A complex link exists between vision and unilateral spatial neglect (USN). Firstly, USN is not a perceptual deficit, secondly, USN is not necessarily accompanied by a visual deficit and finally, USN can be observed in non-visual modalities as well as in mental spatial imagery. This apparent supramodality of USN stands in sharp contrast to the fact that neglect signs are often more severe and more durable in the visual than in other sensory modalities (Chokron et al., 2002).

The influence of vision on spatial representation has rarely been studied. In the present study we assessed six right brain-damaged patients suffering from left USN on two tasks involving spatial representations: a clock-drawing task and a drawing from memory task in two experimental conditions, with and without visual control. We confirm that even in mental imagery, the absence of visual feedback may decrease and even suppress left neglect signs (Bartolomeo and Chokron, 2001b; 2002).

Since vision is largely involved in the orientation of attention in space, suppressing visual control could reduce the magnetic attraction towards the right ipsilesional hemispace and in this way could allow a re-orientation of attention towards the left neglected hemispace. We discuss the theoretical and therapeutic implications of these findings.

Key words: vision, representation, neglect, attention

INTRODUCTION

Unilateral spatial neglect (USN) is the tendency to ignore objects in the contralateral hemispace (Bisiach and Vallar, 2000). A patient with a right parietal lobe lesion may fail to notice or respond to objects in left hemispace and may show a preference for responding to events occurring in ipsilesional space. This bias can range from a mild asymmetry of response latencies to situations in which patients seem to act as if the contralateral half of the world did not exist anymore.

Although many (but not all) neglect patients are also blind in the contralateral hemifield, this hemianopia is not the primary determinant of their behavior. Patients with hemianopia quickly learn to compensate by making more extensive eye and head movements than would normally be required (Marshall and Halligan, 1993).

More convincing evidence that USN is not strictly speaking 'visual' was provided by Bisiach and Luzzatti (1978) who first described 'representational neglect' when a patient was asked to describe a well-known place from memory. In their seminal paper, Bisiach and Luzzatti (1978) reported two left neglect patients who, when asked to imagine and describe from memory the Piazza del Duomo in Milan, omitted to mention the left-sided details regardless of the imaginary vantage point that they assumed, thus showing representational or imaginal neglect. This finding was replicated by Bisiach et al. (1981) in 28 neglect patients and the authors proposed that neglect patients suffer from "a representational map reduced to one half" (Bisiach et al., 1981; p. 549).

The tasks used to assess representational neglect include: describing familiar places from memory, naming the towns or the countries on a map from memory, and drawing objects from memory. In the traditional clock drawing test, a patient presenting with left representational neglect is likely to produce clock drawings with the left half missing. Nevertheless, as pointed out by Vallar and colleagues (1991, p. 230) 'if the basic deficit underlying spatial neglect concerns the inner representation of extrapersonal space, the prediction can be made that sensory parameters, such as the availability of visual cues, should not influence the manifestation of the deficit, in terms for instance, of its severity'. Contrary to this claim, Anderson (1993) described a patient with stroke induced damage to the right parietal lobe and to the right thalamus who reliably produced clock drawings with the left half missing when tested, as is customary, with the eyes open. However, when required to perform the same task with eyes closed, her clock face was drawn normally with all 12 numbers appropriately placed around the full circumference (Anderson, 1993, p. 215). To explain this finding, Anderson argued that "right-sided external percepts are more 'sticky' than internal images" (Anderson, 1993, p. 215). In the same way, Marshall and Halligan (1993) described the case of JR, a left neglect patient, whose performance in geometric shape drawing and in letter cancellation was always better when performed with eyes closed rather than eyes open. In fact, Chedru (1976) was the first to mention, some thirty years ago, the negative effect of vision on the severity of left neglect signs and subsequently Mesulam (1985) and
Anderson (1993) replicated this finding in clock drawings. These are the first observations that visual feedback may exacerbate left neglect in right-brain-damaged (RBD) patients.

Investigating why left neglect patients omit to draw or copy the left side of objects and why they do not notice that the left side is missing even when their drawing remains in free view, Halligan and Marshall (1994) asked left neglect patient PB to copy a butterfly in various conditions. PB had first to copy a regular butterfly, then a butterfly with the left or a right half missing. In a second session, he was requested to draw from memory his copy with eyes open and with eyes closed. Finally in a third session he was asked to draw from memory with eyes open a butterfly with its body vertically aligned, then the same butterfly, but rotated through 90°, and again in the usual vertical body orientation as previously. PB drew a butterfly with two wings only in two conditions: when drawing butterflies with his eyes open and with eyes closed. Finally in a third session he was asked to draw from memory with eyes open a butterfly with its body vertically aligned, then the same butterfly, but rotated through 90°, and again in the usual vertical body orientation as previously. PB drew a butterfly with two wings only in two conditions: when drawing butterflies with his eyes closed, and when drawing a horizontally-oriented butterfly (one wing above the other on the picture plane) with his eyes open. Although all PB’s other butterflies were missing a left wing, PB was insistent that he had drawn a full butterfly. In their paper, Halligan and Marshall (1994) discussed the possibility of a completion phenomenon in neglect preventing the patients from noticing their omissions on the left side. Given the possibility of an interaction between partial perceptual information and preserved conceptual knowledge (revealed by the eyes closed performance) these patients would not experience life in a ‘half-world’.

Taken together, the above findings raise the question of the role of visual feedback and visual context on the representation of space in USN patients. It should be noted that in the vast majority of studies dealing with representational neglect, there is no mention of how vision was controlled during the task, nor even any mention of whether the patient performed the task with eyes open or closed. The aim of the present study was therefore to investigate the influences of vision and more precisely of visual feedback on spatial representations in RBD patients suffering from left USN. In the first experiment, we had patients draw clocks in order to replicate Anderson’s findings (Anderson, 1993); in the second experiment, patients were asked to draw symmetric or asymmetric objects. These two experimental tasks were performed by all control subjects and neglect patients with eyes open and with eyes closed.

**EXPERIMENT 1: CLOCK-DRAWING TEST**

**Methods**

Fourteen normal control subjects (7 men, 7 women) aged between 28 and 75 years (mean: 47.5 years, sd = 14.2) were assessed. All were righthanded according to the questionnaire of Dellatolas et al. (1988).

Six right brain-damaged patients (2 women, 4 men) suffering from severe left unilateral spatial neglect after a stroke were assessed. Neglect signs were evaluated with the Batterie d’Evaluation de la Négligence (BEN: Azouvi et al., 2002; Rousseaux et al., 2002). Subjects’ clinical and demographical data are presented in Table I. Performance on the neglect battery is also shown.

**Procedure**

Subjects were seated in front of a large table. Their trunk and head were aligned at 0°, with the sagittal midplane corresponding to the objective center of the table. Although all patients could sit by themselves and perform the task, trunk and head positions were carefully monitored by the experimenter throughout the task.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender / age / Days from onset</th>
<th>Aetiology</th>
<th>Locus of lesion</th>
<th>Visual deficit</th>
<th>Left extinction</th>
<th>Line bisection (% deviation)</th>
<th>Bells cancellation (max 15/15)</th>
<th>Overlapping figures (max 10/10)</th>
<th>Landscape drawing (max 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient N. 1</td>
<td>F / 81 / 252</td>
<td>Hemorrhagic</td>
<td>TO</td>
<td>LH</td>
<td>no</td>
<td>+ 5.5</td>
<td>0 / 10</td>
<td>4 / 10</td>
<td>4</td>
</tr>
<tr>
<td>Patient N. 2</td>
<td>F / 57 / 728</td>
<td>Hemorrhagic</td>
<td>T</td>
<td>LIQ</td>
<td>no</td>
<td>– 13.15</td>
<td>0 / 8</td>
<td>6 / 10</td>
<td>4.5</td>
</tr>
<tr>
<td>Patient N. 3</td>
<td>M / 56 / 21</td>
<td>Hemorrhagic</td>
<td>PO</td>
<td>LH</td>
<td>yes</td>
<td>+ 15.3</td>
<td>4 / 11</td>
<td>6 / 10</td>
<td>5</td>
</tr>
<tr>
<td>Patient N. 4</td>
<td>M / 63 / 57</td>
<td>Ischemic</td>
<td>TP</td>
<td>LH</td>
<td>no</td>
<td>+ 27.8</td>
<td>8 / 13</td>
<td>7 / 10</td>
<td>4.5</td>
</tr>
<tr>
<td>Patient N. 5</td>
<td>M / 64 / 196</td>
<td>Ischemic</td>
<td>PO</td>
<td>LH</td>
<td>yes</td>
<td>+ 21.8</td>
<td>6 / 14</td>
<td>7 / 10</td>
<td>–</td>
</tr>
<tr>
<td>Patient N. 6</td>
<td>M / 58 / 63</td>
<td>Ischemic</td>
<td>PO</td>
<td>LH</td>
<td>no</td>
<td>+ 52.90</td>
<td>10 / 9</td>
<td>10 / 10</td>
<td>4</td>
</tr>
<tr>
<td>Controls</td>
<td>F: n = 7 / (n = 14)</td>
<td>M: n = 7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean age: 47.5 (sd = 14.2)

Gender: F: female M: male

Lesions: F: frontal, T: temporal, P: parietal, O: occipital

Visual deficit: LH: left hemianopia; LIQ: left inferior quadrant anopia

+ indicates rightward deviation and – indicates leftward deviation.

For the Bells cancellation test, left / right correct responses are reported.

The landscape drawing, consisting of a number of correct responses on the left and on the right is reported.
Participants were asked to complete a clock dial drawing with their right dominant hand with eyes closed and eyes open. Half of the subjects began with the eyes closed condition, whereas the remaining half proceeded in the reverse order. In each condition, the subject’s hand was initially positioned on the sheet of paper at a point corresponding to the centre of the page and to the centre of the clock.

Results

Control Subjects
No omission was recorded in either experimental condition (eyes open or eyes closed) and the clock drawings were fully complete.

Neglect Patients
Figure 1 clearly shows that for patients N. 1, N. 2...
and N. 3 the left neglect was obvious in the eyes open condition (left half or numbers from 6 to 12 missing), whereas the eyes closed condition dramatically reduced the signs of left neglect (all numbers were present). For patient 5, the left neglect was not affected by the visual condition, but the digital numbers were more coherent in the eyes closed condition (Figure 1).

For two out of six patients (patients N. 4 and N. 6) the clock dial was correctly completed independent of the visual condition (Figure 1).

Discussion

The main finding of the first experiment was that in three out of six patients, the clock drawing showed less neglect in the eyes closed condition compared to the eyes open condition. In the three remaining patients, the visual condition had no effect on the patients' performance which was at ceiling in both conditions (patients N. 4 and N. 6). Only for patient N. 5 was the neglect stable in the two conditions. These results confirm Anderson's findings in showing that visual guidance may increase left neglect in clock drawing in some patients. According to Anderson (1993), “right-sided external percepts are more ‘sticky’ than internal images”. Along these lines, eliminating visual control would thus improve the results by eliminating the “magnetic attraction” (see Gainotti et al., 1991) to extraneous visual stimuli in the right hemispace. This hypothesis is consistent with the results of Mark et al. (1988) who tested left neglect patients in a line cancellation task where the targets may be either drawn over or erased. Patients made more omissions in the task where they cancelled with visible marks than in the erasing task, as if they were suffering from both a primary attraction to the right hemispace and from an inability to disengage attention from the right hemispace in order to re-orient it to the left one (Posner et al., 1984). This hypothesis was also proposed by Di Pellegrino (1995), who tested a patient (CB) with severe left visuo-spatial neglect and hemianopia after right hemisphere stroke on three conditions of a clock-drawing task. Both on spontaneous drawing and when the number sequence was provided by the experimenter, CB drew a clock face with left-sided numbers transposed to the right side of the dial; in contrast, when each number was drawn on a separate dial, its location was correct and there was no transposition. Whereas directional hypokinesia or a representational deficit cannot explain these effects, the author proposed that a deficit in disengaging attention from right-sided visual stimuli could play a critical role in clock drawing performance.

Experiment 1, the eyes closed condition may, compared to the eyes open condition, reduce left neglect signs in some neglect patients by decreasing the magnetic attraction toward right-sided details when drawing objects from memory.

EXPERIMENT 2: DRAWING OBJECTS FROM MEMORY

Methods

Subjects

The same subjects examined in Experiment 1 were tested.

Procedure

Subjects were asked to draw 16 objects from memory:
- 8 symmetric objects:
  - 4 manipulable objects (pair of goggles, pair of trousers, earphones, pullover);
  - 4 non-manipulable objects (butterfly, heart, spider, bench);
- 8 asymmetric objects (with a front and a back end)
  - 4 manipulable objects (cup, saucepan, toothbrush, saw);
  - 4 non-manipulable objects: 2 static: (cap, flag); 2 mobile: (truck, child’s scooter);
Each participant drew the objects in a specific randomized order, on a sheet of paper (14.8 cm × 10 cm) with a black pen. For half of the participants, the task was first performed eyes open and then eyes closed, whereas the remaining half performed the task in the reverse order. There was no time limit.

Data Analysis

Several dependent variables were recorded for each visual condition. Our aim was not to conduct a statistical analysis on these data (there were only 16 drawings per subject) but rather to analyse descriptively the drawings with respect to characteristics such as the drawing’s completeness, the symmetry of the drawing, the respective left and right surfaces and the lateralisation of the details.

Drawing completeness: 5 independent judges were requested to decide if the drawing was complete or not. A complete drawing was coded +1 whereas 0 referred to an incomplete drawing.

Drawing symmetry: for symmetrical objects, we recorded the presence or absence of items on each side of the axis of symmetry of the object. The drawing was coded +1 if the left and the right part were symmetric and 0 if they were asymmetric.

Left and right surfaces: Figure 2 illustrates how the left and right surfaces of the drawing were calculated.
When the left half surface was bigger than the right half, the drawing was coded – 1, when the right half surface was bigger than the left half it was coded + 1, and 0 corresponded to a drawing where the two surfaces were equal.

**Lateralisation details:** we recorded the drawing half (left or right) that included the greater number of details.

## Results

### Drawing Completeness

Table II shows the drawing completeness when control subjects and neglect patients performed with eyes closed and eyes open.

In controls, the visual condition had no effect and in all conditions, the object drawn was complete.

By contrast, in some neglect patients, performance was affected by condition. When condition had a positive influence on the performance of neglect patients, it was always in favour of the eyes closed condition.

As shown in Figure 3, in patients N. 1, N. 3 and N. 5, the eyes closed condition led to more complete drawings than the eyes open condition.

For patients N. 2, N. 4 and N. 6, condition had no effect on drawing completeness because it was almost perfect in both conditions (see Table II).

Figure 4 illustrates how in patients N. 3 and N. 5, suppression of visual feedback may improve the completeness of drawings, making them more recognizable.

### Symmetry of the drawing

Again, in normal controls, condition did not affect the symmetry of the drawing (Table II).

---

**Table II**

<table>
<thead>
<tr>
<th>Completeness</th>
<th>Symmetry</th>
<th>Surfaces</th>
<th>Lateralisation details</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EO</td>
<td>EC</td>
<td>EO</td>
</tr>
<tr>
<td>Controls</td>
<td>0.98</td>
<td>0.955</td>
<td>1</td>
</tr>
<tr>
<td>P1</td>
<td>0.5</td>
<td>0.625</td>
<td>0.5</td>
</tr>
<tr>
<td>P2</td>
<td>1</td>
<td>1</td>
<td>0.875</td>
</tr>
<tr>
<td>P3</td>
<td>0.75</td>
<td>0.875</td>
<td>0.875</td>
</tr>
<tr>
<td>P4</td>
<td>0.875</td>
<td>0.875</td>
<td>0.875</td>
</tr>
<tr>
<td>P5</td>
<td>0.5</td>
<td>0.625</td>
<td>0.75</td>
</tr>
<tr>
<td>P6</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Completeness: 1 = complete; 0 = incomplete
Symmetry: 1 = symmetric; 0 = asymmetric
Left and right surfaces: – 1: left surface > right surface; + 1: right surface > left surface; 0: left surface = right surface
Lateralisation of the details: – 1: more details in the left half; + 1: more details in the right half; 0: left details = right details

---

**Fig. 2 – Calculation of the left and right surfaces of the drawing.**

**Fig. 3 – Drawing trousers, a truck, a flag in the eyes open (top) and eyes closed conditions (bottom) for patients #1, #3 and #5. These examples illustrate how in these patients the suppression of visual guidance (bottom) may improve the completeness of the drawings.**
For patients N. 2, N. 3 and N. 6, the symmetry of the drawing was respected independent of condition (see Table II). In contrast, for patients N. 1, N. 4 and N. 5, the drawing symmetry improved in the eyes closed condition compared to the eyes open condition as shown in Figure 5.

Drawing Surface

In controls, performance did not depend on conditions: left and right surfaces were comparable (see Table II).

In all neglect patients, the condition influenced the left and right drawing surfaces mainly for symmetric objects (see Table II).

In patients N. 1, N. 2, N. 3 and N. 6, when drawing symmetric objects, the suppression of visual control increased the surface of the left half or decreased the surface of the right half of the drawing compared to the eyes open condition (see Table II, Figures 6, 7).

In patient N. 4, the right surface was always bigger than the left one, but this discrepancy was reduced when the patient drew with his eyes closed (see Table II).

In patient N. 6, the left and right surfaces were comparable except in the condition where the patient drew symmetric objects with his eyes closed. In this condition, the left surface was bigger compared to the right one (see Table II: a negative score with EC means that the left surface is bigger than the right one).

Laterisation Details

For control subjects, the visual condition did not affect the distribution of the details in each half (left and right) of the drawings (see Table II).

Conversely, as shown in Table II, in all neglect patients except patient N. 6, the eyes closed condition led to less asymmetric (or more symmetric) drawings than the eyes open condition, either by decreasing the details on the right side (patients N. 3, N. 4 and N. 5) or increasing the
The role of vision in spatial representation

Discussion

The main finding of Experiment 2 is that whereas the presence or absence of visual feedback never influenced the performance of normal subjects, all neglect patients were at some point sensitive to it. In addition, when the condition had an affect on their drawing, it was always in the same way, that is, a decrease of left neglect signs when visual feedback was suppressed. Interestingly, the improvement could result from either a decrease of the right half surface and a reduction of the details drawn in the right half, and/or from an increase of the left half surface of the drawing and more details drawn in the left part. These findings indicate that left neglect patients may be hyperattentive to right hemispace. This bias could be due to an inability to disengage attention from the right hemispace (Posner et al., 1984) or to a rightward shift of attention as predicted by Kinsbourne’s hypothesis (1970a; 1970b). In accordance with Experiment 1 and previous findings (Halligan and Marshall, 1994), drawing with one’s eyes closed may improve the performance of left neglect patients by inducing a disengagement from the right half of the drawing and a re-orientation of attention to the left half of the drawing. This hypothesis was also put forward by Hjaltaison and Tegner (1992) to explain why darkness improved line bisection by about 43% in left neglect patients. According to the authors, the improved performance may have been due to the elimination of extraneous visual stimuli from right hemispace.

Taken together, these findings suggest that under visual control, attentional resources are captured and maintained in the right hemispace, thus increasing left neglect behaviour. Eliminating visual control thus improves performance by eliminating the magnetic attraction to extraneous visual stimuli from right hemispace.

General Discussion

The main finding of this study is that suppressing visual control may improve left neglect patients’ performance in a clock drawing task and in drawing objects from memory. Whereas control subjects draw objects in the same manner whether their eyes are open or closed, neglect patients draw more complete and symmetric drawings in the eyes closed compared to the eyes open condition. These findings confirm and extend previous studies. Chedru (1976) designed a test suitable for presentation in equivalent tactile and visual versions: subjects were required, with and without a blindfold, to tap the keys all over a teletype keyboard as quickly as possible. RBD patients with visual field defects showed no impairment in tapping the left-sided keys when vision was obscured, while they preferred the right-sided keys when visual control was available. Chedru’s conclusion (1976) was that the unilateral defect in manual exploration of space is induced by vision. Using the same protocol, Gentilini et al. (1989)
reported that RBD patients with neglect preferred the right-sided keys, both with and without visual control, although this ipsilateral preference was significantly less marked in the tactile condition. Gentilini et al. (1989) have tested space exploration among RBD patients with and without visual control (blindfolded condition) with a modified version of Chedru’s test (pressing the keys of a keyboard). They found that in left neglect patients the ipsilesional preference was significantly less marked in the blindfolded condition, than when performance was assisted by vision. This kind of dissociation was replicated by several authors during space exploration tasks (Cubelli et al., 1991; Ladavas et al., 1993). In the same way, Vallar et al. (1991) submitted 110 unilateral brain-damaged patients to a spatial exploratory task with and without the aid of vision. Like Chedru (1976), the authors reported an association between the modal specificity of the deficit and the presence/absence of visual field impairments. Neglect confined to the visual condition was associated with left homonymous hemianopia or extinction, while about 70% of the patients with neglect in the tactile condition did not show visual field deficits. These findings were interpreted as reflecting the presence of nonsensory (attentional or representational) components in the visual field defects of neglect patients.

Using bisection protocols, Hjaltason and Tegner (1993) found that a rod bisection task performed by left neglect patients while blindfolded elicited less rightward bias than visual line bisection. This discrepancy between visual and tactile conditions may not be due to different spatial search mechanisms (visual or haptic) but can be explained solely by the presence or absence of visual information, as in the present study or in Hjaltason and Tegner (1992), where the line bisection task performed in darkness elicited less rightward bias than in normal illumination. However, it has to be noted that, when submitting left neglect patients to a line bisection task either in a supine or in an upright position in light or dark conditions, Pizzamiglio et al. (1997) did not find any significant effect of illumination. Only a mild tendency toward reduced error in bisecting a line in the dark condition was reported.

Concerning auditory neglect, it has been shown that blindfolding improves the ability of neglect patients to localize correctly sound stimuli originating from the left (Soroker et al., 1997). This suggests that vision, including head turning and eyeball movement, may exacerbate neglect signs in various sensory modalities as well as in mental imagery, as the present findings (Figures 1-7) demonstrate. According to Gentilini et al. (1989), the increase in ipsilateral responses when key pressing was guided by vision in comparison to the blindfolded condition suggests that incoming sensory stimuli from the ipsilateral side play a role in shifting attention towards it and in enhancing neglect of the contralateral side of space. In fact, although several experiments have shown that attention can be allocated to different parts of the spatial field without overt eye movements (see Posner, 1980), experiments performed in healthy subjects have suggested that eye movements cannot be made without shifting the focus of attention in the same direction (see Gainotti, 1993). If neglect behavior results not only from hypotention to contralateral stimuli but also from hyperattention to ipsilateral stimuli (Kinsbourne, 1970; Bartolomeo and Chokron, 1999a; 2001b), it is conceivable that a task carried out in the absence of visual stimulation, such as the tactile test, or drawing while blindfolded as in the present study, entails a less marked imbalance between the two halves of space than the same task carried out with visual assistance. Drawing a clock or objects from memory are tasks that require access to and exploration of visuo-spatial representations. The present results clearly show that the conditions, with or without visual feedback, may affect neglect patients’ performance during a nonvisual, representational task.

As Bisiach and co-workers have demonstrated in their seminal papers, neglect can occur not only in vision, but also in the absence of any physical object in the patient’s visual field (Bisiach and Luzzatti, 1978; Bisiach et al., 1981). In these studies, imaginal neglect co-occurred with visual neglect. This association has often been interpreted as supporting pictorial models of visual mental imagery (Bisiach et al., 1990; Kosslyn, 1994). Neglect patients avoid mentioning left-sided imagined details because they lack the left half of a (spatially organized) mental representation (Bisiach and Luzzatti, 1978). However, the accumulation of neuropsychological evidence of multiple dissociations between imagery and perceptual abilities in brain-damaged patients (recently reviewed in Bartolomeo, 2002), has proved devastating for models of mental imagery based on a functional and anatomical equivalence between these abilities, like Kosslyn’s pictorial model (Kosslyn, 1994, see also Bartolomeo and Chokron, 2001b; 2002). However, as confirmed by the present findings, there is a strong link between vision and spatial representation.

To explore the relationships between visual and imaginal neglect, Bartolomeo et al. (1994) assessed 30 right- and 30 left-brain-damaged patients, and found imaginal neglect only in right brain-damaged patients. Imaginal neglect always co-occurred with visual neglect, and scores measuring the lateral bias in the two types of tasks were positively correlated, thus suggesting that the two disorders share some common underlying mechanism. In fact, about two thirds of left neglect patients showed definite signs of neglect only in visual tasks, and not in imaginal tasks, probably because
right-sided visual details exerted a powerful attraction on patients’ attention (Gainotti et al., 1991). However, when imaginal neglect was present, it was always associated with visual neglect. Additional evidence confirming a relationship between visual and imaginal neglect comes from the outcome of manoeuvres known to modulate visual neglect. When a patient had his eyes and head physically turned toward the left side, his descriptions from memory included more left-sided details (Meador et al., 1987). Similar results were obtained by irrigating patients’ left ears with cold water (Rode and Perenin, 1994), a vestibular stimulation likely to induce a leftward orientation of attention (Gainotti, 1993). Imaginal neglect was also reduced by a short adaptation period to a prismatic rightward shift of the visual field (Rode et al., 2001), another manoeuvre known to ameliorate visual neglect (Rossetti et al., 1998). Thus, sensory-motor procedures can influence imaginal neglect. Conversely, a purely imaginal training can ameliorate visual neglect (Smania et al., 1997). It has been proposed that at least some of these procedures act by facilitating leftward orientation of attention (Gainotti, 1993; Chokron and Bartolomeo, 1999; Bartolomeo and Chokron, 1999b). The present findings support the hypothesis that orienting attention through visual control can influence space-related imagery. Visual imagery may thus involve some of the attentional exploratory mechanisms that are employed in visual behaviour. For this reason, we think that investigations of representational neglect should include two distinct testing conditions: with and without visual guidance. In some cases, the suppression of visual guidance will dramatically reduce what looks like representational neglect.

The present study has some important implications not only for the diagnosis of representational neglect but also for rehabilitation. As mentioned above, it has already been shown that representational training may improve visuospatial neglect (Rode et al., 1996; Smania et al., 1997). In the present study, we show that suppressing visual input may improve left neglect during representational spatial tasks. These findings resemble previous neurophysiological studies on rodents. Vargo et al. (1998; 1999) showed that 48 hours of light deprivation after unilateral traumatic contusion injury to the frontal cortex significantly accelerated recovery from attentional neglect but not sensori-motor deficits. This improvement persisted long after the animal had been placed back under standard light cycles. These findings suggest that there may be a short, early window during which environmental variables promote or deter long term recovery. According to Vargo et al., light deprivation should improve recovery after traumatic contusive brain injury by enhancing dopaminergic function in the ipsilateral basal ganglia.

The present experiments show that in humans, light deprivation may lead to a reduction of neglect during representational tasks. Rehabilitation techniques should perhaps incorporate visuo-spatial training while blindfolded at the acute stage. Regarding normal spatial cognition, the amount and type of available visual information may also, as we have previously shown, influence how extrapersonal space is represented and/or explored (Chokron et al., 1997; Chokron and De Agostini, 2000; Chokron et al., 2002). The interaction between vision, attention and representation should accordingly be more thoroughly studied.

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Independent effects of endogenous and exogenous spatial cueing: inhibition of return at endogenously attended target locations

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Abstract Inhibition of return (IOR) is thought to reflect a bias against returning attention to previously attended locations. According to this view, IOR should occur only if attention is withdrawn from the target location prior to target appearance. In the present study, endogenous attention and exogenous cueing were manipulated orthogonally. IOR was observed both when a target appeared at an unexpected location, and when a target appeared at the expected location. A similar pattern of results was obtained in a reanalysis of data from a study with Neglect patients. These results suggest that IOR is independent of endogenous orienting.

Keywords IOR · Exogenous orienting · Endogenous orienting · Neglect

Introduction

Orienting attention toward the location at which a target stimulus is about to appear facilitates both detection of its onset and discriminative decisions about its perceptual properties. Therefore, if one has information regarding the likely location of a future target stimulus, a beneficial strategy would be to orient attention toward that location in advance. This voluntary, or endogenous, allocation of attention to a spatial location prior to target onset has been thoroughly investigated during the last two decades. In studies of endogenous attention, a symbolic cue that predicts the future target location is often presented. Participants use the predictive value of the cue to orient attention toward the expected location, and then maintain attention at that location until the target appears. The usual result is that performance for targets at this endogenously cued location is more efficient than for targets at uncued locations (Posner et al. 1980).

Alternatively, attention can be captured automatically at the location of a salient stimulus or new object (see Ruz and Lupiáñez 2002 for a review of the attention capture literature). This involuntary, or exogenous, allocation of attention has also been thoroughly studied. In studies of exogenous attention, a salient cue, such as an abrupt change in luminance, is often presented at one of two or more potential target locations, and the cueing effect that occurs using this procedure is attributed to an involuntary, or automatic, shift of attention to the cued location. Evidence for the automaticity of exogenous orienting comes from studies showing that exogenous orienting develops much faster than endogenous orienting (Müller and Rabbitt 1989) and from results showing that even cues of which participants are unaware produce cueing benefits (McCormick 1997).

Furthermore, exogenous cues are typically not predictive (the target appears with the same likelihood at the
cued location as at any other location), so there is no obvious incentive for participants to maintain attention at the location at which it was captured. Thus, if the target does not appear at the cued location shortly after cue onset, then an appropriate strategy would be to withdraw attention from the cued location and reorient attention toward a neutral central location that is equidistant from each potential target location. This strategy of disengaging and reorienting attention would appear to explain why cueing benefits in studies of exogenous orienting are typically observed only at short cue-target intervals.

However, Posner and Cohen (1984) noted that at longer cue-target intervals not only is there no cueing benefit but rather there is a cueing cost, that is, detection responses are slower for targets presented at the cued location than for targets presented at an uncued location. Posner et al. (1985) called this effect inhibition of return (IOR\(^1\)), and it has since been extended to a great variety of tasks and experimental procedures: Maylor (1985) in both target detection and localization RT tasks; Lupiáñez et al. (1997) in choice discrimination RT tasks; and Abrams and Dobkin (1994) and Pratt (1995) in eye movement latency (see Klein 2000; Lupiáñez et al. 1999, for reviews).

From the time that Posner and Cohen (1984) first reported the IOR effect, it has been widely accepted that the effect reflects an inhibition to return attention to a location that has been previously attended (Posner et al. 1985). This conceptualization of the IOR effect presumes that it reflects a mechanism that has adaptive value in situations that require visual search because, by inhibiting attention from returning to previously explored locations, it would promote a more thorough exploration of the visual scene [Danziger et al. 1998; Tipper et al. 1991; Tipper et al. 1996; see “why” section of Klein’s review (2000) for this issue]. In fact, with a variety of procedures, IOR has been shown to occur in the context of visual search tasks, in which participants search serially for a target among distractors (Klein 1988; Klein and MaInnes 1999; Müller and von Mühlener 2000; Takeda and Yagi 2000).

In summary, IOR is widely attributed to a mechanism involved in the orienting of attention, and more specifically to the inhibition of reorienting attention toward a previously attended location. It is clear, then, that the name IOR is not theoretically neutral: there is a perfect correspondence between the name of the effect and the theory explaining it. In other words, IOR is both an empirical effect (slower RT and/or higher error rate to targets appearing at a previously cued location than to those appearing at an uncued location) and an attentional mechanism by which attention is inhibited to reorient to a previously attended location. In our opinion, this ambiguity can impede understanding of exogenous orienting and IOR, because not enough research has been conducted to clearly demonstrate that the IOR effect is caused by an IOR mechanism, that is, by the inhibition of the reorienting of attention. Thus, in the following we will distinguish between IOR as an empirical effect and the reorienting hypothesis as an explanation for the effect.

In fact, several findings give reason to doubt the reorienting hypothesis as an explanation for the IOR effect. If IOR is the result of the inhibition of attention to return to a previously attended location, two predictions can be forwarded: (a) it should always be possible to observe facilitation at SOAs shorter than those at which IOR is measured and (b) no IOR should be found if there is no need to return attention to a previously attended location.

Regarding the first prediction, quite a few studies have reported IOR at long SOAs, without a facilitatory effect at shorter SOAs. Perhaps the clearest example of this finding was reported by Tassinari et al. (1994). They observed IOR at an SOA between the cue and target as short as 0 ms. As noted by Lupiáñez and Weaver (1998), with a cue-target SOA of 0 ms, there can hardly be time to disengage attention from the cued location and then return attention to that location. Interestingly, the absence of a facilitatory effect preceding the IOR effect is more common than one might expect, at least in detection tasks (see Maruff et al. 1999 for a review). Such results contradict the view that IOR is caused by attention being inhibited to reorient to a previously attended location. Far from being a prerequisite for IOR to appear, some authors have argued that orienting of attention might mask the negative effect of cueing at short intervals when no IOR is measured (Danziger and Kingstone 1999; Tassinari et al. 1994).

Regarding the second prediction, several studies have demonstrated that IOR can occur even when there appears to be no need to reorient attention to the cued location. In one such study, Berlucchi et al. (2000) used a procedure in which a target appeared in one of four possible target locations following an unpredictable cue in one of those locations. Within a given block of trials, participants were instructed to attend to one particular location relative to the location of the cue (although cues at each of the four locations were equally likely). The results revealed faster RTs in the endogenously attended location compared to the other three locations, and slower RTs in the exogenously cued location than in the uncued locations (i.e., IOR). However, the most important result was that, at all cue-target SOAs, comparable IOR effects were obtained at endogenously attended and unattended locations. Note that this pattern of results contradicts the predictions set forth above, in that no IOR should be observed when the target appears at a location where attention is endogenously allocated because there is no need for reorienting attention in this situation.

In a separate study of this issue, Rafal and Henik (1994) obtained similar results with a rather different procedure. First, an arrow was presented, which pointed toward the most likely target location (80% predictive), thus producing valid and invalid trials. For both kinds of trials, an exogenous cue (a brightening of the box marker) was presented 500 ms after the endogenous arrow cue. The

\(^1\) The same effect has been called “inhibitory aftereffect” by Tassinari et al. (1987).
target appeared in the same location as the exogenous cue on half of the trials and in the location opposite the exogenous cue on the remaining half of the trials. The target was presented 750 ms after onset of the exogenous cue, and thus 1,250 ms after onset of the endogenous cue. The results revealed additive effects of endogenous and exogenous cueing, thus IOR was independent of endogenous orienting of attention. Similar results were obtained by Berger and Henik (2002), at least in the temporal hemifield. That is, once again, comparable IOR effects seem to be obtained at endogenously attended and unattended locations.

These results are very useful in evaluating the reorienting hypothesis of the IOR effect, as additivity between exogenous and endogenous orienting does not fit well with this hypothesis. As stated above, if the IOR effect is caused by an inhibition to return attention to a previously attended location (the reorienting hypothesis), then it is not at all clear how IOR could occur at an endogenously attended location. Further, even if there were some explanation for how IOR could occur at an attended location, it is hard to envision how it could be as large at endogenously attended as at endogenously unattended locations.

In the present study, we used a new approach to test the plausibility of additivity between exogenous and endogenous orienting processes, and thus to investigate the reorienting hypothesis as an explanation of the IOR effect. An important feature in our procedure is that the same cue was used to manipulate exogenous and endogenous orienting. Because the same cue triggered both types of orienting, we view this study as providing a particularly strong test of the notion that exogenous and endogenous orienting produce additive effects on performance. Furthermore, a range of cue-target SOAs were used to evaluate whether exogenous and endogenous orienting effects perhaps interact at some cue-target SOAs but not at others, depending on whether the exogenous effect is facilitation or IOR.

The procedure we used, first introduced by Posner et al. (1982), combined the general logic of predictive cues to measure endogenous orienting, and abrupt onset cues to measure exogenous cueing. We use the term exogenous cueing to refer to cue-target location correspondence (same or different) and the term endogenous orienting to refer to the location of the target relative to an expectancy derived from the cue (expected or unexpected). Importantly, we included both a condition in which the cue predicted the target to appear at the same location as the cue, and a condition in which the cue predicted the target to appear at the location opposite the cue. By testing both of these conditions, a target that appeared at the same location as the cue could be either expected or unexpected. Similarly, when a target appeared at the location opposite the cue it could be expected or unexpected. In this manner, we were able to study whether exogenous cueing effects are modulated by endogenous orienting of attention when the same cue is used for both exogenous and endogenous orienting manipulations.

The results from the long cue-to-target SOA conditions, for which IOR is often found, are of particular interest in this study. If IOR reflects a bias against returning attention to a previously cued location, then no such effect should be observed when the target appears at an expected location. Note that in this case, when a target appears at an expected location, participants ought to have their attention oriented to that location. Thus, no reorienting should be necessary, and therefore a bias against returning attention to that location should not be reflected in performance. In contrast, when a target appears at an unexpected location, participants should have to reorient their attention to the target location. In this case, if the target location was previously cued, a bias against returning attention to a previously cued location ought to be manifest in performance. In sum, the reorienting hypothesis clearly predicts that exogenous cueing should interact with endogenous orienting. If the results instead show additivity between exogenous cueing and endogenous orienting, then the IOR effect would have to be explained by a mechanism other than the inhibition of the reorienting of attention.

### Materials and methods

#### Participants

The study was carried out by following the guidelines of the ethics committee of the Hôtel-Dieu Hospital in Paris. Thirty-two normal individuals participated in the study after giving written informed consent. They reported normal or corrected-to-normal vision and being right-handed. Their mean age was 60 years (SD=13, range 39–81).

#### Apparatus and stimuli

Stimulus presentation and response collection were controlled by the Psychlab software (Gum 1996). Three black empty square boxes, with sides 10 mm long and 0.34 mm thick, were displayed on a white background on the computer screen. The boxes were horizontally arranged, the central box being located at the center of the screen. The central box contained a small black rectangular fixation point (1.02×1.34 mm) and the distance between boxes was 30 mm. Cues consisted of a 300-ms thickening (from 0.34 to 0.68 mm) of the contour of one lateral box. The target was an asterisk 4.40 mm in diameter, appearing inside one of the lateral boxes, at a retinal eccentricity of about 3.83°.

#### Procedure

Participants sat in front of a computer monitor at a distance of approximately 50 cm. Each trial began with the appearance of the three placeholder boxes for 500 ms.
Then the cue followed for a duration of 300 ms. The target appeared 100, 500, or 1,000 ms after onset of the cue, and remained visible until a response was made. Participants were instructed to maintain fixation on the fixation point and to respond to the target as quickly and accurately as possible, by pressing the center of the space bar with their right index finger. Eye movements were observed by one of the experimenters. After an intertrial interval of 1,000 ms, a new trial began. Participants completed three conditions, in different sessions, according to cue predictiveness. In one condition the cue was unpredictable (50% cued trials; the target appeared with the same probability at the cued as at the uncued location). In the other two conditions the cue was predictive (80% cued trials, 20% uncued trials) or counterpredictive (20% cued trials, 80% uncued trials).

Before each block of trials, participants were informed of the level of predictiveness of the cue (50%, 80%, or 20% cued targets). In the conditions with informative cues (80% and 20% cued targets), it was stressed that cues would in most cases help to respond more rapidly. Before the condition with non-informative cues, it was explained that cues were useless to predict the target position, and thus should be ignored.

Design

Each condition (50%, 20%, and 80% cued trials) was administered on one of three consecutive days, following a Latin square design. A 10-min rest was allowed between blocks. Each block began with 12 practice trials, which were discarded from analyses.

The condition with non-informative cues (50% cued trials) consisted of three blocks of 96 trials, and had a 2 (Cueing; cued, uncued) × 3 (SOA; 100, 500, 1,000 ms) design. The conditions with informative cues (80% and 20% cued trials) consisted of three blocks of 102 trials each. In this case the design was 2 (Cueing; cued, uncued) × 3 (SOA; 100, 500, 1,000 ms) × 2 (Location Expectancy; expected, unexpected).

Cueing refers to whether the target appeared in the same location as the cue (a cued trial) or at the location opposite the cue (an uncued trial), and SOA (100, 500, 1,000 ms) refers to the temporal interval between onset of the cue and onset of the target. Finally, Location Expectancy (only in the conditions with informative cues) refers to whether the target appeared at the location predicted by the cue (cued trials in 80% cued blocks, and uncued trials in 20% cued blocks), or at the location opposite that predicted by the cue (uncued trials in 80% cued blocks, and cued trials in 20% cued blocks). All variables were manipulated within participants, with SOA being manipulated within blocks of trials, and Expectancy and Cueing manipulated within blocks and between sessions, as explained above.

Results

Trials with RT longer than 1,500 ms (0.92%) or shorter than 150 ms (5.19%) were eliminated from the analysis. Mean correct RT for each experimental condition and cueing effects for each SOA level and expectancy condition are presented in Table 1.

Unpredictive cues condition

First, we describe the results from the unpredictable cue condition, to show that our procedure produces the results typically observed with unpredictable exogenous cues. A Cueing (Cued and Uncued) × SOA (100, 500, 1,000 ms) repeated measures ANOVA was conducted on mean RTs from the 50% cued trials condition. As expected, this analysis showed a highly reliable Cueing × SOA interaction, $F_{(2,62)}=38.82$, $P<0.0001$, with significant facilitation at the short SOA, and IOR at the longer 1,000-ms SOA, as revealed by planned comparisons (both $P<0.001$; see top panel of Fig. 1). Thus, the usual transition from facilitation at the short SOA to IOR at the longest SOA was obtained. The main effect of SOA was also significant, showing the usual decrease in RT by increasing SOA, $F_{(2,62)}=29.36$, $P<0.0001$.

Table 1 Mean RT for each experimental condition, and cueing effects

<table>
<thead>
<tr>
<th>SOA (ms)</th>
<th>Predictive cue conditions</th>
<th>Unpredictive cues</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Expected location</td>
<td>Unexpected location</td>
</tr>
<tr>
<td>100</td>
<td>467 427 427</td>
<td>473 443 442</td>
</tr>
<tr>
<td>500</td>
<td>496 430 402</td>
<td>497 452 416</td>
</tr>
<tr>
<td>1,000</td>
<td>463 427 429</td>
<td>499 440 402</td>
</tr>
<tr>
<td>Cued</td>
<td>29 3 24</td>
<td>24 9 25</td>
</tr>
<tr>
<td>Uncued</td>
<td>496 430 402</td>
<td>497 452 416</td>
</tr>
<tr>
<td>Cueing effect</td>
<td>36 12 −26</td>
<td></td>
</tr>
</tbody>
</table>
Fig. 1  Cueing effects across SOA. In the top panel data from the unpredictive cues condition are presented, whereas the data from the predictive cues conditions are presented in the bottom panels (left expected location; right unexpected location).

our hypothesis that IOR can be independent of endogenous orienting.

SOA interacted with Cueing, $F_{(2,62)}=17.47$, $P<0.0001$, in the predicted direction. As with unpredictive cues, the cueing effect was positive (faster responses for cued trials) at the short SOA (27 ms, $P<0.0001$), and negative at the long SOA (−25 ms IOR, $P<0.005$); the positive 6-ms effect at the intermediate 500-ms SOA was not significant ($F<1$). Thus, the typical pattern of exogenous cueing effects was obtained in this analysis. The critical issue, however, concerned the dependence of this interaction on endogenous expectancy. Importantly, the Expectancy × Cueing × SOA interaction was clearly non-significant, $F<1$. As can be seen in the bottom panel of Fig. 1, for both SOAs, the cueing effects were virtually identical.

The only other significant effect was the main effect of SOA, $F_{(2,62)}=30.94$, $P<0.0001$, with RT decreasing linearly as SOA increased ($F_{(1,31)}=36.57$, $P<0.0001$).

**Discussion**

The aim of the present experiment was to investigate the interaction between endogenous orienting of attention and exogenous cueing. More specifically, we were interested in testing whether IOR, conceptualized by many researchers as the manifestation of an exogenous orienting mechanism, indeed depends on the orienting of attention.
We argued that if the IOR effect reflects a bias against returning attention to a previously cued location (the reorienting hypothesis), no such bias should be manifest if, when the target appears, attention is already oriented to the target location. In contrast, if the target appears at an unexpected location, so that participants have to reorient their attention to the target location, a bias against returning attention to a previously cued location would be expressed as an IOR effect.

The results of this experiment are clear-cut. First, the usual transition from facilitation at short SOAs to IOR at long SOAs was observed in both the unpredictable and predictive cues conditions. Second, and more important, Cueing effects did not depend on Location Expectancy, either in the overall analysis (non-significant SOA × Cueing × Expectancy interaction) or in specific analyses carried out for the short and long SOA. Thus, for the first time to our knowledge, we have observed a significant transition from exogenous cueing facilitation to IOR at the expected and the unexpected target location (the same trend was first reported by Posner et al. 1982, although not analyzed this way\(^2\)).

In the specific analyses, significant facilitation and IOR effects were observed, but these effects did not vary as a function of Location Expectancy. It might be argued that the facilitation effect observed at the short SOA did not depend on the expectancy because the expectancy effect was not significant at this SOA. However, Chica and Lupiáñez (2004) have shown recently a lack of interaction between expectancy and short SOA facilitation in a similar procedure with a color discrimination task. They observed at the 100-ms SOA significant positive effects of both exogenous cueing and expectancy, independently of each other.

Thus, our results clearly disconfirm the reorienting hypothesis, which states that the IOR effect is a consequence of a mechanism that biases attention against returning to a previously visited location. Although inconsistent with the most widely accepted explanation for the IOR effect, the results are consistent with those reported in several other studies of exogenous cueing (see Berger and Henik 2002; Berlucchi et al. 2000; Rafal and Henik 1994, for a similar pattern of IOR effects; Riggio and Kirsner 1997, for a similar pattern of short SOA facilitation effects). Thus, there is mounting evidence that the reorienting hypothesis is incorrect, and that an alternative account of IOR is necessary. We outline one such alternative account in the General discussion.

Before doing so, however, we add to the available empirical evidence on this issue by describing the results of a study on the interaction between endogenous orienting and exogenous cueing in brain-damaged patients (see Bartolomeo and Chokron 2001, 2002 for recent reviews). We reanalyzed the data from experiments 2 and 3 of Bartolomeo et al. (2001), in which a procedure similar to that in the present study was used.

Reanalysis of control versus patients data of Bartolomeo et al. (2001)

To better understand the interaction between endogenous orienting and exogenous cueing in Neglect patients we reanalyzed the data of experiments 2 and 3 of Bartolomeo et al. (2001). As in the experiment presented above, we used the term Cueing (cued vs uncued) to refer to whether the target appeared in the same location as the cue (a cued trial) or at the location opposite the cue (an uncued trial). Similarly, after recoding the data, Expectancy\(^3\) referred to whether the target appeared at the expected location (cued trials of experiment 2, and uncued trials of experiment 3), or at the unexpected location (uncued trials of experiment 2, and cued trials of experiment 3). Two further variables were introduced in the analysis: SOA and Target Location. The cue-target SOA had three slightly different values to those in the above experiment (150, 550, 1,000 ms). Given that the focus of this study was the behavior of Neglect patients, who typically neglect information presented in the left hemifield, we analyzed the data separately for Left and Right Targets. All variables were manipulated within participants, with SOA manipulated randomly within blocks of trials, and Expectancy and Cueing manipulated within blocks and between sessions (two of the four experimental conditions in different sessions, as in the previous experiment reported here).

Six brain-damaged patients, with right hemisphere lesions and signs of left spatial neglect, and 18 age-matched participants without brain damage took part in the experiment (see Bartolomeo et al. 2001 for demographic details of both groups of participants).

Results and discussion

The data from the control participants were treated the same way as in the present study. Thus, trials with RT longer than 1,500 ms (0.49%) or shorter than 150 ms (2.05%) were eliminated from the analysis. For the patients’ data, the same cut-offs as in the original Bartolomeo et al. study were used: trials with RT longer than 5,000 ms (3.94%) or shorter than 150 ms (3.86%) were eliminated from the analysis. After the elimination of the outliers, means were computed for each participant and

\(^2\)We thank Giovanni Berlucchi for drawing our attention to this result.

\(^3\)Given that our main interest in this reanalysis was to compare cueing effects for endogenously expected and unexpected locations, the no expectancy data (50% cued, experiment 1 of Bartolomeo et al. 2001) were not included. Note also that in Bartolomeo et al. (2001) the order of different blocks across which cue predictiveness was varied (20% vs 80% predictiveness) were not counterbalanced across participants.
experimental condition. However, to compare the data of the Neglect patients with those of normal controls, and given that the Neglect group was much slower (as is well-known with Neglect patients, see, for example, Robertson 1993), the mean RT for each experimental condition and participant was divided by the mean overall RT for that participant. Thus, the dependent measure of interest was greater than 1.0 when a participant’s RT for a particular condition was greater than his/her mean overall RT, and less than 1.0 when a participant’s RT for a particular condition was smaller than his/her overall mean RT.

These transformed data, recoded according to the design we used in the previous experiment, were submitted to a 2 (Group; Neglect vs Controls) × 2 (Expectancy; Expected vs Unexpected location) × 3 (SOA; 150, 550, 1,000 ms) mixed-factor ANOVA that treated Group as a between-participants variable. Two separate analyses were performed, one for Left Targets and another for Right Targets. Data for each experimental condition are presented in Table 2.

### Left location

Apart from the main effects of Group, Expectancy, and Cueing, the most interesting results were the interactions in which Group was involved. Thus, Neglect patients showed larger than normal main effects of Expectancy and Cueing, as indicated by the Group by Expectancy and Group by Cueing interactions, $F_{(1,22)}=4.89, P<.05$, and $F_{(1,22)}=3.53, P<.073$, respectively. Interestingly, whereas the control group produced similar cueing effects for expected and unexpected locations, the large overall cueing effect produced by Neglect patients was modulated by expectancy, as indicated by the Group × Expectancy × Cueing interaction, $F_{(1,22)}=4.33, P<.05$.

As shown in Fig. 2, Neglect patients showed about 50% RT increment on left uncued trials compared to left cued trials, a result that has been described elsewhere as an extinction-like pattern resulting from a deficit in disengaging attention from a right-sided event when it has to be re-engaged on a left-sided object (Posner et al. 1984; reviews in Bartolomeo and Chokron 2002; Losier and Klein 2001). However, this deficit was completely eliminated by endogenous attention, as it did not occur when Neglect patients expected the target to appear at the left location. Furthermore, the extinction-like pattern of data shown by Neglect patients at the unexpected target location was observed only at the two shortest SOAs, as can be seen in Fig. 2, and is indicated by the four-way interaction between Group, Expectancy, Cueing, and SOA, $F_{(2,44)}=7.52, P<0.005$. These characteristics suggest that the attentional bias shown by these patients concerns primarily exogenous orienting, consistent with abundant previous evidence (reviewed in Bartolomeo and Chokron 2002).

### Right location

Again, the main effects of Group, Expectancy, and Cueing were significant in this analysis. However, the most interesting result was that Neglect patients produced a much bigger cueing effect than the Control group, $F_{(1,22)}=6.07, P<0.05$.

Although the Group × Cueing × SOA interaction only approached significance, $F_{(2,44)}=2.18, P=0.125$, as can be seen in Fig. 3, participants in the control group produced the usual transition from facilitation at the short SOA to IOR at the long SOA, $F_{(2,34)}=7.31, P<0.005$, independently of Expectancy ($F<1$). In contrast, Neglect patients produced a large positive cueing effect (14.12% on average) across the three SOAs, $F_{(1,5)}=7.19, P<0.05$, also independently of Expectancy.

This result is similar to the one observed by Bartolomeo et al. (1999) using a procedure in which cueing was manipulated by comparing target locations in the current and previous trial (target-target procedure). They reasoned that an anomalous IOR for right-sided objects could contribute to the impairment of Neglect patients, and found that Neglect patients indeed showed facilitation instead of IOR for right-repeated targets. The size of this paradoxical “facilitation of return” for right targets showed an inverse correlation with the number of left hits in two cancellation tasks, thus suggesting the presence of a relationship between the paradoxical “facilitation of return” for right targets and left neglect. The bigger the right facilitation of return they showed, the more pronounced was the left neglect on paper-and-pencil tasks. Apart from generalizing this finding to a cue-target

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**Table 2** Proportional mean RT as a function of target location, expectancy, cueing, and SOA. Data from the Neglect patients and control group of Bartolomeo et al. (2001)

<table>
<thead>
<tr>
<th>SOA (ms)</th>
<th>150</th>
<th>550</th>
<th>1,000</th>
<th>Expected</th>
<th>Unexpected</th>
<th>150</th>
<th>550</th>
<th>1,000</th>
<th>Expected</th>
<th>Unexpected</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control group</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cued</td>
<td>0.97</td>
<td>0.94</td>
<td>0.96</td>
<td>1.00</td>
<td>1.01</td>
<td>0.91</td>
<td>0.92</td>
<td>0.87</td>
<td>1.00</td>
<td>0.96</td>
</tr>
<tr>
<td>Uncued</td>
<td>1.04</td>
<td>0.94</td>
<td>0.91</td>
<td>1.11</td>
<td>1.02</td>
<td>1.07</td>
<td>0.96</td>
<td>0.79</td>
<td>1.13</td>
<td>1.05</td>
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<tr>
<td>Cueing effect</td>
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<td>0.01</td>
<td>-0.05</td>
<td>0.11</td>
<td>0.01</td>
<td>0.06</td>
<td>0.01</td>
<td>-0.06</td>
<td>0.12</td>
<td>0.07</td>
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<td><strong>Neglect patients</strong></td>
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</tr>
<tr>
<td>Cued</td>
<td>1.04</td>
<td>1.12</td>
<td>1.12</td>
<td>0.87</td>
<td>1.04</td>
<td>1.35</td>
<td>0.70</td>
<td>0.71</td>
<td>0.79</td>
<td>0.82</td>
</tr>
<tr>
<td>Uncued</td>
<td>1.11</td>
<td>1.12</td>
<td>0.98</td>
<td>1.46</td>
<td>1.48</td>
<td>1.25</td>
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<td>0.89</td>
<td>0.93</td>
<td>0.90</td>
</tr>
<tr>
<td>Cueing effect</td>
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<td>-0.13</td>
<td>0.59</td>
<td>0.44</td>
<td>-0.10</td>
<td>0.17</td>
<td>0.18</td>
<td>0.14</td>
<td>0.08</td>
</tr>
</tbody>
</table>
procedure, the present results are interesting in that, once again, this exogenous cueing effect (facilitatory, instead of IOR) seems not to depend on where attention is endogenously oriented (see Fig. 3).

General discussion

According to the spotlight metaphor of attention, or its neural version (Fernández-Duque and Johnson 1999), attention is conceived as a mechanism that facilitates the processing of stimuli within an attended area of space by improving functioning of the neural areas representing that part of the space. Thus, processing is enhanced at locations to which attention is allocated compared to locations to which attention is not allocated. Within this framework, it is important to know the mechanisms by which the attentional operator moves across space, the parameters of the movement, and the biases inherent to that movement. Thus, as we described in the Introduction, it is widely assumed that exogenous attention is biased against returning to previously attended locations. This bias is the basis for what we call the reorienting hypothesis, which has been used widely to explain the IOR effect.

However, the results of the present experiment, as well as the reanalysis of the results of Bartolomeo et al. (2001), confirm that IOR can be observed for locations at which a target is expected to occur. If IOR reflected a difficulty in returning attention to a previously attended location, then it ought not to occur when attention is endogenously maintained at the cued location. The present results show the opposite outcome, and thus nicely complement those reported in several prior studies in demonstrating a surprising degree of independence between endogenous orienting and exogenous cueing effects. Our methods differed from previous studies that obtained similar results (Berger and Henik 2002; Berlucchi et al. 2000; Rafal and Henik 1994) in that we used exclusively peripheral cues, and modulated participants’ endogenous expectancies by systematically varying the level of cue predictiveness (50%, 80%, or 20% of cued targets). The similarity of the results in the face of this change in method suggests that the independence of IOR from endogenous expectancies is a robust phenomenon.

An important implication of this observation is that the description of spatial attention as a spotlight, and IOR as a byproduct of biases in its movement, might be inadequate. Time and accuracy of target processing seem rather to be the end product of multiple processes, independent to...
some extent and working in parallel. Specifically, the present results suggest that exogenous processes related to bottom-up attentional capture and endogenous mechanisms related to top-down spatial expectancy contribute independently to performance. Similarly, Berlucchi et al. (2000), who observed IOR for locations where participants were told to engage their attention, proposed that their results could be accounted for by the simultaneous operation of multiple independent attentional mechanisms during covert orienting.

The dissociation between exogenous and endogenous orienting shown by the present and previous results should perhaps not come as a surprise, given that these attentional processes serve two often conflicting interests. That is, in order to maintain coherent behavior in the face of a continuously changing environment, an organism needs mechanisms that: (a) allow for the processing of novel, unexpected events, that could be either advantageous or dangerous, in order to respond appropriately with either approach or avoidance behavior, and (b) allow for the maintenance of goal-directed behavior in spite of distracting events (Allport 1989). These two ecological constraints may be satisfied by functionally independent endogenous and exogenous processes. Thus, exogenous and endogenous orienting processes seem to be in a continuous dynamical equilibrium. The salience of distracting events and the strength of the strategic set would establish the relative weight that, respectively, exogenous and endogenous orienting has on performance.

Importantly, however, rather than thinking of exogenous and endogenous attention processes as constituting two means by which a unitary spatial attention operator moves across space, it may be that exogenous and endogenous attention processes perform quite different functions, as has been put forward by Klein and colleagues to explain other dissociations between exogenous and endogenous attention (Hansen and Klein 1990; see Klein and Shore 2001, for a review). One possibility is that exogenous processes are related to perceptual processing, perhaps playing a role in perceptual integration (Kahneman et al. 1992), perceptual competition (Desimone and Duncan 1995), and novelty detection. In contrast, endogenous processes may have more to do with top-down preparation for perceptual processing rather than with perceptual processing itself.

Note that this distinction lends itself to a different explanation of exogenous cueing effects. Rather than making reference to how an abrupt onset cue affects the locus of an attention operator, the explanatory focus shifts to specific ways in which perceptual processing might be altered by an abrupt onset cue. For example, an abrupt onset cue may capture attention (Ruz and Lupiáñez 2002) in the sense that it initiates the encoding of a new perceptual event. If a target appears shortly after the cue, the temporal proximity of the two events may result in the encoding of the cue and target as part of the same perceptual event (Kahneman et al. 1992; Lupiáñez et al. 2001). As this event integration process only occurs efficiently for targets and cues that appear at the same location, and not for those appearing at different locations, it explains why there is often an exogenous cueing benefit at short cue-target SOAs. However, as the temporal interval between cue and target increases, the utility of perceptual integration processes can be expected to decrease, which explains why this facilitation effect is short-lived. Furthermore, if we assume that the perceptual system has an inherent tendency to integrate cue and target events even at longer cue-target SOAs, and even when we try to differentiate them, it follows that cued targets will be treated by the system as “old” events while uncued targets will be treated by the system as “new” events. Assuming that new perceptual events capture attention, then this attention capture could serve as the basis for explaining the IOR effect at long SOAs (cued targets are less new). Note that from this perspective, IOR does not result from inhibited processing at the cued location, but rather from the loss of the benefit that takes place at non-cued locations due to attentional capture from new onsets (Milliken et al. 2000).

In this context, we consider particularly interesting a recent finding by Dorris et al. (2002). They observed that neurons of the superficial and intermediate layers of the monkey superior colliculus (SC) show an attenuated visual response to the target if it has been preceded by a peripheral non-informative cue (i.e., they show IOR for cued targets). However, these neurons were not inhibited during the period of time prior to target onset (i.e., during the interval between cue and target onsets), nor were they inhibited at the time of target onset. In fact, the baseline activity in these cells was actually higher than when the cue was presented at the opposite location to the target (outside the cell’s receptive field). Furthermore, when saccades were elicited artificially by electrical microstimulation of the SC rather than by actual presentation of a target, saccades were faster when the electrical microstimulation was added to the same location as the cue, than when it was added to the uncued location. That is, the presentation of a cue led to an increase in activation of the SC cells, rather than to inhibition of these cells. Interestingly, this increased activation led to a longer saccade latency to an external target (i.e., IOR), but to a shorter latency (facilitation) in artificially induced saccades.

As ironic as it might appear, rather than measuring inhibition allocated to a spatial representation, IOR may measure a negative consequence of some small activation of a spatial representation. Under some conditions (i.e., long SOAs), an activated spatial representation may fail to speed responses to targets presented at that location, but may be sufficient to impede attention from being captured by the target at that location. However, this negative effect (IOR) should only appear if participants treat the cue and target as separate events. If participants integrate cue and target into a single object representation (thus adding to its initial activation), then one might expect to observe facilitation rather than IOR, mirroring Dorris et al.’s (2002) microstimulation data.
Interestingly, this might explain the above-described “facilitation of return” pattern observed for right, non-neglected targets, in Neglect patients. The facilitatory effect might be due to the problems that these patients seem to have in creating separate representations for different objects presented at the same location, revealed in an unusually long Attentional Blink effect (Husain et al. 1997). If Neglect patients are unable to encode separate representations for consecutive stimuli appearing at the same location, then object substitution processes (see Enns and DiLollo, 1997) may lead to the integration of consecutive stimuli within the same event representation, even when they appear at relatively long asynchronies. Thus, in an Attentional Blink procedure the target would be substituted by the following distractor, leading to the Attentional Blink effect. In our cueing procedure the cue would be substituted by the target, leading to a facilitation effect, similar to the one shown by controls at shorter SOAs, and by SC microstimulated cells.

Be that as it may, the findings from Neglect patients also indicate independence between IOR and endogenous allocation of attention, consistent with the evidence suggesting a lateral bias of exogenous orienting with relatively preserved endogenous orienting in left neglect (Bartolomeo and Chokron 2002; Bartolomeo et al. 2001; Ladavas et al. 1994; Smania et al. 1998).

In support of this view, evidence suggests that the two modes of orienting might be subserved by partially distinct neural substrates. Recent neuroimaging studies (reviewed in Corbetta and Shulman 2002) have suggested that the brain contains two partially segregated systems for visual orienting: a dorsal network (intraparietal sulcus and frontal eye field), bilaterally represented and concerned with endogenous orienting, and a more ventral network (temporoparietal junction and inferior frontal gyrus) subserving exogenous orienting. Importantly, the ventral network is lateralized to the right hemisphere, and colocalizes with the brain regions most often damaged in unilateral neglect. A functional MRI study (Rosen et al. 1999), employing a cued RT paradigm to identify the brain areas involved in exogenous and endogenous orienting, demonstrated largely overlapping activations in the parietal and dorsal premotor regions for both modes of orienting, except for an activation in the right dorsolateral prefrontal cortex (BA 46) that was exclusive to the endogenous condition. On the other hand, neural activity in the superior colliculus may be important for the IOR phenomenon (Dorris et al. 2002; Sapir et al. 1999). Thus, exogenous orienting might rely on a frontal-parietal network receiving information from subcortical structures, and modulating its activity, whereas in endogenous orienting the relevant cortical network might be similar, but with a more extensive implication of prefrontal regions.

The functional specialization suggested by our present results may thus reflect a relative modularity of the neural correlates of exogenous and endogenous orienting, in agreement with neurocognitive models postulating attentional processes as resulting from competition among distinct neural networks (Desimone and Duncan 1995).

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The influence of limb crossing on left tactile extinction

P Bartolomeo, R Perri, G Gainotti

Background: Previous research on patients with left tactile extinction has shown that crossing of hands, so that each hand is on the opposite side of the body midline relative to the other, improves detection of stimuli given to the left hand.

Objectives: To study the influence of the spatial position of limbs on left tactile extinction, and its relations with left visual neglect.

Methods: Normal participants and patients with right cerebral hemisphere damage and left tactile extinction were asked to detect single or double light touch stimuli applied to their cheeks, hands, or knees with their arm and legs either in anatomical or in crossed position, increasing the attentional load of the task.

Results: In patients with left extinction, limb crossing caused a deterioration in performance for stimuli applied to right body parts, with only a tendency to an improvement in detection for left body parts (only two of 24 patients showed substantial (>20%) improvement in left extinction after limb crossing). After crossing, left limb detections of double stimuli decreased with increasing degrees of visual neglect.

Conclusions: In conditions of high attentional load, limb crossing may impair tactile detection in most patients with left extinction, and particularly in those showing signs of left visual neglect. These results underline the importance of general attentional capacity in determining tactile extinction. Attentional and somatotopic mechanisms of extinction may assume different weights in different patients.

Brain damaged patients may report only the stimulus ipsilateral to their lesion when stimulated on both sides, despite being able to report a single stimulus wherever applied. This disorder, called extinction or sensory inattention, is clinically defined as the “recognition only on the passively. Accounts of extinction typically emphasize either a sensory problem not severe enough to impair perception of single stimuli, or an attentional disorder favoring ipsilateral over contralateral stimuli, or both. The sensory and attentional mechanisms may reflect damage to different neural structures: the ascending pathways in the subcortical white matter for the sensory mechanism, and frontal or parietal cortical regions for the attentional mechanism.

Concerning extinction in the somatosensory mode, or tactile extinction, several findings suggest that it is not exclusively determined by sensory mechanisms. First, left extinction may appear or be enhanced when patients look towards the right side. On the other hand, contralesional awareness may be improved by looking at or intentionally moving to tactile stimuli rather than receiving them passively. Second, there is the possibility of observing cross modal, visual-tactile extinction, in which a visual stimulus can extinguish a tactile one. Third, there is the fact that tactile extinction seems to be more frequent after right than after left brain damage, thus paralleling the pattern of occurrence of unilateral neglect. Finally, Moscovitch and Behrmann showed that extinction in patients with unilateral neglect may have a directional component. When the wrist of one hand was touched simultaneously on its left and right side, patients extinguished the stimulus contralateral to the brain lesion, independent of the hand that was stimulated (left or right), and of its position (palm up or palm down).

Aglioti and coworkers recently confirmed that tactile extinction does not depend solely on sensory factors. Smania and Aglioti examined the detection of light tactile stimuli applied on one or both hands of normal individuals and 16 right brain damaged patients. Participants were tested with their hands either in anatomical position, or crossed so that the left hand was placed to the right of patient’s midline and vice versa. They found that crossing the hands improved the patients’ performance by 32.5% for the left hand and left detections for the right hand substantially unchanged. In contrast, crossing impaired the controls’ performance by around 5% for either hand.

The investigators proposed that the subjects’ performance relied upon two different representations: a somatotopic representation and an extrapersonal spatial representation. Right brain damage would impair the left part of both representations, and cause the right part of the hemispace to be overrepresented. Accuracy of detection for the left hand would thereby improve when the left hand is placed in the right hemispace. However, this account would have predicted an impairment of right hand detection in the crossed condition, that is, when the right hand is situated on the left, impaired side, but Smania and Aglioti found no substantial change in that condition.

In a second study, Aglioti et al employed a similar experimental paradigm in a larger patient sample (36 right brain damaged patients), but this time the hands (in a crossed or uncrossed position) were either across the body midline or both in the right or in the left hemispace. Results showed an improvement in left hand detection by 30% in the crossed position, which occurred independently of the location of the hands (central or lateral); thus the source of the effect seemed to be the position of the hands with respect to each other, without reference to the body midline. On the other hand, crossing impaired performance for the right hand by 3%, but only in the most severely impaired patients—that is, those omitting at least 70% of left sided stimuli under double stimulation and at least 50% of single left sided stimuli.

However, Vaishnavi et al also explored the effect of limb crossing on extinction and found that crossing induced an
average 5% deterioration in performance for left hand detections in a group of 10 right brain damaged patients. Only two patients showed some improvement (8%) after crossing (see their table 3, patients LAB and GS). Performance for the right hand remained at ceiling both in anatomical and crossed positions.

Perhaps these discrepancies resulted from different impairments being at work in different patients. For example, in Aglioti’s 1999 study, crossing may have impaired stimulus detection on the right hand only for patients with a severe asymmetry in attentional orienting, as suggested by their tendency to omit even single left sided stimuli. If so, then increasing the possible loci of simulation in a tactile extinction paradigm, and thereby taxing the already biased processing capacities of right brain damaged patients, should allow one to observe a more systematic detrimental effect of limb crossing for detections on the right body parts. If, on the other hand, extinction depends on a representational impairment, then increasing the possible stimulus sites should not change the pattern of results observed by Aglioti and coworkers. That is, crossing should improve detection for left body parts and leave performance for right body parts substantially unchanged, at least for patients with milder forms of extinction.

A further question of interest concerns the relations between tactile extinction and signs of visual neglect in the extrapersonal space. There is functional and anatomical segregation of the brain mechanisms which process personal and extrapersonal space, as shown by neurophysiological studies in the monkey and by human lesion studies. In support of this distinction, tactile extinction has been found to correlate poorly with tests of extrapersonal visual neglect. If, however, the effect of limb crossing involves a recoding of personal space into extrapersonal coordinates, then this effect might be found to correlate with neglect signs on paper and pencil tests.

To explore these issues, we examined right brain damaged patients with left tactile extinction and normal individuals, using a task involving the presentation of tactile stimuli on their cheeks, hands, and knees, both in anatomical position and after crossing of arms and legs. Double stimuli were given either to homologous or to non-homologous body parts (for example, left hand and right knee). Thus patients had to monitor six possible loci of stimulation at any given time. The number of patients studied (n = 24) was relatively larger than in most previous studies involving limb crossing, to increase the possibility of observing individual differences in performance. The relation of crossing induced changes with the presence and degree of visual neglect was explored by correlating these changes with patients’ performance on a neglect battery, including tests of target cancellation, line bisection, drawing copy, and identification of overlapping figures.

METHODS

Participants

Twenty four patients with unilateral lesions in the right hemisphere and left tactile extinction and 10 subjects without neurological impairment participated in the study after giving their informed consent. The study was carried out in accordance with the guidelines of the Declaration of Helsinki. Patients and controls did not differ in age or educational level (both t values < 1). All patients underwent a preliminary examination of tactile extinction following a standard clinical procedure consisting of six single unilateral stimuli (left or right hand, left or right knee, left or right cheek) and six double simultaneous stimuli (both hands, both knees, or both cheeks, each repeated twice), delivered to the blindfolded patient according to a previously randomised sequence. Patients were included in the study if they detected at least one single left stimulus per body part and extinguished at least one left stimulus under double stimulation. Table 1 shows the participants’ demographic and clinical characteristics.

Procedure

Tactile detection task

Participants were seated blindfolded in a comfortable chair. The examiner gave light touch stimuli with the index fingertips. In the “anatomical” condition participants seated with hands on their lap. In the “crossed” condition, participants crossed their legs and arms, with the right limbs positioned over their left homologues. Stimulation was given to participants’ cheeks, hands (dorsum), and knees. For each condition (anatomical or crossed), there was a basic sequence of 12 single stimuli (two for each body part and side of space), 24 double stimuli on homologous sites (two for each cheek, five for each hand, and five for each knee), and 12 double stimuli on non-homologous sites (two for each body part and side of space). Double stimuli were always given to body parts on the opposite sides of the body. To avoid ambiguities in the interpretation of responses, participants were asked to respond both by verbally localising the stimulated body part and by moving or touching it. The basic sequence was repeated four times, following an ABBA design, with A = anatomical and B = crossed for half of the participants, and the reverse assignment for the other half. Results of the two repetitions of each condition (anatomical or crossed) were pooled together.

Neglect battery

In the cancellation tests, a horizontal A4 sheet was presented to the patient, who was asked to cancel targets of various kind that were scattered on it: lines or “A’s among other letters. In the overlapping figures task, patients were requested to identify five patterns of overlapping linear drawings of common objects. Each pattern included a central object (for example, a basket) with a pair of objects depicted over each of its sides (such as a lamp and a watch on the left side, a pipe and a key on the right side). The line bisection test was originally described by D’Erme et al. It consists of eight lines horizontally disposed in a vertical A4 sheet, in a fixed random order. There are three 62 mm samples at 38, 81, and 124 mm from the left margin of the sheet, three 100 mm samples at 17, 62, and 90 mm from the margin, and two 180 mm samples at 14 mm from the margin. Finally, patients copied a linear drawing representing a landscape consisting of a house and four trees, presented on a horizontal A4 sheet.

Data analysis

To obtain a quantitative measure of spatial bias in each component test of the visuospatial battery, laterality scores were computed for each of the neglect tests using the following procedure. For the line bisection test, the score was the cumulated percentage of deviation from the true centre for all the lines. Rightward deviation assumed a positive sign, whereas leftward deviations carried a negative sign. For the overlapping figures test and each of the cancellation tests, we estimated the bias toward the right side by using a laterality score, defined as: \( \frac{(x_1 - x_2)^2}{(x_1 + x_2)} \). Values for \( x_1 \) were given by the number of items identified on the right side for the overlapping figures test, or the number of items cancelled on the right half of the page for the cancellation tests. Values for \( x_2 \) were computed in an analogous fashion—that is, by using the number of left sided identified overlapping figures and the number of left sided cancelled items. One advantage of this laterality score is that it provides a quantitative estimate
of spatial bias which is independent of the overall level of performance (for example, of the total number of cancelled targets). Its possible range is from 1 (all the items reported or cancelled on the left side, none on the right side) to +1 (the opposite situation). A correction was needed for cancellation tasks undertaken by patients with severe neglect, who cancelled only the rightmost items, without crossing the midline. In order not to underestimate their neglect, the laterality score obtained by these patients was augmented by subtracting from 6 one point for each tree completely copied, and two points for the house. Scores could range from 0 (all the items reported or cancelled on the right) to 5.5 (only the right half of a single tree copied).

The proportions of correct detections in the tactile detection task for each participant and condition were arcsin transformed and entered into separate repeated measures analyses of variance (ANOVA) for normal participants and for right brain damaged patients. The stimulated body part (cheek*; hand, or knee), its anatomical side (left or right body parts), the type of stimulus (single, double on homologous body parts, or double on non-homologous body parts), and the limb position (anatomical or crossed) were entered as factors. Theoretically relevant results were followed up by Tukey HSD tests.

Although there was no straightforward reason to expect that limb crossing had any effect on detection accuracy on the cheeks, it could have influenced performance in indirect ways (for example, through changes in general arousal due to proprioceptive stimulation).

### RESULTS

Normal participants performed at or near ceiling in all conditions (fig 1A), but were more accurate in the anatomical position (99.7% accuracy) than in the crossed position (99.1%), F(1,9) = 8.65, p < 0.05. This effect interacted with the type of stimulus, F(2,18) = 5.28, p < 0.05, because crossing decreased performance for double homologous stimuli (Tukey test, p < 0.01), but not for the other types of stimuli. No other effects or interactions reached significance.

Right brain damaged patients’ performance (fig 1B) was affected by the stimulated body part, F(2,46) = 65.86, p < 0.0001, because patients detected a touch on cheeks better (87.8%) than stimuli on hands (67.6%) or knees (68.9%) (Tukey test, all p values < 0.0005). Patients detected more stimuli on the right side (93.7%) than on the left side (55.8%), F(1,23) = 151.26, p < 0.0001. These effects interacted (F(2,46) = 19.43, p < 0.0001) because performance was worse for the left hand (43.8%) and knee (46.9%) than for the left cheek (76.7%) (all p values < 0.0005). Accuracy decreased from single stimulation (94.5%) to double homologous stimulation (69.0%) and to double non-homologous stimulation (60.6%), F(2,46) = 339.63, p < 0.0001. As expected in patients with left extinction, these effects interacted (F(2,46) = 37.75, p < 0.0001) because patients detected fewer stimuli on their left body parts with double stimulation than in the other conditions (all p values < 0.0005). The body part interacted with the type of stimulus (F(4,92) = 8.57, p < 0.0001) because the fall in accuracy from single to double stimuli was more substantial for limbs than for cheeks. The limb position (anatomical or crossed) had no effect on overall performance (F(1,23) = 1.35) but interacted with the side (F(1,23) = 10.40, p < 0.005), because crossing non-significantly improved performance for left body parts by 2.6%.
limbs either in anatomical or crossed position. of hits) under single stimulation and under double stimulation in right brain damaged patients on homologous or non-homologous body parts, with limbs either in anatomical or crossed position. (B) Accuracy of detection (percentage (2 homol) or non-homologous (2 non-homol) body parts, with limbs either in anatomical or crossed position. Bartolomeo, Perri, Gainotti

Figure 1  

Concerning, for example, the two patients who showed the larger improvement in left detections after crossing, patient 03 had no signs of visual neglect and patient 05 showed only a moderate rightward deviation on line bisection. The relation between crossing induced effects and visual neglect was explored more formally by calculating the correlation coefficients between the laterality scores obtained from paper and pencil tests and the effect of crossing on limb tactile extinction. If the effect of crossing involved a recoding of personal coordinates into extrapersonal coordinates, then performance on paper and pencil neglect tests should positively correlate with crossing-induced modifications of tactile extinction. Contrary to this prediction, no significant positive correlation emerged between these measures (table 3). Unexpectedly, instead, negative correlations occurred between neglect tests and crossing induced changes of left limbs detection. This was because patients with severe degrees of left visual neglect were the least likely to improve when their left limbs were positioned on the right, non-neglected side (see, for example, patients 16 and 17 in table 2, who had severe left neglect and whose tactile detection for left limbs decreased by more than 20% after crossing).

DISCUSSION
We asked normal participants and right brain damaged patients with left tactile extinction to detect single or double light touch stimuli applied on their cheeks, hands, or knees before and after crossing of hands and legs, so that the left limbs were now on the opposite side relative to their right counterparts. Independently of crossing, patients showed better accuracy for stimuli delivered on their face than for stimuli applied on limbs, confirming previous evidence. This result seems consistent with the view that the cortical sensory representation of the face is organised more bilaterally than that of the limbs, where it is strictly contralateral. Sensation from the face would thus be more resistant to disruption resulting from unilateral brain damage.

Crossing the hands and knees induced changes in accuracy of detection of tactile stimuli. Normal participants showed a slight deterioration of performance in the crossed condition, especially for double simultaneous stimuli, suggesting that these situations are particularly demanding in terms of attention. For right brain damaged patients with tactile extinction, the deterioration of performance on limb crossing was substantial for the right limbs—six times larger than shown by controls. Aglioti et al., using a task similar to ours but with stimuli given only to the hands, found an analogous
Table 2  Accuracy of detection (% of hits) for double stimuli given on limbs in the anatomical and crossed conditions, crossing induced changes (% hits anatomical−% hits crossed), and patients’ performance on the neglect battery

<table>
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<th>Participant</th>
<th>Left anatomical</th>
<th>Left crossed</th>
<th>Left limbs change</th>
<th>Right anatomical</th>
<th>Right crossed</th>
<th>Right limbs change</th>
<th>Line bisection (% deviation)</th>
<th>Line cancellation (max 30/30)</th>
<th>Letter cancellation (max 30/30)</th>
<th>Overlapping figures (max 10/10)</th>
<th>Landscape drawing</th>
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<td>0/23†</td>
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<td>3</td>
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</table>

For line bisection, + indicates rightward deviation and − indicates leftward deviation. For cancellation tests, left/right correct responses are reported. Asterisks indicate pathological performance for standardised tests.

*Rightward or **leftward deviation greater than 2 SD from the mean performance of 30 normal age matched individuals.39

†The same group of normal individuals never omitted more than one item on this task.

C, control; P, patient; –, missing data.
deterioration of performance only in extinction patients with severe impairment, who also omitted most single left stimuli.

In the present study, by contrast, even patients who detected most left single stimuli showed this pattern of performance. This discrepancy may be explained if one considers that increasing the possible loci of stimulation also increases the attentional demands of the task, which thereby becomes more sensitive to disruption when the usual left-right position of the limbs is reversed.

Our results only partially confirmed the improvement of left body part detections after limb crossing shown in previous studies, in which the hands alone were stimulated. We observed only a tendency in this sense for the left knee and cheek, but not for the left hand (see fig 1B).

Inspection of individual performances (table 2) shows that about half the patients had some improvement of left limb extinction after crossing, but only for a third of patients was the improvement larger than 10%, and only for two patients was it larger than 20%. Also this discrepancy may underlie the increased attentional load of our task as compared with the tasks employed by Aglioti and coworkers.

The possibility that the effect of limb crossing varies with the attentional load of the task (left body part improvement with low load, right body part deterioration with high load) supports the view that an attentional component participates in somatosensory extinction after right brain damage. Requested to monitor six possible anatomical loci for brief tactile stimuli, after crossing, patients made many more omissions when they had to orient their attention leftward to detect stimuli given to their right limbs. Although not statistically significant, the tendency for limb crossing to improve left detections on checks in right brain damaged patients (fig 1B) might also suggest that part of the influence of limb crossing observed in previous studies may simply be an arousal effect. Manoeuvres that increase arousal are known to ameliorate left visual neglect.

As mentioned in the introduction, Vaishnavi et al found that limb crossing induced an average deterioration of performance for left hand detections. They argued that extinction patients may suffer from an attentional bias in personal (somatotopic) space, rather than in extrapersonal space. They also proposed that tactile sensation might be biased towards personal rather than extrapersonal space. The alternate pattern could be true in individual cases. Heldmann et al found that repetitive peripheral magnetic stimulation of the left hand led to a significant reduction in left extinction, but had no effect on ipsilesional errors, whereas attentional cueing had no significant influence on left extinction, but increased right hand extinction errors. Our results are not inconsistent with the proposal by Vaishnavi that tactile sensation might be biased towards personal rather than extrapersonal space, and are quite consistent with the proposal by Heldmann that the high attentional demands of their tactile extinction task may account for the detrimental effect of contralesional cueing on ipsilesional performance.

Inspection of tables 2 and 3 and results of the correlational study suggest that there is no clear relation between the results of paper and pencil tests of neglect and the effects of limb crossing on tactile extinction. Contrary to the expectation that neglect patients might particularly benefit from limb crossing when detecting tactile stimuli on their left limbs (now placed on the right, “intact” side of space), the observed tendency was in the opposite sense. Patients with visual neglect tended to omit more left limb stimuli after crossing. If the crossed condition were particularly demanding in terms of attention, then neglect patients might have found this condition especially difficult, in keeping with evidence showing deficits of non-lateralised attentional capacities in these patients. The present results seem also in line with other evidence showing poor correlations between tactile extinction and visuo-spatial tasks in right brain damaged patients, and, more generally, between tasks performed under visual control and tasks carried out without visual control. This evidence can be interpreted as suggesting that right visual objects exert a powerful “magnetic attraction” on patients’ attention, thus enhancing left neglect, as compared with situations in which no visual stimuli are present. Another possible interpretation of these discrepancies is that an attentional bias can manifest itself either in personal or in extrapersonal space, and that tactile sensation may be biased toward personal rather than extrapersonal space. Some patients of the present series showed disassociations in performance between line bisection and target cancellation tasks, consistent with previously reported evidence. The fact that patients with biased performance in either task are represented in the present sample suggests that our results generalise to both these patient populations.

Conclusions
Our results suggest that both somatotopic and attentional factors contribute to tactile extinction, perhaps with different weights in different patients. A rightward attentional bias for the personal space, with the possible addition of a more general, non-lateralised impairment of attentional capacity, may affect right brain damaged patients’ tactile detection by causing a dramatic deterioration in the performance of the right limbs when they are displaced leftward.

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Competing interests: none declared

REFERENCES
Influence of limb crossing on left tactile extinction

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Right spatial neglect after left hemisphere stroke
Qualitative and quantitative study

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Abstract—Objectives: Comparatively little research has been conducted on right neglect after left brain damage. The authors sought to assess contralateral neglect in subacute left hemisphere stroke patients using a comprehensive test battery validated in a large control group after right hemisphere stroke. Methods: Seventy-eight left hemisphere stroke patients were assessed. The test battery included a preliminary assessment of anosognosia and visual extinction, a clinical assessment of gaze orientation and personal neglect, and paper-and-pencil tests of spatial neglect in the peripersonal space. Only nonverbal tests were used. Results: Drawing and cancellation tasks revealed neglect in 10 to 13% of patients. The combined battery was more sensitive than any single test alone. A total of 43.5% of patients showed some degree of neglect on at least one measure. Anatomic analyses showed that neglect was more common and severe when the posterior association cortex was damaged. Conclusions: The frequency of occurrence of right neglect was, as expected, much lower than that reported in a study using the same assessment battery in right brain damage stroke patients. Nevertheless, neglect was found in a substantial proportion of patients at a subacute stage, suggesting that it should be considered in the rehabilitation planning of left brain damage stroke patients.

Unilateral neglect is more frequent, severe, and persistent after right brain damage (RBD) than after left brain damage (LBD). However, patients with right-sided neglect after LBD have been reported. Several cases of right extrapersonal neglect after LBD have been described. Right personal neglect in the absence of extrapersonal neglect has also been observed in LBD patients. A long-term follow-up study, which assessed nearly 100 cases each of LBD and RBD after 4 years, found qualitative differences between the groups in the rate of occurrence of translesional neglect. This asymmetry is usually attributed to a right hemisphere dominance for the distribution of spatial attention. One model proposed to account for this asymmetry postulates that the right hemisphere can direct attention to the ipsilateral and the contralateral hemispace, whereas the left hemisphere directs attention almost exclusively to the contralateral right hemispace. Accordingly, studies using functional neuroimaging have shown a right hemisphere dominance for mediating visual selective attention and more basic aspects of attention, such as arousal and alertness. Right spatial neglect has received much less attention than left neglect. Estimates of the frequency of right neglect after LBD greatly vary from one study to another, ranging from 0 to 76%. Thus, a precise account of the frequency of neglect after LBD is difficult to obtain because the available data are remarkably heterogeneous. Fewer LBD patients are typically studied because they are most likely to be dysphasic and may have problems in understanding the assessment instructions. Timing of assessment and the tests used varied considerably from one investigation to another. A further issue of interest concerns the hypotheses about hemispheric specialization for perceptual-attentional processes. Right and left neglect could differ 1) before underlying mechanisms; and 2) before intrahemispheric lesion locations. For example, 1) right neglect patients may have peculiar patterns of performance on neglect tests; and 2) a large-scale study of right neglect should also be
able to test the proposal that right neglect may result from more anterior lesions than those provoking left neglect.16

In the present study, we assessed the main characteristics of right neglect in patients with subacute left hemisphere stroke. We used a standardized test battery previously validated in a large control group17 and in subacute right hemisphere stroke patients.18 The test battery was adapted for use in aphasic patients to control for the confounding effect of language disorders after left hemisphere damage.

**Patients and methods.** Patients. Eighty-nine patients with a first-ever unilateral left hemisphere stroke were consecutively included in 19 participating centers in France and Belgium. Eleven had to be excluded for severe language (mainly comprehension) disorders. Of the 78 remaining patients, 54 (69.3%) had an ischemic stroke, and 24 (30.7%) had a hemorrhagic stroke. Forty-six of them were men, and 32 were women. Mean (SD) age was 54.6 years (15.7), and time since stroke onset was on average (SD) 10.8 weeks (12.4). Educational level was assessed with a three-level scale, 20 ranging from 0 (no motor-bias tasks) to 2 (severe hemiplegia). Sixteen patients (20.5%) had no hemiplegia; 42 (53.8%) had moderate hemiplegia; and 19 (24.3%) had severe hemiplegia (data were not available for one patient).

Patients were classified in four groups according to stroke localization as assessed by CT, MRI, or both: anterior (lesion limited to the premotor cortex and adjacent white matter; n = 7), posterior (lesion limited to the retroorbital cortex, including, but also temporal or occipital regions, or both; n = 9), anteroposterior (lesion involving premotor, rolandic, and posterior regions; n = 35), and subcortical (lesion limited to internal capsule, centrum semiovale, striatum, or thalamus; n = 20). Anatomic classification was done in each center by examiners who were not informed of the results of neuropsychological evaluation. CT or MRI of the brain were performed on average (SD) 8.9 weeks (6.7) after onset. Anatomic data were not available for seven patients. Testing conditions. The tasks were always given in the same order within one session of ≤1 hour and in the same conditions as in control subjects and RBD patients.17,18 For aphasic patients, the examiner systematically controlled test comprehension before the patient started the task. Only nonverbal tasks were used in the present study to control as much as possible for the confounding effect of language disorders (i.e., tests with an explicit and relevant linguistic component were not used). With this procedure, as previously stated, only a limited number of patients (n = 11) had to be excluded because of severe comprehension deficits. Assessments were conducted under the control of experienced examiners, and three examiners (M.A.K., C.K., and N.M.) from the coordinating center systematically reviewed all the data. Regular meetings with all participating centers also checked homogeneity of testing conditions and scoring.

Test battery. The test battery has been previously reported in detail elsewhere.17,18 To summarize, the test battery included assessment of personal neglect and gaze orientation and several paper-and-pencil tests (bell cancellation test, scene copy, clock drawing, two line-bisection tasks, and identification of overlapping figures), most of which were adapted from the existing literature with their authors’ authorization. Related disorders such as anosognosia and extinction were also addressed. Assessment of gaze orientation and personal neglect. Gaze orientation and head orientation was assessed with a four-level scale19 (0, no deviation; 1, reducible spontaneous deviation; 2, reducible deviation on incentive; and 3, permanent leftward deviation of gaze and head). Personal neglect. Patients were asked to reach their right hand with the left hand, first with eyes open and then with eyes closed. A four-level scale20 was used (0, normal performance; 1, the target is reached with hesitation and is searched; 2, searching is stopped before the target can be reached; and 3, no attempt to reach the target).

Paper-and-pencil tests of extrapersonal neglect. The bells test. Subjects were asked to circle 35 targets (black ink drawings of Bells) presented on a horizontal 21 cm × 29.7 cm (A4) sheet of paper along with 280 distractors.21 The following variables were used: total number of omissions (35) and the difference between right- and left-sided omissions.

Figure copying. Subjects were asked to copy on a horizontal A4 sheet a drawing including (from left to right) a tree, a house with a right-sided chimney, a fence, and a second tree.11,21 A modified five-level16 scale was used, ranging from 0 (no omission) to 4 (omission of the right tree and of at least the right part of another item).

Clock drawing. Patients were required to place the 12 hours in a circle drawn by the examiner. A three-level scale was used, ranging from 0 (normal performance) to 2 (omission or leftward displacement of all right-sided hours).

Line bisection. Patients were asked to mark the middle of four lines of two different lengths (two 5 cm and two 20 cm) presented separately and centered on an A4 horizontal sheet. Deviation from the true middle was measured in millimeters, positively for rightward deviations and negatively for leftward deviations.

Assessment of related disorders. Awareness. Awareness of motor and visual deficits was assessed using a four-level scale20 (0, perfect awareness of the deficit; 1, the deficit is detected only after a specific question about the strength of the left or the right side; 2, the visuospatial difficulties of the patient; 3, the disorder is found only after its clinical demonstration such as a neurologic examination; and 3, the patient never admitted having some impairment despite its demonstration by the examiner).

Visual extinction and hemianopia. The presence of extinction or hemianopia was tested clinically by wiggling fingers for 2 seconds in one or both visual fields while controlling central gaze fixation. Six trials were given in a fixed pseudo-random sequence, including four unilateral trials (two on each side) and two simultaneous bilateral trials. Extinction was considered present when a patient failed at least once to report a contralesional stimulus during bilateral simultaneous presentation while accurately detecting unilateral stimuli.

Data analysis. Descriptive statistics (i.e., mean, SD, and range) were used to describe performance. Statistical analyses were performed using SPSS software (SPSS Inc., Chicago, IL). The performance on paper-and-pencil tests was compared with that of control subjects from a previous study (n = 456 to 576, depending on the tests).11 Patients were considered affected by unilateral neglect if they obtained a score poorer than the fifth percentile of the control group. For some tests, performed without and with cover by all contralesional subjects (e.g., figure copying and clock drawing), any right-sided omission was considered to be an index of unilateral neglect.

Results. Assessment of gaze orientation and personal neglect. A rightward gaze or head deviation was found in nine (11.5%) patients. Personal neglect was found in 7 patients (9%) with eyes open and in 10 patients (12.8%) with eyes closed.

Paper-and-pencil tests of extrapersonal neglect. Ten patients (13.2%) had signs of right neglect on clock drawing, 10 (12.8%) on the bells test, and 8 (10.4%) on figure copying, whereas only 5 (6.4%) and 3 (3.8%) patients had significant leftward deviation on line-bisection tasks (table 1).

Assessment of related disorders. Five patients (6%) had anosognosia for hemiplegia and eight (10%) for visual impairments. Extinction and hemianopia were tested in 74 patients. Seventeen (23%) had a right hemianopia, and three (4%) had a right visual extinction without hemianopia.

The whole battery was more sensitive than any single test alone because 34 patients (43.5%) demonstrated ne-
glect on at least one measure. Comparatively, table 1 also shows a summary of the results obtained in a previous study with RBD patients. Although RBD and LBD patients were not exactly matched for stroke size and severity, the data from the two studies could be reliably compared because they were conducted by the same investigators, in the same units, with the same assessment battery, at a similar subacute stage (mean weeks since stroke onset for LBD patients, 10.8 [12.4]; for RBD patients, 11.1 [13.8]), and for strokes that seemed to be of grossly comparable severity (same amount, 24.3% and 21.4% of patients with severe hemiplegia). Neglect and associated disorders (anosognosia, extinction, and gaze deviation) were more frequent after RBD than after LBD, with a ratio ranging from ~2:1 to 4:1. Only hemianopia and personal neglect had similar frequencies in both groups. The frequency of neglect was roughly similar in patients with ischemic (42.6%) and hemorrhagic (45.8%) stroke (this difference was not significant; $\chi^2 = 3.2; df = 1; p > 0.1$).

To assess the relationships between the different tests within the LBD patients, a correlation matrix was calculated for the six paper-and-pencil tasks (table 2). All but two correlations were weak ($<0.18$). The only two significant correlations concerned the two drawing tasks (clock drawing and figure copying) and the two bisection tasks (long and short lines). No significant correlation existed between performance on paper-and-pencil tests and time since stroke onset, age, educational level, or handedness.

The relationships also tested between neglect and hemianopia or extinction revealed double dissociations between both disorders. One patient with hemianopia and one patient with extinction did not show neglect on any test; conversely, 14 patients who demonstrated neglect on at least one measure had neither hemianopia nor extinction.

<table>
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<th>Cut-off point</th>
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<th>% Neglect after RBD*</th>
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<td>20-cm lines, n = 78</td>
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<td>37.7</td>
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* Data from a previous study. LBD = left brain damage; RBD = right brain damage.

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</table>

* Significant correlations, p < 0.05.
Anatomoclinical correlations. Separate one-way analyses of variance ( \( p = 0.05 \) ) with lesion location as between-subject factor (anterior, posterior, anteroposterior, and subcortical) demonstrated no significant effect of localization for bisection of short lines ( \( F[2,35] = 1.46 \) ), figure drawing ( \( F[2,35] = 0.743 \) ), bells tests ( \( F[2,35] = 0.485 \) ), and clock drawing ( \( F[2,35] = 0.355 \) ). A significant effect of localization was found for gaze deviation ( \( F[2,35] = 3.63; p < 0.05 \) ), anosognosia for visual impairment ( \( F[2,35] = 4.05; p < 0.05 \) ) and motor impairment ( \( F[2,35] = 3.33; p < 0.05 \) ), personal neglect ( \( F[2,35] = 3.55; p < 0.05 \) ), and bisection of long lines ( \( F[2,35] = 3.92; p < 0.05 \) ). Post hoc analyses using Scheffé method showed that this effect was in all cases related to poorer performance in patients with posterior lesions. The figure shows performance on line bisection for the four patient groups defined by the intrahemispheric lesion localization.

Discussion. We assessed the characteristics of contralateral neglect and related disorders in subacute left-hemisphere stroke patients using nonverbal subtests of a comprehensive test battery of unilateral neglect.\(^{17,18}\) A limited number of patients (11/89; 12.3%) had to be excluded because of severe verbal comprehension disorders. This suggests that the patients included in the present study were representative of most left hemisphere stroke patients referred to a rehabilitation facility, although it must be noted that hemorrhagic strokes were a little more frequent and patients’ age was lower than expected.\(^{26}\) The most sensitive tests were drawing tests and the bells test, which was also found to be the case after right hemisphere stroke.\(^{18}\) These tasks each revealed right neglect in 10 to 13.2% of patients, but when the whole battery was taken into account, >43% of patients showed some degree of neglect on at least one test. This is in accordance with previous studies suggesting that a normal performance on one test alone is not sufficient to rule out the presence of neglect in a given patient.\(^{16,18,27}\)

The present data could be compared with those obtained in a study of subacute right hemisphere stroke patients assessed in the same units with the same assessment battery (except for tests including a verbal component) and at a similar subacute stage (11.1 [SD, 13.8] weeks after stroke onset). As can be seen in table 1, for each individual test, neglect and associated disorders were two to four times more frequent after right hemisphere stroke. When the whole battery was considered, neglect was twice as frequent after right-sided than after left-sided lesions (85% vs 43% of patients demonstrated neglect on at least one test). It seems unlikely that this dramatic difference could be related to differences in stroke severity. We acknowledge that the comparison between the present LBD patients with the previously reported RBD group should be taken with caution because the two groups were not exactly matched for stroke severity and lesion size was not systematically measured. It might be possible that larger strokes were excluded from analysis in the LBD group because of patients’ inability to understand the task instructions. Nevertheless, only mild differences existed between the two groups, and particularly the amount of patients with large anteroposterior stroke was similar in both groups (44.9% for LBD; 44.7% for RBD), as was the amount of patients with severe hemiplegia (24.3% for LBD vs 21.4% for RBD), suggesting that stroke severity was similar in both patient groups.

Unlike RBD patients,\(^{18}\) LBD patients demonstrated poor correlations among different paper-and-pencil tests (see table 2). This suggests that left hemispheric neglect is an elusive phenomenon, with less clinical consistency than right hemispheric neglect.

We can confirm that neglect is less frequent and less severe after left than after right hemisphere stroke. This result in a large series of patients and with a comprehensive test battery is important in view of the great variability of previous findings.\(^{2,12,13,16,27-32}\) Reasons\(^{13}\) for this variability include subject selection, lesion localization, and nature and timing of assessment. LBD patients also remain under-represented in most studies because of aphasic disorders. In one of the first studies in the field,\(^{28}\) contralateral neglect was found in 56 of 179 patients with right-sided lesions and in 1 of 286 patients with left-sided lesions. Similar results have been reported\(^{2}\) in 23 of 66 (35%) RBD patients and in 4 of 44 (9%) LBD patients with visual or tactile contralateral neglect. Similarly, in a large community-based study, in which a simple screening procedure was used, neglect was found in 42% of patients with right hemisphere lesions and in 8% of patients with left hemisphere lesions.\(^{32}\) Therefore, other studies reported contrasting results. The frequency of neglect\(^{29}\) assessed using a simple line cancellation test was not markedly different after RBD (37%) or LBD (30%), although neglect was much more severe after right hemisphere damage. Similar findings have been reported.\(^{16}\) Timing of as-
Assessment may be an important factor explaining these discrepancies. For example, another study using a comprehensive test battery has demonstrated that neglect was equally common at the acute stage (3 days) after right and left hemisphere stroke (72% vs 62%). A different picture was observed 3 months later when neglect had dramatically decreased in left hemisphere stroke patients (33%), whereas it remained frequent after right hemisphere stroke (75%). Results of a meta-analysis of 17 studies including left and right hemisphere stroke patients supported the frequency of occurrence of right neglect, ranging from 0 to 76% (median = 21%). By contrast, the frequency of left neglect after right hemisphere stroke ranged from 13 to 82%, with a median frequency of 43%. Despite their variability, these data suggest that left neglect is about twice as frequent as right neglect and are consistent with our present findings. Moreover, formal quantitative and qualitative testing was necessary to identify the type and the severity of neglect. It may be also important to distinguish different types of neglect to design appropriate rehabilitation strategies to target specific problems.

Previous study of neglect has compared the frequency of neglect after unilateral and bilateral cerebral lesions and has shown in a retrospective survey that lesions confined to the left hemisphere usually give rise to minor and short-lasting spatial impairments in the contralesional side, but bilateral lesions were necessary to produce persistent and severe right neglect. In the present study, only patients with a first-ever unilateral stroke were included (although previous silent contralateral lesions, not detected on standard CT or MRI, cannot be completely excluded).

In most clinical studies, neglect was measured with paper-and-pencil tests in the peripersonal space. However, accumulating evidence suggests that neglect is a heterogeneous disorder that may underlie distinct clinical phenomena. Personal neglect has been found to be dissociable from peripersonal or extrapersonal neglect. Surprisingly, in the present study, the frequency of occurrence of personal neglect did not significantly differ from that found after RBD. The putative right hemisphere specialization for spatial selective attention may mainly concern the extrapersonal space.

These conflicting results are broadly consistent with the hypothesis that different mechanisms may underlie left and right unilateral neglect. For example, a deficit of contralesional space exploration when searching for targets on a relatively large board (75 cm × 50 cm) was reported in RBD and LBD patients. However, only RBD patients omitted contralesional targets in a task in which the search was restricted to a smaller (14 cm × 21 cm) portion of space. A specific problem of exogenous, or stimulus-related, orienting of attention was suggested in RBD patients. This problem impaired the extraction of information from the left half of stimuli during single eye fixations. Supporting evidence for this claim comes from response time studies and neuroimaging evidence. An earlier study suggests that the brain contains two partially segregated systems for visual orienting: a dorsal network (intraparietal sulcus and frontal eye field), bilaterally represented and concerned with endogenous orienting, and a more ventral network (temporoparietal junction and inferior frontal gyrus), suberving exogenous orienting. Importantly, the ventral network is lateralized to the right hemisphere and colocalizes with the brain regions most often damaged in left neglect. These notions seem to comply with our finding of right neglect mainly in tasks stressing spatial exploration (cancellation tasks), with a relative sparing of tasks involving perceptual analysis (line bisection). Thus, consistent with the hypothesis of a left hemisphere dominance for action selection, right neglect may involve a bias affecting the processing stages more closely related to action than left neglect. A previous study has revealed that right neglect was preferentially associated with anterior lesions, whereas left neglect was related to retrorolando lesions. However, our results did not replicate this finding and suggested that right neglect is preferentially associated with posterior cortical lesions similar to left neglect.

Anosognosia is a major concern in neglect patients and has been found associated with poor functional recovery. Anosognosia for visual impairments was more frequent (10%) than anosognosia for hemiplegia (6%). The frequency of anosognosia was much lower than that found after right-sided lesions (46% and 17%). Our results are similar to those reported in several previous reports, although there remains considerable variability across studies. For example, in five previous studies, anosognosia was found in 28 to 68% of patients after RBD and in 5 to 32% of patients after LBD.

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References

Neglected attention in apparent spatial compression

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Abstract

Halligan and Marshall [Cortex 27 (1991) 623] devised a new test to evaluate the hypothesis that in visual neglect, left space is systematically compressed rightwards. In the critical condition of the original study, rows of horizontally arranged numbers with a target arrow pointing to one of them from the opposite margin of the display were presented. When asked to verbally identify the number indicated by the arrow, a right brain-damaged patient with left neglect and hemianopia often indicated a number to the right of the target. The more the target was located on the left, the greater the response shift rightward, as if rightward compression were linearly proportional to the co-ordinates of Euclidian space. However, a possible alternative account could be that the patient’s attention was attracted by the numbers located to the right of the target digit, thus biasing her responses toward numbers on the right. To explore this hypothesis, we asked normal participants and patients with right hemisphere lesions, with and without neglect or hemianopia, to mark on the margin of a sheet the approximate location indicated by an arrow situated on the opposite margin. In three different conditions, the arrow indicated either one of several numbers or lines in a row, or a blank location on the sheet margin. Only patients with left neglect, and especially those with associated hemianopia, deviated rightward, and then crucially only on those conditions where visible targets were present, consistent with the attentional bias account.

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Keywords: Unilateral neglect; Visual field defect; Space processing; Attentional and representational disorders

1. Introduction

Visual neglect is no longer considered a single monolithic disorder but rather a multiplicity of cognitive deficits that can collectively result in a lateralised disturbance of behavioural responses in different domains of space (Heilman, Watson, & Valenstein, 2002; Vallar, 1998). Most neglect patients, however, might suffer from a combination of component (potentially dissociable) deficits (Driver & Husain, 2002; Gainotti, D’Erme, & Bartolomeo, 1991). In particular, the frequency and severity of attentional problems in neglect patients have been often underlined (Bartolomeo & Chokron, 2001, 2002). Many neuropsychology tests present discussions of visual neglect in terms of an opposition between ‘attentional’ (e.g. Kinsbourne, 1993) and ‘representational’ accounts (e.g. Bisiach, 1993). While such an approach permits unification of a large and growing body of findings — the adequacy of the explanation offered given the nature of the many different tasks involved can be simplistic and theoretically premature.

In considering left unilateral neglect as an impairment of mental representations, Bisiach and colleagues proposed that neglect patients suffered from a “representational scotoma” (Bisiach, Bulgarelli, Sterzi, & Vallar, 1983, p. 36), or “a representational map reduced to one half” (Bisiach, Capitani, Luzzati, & Perani, 1981, p. 549). Another type of hypothetical representational impairment in neglect holds that space representation in neglect is characterised by some
form of horizontal anisometry (Chatterjee, 2002; Chokron, Bernard, & Imbert, 1997; Milner & Harvey, 1995), where spatial co-ordinates progressively relax from the right to the left side. For example, Bisiach, Pizzamiglio, Nico, and Antonucci (1996) had neglect patients mark the left and right endpoints of a virtual horizontal line on the basis of a given midpoint. Patients misplaced the left endpoint leftwards (over-extension of left side), as if they had to travel further leftward than rightward to equalise the amount of perceived spatial extent (see also Chokron et al., 1997; Kerkhoff, 2000). Milner and Harvey (1995) maintained that neglect patients perceive left-sided horizontal physical segments as shorter than identical right-sided segments. However, Doricchi and Angelelli (1999) showed that only patients with an association of left neglect and hemianopia demonstrate this pattern of behaviour, suggesting that an interaction between cognitive and sensory disorders is necessary in order to produce the perceptual anisometry of horizontal extension.

In a different account, Halligan and Marshall (1991) suggested that space representation in left neglect was distorted—such that the left part was ‘compressed’ toward the right, similar to a shrunk scarf or a spring being compressed (see also Milner, 1987; Werth & Poppel, 1988). Evidence in support of this account came from the pattern of performance of a single right brain-damaged patient with visual neglect and hemianopia. When on the critical horizontal conditions, the patient was presented with rows of numbers (from 1 to 15) either at the top or bottom of the display, and had to identify the number aligned with an arrow presented near the opposite margin of the display, she frequently indicated the number to the right of the target. The more the target was located on the left, the greater the response shift rightward. On the basis of this performance, Halligan and Marshall (1991) concluded that left space had been compressed rightward. However, as pointed out by Milner and Harvey (1995), a potential problem with this task is that the perception of the arrow location should be matched by similar changes in the perceived location of the targets. Thus, a putative spatial compression would affect both the arrow and the target location, and result in no apparent deviation in target identification. This possibility, however, prompts the question of why the patient described by Halligan and Marshall (1991) demonstrated a consistent rightward shift in target selection. A possible answer to this question could be that an attentional bias was at work, which determined neglect of the left-sided target stimuli and enhanced the relative salience of numbers located to the right of the target digit.

From a purely representational account of unilateral neglect (one where attentional factors were not held to play a contributing role), it would be relatively unimportant whether or not objects are presented in the non-neglected space, since it is the relative left part of the spatial representation (i.e. in this case of the page or TV screen) that is impaired irrespective of what happens in the other half. Per contra, some attentional accounts of neglect (e.g. Gainotti et al., 1991; Kinsbourne, 1993) have stressed that right-sided items are likely to attract patients’ attention; the more objects presented on the ‘unaffected’ side, the greater the neglect (Mark, Kooistra, & Heilman, 1988). In the present study, the aim was to explore the effect of the presence or absence of such competing stimuli on a task similar to that employed by Halligan and Marshall (1991), in the expectation that this additional experimental condition would help elucidate the effects of any attentional deficit.

Participants marked on a margin of the sheet the location indicated by an arrow situated on the opposite margin. In three different conditions, the arrow indicated either one of several numbers or lines in a row, or a blank location in a margin without any targets. The arrows were either presented on the top margin, pointing toward the bottom margin, or with the opposite spatial arrangement.

If a rightward attentional bias for objects is at work, then patients should show a differentially greater rightward deviation with competing targets. If, on the other hand, the representational problem consists of an anisometry of space representation with spatial co-ordinates progressively relaxing from the right to the left side on the horizontal plane (Bisiach et al., 1996), patients should show no deviation at all in either condition, because in performing the task they would proceed along the (presumably intact) radial dimension of spatial co-ordinates. Problems in programming left-directed arm movements (Bartolomeo, D’Erme, Perri, & Gainotti, 1998; Heilman, Bowers, Coslett, Whelan, & Watson, 1985; Mattingley, Bradshaw, & Phillips, 1992) are also unlikely to influence the outcome of the present paradigm (like the original study by Halligan and Marshall (1991)) since all conditions required the same movements in the axial plane, without a major horizontal component. In any case, pre-motor deficits should not differentially affect performance in the three conditions of the task, which differ mainly in perceptual aspects and require similar motor responses.

A further issue of interest that could not be addressed in the single case study by Halligan and Marshall (1991) is the effect of left hemianopia. Hemianopia may interact with neglect in determining perceptual asymmetries (Doricchi & Angelelli, 1999). Could this also apply to the ‘spatial compression’ task paradigm? The performance of patient P.P. (Halligan & Marshall, 1991) cannot settle the issue, because she had an association of neglect and hemianopia. To explore the effects of hemianopia on this task performance, we also tested patients either with isolated neglect or hemianopia, or with an association of these two disorders. Normal participants and right brain-damaged patients without either neglect or hemianopia also participated to the study as control groups.

Finally, we aimed to explore not only accuracy of performance, but also its variability. This is an important but often neglected aspect of the clinical performance and has relevance for both attentional and representational accounts. Left neglect patients may show not only decreased performance.
for left-sided targets, but also increased variability for detection of these targets (Anderson, Menneemeier, & Chatterjee, 2000). This may depend on the fact that left targets often, but not always, fail to capture patients’ attention (Bartolomeo, Siroff, Chokron, & Decaix, 2001). In the few cases, in which attentional capture is adequate, patients may provide relatively good responses to these targets. This results in increased variability of response for these targets. Also normal participants show increased variability when their attention is diverted from the targets, both in terms of accuracy of response (Prinzmetal, Amiri, Allen, & Edwards, 1998; Prinzmetal, Nwachuku, Bodanski, Blumenfeld, & Shima, 1997; Prinzmetal & Wilson, 1997) and of response time (Bartolomeo et al., 2001). Hence, increased variability of response again can be used to suggest that attention is being diverted from the current target. The finding of an increased variability of responses for left-sided targets in neglect patients may thus represent converging evidence for an attentional account of their performance on the spatial compression paradigm.

2. Methods

2.1. Participants

A total of 18 patients with unilateral lesions in the right hemisphere and eight age-matched controls consented to participate in the experiment. The presence and degree of neglect were evaluated using a test battery consisting of tasks of target cancellation, line bisection, and drawing copy (Bartolomeo & Chokron, 1999). Individual results are shown in Table 1. All patients were examined for visual field defects using the confrontation task, which was administered following a previously described procedure (Bartolomeo & Chokron, 1999; Gainotti et al., 1991). The patient was seated at a distance of about 1 m from the confronting examiner, and requested to fixate his or her gaze on the examiner’s nose. Once fixation was stable, the examiner, who held his or her arms outstretched, briefly moved his or her fingers either in one hemifield or in both hemifields simultaneously. Patients were asked to report each movement of the examiner’s fingers. In its basic form, the test consisted of six single unilateral stimuli (respectively delivered in left and right upper visual quadrants, left and right lower visual quadrants, and in left and right hemifields along the equatorial line) and six double simultaneous stimuli (two in the upper visual quadrants, two in the lower visual quadrants, and two on the equatorial line). The stimuli were displayed within the square. Each square contained a single 15 mm long and 1 mm thick black vertical arrow. The arrow was printed 5 mm from the square’s contour, either at its upper or bottom side, pointing to the opposite side. There were 12 possible positions of the arrow corresponding to a division of the side of the square into 12 equal intervals. The distance between intervals was 15 mm. The first position was 15 mm from the left side of the square’s contour. Consequently, there were 24 possible stimuli for each condition. 12 with the arrow at the upper side and 12 with the arrow at the bottom side of the square. In the “blank” condition, only the arrow was presented on the sheet. In the “lines” condition, the side of the square pointed at by the arrow was segmented at 5 mm intervals by 38 vertically-oriented black lines. The lines were 5 mm long and 1 mm thick. In the “numbers” condition each line was replaced by a single-digit number. Numbers were random and ranged between 1 and 9, with a different order for each arrow position. They were printed in 12-point Times New Roman style, bold type.

2.2. Stimuli

Two classes of targets and one without any stimuli were constructed, each corresponding to one of the three experimental conditions: (1) “numbers”, (2) “lines”, and (3) “blank” (see Fig. 1).

Participants were presented with a 195 mm × 195 mm white square centred on a horizontal A4 paper sheet. The contours of the square were black and 1 mm thick. All the stimuli were displayed within the square. Each square contained a single 15 mm long and 1 mm thick black vertical arrow. The arrow was printed 5 mm from the square’s contour, either at its upper or bottom side, pointing to the opposite side. There were 12 possible positions of the arrow corresponding to a division of the side of the square into 12 equal intervals. The distance between intervals was 15 mm. The first position was 15 mm from the left side of the square’s contour. Consequently, there were 24 possible stimuli for each condition. 12 with the arrow at the upper side and 12 with the arrow at the bottom side of the square. In the “blank” condition, only the arrow was presented on the sheet. In the “lines” condition, the side of the square pointed at by the arrow was segmented at 5 mm intervals by 38 vertically-oriented black lines. The lines were 5 mm long and 1 mm thick. In the “numbers” condition each line was replaced by a single-digit number. Numbers were random and ranged between 1 and 9, with a different order for each arrow position. They were printed in 12-point Times New Roman style, bold type.
Table 1
Demographical and clinical data for the four groups of patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender/age/education (years of schooling)</th>
<th>Days from lesion onset</th>
<th>Aetiology</th>
<th>Locus of lesion</th>
<th>Line bisection (% deviation)</th>
<th>Line cancellation (max 30/30)</th>
<th>Bells cancellation (max 15/15)</th>
<th>Letter cancellation (max 30/30)</th>
<th>Overlapping figures (max 10/10)</th>
<th>Landscape drawing (max 6)</th>
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</thead>
<tbody>
<tr>
<td>N+H− 1</td>
<td>F/72/14</td>
<td>107</td>
<td>Ischemic</td>
<td>Temporal parietal</td>
<td>+1.86 29/30 10/14^a</td>
<td>26/29 10/10 5.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N+H− 2</td>
<td>M/44/17</td>
<td>1470</td>
<td>Ischemic</td>
<td>Parietal</td>
<td>-13.46^a 29/30 13/12</td>
<td>30/28 10/10 5.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N+H− 3</td>
<td>F/32/14</td>
<td>110</td>
<td>Hemorrhagic</td>
<td>Internal capsule, basal ganglia</td>
<td>+6.26 30/30 11/15^a</td>
<td>27/28 10/10 6</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>N+H− 4</td>
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<td>Ischemic</td>
<td>Temporal parietal</td>
<td>+10.44 9/14^a 8/14^a</td>
<td>25/29 10/10 5</td>
<td></td>
<td></td>
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<tr>
<td>N+H− 5</td>
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<td>Temporal parietal</td>
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<td>Hemorrhagic</td>
<td>Basal ganglia, temporal occipital</td>
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<td>0/22 8/10 3</td>
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</tr>
<tr>
<td>N+H− 2</td>
<td>M/59/12</td>
<td>207</td>
<td>Ischemic</td>
<td>Occipital</td>
<td>+52.90^b 30/30 10/9</td>
<td>28/24 10/10 4</td>
<td></td>
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<tr>
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<td>127</td>
<td>Hematoma</td>
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<td>+32.71^c 0/19 0/8^c</td>
<td>6/26 6/10 2</td>
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<tr>
<td>N+H− 4</td>
<td>M/43/12</td>
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<td>Neoplastic</td>
<td>Temporal parietal</td>
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<td>27/30 10/10 5.5</td>
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<td></td>
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<tr>
<td>N+H− 5</td>
<td>M/52/14</td>
<td>137</td>
<td>Ischemic</td>
<td>Occipital</td>
<td>-6.03 26/30 0/13^a</td>
<td>13/28 9/10 3.5</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Performance on the neglect battery is also shown. –, Missing data. For line bisection, + indicates rightward deviation and − indicates leftward deviation. For cancellation tests, left/right correct responses are reported. The landscape drawing, consisting of a central house with two trees on each side, was scored by assigning two points to the house and one point to each tree completely copied. Footnotes (a–c) indicate pathological performance for standardised tests.

^a Left-right difference of omissions beyond the 95th percentile of normal performance (Rousseaux et al., 2001; test originally described in Gauthier, Dehaut, & Joanette, 1989).

^b Rightward deviation larger than 2S.D. from the mean performance of 30 normal individuals (Bartolomeo et al., 1994).

^c The same group of normal individuals never omitted more than one item on these tasks.
counterbalanced across participants. For each stimulus, participants were requested to mark with a fluorescent marker the position indicated by the arrow on the opposite side of the square. Before administering the experimental trials the experimenter ensured that each participant had understood the task instructions. To this end, each participant had three practice trials or more as needed. There was no time limit. In total, the whole task took 2–3 h (depending on individual participants), and this was often divided in two or three test sessions, separated by a maximum of 1 week interval. Participants examined in two sessions received three blocks per session; participants examined in three sessions received two blocks per session. Deviation from the target was measured in mm. To ensure a uniform measurement procedure across the different conditions, after the task was performed the sheet margin of the items for the blank condition was horizontally divided in 5 mm steps, corresponding to the locations of the targets in the other conditions. Deviation
was then measured to the nearest 5 mm division. Rightward deviations were given a plus sign and leftward deviations carried a minus sign.

3. Results

3.1. Accuracy

Controls performed the task accurately, with more than 97% of their performance being situated within 5 mm left or right of the target (mean ± 95% confidence interval, 0.01 ± 0.17 mm), thus indicating that the task was relatively easy to perform (see also Halligan & Marshall, 1991). A repeated-measures analysis of variance (ANOVA) was performed on the accuracy data with group (N-H−, N+H−, N-H+, N+H+ and controls) as between factor and condition (blank, lines, numbers), horizontal arrow position (1–12, from the left to the right), and vertical arrow position (up-pointing or down-pointing) as within factors. There was an effect of group, F(4, 21) = 19.77, P < 0.0001, because N+H+ and N+H− deviated rightward (by 5.56 and 1.37 mm on average, respectively), whereas the other groups shifted leftward of less than 1 mm on average. On post hoc tests (Fisher’s LSD), the N+H+ group differed from all the other groups (all, P < 0.0001); the N-+H− group differed only from the N-H− group, P = 0.018. Importantly, there was an effect of the condition, F(2, 42) = 24.75, P < 0.001, in the direction predicted by the attentional account; there was less rightward deviation in the blank condition than in the conditions with numbers or lines, P < 0.001; these two last conditions did not differ from each other. Again as predicted by the attentional account, the group and condition factors interacted, F(8, 42) = 9.17, P < 0.0001; only neglect patients (and especially those with neglect and hemianopia) deviated in conditions with visual targets (Fig. 2).

The relative horizontal position of the arrow influenced performance, F(11, 231) = 21.09, P < 0.0001, and interacted with the group, F(44, 231) = 11.19, P < 0.0001, with the condition, F(22, 462) = 2.56, P = 0.001, and with both group and condition, F(88, 462) = 1.61, P = 0.001. These interactions reflected the fact that neglect patients showed a gradient-shaped performance, with greater rightward deviation when the arrow was located more to the left (see Fig. 2), similar to that found in P.P.’s performance (Halligan & Marshall, 1991). The interactions again involved the task condition because the gradient was particularly evident in the conditions with visual targets. Although there was no influence of the vertical position of the arrow on overall performance, F < 1, this factor interacted with the group, F(4, 21) = 4.00, P = 0.01, with the horizontal position, F(11, 231) = 13.22, P < 0.001, and with both horizontal position and group, F(88, 462) = 2.72, P < 0.001. This came about because only brain-damaged patients, and not normal participants, showed a vertical-horizontal interaction (see below for a description of this interaction in neglect patients).

To follow up these results, separate ANOVAs were conducted on each of the two groups of neglect patients (with or without hemianopia). For N+H+ patients, the analysis confirmed that the conditions with visual targets evoked more rightward deviation than that without targets, F(2, 8) = 25.88, P = 0.0003 (blank versus lines or numbers, P < 0.0005; lines versus numbers, ns). The deviation varied with the horizontal position of the arrow, F(11, 44) = 26.70, P < 0.0001, because it was maximal with the arrow on the left side and decreased gradually with more rightward positions (see Fig. 2E). This effect interacted with the condition, F(22, 88) = 2.86, P = 0.0003, because it was most evident in the conditions with visual targets. The vertical position of the arrow interacted with the horizontal position, F(11, 44) = 4.80, P < 0.0001, because down-pointing arrows evoked gradients with steeper slopes than up-pointing arrows. Linear models provided an adequate description of data from the conditions with visual targets, as shown by regression analyses with the objective horizontal position as independent variable and the deviation from the target as dependent variable, which explained from 39 to 97% of the total variance, F(1, 11) > 6.33, all P < 0.05.

Despite the fact that N+H− patients showed a lesser rightward deviation than N+H+ patients (see Fig. 2), they presented a qualitatively similar pattern of effects and interactions. The presence of visual targets increased the shift, F(2, 4) = 4.93, P = 0.04 (although on paired comparisons the blank versus lines contrast only approached significance, P = 0.0676; blank versus numbers, P = 0.015; lines versus numbers, ns). The horizontal location of the arrow again affected performance, F(11, 44) = 7.57, P < 0.0001, and interacted with the vertical position, F(11, 44) = 6.96, P < 0.0001, because down-pointing arrows were associated with gradients of performance with steeper slopes than up-pointing arrows.

In contrast to the generally negative slopes observed for neglect patients, which reflected a gradient of performance similar to that shown by P.P. (Halligan & Marshall, 1991), the other groups of participants usually showed positive slopes when their errors were regressed on the horizontal position of the arrow. In descriptive terms, the non-neglect participants usually showed positive slopes (except for the leftmost position), and tended to become more and more accurate as the arrow moved towards the right (see Fig. 2A–C). However, with a few exceptions, for the non-neglect groups, linear models accounted for less than 33% of the variance, F(1, 11) < 4.80, ns.

3.2. Variability

We calculated the within-subjects S.D. for each position of the arrow and conducted a repeated-measures ANOVA on these data with group (N-H−, N+H−, N+H+, N+H+)...
Fig. 2. (A–E) Performance of the different groups of participants as a function of task condition and horizontal arrow position. Error bars: 1 S.E.
Fig. 2. (Continued)
N−H+ and controls) as between factor and condition (numbers, lines, blank), horizontal position (1–12), and vertical position (up-pointing, down-pointing) as within factors. Average S.D.s for each group were as follows: controls, 1.78 mm; N−H−, 2.48 mm; N−H+, 1.47 mm; N+H−, 3.87 mm; N+H+, 4.47 mm. There was an effect of the group, $F(4, 21) = 16.85$, $P < 0.001$, because neglect patients had more variable performance than each of the other groups (Fisher’s PLSD, all $P < 0.01$); no difference in variability emerged between neglect patients with or without hemianopia. The horizontal position of the arrow influenced variability of performance, $F(11, 231) = 45.88$, $P < 0.0001$, because there was progressively less variability with targets presented from the left to the right side. This was only true for neglect patients, which resulted in an interaction with the group factor, $F(44, 231) = 8.91$, $P < 0.0001$. The task condition had no effect on overall variability, $F < 1$, but interacted with the vertical position of the arrow, $F(2, 42) = 27.84$, $P = 0.005$, and with both the vertical and the horizontal positions, $F(22, 462) = 5.54$, $P = 0.04$. These interactions originated from a particularly high variability of performance for numbers presented at the bottom-left part of the sheet.

Regression analyses showed that variability of performance decreased monotonically from the left to the right only for the N+H+ group, and then only on the conditions with visual targets.

4. Discussion

This study was inspired by the results reported in a single case study by Halligan and Marshall (1991), where the findings were used to support the case that a systematic compression of space was responsible for the patients’ neglect. These authors found that their patient with left-sided neglect and hemianopia deviated significantly rightward when she was required to indicate the number of a horizontal array which has been designated by a vertical arrow located on the opposite side of the display. The main aims of the current study were to confirm and replicate the original findings in a large group study and establish whether the original account could be explained by attentional deficits. We confirmed a rightward deviation similar to that described by Halligan and Marshall (1991), i.e. a lateral gradient of performance with decreasing rightward deviation from the left to the right side of the display. Significantly, however, the rightward shift was present only when the target had to be selected from among other physical candidates (lines or numbers). Patients with left neglect and hemianopia demonstrated the most severe rightward shift, whereas neglect patients without hemianopia showed milder deviations. Thus, it appears that the pattern of results can be best predicted by a hypothesis that assumes a biased orienting of attention.
On this attentional account, the patients deviate rightward in conditions with visible targets because items on the right side of the target attract their attention, and as such present as the more plausible candidate for response. The alternative hypotheses mentioned in the introduction, such as failure to properly represent left-sided space or directional motor deficits, fail to fully capture the crucial difference between target-present and target-absent conditions. A directional motor deficit affecting the right arm could be consistent with the present results if it was hypothesised that only leftward movements aimed at left-sided visual targets would be compromised by the putative deficit and not left-directed movements per se. Although such a possibility has been suggested (Mattingley, Husain, Rorden, Kennard, 1998) it does not seem to correspond to the original definition of limb directional hypokinesia as a problem related to movement direction (Heilman et al., 1985). Note, moreover, that such an account would have left unexplained the performance of patient P.P. in the original study by Halligan and Marshall (1991), where the task was to verbally identify a visual target, without the need of producing any arm movement. A further possibility could be that, when performing the present task, neglect patients' gaze drifted rightward when moving from one horizontal side of the sheet to the other. Neglect patients are indeed prone to orient their gaze towards ipsilesional visual targets (Gainotti et al., 1991). However, this possibility would not be inconsistent with the attentional account, because gaze shifts are usually preceded by analogous shifts in spatial attention (Hoffman & Subramaniam, 1995; Kowler, Anderson, Dosher, & Blaser, 1995; Shepherd, Findlay, & Hockey, 1986). Thus, a rightward ocular drift might well have resulted from patients' attention being attracted by rightward targets. Our crucial result that no deviation was present in the absence of visible targets seems inconsistent with any account based on a purely directional bias of gaze shifts, such as, for example, the possibility that patients produced hypometric leftward saccades (Butter, Rapcsak, Watson, & Heilman, 1988).

The interaction between the horizontal and the vertical positions of the arrow, with top arrows pointing to bottom targets that engendered steeper gradients of performance than the opposite assignment, is more difficult to interpret. It is, however, broadly consistent with the performance of patient P.P. (Halligan & Marshall, 1991), who presented slightly steeper slopes with bottom targets than with top targets. The steeper slopes that we observed with down-pointing arrows reflect more rightward deviation for left-bottom targets than for left-top targets. This is reminiscent of the fact that in cancellation tasks, neglect patients often omit more targets in the left-inferior quadrant than in the left-superior quadrant (Chatterjee, Thompson, & Ricci, 1999; Halligan & Marshall, 1991; Mark & Heilman, 1997). This radial asymmetry of performance may represent a lesional correlate of a possible specialisation of the parietal lobe for operations directed in near and lower space (Previc, 1990).

Our results on accuracy of response were paralleled by analogous findings when variability of response was used as a dependent variable. In patients with neglect and hemianopia, we found a gradient of variability of response, with maximal variability for left-sided targets and a gradual decrease toward the right. An analogous gradient was observed in response time studies with neglect patients (Anderson et al., 2000). Increased variability of response is often observed when attention tends to be diverted from the target (Bartolomeo et al., 2001; Prinzmetal et al., 1997, 1998, 1999; Prinzmetal & Wilson, 1997). A possible explanation of this effect relies on the probabilistic nature of attentional orienting. If left neglect patients tend to orient their attention rightward, left targets will often, but not always, fail to capture patients' attention. This will result in normal or near-normal performance on those rare trials in which a left target does capture patients' attention. The coexistence of relatively accurate performance for attended left targets with impaired performance for non-attended left targets could engender the observed space-based variability in neglect. Thus, the present results on variability of performance are again consistent with the hypothesis that patients' attention was biased towards the right side when they performed the spatial compression task.

There is compelling evidence for the important role that right visual stimuli can make in exacerbating neglect behaviour (Chokron, Colliot, & Bartolomeo, in press; De Renzi, Gentilini, Faglioni, & Barbieri, 1989; Gainotti et al., 1991; Kinsbourne, 1993; Marshall & Halligan, 1989). Mark et al. (1998) required neglect patients to draw on targets scattered on a sheet with a pencil mark or to erase them, found more left omission in the 'draw' than in the 'erase' condition, and concluded that right-sided (cancelled) targets continued to attract patients' attention, thereby increasing left neglect. In a Posner-type reaction time paradigm (see Posner, Walker, Friedrich, & Rafal, 1984), D'Erme, Robertson, Bartolomeo, Daniele, and Gainotti (1992) found slower responses to left-sided targets when targets occurred in one of two bilateral boxes than when they occurred without boxes, as if the right-sided box again attracted patient's attention. Bartolomeo, D'Erme, and Gainotti (1994) explored visual neglect and imaginal neglect (i.e. neglect during description from memory of known places, see Bisiochi & Luzzatti, 1978) in the same patients and found that neglect was more frequent and severe in the visual than in the imaginal domain. Again, it is possible that right-sided visual targets attracted patients' attention in the visual condition, but not in the imaginal condition. Our results are consistent with these earlier proposals, and also help extend these by showing that rightward bias after left neglect may be sufficiently powerful to influence perceptual judgements tasks (radial imagined extension of an arrow) that do not explicitly involve lateral exploration of space.

In the present study, we confirmed Halligan and Marshall's (1991) observation of a spatial gradient of response; in neglect patients, the more leftward the arrow, the...
more rightward-deviated the response. This gradient could result from the fact that the more leftward the stimulus arrow was (relative to the centre of the page), the greater the number of potential stimulus items were on the right of the target. This would increase the possibility of choosing one of these right distracters.

Our finding that the rightward deviation was more severe in patients with both neglect and hemianopia than in patients with neglect alone, is again consistent with previous observations reporting analogous differences in performance with other experimental paradigms (Daini, Angelelli, Antonucci, Cappa, & Vallar, 2002; D’Erme, De Bonis, & Giannotti, 1987; Doricchi & Angelelli, 1999). If the chosen target in our task was the result of competition between other potential targets, and this competition was attentionally rightward-biased due to neglect, then the co-presence of a left hemianopia might be expected to reinforce this rightward shift by completely suppressing the contribution of items to the left of fixation. An attentional component seems nonetheless necessary to produce much of the observed biased performance: patients with hemianopia but without neglect did not show any consistent deviation on our task. In patients with neglect and hemianopia, left neglect was often more severe than in patients with neglect alone (see Table 1), perhaps because N+H+ patients were more likely to have larger lesions than N-H- patients. This raises the possibility that the pattern of results obtained were in fact determined by the severity of neglect alone, with more severe patients deviating more than milder patients, rather than by the association of neglect plus hemianopia. Although the present results cannot be regarded as conclusive concerning this possibility, the performance of a patient in the N+H+ group argues against this interpretation. Patient 4 had only mild signs of neglect in association with left hemianopia (see Table 1), but showed a substantial rightward deviation in the lines and numbers conditions (6.05 and 5.13 mm on average, respectively), suggesting that it was the association of neglect and hemianopia, and not the extent of neglect, that was responsible for the increased shift.

The detrimental effect of hemianopia in neglect patients’ performance on the present task is reminiscent of the similar effect of visual field defect on line bisection, a widely used diagnostic test for neglect. Despite some negative results (Halligan, Marshall, & Wade, 1990), and the fact that patients with visual field defects reliably produce a contralateral bias on line bisection (Burt & Black, 1998; Fuchs, 1920), it has been repeatedly shown that patients with neglect and hemianopia show a greater rightward deviation on line bisection than patients with neglect only (Daini et al., 2002; D’Erme et al., 1987; Doricchi & Angelelli, 1999). Our finding that the presence of non-relevant (right-sided) target stimuli may produce a rightward bias in perceptual judgements suggests a possible shared account for this pattern of performance with line bisection. In line bisection, it has been hypothesised that the subjective midpoint is treated as a virtual target (Halligan & Marshall, 1998), chosen from several possible candidates (other points of the line), on the basis of the relative salience of the two segments. Under the influence of left neglect, this perceptual decision is biased to the right and this pathological bias may be responsible for the present results on our compression task. The presence of a concurrent left hemianopia would therefore increase the likelihood that left-sided targets would be not be chosen, all of which would contribute to a performance reflecting a greater rightward bias of attention.1

Our results also suggest the need to reappraise other findings previously ascribed to the operations of purely representational mechanisms. For example, Ricci, Callhoun, & Chatterjee (2000) recently argued that a limitation in patients’ ability to represent horizontal magnitudes determines the length effect in line bisection (that is, the fact that left neglect patients bisect longer lines further to the right than shorter lines), and denied that this effect could result from an attentional bias (longer lines extend further ipsilaterally and thus shift patients’ attention rightward to a greater extent than shorter lines). Ricci et al. took ingeniously advantage of the Oppel-Kundt illusion, which makes normal subjects perceive as longer lines made of several short segments, compared with lines of equal physical length, but made of a lesser number of longer segments. They constructed two classes of 200 mm long lines, either made of shorter or of longer segments. When three left neglect patients were asked to bisect these lines, their rightward error was greater for the lines made of shorter segments than for the lines made of longer segments. Because the physical length of the lines was the same, the authors concluded that patients’ performance was determined by their (illusory) internal representation of the lines, and cannot be explained by attentional mechanisms directed to the external stimulus. However, our present results suggest that an attentional account is both possible and likely. Despite the instructions to “treat the stimuli as if they were solid lines” (p. 674), Ricci et al.’s patients in fact saw a horizontal row of discrete segments. If an attentional bias favouring right-sided objects and penalising left-sided stimuli is at work in neglect, then right-sided segments were likely to attract patients’ attention. In keeping with our present results, attentional bias could have influenced patients’ perceptual judgement about the centre of the lines, for example by pushing rightward the candidate segment or the interval between segments to be chosen to mark the transaction. If so, increasing the number of segments (as in the illusory ‘longer’ lines) would increase the number of right-sided ‘attractors’, thus increasing the probability of making a greater rightward error in bisection.

1 Interestingly, computational models of line bisection also suggest an important role of competition between portions of the line in shaping normal and pathological performance on this task (Anderson, 1996; Mousser, Halligan, & Marshall, 1997).
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of this reduction remain to be spell out. Our results indicate that currently available models of selective attention, with their emphasis on competition for selection (Desimone & Duncan, 1995), may provisionally offer a suitable framework to interpret significant aspects of neglect patients’ behaviour.


Direct Evidence for a Parietal-Frontal Pathway Subserving Spatial Awareness in Humans

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Intraoperative electrical stimulation, which temporarily inactivates restricted regions during brain surgery, can map cognitive functions in humans with spatiotemporal resolution unmatched by other methods. Using this technique, we found that stimulation of the right inferior parietal lobule or the caudal superior temporal gyrus, but not of its rostral portion, determined rightward deviations on line bisection. However, the strongest shifts occurred with subcortical stimulation. Fiber tracking identified the stimulated site as a section of the superior occipitofrontal fasciculus, a poorly known parietal-frontal pathway. These findings suggest that parietal-frontal communication is necessary for the symmetrical processing of the visual scene.

Left unilateral neglect is a neurological condition resulting from right hemisphere damage (1, 2). Neglect patients ignore left-sided events in everyday life (3) and have a poor functional outcome. They typically bisect horizontal lines to the right of the true center (2, 4), perhaps because they perceive the left half of the line as being shorter or less salient than the right half (5, 6). The study of unilateral neglect is important if we are to understand the mechanisms of spatial cognition, but its anatomical correlates are controversial. Most studies implicate the inferior parietal lobule (IPL) (7, 8), consistent with the known role of posterior parietal cortex in spatial attention (9, 10) and perceptual salience (11). Others implicate the rostral superior temporal gyrus (rSTG) (12), suggesting a segregation of spatial awareness in the ventral cortical visual stream (13, 14). The underlying subcortical association circuits have received less attention (15).

We used intraoperative direct electrical stimulation (16) to study line bisection performance. During brain surgery for tumor resection, it is common clinical practice to awaken patients in order to assess the functional role of restricted brain regions (the brain has no receptors for pain), so that the surgeon can maximize the extent of the excision without provoking cognitive impairment. Patients perform cognitive tasks, such as counting or figure naming, while the surgeon temporarily inactivates restricted regions (~5 mm) around the tumor by means of electrical stimuli (16). If the patient stops talking or produces incorrect responses, the surgeon avoids removing the stimulated region.

CAL, a 27-year-old woman, and SB, a 28-year-old man, both left-handed, underwent surgical resection of a low-grade glioma (WHO II). In CAL, the glioma was centered on the caudal part of the right temporal lobe (17). CAL showed a rightward deviation upon stimulation of two cortical sites: the supramarginal gyrus (SMG, the rostral subdivision of the IPL) and the caudal portion of the superior temporal gyrus (cSTG) (Fig. 1) (table S2). There was no deviation during stimulation of the rSTG or of the frontal eye field.

In SB, the glioma was centered on the right inferior parietal lobule (17). SB showed a rightward deviation remarkably identical in amplitude to that shown by CAL (Fig. 2) (table S2) upon stimulation of the SMG. SB also deviated rightward during cSTG stimulation, again consistent with CAL’s performance. Stimulation of other neighboring areas (“control 1” in Fig. 2B) did not determine pathological shifts. During tumor resection, subcortical regions on the floor of the surgical cavity were stimulated.

SB showed a large rightward deviation upon stimulation of the restricted region labeled as 42 in Fig. 2A, but not of neighboring cortical or subcortical areas (“control 2” in Fig. 2B). Stimulation of region 42 was repeated after additional excision of the surgical cavity, causing even greater deviations (“control 3” in Fig. 2B). SB showed no signs of neglect (table S1).

Using diffusion tensor magnetic resonance tractography (18) on postoperative magnetic resonance imaging (MRI) scans and diffusion tensor imaging (DTI) scans, we were able to precisely map the course of long association fibers in the white matter of this patient (19). The region labeled as 42 in Fig. 2A, whose inactivation had produced the maximal rightward shifts on line bisection, corresponded exactly to a portion of the superior occipitofrontal fasciculus (18, 20) that connects the parietal to the frontal lobe (21) (Figs. 2, C and D) (figs. S1 and S2). The stimulated region was both distinct and remote from other corticocortical pathways, such as the optic radiations or the parietal-temporal connections.

Our findings demonstrate that the SMG, the cSTG, and a poorly known parietal-frontal pathway, the superior occipitofrontal fasciculus (18, 20), but not the rSTG, are critical to the symmetrical processing of the visual scene in humans (22). These results provide evidence relevant to the debate about the lesion correlates of neglect, based until now on the relatively imprecise lesion-overlapping methods in stroke patients, and support the proposal that damage to the temporal-parietal junction (7, 8, 23) and the underlying white matter (15) is a crucial antecedent of left neglect. As a consequence, there is no need to postulate a segregation of spatial awareness, specific to humans, in the rostral part of the right STG (14).

We observed the maximal deviation upon inactivation of the superior occipitofrontal fasciculus in the depth of the IPL. This result specifies the precise anatomical locus of the parietal-frontal pathway in which neglect

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Materials and Methods
Figs. S1 to S3

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Fig. 1. Performance of patient CAL. (A) The surgical field. (B) Mean deviation (in millimeters) with 95% confidence intervals during stimulation of the rostral part of the superior temporal gyrus (rSTG, label A; \( n = 4 \)), of the caudal part of the STG (cSTG, label B; \( n = 2 \)), of the supramarginal gyrus (SMG, label 50; \( n = 4 \)), of the frontal eye field (FEF, label F; \( n = 5 \)), and of control neighboring regions (superior frontal gyrus, medial frontal gyrus, precentral gyrus, postcentral gyrus, and tumor, \( n = 16 \)). *\( P < 0.05 \) (two-tailed) as compared to controls’ performance (32). (C) Three-dimensional reconstruction of the tumor mass (in purple) and of the stimulated regions (in yellow). (D) Lateral view.

Fig. 2. Performance of patient SB. (A) The surgical field. (B) Mean deviation (in millimeters) with 95% confidence intervals during stimulation of the caudal part of the STG (cSTG, label 31; \( n = 6 \)), of the supramarginal gyrus (SMG, label 30; \( n = 4 \)), of the superior occipitofrontal fasciculus (label 42) during (O-FF 1; \( n = 4 \)) and after tumor resection (O-FF 2, \( n = 4 \)), and of control neighboring regions (postcentral gyrus, lateral occipital gyri, and tumor) before resection (control 1, \( n = 27 \)), during resection (control 2, \( n = 38 \)), and after resection (control 3, \( n = 12 \)). Performance 5 days after surgery is also shown (day +5). *\( P < 0.05 \), **\( P < 0.01 \) (both two-tailed) as compared to controls’ performance (32). (C) Three-dimensional reconstruction of the surgical resection (in red) and of the stimulated regions (in yellow), showing their relationships with the superior occipitofrontal fasciculus (in yellow) and the superior longitudinal fasciculus (in blue) (18). The head of the caudate nucleus and the putamen are shown in green. (D) Lateral view.
patients’ lesions overlap (15). Our findings are similar to those obtained in nonhuman primates. Monkeys showed persistent signs of neglect after unilateral section of the white matter between the fundus of the intraparietal sulcus and the lateral ventricle (24). The greater effect of subcortical inactivation, as compared to cortical inactivation, is consistent with the idea that symmetrical space processing requires the integrity of a parietal-frontal network (1, 15). Damage to restricted regions of the white matter can cause the dysfunction of large-scale neurocognitive networks. According to an influential model (1), signs of left neglect result from impairment of a right-hemisphere network, including prefrontal, parietal, and cingulate components. The parietal component of the network could be especially important for the perceptual salience of extra-personal objects, whereas the frontal component might be implicated in the production of an appropriate response to behaviorally relevant stimuli (1), in the online retention of spatial information (1, 25), or in the focusing of attention on salient items through reciprocal connections to more posterior regions (20).

Models of line bisection postulate a competition between the relative salience of the two lateral segments (6). The bisection mark is drawn at the point of subjective equality between the two segments (5). Bisection-related tasks activate the IPL in humans (26). Transcranial magnetic stimulation over the right posterior parietal cortex, but not over the STG, was found to bias the comparison of the lengths of the component segments of pretransected lines in a direction coherent with rightward shifts in line bisection (27). In the monkey, regions adjacent to the intraparietal sulcus, such as the lateral intraparietal area, are related to visual perceptual salience (11) and can reinforce the stimulus attentional priority (10). Parietal inactivation may thus bias the perceptual decision by modulating the salience of the line segments (6).

The assessment of spatial cognition during intraoperative stimulation offers the double opportunity of preserving spatial processing functions during brain surgery and of pinpointing the neurocognitive systems devoted to spatial processing in humans. Spatial awareness is dependent not only on the cortical areas of the temporal-parietal junction, but also on a larger parietal-frontal network communicating via the superior occipitofrontal fasciculus.

References and Notes

17. C. Rorden and J. B. Pochon, L. Thivard, and the staff of BrainVISA.
19. The neurorosurgeon stopped the resection after stimulation of the region labeled as 42 (Fig. 2A). As a consequence, region 42 corresponded to the deepest point on the floor of the rostral-superior part of the surgical cavity, and was thus easily identified on postoperative anatomical MRI scans. The white matter tract underlying region 42 was identified by overlapping the MRI scans with the DTI scans (fig. S1) (Fig. 2 C and D).
21. The superior occipitofrontal fasciculus is a poorly known long association pathway. It terminates rostrally in the lateral prefrontal cortex of the inferior and middle frontal gyrus (18). Its caudal terminations are less known (18, 30), but despite its name, derived from early descriptions (31), the superior occipitofrontal fasciculus seems to terminate caudally in the superior parietal gyrus (18) in the intraparietal sulcus (30), p. 367.
22. We used line bisection because it is an easy task for patients to perform and allows repeated assessments in the time scale required by intraoperative testing. Bisection of centrally presented 20-cm lines correlates positively and significantly with cancellation tests and is a good predictor of clinical neglect as assessed by standardized scales (2, 28).
28. See supporting data on Science Online.
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Supporting Online Material

www.sciencemag.org/cgi/content/full/309/5744/2226/DC1
Materials and Methods
SOM Text
Tables S1 and S2
Figs. S1 and S2
References

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Breakdown of Cortical Effective Connectivity During Sleep

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When we fall asleep, consciousness fades yet the brain remains active. Why is this so? To investigate whether changes in cortical information transmission play a role, we used transcranial magnetic stimulation together with high-density electroencephalography and asked how the activation of one cortical area (the premotor area) is transmitted to the rest of the brain. During quiet wakefulness, an initial response (~15 milliseconds) at the stimulation site was followed by a sequence of waves that moved to connected cortical areas several centimeters away. During non–rapid eye movement sleep, the initial response was stronger but was rapidly extinguished and did not propagate beyond the stimulation site. Thus, the fading of consciousness during certain stages of sleep may be related to a breakdown in cortical effective connectivity.

When awoken early in the night from non–rapid eye movement (NREM) sleep, people often report little or no conscious experience (1). It was first thought that this fading of consciousness was due to the brain shutting down. However, although brain metabolism is re-
Supporting Online Material for

Direct Evidence for a Parietal-Frontal Pathway Subserving Spatial Awareness in Humans

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This PDF file includes:

Materials and Methods
Tables S1 and S2
Figs. S1 and S2
References
Supporting Online Material

Participants. CAL and SB attended clinical observation because of epileptic seizures. They showed no abnormality on pre-operative neurological and neuropsychological examination. In particular, there were no signs of neglect on paper-and-pencil tests (S1) (see Table S1). Eight healthy left-handed subjects (mean age, 31 years; SD, 5.3, range 26-38) served as controls. They performed 30 line bisections each, with the same test material and in a similar body position as the patients.

Surgical procedure. Patients were placed in a semidecubitus position on their left side and used their left, dominant hand to perform line bisection tasks. Intraoperative cortico-subcortical mapping was performed under local anesthesia using the technique of direct intraoperative electrical stimulation (S2). A bipolar electrode with 5-mm spaced tips delivering a biphasic current with parameters non-deleterious for the CNS (pulse frequency of 60 Hz, single pulse phase duration of 1 ms, amplitude from 2 to 8 mA) was applied to the brain of awake patients. In addition to line bisection, sensori-motor and language functions were assessed (counting and naming). In order to perform a successful tumour removal while sparing functional areas, all resections were pursued until functional pathways were encountered around the surgical cavity, then these were followed according to functional boundaries. These procedures allow the surgeon to minimize the residual morbidity while increasing the quality of the resection, and thereby to improve patient survival by minimizing the anaplastic transformation of low-grade gliomas (S2).

Line bisection task. Twenty-cm long, 1-mm thick black lines were centered on a horizontal A4 sheet (one line per sheet) (S3, S4), and presented aligned to the subjects’ eye-axis, in central position with respect to the patient’s sagittal head plane. Subjects were instructed to mark with a pencil the center of each line. Patients and examiners were blind concerning the stimulated sites. One examiner said “go” just before presenting each line, upon which the surgeon immediately started the stimulation. After each bisection, another examiner assessed the accuracy of the
bisection mark by overlapping the test sheet with a transparency indicating 5% and 10% deviations. When a deviation greater than 5% occurred, the examiner said “yes”, and the neurosurgeon put a numbered label on the stimulated area. Patients kept bisecting lines without further stimulation until their performance reverted to normality. During the surgical intervention, CAL performed a total of 31 line bisections; SB performed 106 line bisections.

**Data analysis.** For each trial, we calculated the deviation in mm from the true center of the line, with leftward errors scored as negative deviations and rightward errors scored as positive deviations. Patients’ bisection performance for each stimulated site was compared to controls’ using a significance test for comparing an individual case with small control samples ($S5$).

**Diffusion tensor analysis.** Diffusion tensor imaging (DTI) was performed using echo-planar imaging at 1.5 T (General Electric) with standard head coil for signal reception. DTI axial slices were obtained using the following parameters: repetition time, 10s; echo time, 88ms; flip angle, 90°; matrix, 128 × 128; field of view; 380 × 380mm², slice thickness, 3mm; no gap (3mm isotropic voxels); acquisition time, 320s. Four averages were used with signal averaging in the scanner buffer. Diffusion weighting was performed along six independent directions, with a b-value of 900 s/mm². High-resolution 3-D anatomical images were used for display and anatomical localization (110 axial contiguous inversion recovery three dimensional fast SPGR images, 1.5mm thick; TI, 400ms; FOV, 240 × 240mm²; matrix size, 256 × 256). BrainVisa, a software platform for visualization and analysis of multi-modality brain data (http://brainvisa.info/), was used to visualize the anisotropy data, define the regions of interest, track fibres and register T1-weighted MRI with DTI.
Supplementary discussion. It has been claimed (S6) that line bisection is not a specific task for neglect, because neglect patients (as assessed by cancellation tests) would often perform normally on this task. In this study (S6), however, the lines were presented with their right extremity aligned with the right margin of the sheet. This procedure likely resulted in an underestimation of pathological performance on line bisection, because it is well known that displacing the lines towards the right side decreases patients' rightward errors (S7). Dissociations between line bisection and cancellation tests may occur (S8), and suggest that these tasks recruit different processes or strategies, depending perhaps on the different number of objects that compete for attention, e.g. two segments meeting in an imaginary midpoint target for line bisection, or several physical targets for target cancellation. However, in a study (S3) with greater statistical power, which employed centrally placed, 20-cm lines, line bisection performance correlated positively and significantly with cancellation tests and clinical scales of neglect. Thus, in conditions similar to those of the present study, line bisection performance did capture significant aspects of neglect behavior.
<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender / Age</th>
<th>Time between test and surgery</th>
<th>Line Bisection % deviation</th>
<th>Line cancellation max 30 / 30</th>
<th>Bells cancellation max 15 / 15</th>
<th>Letter cancellation max 30 / 30</th>
<th>Overlapping figures max 10 / 10</th>
<th>Landscape drawing max 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAL</td>
<td>F / 27 / 12</td>
<td>Day before surgery</td>
<td>0.00</td>
<td>30 / 30</td>
<td>15 / 15</td>
<td>30 / 29</td>
<td>10 / 10</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>114 days after surgery</td>
<td>-1.63</td>
<td>30 / 30</td>
<td>14 / 15</td>
<td>29 / 30</td>
<td>10 / 10</td>
<td>6</td>
</tr>
<tr>
<td>SB</td>
<td>M / 29 / 12</td>
<td>Day before surgery</td>
<td>+0.04</td>
<td>30 / 30</td>
<td>15 / 14</td>
<td>30 / 30</td>
<td>10 / 10</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 days after surgery</td>
<td>-1.00</td>
<td>28 / 25</td>
<td>13 / 12</td>
<td>28 / 29</td>
<td>10 / 10</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>51 days after surgery</td>
<td>-0.03</td>
<td>30 / 30</td>
<td>14 / 15</td>
<td>29 / 30</td>
<td>10 / 10</td>
<td>6</td>
</tr>
</tbody>
</table>
See (SI) for detailed test description. For line bisection, + indicates rightward deviation and - indicates leftward deviation. For the cancellation tests and the overlapping figures test, left / right correct responses are reported. The landscape drawing, consisting of a central house with two trees on each side, was scored by assigning 2 points to the house and 1 point to each tree completely copied.
Table S2. Intraoperative bisection task: Talairach coordinates (S9) of the stimulated sites and patients’ performance

<table>
<thead>
<tr>
<th>Patient</th>
<th>Talairach coordinates</th>
<th>Anatomical area*</th>
<th>Mean deviation (mm)**</th>
<th>SD (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X y z</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAL</td>
<td>60 22 -15</td>
<td>rSTG</td>
<td>+1.50</td>
<td>1.29</td>
</tr>
<tr>
<td></td>
<td>71 -21 13</td>
<td>cSTG</td>
<td>+6.50</td>
<td>2.12</td>
</tr>
<tr>
<td></td>
<td>70 -22 32</td>
<td>SMG</td>
<td>+6.25</td>
<td>2.22</td>
</tr>
<tr>
<td></td>
<td>17 2 75</td>
<td>FEF</td>
<td>-0.80</td>
<td>1.92</td>
</tr>
<tr>
<td>SB</td>
<td>71 -23 15</td>
<td>cSTG</td>
<td>+8.83</td>
<td>1.86</td>
</tr>
<tr>
<td></td>
<td>67 -40 37</td>
<td>SMG</td>
<td>+6.25</td>
<td>0.96</td>
</tr>
<tr>
<td></td>
<td>39 -52 39</td>
<td>O-FF1</td>
<td>+26.13</td>
<td>1.41</td>
</tr>
<tr>
<td></td>
<td></td>
<td>O-FF2</td>
<td>+40.25</td>
<td>11.62</td>
</tr>
</tbody>
</table>

*rSTG, rostral superior temporal gyrus; cSTG, caudal superior temporal gyrus; SMG, supramarginal gyrus; FEF, frontal eye field; O-FF, superior occipito-frontal fasciculus

** + indicates rightward deviation and - indicates leftward deviation.
Fig. S1. Orientation colored coding of the post-operative DTI maps for patient SB, illustrated on axial slices. Fiber directions of the right-left, rostral-caudal, and superior-inferior orientations were coded in red, green, and blue, respectively. The orange circle corresponds to region 42 in Fig. 2A.
Fig. S2. Additional 3D reconstructions of the superior occipito-frontal fasciculus (in yellow) and of the superior longitudinal fasciculus (in blue) for patient SB. The orange circle corresponds to region 42 in Fig. 2A.
References and Notes

“Can” happen, Haidt fails to mention that the overwhelming conviction among evolutionary theorists remains that they are most unlikely, since the selection differential between groups would have to exceed the cost differential experienced by self-sacrificing individuals within groups.

By a rhetorical sleight of hand, after describing D. S. Wilson’s group-selection hypothesis for the evolution of religion, Haidt then announces—as though it were fact—that “group selection greatly increased cooperation within the group” (p. 1001). This is pure speculation, not fact, and highly controversial, contrarian speculation at that.

In another case of substituting opinion for reality, Haidt proposes his “Principle 4,” arguing for the biological legitimacy of “patriotism, respect for tradition, and a sense of sacredness” (p. 1001). Perhaps, in the future, these supposed components of morality will be found to have genuine evolutionary underpinnings, but for now they seem closer to a political platform plank for the religious right; psychologists interested in achieving a new synthesis by applying evolutionary biology to human morality should bear in mind that just because these notions appeared in a Science Review does not make them genuine science.

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Response
BARASH IS CORRECT THAT A SURVEY OF ALL evolutionary theorists would show a great deal of skepticism about group selection. That consensus, however, was forged in the 1960s and 1970s on the basis of some simplifying assumptions, most notably that phenotypes are determined solely by genotypes and that culture can be ignored. Models incorporating these assumptions showed that selection pressures operating at the individual level were almost always stronger than selection pressures operating at the group level, leading to the conclusion that genes for apparently altruistic traits can only spread if those genes are in fact “selfish” (1) via one of the two mechanisms of kin selection or reciprocal altruism.

But evolutionary models have become more realistic in recent years. Phenotypes (e.g., cooperators or defectors) can now be modeled as joint products of genes, cultural learning, and culturally altered payoff matrices. When culture is included, the old consensus must be reexamined. The time frame shrinks from millennia to years (or less) as groups find culturally innovative ways to police themselves, to increase their phenotypic homogeneity, to lower the costs of prosocial action, and to increase the size of the pie they then share. Just look at eBay: Its genius was to make the prosocial behaviors of gossip and punishment nearly costless through its feedback systems. The eBay community is an emergent group that wiped out many other auction-related groups, without malice or genetic change. If we limit our survey of evolutionary theorists to those who study humans as cultural creatures and who allow for the bidirectional interplay of genetic and cultural evolution, we find the opposite of Barash’s view: Most such theorists believe that cultural group selection has occurred and is occurring, and that such selection might well have shaped human genes whenever culturally altered selection pressures remained constant locally over many centuries. In writing my Review, I ignored the old consensus and drew instead on the new and exciting work of leading theorists such as Richerson and Boyd (2), Boehm (3), Fehr (4), Henrich (5), Maynard Smith (6), and Wilson (7), all of whom believe that natural selection works at multiple levels, including the group level. As for Barash’s final point about conservative morality, I do not believe that descriptive biology confirms normative legitimacy. In my Review, I identified some areas of moral life that are highly elaborated in most cultures, but that are disliked by political liberals and dismissed by moral psychologists. I suggested that evolution may have shaped our intuitions about in-groups, authority, and purity, just as it shaped our intuitions about harm and fairness. If Barash believes that this suggestion is irresponsible because it may strengthen the religious right, then he has demonstrated the danger of moralism in science and has inadvertently illustrated all four of the principles that I proposed as comprising the new synthesis in moral psychology.

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References

CORRECTIONS AND CLARIFICATIONS
Reports: “Direct evidence for a parietal-frontal pathway subserving spatial awareness in humans” by M. Thiebaut de Schotten et al. (30 September 2005, p. 2226). This study employed a neuroimaging method, diffusion tensor imaging tractography, to identify a fronto-parietal pathway important for spatial awareness. On the basis of the available literature [see, e.g., J. Bossy, Les hémisphères cérébraux, Neuroanatomie, Ed. (Springer, Berlin, 1991)], this pathway was labeled as “superior occipito-frontal fasciculus.” However, further evidence from the author’s laboratory (see Supporting Online Material at www.sciencemag.org/cgi/content/full/317/5838/597/DC1) led them to reconsider this labeling. The authors are now convinced that the pathway likely corresponds to the homologous of the second branch of the superior longitudinal fasciculus (SLF II), described in the monkey brain by Schmahmann and Pandya [J. D. Schmahmann, D. N. Pandya, Fiber Pathways of the Brain (Oxford Univ. Press, New York, 2006)]. In the monkey, the SLF II originates in the caudal inferior parietal lobe (corresponding to the human angular gyrus) and the occipito-parietal area and projects to the dorsolateral prefrontal cortex. This modification does not change the main point of the Report, that damage to the fronto-parietal pathways is important to produce neglect. On the contrary, it renders the results even more consistent with the data reported by Dorich and Tomaiuolo [F. Dorich, T. Tomaiuolo, NeuroReport 14, 2239 (2003)], which demonstrated that damage to the SLF II in human patients with vascular lesions correlates with the presence of spatial neglect. Future studies on the implication of white matter pathways in human cognition would greatly benefit from a stereotaxic atlas of the white matter tracts in the human brain.
Time to imagine space: a chronometric exploration of representational neglect

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Abstract

When describing known places from memory, patients with left spatial neglect may mention more right- than left-sided items, thus showing representational, or imaginal neglect. This suggests that these patients cannot either build or explore left locations in visual mental imagery. However, in place description there is no guarantee that patients are really employing visual mental imagery abilities, rather than verbal-propositional knowledge. Thus, patients providing symmetrical descriptions might be using other strategies than visual mental imagery. To address this issue, we devised a new test which strongly encourages the use of visual mental imagery. Twelve participants without brain damage and 12 right brain-damaged patients, of whom 7 had visual neglect, were invited to conjure up a visual mental image of the map of France. They subsequently had to state by pressing a left- or a right-sided key whether auditorily presented towns or regions were situated to the left or right of Paris on the imagined map. This provided measures of response time and accuracy for imagined locations. A further task, devised to assess response bias, used the words “left” or “right” as stimuli and the same keypress responses. Controls and non-neglect patients performed symmetrically. Neglect patients were slower for left than for right imagined locations. On single-case analysis, two patients with visual neglect had a greater response time asymmetry on the geographical task than predicted by the response bias task, but with symmetrical accuracy. The dissociation between response times and accuracy suggests that, in these patients, the left side of the mental map of space was not lost, but only “explored” less efficiently.

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Keywords: Unilateral neglect; Visual mental imagery; Attention; Brain-damaged patients; Space processing

1. Introduction

Patients with left spatial neglect may mention more right-sided than left-sided items when describing known places from memory (Brain, 1941; Denny-Brown, Meyer, & Horenstein, 1952; Bisiach, Capitani, Lazarzatti, & Perani, 1981; Bisiach & Lazarzatti, 1978) asked left neglect patients to imagine and describe familiar surroundings from memory (the Piazza del Duomo in Milan). Patients omitted to mention left-sided details regardless of the imaginary vantage point that they assumed, thus showing representational, or imaginal neglect. Bisiach and co-workers proposed that imaginal neglect could either result from “a representational map reduced to one-half” (Bisiach et al., 1981, p. 549), or from patients’ failure to explore the left part of an intact map, and preferred the amputation hypothesis on grounds of parsimony. Bartolomeo, D’Erme, and Gainotti (1994) assessed quantitatively the amount of neglect in 30 right brain-damaged and 30 left brain-damaged patients, tested consecutively on both visuospatial tasks and place description tasks. Three different geographical domains (Roman squares, a map of Europe and the coast of Italy as it could be seen from Sardinia) were used to obtain a sufficient amount
of data for analysis. Right brain-damaged patients had a rightward bias in both visual and imaginal tasks, while left brain-damaged patients performed no differently from controls. For right brain-damaged patients, the amount of spatial bias in imaginal tasks correlated with that in visuospatial tasks, thus supporting the hypothesis of a relationship between the two impairments. However, analysis of individual performance revealed that only five of the 17 patients with left visuospatial neglect also showed neglect in the imaginal domain, contrary to the predictions of the map amputation hypothesis. The greater frequency of left neglect in visuospatial than imaginal tasks may result from right visual objects being more likely than right imagined items to capture neglect patients’ attention (Bartolomeo & Chokron, 2002b; D’Erme, Robertson, Bartolomeo, Daniele, & Gainotti, 1992; Gainotti, D’Erme, & Bartolomeo, 1991; Mark, Kooistra, & Heilman, 1988).

A problem with the description from memory of known places is that abilities other than visual imagery might be used to perform this task. In the Bartolomeo et al.’s study (1994), patients were invited to imagine the places “as if they were in front of them”. Despite these instructions, some patients might simply have produced a list of items from verbal semantic memory. If so, imaginal neglect would be underestimated in these tasks, and might thus ultimately appear to be less common than visuospatial neglect, whereas the two disorders would in fact have a similar frequency. On the other hand, even when naming an imagined detail, participants could then verbally associate this detail with others nearby, which would thus be mentioned without being imagined (e.g., when describing a map of France, Paris could be verbally associated with the Seine river). If so, there could be a local inflation of details, which would also complicate estimates of frequency of imaginal neglect. The issue is of theoretical importance, because if imaginal neglect occurs with similar or increased frequency as visual neglect, than the two deficits may stem from a loss of the left part of the mental representation of space (Bisiach, 1993). On the other hand, a larger frequency of visual than imaginal neglect across patients, as suggested by the results reviewed earlier, would rather be consistent with an attentional impairment typically affecting visual objects, and in some cases imagined items too (Bartolomeo et al., 1994). A third possibility is that these two forms of neglect result from entirely different disorders. This possibility is consistent with reports of double dissociations between imaginal and visual neglect (Coslett, 1997; Denes, Beschin, Logie, & Della Sala, 2002; Guariglia, Padovani, Pantano, & Pizzamiglio, 1993; Ortigue et al., 2001), but increases the need for explanation.

But place descriptions have other problems. Idiosyncratic responses are possible, depending, for example, on patients’ place of residency or vacation. There is a strong influence of pre-morbid cultural level. Often, too few items are available for statistical analysis. Finally, there is no way to know where patients place the center of their mental images, and consequently on which side the produced items are situated in patients’ mental map of space. For example, a lateralized item just imagined could easily become the center of further exploration.

To address these concerns, we developed a response time (RT) task for imagined locations, and compared performance on this task to the widely used task of describing an imaginary map of France (Rode, Perenin & Boisson, 1995). Participants heard the spoken names of geographical locations (towns and regions of France), and had to press a left- or a right-sided key according to the corresponding imagined location in a mentally-generated map of France with Paris as its center. Participants had no obvious way of performing this task without conjuring up a visual mental image of a map of France, because geographical locations are rarely understood in terms of being situated to the “left” or “right” of Paris. By providing participants with the place names, instead of asking them to list the names, we tried to minimize the influences of particular cultural backgrounds. Our task enabled us to record two measurements, response time and accuracy, that should allow a finer quantitative evaluation of patients’ performance than place descriptions. Finally, an imaginary center of the mental map was supplied on each trial by asking participants to start their exploration from the imagined location of Paris. Results of this task should allow one to adjudicate between competing hypotheses of representational neglect. If patients have lost the left part of their mental map of space (Bisiach & Luzzatti, 1978), then left-sided items should either evoke “right” responses or no response at all. If, on the other hand, imaginal neglect results from an impairment of image exploration (Bartolomeo et al., 1994), then patients might respond more slowly to left than to right imagined items, much as they are slowed in responding to left visual targets (Bartolomeo & Chokron, 2002b).

To allow an intuitive matching between stimulus and response, we asked patients to use their right, unaffected hand to press a left- or a right-sided key for the corresponding imagined locations. This, however, introduced a potential problem in the interpretation of the results. Patients with left neglect may show a response bias when asked to press lateralized keys (even if they are close to each other, as in the present study), with faster responses for right-sided keys than for left-sided keys (Behrmann, Bläck, & Murji, 1995; Ládavas, Farne, Carletti, & Zeloni, 1994). Thus, slower RTs for left-sided imagined locations might in fact originate from a response bias, and not from an imaginal impairment. To address this concern, we asked participants to perform an additional task, employing the same keypress responses but different stimuli. In this control task, participants heard the

1 Using vocal, instead of manual, responses would not eliminate the possibility of response biases. Some neglect patients are unwilling even to utter the word “left”. This may be an additional problem with place description tasks. For example, Brain (1841) described a patient who, when asked to describe how she would find her way from the tube station to her flat she described this in detail correctly and apparently visualizing the landmarks, but she consistently said right instead of left for the turning except on one occasion (p. 259).
words “left” or “right”, and had to press the corresponding key. If an asymmetry of performance occurred only in the geographic task, but not in the response bias task, then it could not be considered to result from a mere response bias.

2. Methods

2.1. Participants

A total of 12 patients with unilateral right hemisphere lesions, at a distance of at least 3 weeks from lesion onset, and 12 age- and education-matched individuals without brain damage (mean age ± S.D. 84.42 ± 17.73 years, mean years of schooling ± S.D. 12.00 ± 3.33) consented to participate in the study, which was carried out by following the guidelines of the Ethical Committee of the Sainte-Anne Hospital in Paris. Neglect was assessed by using a standardized battery of paper-and-pencil tests (Azouvi et al., 2002). Seven patients were considered as showing signs of left visual neglect, 5 performed within normal limits. Table 1 reports patients’ demographical and clinical data.

2.2. Description from memory of a map of France

We asked participants to imagine a map of France “like the one shown in TV weather forecasts”, and to name as many geographical locations as possible which they imagined “seeing” on the map. Responses given during 2 min were collected and classified as left- or right-sided depending on the items’ location with respect to the Paris meridian (Rode et al., 1995). Items situated near the meridian, or items with ambiguous laterality (e.g., the Seine river), were excluded from analysis.

2.3. Geographical RT task

2.3.1. Stimuli

Twenty pairs of geographical locations (names of towns and regions of France) were selected. Each pair consisted of items situated east and west of Paris, in a roughly symmetrical fashion (see Fig. 1 below). Care was taken to choose locations of approximately equal importance, as estimated by the number of inhabitants (mean ± S.D., left, 441,567 ± 897,152; right, 455,668 ± 619,475; t < 1). The items were recorded in a soundproof room by one of the authors (ACBL). The sound files were subsequently edited to eliminate parasitic noise, respiration, stuttering, etcetera, and to ensure a relatively homogeneous onset and offset of each item. Stimuli were matched for duration (left: 720 ± 149 ms; right: 702 ± 130 ms; t < 1).

2.3.2. Procedure

Stimuli were presented on a Macintosh computer using the SuperLab software.
Participants were comfortably seated and wore a pair of headphones. They had their right hand on the computer keyboard, with their index and ring fingers placed on, respectively, the “k” and the “;” keys of the American keyboard. Before starting, participants were asked to imagine a map of France. Then, on each trial they heard the words “Paris” and, after 200 ms, another French town or region (e.g., “Bordeaux”). Participants were instructed to press the “k” key if the second stimulus referred to a location left of Paris, or the “;” key if the stimulus indicated a location right of Paris. The intertrial interval was set to 3 s starting from the participant’s response to the previous trial. A maximum of 5 s was allowed for response on each trial. Stimuli were given in a random sequence, preceded by six additional practice items, referring to three left locations and three right locations. Responses to practice items were subsequently discarded from analysis. To avoid responses to particular stimuli becoming automatic with practice, each target was presented only once. Accuracy and response times were recorded.

2.4. Response bias RT task

The procedure was identical to that used for the geographical RT task, with the exception that, instead of geographical locations, participants heard the words gauche (“left”) or droite (“right”), and were invited to press the corresponding
key as fast as possible. The interval interval was set to 1 s. There were 12 left and 12 right stimuli, which were given in random order.

3. Results

3.1. Description from memory of a map of France

Normal participants produced an average of 9.58 items for the left side (S.D. 3.96), and of 9.75 items for the right side (S.D. 4.71). No individual participant showed a significant asymmetry on this task (binomial test, all ps > 0.10).

Table 2 reports patients’ performance. Only patient N − 4, showing no signs of visual neglect, had a reliable asymmetry of performance on this task (binomial test, p < 0.03). The asymmetry resulted from the enumeration in succession of several towns situated in the south-east part of France.

3.2. RT tasks

RTs < 100 ms were excluded as anticipations. This resulted in the exclusion of less than 0.5% of the responses. Fig. 1 shows controls’ mean RTs for each item of the geographical RT task. Performance was symmetrical concerning both RTs (mean ± S.D. in ms, left, 737 ± 28; right, 752 ± 146), r(1) and accuracy (average hits/20 items ± S.D., left, 18.50 ± 1.38; right, 18.83 ± 0.94). Remarkably, patients also showed symmetrical accuracy, although at a lower level than controls (neglect: left, 14.29 ± 4.96; right, 14.86 ± 4.02; non-neglect: left, 13.00 ± 2.65; right, 11.80 ± 3.11). Patient N − 4, the only participant who mentioned significantly more right-sided than left-sided items on the map description task, had symmetrical performance on the geographical RT task (see Table 2; if anything, there was a tendency to misplace right-sided details to the left, in the opposite sense to that predicted by imaginal neglect). This suggests that her biased performance on map description resulted from one or more of the possible confounds described in the introduction (residence or vacation habits, local inflation of items resulting from verbal association, rightward shift of the center of the visual image consequent upon the description of a right-sided item).

For RTs (Fig. 2), we needed to take into account the possibility of a response bias favoring right-sided over left-sided responses (Behrmann et al., 1995; L’Adavas et al., 1994). Accuracy on the response bias task was at or near ceiling for all participants. We conducted a repeated-measures analysis of variance on mean RTs with group (controls, neglect, non-neglect), task (geographical, response bias) and side (left, right) as factors. All main effects were significant. Controls were faster than brain-damaged patients, F(2,21) = 19.04, p < 0.0001 (Tukey HSD test, controls versus each of the 2 groups of patients, ps < 0.005; neglect versus non-neglect patients, p > 0.32). the response bias task evoked faster responses that the geographical task, F(1,21) = 29.55, p < 0.0001, and right responses were faster than left responses, F(1,21) = 14.02, p = 0.001. The group interacted with the task, F(2,21) = 5.19, p = 0.015, with the side, F(2,21) = 7.18, p = 0.004, and, most importantly, with task and side, F(2,21) = 4.45, p = 0.024, because neglect patients had the most severe left-right RT asymmetry, and especially on the geographical task (left-right difference for neglect patients on the geographical task, 563 ms; Tukey HSD test, p < 0.001; left-right differences for all the other conditions and groups, ps > 0.53) (see Fig. 2). Thus, neglect patients as a group showed an asymmetry of RTs with responses to left-sided imagined items being slower than RTs to right-sided items, consistent with the notion of imaginal neglect. This asymmetry cannot be entirely accounted for by a response bias, because neglect patients showed a lesser asymmetry when asked to produce the same responses without using visual mental imagery abilities.

To explore individual patient performances, we normalized each RT by dividing it by the average RT for each patient on each task, then calculated scores of laterality for each patient and task (normalized left-right RTs), and plotted these scores along with the 95% inferential confidence intervals (Tryon, 2001) of the left-right difference for each patient (Fig. 3). In this way, one can be 95% confident that

Table 2

<table>
<thead>
<tr>
<th>Patient</th>
<th>Left Details</th>
<th>Right Details</th>
<th>Left Errors</th>
<th>Right Errors</th>
<th>Left Omissions</th>
<th>Right Omissions</th>
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<tbody>
<tr>
<td>N+1</td>
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<td>3</td>
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<tr>
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<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
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<td>6</td>
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<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
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<td>8</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>N−6</td>
<td>3</td>
<td>4</td>
<td>9</td>
<td>6</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
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<td>7</td>
<td>2</td>
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</tr>
<tr>
<td>N−1</td>
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<td>5</td>
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<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>N−2</td>
<td>4</td>
<td>8</td>
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<td>6</td>
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<tr>
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<td>8</td>
<td>11</td>
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<td>0</td>
</tr>
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<td>12</td>
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<td>N−5</td>
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<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>9</td>
</tr>
</tbody>
</table>
Fig. 2. Performance of normal controls and of right-brain damaged patients with or without visual neglect for left-sided items (hatched bars) and right-sided items (empty bars) on the geographical RT task and on the response bias RT task. Error bars denote 95% confidence intervals.

Fig. 3. Laterality scores of each individual patient on the geographical RT task and on the response bias RT task. Positive values, rightward bias; negative values, leftward bias. Error bars denote inferential 95% confidence intervals.
intervals which do not cross the horizontal axis at 0 indicate a rightward bias (for positive values) or a leftward bias (for negative values). For each patient, non-overlapping intervals indicate a difference in bias between the two tasks.

Five neglect patients of seven and one non-neglect patient demonstrated a reliable rightward bias on the geographical task. However, only for two patients (N = 1 and 4) could this bias be confidently attributed to an imaginal impairment, because for the other patients there was substantial overlapping with performance on the motor task. The two patients with imaginal bias also had neglect on paper-and-pencil tests. Importantly, they had symmetrical accuracy on the geographical RT task (see Table 2).

4. Discussion

We used a response time task to explore imaginal neglect. Participants heard the name of towns or regions of France and pressed the key corresponding to their localization. This task: (1) strongly incites participants to conjure up a visual mental image of a geographic map, and discourages strategies based on purely verbal recall of locations; (2) supplies both the center of exploration and the item to be localized on each trial, and is thus less subject to idiosyncratic responses than place descriptions; (3) provides quantitative measures of performance (accuracy and RTs). Thus, the geographical RT task does not suffer from problems affecting place description tasks. It can be used to test hypotheses about imaginal neglect and its relationships with visual neglect, and can be repeated to assess patients' performance before and after rehabilitation.

Participants found the geographical task more difficult than the response bias task, as shown by longer RTs and higher error rates in the former than in the latter task. It is sometimes suggested that difficulty may increase biases in neglect patients. Thus, it might be that a mere response bias determined the present pattern of results in neglect patients, including the increased asymmetry of response on the geographical task. However, we deem this possibility implausible, because: (1) most of our patients did not show a greater bias on the response bias task than on the geographical task (see Fig. 3); (2) the two forms of biases seemed unrelated, as suggested by the lack of significant correlation between their amounts across patients (r = 0.24, z < 0.45), and (3) in previous research, motor biases were hardly affected by the difficulty of the task.2

Denis et al. (2002) proposed other methods to explore imaginal neglect. They presented patients with visual layouts or verbal descriptions of layouts and subsequently asked them to recall the presented material (Halligan, Marshall, & Wade, 1992, had previously proposed a similar technique of recall from verbal description). Neglect patients reported fewer items from the left than from the right side in both conditions, but especially in the “memory after perception” condition, which resulted in a significant interaction between conditions. However, in the “memory after perception” condition visual neglect could have biased the perceptual apprehension of the visual scene, consistent with the increased neglect demonstrated in this condition. On the other hand, in the “memory after description” condition normal controls also had a tendency to report fewer items from the left than from the right side, which might suggest a task-dependent bias.

Bächtold, Baumüller, and Brugger (1998) visually presented numbers 1 to 11 in the center of the visual field, and found asymmetries of RTs in normal individuals, with faster left-hand RTs for numerals <6 and a right-hand RT advantage for those >6 for subjects who conceived of the numbers as distances on a ruler, and a reversed asymmetry for subjects who conceived numbers as hours on a clock face. They attributed this pattern of results to a spatial stimulus-response compatibility effect, and suggested that their task could be usefully applied to the study of imaginal neglect. Kokolija, Marshall, and Fink, 2004 asked normal participants to judge whether the angle of imagined clock hands corresponding to a time visually given as digital numbers (e.g., 06:50) was greater than or less than 90°. Participants had longer RTs and greater error rates when the imagined angle was located in the left hemispace than when it was in the right hemispace, perhaps because they mentally rotated the imaginary minute hand in a clockwise direction starting from the “noon” position. The present RT tasks share with these tasks the advantage of obtaining quantitative measures of performance on a continuous scale, and have the additional advantage of excluding any visual input.3 The geographical RT task consequently allows an even more clear-cut exploration of imaginal neglect, without any risk of contamination from perceptual neglect.

Our finding of a reliable rightward RT bias in two of seven patients with visual neglect,4 and of no such bias in patients...

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2 For example, in their Exp. 1, Lichav et al. (1994), asked neglect patients to respond to visual stimuli by pressing two horizontally aligned adjacent keys. Patients showed slower responses with the right-sided key than with the right-sided key, consistent with a response bias. In a further condition, the keyboard was reversed by 180°. Again patients were slower when pressing the key in the relative left spatial position. Patients found the reversed condition more difficult than the standard condition, as shown by an increased error rate in the reversed condition. However, their asymmetry of response (57 ms) was the same as in the standard condition (56 ms). Another study on motor bias in neglect (Bartolomeo et al., 1998) reported left RT asymmetry in a relatively difficult test in which patients had to press left- or right-sided keys in response to central visual stimuli, compared to a much easier task requiring patients to respond with a unique, centrally placed key to lateralized visual targets.

3 Although the numbers were centrally presented in the tasks devised by Bächtold et al. (1998) and Kokolija et al. (2004), one cannot exclude the possibility that, for example, neglect patients would process more efficiently the right digits than the left digits with multi-digit numbers.

4 Caution is needed concerning the present estimate of the frequency of imaginal neglect, because imagery and motor biases can co-exist in the same...
without visual neglect, confirms previous evidence obtained with place descriptions (Bartolomeo et al., 1994), that only about a third of patients with visual neglect demonstrate imagnal neglect too, and that neglect confined to visual mental imagery is a rare occurrence. Group studies (Halband, Graf, & Etlinger, 1985), the detailed report of two cases (Anderson, 1993), and a study conducted during intracarotid injection of amobarbital (Manoach, O’Connor, & Weintraub, 1996) also confirmed that visuospatial neglect often occurs without representational neglect. At least some of the rare cases of representational neglect in isolation could originate from selective recovery of visual neglect in patients originally showing an association of visual and imaginal neglect. Patients might learn to endogenously orient their attention to left visual objects (Bartolomeo, 1997, 2000; Bartolomeo, Siéroff, Decaix, & Chokron, 2001), but not to left visual images, which are not usually the object of rehabilitation or of verbal eortations from the caregivers. Follow-up studies, in which visual and imaginal neglect were repeatedly assessed, show several examples of this pattern of selective recovery (Bartolomeo & Chokron, 2001; Bartolomeo et al., 1994; Coslett, 1989, 1997; Rode, Rossetti, Pererin, & Boisson, 2004).5

In their seminal report, Bisiach and Luzzatti (1978) suggested that imaginal neglect could either result from an amputation of patients’ mental representation of space, or from patients’ inability to explore the left part of an intact map, and preferred the amputation hypothesis. Our result of asymmetric RTs with symmetrical accuracy in the geographical task suggests, instead, that attentional biases resulting in visual neglect (Bartolomeo & Chokron, 2002b) may also operate in visual mental imagery (Bartolomeo & Chokron, 2002a). Consistent with this hypothesis, imaginal neglect can be offset by the same sensory-motor maneuvers which favorably affect visual neglect, such as leftward eye and head turning (Meador, Loring, Bowers, & Heitman, 1987), vestibular stimulation (Rode & Pererin, 1994), and visuormotor adaptation to right-deviating prisms (Rode, Rossetti, & Boisson, 2001). These procedures may act by facilitating leftward orienting of attention (Chokron & Bartolomeo, 1999; Gainotti, 1993). Also the evidence of an asymmetry of REMs during sleep in neglect patients (Dorichci, Guariglia, Paolucci, & Pizzamaglio, 1993) is in agreement with the idea that the attentional bias in neglect need not be restricted to real visual objects. Rather than sharing low-level mechanisms with vision (Kosslyn, Ganis, & Thompson, 2003), visual mental imagery may involve some of the attentional-exploratory mechanisms that are employed in visual behavior (Bartolomeo, 2002; Chokron, Colliot, & Bartolomeo, 2004; Griffin & Nobre, 2003; Thomas, 1999). It may be precisely the utilization of these processes of “active” vision that renders visual mental imagery so similar to “real” visual experience (O’Regan & Noe, 2001). The definition of the exact conditions under which an attentional bias can result in visual neglect only, or spread to mental imagery abilities, constitutes a fascinating challenge for future research.

Acknowledgment

Results from this study were presented at the 22nd European Workshop on Cognitive Neuropsychology, Bressanone, Italy, 2004.

References


5 In two other cases (Bosch, Cocchini, De Sar & Logie, 1997; Ottiger et al., 2001), imaginal neglect appeared to have occurred at disease onset without any signs of visual neglect. Concerning these cases, one may note that patients may sometimes show only subtle signs of visual neglect, whose clinical compensation may occur in a few days (see e.g., Fig. 5 in the off tests & Chokron, 2001). Other patients may demonstrate even milder signs of visual spatial bias (e.g., only on RT tests). We acknowledge, however, that evidence of an isolated imaginal neglect at onset would render our present account less generally applicable (see also the discussion in Marshall & Halligan, 2002).


A battery of tests for the quantitative assessment of unilateral neglect

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INSERM U 610, Hôpital de la Salpêtrière, Paris, France
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Abstract. Purpose: The lack of agreement regarding assessment methods is responsible for the variability in the reported rate of occurrence of unilateral neglect (UN) after stroke. In addition, dissociations have been reported between performance on traditional paper-and-pencil tests and UN in everyday life situations.

Methods: In this paper, we present the validation studies of a quantitative test battery for UN, including paper-and-pencil tests, an assessment of personal neglect, extinction, and anosognosia, and a behavioural assessment, the Catherine Bergego Scale (CBS). The battery was given to healthy subjects (n = 456 – 476) and to patients with subacute stroke, either of the right or the left hemisphere.

Results: In healthy subjects, a significant effect of age, education duration and acting hand was found in several tasks. In patients with right hemisphere stroke, the most sensitive paper and pencil measure was the starting point in the cancellation task. The whole battery was more sensitive than any single test alone. An important finding was that behavioural assessment was more sensitive than any other single test. Neglect was two to four times less frequent, but also less severe and less consistent after left hemisphere stroke.

Conclusion: Assessment of UN should rely on a battery of quantitative and standardised tests. Some patients may show clinically significant UN in everyday life while obtaining a normal performance on paper-and-pencil measures. This underlines the necessity to use a behavioural assessment of UN.

Keywords: Unilateral neglect, assessment, stroke

1. Introduction: why a quantitative test battery for unilateral neglect?

Unilateral neglect (UN) is a failure to attend to the contralesional side of space. It is a puzzling disorder commonly encountered after stroke, particularly of the right hemisphere. The study of UN is of con-
siderable interest for neuroscientists interested in spatial cognition or attention [38]. However, UN also has major practical significance for clinicians and rehabilitation professionals dealing with stroke patients. Indeed, UN may affect many daily living skills and has been found associated with poor functional recovery from stroke. Denes et al. [30] found that neglect was the worst prognostic factor for functional recovery in hemiplegia, when compared to other cognitive disorders, such as aphasia, intellectual deterioration, or disturbed emotional reactions. These findings have been subsequently largely reproduced by other authors, who showed that neglect had an adverse influence upon functional outcome, improvement on rehabilitation, length of hospital stay and discharge to home [2, 3, 25, 45, 53], although contradictory results have been reported [35, 54].

In most severe cases, after a large right hemisphere stroke, UN is obvious and can be detected by simple observation of the patient in his bed. However, in most patients, UN is not clinically apparent and specific testing is needed to reveal the disorder. Specific testing is also necessary to give objective measures of the severity of neglect and to monitor recovery during rehabilitation. However, objective assessment of neglect is not easy, for at least two reasons. Firstly, it is now widely accepted that UN is not, at least from a clinical point of view, a unitary disorder [14]. Clinical manifestations of UN may vary from one patient to the other, and in a given patient, according to time and nature of assessment. The different clinical manifestations of UN, that can dissociate one from each other, include viewer- or object-centred neglect, neglect for near or far extrapersonal space, personal neglect, representational neglect, motor neglect, directional hypokinesia [43]. However, most commonly used tests only take into account visual or visuo-motor aspects of UN in the near peripersonal space [42]. Secondly, UN is not an all-or-nothing phenomenon. Neglect can vary in a given patient according to the test used, its nature, its complexity, but also according to extraneous factors, such as fatigue, motivation, or mood status.

**Assessment of UN.** A great number of clinical tests of UN have been reported in the literature. However, despite a large amount of research, there is still no consensus among clinicians regarding the methods of identifying neglect and monitoring changes after treatment [22, 59]. A recent review [51] identified 62 assessment tools for UN. Only 28 of them were standardised, thus allowing objective quantified measurement of the disorder. In a recent systematic review of published reports, Bowen et al. [22] found that the frequency of occurrence of neglect in patients with right brain damage ranged from 13% to 82%. The assessment method used was one of the main factors explaining the discrepancies between the different studies. Thirty studies were included in this latter review, most of them using a battery of paper-and-pencil tests. Only one study [46] did not specify how UN was assessed. Nineteen studies used a battery of up to 7 different tests. The most frequently used single task was a cancellation task. Figure copying was also commonly used. Only occasionally did the assessment of UN involve an ecological assessment of neglect in everyday life.

Many clinicians are familiar with several simple bedside screening tests, such as object copying [33, 52], object-centred neglect, or drawing. However, such tests are not very sensitive and are difficult to score in a quantitative way. Cancellation tasks are more sensitive and may give quantitative scores. There are several versions, but all of them require the patient to find and cancel target items displayed on an A4 paper sheet. In the classical line cancellation task [1], there are no distractors, only lines to cancel. In most other tests, such as the bells test [34], or the star cancellation test [71], distractors are mixed with targets in a pseudo-random fashion, thus improving the sensitivity of the task. Line bisection is another widely used test. Patients with UN tend to show a rightward deviation of the subjective midpoint [64]. The sensitivity of line bisection depends on the length of the line to bisect, longer lines being more sensitive [16]. With short lines, neglect patients show a paradoxical leftward deviation ("crossover effect") [39]. Other clinical tests have been proposed, such as the overlapping figures test [32], in which patients are asked to name four overlapping figures, two on the right and two on the left of a fifth centrally located figure, and reading and writing tasks. These different tests assess visual or visuo-motor aspects of UN in the close peripersonal space. Personal neglect can be assessed by asking the patient to comb his hair, shave or put on make-up [15, 50, 73], or to reach his left arm with his right hand [18]. The Fluff test has been recently proposed as a simple test for studying personal neglect [27]. This latter test requires patients to remove, with one’s eyes closed, 24 2-cm diameter circles attached with velcro to the front of their clothes. Neglect in the far extrapersonal space can be assessed by requiring a patient to describe objects in the room around him, or to bisect lines or cancel items located outside hand reach, for example with a laser pointer [40]. However, these tests cannot easily be replicated across different settings. Repre-
sentational neglect is addressed by asking the patient to describe from memory a familiar place [17], although such a procedure cannot be scored quantitatively. Rode and Perenin [61] devised a simple test that permits to obtain a quantitative score of representational neglect for French patients. Patients have to generate a mental image of the map of France and to cite as many cities they can mentally visualize on the right and the left of an imaginal line. Motor neglect is usually observed by therapists who remark the lack of spontaneous use of the contralesional limb. However, there is no simple way to quantitatively score motor neglect or directional hypokinesia in a routine clinical setting. A few standardised assessment batteries including various clinical tests have been published. The Behavioural Inattention Test (BIT) [37, 71] is a comprehensive and well validated one, including both paper and pencil and behavioural tests.

Ecological assessment of UN. Although paper-and-pencil tests are useful for rapid clinical screening, they fail to consider the patient’s actual performance in his everyday life. Some patients obtain a normal performance on conventional tests, while showing a directional bias in daily life skills. Such dissociations have been attributed to the relative sparing of voluntary orientation of attention (involved in conventional tests) contrasting with an impairment of automatic orienting which allows attention to be automatically captured by relevant stimuli in everyday life [10, 65]. There is a need for standardised ecological measures of neglect to quantify the extent of neglect in everyday life, to adapt rehabilitation to the individual patient’s limitations, to monitor changes and to assess the effectiveness of rehabilitation. This last point is of great importance for rehabilitation. This battery demonstrated good inter-rater and test-retest reliability. However, it did not seem to be more sensitive than paper-and-pencil tests. An Italian team has devised a semi-structured scale of both personal and extrapersonal neglect [56, 72, 73]. Extrapersonal neglect is assessed by asking the patients to serve tea or to distribute cards to four persons around a square table, to describe complex figures and objects in a room. Personal neglect is assessed by requiring to use common objects (razor or powder, comb, glasses). Inter-rater reliability is good [72]. Only extrapersonal subtests were significantly correlated with paper-and-pencil tests. A modified version of the personal subscale has been proposed, the comb and razor test, with a more precise quantitative scoring system [15, 50]. The Baking Tray Task consists of 16 wooden cubes, that the patient is required to place as evenly as possible over a 75 × 100 cm board, “as if they were buns on a baking tray” [68]. Patients with UN tend to place the cubes preferentially on the right part of the board.

Although these different tasks are all simulations of real-life situations, they do not provide any objective information on the patient’s behaviour in his actual everyday environment. Most of these ecological tests still represent quite artificial situations which may rely more on voluntary rather than automatic orienting of attention. Moreover, they do not take into account anosognosia. Considering the above mentioned limitations and difficulty of assessment of UN, a collaborative study was decided in the French-speaking community, with the objective to design and validate a test battery of UN, that could be both psychometrically sound and easy to complete within a rehabilitation setting. This battery (“Batterie d’évaluation de la négligence spatiale”, BEN) comprises two different parts. The first one includes traditional clinical and “paper and pencil” tests of neglect and related disorders, the second one is a standardised observational scale, aimed at providing an ecological assessment of neglect in the patient’s everyday life.

2. Paper-and pencil tests of the French test battery for UN (“Batterie d’évaluation de la négligence spatiale”, BEN)

2.1. Materials and methods

2.1.1. Subjects

As a first step, normative data were collected in a group of healthy individuals (n = 456 to 576 depend-
The objective was to determine norms and a pathological threshold for each task, and to assess the effect on performance of five factors: gender; age (four age groups: 20–34; 35–49; 50–64; 65–80); education duration (≤8 years; 9–12 years; ≥13 years); handedness; and acting hand (half of the subjects performed the task with their preferred hand, half of them with their non-dominant hand).

Two groups of patients were included, at the subacute stage after a stroke either in the right (\(n = 206\)) [6] or the left (\(n = 89\)) [11] hemisphere. For patients with left hemisphere stroke, only non-verbal subtests were given, to control for any confounding effect of associated language impairments. Nevertheless, 11 patients with left hemisphere stroke were excluded from the study due to severe aphasia with major comprehension deficits. The main characteristics of the two groups are displayed on Table 1. It appeared that, as compared to the general stroke population, these patients were relatively younger, probably due to a selection bias related to the fact that most of them were recruited through specialised stroke rehabilitation units, and not from geriatric wards. These patients should be regarded as representative of stroke patients referred to a rehabilitation facility. Not surprisingly, the majority of patients also had motor deficits (hemiparesis or hemiplegia). Severity of motor impairments (which reflects overall stroke severity) was assessed with a four-level scale, ranging from 0 (no motor deficit) to 3 (severe hemiplegia). The amount of patients with severe hemiplegia was quite similar in both groups (see Table 1). In addition, patients were classified in four groups according to stroke localisation (anterior; posterior; antero-posterior; subcortical) as assessed with CT and/or MRI scans by examiners blind to neuropsychological assessment. Anatomic data were not available for 49 patients in the right hemisphere group and for seven patients in the left hemisphere group.

### 2.1.2. Methods: Paper-and-pencil tests of the BEN

Most of paper-and-pencil tests included in the battery were adapted from the existing literature, with their authors’ permission. In addition to these traditional tests, personal UN and related disorders, such as anosognosia and extinction were also addressed.

#### 2.1.2.1. Paper-and-pencil tests of extrapersonal neglect

**The bells test** [34]. Subjects were asked to circle 35 targets (black-ink drawings of bells), presented on a horizontal A4 paper sheet, along with 280 distractors in a pseudo-random array. The total number of omissions and the difference between left- and right-sided omissions were recorded. In addition, a special care was given to identifying the subject’s starting point. Targets were equally distributed in seven columns (three left, three right, and one central) numbered from 1 to 7 starting from the left. The starting point was operationally defined as the number (1–7) of the column including the first circled bell.

**Figure copying** [33,52]. Subjects were asked to copy on a horizontal A4 sheet a drawing including (from the left to the right) a tree, a fence, a house with a left-sided chimney, and a second tree. Following Ogden [52], a five-level scale was used, ranging from 0 (no omission) to 4 (omission of the left tree and of at least the left part of another item).

**Clock drawing**. Patients were required to place the 12 hours in a circle drawn by the examiner. A three-level scale was used, with a score of 0 in case of a normal symmetrical performance, of 1 in case of omissions of a part of left-sided hours and of 2 in case of omission or rightward displacement of all left-sided hours.

**Line bisection**. Patients were asked to mark the middle of four lines of two different lengths (5-cm and 20-cm), presented separately centred on an A4 horizontal sheet. Deviation from the true middle was measured in mm, positively for rightward deviation, negatively for leftward deviation.

**Overlapping Figures Test** [32]. Test stimuli consisted of two figures overlapping on the right and two on the left side of a card, all of them overlapping a fifth centrally located figure. Patients were asked to name all the figures they could detect. The total number of omitted figures, and the difference between left- and right-sided omissions across five trials were recorded.

**Reading** [70]. Patients were asked to read a short 12-line text, horizontally printed on an A4 sheet. The total
Table 2
Performance of healthy controls on the BEN (adapted from Rousseaux et al., 2001)

<table>
<thead>
<tr>
<th>Test variables</th>
<th>Maximal possible score</th>
<th>Mean (SD)</th>
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<th>Percentile 5/95</th>
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</thead>
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<tr>
<td>Bells test ( (n = 576) )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omissions (total number)</td>
<td>35</td>
<td>2.06 (1.49)</td>
<td>0 / 10</td>
<td>0 / 6</td>
</tr>
<tr>
<td>Omissions (left minus right)</td>
<td>15</td>
<td>−0.05 (1.39)</td>
<td>−6 / 5</td>
<td>−2 / 2</td>
</tr>
<tr>
<td>Starting point</td>
<td>7</td>
<td>1.88 (1.49)</td>
<td>1 / 7</td>
<td>1 / 5</td>
</tr>
<tr>
<td>Figure copying ( (n = 487) )</td>
<td>4</td>
<td>0.04 (0.21)</td>
<td>0 / 2</td>
<td>0 / 0</td>
</tr>
<tr>
<td>Clock drawing ( (n = 457) )</td>
<td>2</td>
<td>0.01 (0.09)</td>
<td>0 / 1</td>
<td>0 / 0</td>
</tr>
<tr>
<td>Bisection (mm) ( (n = 457) )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-cm lines</td>
<td>100</td>
<td>−0.95 (4.15)</td>
<td>−16 / 15</td>
<td>−7.2 / 6.5</td>
</tr>
<tr>
<td>5-cm lines</td>
<td>25</td>
<td>−0.17 (1.45)</td>
<td>−7 / 5</td>
<td>−2.5 / 2</td>
</tr>
<tr>
<td>Test reading ( (n = 457) )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omissions (total number)</td>
<td>0.04 (0.26)</td>
<td>0 / 3</td>
<td>0 / 0</td>
<td></td>
</tr>
<tr>
<td>Omissions (left minus right)</td>
<td>0.02 (0.26)</td>
<td>−1 / 3</td>
<td>0 / 0</td>
<td></td>
</tr>
<tr>
<td>Writing (left margin, cm) ( (n = 456) )</td>
<td>3.0 (2.54)</td>
<td>0 / 25</td>
<td>0.79 / 7.72</td>
<td></td>
</tr>
</tbody>
</table>

number of words omitted, and the difference between left- and right-sided omissions within the first five lines were recorded.

Writing. Patients were asked to write, on three separate lines, their first and last names, address, and profession (or the current date if they had no profession). The score was the maximal left margin width (in cm).

2.1.2.2. Assessment of gaze orientation and personal neglect

Spontaneous gaze and head orientation was assessed with a four-level scale [60] ranging from 0: no deviation, to 3: permanent rightward deviation of gaze and head.

Personal neglect was assessed following Bisiach et al. [18] methodology. Patients were asked to reach their left hand with the right hand, first with eyes open, then with eyes closed. A four-level scale was used, ranging from 0: normal performance, to 3: no attempt to reach the target.

2.1.2.3. Assessment of related disorders

Awareness of motor and visual deficits was assessed following Bisiach et al. methodology [19], using a four-level scale, both for motor and visual impairments (range: 0 = perfect awareness to 3 = the patient never admitted having some impairment, despite its demonstration by the examiner).

Visual extinction and hemianopia were tested clinically by wiggling fingers for two seconds in one or both visual fields (six trials). Extinction was considered as present when a patient failed at least once to report a contralesional stimulus during bilateral simultaneous presentation, while accurately detecting unilateral stimuli.

2.2. Results

2.2.1. Performance of healthy controls

Some tasks showed a ceiling effect due to a nearly perfect performance: clock drawing, overlapping figures, reading, head and gaze deviation, personal neglect, and visual extinction. For these tasks, any deviation from optimal performance should be considered as abnormal. The other tasks showed a more variable pattern of performance, allowing the determination of a pathological threshold that was arbitrary set below the fifth percentile of the control group. The main results of the performance of the control group are displayed in Table 2.

There was no significant effect of gender, for any task. However, performance in several tasks appeared to be significantly affected by age, education, and by the acting hand [62]. In the bells test, the total number of omissions was significantly higher in older or less educated people. The difference between left and right omissions was also significantly associated with education (more left-sided omissions for lower education levels and more right-sided omissions for higher education duration). Although only a minority of subjects showed one omission in the Figure copying test, the effect of education was significant, due to less omissions in the highest education group. There was a mild, but significant, leftward deviation in line bisection. This deviation was significantly influenced by the acting hand (larger leftward deviation with the left hand), but only for short lines (5-cm). Other factors, including age, gender or handedness, had no significant influence on performance in line bisection. Finally, the left margin in the writing test was significantly larger in older persons, when using the left hand or in left-handers.
2.2.2. Patients with right hemisphere stroke

The main result was that test sensitivity greatly varied from one test to another (Table 3) [6]. The amount of patients with neglect on each individual subtest ranged from 19.0% to 50.5%. However, more than 85% of patients showed UN on at least one test. The two most sensitive tests were the bells test and the reading test. In the bells test, the most sensitive measure was not the number of omissions, but rather the spatial location of the starting point spontaneously used by the patient. While 80% of controls used a left to right scanning strategy, a majority of patients used a reverse pattern, starting with a right-sided target (Fig. 1).

In the line bisection test, a length effect was found. Indeed, longer lines (20-cm) were nearly twice as sensitive than shorter (5-cm) ones. Bisection of short lines was the less sensitive test in the battery. A paradoxical leftward deviation (cross-over effect) was found in some patients, more frequently with short lines.

To assess the relationships between the different tests, a correlation matrix was calculated for paper-and-pencil measures. The great majority of correlation coefficients was positive and significant ($p < 0.0001$), and about one third of these coefficients had a value of 0.50 or more.

2.2.3. Patients with left hemisphere stroke

Neglect was clearly less frequent and less severe in the left hemisphere group [11]. As indicated in Table 3, paper-and-pencil tests revealed right neglect in 3.8% to 13.2% of patients, depending on the task. However, as far as 43.5% of patients demonstrated some degree of UN on at least one task. Personal neglect was just as frequent as extrapersonal neglect (9 and 13% with eyes open and eyes closed respectively), and was nearly as frequent as after right hemisphere stroke (16% and 13%). Anosognosia for motor and visual deficits was much less frequent than after right hemisphere stroke. Inter-tests correlations were low ($<0.50$).

2.3. Discussion

In healthy controls, there was a significant effect of age and/or education for the bells test, figure copying and writing, suggesting that these factors should be taken into account in the assessment of a patient suspect of UN. A significant effect of the acting hand was found only in line bisection. In this latter test, controls showed a mild but significant leftward deviation, a phenomenon known as “pseudo-neglect” [23,24,44]. This effect was larger with the left hand and with short lines, a result in accordance with a meta-analysis [44]. The effect of handedness is debated in the literature, and the lack of effect found in the present study should be taken with caution, due to the relatively low number of left-handed individuals ($n = 49$).

The battery was found sensitive to detect UN in patients with right hemisphere stroke. Indeed, more than 85% of patients showed UN on at least one test. An important finding was that an assessment across several different tests was more sensitive than any single test alone. This finding, in accordance with previous reports [41,52], suggests that a normal performance on one test alone is not sufficient to rule out the presence of UN. The two most sensitive tests were the bells test and the reading test, both including a strong visual component that has been suggested to exacerbate UN [9]. However, it should be emphasised that the number of left-sided omissions should not be considered as the sole marker of UN. The pattern of visual scanning used by the patient should be taken into consideration. Indeed, in the bells test, the most sensitive measure was the spatial location of the first circled bell. Contrary to controls, who used preferentially a left to right scanning strategy, a majority of patients started with a right-sided target. This supports the assumption that an early automatic orientation of attention toward the ipsilesional half of space is a major component of unilateral neglect [29,32,49]. Previous studies found that a rightward orientation bias was the only detectable residual impairment in patients who had apparently recovered from neglect [26,49]. In the line bisection tests, a length effect was found, in accordance with previous studies.
showing a linear increase in rightward displacement as a function of line length in most neglect patients [16, 39]. The cross-over effect for short lines has been reported in previous studies [39, 48], although its mechanism remains a matter of debate. Nevertheless, these results suggest that bisection of short lines should not be recommended as a screening test for neglect.

Neglect was clearly less frequent and less severe in the left hemisphere group, in accordance with a large amount of previous studies, although this has been a matter of debate [1, 7, 22, 31, 41, 52, 54, 66]. The present data showed that, depending on the criteria used, right UN was two to four times less frequent than left UN. Neglect was not only less frequent, it was only much less severe in the left hemisphere group as compared to patients suffering from a right hemisphere stroke. An other difference between right and left UN was that paper-and-pencil tests were significantly correlated one with each other in the right hemisphere group, while there were only poor inter-tests correlations in the left hemisphere group. This finding suggests that right neglect is a somewhat elusive phenomenon, with less clinical consistency than left UN. In opposition with the findings obtained with paper-and-pencil tests, there was no such asymmetry with personal neglect that was not significantly more frequent after right hemisphere stroke. It should be acknowledged that the two groups were not systematically matched in terms of stroke size and severity, and that a few patients \((n = 11)\), presumably with the most severe strokes, had to be excluded from the left hemisphere group due to comprehension deficits. Moreover, data on stroke localisation showed that the right hemisphere group tended to present more frequent antero-posterior and posterior strokes. Nevertheless, the two groups appeared to be quite similar in terms of associated motor impairments, suggesting that differences in stroke severity could not readily account for the dramatic differences in the frequency and severity of UN.

3. Behavioural assessment of UN: the Catherine Bergego Scale (CBS)

3.1. Materials and methods

3.1.1. Subjects

Several studies have been conducted successively with the CBS. Most of them were conducted in patients with subacute right hemisphere stroke in a rehabilitation setting. The first, preliminary study, included 18 patients, with the objective to assess inter-rater reliability. Further studies on psychometric properties of the scale have been conducted on two successive groups of patients with subacute-chronic right hemisphere stroke \((n = 50\) and \(n = 83\) respectively) [4, 5]. The CBS was also used in a subgroup of 69 patients in two participating centres of the previously mentioned validation study of the BEN [6].

### Table 3

Performance of patients (adapted from Azouvi et al., 2002 and Beis et al., 2004). LH = left hemisphere; RH = right hemisphere

<table>
<thead>
<tr>
<th>Test variables</th>
<th>Cut-off</th>
<th>LH stroke Mean (SD)</th>
<th>% pathologic</th>
<th>RH stroke Mean (SD)</th>
<th>% pathologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bells test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omissions (total number)</td>
<td>&gt; 6</td>
<td>3.7 (2.5)</td>
<td>12.8</td>
<td>8.4 (9.4)</td>
<td>41.3</td>
</tr>
<tr>
<td>Omissions (left minus right)</td>
<td>&gt; 2</td>
<td>0.5 (2.1)</td>
<td>11.7</td>
<td>3.1 (4.4)</td>
<td>44.9</td>
</tr>
<tr>
<td>Starting point</td>
<td>&gt; 5</td>
<td>4.6 (2.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Figure copying</td>
<td>&gt; 0</td>
<td>0.4 (1.2)</td>
<td>10.4</td>
<td>1.2 (1.6)</td>
<td>42.7</td>
</tr>
<tr>
<td>Clock drawing</td>
<td>&gt; 0</td>
<td>0.2 (0.6)</td>
<td>13.2</td>
<td>0.4 (0.6)</td>
<td>27.8</td>
</tr>
<tr>
<td>Bisection (mm) 20-cm lines</td>
<td>&gt; 6.5</td>
<td>0.4 (19.7)</td>
<td>6.4</td>
<td>10.1 (19.4)</td>
<td>37.7</td>
</tr>
<tr>
<td>5-cm lines</td>
<td>&gt; 2.0</td>
<td>0.2 (2.9)</td>
<td>3.8</td>
<td>0.6 (3.7)</td>
<td>19.0</td>
</tr>
<tr>
<td>Text reading</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omissions (total number)</td>
<td>&gt; 0</td>
<td>11.9 (25.3)</td>
<td>46.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omissions (left minus right)</td>
<td>&gt; 0</td>
<td>5.6 (11.4)</td>
<td>41.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Writing (left margin, cm)</td>
<td>&gt; 7.7</td>
<td>6.8 (5.0)</td>
<td>34.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gaze and eye deviation</td>
<td></td>
<td>12</td>
<td>32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal neglect</td>
<td></td>
<td>9</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eyes open</td>
<td></td>
<td>13</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eyes closed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anosognosia</td>
<td></td>
<td>For hemiplegia 6</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>For hemianopia 10</td>
<td>46</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Two of us (DP, PA) have more recently investigated behavioural aspects of right neglect in patients suffering from a left hemisphere stroke (unpublished data). Fifty-four patients suffering from a first-ever left hemisphere stroke were included. They were all right-handed. Time since stroke onset was 65.9 days (SD = 40.5). Stroke was ischaemic in 71.7% of cases.

3.1.2. Methods
The Catherine Bergego Scale (CBS) is based on a direct observation of the patient’s functioning in ten real-life situations, such as grooming, dressing, or wheelchair driving [4,5,13]. For each item, a four-point scale is used, ranging from 0 (no neglect) to 3 (severe neglect). A total score is then calculated (range: 0–30). Arbitrary cut-off points were drawn in the CBS, to distinguish different levels of impairment. Patients with a total score of 0 were considered as having no UN, a score ranging from 1 to 10 was considered as mild behavioural UN, a score 11–20 as a moderate UN and a score 21–30 as a severe UN. To assess patients’ awareness of neglect-related everyday difficulties, a parallel form of the CBS has been designed as a questionnaire, with the same ten items previously described. An anosognosia score can be computed by recording the difference between the observer’s and the patient’s scores.

3.1.3. Statistical analyses
Reliability was assessed by computing Cohen’s kappa coefficients on each of the ten items of the scale, and the correlation coefficient between the total scores given by two independent examiners [13]. Concurrent validity was assessed by comparison of behavioural assessment with the CBS to the results of conventional paper-and-pencil tests. Correlation coefficients between the CBS total score and conventional measures were computed. To further address the relationships between conventional and behavioural assessment, a stepwise multiple regression analysis was performed in the 69 patients from the validation study of the BEN. The total score on the CBS was used as dependent variable, and paper and pencil measures as explicative variables.

Internal consistency of the scale was established by measuring Spearman rank correlation between the scores on each individual question and the total score. The internal structure of the scale was assessed by two different methods on the data from 83 right hemisphere stroke patients from our department [5]. Firstly, a principal component analysis with varimax rotation was computed. In a second step, a Rasch analysis was computed (Bigsteps software) [47]. Rasch analysis is a method specifically designed for evaluating characteristics of rating scales with the expectation of unidimensionality [57,67]. Briefly, the Rasch model has been designed to assess the validity of ordinal scales and to permit the transformation of raw discontinuous scores into an equal interval measure.

3.2. Results
Inter-rater reliability was found satisfactory in the first group of patients (n = 18) who were scored simultaneously by two independent raters [13]. The kappa coefficients for the ten items of the scale ranged from 0.59 to 0.99, demonstrating a fair to high inter-rater reliability [13]. In addition, the total scores of the two examiners were strongly correlated one with each other (Spearman rank order correlation coefficient = 0.96, p < 0.0001) [13].

Spearman’s correlation coefficients between the scores on each individual question and the CBS total score were all significant, ranging between 0.58 to 0.88 [4]. A principal component analysis with varimax rotation (n = 83) extracted only one factor with an eigenvalue higher than 1, explaining 65.8% of total variance. All items of the CBS obtained a high loading on this factor (range: 0.77–0.84). Rasch analysis revealed that the ten items defined a common, single ability continuum with widespread measurement range and quite regular item distribution, and showed a satisfactory reliability [5].

In our three different studies [5,6,13], the three following items were found to be the most sensitive of the scale: neglect of left limbs, collisions while moving, and neglect in dressing. Behavioural assessment with the CBS was compared to the results of conventional paper-and-pencil tests. In our different studies previously mentioned, the total CBS score correlated significantly and relatively strongly with most paper-and-pencil tests. Bisection of short lines was the only test that did not correlate with behavioural neglect. The strongest correlations were obtained with the bells test with correlation coefficients always above 0.7 [4,5]. However, an important finding was that the CBS was constantly found to be more sensitive than conventional tests [4–6]. This point was addressed in the previously mentioned validation study of the BEN [6]. In this latter study, the highest incidence of UN found with any individual paper-and-pencil test was 50%, while 76% of patients demonstrated neglect on at least one item
of the CBS. Six patients performed within the normal range on the bells test and nevertheless showed a moderate to severe behavioural neglect on the CBS [6]. A stepwise multiple regression analysis found that four variables, from three paper-and-pencil tasks, significantly predicted the total CBS score (R square = 0.79, F(4,57) = 54.2, p < 0.0001): the total number of omissions and the starting point in the bells test, figure copying and clock drawing. These three tasks in combination revealed neglect in 148 patients (71.84%), and missed only 29 neglect patients (16.38%), most of whom had a mild neglect [6].

Patient’s self-assessment with the CBS was significantly lower than the examiner’s score (t(66) = −4.4, p < 0.0001), indicating some form of anosognosia of neglect-related difficulties in everyday life [6]. The difference was of 5 or more in 25 patients (37.3%). Anosognosia for behavioural neglect correlated significantly, although moderately, with anosognosia for motor and visual impairment (r = 0.29 and 0.37 respectively, p < 0.05). The anosognosia score correlated strongly with neglect severity, as assessed with the CBS (r = 0.82, p < 0.0001), or with paper and pencil tests (r ranging from 0.47 to 0.70, p < 0.0001), except for short-line bisection [6]. However, individual analysis revealed dissociations between anosognosia and neglect, some patients with moderately severe neglect obtaining anosognosia scores close to 0.

The study with the CBS in patients with left hemisphere stroke (unpublished data) revealed that 41 (77.3%) patients showed at least some neglect on one item of the scale (i.e. had a CBS score of 1 or more). However, only three (5.4%) had a CBS score higher than 10, corresponding to a clinically significant behavioural UN. This should be compared to the much higher rate of clinically significant neglect in patients with right hemisphere stroke (36%) [6]. The items from the CBS that obtained the highest scores (more severe neglect) were neglect of right limbs, neglect in dressing and mouth cleaning after eating, all corresponding to personal neglect. In opposition, items related to extrapersonal neglect, such as collisions while walking or wheelchair driving, obtained lower scores (Fig. 2). The CBS score was significantly correlated with the bells test (r = 0.41 with total omissions and 0.34 with right minus left omissions, both ps < 0.01), although the correlation coefficients were of lower magnitude than those observed in studies with right brain damaged patients (above 0.7). The CBS did not significantly correlate with line bisection. There were also significant correlations with functional disability, particularly with independence in basic activities of daily living (the Functional Independence Measure (FIM) [36] (r = −0.48, p < 0.01) and with posture and balance (Postural Assessment for Stroke Scale, PASS) [12] (r = −0.55, p < 0.001). Similarly to the findings obtained after right hemisphere stroke, the CBS score was significantly correlated with the presence of lesions in the left parietal cortex.

3.3. Discussion

These results suggest that the CBS is reliable and valid, and that the ten items define a homogeneous construct. The discrepancies between paper-and-pencil and behavioural assessments are very important to consider. We have repeatedly found that behavioural assessment was more sensitive to the presence of UN than any single paper-and-pencil test. This suggests that the diagnosis of UN should not be ruled out based on the performance on paper-and-pencil tests alone, without a careful examination of how the patient behaves in his real environment. In addition, it should also be mentioned that the CBS has been used in a rehabilitation trial in severe neglect patients, and was found sensitive to change, and useful to monitor patients’ improvement after rehabilitation [63].

The CBS is also useful to assess anosognosia of neglect in everyday life. Although anosognosia significantly correlated with UN, double dissociations were found between both disorders, in accordance with previous studies [19,28] Moreover, the data presented here suggest that anosognosia is not a unitary phenomenon [55] and that anosognosia for motor, visual or cognitive deficits can be dissociated from each other.

Findings from the study with left hemisphere stroke patients again suggested that right UN is much less severe than left UN. Clinically significant behavioural neglect (about 5% of patients) is much less frequent than after right hemisphere stroke. It seems that right UN is, like left UN, significantly associated with functional and balance impairments. These results may also raise the intriguing possibility of a qualitative difference between right and left neglect, with right neglect involving preferentially the personal rather than the extrapersonal space.

4. General discussion and conclusion

The studies summarised here illustrate the necessity to use a quantitative and validated test battery for...
assessment of UN. It is necessary to compare performance of patients with that of matched healthy controls. A significant effect of age and/or education was found for several tests in healthy controls, suggesting that these factors should be taken into account. Moreover, it is clear that clinical tasks for UN are of variable sensitivity. Tasks including a strong visual component were the most sensitive in our battery, and the automatic rightward orientation bias appeared to be the best indicator of unilateral neglect. In addition, several tests were more likely to uncover evidence of neglect than a single test. The BEN also addresses disorders such as personal neglect, anosognosia and extinction, that are not addressed in other widely used batteries.

Surprisingly, although UN in the extrapersonal space was more frequent and severe after right than left hemisphere stroke, personal neglect was of quite similar frequency in the two groups of patients.

An important finding, replicated across several studies with different groups of patients, was that behavioural assessment of neglect in daily life was more sensitive than any other single measure of neglect. As recently suggested [21], such behavioural measures should be included in any therapeutic trial of UN. The CBS is a reliable, valid and sensitive measure of behavioural neglect, that can easily be used in a rehabilitation setting. It also permits an assessment of anosognosia for neglect in everyday life, that can be dissoci-
ated from anosognosia for hemiplegia or hemianopia. Finally, it should be reminded that neglect is not an all-or-nothing phenomenon. Apparently recovered neglect patients may demonstrate signs of spatial bias when confronted to a novel situation [8]. Non specific factors, such as motivation, fatigue, emotional state, may also be of influence and should be taken into consideration in the assessment of neglect patients.

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References


Inhibition of return: Twenty years after

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When responding to a suddenly appearing stimulus, we are slower and/or less accurate when the stimulus occurs at the same location of a previous event than when it appears in a new location. This phenomenon, often referred to as inhibition of return (IOR), has fostered a huge amount of research in the last 20 years. In this selective review, which introduces a Special Issue of Cognitive Neuropsychology dedicated to IOR, we discuss some of the methods used for eliciting IOR and its boundary conditions. We also address its debated relationships with orienting of attention, succinctly review findings of altered IOR in normal elderly and neuropsychiatric patients, and present results concerning its possible neural bases. We conclude with an outline of the papers collected in this issue, which offer a more in-depth treatment of behavioural, neural, and theoretical issues related to IOR.

Given the complexities of our interaction with the environment, the attentional system has evolved in humans to help the perceptual system to pick up the most relevant information, while ignoring less important information. In order to understand how information is selected from the environment it is important to know how attention operates, how it is oriented to the most relevant stimuli and events, whilst it is withdrawn from irrelevant information. Thus, attention in general and attentional orienting in particular has become one of the most important topics of research on cognitive psychology, cognitive neuropsychology, and cognitive neuroscience during the last decades, with much research being devoted to the study of the attentional mechanisms that modulate perception.

In this sense, it is nowadays well established that orienting can be performed in two different ways: an exogenous way, triggered bottom-up by external stimuli, and another more top-down, endogenous way, voluntarily triggered by the expectancies of the individual. This distinction between endogenous and exogenous spatial orienting is supported by a wealth of behavioural evidence in normal individuals (e.g., Funes, Lupiáñez, & Milliken, 2005; Klein, 2004, for reviews) and brain-damaged patients (see Bartolomeo & Chokron, 2002; Losier & Klein, 2001), as well as by the existence of different
neural substrates (Corbetta & Shulman, 2002, for a review; see also Kincade, Abrams, Astafiev, Shulman, & Corbetta, 2005).

Much of this research has been influenced by the pioneer work of Michael Posner and colleagues who developed in the late seventies an experimental procedure, the cost and benefits paradigm (Posner, 1980; Posner, Nissen, & Odgen, 1978), to study attention. This procedure has become so useful in the research of attention because it allows us to study, with simple manipulations, different modes of orienting and their boundary conditions and is simple enough as to be used not only with normal participants but also with different populations of patients and even in animals (Bartolomeo, Siéroff, Decaix, & Chokron, 2001; Dorris, Klein, Everling, & Munoz, 2002; Fuentes, Boucart, Vivas, Alvarez, & Zimmerman, 2000; Posner, Rafal, Choate, & Vaughan, 1985; Posner, Walker, Friedrich, & Rafal, 1984).

Target stimuli are presented on a computer screen at one of two locations marked by one box each, one to the right and the other to the left of a central fixation point. A variable time before the target appears, a cue is presented to cue the target appearance at one of the two possible locations. Two different kinds of cue can be used with this procedure in order to study different types of attention. On the one hand, the cue can be presented at the centre and be predictive of target location with a probability above chance (e.g., a central arrow pointing either left or right). This way, the cue is to be interpreted, and participants have to develop an expectancy of target location according to the meaning of the cue. Attention can then be voluntarily orientated to the predicted location, leading to faster and/or more accurate responses at this location than at the opposite location, supposedly mediated by an involuntary shift of attention to the cued location.

Although these two types of attentional orienting lead to similar effects on performance, at least under some circumstances—that is, faster and/or more accurate responses (facilitation effects)—there are important differences between the two modes of orienting (see Klein, 2004; Klein & Shore, 2000, for reviews). One of the more important differences refers to the time course of exogenous versus endogenous orienting of attention, which has been studied by manipulating the asynchrony between the onset of the cue and the onset of the target (cue–target onset or stimulus onset asynchrony, CTOA or SOA). Exogenous cues lead to faster shifts of attention than do endogenous cues, as indexed by facilitation effects at the cued location (Müller & Rabbitt, 1989). More importantly, the duration of the facilitation effect dramatically depends on the type of cue that is used. Whereas the effect of central symbolic cues remains positive (i.e., facilitation effect) for long intervals up to one second, the effect of peripheral nonpredictive cues is quite transient, so that it usually disappears after a few hundreds milliseconds.

Furthermore, and importantly for the present Special Issue, the facilitation effect observed with peripheral cues not only disappears after some time interval, but is reversed, so that after about 300 ms responses are now slower and/or less accurate at the location where the cue was presented than at the opposite location (see Klein, 2000, for a review). This phenomenon was discovered independently in the 1980s by the Posner group (Posner & Cohen, 1984) in the US and by the Berlucchi group (Tassinari, Aglioti, Chelazzi, Marzi, & Berlucchi, 1987) in Italy, and it has since inspired an impressive and ever-increasing number of studies in the cognitive neuroscience community. The effect has received different names such as “inhibitory aftereffect” (Tassinari et al., 1987) or “inhibitory tagging”
(Fuentes, Vivas, & Humphreys, 1999; Klein, 1988). However, Posner, Rafal, and colleagues (Posner et al., 1985) termed this phenomenon “inhibition of return” (IOR), and this is the name that is used most often in the cognitive neuroscience and experimental psychology laboratories.

Since the discovery of the phenomenon, IOR has lead to an important amount of research in cognitive neuroscience, having a big impact in the field of attention, as the effect has been used to study different issues on attention and spatial cognition and attentional deficits in different clinical and subclinical populations and brain-damaged patients. To get an idea of the impact that the phenomenon has had in the field, we should note that the original paper by Posner and Cohen (1984) has been cited more than 800 times in journals of the Science Citation Index (ISI Web of Science. Thomson ISI. Philadelphia, PA, USA). The paper by Posner et al. (1985) has been cited nearly 300 times (122 times in the last 5 years from 2000 to 2004). See Table 1 for the 20 most cited papers on IOR in journals of the ISI web of knowledge. More importantly, as can be observed in Figure 1, more than 300 papers have been published on IOR since its discovery in 1984, with around 40 papers per year being published during the last years.

IOR: Methods, findings, and theories
The model task pioneered by Posner for exploring covert orienting, as described above, has provided the methodological foundation for most studies of IOR. An uninformative peripheral cue is presented at one of two locations followed after various delays by a target at the cued or uncued location. In the earliest studies the target called for a simple detection response, and catch trials were used to discourage anticipatory responding. At short intervals performance is usually better at the cued location, an advantage attributed to attentional capture by the cue. In Posner and Cohen’s (1984) implementation of this task, two different methods were used to ensure that when testing at longer intervals, attention would not simply remain at the cued location: Either a second cue was presented at fixation after the peripheral cue; or targets were presented at fixation with a higher probability than that of either peripheral location. The former method would return attention exogenously to fixation (a neutral state with regard to the potential targets) while, with the latter method, it is reasonable to assume that the participant would do this endogenously. Many studies have successfully elicited IOR in normal adults using neither of these methods, suggesting that the equal probability of receiving a target at the possible target locations provides sufficient incentive for these participants to place their attention in a neutral state some time after the cue. In participants with poor volitional control of attention (e.g., children, schizophrenics, the elderly), however, the endogenous removal of attention from the cue may be sluggish, and therefore the appearance of IOR may be significantly delayed, or even absent, if measures are not taken to exogenously return attention to fixation after it is captured by the peripheral cue (for a review, see Klein, 2005).

The timecourse and spatial distribution of IOR has been explored by varying the time and distance between the cue and target. These studies have shown that IOR is relatively long lasting (persisting for up to 3 seconds in some studies, see Samuel & Kat, 2003, for a review) and that there is a gradient of inhibition around the originally cued location (Bennett & Pratt, 2001; Dorris, Taylor, Klein, & Munoz, 1999; Maylor & Hockey, 1985). When a return cue at fixation is not used, the time when facilitation at the cued location is replaced by inhibition may be delayed when the difficulty of the target task is increased (Lupiáñez, Milan, Tornay, Madrid, & Tudela, 1997) and when a verbal memory load interferes with the endogenous return of attention from the cued location (Klein, Castel, & Pratt, in press). When the participant is given reason to attend to a location endogenously, whether through instruction without a probability manipulation (Berlucchi, Chelazzi, & Tassinari, 2000) or because targets are likely to occur there
IOR is observed at the endogenously attended location. This finding has been used to argue against the assertion that IOR is the result of the inhibition of the return of attention to the originally cued and attended location and hence against the very label “inhibition of return” (Berlucchi, 2006). Another possibility is that there are in fact two “beams” of attention: the one controlled “top-down” or endogenously, usually in the absence of asymmetric visual stimulation, and the one controlled exogenously by virtue the “bottom-up” salience of array elements (Briand & Klein, 1987; Klein, 1994; Klein & Shore, 2000). By operating on the salience map, IOR may delay exogenous orienting based on bottom-up signals without affecting endogenous orienting. Converging evidence for this view comes from the finding that IOR follows exogenously but not endogenously generated shifts of attention (Posner & Cohen, 1984;
According to this view, from the perspective of both cause and effect, endogenous orienting might be independent of IOR. Interposing a saccade between the cue and target, Posner and Cohen (1984) and Maylor and Hockey (1985) found that it was not the retinal location of the cue that was inhibited, but rather the location of the cue in the environment. Similarly, interposing motion of the array elements between a cue and target, Tipper, Driver, and Weaver (1991) found that targets presented on the originally stimulated object were inhibited, even when that object had moved to the location where the uncued object had been at the time of the cue. These studies show that, when necessitated by ocular or object movements, IOR can be coded in an environmental or object frame of reference. Suggesting that IOR may be encoded in a multimodal structure, IOR has also been obtained in touch and audition, and between all cue–target pairings of vision, touch, and audition (Spence, Lloyd, McGlone, Nicholls, & Driver, 2000). All these findings place the cause of IOR at some distance from the early sensory pathway stimulated by the cue.

When entertaining assertions about the perceptual, attentional, and motoric nature of IOR it is necessary to consider whether these assertions are about what causes IOR or, once IOR has been caused, what kinds of information processing are affected by the hypothetical inhibition (Taylor & Klein, 1998). Rafal et al. (1989) used central arrows or peripheral cues to induce their participants to generate overt orienting (a saccade), covert orienting (a shift of attention) or to prepare a saccade. After an endogenously or exogenously elicited saccade, the eyes returned to fixation, and, reflecting IOR, a target calling for a detection response was responded to slower when presented at the previously fixated location. On a proportion of trials calling for a shift of attention or preparation of a saccade, a stimulus at fixation informed the participant to cancel the shift or cease the preparation. The cancellation of saccadic preparation caused IOR whether an endogenous or exogenous cue had been used to generate the preparation. Finally, replicating Posner and Cohen (1984), IOR was found after an exogenous but not after an endogenous shift of attention. Because the conditions that elicited IOR in this study have in common an oculomotor programme (either executed or activated), oculomotor programming is strongly implicated as playing a critical role in causing IOR.

Once caused does IOR affect perceptual, attentional, or motor processing? When a choice task is used, IOR interacts with the Simon effect (Ivanoff, Klein, & Lupiáñez, 2002), and when a detection...
response is used IOR doubles when the nonresponding hand is placed on the keyboard (Ivanoff & Klein, 2001). These findings implicate an effect at the level of motor processing. The effect seems to be related to a bias to avoid responses to targets at a previously cued location (Ivanoff & Klein, 2001) rather than inhibition of such responses (Prime & Ward, 2004). On the one hand, as indexed by temporal order judgements (Klein, Schmidt, & Muller, 1998) and illusory line motion (Schmidt, 1996) perceptual arrival times do not seem to be affected by IOR. On the other hand, perceptual sensitivity (d') is reduced at a previously cued location both with masked targets (Handy, Jha, & Mangun, 1999) and as a function of response speed using a deadline procedure (Ivanoff & Klein, in press). Taken together these findings suggest that IOR may operate at several stages of processing to discourage orienting toward previously cued locations. Two “flavours” of IOR were reported by Taylor and Klein (2000) using central arrows and peripheral events as the first or second of two successive stimuli. When the oculomotor system was engaged (by either the first or the second stimulus) the inhibition laid down by the first stimulus had a motoric effect (responses in the same direction as that indicated by the first stimulus were retarded even when the second stimulus was a central arrow). In contrast, when the oculomotor system was quiescent (manual responses were made to the second stimulus after the first one was ignored, or responded to manually) the effect was upon attention/perception: Inhibition was only observed in response to peripheral events. A similar dissociation has been reported by Sumner and coworkers (Sumner, 2006; Sumner, Nachev, Vora, Husain, & Kennard, 2004). Following typical stimuli they found IOR for manual and saccadic targets, while for cues that were invisible to the superior colliculus, IOR was observed for manual but not saccadic responses. Unlike Taylor and Klein’s dissociation, which is about the effect(s) of IOR, Sumner’s is about the generation of IOR: When IOR is generated by stimuli that bypass the superior colliculus the inhibition does not affect reflexive saccades.

Posner and Cohen (1984) speculated that IOR might serve to encourage orienting toward novel objects and events. Extending this suggestion, Klein (1988) proposed that IOR might operate in visual search to discourage wasteful reinspections. Using a probe-after-search procedure, he confirmed this proposal by finding IOR at the locations of distractors during difficult, but not easy (popout), visual search (see also Takeda & Yagi, 2000). Klein and Maclnnnes (1999) extended this finding to oculomotor search of complex scenes (from Martin Handford’s “Where’s Waldo” books). When probe targets interrupted search or when they were presented after the participant had temporarily ceased searching (Maclnnes & Klein, 2003) the time to foveate the probe declined as the distance of the probe from a recently fixated region of the scene increased. When observers are free to search a scene for a target, a tendency to avoid reinspections could be due to a passive inhibitory tagging system like IOR or to the adoption of a deliberate strategy to scan the array in a particular order. This ambiguity was eliminated by McCarley, Wang, Kramer, Irwin, and Peterson (2003) using a task in which the experimenter guides oculomotor behaviour by presenting a sequence of targets. Here there is no possibility of the observer planning the scanpath for inspecting objects in a scene because the experimenter is presenting items one at a time. When the observer is given a choice between targets, with one presented at a new location and one presented at an old location, there is a strong bias to inspect the target at the new location (McCarley et al., 2003). This bias, reflecting IOR, is so strong that observers find it difficult to follow an instruction to select the old object when it is presented with a new one (Boot, McCarley, Kramer, & Peterson, 2004). IOR and cognitive neuroscience

Inhibition of return has been used to study different issues in cognitive neuroscience, more specifically in the fields of attention and spatial cognition, as a tool to study both the underlying mechanisms and the neural structures on which
they are subtended. Thus, IOR has been used to study the development of the attentional orienting mechanism from the first days after birth (i.e., in newborns) to the late stages of decline in the elderly, to study attention on patients with psychological and psychiatric disorders and on neuropsychological patients, and to search the brain for areas involved in attention. As discussed above, IOR has been used to investigate the frames of reference on which attention can act and whether attention is unimodal versus crossmodal, and not only to study attention but to investigate how attention modulates and can be subserved by other processes such as perception and memory.

IOR has been used to study the development of the visual and attentional system in infants from the early newborn stages until the decline with age in the elderly. Thus, newborns show IOR from the first day after birth (Valenza, Simion, & Umiltà, 1994). Nevertheless, it was shown that the eccentricity at which infants show IOR varies with age, in close relation with the eccentricity at which they can make accurate saccades (Harman, Posner, Rothbart, & Thomas-Thrapp, 1994), which suggest that IOR can be taken as an index of the maturation of the eye-movement system. Studies which included a longer range of ages showed that the IOR effect observed in children and adolescents from around 1 up to 17 years old varies and depends on the cue–target SOA that is used and the presence versus absence of a central reorienting cue (MacPherson, Klein, & Moore, 2003; Richards, 2000).

Moving now to the late decline with age, IOR has also been used to study attentional dynamics in the elderly and in patients with Alzheimer’s disease. Although previous studies showed no differences in IOR between young and older adults (Hartley & Kieley, 1995), when the time course is taken into account elderly people have shown IOR at later cue–target intervals (Castel, Chasteen, Scialfa, & Pratt, 2003). Similarly, they have shown a deficit when object-based IOR is measured, but not when location-based IOR is measured (McCrae & Abrams, 2001). In the same guise, several studies have shown relatively normal IOR in patients with Alzheimer’s disease (Danckert, Maruff, Crowe, & Currie, 1998; Faust & Balota, 1997; Langley, Fuentes, Hochhalter, Brandt, & Overmier, 2001; for a review, see Amieva, Phillips, Della Sala, & Henry, 2004). However, when some parameters of the procedure such as the task (Langley et al., 2001), time course (Langley et al., 2001), or the presence versus absence of a central reorienting cue (Faust & Balota, 1997) were studied, Alzheimer’s disease patients did show some deficits of IOR. Similarly, a reduction or elimination of IOR has been documented in patients with Parkinson’s disease (Poliakoff, O’Boyle, Moore, McGlone, Cody, & Spence, 2003).

Several psychological and psychiatric populations have been shown to have attentional deficits as revealed by abnormal patterns of IOR. Thus, patients with obsessive-compulsive disorder have been observed to show reduced IOR (Nelson, Early, & Haller, 1993; Rankins, Bradshaw, Moss, & Georgiou-Karistianis, 2004), with perhaps this mechanism explaining their difficulties in disengaging from actions, whereas deaf subjects can disengage their attention faster than can hearing subjects, as indexed by a faster decay of IOR (Colmenero, Catena, Fuentes, & Ramos, 2004). Regarding attention deficit hyperactivity disorder, it is not clear whether these subjects have really an impairment in the attentional mechanism subserving IOR, as they only show a slightly smaller IOR effect than do controls (Li, Chang, & Lin, 2003). Children and adolescents with spina bifida meningomyelecele show attenuated IOR in the vertical plane (Dennis et al., 2005), which is taken as evidence for their problems in orienting to salient stimuli.

Schizophrenic patients have been reported to show abnormal IOR depending on the type of patient and the specific procedure that was used to measure the IOR effect. Thus, Huey and Wexler (1994) showed smaller and delayed IOR on medicated and clinically stable schizophrenic outpatients than on healthy control participants. Similarly, Gouzoulis-Mayfrank, Heekeren, Voss, Moerth, Thelen, and Meincke (2004) reported blunted IOR, and Larrison-Faucher, Briand, and Sereno (2002) reported delayed onset in
schizophrenic patients, as compared to control participants. However, Fuentes and colleagues have reported normal levels of IOR on medicated schizophrenic patients (Fuentes, Boucart, Alvarez, Vivas, & Zimmerman, 1999; Fuentes & Santiago, 1999), and Sapir, Henik, Dobrusin, and Hochman (2001) reported IOR as being present or not on medicated patients depending on whether a central reorienting cue was presented at fixation. Important parameters of the procedure that is used to measure IOR, such as the duration of the cue, the SOA and the presentation of a reorienting cue at fixation, could explain the different results observed in the different studies.

Damage to the central nervous system may or not influence IOR. Patients with damage to the pulvinar nucleus of the thalamus have been reported to show normal IOR (Danziger, Ward, Owen, & Rafal, 2001; Sapir, Rafal, & Henik, 2002). Similarly, Danziger, Fendrich, and Rafal (1997) reported normal IOR in hemianopic patients, even when the cues were presented in the blind field. However, patients with conversion paresis seem to show blunted or no IOR (Roelofs, van Galen, Eling, Keijsers, & Hoogduin, 2003), whereas patients with parietal damage with or without spatial neglect seem to show quite unaltered IOR at the contralesional side, in contrast to reduced IOR, a lack of effect or even facilitation (instead of IOR) at the ipsilesional side (Bartolomeo, Chokron, & Séroff, 1999; Bartolomeo et al., 2001; Lupiáñez et al., 2004; Sapir, Hayes, Henik, Danziger, & Rafal, 2004; Vivas, Humphreys, & Fuentes, 2003).

Sapir, Soroker, Berger, and Henik (1999) reported a lack of IOR in a patient with damage to the superior colliculus (no IOR only in the visual fields projecting to the damaged right SC, i.e., the left temporal hemifield and the nasal right hemifield). On the other hand, Tipper, Rafal, and colleagues (Tipper et al., 1997) reported that object-based IOR could be observed in two split-brain patients, provided that the cued object remained in the same hemifield; as soon as it crossed the midfield IOR disappeared (in fact, it reversed to facilitation). These two studies clearly show that, although the superior colliculus seems to be an important structure related to IOR, cortical structures are also involved. Depending perhaps on the frames of reference on which attention is acting, and therefore in which IOR is being measured, different neural cortical and subcortical structures might be involved in the generation of IOR.

Outline of the special issue

The papers collected in this Special Issue largely result from a session of the 23rd European Workshop on Cognitive Neuropsychology, Bressanone, Italy, organized in 2005 by the guest editors of this issue, in the 20th anniversary of the publication of the IOR eponymous paper in Cognitive Neuropsychology (Posner et al., 1985).

The first article is devoted to the behavioural exploration of IOR. Chica et al. (2006) replicated the demonstration that IOR can occur at endogenous attended locations and extended this finding to both detection and discrimination tasks. These results cast doubts on the traditional account of IOR as resulting from the inhibition of the return of attention to a previously inspected location, at least as far as endogenous attention is concerned.

Petroc Sumner’s contribution (Sumner, 2006) focuses on the neural bases of IOR. Sumner developed an elegant paradigm for identifying collicular contributions to visual orienting. Either standard luminance cues or S-cone cues, which are invisible to the direct collicular pathways, are presented. The results show that there are (at least) two types of IOR: one affecting both manual and ocular responses, presumably depending on the superior colliculus, and the other affecting only manual responses, presumably depending on the cortex. This study indicates directions for a possible taxonomy of distinct types of IOR.

If IOR requires, at least in part, cortical processes, then it should be impaired in brain-damaged patients. Vivas, Humphreys, and Fuentes (2006) show that this is actually the case. Patients with parietal lesions had decreased IOR for stimuli occurring on the same side as...
their brain lesion, perhaps as a consequence of an imbalance of the relative salience of signals.

In the last paper, Giovanni Berlucchi (2006), one of the discoverers of the phenomenon, further stresses the difficulties of interpreting IOR as a mere bias against returning to a previously explored location. Consequently, the very name of inhibition of return might be inappropriate. Berlucchi makes the intriguing suggestion that these after-effects might actually result from two processes; a first, sensory effect would determine a consequent orienting effect. In other words, sensory attenuation immediately following a peripherally presented stimulus might produce a subsequent deficit of (exogenous) orienting towards stimuli occurring in the same location.

We hope that this collection of papers will provide the reader with a state-of-the-art knowledge of inhibitory after-effects in spatial processing and with a flavour of the exciting perspectives that these phenomena open for the cognitive neuroscience community.

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REFERENCES


Dissociating inhibition of return from endogenous orienting of spatial attention: Evidence from detection and discrimination tasks

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In the present series of experiments peripheral informative cues were used in order to dissociate endogenous and exogenous orienting of spatial attention using the same set of stimuli. For each block of trials, the cue predicted either the same or the opposite location of target appearance. Crucially, using this manipulation, both expected and unexpected locations could be either cued or uncued. If one accepts the hypothesis that inhibition of return (IOR) is an attentional effect that inhibits the returning of attention to a previously attended location (Posner & Cohen, 1984), one would not predict an IOR effect at the expected location, since attention should not disengage from the location predicted by the cue. Detection and discrimination tasks were used to examine any potential difference in the mechanism responsible for IOR as a function of the task at hand. Two major results emerged: First, IOR was consistently observed at the expected location, where, according to the traditional “reorienting” hypothesis, IOR is not supposed to occur. Second, a different time course of cueing effects was found in detection versus discrimination tasks, even after controlling for the orienting of attention. We conclude that IOR cannot be accounted for solely by the “reorienting of attention” hypothesis. Moreover, we argue that the observed time course differences in cueing effects between detection and discrimination tasks cannot be explained by attention disengaging from cues later in discrimination than in detection tasks, as proposed by Klein (2000). The described endogenous-exogenous dissociation is consistent with models postulating that endogenous and exogenous attentional processes rely on different neural mechanisms.

INTRODUCTION

Unexpected, novel, salient, and potentially dangerous events take high priority in the brain. There is now a wealth of literature showing that these stimuli are typically processed in an automatic (or bottom-up) fashion, involving what has been labelled exogenous or involuntary attention
(Corbetta & Shulman, 2002; Egeth & Yantis, 1997; Jonides, 1981; see Ruz & Lupiáñez, 2002, for a review about attentional capture). Spatial attention, however, can be voluntarily directed to a particular location or object depending on the goals or expectancies of the task at hand, involving more endogenous or voluntary forms of attention. According to the spotlight metaphor (Posner, Snyder, & Davidson, 1980), exogenous and endogenous attention are the behavioural expression of the same unitary mechanism. This metaphor assumes that attention is a unique spotlight that can be oriented to a location either voluntarily (endogenously) or involuntarily (exogenously), favouring the processing of objects and locations illuminated by this focus.

In a seminal study, Posner and Cohen (1984) developed the cost and benefits paradigm, in order to investigate the processes that were involved in the orienting of attention. In this paradigm, a fixation point is normally presented at the centre of the screen, and two boxes appear to the left and right of fixation. An uninformative peripheral cue (e.g., a brief flash in one of the boxes) is normally used when investigating exogenous attention, while endogenous cueing studies usually involve central informative cues (e.g., an arrow pointing left or right). Uninformative peripheral cues are supposed to capture spatial attention exogenously (or involuntarily), while central informative cues are presumed to produce a voluntary orienting of spatial attention.

The behavioural effects of both types of cue are clearly different. Central informative cues normally produce faster and/or more accurate target responses at the expected than at the unexpected location, even for long cue–target time intervals (Posner, 1980). However, the use of uninformative peripheral cues leads to two different effects in the detection of a subsequent target across time. If the target appears soon after the appearance of the cue (less than 300 ms), a facilitatory effect is observed—that is, response times (RTs) are faster at cued than at uncued locations. However, if the target appears 300 ms after cue onset or later, an inhibition of return (IOR) effect is observed (i.e., RT is slower for cued than for uncued trials, Posner & Cohen, 1984).

IOR was proposed to be a mechanism that evolved to maximize sampling of the visual environment. The effect was observed for peripheral but not central cues. In addition, Posner and Cohen (1984) found IOR when attention was redirected to the central fixation, supposedly producing a disengagement of attention from the cued location. Taking into account these results, and considering attention as a single spotlight (which may be oriented in two modes, endogenously or exogenously), Posner, Rafal, Choate, and Vaughan (1985) concluded that IOR was an attentional effect, consisting of an inhibition of the return of attention to a previously attended position. According to this hypothesis, when a peripheral cue appears, attention is automatically drawn to its position, but subsequently attention is disengaged from that particular spatial position, and an inhibitory mechanism starts to operate, inhibiting the return of attention to that previously attended position. This hypothesis, which we call the reorienting hypothesis from now on, has been widely accepted by many researchers (see Klein, 2000, for a review).

According to the reorienting hypothesis, no inhibition should be measured until attention is disengaged from the cued location. However, Berlucchi, Tassinari, Marzi, and Di Stefano (1989) reported an experiment in which, even though participants knew in advance where the target would appear, RTs were slower when the target was presented at the same position as the peripheral exogenous cue. In this study, the target always appeared at the same spatial position within a block of trials. Thus, although these results seemed to challenge the reorienting hypothesis, a potential problem with this interpretation could be that a habituation process decreased the effect of the voluntary allocation of attention at the cued position. This concern was resolved in a more recent study, where Berlucchi, Chelazzi, and Tassinari (2000) presented targets at one of four possible locations randomly. Targets were preceded by nonpredictive exogenous cues. In each block of trials, participants were
asked to voluntarily attend to a position related to the exogenous cue (e.g., to attend to the position symmetrical to the cued location). Overall, RTs were faster at the voluntarily attended position and slower at the cued location (i.e., a main effect of IOR was observed). Importantly, these effects were completely independent from each other: IOR was observed at both the endogenously attended and the unattended position.

Recently, Berger, Henik, and Rafal (2005) presented a paradigm in which a central informative cue (an arrow with 80% validity) was followed by a peripheral uninformative cue. After a variable stimulus onset asynchrony (SOA) the target was presented, and the participants were asked to complete a detection task, a two-choice localization task, or a saccadic eye movement to the target (Experiments 1, 2, and 3, respectively). The results of the three experiments showed that the endogenous orienting of attention (elicited by the central informative cue) was independent of the exogenous orienting of attention (elicited by the peripheral uninformative cue), with IOR being observed at endogenously attended and unattended locations. These results are opposite to those predicted by the reorienting hypothesis, according to which IOR is not supposed to occur until attention is disengaged from the cued location. At the expected location, since attention is allocated at that position, no IOR effect should be observed.

It is worth noting here that Posner, Cohen, and Rafal (1982) reported an experiment where the cue predicted either the same or the opposite position of target appearance. The authors’ main conclusion was that the appearance of the cue produced an early facilitatory effect even though the cue predicted the target to appear at the opposite location. However, they did not take into account that the inhibitory effect (IOR) was also observed when the target appeared at the position to which participants were attending (as was predicted by the cue). Recently, Lupiánez et al. (2004) employed a similar experimental setting and compared RTs to targets appearing at cued versus uncued positions at endogenously attended locations (i.e., cued location trials in a 80% valid condition and uncued location trials in a 20% valid condition). The main result that emerged from this study was that IOR was consistently found at the endogenously attended location. Additionally, a similar IOR effect was also observed when the target appeared at an unexpected location (i.e., cued location trials in the 20% valid condition vs. uncued location trials in the 80% valid condition). Thus, IOR appeared in both endogenously expected and unexpected locations.

Similar findings emerged from the reanalysis (Lupiánez et al., 2004) of the results of a previous study by Bartolomeo, Sieroﬀ, Decaix, and Chokron (2001) exploring performance of normal individuals and of patients with left unilateral neglect. These patients showed a lack of IOR for right, ipsilesional targets, conﬁrming previous ﬁndings (Bartolomeo, Chokron, & Sieroﬀ, 1999; see also Vivas, Humphreys, & Fuentes, 2003). This result is also consistent with the idea that these patients’ attention is biased towards right, ipsilesional objects (Bartolomeo & Chokron, 2002). Lupiánez et al.’s (2004) reanalysis of Bartolomeo et al.’s results demonstrated that the lack of IOR was present for both expected and unexpected right-sided targets.

In summary, previous research has shown that it is possible to observe cueing effects (speciﬁcally IOR at long cue–target intervals) at a position were attention is being maintained voluntarily (by means of instructions to attend to a position related to a peripheral, Berlucchi et al., 2000; Berlucchi et al., 1989; Lupiánez et al., 2004, or a central cue, Berger et al., 2005).

In the present study, we attempted further to dissociate endogenous and exogenous orienting of spatial attention using the same set of stimuli. As in Lupiánez et al.’s (2004) study, an informative peripheral cue was used, which predicted, in each block of trials, either the same or the opposite position of target appearance (see Procedure section for details). Crucially, with this manipulation, expected and unexpected positions could be either cued or uncued. If IOR is observed at the position predicted by the cue (at which attention is supposed to be allocated), this effect would
be difficult to explain as the inhibition of the return of attention to the cued location (because no return of attention is supposed to take place in this condition).

A second aim of the present study was to investigate the time course of cueing effects (facilitation followed by IOR) in detection and discrimination tasks. It has been shown that IOR appears later in discrimination than in detection tasks (Lupiáñez, Milán, Tornay, Madrid, & Tudela, 1997). Klein (2000) proposed that these differences might be due to a later disengagement of attention in discrimination than in detection tasks. He argued that discrimination tasks are more difficult than detection tasks, and as such they demand a more effortful set for the processing of the target. Furthermore, it would be very difficult to adopt and implement a different set for the processing of the cue and target when they are presented very close in time. For that reason, in cueing discrimination tasks, the author proposed that more attentional resources would be allocated to the processing of the cue, and thus the disengagement of attention from the cued location would take longer than in detection tasks. This would delay the occurrence of IOR in discrimination tasks, as compared to detection tasks. In the paradigm used here, the allocation of endogenous attention is controlled by the predictiveness of the cue. At the expected location, no disengagement of attention is supposed to occur, whereas at the unexpected location attention should be disengaged, at least at long enough SOAs. If the time course differences in cueing effects between detection and discrimination tasks are due to differences in the disengagement of attention, no such differences should be found with our procedure.

If the results of the present series of experiments show that IOR can be observed at the attended location and/or if IOR still appears later in the discrimination than in the detection task, it could be argued that these effects cannot be solely explained by the orienting disengagement of attention. Instead, one would have to invoke other processes, perhaps related to the presence or absence of an object (the cue) before the onset of the target (Lupiáñez et al., 2004; Milliken, Tipper, Houghton, & Lupiáñez, 2000).

EXPERIMENT 1

An informative peripheral cue was presented that could predict (with 75% validity) in each block of trials, either the same or the opposite position of target appearance. With this manipulation, both expected and unexpected locations can be either cued or uncued, making it possible to dissociate endogenous and exogenous orienting of attention using the same set of stimuli. Two SOAs (100–1,000 ms) were used, in order to study both facilitation, normally observed at short SOAs, and IOR, usually observed at longer SOAs. Detection and discrimination tasks were used, in order to compare the cueing effect at expected and unexpected locations in both tasks.

Method

Participants
A total of 48 psychology students from the Faculty of Psychology of the University of Granada participated in this experiment (24 performed the detection, and 24 the discrimination task). The average age of the participants was 20 years. All of the participants reported to have normal or corrected-to-normal vision, were naïve as to the purpose of the experiment, and participated voluntarily for course credits.

Apparatus and stimuli
The stimuli were presented on a 15-in. colour VGA monitor. An IBM-compatible PC running MEL2 software (Schneider, 1988) controlled the presentation of stimuli, timing operations, and data collection. The participants sat 57 cm from the monitor with their head resting on a chinrest. At the beginning of each trial a fixation point (a plus sign) was displayed at the centre of the screen, on a black background. Two grey boxes (17 mm in height by 14 mm in width) were displayed to the left and right of fixation. The inner edge of each box was 77 mm from fixation.
As the orientation cue, one of the boxes flickered (turned to white) for 50 ms, giving the impression of a brief flash. The target was either a red or a yellow asterisk appearing at the centre of one of the boxes. A 400-Hz sound, 100 ms in duration, was used to provide response feedback.

**Procedure**

A fixation point (plus sign) and two boxes (to the left and right of fixation) were displayed at the beginning of each trial. The peripheral cue appeared 1,000 ms later, for 50 ms. After a random variable SOA (100–1,000 ms) the target was presented. It could be either a red or a yellow asterisk presented at the centre of one of the boxes for 33 ms. If no response was made after 1,800 ms or the wrong response was made, auditory feedback was provided for 100 ms. The intertrial interval (on which the screen remained in black) was 1,000 ms duration.

On 20% of the trials (catch trials) no target was presented, and no response was required. On the remaining 80% of the trials a target was presented, and the participants were asked to detect the target or to discriminate its colour (depending on the experimental group). In the detection task the participants were instructed to press the “m” or “z” key on a keyboard as soon as they saw the asterisk (independently of its colour), while in the discrimination task, the participants were asked to press one of the keys when the asterisk was red and the other key when it was yellow (the response mapping was counterbalanced across participants).

The experiment consisted of two blocks of trials. In one of them, the cue predicted the likely position of target appearance on 75% of trials (i.e., in 75% of the trials the target appeared at the same position as the cue). These were expected trials (because the target appeared where the participants were expecting it to appear) and cued trials (because the cue and target appeared at the same position). However, in the remaining 25% of the trials, the target appeared at the opposite location to that of the cue. These were unexpected trials (because the target did not appear at the position predicted by the cue) and uncued trials (because the cue and target appeared at different locations). In the other block of trials, the cue predicted the target to appear at the opposite position on 75% of the trials. Thus, when the target was presented at the position opposite to the cue, these were expected but uncued trials. However, when the cue and target were presented at the same position (25% of trials), these were unexpected and cued trials. The order of blocks was counterbalanced across participants. The participants were informed about the most likely location of target appearance at the beginning of each trial and were encouraged to take this information into account. The task lasted about 45 minutes, and the participants were allowed to take a short break after every 36 trials.

**Design**

The experiment had a 2(task) × 2(expectancy) × 2(cueing) × 2(SOA) design, with the first variable being manipulated between participants, and the remaining three variables being manipulated within participants. Task had two levels: detection and discrimination tasks. Expectancy had two levels: expected and unexpected location trials.1 Cueing had two levels: cued and uncued location trials. Finally, SOA had two levels: 100 and 1,000 ms.

The experiment consisted of two series of three experimental blocks of 72 trials. Each series was preceded by a practice block of 36 trials. There were a total of 432 experimental trials. For each experimental condition of cueing and SOA, there were 81 observations for expected trials and 27 for unexpected trials.

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1 Note that expected trials refer to expected cued trials in one block (where the cue predicts that the target would appear at the same position), and expected uncued trials in the other block (where the cue predicts that the target would appear at the location opposite to the cue). Similarly, unexpected trials refer to unexpected uncued trials in one block (where the cue predicts that the target would appear at the same position), and unexpected cued trials in the other block (where the cue predicts that the target would appear at the location opposite to the cue).
Results

Responses to catch trials (false alarms) were 5.1% of the trials in the detection task and 3.1% in the discrimination task. Trials on which no response was made (misses) were 1.7% and 1.5% of trials in the detection and discrimination task, respectively. In the discrimination task, incorrect responses (7.06%) were discarded from the RT analysis. Finally, trials with responses faster than 100 ms or slower than 1,200 ms were also removed from the RT analysis, which discarded 0.44% and 1.34% of trials in the detection and discrimination task, respectively.

As opposite cueing effects (facilitation vs. IOR) were expected for the short and long SOA, two separate analyses of variance (ANOVAs) with the factors 2(task) × 2 (expectancy) × 2 (cueing) were performed, one for each SOA condition, in order to explore the effect of task, expectancy, and cueing separately for the short and long SOA (see Table 1).

SOA 100 ms

The analysis of the mean RTs showed a significant main effect of task, $F(1, 46) = 98.79, \text{MSE} = 15,732, p < .0001$, with RT being faster in the detection ($M = 436$ ms) than in the discrimination task ($M = 616$ ms). The expectancy effect was significant, $F(1, 46) = 39.88, \text{MSE} = 342, p < .0001$, with participants responding faster when the target was presented at the expected position ($M = 518$ ms) than at the unexpected position ($M = 535$ ms), revealing that they were able to voluntarily orient their attention to the expected location with an SOA as short as 100 ms. The interaction between cueing and task was significant, $F(1, 46) = 13.77, \text{MSE} = 787, p < .001$, while in the detection task, a marginally significant IOR effect was shown, $F(1, 46) = 3.21, \text{MSE} = 787, p = .07$. The interaction between expectancy, cueing, and task was significant, $F(1, 46) = 6.32, \text{MSE} = 2,235, p = .01$, revealing that, at the expected location, no cueing effect appeared in either the detection or the discrimination task, $F < 1$. However, at the unexpected location, the cueing effect was different in the detection and the discrimination task, $F(1, 46) = 12.15, \text{MSE} = 2,140, p < .001$, with a significant facilitatory effect being observed in the discrimination task, $F(1, 46) = 7.13, \text{MSE} = 2,140, p < .01$, while a significant IOR effect was observed in the detection task, $F(1, 46) = 5.10, \text{MSE} = 2,140, p < .05$.

SOA 1,000 ms

The analysis of the mean RTs revealed significant main effects of task, $F(1, 46) = 126.18, \text{MSE} = 14,834, p < .0001$, and expectancy, $F(1, 46) = 15.94, \text{MSE} = 514, p < .001$, with participants responding faster when the target was presented at the expected position ($M = 518$ ms) than at the unexpected position ($M = 535$ ms), revealing that they were able to voluntarily orient their attention to the expected location with an SOA as short as 100 ms. The interaction between cueing and task was significant, $F(1, 46) = 39.88, \text{MSE} = 342, p < .001$, while in the detection task, a marginally significant IOR effect was shown, $F(1, 46) = 3.21, \text{MSE} = 787, p = .07$. The interaction between expectancy, cueing, and task was significant, $F(1, 46) = 6.32, \text{MSE} = 2,235, p = .01$, revealing that, at the expected location, no cueing effect appeared in either the detection or the discrimination task, $F < 1$. However, at the unexpected location, the cueing effect was different in the detection and the discrimination task, $F(1, 46) = 12.15, \text{MSE} = 2,140, p < .001$, with a significant facilitatory effect being observed in the discrimination task, $F(1, 46) = 7.13, \text{MSE} = 2,140, p < .01$, while a significant IOR effect was observed in the detection task, $F(1, 46) = 5.10, \text{MSE} = 2,140, p < .05$.

Table 1. Mean reaction time* and percentage of incorrect responses in the discrimination task in Experiment 1, as a function of cueing, stimulus onset asynchrony, task, and expectancy

<table>
<thead>
<tr>
<th></th>
<th>Detection task</th>
<th>Discrimination task</th>
<th>Detection task</th>
<th>Discrimination task</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Expected</td>
<td>Unexpected</td>
<td>Expected</td>
<td>Unexpected</td>
</tr>
<tr>
<td>Cued</td>
<td>RT</td>
<td>422</td>
<td>607 (6.0)</td>
<td>606 (8.4)</td>
</tr>
<tr>
<td></td>
<td>RT</td>
<td>432</td>
<td>614 (6.0)</td>
<td>641 (7.2)</td>
</tr>
<tr>
<td>Mean cueing effect</td>
<td>−10</td>
<td>7</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Uncued</td>
<td>RT</td>
<td>432</td>
<td>614 (6.0)</td>
<td>641 (7.2)</td>
</tr>
<tr>
<td></td>
<td>RT</td>
<td>382</td>
<td>581 (5.9)</td>
<td>600 (8.1)</td>
</tr>
<tr>
<td>Mean cueing effect</td>
<td>−30</td>
<td>−54</td>
<td>−30</td>
<td></td>
</tr>
</tbody>
</table>

Note: Percentages of incorrect responses are in parentheses. The bottom row shows the mean cueing effect for each condition. The headings 100 and 1,000 denote stimulus onset asynchrony (SOA), in ms. RT = reaction time.

*aIn ms.
responding faster in the detection task and at the expected ($M = 496$ ms) than at the unexpected location ($M = 509$ ms) overall. The cueing effect also reached significance, $F(1, 46) = 53.99$, $MSE = 926$, $p < .0001$, and interacted with task, $F(1, 46) = 5.38$, $MSE = 926$, $p < .05$, showing a significant IOR effect both in the detection, $F(1, 46) = 46.73$, $MSE = 926$, $p < .0001$, and in the discrimination task, $F(1, 46) = 12.64$, $MSE = 926$, $p < .001$, although the effect was larger in the former. Expectancy did not interact with cueing, $F < 1$, but the interaction between task, expectancy, and cueing was marginally significant, $F(1, 46) = 3.48$, $MSE = 1,340$, $p = .06$. This interaction showed that, although the IOR effect was significant in both expected and unexpected locations, $F(1, 46) = 29.47$, $MSE = 739$, $p < .0001$, and $F(1, 46) = 18.62$, $MSE = 1,527$, $p < .0001$, respectively, at the expected location, the IOR effect was similar in magnitude in the detection and the discrimination tasks, $F < 1$. However, at the unexpected location, IOR was larger in the detection (mean cueing effect, defined as the mean RT difference between uncued and cued trials, $-54$ ms) than in the discrimination task (mean cueing effect $-14$ ms), $F(1, 46) = 6.32$, $MSE = 1,527$, $p < .01$ (see Figure 1).

The mean error data in the discrimination task were submitted an ANOVA with the factors 2(expectancy) × 2(cueing) × 2(SOA). In this analysis only the main effect of expectancy reached significance, $F(1, 23) = 5.66$, $MSE = .001$, $p < .05$, with participants’ responses being more accurate for expected ($M = .06$) than for unexpected location trials ($M = .07$).

**Discussion**

The results of the present experiment show that participants are able to attend to the likely position predicted by the cue, since the effect of expectancy reached significance at a SOA as short as 100 ms. At this short SOA, when the target appeared at the expected location, no cueing effect was observed either in the detection or in the discrimination task. However, when the target was presented at an unexpected position, a facilitatory effect appeared in the discrimination task, while an IOR effect was observed in the detection task. At the longer SOA, a significant IOR effect appeared at both the expected and the unexpected location. At the expected location, this IOR effect was similar in magnitude for the detection and discrimination tasks. However, at the unexpected location, the IOR effect was larger in the detection than in the discrimination task.

These results clearly differ from those predicted by the reorienting hypothesis of IOR. If IOR is a mechanism that inhibits the returning of attention to a previously attended position, no IOR effect should be observed until attention is disengaged from the cued location. At the expected location, since attention has not been disengaged, no IOR effect is supposed to occur. However, in the present experiment, IOR was observed at the expected location in both the detection and the discrimination task.

An important result that emerged from this experiment was that at the expected location, the detection and discrimination tasks yielded similar IOR effects, whereas, at the unexpected location, IOR was larger in the detection than in the discrimination task. Experiment 2 was designed in order to replicate the results of Experiment 1 and to study the temporal course of cueing effects in detection and discrimination tasks while controlling the locus of endogenous orienting of attention.

![Figure 1. Mean reaction time (RT, in ms) for cued and uncued trials, in Experiment 1, as a function of expectancy, task, and stimulus onset asynchrony (SOA).](image-url)
EXPERIMENT 2

This experiment was designed to confirm the results of Experiment 1, in which we demonstrated that IOR can be observed at both expected and unexpected peripheral cue. A further aim of Experiment 2 was to study the time course of cueing effects across SOAs in both detection and discrimination tasks. For this purpose, SOA was manipulated at four levels: 100, 300, 500, and 700 ms. Previous research has shown that the time course of cueing effects is different in detection and discrimination tasks (Lupiáñez et al., 1997). As described in the Introduction, the “later disengagement” hypothesis (Klein, 2000) proposes that, as discrimination tasks are more difficult than detection tasks, once attention is engaged at the cued location, the disengagement of attention from that position requires a longer period of time than in detection tasks. As a consequence, IOR is observed at longer SOAs. With our paradigm, the allocation of attention is controlled by the predictivity of the cue, so attention is held at the expected location (or disengaged from the unexpected location). If cueing effects between detection and discrimination tasks show the same time course differences, the explanation that attention is disengaged later from the cued location in discrimination than in detection tasks cannot hold, as the disengagement of attention is being controlled and measured by the expectancy effect.

Method

Participants
A total of 40 psychology students from the Faculty of Psychology and the Faculty of Physical Education and Sport Sciences of the University of Granada participated in this experiment (20 for the detection and 20 for the discrimination task), 22 women and 18 men. A total of 38 of the participants were right-handed, 1 left-handed, and 1 ambidextrous by self-report. The average age of the participants was 20 years, and all reported to have normal or corrected-to-normal vision. They were naïve as to the purpose of the experiment and participated voluntarily for course credits.

Apparatus and stimuli
Apparatus and stimuli were the same as those in Experiment 1, with the following exceptions: An IBM-compatible PC running E-prime software (Schneider, Eschman, & Zuccolotto, 2002) controlled the presentation of stimuli, timing operations, and data collection. As an orientation cue, the contour of one of the boxes briefly thickened, giving the impression of a flash. When participants made a mistake, a 1997-Hz sound occurred for 50 ms.

Procedure
The procedure was the same as that in Experiment 1, except that the SOA variable had four levels: 100, 300, 500, and 700 ms.

Design
The experiment had a 2(task) × 2(expectancy) × 2(cueing) × 4(SOA) design, with the first variable being manipulated between participants, and the remaining three variables being manipulated within participants. Task had two levels: detection and discrimination. Expectancy had two levels: expected and unexpected location trials. Cueing had two levels: cued and uncued location trials. Finally, SOA had 4 levels: 100, 300, 500, and 700 ms.

The experiment consisted of two experimental blocks of 320 trials, each being preceded by a practice block of 24 trials. For each experimental condition of cueing and SOA, there were 48 observations for expected trials and 16 for unexpected trials.

Results
False alarms accounted for 0.59% and 0.17% of trials in the detection and discrimination task, respectively. Misses were 0.88% of trials in the detection and 0.17% in the discrimination task. In the discrimination task, trials with an incorrect
The main effects of task and SOA were significant. The interactions between cueing and SOA and between cueing and task were also significant. The interaction between cueing and SOA was significant.

To this aim, two repeated-measures ANOVAs were performed, one for the expected and the other for the unexpected location trials. The first variable was manipulated between participants, while the remaining three variables were manipulated within participants (see Table 2). As in the previous experiment, the RT analysis revealed a significant main effect of task, $F(1, 38) = 105.54$, $MSE = 47,641$, $p < .0001$, expectancy, $F(1, 38) = 63.81$, $MSE = 763$, $p < .0001$, cueing, $F(1, 38) = 5.64$, $MSE = 1,145$, $p < .05$, and SOA, $F(3, 114) = 45.91$, $MSE = 846$, $p < .0001$. The interaction between cueing and task was also significant, $F(1, 38) = 19.35$, $MSE = 22,149$, $p < .0001$, as was the interaction between cueing and SOA, $F(3, 114) = 9.73$, $MSE = 763$, $p < .0001$. Importantly, expectancy and cueing again did not interact, $p > .1$, the cueing effect being −7 ms at the expected position and −5 ms at the unexpected position.

In order to test the later disengagement hypothesis about IOR (which postulates that IOR appears later in discrimination than in detection tasks because attention is disengaged later in both tasks at the time course of cueing effects in the cued location), it is important to analyse the time course of cueing effects in both tasks at the expected location (where attention is not supposed to be disengaged in either task) and at the unexpected location (where attention is supposed to be disengaged in both tasks). To this aim, two repeated-measures ANOVAs were performed, one for the expected and the other for the unexpected location trials. The first variable was manipulated between participants, while the remaining three variables were manipulated within participants (see Table 2). As in the previous experiment, the RT analysis revealed a significant main effect of task, $F(1, 38) = 105.54$, $MSE = 47,641$, $p < .0001$, expectancy, $F(1, 38) = 63.81$, $MSE = 763$, $p < .0001$, cueing, $F(1, 38) = 5.64$, $MSE = 1,145$, $p < .05$, and SOA, $F(3, 114) = 45.91$, $MSE = 846$, $p < .0001$. The interaction between cueing and task was also significant, $F(1, 38) = 19.35$, $MSE = 22,149$, $p < .0001$, as was the interaction between cueing and SOA, $F(3, 114) = 9.73$, $MSE = 763$, $p < .0001$. Importantly, expectancy and cueing again did not interact, $p > .1$, the cueing effect being −7 ms at the expected position and −5 ms at the unexpected position.

Table 2. Mean RT* and percentage of incorrect responses in the discrimination task in Experiment 2, as a function of cueing, expectancy, task, and stimulus onset asynchrony

<table>
<thead>
<tr>
<th>Task</th>
<th>Cueing</th>
<th>Detection</th>
<th>Discrimination</th>
<th>Expected</th>
<th>Unexpected</th>
<th>Detection</th>
<th>Discrimination</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>100</td>
<td>300</td>
<td>500</td>
<td>700</td>
<td>100</td>
<td>300</td>
</tr>
<tr>
<td>Cued</td>
<td>RT</td>
<td>371</td>
<td>336</td>
<td>343</td>
<td>365</td>
<td>537</td>
<td>505</td>
</tr>
<tr>
<td>Uncued</td>
<td>RT</td>
<td>364</td>
<td>326</td>
<td>321</td>
<td>334</td>
<td>552</td>
<td>516</td>
</tr>
<tr>
<td>Mean cueing effect</td>
<td>−7</td>
<td>−10</td>
<td>−22</td>
<td>−31</td>
<td>15</td>
<td>11</td>
<td>−4</td>
</tr>
</tbody>
</table>

Note: Percentages of incorrect responses are in parentheses. The bottom row shows the mean cueing effect for each condition. The headings 100, 300, 500, and 700 denote stimulus onset asynchrony (SOA), in ms. RT = reaction time.

*In ms.
was not significant, $F < 1$, showing that the cueing effect became more negative (or less positive) across SOA in both the detection and the discrimination task. The absence of Task × Cueing × SOA interaction can be taken as an indication that the orienting of attention was controlled, since the same attentional orienting (Cueing × SOA interaction) occurred in both tasks. However, in the detection task, IOR reached significance beginning at the 500-ms SOA, $F(1, 38) = 9.54$, $MSE = 497$, $p < .005$, while in the discrimination task, no cueing effect appeared at the 500-ms SOA, $F < 1$, with IOR being only observed at the 700-ms SOA, $F(1, 38) = 4.80$, $MSE = 428$, $p < .05$ (see Figure 2).

Thus, at the expected location (where attention is not supposed to be disengaged), IOR still appears, and it still does so later in the discrimination than in the detection task.

**Unexpected location**

Again, the main effects of task and SOA were significant. Significant interactions between cueing and SOA and between cueing and task were also observed. Once again, the cueing effect became more negative (or less positive) across SOAs in both the detection and the discrimination task, as can be observed in the absence of Task × Cueing × SOA interaction, $F < 1$. However, IOR was observed beginning at the 500-ms SOA in the detection task, $F(1, 38) = 10.42$, $MSE = 1,134$, $p < .005$, while, in the discrimination task, no IOR appeared even at the 700-ms SOA, $F < 1$.

The mean error data in the discrimination task were submitted to a repeated measures ANOVA, with the following factors: expectancy(2), cueing(2), and SOA(4). In this analysis, only the cueing effect reached significance, $F(1, 38) = 7.55$, $MSE = 0.002$, $p < .05$, with responses being more accurate for cued ($M = .04$) than for uncued ($M = .06$) trials overall.

**Discussion**

In Experiment 2, as in the previous experiment, participants were able to attend to the likely position predicted by the cue, which can be measured by a main effect of expectancy. However, at a long enough SOA (700 ms), IOR did occur at the expected location (where attention was being voluntarily allocated) in both detection and discrimination tasks. This IOR effect is difficult to explain by the inhibition of the return of attention to that position, as attention is supposed to be endogenously maintained there.

Concerning the differences in the time course of cueing effects in detection and discrimination tasks, the present results showed that IOR still appears later in the discrimination than in the detection task, even when the orienting of attention is controlled. This result is opposite to the prediction of the later disengagement hypothesis, which postulates that IOR is observed later in discrimination tasks because attention is disengaged later from the cued location than it is in detection tasks. With our paradigm, we controlled the allocation of attention at the position predicted by the cue, so the differences in the time course of cueing effects between the detection and discrimination tasks cannot be explained, at least in the present experiment, by factors related to the disengagement of attention from the cued location.

As in the previous experiment, cueing effects in detection and discrimination tasks were more similar at the expected location than at the unexpected location. At long SOAs (more than 500 ms), when the target appeared at the position predicted by the cue, IOR was observed in both
the detection and the discrimination task. A planned comparison revealed that, at the expected location, the IOR effect was not significantly different between tasks, \( p > .05 \). However, when the target was presented at an unexpected position, the cueing effect was different in both tasks, \( p < .05 \), with IOR being observed in the detection task but not in the discrimination task.

**EXPERIMENT 3**

Could IOR be further delayed when participants are asked to discriminate targets appearing at an unexpected location? To test this possibility, we conducted a further experiment, with a larger range of SOAs: 100, 400, 700, and 1,000 ms.

**Method**

**Participants**

A total of 40 psychology students from the Faculty of Psychology and the Faculty of Physical Education and Sport Sciences of the University of Granada participated in this experiment (20 for the detection and 20 for the discrimination task), 29 women and 11 men. A total of 36 of the participants were right-handed, 3 left-handed, and 1 ambidextrous by self-report. The average age of the participants was 20 years. All of them reported to have normal or corrected-to-normal vision, were unaware of the purpose of the experiment, and participated voluntarily for course credits.

**Apparatus, stimuli, procedure, and design**

The apparatus, stimuli, set-up, procedure, and design were the same as those in Experiment 2, with the exception of the SOA variable, which was manipulated at four different levels: 100, 400, 700, or 1,000 ms.

**Results**

False alarms accounted for 0.97% of trials in the detection task and 0.89% in the discrimination task. Responses to catch trials were 0.52% and 0.50% of trials in the detection and discrimination task, respectively. Responses faster than 100 ms and slower than 1,200 ms were also excluded from the RT analysis, which discarded a further 0.95% and 0.50% of trials in the detection and the discrimination task, respectively. Finally, trials with an incorrect response in the discrimination task (4.03%) were also removed from the RT analysis.

The mean RT data were submitted to a mixed ANOVA, with the factors task(2), expectancy(2), cueing(2), and SOA(4). Table 3 shows the mean RT and mean error data for each experimental condition. The analysis showed a significant main effects of task, \( F(1, 38) = 115.51, MSE = 44,349, p < .0001 \), expectancy, \( F(1, 38) = 94.65, MSE = 693, p < .0001 \), cueing, \( F(1, 38) = 37.13, MSE = 976, p < .0001 \), and SOA, \( F(3, 114) = 38.76, MSE = 669, p < .0001 \). The interactions between cueing and SOA, \( F(1, 38) = 11.52, MSE = 336, p < .0001 \), and cueing and task, \( F(1, 38) = 21.94, MSE = 976, p < .0001 \), were significant. Once again, the interaction between expectancy and cueing was not significant. However, the interaction between expectancy, cueing, and task was marginally significant, \( F(1, 38) = 3.54, MSE = 2,470, p = .06 \). Importantly, this interaction showed that at the expected location, the cueing effect in the detection and discrimination task did not differ, \( F(1, 38) = 1.14, MSE = 1,213, p = .29 \). However, at the unexpected location, the cueing effect differed between tasks, \( F(1, 38) = 12.89, MSE = 2,231, p < .001 \). IOR occurred in the detection task, \( F(1, 38) = 23.04, MSE = 2,231, p < .0001 \), but not in the discrimination task, \( F < .1 \) (see Figure 3).

In order to test the later disengagement hypothesis, separate ANOVAs were carried out, for the expected and unexpected location, with the following factors: Task(2) × Cueing(2) × SOA(4).

**Expected location**

The analysis revealed significant main effects of task and SOA. The interaction between cueing and SOA was also significant. Again, the
interaction between task, cueing, and SOA was not significant. However, IOR was observed from the 400-ms SOA in the detection task, $F(1, 38) = 9.65, MSE = 652, p < .005$, while in the discrimination task, no cueing effect appeared at the 400-ms SOA, $F(1, 38) = 1.72, MSE = 652, p = .19$, with IOR being observed beginning at the 700-ms SOA, $F(1, 38) = 6.26, MSE = 494, p < .05$.

**Unexpected location**

The main effects of task and SOA were again significant, and the interaction between cueing and SOA was borderline significant, $F(3, 114) = 2.64, MSE = 524, p = .05$. Cueing also interacted with task. Once again, the interaction between task, cueing, and SOA was not significant, $F < 1$. However, in the detection task, IOR was observed beginning at the 100-ms SOA, $F(1, 38) = 6.22, MSE = 1,028, p < .05$, whereas, in the discrimination task, no such cueing effect was observed even at the 1,000-ms SOA, $F < 1$.

The mean error data in the discrimination task were initially submitted to a repeated measures ANOVA, with the factors task(2), expectancy(2), cueing(2), and SOA(4). In this analysis, only the expectancy effect reached significance, $F(1, 38) = 5.00, MSE = 0.002, p < .01$, with the participants being more accurate when the target appeared at the expected position ($M = .04$) than when it appeared at the unexpected position ($M = .06$).
Discussion

Experiment 3 replicated the results from Experiments 1 and 2. IOR was again observed at the expected location in both the detection and the discrimination task. At this expected location, IOR appeared for SOAs greater than 400 ms in the detection task, while in the discrimination task no cueing effect was observed at the 400-ms SOA, with IOR being observed for SOAs greater than 700 ms. At the unexpected location, IOR appeared from the shortest SOA in the detection task, while this effect did not reach significance in the discrimination task, even at the longest SOA. Thus, as shown by the interaction between expectancy, cueing, and task, which approached significance, at the expected location, the cueing effects were similar in the detection and the discrimination task. However, at the unexpected location, a more negative cueing effect was observed in the detection than in the discrimination task.

GENERAL DISCUSSION

In the present series of experiments endogenous and exogenous orienting have been dissociated using the same set of stimuli. An informative peripheral cue was used, which predicted, in each block of trials, that the target would appear at either the same or the opposite position to the cue. Crucially, both expected and unexpected locations were either cued or uncued. The results revealed that the expectancy effect was significant at all the SOAs used here, showing that participants were able to attend to the position predicted by the cue. As noted above, if participants were already attending to the position predicted by the cue, no disengagement of attention from that location was supposed to occur when the target appeared at this position (expected location trials). However, in the three experiments reported here, IOR was observed at the expected location, both in the detection and the discrimination task. This result argues against the reorienting hypothesis (Posner & Cohen, 1984), which predicts no IOR effect until attention leaves the cued location (see Klein, 2000, p. 139, line 22).

It could be argued that endogenous attention was not completely engaged in the expected location as the cue was not 100% predictive of target’s appearance. In support of this idea, it has been demonstrated that attentional capture (i.e., facilitatory effects) can be overridden by 100% informative cues, but not by 80% informative cues (Yantis & Jonides, 1990). However, in Berlucchi et al.’s (1989) experiment, although participants knew in advance where the target would appear (as it was presented at the same spatial position on all trials within a block), IOR was still observed at the expected location. In the experiments presented here (75% informative cue) we cannot be sure that attention was completely oriented endogenously at the expected location (as it might be using a 100% informative cue). Moreover, we reckon that attention might be always more oriented to the position predicted by the cue (expected location) than to the opposite location (unexpected location). Nevertheless, Experiments 2 and 3 showed that in the discrimination task IOR was observed at the expected location, but not at the unexpected location. Thus, it can be concluded, at least concerning the present experiments, that attentional disengagement from the cued location is not necessary to observe IOR.

Moreover, given that the predictivity of the cue was manipulated between blocks of trials, one might wonder whether the expectancy effect observed in the three experiments actually reflects the orienting of attention. Note that, within a block of trials, one type of trial was more frequent than the others, which might have elicited other processes than the orienting of attention. For instance, in the block where the cue predicted the target to appear at the opposite location, the participants would have been habituated to a stimulation pattern consisting of the cue and target appearing at opposite locations. A target appearing at the same location as the cue would have broken this pattern, increasing RT on those trials, resulting in an “expectancy effect”. However, we have shown elsewhere that the
same pattern of results emerges when the expectancy is manipulated within a block of trials (Chica & Lupiáñez, 2004). In that study, the central fixation point (a “+” or “−” sign) informed the participants regarding the predictivity of the upcoming peripheral cue. When the fixation point was a “+” sign, the peripheral cue predicted the target to appear at the same location (75%). In contrast, when the fixation point was a “−” sign, the peripheral cue predicted (75%) the target to appear at the opposite location. Therefore, all kinds of cue–target combinations were equally frequent. The only way to account for the expectancy effect that was observed in our study is to assume that participants were taking into account the information provided by the fixation point and orienting attention according to it, either to the same location as the cue or to the opposite location. As in the experiments presented here, the results of Chica and Lupiáñez showed that IOR can be observed at endogenously attended locations, from where attention is not supposed to be disengaged.

The second important aim of the present study was to test the later disengagement hypothesis—that is, the later appearance of IOR in discrimination than in detection tasks (Klein, 2000). According to this hypothesis, since discrimination tasks are more difficult than detection tasks, more attentional resources are needed for the processing of the target. Klein proposed that it would be difficult to implement a different set for the processing of the cue and target, since they are normally presented very close in time. Thus, more attentional resources are also allocated to the processing of the cue when discrimination instead of detection tasks are used. As a consequence, the disengagement of attention from the cued location occurs later, and IOR is observed later in discrimination than in detection tasks.

The results of Experiments 2 and 3, in which orienting of attention was controlled (in both tasks, attention could be allocated either to the position predicted by the cue or to the opposite location), showed that IOR still appears later in discrimination than in detection tasks, especially in unexpected location trials, in which attention is already disengaged from the cued location when the target appears. It is important to note that the interaction Task × Cueing × SOA did not approach significance (in either experiment). This can be taken as an indication that the orienting of attention was controlled, since the same orienting of attention (Cueing × SOA interaction) appeared in the two tasks (Lupiáñez, Milliken, Solano, Weaver, & Tipper, 2001). In expected location trials, attention was allocated to the position predicted by the cue (i.e., no disengagement of attention from that location is supposed to occur when the target appears). At the unexpected location, attention is supposed to be disengaged already from the cued location when the target appears. However, at both the expected and the unexpected location, IOR appeared later in the discrimination than in the detection task. Therefore, the time course differences between the detection and the discrimination task observed in these experiments cannot be explained solely by attention being disengaged later from the cued location in the discrimination than in the detection task.

The present results (i.e., IOR at the expected location and IOR appearing later in the discrimination than in the detection task) are difficult to explain solely by the orienting of attention, the disengagement from the cued location, and the subsequent inhibition of the return of attention. Alternatively, we propose that the appearance of a cue shortly before the target can capture spatial attention so that it is oriented to its position, but other perceptual processes can also affect the processing of the subsequent target (see e.g., Handy, Jha, & Mangun, 1999; Hawkins, Hillyard, Luck, & Mouloua, 1990; Li & Lin, 2002). When the cue appears, it is encoded as a new perceptual event, and this is why it captures attention. If the target is presented shortly after the cue, at the same spatial position, it is possible to encode the two objects as the same perceptual event (Kahneman, Treisman, & Gibbs, 1992; Lupiáñez et al., 2001). This would lead to a facilitatory effect at short cue–target SOAs. However, at a longer SOA, if the target appears at the same position as the cue, the perceptual analysis of the
cue would have finished, and no integration within
the same perceptual event will occur. Alternatively,
the target could be labelled as an “old” object,
since that position has not been recently analysed
and therefore will benefit from attentional capture.
This would lead to a faster processing of the target
at uncued locations (i.e., IOR). Thus, IOR is not
conceived as the inhibition of orienting attention to
the cued location, but as the loss of advantage for
objects appearing at “old” (previously cued) locations
(Milliken et al., 2000).

In addition, the analysis of the cue and its influence
on target processing could be different when
detection and discrimination tasks are used.
Lupiañez et al. (2004) proposed that when
performing a detection task, the most important
process might be to dissociate the new object
(the target) from the previous one (the cue).
Thus, participants would need to implement a
set to dissociate events. For that reason, the
presence of an object before the target usually
produces a “detection cost” for very short SOAs.
However, when performing a discrimination
task, it is not as important to dissociate events as
it is to analyse the features of the target required
to select the appropriate response. Here, the presence
of the cue before the target might facilitate
its discrimination, by helping to select the spatial
position where the analysis of the features is
going to occur. This “spatial selection benefit”
finishes when the analysis of the cue is completed,
giving rise to a later appearance of IOR in discrimina-
tion than in detection tasks.

In Experiments 1 and 3, IOR was observed at
the unexpected location at a SOA as short as
100 ms. Although this result is not common in
cueing studies (Lupiañez et al., 1997, 2001;
Posner & Cohen, 1984), Danziger and
Kingstone (1999) obtained similar results using a
cueing paradigm with four possible locations. In
Danziger and Kingstone’s experiment, the cue
was presented in one of the locations, and the
participants were told to attend to the clockwise
position related to its location. With this manipu-
lation, IOR was found at a SOA as short as 50 ms.
The authors proposed that, in a typical cueing
paradigm (e.g., Posner & Cohen, 1984), the
IOR effect at short SOAs is masked by the orient-
ing of attention to the peripheral cued location:
When the cue appears, attention is automatically
summoned to its position (Posner et al., 1982).
But if the cue predicts that the target would
appear at another location, attention quickly
moves away from that position. Thus, when the
target appears at the cued location, a cost in per-
formance (IOR) is observed. However, Danziger
and Kingstone’s results can also be explained by
factors related to the perceptual analysis of the
cue. As the cue predicted a clockwise position,
its perceptual analysis would have to be fast, in
order to start the analysis of the target at the
other location. This would lead to an early appear-
ance of IOR, since the cued location becomes “old”
when the analysis of the cue finishes. This result is
observed more in detection than in discrimination
tasks, as IOR was observed from very short SOAs
in the former task.

It is important to note that Danziger and
Kingstone (1999) proposed that it was IOR that
was unmasked by their procedure. However,
using detection and discrimination tasks, we have
shown that it is not always IOR that is unmasked,
with facilitation being unmasked under some
conditions. Therefore, one may conclude that it
is cueing effects that are unmasked by making
the cue counterpredictive. At unexpected
locations, IOR was observed in the detection
task, while a facilitatory effect emerged in the
discrimination task. Therefore, cueing effects
manifest differently depending on the task that
the participants are asked to complete (detection
vs. discrimination). These cueing effects are
usually more negative in detection than in
discrimination tasks. In fact, we have constantly
found that at the expected location there were
no differences in cueing effects between the detec-
tion and discrimination tasks. However, at the
unexpected location cueing effects were more
negative in the detection than in the discrimi-
nation task.
A reanalysis of the three experiments described in this paper confirmed these results. We pooled together the data for short SOA (i.e., 100 ms) and compared them with those for long SOAs (i.e., 700 ms for Experiment 2 and 1,000 ms for Experiments 1 and 3; see Figure 4). At the expected location, the cueing effect was not significantly different between the detection and discrimination tasks, either at the short or at the long SOA, $F(1, 126) = 2.66, \text{MSE} = 677, p = .10$, and $F < 1$, respectively. However, at the unexpected location, the effect of cueing was significantly different between the tasks, both at the short and at the long SOA, $F(1, 126) = 17.40, \text{MSE} = 1,656, p < .0001$, and $F(1, 126) = 19.06, \text{MSE} = 1,204, p < .0001$, respectively. Therefore, when attention has already disengaged (unexpected locations), it is not IOR that is unmasked, but the cueing effect, which could be either negative (IOR) or positive (facilitation) depending on other factors such as the type of target or the task to be performed with it.

The dissociation of IOR from endogenous orienting that we show in the present study is not consistent with views of spatial attention as a single spotlight, which could be oriented either endogenously or exogenously. However, the described dissociation fits well with the mounting evidence suggesting the presence of distinct neurocognitive systems for endogenous and exogenous attention. There is now extensive behavioural evidence (e.g., Funes, Lupiáñez, & Milliken, 2005; see Klein & Shore, 2000, for a review) that exogenous and endogenous attention are in fact two qualitatively different processes. Consistent with behavioural results, neuroimaging studies suggest that the brain contains two partially segregated systems for visual orienting: a dorsal network (including parts of the intraparietal sulcus and frontal eye field), bilaterally represented, and concerned with endogenous orienting, and a more ventral, right-lateralized network (temporo-parietal junction and inferior frontal gyrus) subserving exogenous orienting (Corbetta & Shulman, 2002). There is also some suggestion that IOR might correlate with activity in right-hemisphere frontal regions such as the right medial frontal gyrus (SEF) and the right inferior prefrontal sulcus (FEF; Lepsien & Pollmann, 2002; see also Ro, Farné, & Chang, 2003). Compelling neuropsychological evidence also indicates dissociations between exogenous and endogenous attention. In left unilateral neglect, exogenous orienting is heavily biased rightward (Bartolomeo & Chokron, 2001, 2002). However, endogenous processes are largely spared, if slowed, in neglect patients (Bartolomeo et al., 2001). Importantly, as mentioned in the Introduction of this paper, these same patients may show a lack of IOR for right, ipsilesional stimuli (Bartolomeo et al., 1999, 2001; Lupiáñez et al., 2004), consistent with their rightward exogenous bias.

The possible preferential implication of right-hemisphere regions in IOR suggests a relation of this phenomenon with exogenous attention. This relationship was initially suggested by Maylor and Hockey (1985) and was recently confirmed by the demonstration of the tendency of normal individuals to make microsaccades away from a task-irrelevant, peripherally presented visual stimulus (Galfano, Betta, & Turatto, 2004). Microsaccades are small, automatic eye movements occurring during fixation, and their direction may correlate with covert exogenous orienting of attention (Engbert & Kliegl, 2003; Hafed & Clark, 2003).
Also the well-established importance of the activity of the superior colliculus to the expression of IOR (Dorris, Klein, Everling, & Munoz, 2002; Posner et al., 1985; Sapir, Soroker, Berger, & Henik, 1999) underlines the relationship of this phenomenon to exogenous attention.

Taken together, the evidence suggests that the brain may contain multiple attentional mechanisms that influence perception and action independently from one another, by biasing the competition among objects in the visual field (Desimone & Duncan, 1995). In this framework, IOR could be seen as one process (or perhaps several processes; see Sumner, 2006; Sumner, Nachev, Vora, Husain, & Kennard, 2004) decreasing attentional capture for “old” visual objects (Lupiañez et al., 2004; Milliken et al., 2000), which are less likely to constitute a menace for the exploring organism. It makes ecological sense that such a basic ability for survival would be automatic and independent of more top-down influences on perception as is the case of endogenous attention.

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Unilateral spatial neglect is a disabling neurological condition that typically results from right hemisphere damage. Neglect patients are unable to take into account information coming from the left side of space. The study of neglect is important for understanding the brain mechanisms of spatial cognition, but its anatomical correlates are currently the object of intense debate. We propose a reappraisal of the contribution of disconnection factors to the pathophysiology of neglect based on a review of animal and patient studies. These indicate that damage to the long-range white matter pathways connecting parietal and frontal areas within the right hemisphere may constitute a crucial antecedent of neglect. Thus, neglect would not result from the dysfunction of a single cortical region but from the disruption of large networks made up of distant cortical regions. In this perspective, we also reexamined the possible contribution to neglect of interhemispheric disconnection. The reviewed evidence, often present in previous studies but frequently overlooked, is consistent with the existence of distributed cortical networks for orienting of attention in the normal brain, with implications for theories of neglect and normal spatial processing, opens perspectives for research on brain-behavior relationships, and suggests new possibilities for patient diagnosis and rehabilitation.

**Keywords:** attention, brain lesions, perceptual disorders, spatial cognition, white matter fiber pathways

No wonder Lashley thought the whole brain was involved in mental tasks. It was not the whole brain, but a widely dispersed network of quite localized neural areas

Michael I. Posner (2005, p. 239)

**Introduction**

Patients with right hemisphere damage often show signs of left unilateral neglect, an inability to take into account information coming from the left side of space (Mesulam 1985; Heilman et al. 1993; Bartolomeo and Chokron 2001, 2002; Vallar 2001; Parton et al. 2004). Neglect patients do not eat from the left part of their dish, they bump with their wheelchair into obstacles situated on their left, and when questioned from the left side they may either fail to answer or respond to a right-sided bystander. When presented with bilateral stimuli, they may immediately look toward the rightmost stimulus, as if their attention were “magnetically” attracted (Gainotti et al. 1991). On visuo-spatial testing, they omit targets on the left in search tasks, deviate rightward when bisecting horizontal lines, and do not copy the left part of drawings. This neurological condition is a significant source of handicap and disability for patients and entails a poor functional outcome. A better understanding of neglect is thus required both on clinical grounds, for purposes of diagnosis and rehabilitation, and in order to comprehend the brain mechanisms of attention and spatial processing. Unfortunately, however, despite decades of research there are still important disagreements on the interpretation of the neglect syndrome, even on basic matters such as its lesional basis. This question constitutes the specific focus of the present review.

Most studies devoted to the anatomical correlates of neglect indicate the temporal–parietal junction (TPJ) and the inferior parietal lobule (IPL) (Vallar 2001; Mort et al. 2003), consistent with the known role of posterior parietal cortex in spatial attention (Colby and Goldberg 1999; Gitelman et al. 1999; Corbetta and Shulman 2002). In contrast with this view, another line of findings implicated more rostral portions of the superior temporal gyrus (Karnath et al. 2001, 2004), emphasizing the role of the ventral visual stream in spatial awareness originally hypothesized by Milner and Goodale (1995). In addition, damage to several other brain structures has been reported to determine neglect, including the thalamus, the basal ganglia, and the dorsolateral prefrontal cortex (Vallar 2001; Karnath et al. 2002).

However, at variance with interpretations of neglect stressing the role of damage to local brain modules, it has long been proposed that attentional spatial processes that may be disrupted in neglect do not result from the activity of single-brain areas but rather emerge from the interaction of large-scale networks (Mesulam 1981; Heilman et al. 1993). If so, then damage to the connections making up these networks is expected to impair their integrated functioning and consequently to bring about signs of neglect. Consistent with this prediction, here we review accumulating evidence that long-lasting signs of left unilateral neglect may also result from the important influence of intra- and interhemispheric disconnection.

**Intra- and Interhemispheric Disconnection**

**Frontoparietal Networks of Spatial Attention**

Within each hemisphere, large-scale cortical networks coordinate the operations of spatial attention (Mesulam 1981; Posner and Petersen 1990; LaBarge 2000; Corbetta and Shulman 2002). Important components of these networks include the dorsolateral prefrontal cortex and the posterior parietal cortex. Physiological studies indicate that these 2 structures show interdependence of neural activity. During memory-guided saccades, cooling of parietal neurons engenders changes in neural activity in prefrontal neurons, and vice versa (Chafee and Goldman-Rakic 2000). Not surprisingly, in the monkey, these 2 structures are directly and extensively interconnected (Seleson and Goldman-Rakic 1988; Morecraft et al. 1993). Several distinct frontoparietal long-range pathways have been identified (Petrides and Pandya 2002; Schmahmann and Pandya 2006).
These pathways include the arcuate fasciculus (AF), the superior longitudinal fasciculus (SLF), and the frontoocipital fasciculus (FOF). The AF links the caudal portions of the temporal lobe, at the junction with the parietal lobe, with the dorsal portions of the areas 8, 46, and 6 in the frontal lobe (Schmahmann and Pandya 2006). Within the SLF, 3 distinct branches can be identified on the basis of cortical terminations and course (Fig 1; Petrides and Pandya 2002; Schmahmann and Pandya 2006). The SLF I links the superior parietal region and the adjacent medial parietal cortex with the supplementary and premotor areas in the frontal lobe. The SLF II originates in the caudal inferior parietal lobe (corresponding to the human angular gyrus) and the occipitoparietal area and projects to the dorsolateral prefrontal cortex. The SLF III connects the rostral portion of the inferior parietal lobe (homologous to the human supramarginal gyrus) with the ventral premotor area 6, the adjacent area 44, the frontal operculum, and the area 46. The FOF links the medial preoccipital area PO, the lateral--dorsal occipital area DP, the medial parietal area PGm, the caudal cingulate gyrus, and the caudal IPL to the dorsal premotor (area 6) and the dorsal prefrontal cortices (areas 8, 9, and 46) (Schmahmann and Pandya 2006). Rizzolatti and Matelli (2003) proposed to dissociate the dorsal cortical visual stream (see Mishkin et al. 1983; Milner and Goodale 1995) into 2 components, a dorsoventral stream, which controls actions “on line” and whose damage leads to optic ataxia, and a ventrodorsal stream, implicated in space perception and action understanding. In this framework, FOF and SLF II may be considered to connect, respectively, the dorsodorsal and the ventrodorsal cortical networks (Schmahmann and Pandya 2006). Although it is not a frontoparietal pathway, the inferior longitudinal fasciculus (ILF) may also be relevant here because its lesion has been implicated in neglect (Leibovitch et al. 1998; Bird et al. 2006). In the monkey, the ILF originates in the ventral lateral and ventral preoccipital areas and runs in the depth of the temporal lobe to terminate in the superior temporal sulcus, the inferior temporal gyrus, and other temporal areas; moreover, it connects the caudal part of the cingulate gyrus, the IPL, and the superior temporal gyrus (STG) to the parahippocampal gyrus (Schmahmann and Pandya 2006).

Diffusion tensor imaging (DTI), a new technique to map the course of white matter tracts in the living human brain (Basser et al. 1994), has demonstrated a similar organization of frontoparietal pathways in humans (Catani et al. 2002; Makris et al. 2005; Rushworth et al. 2005), although the identification of the cortical terminations remains uncertain due to the technical limitations of the DTI method.

**Frontoparietal Disconnection and Spatial Neglect**

How is visuospatial processing affected by damage to these frontoparietal networks? In a groundbreaking study in the monkey, Gaffan and Hornak (1997) showed that severe neglect may arise after a unilateral section of the white matter between the fundus of the intraparietal sulcus and the lateral ventricle, interrupting long-range communication pathways between the parietal and the frontal lobes. When exposed to horizontally arranged stimuli, neglect monkeys often omitted to respond to targets contralateral to the lesion, choosing instead an ipsilateral distractor. Interestingly, in this study monkeys demonstrated little, if any, contralateral neglect after isolated ablations of the frontal cortex and the posterior parietal cortex or even after a combined lesion of both of these structures. The monkeys with neglect also had clear impairments in everyday activities such as visual searching for food in free vision in the home cage. When offered 2 handfuls of food by an observer, they failed to find the food in the observer’s hand that was contralateral to the monkey’s lesion. This was in marked contrast to the monkeys with hemianopia alone that had efficient visual searching which compensated for their hemianopia in free vision (Gaffan D, personal communication, 2006). Thus, disconnection really proved crucial to observe neglect in monkeys in this study (for analogous results obtained in rodents, see Burcham et al. 1997; Reep et al. 2004).

Importantly, analogous findings were reported in different studies in human patients. Using computed tomography scans and single photon emission computed tomography, Leibovitch et al. (1998) investigated the anatomical correlates of neglect in a large sample of right brain-damaged patients not selected for the presence or absence of concomitant visual field defects. These authors found that the main correlate of chronic neglect was the combined lesion involvement and hypofunctioning of fibers connecting the parietal and temporal lobes (ILF), as well as those linking the parietal and frontal lobes (SLF), loaded in the white matter beneath the TPJ.

More recently, Doricchi and Tomaiuolo (2003) made a further step and disentangled the contribution of SLF and ILF disconnection to spatial neglect. In their study, lesion overlap was mapped in a sample of chronic neglect patients without visual field defects. Patients were further divided in 2 subgroups based on whether the lesion involved or spared the basal ganglia. In both subgroups, areas of maximal lesion overlap were found in the SLF beneath the rostral sector of the supramarginal gyrus. This finding revealed that, in humans, damage limited to frontoparietal connections in the SLF is sufficient to contribute to the development of chronic neglect. The authors concluded that while “a brain damage affecting circumscribed portions of the IPL could… disrupt only a subset of those different spatial abilities that, with different emphasis and by different authors, are currently considered to be specifically defective in neglect patients,…disconnection of the parietal-frontal spatial attentional network… might render neglect more persistent by extensively compromising the sensory–motor mapping of the contralesional space even in those patients who, suffering only partial damage of the functionally
heterogeneous IPL-TPJ area, would otherwise show more selective (and perhaps transitory) parietal related spatial deficits” (p. 2242).

More compelling and direct evidence stressing the importance of frontoparietal disconnection in neglect came from a recent study employing intraoperative electrical stimulation in human patients (Thiebaut de Schotten et al. 2005). During brain surgery for resection of low-grade gliomas, neurosurgeons often awaken patients in order to assess the functional role of restricted brain regions so that the extent of the exeresis can be maximized without provoking cognitive impairments. Patients perform cognitive tasks, such as counting or naming, while the surgeon temporarily inactivates restricted regions around the tumor, using electrical stimuli. If the patient stops talking or produces incorrect responses, the surgeon avoids removing the stimulated region. This technique allows researchers to map cognitive functions in humans with unrivaled spatiotemporal resolution (~5 mm by 4 s). Thiebaut de Schotten et al. (2005) asked 2 patients with gliomas in the right temporoparietal region to mark the midpoint of 20-cm horizontal lines (a typical neglect task; Azouvi et al. 2002) while being stimulated. Electrical stimulation of the right IPL or the caudal STG, but not of its more rostral portions, determined rightward deviations on line bisection.

However, the strongest shifts occurred when one of the patients was stimulated subcortically. Fiber tracking using DTI identified the stimulated site as the likely human homologue of the SLF II (in the original article, which was published before the atlas of Schmahmann and Pandya became available, the pathway was incorrectly labeled as FOF; this, however, does not hamper the main point made by Thiebaut de Schotten and co-workers that damage to the frontoparietal pathways is important to produce neglect), consistent with the postulated role of this pathway in space perception (Rizzolatti and Matelli 2003; Schmahmann and Pandya 2006). Thus, there is a remarkable consistency between the behavioral consequences of frontoparietal disconnection in humans and monkeys, despite the fact that different behavioral tests were used: line bisection (Thiebaut de Schotten et al. 2005) or target cancellation (Doricchi and Tomaiuolo 2003) in humans and target search in monkeys (Gaffan and Hornak 1997). This convergence of results strongly suggests a similar organization of space-processing mechanisms across the 2 species. The demonstration of the role of frontoparietal disconnections in neglect supports models of neglect postulating an impairment of large-scale right hemisphere networks (Mesulam 1999), including prefrontal, parietal, and cingulate components. The parietal component could determine the perceptual salience of extrapersonal objects, whereas the frontal component might be implicated in the production of an appropriate response to behaviorally relevant stimuli (Mesulam 1999), in the online retention of spatial information (Husain and Rorden 2003) or in the focusing of attention on salient items through reciprocal connections to more posterior regions (Petrides and Pandya 2002). We also note that, as a consequence of frontoparietal disconnection, inaccurate or slowed communication between posterior and anterior brain regions, whether coupled or not with a general deficit in responding to unattended stimuli, might delay the information transfer from sensory-related areas to response-related regions to the point of exceeding an elapse of time after which this information is no longer useful for affecting behavior (Bartolomeo and Chokron 2002).

Reappraisal of Previous Lesion Overlap Studies

To explore the consistency of the above reviewed results with previous evidence from vascular patients, we plotted on a standardized brain the subcortical lesions of the stroke patients with neglect from the lesion overlapping studies that contained sufficient details (Doricchi and Tomaiuolo 2003; Mort et al. 2003; Karnath et al. 2004; Corbetta et al. 2005). Long-range connections were visualized using fiber tracking (Thiebaut de Schotten et al. 2006) (see Supplementary Material). Most interestingly, neglect patients’ lesions invariably overlapped at or near the subcortical long-range pathways linking the parietal to the frontal lobes (Fig. 2). The same meta-analysis revealed the presence of an important lesion overlap in the white matter frontoparietal connections in the study by Karnath et al. (2004). This overlap shows striking resemblance with the lesion overlap documented by Doricchi and Tomaiuolo (2003) in the same area, indicating that in the sample of patients studied by Karnath et al. (2004), lesion overlap in the STG was not selective and that neglect could have been due to frontoparietal disconnection rather than STG damage.

Further Evidence on Frontoparietal Disconnection in Neglect

In a recent group study on 52 right brain–damaged patients with vascular lesions, Committeri et al. (2007) investigated the anatomical correlates of personal neglect (i.e., neglect concerning the patient’s own body) and extrapersonal neglect (concerning the space external to the patient’s body). Committeri et al. concluded that personal neglect is due to lesion involvement of the supramarginal gyrus in the parietal lobe, whereas extrapersonal neglect results from damage of more ventral areas including the STG and the inferior frontal gyrus (IFG).

In a first series of comparisons, the authors made voxel-by-voxel subtractions between 1) patients with extrapersonal neglect (whether isolated or in combination with personal neglect) versus patients with pure personal neglect or no neglect at all; 2) patients with personal neglect (whether isolated or in combination with extrapersonal neglect) versus patients with pure extrapersonal neglect or no neglect. The results of these subtractions are reported in their Figure 2. In the first row of axial slices, a distinct area of overlap is clearly present in the white matter of the axial slice $z = +28$. We found that this spot is perfectly centered on the SLF on the matching Talairach template and is only 9 mm caudal and 1 mm superior to the maximum lesion overlap previously found by Doricchi and Tomaiuolo (2003) in a group of patients showing extrapersonal neglect on both line-bisection and multiple-item cancellation tasks (see Supplementary Fig. 2).

In a second series of subtractions, Committeri et al. compared patients with pure extrapersonal neglect or pure personal neglect with patients without neglect. Also in this case, a similar maximum lesion overlap on the SLF was found in patients with pure extrapersonal neglect (see the axial slice $z = +28$ in the third row of their Fig. 2). These anatomical findings went probably unnoticed because for the quantitative analysis, Committeri et al. considered the percentage of white matter damaged within 3 ample regions of interest: the centrum semiovale, the suprалenticular and sublenticular corona radiata, and the external and internal capsulae. They found that the white matter immediately dorsal (suprалenticular corona radiata and centrum semiovale) and ventral (sublenticular corona radiata) to
the insula was significantly more damaged in patients with extrapersonal neglect and that the white matter underlying the supramarginal gyrus was more damaged in patients with personal neglect. However, with respect to a more precise anatomical localization of these areas, the higher spatial resolution provided by voxel-by-voxel subtractions reported in their Figure 2 is instructive and unequivocal in indicating specific damage of white matter fasciculi linking parietal and frontal areas in patients with extrapersonal neglect. With reference to the distinct branches of the SLF identified in the monkey by Schmahmann and Pandya (2006) (see Supplementary Fig. 1 and Supplementary Material), we found that the maximum lesion overlap found by Committeri et al. locates itself at the boundary between the likely human homologous of SLF II and SLF III (see Supplementary Fig. 2). Thus, the involvement of dorsal SLF underneath the central sulcus documented by Doricchi and Tomaiuolo (2003) cannot be merely attributed to the presence of concomitant and undetected personal neglect that, as proposed by Committeri et al. in the discussion section, would have shifted the lesion overlap dorsally with respect to more ventral areas which, in their proposal, would subserve awareness of the extrapersonal space.

In a third analysis of their data, Committeri et al. used voxel-based lesion–symptom mapping (VLSM; see Bates et al. 2003). For each voxel, patients were divided into 2 groups according to whether or not their lesion affected that voxel. Scores for extrapersonal and personal neglect were then compared for these 2 groups, yielding a \( t \)-statistics for each voxel and a corresponding \( t \)-test–based statistical map for the entire voxel-based brain volume. Also in this case, white matter involvement was present for extrapersonal neglect in fibers feeding the frontal eye field (first row of their Fig. 4, sagittal slice \( x = +36 \); a more ventral white matter involvement is evident in axial slice \( z = +20 \)) as well as for personal neglect (second row of their Fig. 4, axial slice \( z = +32 \) and sagittal slice \( z = +36 \)). VLSM analysis also allows researchers to evaluate the similarity between the \( t \)-test–based statistical maps by calculating the correlations between the \( t \)-scores of personal and extrapersonal neglect for each voxel (Bates et al. 2003). A positive correlation for one voxel suggests that this voxel performs a core function common to both types of deficit (Bates et al. 2003). Committeri et al. obtained a strong positive correlation of 0.84 (reflecting 70% of overlap in the variance) for the IFG (see Husain and Kennard 1996), the posterior insular–opercular temporal–parietal cortex, and most importantly, the white matter underlying the central sulcus (see Doricchi and Tomaiuolo 2003). Therefore, also the VLSM analysis demonstrated that this region of the white matter is implicated in a core function for spatial awareness, as originally suggested by the results of Doricchi and Tomaiuolo (2003) and Thiebaut de Schotten et al. (2005).

In support of this interpretation, another recent VLSM study on 80 stroke patients (Verdon et al. 2006) found that damage to
frontoparietal white matter fibers, which the authors identified with the pathway described by Thiebaut de Schotten et al. (Thiebaut de Schotten et al. 2005), correlated with the presence of generalized and severe neglect.

Relation to Spatial Working Memory Impairment

A cognitive function that could be particularly sensitive to frontoparietal disconnection is the building up and maintenance of memory for inspected spatial locations. In a series of studies, Husain et al. (2001) showed that neglect in cancellation tasks is significantly increased by the failure to remember the location of already canceled items. In a study addressing the anatomical correlates of poor spatial working memory (SWM) in neglect patients, Malhotra et al. (2005) concluded that “...a deficit in SWM would not be expected in all neglect patients, but it would be anticipated to occur in those who have damage to critical areas in the right parietal and frontal lobe that support SWM performance. ... lesion locations associated with the poorest SWM performance among neglect patients were in right parietal white matter and ... the right insula. Damage to both these sites would be consistent with deafferentation and/or loss of cortical regions known to support SWM based on functional neuroimaging evidence” (Malhotra et al. 2005, p. 434, our italics). This conclusion clearly suggests the possibility that a lesion of the white matter can disrupt the whole frontoparietal network subserving SWM capacities.

Other Intrahemispheric Pathways

A recent anatomical investigation suggests that frontoparietal disconnection due to middle cerebral artery infarctions might not be the only type of intrahemispheric disconnection related to neglect. Bird et al. (2006) showed that in patients with infarctions in the territory of the right posterior cerebral artery, disconnection of white matter fiber tracts between the parahippocampal gyrus and the angular gyrus was correlated with left neglect. Interestingly, the authors also noted that when this type of intrahemispheric disconnection was coupled with lesions of the splenium of the corpus callosum (producing interhemispheric disconnection, see Interhemispheric Interactions and Disconnection below), neglect tended to be more severe.

Intrahemispheric Disconnection and Neglect: Discussion

Disconnection and Cortical Deactivation

Despite the abundant evidence reviewed above, an apparent challenge to the role of subcortical disconnection in the pathogenesis of neglect comes from a number of investigations on the correlation between levels of cortical perfusion and the presence of neglect in the acute, or hyperacute, poststroke phase. Using perfusion weighting imaging, based on estimates of arrival and clearance of a bolus of contrast indicating the level of functional activity in otherwise structurally spared cortical areas, Hillis et al. (2002) investigated the functional correlates of neglect and aphasia due to hyperacute (within 48 h from stroke) subcortical infarction. They found that, independent of the lesion localization (corona radiata or caudate/capsular structures), neglect was only present in patients who had associated cortical hypoperfusion and absent in those having no cortical hypoperfusion. Importantly, though only tested in aphasic patients, pharmacological or surgical intervention restore cortical perfusion led to substantial improvement of cognitive impairments and prevented the development of cortical infarcts. This study shows that a lesion in the white matter does not necessarily cause neglect; however, no precise mapping of white matter lesions was made, thus leaving unexplored the relationship between lesion location and extent, cortical hypoperfusion and neglect. Notwithstanding this limitation, the findings by Hillis et al. (2002) are relevant in that they confirm that a subcortical disruption of frontoparietal connections, whether resulting from vascular damage (Doricchi and Tomaiuolo 2003), surgical section (Gaffan and Hornak 1997), or temporary/functional lesions (Thiebaut de Schotten et al. 2005), might cause neglect by reducing functional activity in the entire cortical–subcortical frontoparietal network connected by these pathways.

Following the terminology recently proposed by Catani and ffytche (2005), the present pathophysiological interpretation of the neglect syndrome emphasizes the combined role of “topological” factors, related to dysfunction of cortical specialized areas, and “hodological” factors, related to dysfunction of connecting pathways among the same areas. Furthermore, we propose that disconnection might produce more of a deficit than cortical damage/dysfunction alone through several, not mutually exclusive, mechanisms: 1) Damage to the tightly packed fibers of the white matter may result quantitatively more disrupting than damage to equivalent cortical volumes, by impairing the functioning of larger cortical areas (Fig. 3). 2) Brain networks are composed of cortical modules interacting with each other. Disturbed communication between modules might thus produce not only cortical hypofunctioning but also hyper- or inadequate functioning of several cortical areas, resulting in a more severe disintegration of complex functions than the deficit relative to lesion to isolated modules (Catani and ffytche 2005). 3) Cortical lesions may leave the possibility for other cortical areas to functionally compensate for the deficit, through the phenomena of brain plasticity (see, e.g., Duffau 2005); on the other hand, white matter damage, which provokes the dysfunction of a whole network of connected areas, might render compensation more difficult to obtain.

It remains to be seen whether frontoparietal disconnection is sufficient to produce signs of neglect, as suggested by some of the results reviewed here, or whether concomitant cortical damage is necessary. A prediction resulting from the first hypothesis is that patients with relatively pure white matter

![Figure 3](image-url)
damage, resulting for example from multiple sclerosis or cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), may show signs of neglect. To the best of our knowledge, in the literature there are only a case report (Griff-Radford and Rizzo 1987) and a group study (Gilad et al. 2006) describing the possible occurrence of left neglect in patients with multiple sclerosis. Together with reports of patients with lesions of vascular origin, which affected primarily or exclusively the posterior limb of the right internal capsule (Healton et al. 1982; Ferro and Kertesz 1984; Ferro et al. 1987), this evidence does suggest the possibility of a purely disconnection basis of neglect. The apparently rare occurrence of neglect in diseases selectively affecting the white matter may depend on the frequently bilateral hemispheric involvement in these diseases, which may prevent unilateral neglect to occur (see the discussion on interhemispheric interactions in Neglect, Orienting of Attention and Interhemispheric Interactions: Callosal or Collicular? below), but probably also on the relative lack of interest for neglect of clinicians whom these patients are referred to. Signs of neglect may easily pass undetected without proper testing, as confirmed by the substantial lack of neglect literature before the mid-twentieth century. Only a systematic assessment of neglect in patients with selective damage of the white matter can shed light on this issue.

**Perspectives for Neglect Research**

The above reviewed evidence suggests that there are at least 2 long-range pathways linking the parietal to the frontal lobes whose dysfunction could be implicated in neglect (see Fig. 1). As previously mentioned, the inactivation of the SLF II in the right hemisphere causes rightward deviation on line-bisection tasks (Thiebaut de Schotten et al. 2005). Lesion of the more ventrally located SLF III in the right hemisphere correlates with rightward deviation on line-bisection and left omissions on visual search tasks (Doricchi and Tomaiuolo 2003). Although the combined lesion of these pathways might well generally disrupt the right hemisphere attentional networks (Corbetta et al. 2005), thus giving rise to generalized left neglect, future studies might be able to correlate selective lesions of one of these 2 pathways with particular patterns of functional deactivation in the cortex and behavioral dissociations in neglect symptoms. For example, the identification of white matter pathways disrupted in a particular patient, and the cortical areas consequently hypoactive even if undamaged (Corbetta et al. 2005), might help detailing the anatomical correlates of the many dissociations of performance described in neglect patients (near vs. far, perceptual vs. imaginal, etc.). Until now, the neural correlates of neglect dissociations have proved difficult to assess, perhaps because only gray matter lesions were considered. These considerations might prove important for patient diagnosis because a particular form of disconnection might have greater predictive value than the localization of gray matter lesions concerning the patients’ deficits and disabilities. The demonstration of anatomically intact but functionally inactivated areas might also open perspectives for treatments (whether pharmacological or rehabilitative), aimed at restoring normal neural activity in these areas.

**Implications for Theories of Neglect**

The role of damage to different sectors of the cerebral networks linking the parietal and frontal lobes in the pathogenesis of unilateral neglect is currently a matter of intense debate. One thesis proposes that the higher frequency, severity, and duration of left neglect after right brain damage, compared with right neglect after left brain damage, are due to the different competence of the 2 hemispheres in dealing with the left and the right side of space. According to this theory, the left hemisphere is able to represent only the right hemispace, whereas the right hemisphere is endowed with sensory-motor representations of both sides of space. Therefore, the higher frequency of neglect following right hemisphere damage is linked to the limited capacity of the left hemisphere in dealing with the left hemispace; conversely, the lower frequency of neglect after left hemisphere damage depends on the ability of the right hemisphere to deal with the whole horizontal space (Heilman et al. 1993; Mesulam 1999).

A second theory based on neuroimaging studies (Corbetta and Shulman 2002) holds that what is lateralized in the right hemisphere is not the sensory-motor representation of both hemispaces but, rather, a network including the IPL, the posterior part of the STG, the inferior and middle frontal gyri, and the frontal operculum, especially concerned with the detection of novel unexpected stimuli (such as those appearing at an unexpected spatial location following the presentation of an invalid spatial cue). This right hemisphere network triggers reorienting of attentional resources in dorsal bilateral networks including the superior parietal lobule and the frontal eye field (Corbetta et al. 2005). At variance with the previous hypothesis, Corbetta and co-workers surmise that each hemisphere is endowed with a dorsal network guiding endogenous orienting in the contralateral space and that the higher frequency of neglect following right hemisphere damage is due to the disruption of the alerting ventral network lateralized in the right hemisphere (Corbetta and Shulman 2002). A precise reconstruction of the section of the SLF damaged by the lesion causing neglect might therefore constitute a crucial test of these 2 hypotheses. Frontoparietal disconnection in the right hemisphere may disrupt the function of one or both of these networks or impair the integrated functioning of the 2 networks (Doricchi and Tomaiuolo 2003; Mort et al. 2003; Corbetta et al. 2005). For instance, showing that a selective lesion of SLF II, connecting the dorsal network, is sufficient to produce neglect signs would favor the first hypothesis, whereas linking neglect to a selective damage to the SLF III or the AF, connecting the ventral network, would be consistent with the theory of Corbetta and co-workers.

However, more complex anatomical–functional scenarios consistent with the heterogeneity of the neglect syndrome can be envisaged. For example, selective lesions of the different sectors of the SLF could be associated with different types of neglect or the presence of different neglect signs (e.g., behavioral dissociations in the performance of different tasks as, e.g., line bisection vs. multiple-item cancellation). We strongly argue that such a differential approach to the study of neglect syndrome could be by far more fruitful, from both clinical and theoretical standpoint, than trying to attribute neglect to the main influence of disruption of a single anatomical–functional brain module.

**Interhemispheric Interactions and Disconnection**

Neglect, Orienting of Attention and Interhemispheric Interactions: Callosal or Collicular?

Patients with left neglect typically show an asymmetry of attentional orienting, whereby orienting to right-sided objects
is easier and faster than orienting to left-sided objects (for review, see Bartolomeo and Chokron 2002). Thus, it has been suggested that left neglect essentially results from a rightward attentional bias (Kinsbourne 1970), from a deficit in disengaging attention from the right side to reorient it to the left side (Posner et al. 1984; Morrow and Ratcliff 1988), or from a deficit in orienting attention to the left contralesional hemisphere (Heilman and Valenstein 1979). A well-articulated account of neglect based on orienting of attention is the opponent processor model (Kinsbourne 1970, 1977, 1987, 1993). According to this hypothesis, each hemisphere shifts attention toward the contralateral hemisphere by inhibiting the other hemisphere. Moreover, in the normal brain there is a tendency to rightward orienting supported by the left hemisphere, which has a stronger orienting tendency than the right hemisphere. Right hemisphere lesions, by disinhibiting the left hemisphere, exaggerate this physiological rightward bias, thus giving rise to left neglect. Left neglect does not reflect an attentional deficit but an attentional bias consisting of enhanced attention toward the right. The verbal interaction between patient and examiner would further enhance left neglect by further activating the already disinhibited left hemisphere. Furthermore, left neglect patients would suffer from an abnormally tight focus of attention, which would deprive them of the possibility of a more general overview of the visual scene (Kinsbourne 1993). Right neglect would rarely be observed because much larger lesions of the left hemisphere are needed to overcome its stronger tendency to rightward orienting and because the verbal exchanges with the examiner would now work in the opposite direction, activating the left hemisphere and minimizing right neglect. Evidence supporting the opponent processor model came from the pioneering report of a patient who showed a severe left neglect following a first right-sided parietal infarct but abruptly recovered from neglect 10 days later, when he suffered from a second infarct in the dorsolateral frontal cortex of the left hemisphere (Vuilleumier et al. 1996). However, conclusive anatomical inferences from this case report seem not easy because the patient was studied in the acute phase of the disease, when transient phenomena of neural depression in areas remote from the lesion can occur (diaschisis; Meyer et al. 1993). As noted by the authors, the second stroke induced a tonic leftward deviation of head and gaze: this occurrence might have contributed to minimizing left neglect signs, similarly to the effects of vestibular or optokinetic stimulations (see Gainotti 1993; Vallar et al. 1997; Chokron and Bartolomeo 1999).

According to the opponent-processing model, increasing severity of neglect should result from an increasingly stronger bias toward the right, reflecting increasing disinhibition of the left hemisphere. Thus, response times to right-sided targets should become progressively faster as neglect increases in severity across patients. Contrary to this prediction, a group study of patients with varying degrees of neglect on paper-and-pencil tests demonstrated that not only patients’ response times to left targets but also those to right targets increased with increasing neglect (Bartolomeo and Chokron 1999b). However, the 2 regression lines were not parallel. With increasing neglect, responses to left targets increased more steeply than those to right targets. Thus, a rightward attentional bias is present in patients with left neglect, together with left hypotension. However, the rightward bias is one of the defective, and not enhanced, attention.

Full understanding of the interactions between the opponent processors in the 2 hemispheres requires the identification of neural mechanisms and pathways mediating such interactions. Mutually inhibitory interhemispheric interactions would intuitively appear to implicate the callosal connections; however, also the superior colliculi (SC), which mutually inhibit one another, are plausible candidates (Kinsbourne 1987). In the cat, lesion of one SC produces contralateral neglect, which can be reversed by lesion to the contralateral SC or by section of the intertectal commissure (Sprague 1966).

A more recent study (Rushmore et al. 2006) showed that ablation or cooling of the posterior parietal cortex induced contralateral neglect, which corresponded to decreased metabolic activity (as measured by 2-deoxyglucose uptake) of the ipsilateral SC and increased activity of the contralateral SC, but not of the contralateral parietal cortex; cooling of the opposite parietal cortex or SC restored orienting reactions to the previously neglected stimuli; and, correspondingly, collicular activity reverted to symmetry.

Weddell (2004) reported a possible human analogue of the Sprague effect (see also Zihl and von Cramon 1979). In a patient with a midbrain tumor, right frontal damage resulting from a surgical procedure provoked signs of left neglect, which disappeared abruptly 7 months later, when the tumor extended into the left SC. Most of the retinal afferents to the SC come from the contralateral eye. Thus, patching the right eye should decrease the visual input to the left SC, thereby decreasing its inhibition on the right SC. Consistent with the collicular hypothesis, neglect patients were found to show some improvement during the period when the patch was worn (Butter and Kirsch 1992). However, another study, contrasting monocular eye patching with patching of the 2 right visual hemifields that decreases the visual input to the left hemisphere, found an improvement of neglect only in the hemifield-patching group (Beis et al. 1999). Thus, a corticosubcortical system including both cortical and subcortical systems (respectively, the frontoparietal regions and the SC) might constitute the neural basis for the opponent processor model.

Results from transcranial magnetic stimulation (TMS) and functional magnetic resonance imaging (fMRI) studies in humans are also relevant for the opponent processor model. Oliveri et al. (1999) studied the effects of temporary inactivation by TMS of parietal and frontal sites in the intact hemisphere upon contralateral tactile extinction to bilateral simultaneous in right- and left brain-damaged patients. In right brain-damaged patients, TMS over the intact left frontal site significantly reduced extinction as compared with controls, whereas the same effect was not observed upon stimulation of the homologous site in the intact right hemisphere of left brain-damaged patients. These results are in keeping with the idea that TMS reduces inhibition from the stimulated to the unstimulated hemisphere and that mutual inhibition between the 2 hemispheres is asymmetrical, with more prominent inhibition directed from the left to the right hemisphere. Without excluding the possible contribution of subcortical mechanisms, the authors argued that TMS effects on extinction of tactile digit stimuli could have been well mediated by callosal fibers connecting “hand representations of associative parietal and frontal areas” as these connections “are more powerful and widespread than those between the primary hand motor and sensory areas” (p. 1737). As far as tactile modality is concerned, the authors further argued that this callosal mechanism might be particularly plausible because subcortical
mechanisms as the Sprague effect “seem to be valid especially for the visual system” (p. 1737).

A recent fMRI investigation (Corbetta et al. 2005) explored 11 stroke patients with left neglect who, in keeping with previous overlap studies (Doricchi and Tomaiuolo 2003; Mort et al. 2003), showed a maximal lesion overlap in the white matter beneath the IPL (see their Fig. 2 and the present Fig. 2). Four weeks after the stroke, when performing a response time task to lateralized stimuli, neglect patients had decreased activation of structurally intact frontoparietal regions in the right hemisphere (especially the intraparietal sulcus, the superior parietal lobule, and the dorsolateral prefrontal cortex), coupled with robust activation of the homologous regions in the left hemisphere. Thirty-nine weeks after lesion onset, recovery of neglect signs was paralleled by the disappearance of the imbalance between the 2 superior parietal lobules. According to the authors, this pattern of results suggests that lesions of the right TPJ determine a functional imbalance of the superior parietal lobules, which are structures important to attentional orienting. Consistent with the many previous findings and interpretations of neglect summarized in the present review, Corbetta et al. concluded that their results “rule out the possibility that neglect results form the critical dysfunction of one brain area” (p. 1608).

In conclusion, the reviewed evidence indicates that insight in the anatomical basis of the dynamic interplay between homologous structures in the 2 halves of the brain is of importance for the diagnosis and treatment of neglect and for the understanding of the mechanisms of spontaneous recovery or relevant clinical changes during the transition from the acute to the postacute and chronic phase.

**Confabulations and Implicit Processing**

Four decades ago, in his seminal review of disconnection syndromes, Geschwind (Geschwind 1965) suggested that some neglect signs reflected the activity of the left hemisphere being deprived of information from the right hemisphere. In Geschwind’s view, the left hemisphere is dominant not only for language but also for cognition in general; thus, if the right visual and somesthetic cortex are isolated from the left hemisphere, “[t]he left side of the body and of space is then ‘lost’. The patient will then respond in many instances by using [a] technique of confabulatory completion” (p. 600). These confabulatory responses would be the result of an isolated left hemisphere, with no access to the left-sided information processed by the right hemisphere. In other words, interhemispheric disconnection would produce a deafferentation of the left hemisphere, degrading the information coming from the left part of space, processed by the right hemisphere. To address the “vexing problem of why a left parietal lesion less often produces neglect of half space than does a right parietal lesion” (p. 601), Geschwind further proposed that “disease may simply aggravate the normal disadvantage of the right hemisphere in being further away and responding less well to stimuli” (p. 601), thus anticipating the above reviewed hypothesis later developed by Kinsbourne (see Neglect, Orienting of Attention and Interhemispheric Interactions: Callosal or Collicular? above).

Although the idea of a generally dominant left hemisphere is no longer accepted, other aspects of Geschwind’s proposal might help interpreting patterns of performance later described in split-brain patients and neglect patients. Following surgical section of the corpus callosum, it has been reported that the left hemisphere sometimes provides post hoc confabulatory verbal explanations of actions performed by the right hemisphere (Gazzaniga and Baynes 2000). In a well-known example (see Gazzaniga and Baynes 2000), a split-brain patient was shown tachistoscopically the pictures of a snow scene in the left visual field/right hemisphere and a rooster claw in the right field/left hemisphere. When the patient was presented with multiple pictures and asked to use each hand to choose those matching the bilateral displays, his right hand chose the picture of a rooster, and his left hand, driven by the right hemisphere, appropriately chose a shovel as a match for the snow scene. At debriefing, however, the patient, whose left hemisphere had not seen the snow scene, confabulated that the shovel was needed to clean out the chicken house.

Right brain–damaged patients with left-sided extinction or neglect may show remarkable implicit processing without overt verbal recognition of stimuli tachistoscopically presented in the left hemifield. Patients can perform better than chance when forced to make same/different judgments or to select in a multiple choice the identity of a nonexplicity detected item (Volpe et al. 1979) and can show implicit semantic processing of the stimulus presented in the neglected hemifield (McGlinchey-Berroth et al. 1993; Berti et al. 1994), although only a minority of neglect patients may show such effects (D’Erme et al. 1993). One may also wonder whether any interhemispheric disconnection factors may contribute to the implicit processing and the confabulations concerning the neglected left side of visual stimuli presented in free vision. For example, in an often-cited case report (Marshall and Halligan 1988), patient P.S. was unable to tell the difference between 2 vertically arranged houses, one of which had its left side on fire. However, when asked in which of the 2 she would live, P.S. consistently chose the house that was not burning. In Geschwind’s view, this behavior could be accounted for by postulating 1) an inability of the left hemisphere to access left-sided information (the fire), with consequent lack of verbal acknowledgment of the difference between the 2 houses; 2) some residual (right hemisphere–based?) knowledge of this difference, either resulting in the appropriate behavioral choice or causing misinterpretation of the difference and resulting in a choice consistent with the misinterpretation. A further prediction coming from this hypothesis is that, if patients are asked “why” they prefer the nonburning house, their left hemisphere should either admit ignorance or produce confabulatory responses. In the case of P.S., no comments about her choices are available, except that she deemed “silly” the task of choosing between 2 “identical” houses. However, other studies provide this information and report a variety of responses at debriefing. For instance, a patient described by Manning and Kartsounis (1993) chose the non-burning house confabulating that it had an extra fireplace, consistent with Geschwind’s hypothesis. Another patient described by Bisiach and Rusconi (1990) consistently chose the “burning” house, considering it more “spacious” on the burning side, where the contour of the flames actually enlarged the shape of the house, an example of choice based on an implicit misinterpretation of the difference. In a group of 13 neglect patients (Doricchi et al. 1997), responses motivating correct implicit choices of the “non-burning house” were equally distributed into two categories: 1) “there is no specific reason for my choice, the 2 houses are the same anyway,” suggesting complete uncoupling of verbal output from
implication of reporting the same contralesional stimulus when presented alone. Extinction can occur both within and between different sensory modalities. It is often clinically detected in the recovery phase of neglect, though it can doubly dissociate from it. Marzi and co-workers (Smania et al. 1996) argued that right brain-damaged patients with extinction might suffer a partial interhemispheric disconnection syndrome, "whereby the information on the stimulus presented to the damaged right hemisphere cannot be efficiently integrated with that available to the left hemisphere" subserving the verbal response or mastering the task of deciding about the number of stimuli presented ("1" or "2"). These authors studied a right brain-damaged patient in whom disruption of interhemispheric transfer of visual information was demonstrated by recording of evoked potentials (Smania et al. 1996). In this patient, extinction of contralesional visual stimuli on double simultaneous presentation dropped dramatically when, instead of a verbal response (saying "2"), a motor response with no preferential triggering by one hemisphere (e.g., moving the eyes upward) or a response requiring bilateral muscular control (e.g., lowering the chin) was required to report double stimuli. According to the authors, when 2 stimuli are simultaneously presented to a right brain-damaged patient, the one perceived directly by the intact left hemisphere (dominating the verbal response) has stronger central representation, thus masking the weaker callosal input coming from the damaged hemisphere. In case of unilateral presentation to the damaged right hemisphere, the same callosal input triggers normal verbal recognition because no other stimulus competes for response in the left hemisphere. Impaired verbal report of stimuli arriving at the right hemisphere when simultaneously presented with stimuli to the left hemisphere was documented in a split-brain patient (Reuter-Lorenz et al. 1995). In line with the hypothesis that weak or impaired access to the responding hemisphere can modulate extinction and neglect phenomena, Corballis et al. (2005) recently described a callosotomized patient showing striking neglect for stimuli presented to the right hemisphere when these had to be reported verbally (i.e., by the left hemisphere). Neglect, however, disappeared when nonverbal responses were required, and the report was no more under the control of the left hemisphere. Thus, callosal damage might contribute, at least in some cases, to the appearance of split-brain-like confabulations or extinction of stimuli presented to the damaged hemisphere.

**Extinction**

An important clinical phenomenon that has been interpreted in terms of interhemispheric disconnection is extinction after unilateral brain damage. Extinction refers to the failure of verbally reporting the most contralesional of a pair of simultaneous stimuli while maintaining an intact or largely preserved ability of reporting the same contralesional stimulus when presented alone. Extinction can occur both within and between different sensory modalities. It is often clinically detected in the recovery phase of neglect, though it can doubly dissociate from it. Marzi and co-workers (Smania et al. 1996) argued that right brain-damaged patients with extinction might suffer a partial interhemispheric disconnection syndrome, "whereby the information on the stimulus presented to the damaged right hemisphere cannot be efficiently integrated with that available to the left hemisphere" subserving the verbal response or mastering the task of deciding about the number of stimuli presented ("1" or "2"). These authors studied a right brain-damaged patient in whom disruption of interhemispheric transfer of visual information was demonstrated by recording of evoked potentials (Smania et al. 1996). In this patient, extinction of contralesional visual stimuli on double simultaneous presentation dropped dramatically when, instead of a verbal response (saying "2"), a motor response with no preferential triggering by one hemisphere (e.g., moving the eyes upward) or a response requiring bilateral muscular control (e.g., lowering the chin) was required to report double stimuli. According to the authors, when 2 stimuli are simultaneously presented to a right brain-damaged patient, the one perceived directly by the intact left hemisphere (dominating the verbal response) has stronger central representation, thus masking the weaker callosal input coming from the damaged hemisphere. In case of unilateral presentation to the damaged right hemisphere, the same callosal input triggers normal verbal recognition because no other stimulus competes for response in the left hemisphere. Impaired verbal report of stimuli arriving at the right hemisphere when simultaneously presented with stimuli to the left hemisphere was documented in a split-brain patient (Reuter-Lorenz et al. 1995). In line with the hypothesis that weak or impaired access to the responding hemisphere can modulate extinction and neglect phenomena, Corballis et al. (2005) recently described a callosotomized patient showing striking neglect for stimuli presented to the right hemisphere when these had to be reported verbally (i.e., by the left hemisphere). Neglect, however, disappeared when nonverbal responses were required, and the report was no more under the control of the left hemisphere. Thus, callosal damage might contribute, at least in some cases, to the appearance of split-brain-like confabulations or extinction of stimuli presented to the damaged hemisphere.

**Anatomical Evidence Supporting the Influence of Interhemispheric Disconnection on Neglect**

From an anatomical standpoint, the hypothesis of a contribution of interhemispheric disconnection to some of the behavioral features characterizing neglect has received empirical support from studies in animals and humans. Watson et al. (1984) found that on several behavioral measures (i.e., responses to auditory, visual, and somesthetic stimuli, circling behavior, and asymmetric orienting), postoperative neglect was more severe in monkeys that underwent callosotomy prior to ablation of the frontal arcuate gyrus as compared with monkeys that underwent only equivalent cortical ablation. Gaffan and Hornak (1997) showed that monkeys with combined resection of the right optic tract (causing complete left hemianopia) and the corpus callosum (causing complete interhemispheric forebrain disconnection) showed more severe neglect than monkeys undergoing section of frontoparietal connections (also causing substantial neglect, see Frontoparietal Disconnection and Spatial Neglect above) or resection of the parietal and/or prefrontal cortex (causing very mild and transitory neglect). The authors argued that severe neglect in monkeys with combined optic tract–callosal disconnection depended on the impossibility of the intact attentional frontoparietal system of the blind hemisphere to receive visual information gathered by the seeing hemisphere and to build up an adaptive compensatory mnemonic representation of the space contralateral to the blind hemisphere. In keeping with the proposal of Gaffan and Hornak, the defective integration of visual input from the intact left hemisphere with damaged mechanisms of space representation in the right hemisphere appears to produce erroneous compensation of the visual field defect in patients with neglect and concomitant hemianopia. This is revealed by horizontal distance-reproduction tasks forcing patients to set distance end points toward the attended or the otherwise spontaneously unattended hemispace (Bisiach et al. 1996; Doricchi and Angelelli 1999; Nico et al. 1999; Doricchi et al. 2005). In these tasks, the combination of neglect and hemianopia leads to marked and paradoxical hypometric distance reproductions in the ipsilesional direction (probably as a consequence of saccadic undershooting made in order to keep the endpoint from falling into the blind hemifield) and hypermetric responses in the contralesional direction (as a consequence of saccadic overshooting made to shift the blind hemifield away and bring the endpoint position into the seeing hemifield moving contralesionally; Ishii 2002). Also in keeping with the findings of Gaffan and Hornak, the greater severity of neglect symptoms in patients with concomitant neglect and hemianopia, as compared with those with neglect unaccompanied by hemianopia, is well documented by studies from several laboratories and can be particularly evident in tasks requiring parallel processing of stimuli extending along the horizontal space such as, for example, the line-bisection task (D’Erme et al. 1987; Binder et al. 1992; Harvey et al. 1995; Bartolomeo and Chokron 1999a; Harvey and Milner 1999; Doricchi et al. 2005).

Results analogous to those obtained by Gaffan and Hornak with hemianopic-callosotomized monkeys were recently reported in human patients by Park et al. 2006, who found that among “...the various combinations of occipital plus adjacent lesions, only occipital injury together with complete injury to the splenium of the corpus callosum significantly contributed to the frequency and severity” of spatial neglect (p. 60). Park et al.
further observed that in their group of patients with unilateral damage in the territory of the posterior cerebral artery, visual field defects per se did not predict the severity of neglect. We notice, however, that the absence of a significant correlation between hemianopia and severity of neglect only reconfirms the well-established double dissociation between visual neglect and hemianopia (McFie et al. 1950; Gainotti 1968) and is not surprising to be found in a group of unselected right brain-damaged patients. In such an unselected group including hemianopic patients both with and without neglect, the compensatory leftward attentional bias of pure hemianopic patients (Fuchs 1920; D’Erme et al. 1987; Barton and Black 1998) will tend to cancel out the relationship between presence of hemianopia and severity of neglect that is observed when only patients with neglect are considered (Halligan et al. 1990; Gaffan and Hornak 1997; Doricchi and Angelelli 1999).

Finally, it is worth emphasizing that in patients with neglect, the influence of interhemispheric disconnection might be at work independently from the presence of concomitant visual field defect. Kashiiwagi et al. (1990) described a patient who demonstrated left neglect signs after callosal infarction, with magnetic resonance imaging showing no lesion in the right hemisphere. This patient had neglect when performing paper-and-pencil tasks with his right hand but not when using his left hand (see also the already mentioned study by Corballis et al. 2005). More recently, the above reviewed lesion overlapping study by Doricchi and Tomaiuolo (2003) found that damage to callosal radiation can be a lesional correlate of chronic neglect unaccompanied by hemianopia.

In conclusion, though interhemispheric disconnection might not be a sufficient cause of neglect per se, as also suggested by the fact that split-brain patients do not systematically show signs of left neglect (Plourde and Sperry 1984; Gazzaniga and Baynes 2000), it could still explain some neglect-related phenomena. In this sense, the confabulations produced by split-brain patients and those generated by neglect patients might have at least partially superimposed functional causes, with the left hemisphere being totally deprived of right hemisphere processing in the first case or being provided with incompletely processed right hemisphere information in the second case.

**Conclusion**

A wealth of data from cognitive neurosciences indicate that the brain is a mosaic of functionally interconnected areas. The anatomical basis of these functional links begins now to be explored in detail (Mesulam 2005). Recent developments in neuroimaging techniques, such as DTI and fiber-tracking techniques, permit to map in vivo the white matter pathways, both in normal individuals (Catani et al. 2002) and in neurological patients (Thiebaut de Schotten et al. 2005). These new and exciting developments are likely to change our way of looking at brain-behavior relationships, for example, by giving the possibility of directly testing the disconnection hypotheses put forward by Geschwind (1965) 40 years ago (Catani and ffytche 2005), and more specifically, the interhemispheric disconnection hypothesis of neglect as well as the frontoparietal disconnection hypothesis reviewed here. Full consideration of the pathways of communication between functional regions of the brain will help avoid the risk of interpreting in a localist, “phrenological” way, patterns of performance which reflect instead the complexity of multiple, highly interactive processes.

**Supplementary Material**

Supplementary Material can be found at http://www.cercor.oxfordjournals.org/.

**Notes**

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**References**


Chafee MV, Goldman-Rakic PS. 2000. Inactivation of parietal and prefrontal cortex reveals interdependence of neural activity


Re-appraisal of previous lesion overlap studies: Methods

Overlap Region of Interest (ROI). Data from the original overlapping maps were used to define the maximum overlap described by Doricchi and Tomaiuolo (Doricchi and Tomaiuolo 2003) (see Table 1 for MNI coordinates). The subcortical maximum lesion overlaps of the Karnath et al study (Karnath et al. 2004, Fig. 2) were manually drawn on the same Montreal Neurological Institute (MNI) template using MRIcro 1.40 (Rorden and Brett 2000) (http://www.sph.sc.edu/comd/rorden/mricro.html). For the remaining studies (Mort et al. 2003; Corbetta et al. 2005), the maximum overlap was manually drawn in MRIcro, using the MNI coordinates reported in the studies for the lesion overlaps correlated to spatial neglect. Supplementary Table 1 reports the MNI coordinates of the centroids of the subcortical maximum overlap areas in these studies.

DTI acquisition. Diffusion-weighted magnetic resonance imaging data were acquired from a healthy 41-year-old male right-handed volunteer, using DTI at 1.5T. Diffusion parameters were TR/TE/angle: 12.5s/66.2ms/90°, voxel size: 1.88x1.88x2 mm³, b-value: 700 s/mm², 41 directions and 1 B0 image. Data were acquired with NMR pulse sequences, reconstructed with NMR reconstructor package and post processed with AIMS/Anatomist/BrainVisa software, available at http://brainvisa.info.

Tractography. Diffusion image analysis was performed using tensor diffusion imaging and deterministic fiber algorithm using Brainvisa 3.0.2 (http://brainvisa.info/). Fiber tracking was performed using two manually drawn ROIs: (1) a global ROI based on previously published methods (Catani et al. 2005) and (2) caudal selective ROIs (Thiebaut de Schotten et al. 2006), which allowed us to differentiate the single fasciculi (Supplementary Figure 1).

Bundle normalization and visualization. EPI B0 image was normalized with default parameters to the EPI template space provided by statistical parametric mapping software (SPM2, Welcome Department of Cognitive Neurology, Institute of Neurology, London, UK,
http://www.fil.ion.ucl.ac.uk/spm/), in association with MATLAB version 7 (The Mathworks, Inc., MA, USA). The resulting deformation matrix was applied to the fiber bundles (Thiebaut de Schotten et al. 2006). The maximum overlaps and the normalized bundles were visualized using Anatomist 3.0.2 (http://brainvisa.info).

References


## Supplementary Table 1

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Coordinates of the centroids of the subcortical maximum overlap areas
Supplementary Figure 1

ROIs used to track the SLF II, the SLF III and the AF.
The red cross indicates the subcortical maximum lesion overlap found in patients with extrapersonal neglect by Committeri et al. (Committeri et al. 2006, Fig. 2, first row, axial slice Z = +28)). The lesion overlap described in patients with extrapersonal neglect by Doricchi and Tomaiuolo (Doricchi and Tomaiuolo 2003) is indicated in green. The matching MNI templates showing the trajectories of SLF II, III and AF are also shown.
The phenomenology of endogenous orienting

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Abstract

Can we build endogenous expectations about the locus of occurrence of a target without being able to describe them? Participants performed cue–target detection tasks with different proportions of valid and invalid trials, without being informed of these proportions, and demonstrated typical endogenous effects. About half were subsequently able to correctly describe the cue–target relationships (‘verbalizers’). However, even non-verbalizer participants showed endogenous orienting with peripheral cues (Experiments 1 and 3), not depending solely on practice (Experiment 2). Explicit instructions did not bring about dramatic advantages in performance (Experiment 4). With central symbolic cues, only verbalizers showed reliable endogenous effects (Experiment 5). We concluded that endogenous orienting with peripheral cues can occur independently of participants developing explicit hypotheses about the cue–target relationships.

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Keywords: Spatial attention; Response time; Consciousness; Implicit knowledge

1. Introduction

Attention can be directed to an object in space either in a relatively automatic way (e.g., when a honking car attracts the attention of a pedestrian), or in a more controlled mode (e.g., when the pedestrian monitors the traffic light waiting for the ‘go’ signal to appear). The distinction goes back at least to William James, who distinguished between “passive, reflex, non-voluntary, effortless” attention and “active and voluntary” attention (James, 1890, p. 416). More recently, this distinction has been variously referred to as reflexive/voluntary, bottom-up/top-down, stimulus-driven/goal-directed or strategy-based, or exogenous/endogenous (see Egeth & Yantis, 1997, for review). It is important to note that, logically speaking, this dichotomy must be relative rather than absolute. A strictly defined exogenous mechanism would leave no room for psychological variables such as attentional orienting (Pashler, 1998). On the other hand, it is possible that, to endogenously direct one’s attention toward an object, this object must previously have been selected as such by exogenous
processes. Endogenous orienting by itself may only facilitate location-based, and not object-based, processing (He, Fan, Zhou, & Chen, 2004; Macquistan, 1997). Thus, exogenous and endogenous mechanisms normally interact during visual exploratory behavior. Several lines of evidence indicate that, rather than being two modes of orienting of the same attentional system, they may be qualitatively different, albeit interacting, processes. This evidence includes data from normal participants, both in behavioral studies (Berger, Henik, & Rafal, 2005; Briand, 1998; Briand & Klein, 1987; Klein & Shore, 2000; Lupiáñez et al., 2004; Prinzmetal, McCool, & Park, 2005) and in neuroimaging studies (Corbetta & Shulman, 2002). The dichotomy is also supported by the patterns of performance shown by brain-damaged patients (Bartolomeo & Chokron, 2002; Bartolomeo, Siéroff, Decaix, & Chokron, 2001; Losier & Klein, 2001).

Exogenous and endogenous orienting can be studied in relative isolation from one another by using cue–target detection tasks (Posner, 1980). In a typical experiment, participants are presented with three horizontally arranged boxes. They fix their gaze on the central box and respond by pressing a key when a target (an asterisk) appears in one of two lateral boxes. Each target is preceded by a cue at various time intervals, or stimulus-onset asynchronies (SOAs). Cues can be central (an arrow presented in the central box pointing toward one lateral box) or peripheral (a brief brightening of the contour of one lateral box). Valid cues correctly predict the location of the impending target, whereas invalid cues indicate the box on the opposite side. Cues can be either informative, when targets usually appear in the cued box (e.g., 80% of the time), or non-informative, when targets can appear with equal probabilities at the cued or at the uncued location.

Peripheral non-informative cues attract attention automatically, or exogenously (Jonides, 1981; Müller & Rabbitt, 1989). This exogenous attentional shift, revealed by faster response times (RTs) for cued than for uncued trials, is typically observed only for short SOAs between cue and target. For SOAs longer than ~300 ms, uncued targets evoke faster responses than cued targets (Posner & Cohen, 1984), a phenomenon known as inhibition of return (IOR; Klein, 2000; Posner, Rafal, Choate, & Vaughan, 1985) or inhibitory after-effect (Tassinari, Aglioti, Chelazzi, Marzi, & Berlucchi, 1987).

With peripheral informative cues, the cue validity effect persists even at longer SOAs, thus suggesting that the initial exogenous shift is later replaced by a more controlled, endogenous shift toward the same location (Müller & Findlay, 1988). This endogenous shift would be motivated by strategic considerations, because subjects know that targets will appear with high probability at the cued location.

Endogenous shifts are more often studied using central, symbolic cues (arrows). However, this approach may introduce potential confounds. For example, more levels of processing, such as the interpretation of the symbol, may be involved in central cueing than in peripheral cueing. Central and peripheral cues might act on distinct stages of information processing, e.g., an early perceptual stage for peripheral cues, and a late perceptual or a decision stage for central cues (Riggio & Kirnser, 1997). Consistent with this hypothesis, facilitation induced by symbolic cues develops more slowly than with peripheral cues, requiring at least 300 ms to reach optimum (see, e.g., Müller & Findlay, 1988). Indeed, orienting in response to central and peripheral cues may implicate distinct attentional systems (Briand, 1998; Briand & Klein, 1987; Klein, 1994).

In view of these concerns, endogenous and exogenous processes can be explored and compared using exclusively peripheral cues, whose degree of informativeness about the location of the impending target is varied in different experiments (Müller & Rabbitt, 1989). Typically, one may employ cues that most frequently predict the target to occur at the cued box, or cues that are most frequently invalid, thus indicating the uncued box as the probable site of target occurrence (Posner, Cohen, & Rafal, 1982).

It is traditionally maintained that endogenous orienting is voluntary and requires conscious awareness, whereas exogenous orienting is more reflexive in nature. For example, Jonides proposed that “on the one hand, certain salient stimuli have reflexive control over attention allocation... On the other hand, subjects have internal control over the spatial allocation of attention so that, when motivated, they can voluntarily shift attention from one part of the field to another” (Jonides, 1981, p. 188). It is hard to imagine how such a voluntary shift, requiring appropriate motivation, could take place without conscious effort. Concerning the relationship between strategies and awareness, Posner and Snyder explicitly related “conscious attention” to “strategies,” defined as “programs... which are under the conscious control of the subject” (Posner & Snyder, 1975, p. 73). Consistent with these views, McCormick (1997) demonstrated that exogenous cues presented below a subjective threshold of awareness can capture attention without awareness. He employed a cue–target
From near-threshold normal vision (Kentridge, Heywood, & Weiskrantz, 1999b), G.Y.’s performance suggested that information provided by cues presented in a blind field, and thus not consciously perceived, can be used to orient attention. However, in sharp contrast with the results of normal participants in the McCormick study, G.Y. could benefit from cue-associated information even when cues and targets were spatially separated (i.e., 68.35% of the cues indicated a target appearing at the opposite location). In other words, G.Y. could engage endogenous orienting processes as a consequence of cues which he denied to have seen. Although direct comparison between the two studies is difficult, because blindsight can be qualitatively different from near-threshold normal vision (Kentridge, Heywood, & Weiskrantz, 1999b), G.Y.’s performance suggests that, at least in some cases, endogenous orienting can occur without explicit awareness.

Forms of attentional orienting different from exogenous shifts can also take place in the absence of explicit awareness, as was shown by Lambert (2003), Lambert, Naikar, McLahan, and Aitken (1999), and Lambert and Sumich (1996). They presented bilateral letter cues to participants. The relative locations of the letters predicted the side of target onset. Results showed benefits at the cued locations, independent of the participants’ capacities of describing the cue–target relationships in a post-experiment questionnaire, and even of the participants’ ability to acknowledge that a cue had been presented (Lambert et al., 1999). In a similar vein, Lambert and Sumich (1996) found cueing benefits for target detections preceded by words whose semantic category (living or non-living) predicted the side of occurrence of the target, again in the absence of any explicit acknowledgment of the word–target relationship. These effects cannot be attributed to purely exogenous shifts, because there was no spatial co-occurrence of valid cues and targets.

The present study originated from comments that some normal participants made after performing the experiments reported in a study devoted to orienting of attention in left spatial neglect (Bartolomeo et al., 2001), wherein we explored exogenous and endogenous orienting processes in normal participants and neglect patients using a cue–target detection paradigm with peripheral cues. In different experiments, we used different proportions of valid trials (50, 80 or 20%), and found in normal participants the typical effects of endogenous orienting. Cues gave an advantage to valid trials in the 80% valid condition, and, at long enough SOAs, a benefit for invalid trials in the 20% condition (see also Posner et al., 1982; Warner, Juola, & Koshino, 1990). Before each experiment, participants were informed of the level of cue predictiveness. Despite this, at informal debriefing some participants claimed not to have paid attention to the cues at all. Instead, they just tried to respond as fast as possible to the targets. And yet, these participants’ performance showed the typical effects of cue predictiveness: Not only effects related to exogenous orienting, like IOR with non-informative cues, but also a durable advantage for cued locations with 80% valid cues and a cost for cued locations larger than IOR with 20% valid cues. Since these last effects are usually taken as resulting from endogenous orienting, we wondered whether this form of orienting is really based on volitional strategies, as is usually maintained (Jonides, 1981; Posner & Snyder, 1975), or it can rather result from more implicit processes.

To address this question, in the present study we asked normal participants to perform cue–target detection tasks with different degrees of cue predictiveness. We also varied the information about cue predictiveness given to the participants prior to the testing session, and tried to assess participants’ awareness of the cue–target relationships by using a post-experiment questionnaire. In Experiments 1–3 and 5, no information was given about the relationships between cue and target positions. Participants had to figure out these relationships on their own. To obtain an internal, within-subjects control for participants’ performance, in a first block of trials cues were not informative about the localization of the impending target. In a second block, which followed the first without interruption, the level of cue predictiveness varied across experiments. Any change in performance between the first and the second experimental block can only result either from practice, or from
participants’ reactions to changes in cue predictiveness. In addition to provide an internal control for participants’ performance, this two-block structure can also be informative about the participants’ capacities of developing strategies in response to unexpected changes in the cue–target relationships.

These issues are of obvious importance for theoretical accounts of attention and consciousness. In the words of Posner and Raichle, “there seems to be some general relationship between voluntary programming and awareness, since both depend on attentional systems, yet these functions may themselves be dissociated. During REM sleep we are aware of dreams but often cannot exercise voluntary control over them... The exact connection between awareness and control, and the connection of both to the attentional networks, remain for future research to resolve” (Posner & Raichle, 1994, p. 204). Moreover, because in most of our experiments participants were not informed of the cue–target relationships, but had to find out this information by themselves, our study bears implications for theories of explicit and implicit learning, and their relationship with awareness (see Jiménez, 2003). Finally, cue–target paradigms similar to the ones we employed are widely used in clinical settings, to explore performance of patients with focal brain damage (Bartolomeo & Chokron, 2001; Losier & Klein, 2001; Posner, Walker, Friedrich, & Rafal, 1984), degenerative dementia (Danckert, Maruff, Crowe, & Currie, 1998), Parkinsonian syndromes (Posner et al., 1985; Rafal, Posner, Friedman, Inhoff, & Bernstein, 1988), schizophrenia (Posner, Early, Reiman, Pardo, & Dhawan, 1988) and other pathological conditions, as well as of normal elderly participants (Castel, Chasteen, Scialfa, & Pratt, 2003). The present study intended to contribute to a better knowledge of such an elegant and widely used neuropsychological diagnostic tool as is the Posner RT paradigm.

2. General method

2.1. Participants

A total of 100 undergraduates from the Paris 5 University (27 males, median age 26 years, range 20–46) took part in a series of five experiments for course credit (20 participants for each experiment). All were right-handed and reported normal or corrected-to-normal vision. All participants were naïve to the purposes of the experiments. No participant took part in more than one experiment.

2.2. Apparatus and stimuli

Stimulus presentation and response collection were controlled by the Psychlab software (Gum, 1996). Three black empty square boxes, with a 10-mm long, 0.34-mm thick side, were displayed on a white background. The boxes were horizontally arranged, the central box being located at the center of the screen. The central box contained a small black rectangular fixation point (1.02\texttimes 1.34 mm). Distance between boxes was 30 mm. Cues consisted of a 300-ms thickening (from 0.34 to 0.68 mm) of the contour of one box (Experiments 1–4), or in the presentation for 300 ms of a central horizontal arrow indicating one of the two lateral boxes (Experiment 5). The target was an asterisk 4.40-mm in diameter, appearing inside one of the lateral boxes, with its center at a retinal eccentricity of about 3.83°.

2.3. Design and procedure

Participants sat in front of a computer monitor at a distance of approximately 50 cm. Each trial began with the appearance of the three placeholder boxes for 500 ms. Then a cue was displayed for 300 ms. The target appeared at a variable SOA (600, 800 or 1000 ms) from cue onset, and remained visible until a response was made. These SOAs were chosen to render the target onset difficult to predict on a temporal basis, while maintaining the cue–target interval in a range apt to explore endogenous shifts of attention. Participants were instructed to maintain fixation on the fixation point and to respond to the target as quickly and accurately as possible, by pressing the center of the space bar with their right index finger. They were told that targets would be preceded by cues, indicating either the box in which the target was to appear, or the opposite box; however, participants were invited to concentrate exclusively on targets and to pay no attention to cues. After an intertrial interval of 1000 ms, a new trial began.
Unknown to the participants, two blocks of trials followed one another without interruption. In the first block, consisting of 24 trials preceded by 12 practice trials, valid and invalid cues were presented in equal proportion. In the second block, made of 90 trials preceded by 18 practice trials, the level of predictability of cues varied according to the experiment. In 12 additional catch trials, interspersed within the second block, only cues were presented and participants had to refrain from responding. Trials within each block were presented in a previously randomized sequence. The same sequence of trials was used for all participants. In Experiments 1–3 and 5, participants were not informed of the cue–target relationship; they were told about the presence of the cues, but asked not to pay attention to them and invited just to respond to the targets as fast as possible.

Immediately after the experiments, participants filled out a questionnaire (inspired by Lambert et al., 1999), asking (1) whether there was any cue–target relationship, and (2) whether cues predicted most frequently the target location or the wrong location. On the basis of their responses to the questionnaire, participants were classified as ‘verbalizers,’ if they answered correctly either to both questions, or as ‘non-verbalizers,’ if their answer to question 1 was incorrect. Participants who declared that there was a consistent relationship between the cues and the targets in response to question (1), but chose the wrong possibility in response to question (2), were discarded from RT analysis. Following Lambert et al. (1999), after completion of the questionnaire we asked participants to rated their confidence in their judgment on the following scale: 1 (pure guess), 2 (mainly guesswork), 3 (possibly the correct choice), 4 (probably the correct choice), 5 (very likely the correct choice), 6 (certainly the correct choice).

2.4. Analysis of results

The first 12 trials of block 1 and the first 18 trials of block 2 were discarded as practice. Response times exceeding the 100–1000 ms range were discarded from analysis. After this first trimming, the mean RT and SD were calculated for each participant. RTs exceeding the range of 2.5 SDs around the participant’s mean were considered as outliers and discarded from further analysis. Overall, the trimming procedures resulted in the exclusion of 2% of responses. For each experiment, mean RTs were entered in a repeated-measures analysis of variance (ANOVA), with Group (verbalizers, non-verbalizers) as between-participants factor and Block (1, 2), Cue (valid, invalid) and SOA (600, 800, 1000 ms) as within-participants factors. The z level was set to 0.05. The critical comparisons to evaluate the hypothesis that endogenous orienting is possible independent of explicit awareness concerned the Cue Validity effect in the two experimental blocks for each group of participants. Thus, two comparisons (one per participant group) were planned in advance, with the z level set to 0.05 according to the modified Bonferroni procedure proposed by Keppel (1991).

3. Experiment 1: 50% → 80% valid trials

The first experiment addressed the following questions: Can people use a probabilistic cue–target relationship, such as the fact that most of the cues are valid, despite the absence of explicit information about this relationship? And, if yes, does this knowledge always have an explicit, declarative correlate? To explore these issues, we presented participants with a Posner-type RT paradigm with 80% valid peripheral cues, without giving any explicit instruction as to the informative value of the cue. Moreover, unknown to participants the 80% valid block started after a first block of trials with non-informative cues. Immediately before the experimental session, participants were orally given the following instructions: “You are going to see three boxes on the screen. Keep your gaze fixed on the central box and press this key as soon as you see an asterisk appearing in one lateral box. Try to be as fast as possible. Before the asterisk appears, the contour of one lateral box will briefly become thicker. Do not pay attention to this occurrence and be sure to respond only to the asterisk.” Participants were asked to fill a post-experiment questionnaire (inspired by Lambert et al., 1999) soon after the RT session was completed.

1 We preferred these more theoretically neutral terms to ‘aware’ and ‘unaware.’ Although in the following sections we occasionally used ‘awareness’ as a shorthand for ‘ability to produce an accurate verbal report,’ we would like to postpone to the Section 7 any considerations about the implications of our results for phenomenal awareness.
In this experiment, we expected to observe a cost for valid trials with respect to invalid trials (i.e., IOR) in the first block. In the second block, this cost should persist if RTs are not influenced by the change in informative value of the cues. If, on the other hand, this change modifies participants’ expectations, in the sense that they now look forward to detecting the target at the cued location, this endogenous orienting should offset the cost for valid trials (IOR). Thus, IOR should be masked by this concomitant, strategy-based endogenous orienting (see Berlucchi, Chelazzi, & Tassinari, 2000; Danziger & Kingstone, 1999; Lupiáñez et al., 2004).

3.1. Methods

The task consisted of a first block with uninformative cues; a second block with 80% valid cues followed without interruption and unknown to the participants. The post-experiment questionnaire was given soon after completion of the RT session.

3.2. Results and discussion

One participant was excluded from analysis because he responded to all the catch trials. Three further participants were discarded because they gave inconsistent responses to questions (1) and (2) of the post-experiment questionnaire. They stated that there was a consistent relationship between cues and target, but chose the wrong one, i.e., that targets most often appeared at the uncued location, when answering question (2). The remaining participants were divided into verbalizers \( (N = 7) \) and non-verbalizers \( (N = 9) \) as described under Section 2. Table 1 reports the results for the two groups. The main effect of Group did not approach significance, \( F < 1 \), nor did this factor interact with other factors. In particular, the Group \( \times \) Block \( \times \) Validity interaction was not significant, \( F < 1 \). Overall, valid trials evoked responses slower by 18 ms than invalid trials, \( F(1,14) = 4.65, p = .049 \). There was an effect of SOA, \( F(2,28) = 7.89, p = .002 \), because RTs tended to speed up with increasing SOA. Importantly, an interaction between Block and Cue Validity emerged, \( F(1,14) = 30.54, p < .0001 \) (Fig. 1A).

In the block with non-informative cues, RTs were faster for invalid trials (372 ms) than for valid trials (409 ms), consistent with the phenomenon of IOR. In the 80% validity block, instead, valid trials evoked similar RTs (380 ms) to invalid trials (388 ms), as if an endogenous facilitation for validly cued targets masked IOR. If this interpretation is correct, it would imply that people can use endogenous, strategy-based processes even in the absence of explicit instructions to do so. No other effect or interaction reached significance.

The planned comparisons showed that the Block \( \times \) Validity interaction was statistically reliable both for verbalizers, \( F(1,14) = 17.61, p < .0001 \), and for non-verbalizers, \( F(1,14) = 12.94, p = .0029 \). All verbalizers gave a confidence rating of 3 (“possibly the correct choice”) or more to their answers to the questionnaire (mean, 4.14; \( SD, 1.21 \)). The mean confidence rating for non-verbalizers was 2.22 (\( SD, 0.83 \)), with a single

<table>
<thead>
<tr>
<th>Table 1</th>
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<tr>
<td>Mean response times (in ms) for verbalizer and non-verbalizer participants to Experiment 1 (block 1: 50% valid trials; block 2: 80% valid trials) and Experiment 2 (block 1: 50% valid trials; block 2: 50% valid trials)</td>
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<tr>
<td>SOA (ms)</td>
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<td>Block 1</td>
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<td>Block 2</td>
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participant giving a score of 1 ("pure guess") to his response. Excluding this participant from analysis did not change the significance of the Block \times Validity interaction for non-verbalizers, $F(1,13) = 9.76, p = .008$. Thus, even participants unable to verbally report about the correct relationships between cues and targets were able to employ these relationships to speed up their responses to validly cued targets in block 2. This result suggests that endogenous processes may be unavailable to verbal report.

However, before concluding that the results of Experiment 1 show endogenous masking of IOR in block 2, we had to consider a possible alternative account. IOR has been shown to decrease with practice (Weaver, Lupiáñez, & Watson, 1998; but see Pratt & McAuliffe, 1999). Thus, it might be that participants continued to employ exclusively exogenous processes in the second block of Experiment 1, but the RT cost for valid trials gradually decreased as a result of practice. This seems unlikely, because we did not simply observe a decrease of IOR in the second block, but its complete disappearance. Nevertheless, to address more directly this concern, we performed an additional experiment, with an identical number of trials, but in which the percentage of valid trials remained 50% throughout the whole task.

4. Experiment 2: 50% > 50% valid trials

In this experiment, we asked a new group of participants to perform a task identical to Experiment 1, with the only exception that now the cues of the second block continued to be nonpredictive as in the first block. In other words, the proportions of valid and invalid cues remained 50% throughout the experiment. If the lack of IOR in the second block of Experiment 1 were due to practice, we expected a similar outcome in Experiment 2. If, on the other hand, IOR persisted even in the second block of Experiment 2, then practice cannot account for the difference between blocks observed in Experiment 1.

4.1. Methods

The task and the instructions were identical to Experiment 1, with the exception that now the proportion of valid and invalid trials in the second block was equal. Both in the first and in the second block of trials cues were non-informative of the location of the impending target.

![Fig. 1](image_url). Response times (in ms) for verbalizer and non-verbalizer participants as a function of the percentage of valid trials in the two consecutive blocks of Exp. 1 (block 1: 50% valid cues; block 2: 80% valid cues) (A), and for the two blocks of Exp. 2 (both with 50% valid cues) (B).
4.2. Results and discussion

Table 1 shows the results of Experiment 2. One participant was excluded because he responded to most catch trials. On the post-experiment questionnaire, 13 participants correctly responded that there was no special relationship between cue and target location, and were thus considered as verbalizers; six mistakenly concluded that there was one, and were included in the non-verbalizer group. The mean confidence ratings for the two groups were, respectively, 2.50 (SD, 1.38) and 2.31 (SD, 1.25). One non-verbalizer and two verbalizers stated that their response was a pure guess. The two groups of participants did not perform differently on the RT task, \( F < 1 \), nor the Group factor interacted with any other factor. In particular, the Group \( \times \) Block \( \times \) Validity interaction did not reach significance, \( F(1,17) = 1.60, p = 0.22 \). Valid trials evoked slower responses (370 ms) than invalid trials (341 ms), \( F(1,17) = 23.88, p = .0001 \), thus showing a typical IOR of around 30 ms. In particular, both groups of participants showed IOR in both blocks of the experiment (Fig. 1B). No other effect or interaction reached significance. Planned comparisons confirmed a significant IOR for both groups of participants in block 2 (35-ms IOR for verbalizers, \( F(1,17) = 46.72, p < .0001 \); 31-ms IOR for non-verbalizers, \( F(1,17) = 18.22, p = .0005 \)).

The results of Experiment 2 strongly suggest that the Block \( \times \) Validity interaction observed in Experiment 1 was not an effect of practice, but was the consequence of an advantage for valid trials (or of a cost for invalid trials) that masked IOR in block 2.

The discrepancy between our results (unchanging IOR over two consecutive experimental blocks) and Weaver et al.’s (1998) results (decreasing IOR with practice) may easily be explained if one consider that in the Weaver et al.’s setting the overall number of trials per participant \((N = 2040)\) was much larger than in our procedure \((N = 156)\). Thus, in the Weaver et al.’s experiments, the duration of practice was much more extended than in ours, allowing for a detrimental effect on IOR to occur. Indeed, in detection tasks practice-related reductions of IOR typically occur after 200 or more trials (Lupiañez, Weaver, Tipper, & Madrid, 2001).

4.3. Experiment 3: 50% \( \rightarrow \) 20% valid trials

Thus far, our results suggest that one can show facilitation for validly cued targets in a RT task with peripheral informative cues by employing processes that (1) can be learned without explicit instructions and (2) may not be available for subsequent verbal report. This outcome is surprising in view of the traditional account of the effect of informative cues as being propositional and strategy-based; it might, instead, reflect implicit processing of the cue–target relationships. As already mentioned, McCormick (1997) showed that cues presented below a subjective threshold for awareness can capture attention without awareness, but cannot endogenously redirect attention to the uncued location. Awareness of cues seemed necessary to inhibit the cued location to reorient attention elsewhere. In other words, people might be able to “inhibit their reflexive orienting only when they can predict its location and develop a strategic set to inhibit signals there” (Rafal & Henik, 1994, p. 18). More generally, strategies of attentional orienting might primarily consist of inhibition of irrelevant objects (see Johnston & Hawley, 1994; McCormick, 1997). In light of these considerations, we wondered whether the active, strategy-based inhibition implicated in reorienting attention from a cued to an uncued location might involve a more explicit processing of cue–target relationship, which would allow participants to correctly recount it in the post-experiment questionnaire. Experiment 3 aimed at answering this question, by employing an experimental design similar to Experiment 1, but with a majority of invalid trials in the second block. Thus, the optimal strategy to produce fast responses to targets in the second block would be to inhibit the attentional capture exerted by the peripheral cue and to reorient attention toward the uncued box. This should result in an advantage of invalid over valid trials for long enough SOAs (Bartolomeo et al., 2001; Posner et al., 1982), in the range of those employed in the present study.

4.4. Methods

The task and instructions were identical to the preceding experiments, with the exception that now the second block consisted of 20% valid and 80% invalid trials.
4.5. Results and discussion

Results are presented in Table 2 and Fig. 2A.

Two participants responded to more than half of the catch trials, two other participants gave inconsistent responses to the post-experiment questionnaire. These four participants were therefore excluded from analysis. Six of the remaining participants gave correct responses to the questionnaire and were classified as verbalizers; 10 responded incorrectly and were labeled as non-verbalizers. As in Experiment 1, no effect of Group emerged, $F < 1$, nor this factor interacted with other factors. In particular, the Group $\times$ Block $\times$ Validity interaction did not reach significance, $F < 1$. The Block factor was significant, $F(1,14) = 17.57$, $p < .001$, because responses were 45-ms faster in block 1 than in block 2, perhaps as a consequence of an increased cost for valid trials in block 2 (see the Block $\times$ Validity interaction below). Invalid trials evoked faster responses than valid trials, $F(1,14) = 35.83$, $p < .0001$. RTs decreased with increasing SOAs, $F(2,28) = 7.81$, $p = .002$. A 21-ms IOR was present in the first block. In the second block, this inverse validity effect increased to 54 ms, as if an endogenous process, driven by the fact that most trials were invalid,

Table 2
Mean response times (in ms) for verbalizer and non-verbalizer participants to Experiment 3 (block 1: 50% valid trials; block 2: 20% valid trials) and Experiment 4 (same design with explicit instructions)

<table>
<thead>
<tr>
<th>SOA (ms)</th>
<th>Verb</th>
<th>Non-verb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Valid</td>
<td>Invalid</td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Block 1</td>
<td>600</td>
<td>391</td>
</tr>
<tr>
<td></td>
<td>800</td>
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<tr>
<td>Block 2</td>
<td>600</td>
<td>449</td>
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<tr>
<td></td>
<td>800</td>
<td>437</td>
</tr>
<tr>
<td></td>
<td>1000</td>
<td>442</td>
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</table>

Exp. 3: 50% > 20%

Exp. 4: 50% > 20%, explicit instructions

Fig. 2. Response times (in ms) for verbalizer and non-verbalizer participants as a function of the percentage of valid trials in the two consecutive blocks of Exp. 3 (block 1: 50% valid cues; block 2: 20% valid cues) (A), and for the two blocks of Exp. 4 (B) (same cue–target relationships, but with explicit instructions).
added to IOR in determining an extra cost for valid trials. This resulted in an interaction between Block and Cue Validity, $F(1,14) = 10.97, p = .005$. No other effect or interaction reached significance. Planned comparisons showed that the Block by Validity interaction was reliable in verbalizers, $F(1,14) = 7.58, p = .02$, and approached significance in non-verbalizers, $F(1,14) = 3.43, p = .085$ (see Fig. 2A). After excluding a single non-verbalizer participant, the interaction became reliable, $F(1,13) = 5.18, p = .040$. This participant showed IOR in the first block, and no valid/invalid difference in the second block, as if she had adopted the strategy of orienting her attention towards the cued box in the second block. Thus, except for this single non-verbalizer participant, the results of Experiment 3 suggest that explicit awareness of the cue/target contingencies may not be necessary to inhibit cued locations. The mean confidence ratings for verbalizers and non-verbalizers were, respectively, 2.83 ($SD$, 0.75) and 2.70 ($SD$, 0.82). No participant rated his or her response as resulting from pure guess.

5. Experiment 4: 50% → 20% valid trials with explicit instructions

Results of Experiments 1–3 suggested that phenomena related to endogenous orienting of attention following peripheral cues may result from processes that (1) can be learned without explicit instructions and (2) may not be accessible to subsequent verbal report.

We decided to pursue the issue of possible differences in performance related to the awareness of the cue–target relationships in a more direct way, i.e., by giving participants explicit information about these relationships and by comparing their performance with that of participants who had not received explicit instructions.

5.1. Methods

The procedure was identical to Experiment 3, with the only exception that participants were given explicit instructions about the information conveyed by the cue in block 2. Specifically, participants were told that the experiment would consist of two parts. In the first part, cues would not be informative about the localization of the target; targets would appear in the cued or in the uncued box with equal probability. In the second part, most targets would appear in the uncued box, so the best strategy when a cue occurs would be to expect the target appear in the other box. However, as in the previous experiments, there was nothing to alert participants that they were passing from block 1 to block 2.

5.2. Results and discussion

Three participants were excluded from analysis; two because they responded to most of the catch trials, one because he gave inconsistent responses to the post-experiment questionnaire. Of the remaining participants, 12 gave correct responses to the questionnaire, and were thus classified as verbalizers; five responded incorrectly, despite the fact that before performing the experiment they had received an accurate description of the cue–target relationships. These five participants were classified as non-verbalizers. The mean confidence ratings for verbalizers and non-verbalizers were, respectively, 4.17 ($SD$, 1.85) and 3.40 ($SD$, 1.52). No participant rated his or her response as resulting from pure guess. Results are reported in Table 2 and Fig 2B.

There was no effect of Group on performance, $F(1,16) = 1.64, p = .22$, nor did this factor interact with other factors. In particular, the Group × Block × Validity interaction did not reach significance, $F < 1$. RTs were faster in the first (335 ms) than in the second block of trials (367 ms), $F(1,16) = 15.23, p = .001$. Valid trials evoked slower responses (378 ms) than invalid trials (324 ms), $F(1,16) = 25.49, p = .0001$. RTs decreased with increasing SOA, $F(2,32) = 21.27, p < .0001$. As in Experiment 3, there was a Block × Validity interaction, $F(1,16) = 5.10, p = .038$, because the 43-ms inverse validity effect (IOR) in the first block increased to 65 ms in the second block. There was also a Block × Validity × SOA interaction, $F(2,32) = 4.84, p = .014$, probably a spurious finding resulting from unusually fast RTs (284 ms) in the invalid condition of the first block at 800-ms SOA. No other effect or interaction reached significance.
5.3. Comparison between implicit and explicit instructions

The principal aim of this study was to better understand the relationships between conscious/declarative processes and orienting of attention. A critical comparison to address this issue is that between the results of the present experiment and those of Experiment 3, in which the same stimulus and procedure was used, but with the notable exception that participants were not informed in advance of the cue/target relationship. As we have seen, some of the participants in Experiment 3 (those labeled as ‘verbalizers’) were able to guess the correct cue/target relationship by themselves. However, this knowledge yielded no substantial advantage to their performance. It might be that this occurred because verbalizers understood the cue/target relationships relatively late in the course of the experiment. As a result, their knowledge had perhaps no measurable influence on their overall performance. If so, then providing participants with the appropriate knowledge before the experiment starts should yield an observable increase in the inverse validity effect, as suggested by comparing the two panels of Fig. 2. To test this prediction, we analyzed the combined results of Experiments 3 and 4 using a repeated-measures ANOVA with the additional between-participants factor of Instructions (implicit, Experiment 3; explicit, present experiment). The Block × Cue interaction was present both for verbalizers, \( F(1,28) = 11.47, p = .002 \), and for non-verbalizers, \( F(1,28) = 5.12, p = .032 \). The Instructions factor only tended to significance, \( F(1,28) = 3.46, p = .073 \). The overall RTs were 348 ms with explicit instructions and 380 ms with implicit instructions. The only significant effect involving the Instructions factor was an interaction with SOA, \( F(2,56) = 3.46, p = .007 \). RTs decreased linearly with increasing SOA for participants having received implicit instructions (respectively 389, 380, and 370 ms at the 3 SOAs). With explicit instructions, on the other hand, the already tendentially faster RTs decreased more abruptly with longer SOA, especially between the two shorter SOAs (370, 338, and 334 ms at the 3 SOAs). This effect may reflect an increased readiness to respond after 600-ms SOA for participants knowing from the beginning of the task the actual cue–target relationships. However, the three-way interaction with Instructions, SOA and Cue Validity did not approach significance, \( F < 1 \), suggesting that the effect was unspecific, because it occurred both for valid and for invalid trials. No other effect or interaction reached significance. Thus, comparing explicit and implicit instructions did not bring about robust evidence that knowing in advance the cue–target relationships lead to a substantial advantage in performance. To explore more directly the effect of explicit awareness, as resulting from verbal instructions, on endogenous processes, we subtracted the validity effects for the two blocks to obtain an index of endogenous orienting, and compared the index of verbalizers in Experiment 4 with that of non-verbalizers in Experiment 3 (i.e., compared the performance of those whom we can be confident were aware, with the performance of those whom we can be confident were not). The endogenous index was 26 ms for verbalizers in Experiment 4 and 23 ms for non-verbalizers in Experiment 3. The 3-ms difference was far from statistical significance, \( F < 1 \). If one makes the arbitrary but conservative assumption that the magnitude of the advantage conferred by explicit awareness should amount at least to 30 ms, then the likelihood ratio (Glover & Dixon, 2004) in favour of a null effect is 9.2. This result indicates a lack of substantial effects of explicit instructions on participants’ endogenous processes.

6. Experiment 5: 50% → 80% valid trials with central cues

We have thus far found evidence suggesting the presence of components of endogenous orienting to peripheral cues in the absence of a verbal-declarative correlate. Perhaps the importance of such a correlate would emerge if participants saw not a mere luminance change in their visual periphery, but an arrow, with its associated symbolic value, in central vision. Experiment 4 aimed at testing this possibility.

6.1. Methods

The task was identical to Experiment 1, with 50% valid cues in block 1 and 80% valid cues in block 2, except that the cue was not peripheral, but consisted of a horizontal arrow presented inside the central box, and

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2 We thank a reviewer of the present article for suggesting this comparison.
pointing to one of the lateral boxes. Prior to the task, participants were informed that an arrow would appear in the central box prior to the targets, and were invited not to pay attention to this occurrence, but to concentrate upon responding to targets.

6.2. Results and discussion

Seven participants correctly responded to the questionnaire, 11 gave incorrect responses. The two remaining participants gave inconsistent responses and were excluded from analysis. Table 3 and Fig. 3 report the results.

The Group factor did not reach significance, $F(1,16) = 1.12, p = 0.31$. Responses were faster in block 1 (321 ms) than in block 2 (370 ms), $F(1,16) = 47.67, p < .0001$, perhaps as a consequence of the introduction of catch trials in the second block.\(^3\) Validly cued trials evoked faster responses than invalid trials, $F(1,16) = 5.36, p = .034$. There was an interaction between Block and Cue Validity, $F(1,16) = 6.11, p = .025$, because the validity effect was 19 ms in the 80% valid cue block, but only 5 ms in the first block with uninformative cues. We recall that a similar interaction had occurred in Experiment 1, which employed identical cue–target relationships but used peripheral cues. Increasing SOA led to faster RTs, $F(2,32) = 6.69, p = .004$.

The Group $\times$ Block $\times$ Validity interaction did not reach significance, $F(1,16) = 2.58, p = 0.13$, although inspection of Fig. 3B does suggest that awareness of the cue/target relationships increased validity effects. No other effect or interaction reached significance. The planned comparisons showed that the Block $\times$ Validity interaction resulted significant for verbalizers, $F(1,16) = 6.81, p = .02$, but not for non-verbalizers, $F < 1$. The mean confidence ratings for the two groups were, respectively, 3.43 ($SD$, 1.51) and 1.73 ($SD$, 0.65). One verbalizer and three non-verbalizers stated that their response was a pure guess. Excluding these participants from analysis did not change the overall pattern of results, and in particular the Block $\times$ Validity interactions (verbalizers, $F(1,12) = 7.06, p = .02$; non-verbalizers, $F(1,12) = 2.64, p = 0.13$). Thus, at variance with the results of Experiment 1, results of Experiment 4 do not unambiguously show that participants incapable of giving an appropriate verbal description of the cue–target relationships can make use of the informative value of a central, symbolic cue.

Hommel, Pratt, Colzato, and Godijn (2001) gave participants arrows or words (the German words for LEFT, RIGHT, UP, and DOWN) indicating a possible target location without any informative value (e.g., the target location was equiprobable and independent of the indications given by the cue), with explicit instructions stressing the non-informativeness of the cues (see also Ristic, Friese, & Kingstone, 2002; Tipples, 1997). Despite participants’ knowledge of the uselessness of the cues, their RTs to cued locations resulted faster than those to uncued locations, thus showing an automatic orienting in reaction to a symbolic cue. Perhaps

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\(^3\) Except for Experiment 3, this effect was not significant in the preceding experiments, which seems to argue against our conjecture. A tendency in the same sense was, however, always present, with the exception of Experiment 1, in which it occurred only for invalid trials. The endogenous advantage for valid trials in the second block of Experiment 1 may have offset the cost resulting from the introduction of catch trials.
the larger number of trials used in the Hommel et al.’s study encouraged their participants to develop the (erroneous) hypothesis that cues could help target detection, and their attention was consequently oriented toward the cued location. Alternatively or in addition, our task instructions, which explicitly asked participants not to pay attention to the arrows, might have been literally followed by some of our participants. Thus, our results partially support Hommel et al.’s (2001) conclusions in showing that orienting effects in response to symbolic cues can occur in the absence of explicit instructions. Nevertheless, our finding of a reliable validity effect only for the group of participants capable of giving an appropriate verbal description of the relationships between cue and target further qualifies this hypothesis by suggesting that, with symbolic cues, validity effects might depend on participants developing explicit hypotheses about these relationships. We note, however, that the lack of a significant interaction between Group, Block and Validity in the present experiment calls for further experimental evidence to settle this issue.

7. General discussion

In cue–target detection tasks, cues can influence response times to subsequent targets as a function of the proportion of valid and invalid trials. This influence is not a direct consequence of the sensory properties of the cue, but results from higher-order knowledge about the probability that the target will appear in the cued or in the uncued box. Thus, these effects are often characterized as being “endogenous” in nature, as opposed to being “exogenous” cueing effects. Exogenous effects, on the other hand, would occur on a trial-by-trial basis. Examples are the transient facilitation in responding to validly cued targets (Carrasco, Ling, & Read, 2004; Jonides, 1981; Nakayama & Mackeben, 1989), or the cost for these same targets observed with longer SOAs (IOR; Klein, 2000; Posner & Cohen, 1984; Tassinari et al., 1987). In the present experiments, most participants were able to build endogenous expectations about the side of occurrence of a target preceded by informative cues, despite the absence of previous knowledge about cue–target relationships in Experiments 1–3 and the presence of a first block of trials with non-informative cues. Thus, participants could adapt their response strategies to an unexpected change in the cue–target relationships. Additionally, the block with
non-informative cues provided an important internal control for performance in the block with informative cues. Any differences in cue validity effect between the two blocks would indicate that the informative value of cues in the second block influenced performance. With peripheral cues, around half of these participants were unable to describe the strategy they used, even when prompted by a two-answer, forced-choice question. Despite this, participants demonstrated an offset of IOR with 80% valid cues in Experiment 1 (which did not simply depend on a practice effect, as shown by Experiment 2), and an increase of the cost for valid trials in Experiment 3. The results of Experiment 4 showed that the fact of providing participants with advance knowledge of the cue–target relationships did not dramatically change their target detection times with peripheral cues. In Experiment 5, we observed a similar pattern of results for central symbolic cues, with the important exception that only participants capable of giving a verbal description of the cue–target relationship demonstrated a reliable RT advantage for targets occurring at the cued position.

As mentioned in Section 1, Lambert et al. (1999) showed that people can implicitly learn contingencies relating the position of the upcoming target with the identity of bilateral letter cues presented near the position expectancy boxes (e.g., W and S predicted a right-sided target). Although most participants did not answer appropriately to a post-experiment questionnaire, they showed an early facilitation for cued locations, followed by a cost for these same locations reminiscent of IOR (Lambert et al., 1999, Experiment 1). The characteristics of these attentional effects differed both from exogenous orienting, because Lambert et al.’s results implied a learned association between cue identity and target location, and from endogenous orienting, because when participants were made aware of the cue–target relationships, the late cost for cued targets reversed to a facilitation (Lambert et al., 1999, Experiment 4). Our present findings differ by those of Lambert et al., because here we show that even processes usually labeled as endogenous (late facilitation for cued targets with 80% valid cues in Experiment 1, or increased inhibition for cued targets with 20% valid cues in Experiment 3) can be learned without explicit instructions and be nevertheless impervious to subsequent verbal description. As already mentioned, McCormick (1997) ingeniously employed an orienting analogue of the process-dissociation procedure (Jacoby, Toth, & Yonelinas, 1993), and showed that below-threshold cues can capture attention, but one needs supra-threshold cues to direct attention to an uncued spatial position. An obvious difference between the present study and McCormick’s is that in our study all cues were clearly perceptible; what some of our participants were not able to realize was the relationship between the cued side and the target side.

One might surmise that non-verbalizer participants elaborated an ‘unconscious’ strategy. According to this view, our participants might have used a form of implicit learning independent of hypothesis-testing strategies, and which yielded a form of knowledge that was inaccessible to consciousness (see Jiménez, 2003). It has indeed been proposed that even metacognitive processes labeled as “monitoring,” and therefore implying awareness, may in fact operate without much awareness (Reeder & Schunn, 1996). For example, the blindsight patient G.Y. learned to change his strategy of response during the course of an experiment with a majority of invalid cues, shifting from an advantage to validly cued targets to an advantage for invalid trials, without being able to describe this change (Kentridge & Heywood, 2000). However, although an appropriate verbalization can be considered as a reliable indicator of conscious processing (Merikle, Smilek, & Eastwood, 2001), the converse is not necessarily true. Lack of verbalization cannot be conclusively considered to indicate lack of awareness (Perruchet & Vinter, 2002; Shanks, 2003). For example, it might simply indicate lack of memory (Allport, 1988) (although in the present study this would seem unlikely, given that the post-experiment questionnaire was administered soon after the completion of each experiment; it is also hard to imagine that G.Y.’s lack of commentary about the use he made of anti-cues can be the result of a memory problem).

The phenomenological tradition has often distinguished between direct forms and more reflexive forms of consciousness, a distinction endorsed, among others, by Husserl, Sartre and Ricoeur (reviewed by Vermersch, 2000) (see Dalla Barba, 2002; Dulany, 1997; Edelman & Tononi, 2000; Marcel, 1988, for more recent proposals of similar dichotomies). In particular, the distinction between “experiential” sensitivity, which is related to phenomenal consciousness, and “informational” sensitivity, which may guide one’s actions without the

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4 To avoid perturbing the participants’ inferences about the cue–target relationships in the second block, the number of trials of the first block was kept to a minimum. This renders all the more impressive the significance of the Block × Validity interaction in all experiments apart from number two, which was a control for practice effects.
existence of conscious sensations (Flanagan, 1992), seems consistent with the present findings. Also relevant to our results, Merleau-Ponty (1942) distinguished between ‘spoken’ and ‘acted’ forms of perception (perception parlée and perception vécue). For example, as we enter a room we may feel an impression of disorder, only to later discover that it comes from a crooked picture on the wall. Before realizing this, our consciousness was experiencing things impervious to verbal report. This would by no means imply that the first impression on entering the room was unconscious. Rather, it was a form of consciousness not immediately amenable to verbal description. In Merleau-Ponty’s words, “consciousness is a network of significant intentions, sometimes clear by themselves, sometimes experienced rather than spoken out” (Merleau-Ponty, 1942, p. 187). Our present results extend to endogenous orienting of attention the general notion that “doing” often precedes “understanding.”

Neuropsychological evidence from brain-damaged patients offers instances of dissociations between direct consciousness and reflexive consciousness (Bartolomeo & Dalla Barba, 2002). An amnesic patient with anosognosia was able to intellectually acknowledge the presence of his deficits, as well as his incapacity to directly appreciate them (Dalla Barba, Bartolomeo, Ergis, Boisés, & Bachoud-Lévi, 1999). Patients with left unilateral neglect typically lack explicit awareness for events occurring in the neglected part of space, perhaps because these events fail to capture their attention (see Bartolomeo & Chokron, 2002, for review). However, some patients may show signs of more implicit knowledge of neglected items (D’Erme, Robertson, Bartolomeo, & Daniele, 1993). When shown two drawings of a house, identical with the exception that red flames emerged from the left side of one of the houses, a patient with neglect failed to note any difference between the drawings, but consistently chose the non-burning house when asked which one she would have preferred to live in (Marshall & Halligan, 1988). It would seem that this patient had some access to the semantics of the drawings, but could not develop the reflexive consciousness necessary to explicitly acknowledge it in verbal report. When another neglect patient showing a similar pattern of performance was asked to explain why he should prefer the non-burning house, he produced confabulatory responses, such as that the non-burning house had an extra fireplace (Manning & Kartsounis, 1993). This example further underlines the inaccessibility of these processes to reflexive consciousness. On the other hand, the celebrated film director Federico Fellini was perfectly conscious of suffering from neglect at an intellectual level, to the point of jokingly asking to include his new condition in his calling card; nevertheless, he persisted in producing funny drawings of women lacking their left half (Cantagallo & Della Sala, 1998). These dissociations between immediate and reflexive forms of consciousness in brain-damaged patients, together with the present results showing the possibility of endogenous orienting without verbal reports in normal participants, call into question the nature of the relatively preserved endogenous processes in left neglect patients.

As mentioned in Section 1, we showed that neglect patients are able to endogenously direct their attention to left targets preceded by right cues, if they have sufficient time to do it and if they know that most cues are invalid (Bartolomeo et al., 2001). Patients’ RTs to left invalidly cued targets were in the range of their responses to right-sided targets at 1000-ms SOA, thus reversing in this particular condition the typical disengage deficit of neglect patients (see Losier & Klein, 2001, for review). This result suggested the relative preservation of endogenous processes in left neglect and therefore stressed the importance of an exogenous attentional bias in this condition (Bartolomeo & Chokron, 2002; Losier & Klein, 2001). In the light of the present results, one may wonder whether the patients’ ability to endogenously direct their attention towards the neglected side resulted from explicit strategies, or from more implicit processes, similar to those demonstrated in the present study by non-verbalizer participants (patients in the Bartolomeo et al.’s study received the usual instructions before performing the RT tasks, and were thus informed about the predictive value of the cues).

The study of the relationships between immediate and high-order forms of consciousness in normal participants and brain-damaged patients is likely to put constraints on cognitive models of consciousness, to promote specific attempts to search for their neural correlates, and to suggest theoretically motivated techniques of rehabilitation for neuropsychological deficits.

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Bressanone, Italy, January 2002. The presentation was subsequently selected for publication as a short note (Decaix, Sieroff, & Bartolomeo, 2002). Caroline Decaix is now at the Hopital Charles Foix, Ivry, France. We thank Gianfranco Dalla Barba, William Prinzmetal and two anonymous reviewers for their insightful comments on previous versions of the manuscript.

References


Visual neglect
Paolo Bartolomeo

Purpose of review
Left visual neglect is a frequent and dramatic consequence of right hemisphere lesions. Diagnosis is important because behavioural and pharmacological treatments are available. Furthermore, neglect raises important issues concerning the brain mechanisms of consciousness, perception and attention.

Recent findings
Recent behavioural findings and new techniques, such as transcranial magnetic stimulation, direct cortical and subcortical stimulation during brain surgery, and diffusion tensor imaging tractography, have provided evidence relevant to the debate concerning the functional mechanisms and the anatomical bases of neglect.

Summary
Several component deficits appear to interact in producing different forms of neglect. Rather than lesions at single cortical levels, dysfunction of large-scale brain networks, often induced by white matter disconnection, may constitute the crucial antecedent of neglect signs.

Keywords
attention, mental imagery, perception, spatial cognition, white matter fibre pathways

Introduction
In a neurological ward, it is frequent to come upon patients who look at objects on their right side with intense interest, while paying no attention to what happens on their left. Visual neglect is a dramatic but often overlooked consequence of right hemisphere damage, usually of vascular origin. Patients do not eat from the left part of their dish, they bump their wheelchair into obstacles situated on their left, and have a tendency to look to right-sided details as soon as a visual scene deploys, as if their attention were ‘magnetically’ attracted by these details [1]. They are usually unaware of their deficits (anosognosia), and often obstinately deny being hemiplegic [2]. Patients with left brain damage may also show signs of contralesional, right-sided neglect, albeit more rarely and usually in a less severe form [3]. Diagnosis is important, because neglect predicts poor functional outcome in stroke [4]. Moreover, effective rehabilitation strategies are available [5], and there are promising possibilities for pharmacological treatments [6].

Bedside testing
A few paper-and-pencil tests, which may be administered at the bedside, can confirm diagnosis [7]. Neglect patients omit to cancel left targets in search tasks, deviate rightward when bisecting horizontal lines, and fail to copy the left part of drawings [8].

Patients’ asymmetries of performance in cancellation tasks can vary from a few left-sided omissions to cancellation of only the rightmost items. Some patients will cancel again and again the same right-sided items, thus showing a pathological ‘revisiting behaviour’ for objects presented in the supposedly ‘normal’ sector of space [9]. Patients who can compensate for their deficit to some extent, either as a result of spontaneous recovery or after rehabilitation, may cancel out all the elements, but keep starting from the right extremity of the sheet, at variance with normal participants, who most often start from the left part of the sheet [10], perhaps as a consequence of the left-to-right reading habits typical of Western cultures (see [11]).

Line bisection is also a useful tool to discriminate between neglect and visual field defects, such as left homonymous hemianopia, which was once thought to cause neglect. Contrary to this hypothesis, there are patients with left hemianopia but no neglect, who deviate leftward on line bisection [12–14]. The association of left
neglect and hemianopia, however, produces the largest rightward deviations on line bisection [12,13,15]. When given relatively short lines to bisect (e.g. 5 cm or less), patients may paradoxically shift the bisection point leftwards (the so-called crossover effect) [16]. The copresence of visual field defects may be a necessary condition for this [17] and other neglect-related behaviours [15] to occur.

When copying a drawing, neglect patients often omit left-sided details (more rarely, patients may increase the number and spatial extension of left-sided details [18]). When drawing well known objects from memory, patients may demonstrate similar omissions of left-sided details. Surprisingly, however, some of these patients make more symmetrical drawings when blindfolded than in free vision (Fig. 1) [19]. Thus, even in drawing from memory, patients’ attention may be ‘magnetically’ drawn to the right-sided details they just drew, rendering difficult the completion of the drawing on the left, neglected side. Perhaps sensory deprivation may be used in neglect rehabilitation to offset the attention-capturing power of right-sided visual details.

**Imaginal neglect**

Despite these demonstrations of the importance of right-sided visual stimuli in eliciting left neglect, neglect can manifest itself in the absence of visual stimuli. When describing known places from memory, patients may omit details situated in the left part of the (mental) scene [20]. Only a minority of patients with visual neglect, however, also show imaginal neglect, perhaps because imagined details have less attention-capturing power than real ones [10,21]. Imaginal neglect can also occur in the absence of signs of perceptual neglect, either at onset [22] or, perhaps more commonly, as a result of selective compensation for the perceptual aspects of the syndrome [10]. Patients often learn with time (and possibly the help of people around them) to explore more thoroughly their visual environment. Compensation, however, may be more difficult to obtain in the more abstract imaginal domain, which is rarely the object of rehabilitation or of more informal reminders to ‘look to your left’.

Neglect patients may also deviate rightwards on the mental bisection of number intervals; for example, when asked which is the median number between 11 and 19, they may answer ‘17’ [23]. In this domain as well, visual and imaginal performance may dissociate. Biased performance with mental number lines may be related to concomitant prefrontal damage and spatial working memory impairment [24]. It would indeed be surprising to find that all neglect patients demonstrate such a mental bias, given that people do not always imagine numbers in spatial arrangements, and even when they do, their mental diagrams are not necessarily oriented along the horizontal direction [25].

When a patient was asked to use a black touch screen to represent the night sky, and to touch the locations occupied by (imaginary) stars [26], he put significantly more stars to the right of the screen midline, but especially when the stars remained illuminated after the touch. If the screen remained black, the asymmetry was less evident. This again suggests an attention-capturing influence of real right-sided visual stimuli on patients’ neglect [19,27]. Perceptual influences on spatial imagery, however, seem less relevant for casual, task-unrelated stimuli. When patients were asked to imagine and describe the map of France with eyes open or blindfolded, performance was similar regardless of the condition [28]. During sleep, neglect patients may show suppression of leftward-directed rapid eye movements (REMs). A recent case report described a patient with left visual neglect and frequent nystagmoid REMs with alternating leftward slow/rightward fast phases, corresponding to dreams with consistent visual events, such as a train running leftward, but virtually no nystagmoid REMs in the opposite direction [29]. The complex relationships between perception and imagery in general [30], and concerning neglect in particular, are difficult to predict from the available theoretical models.

**Functional mechanisms**

Even from this brief description, it should be clear that left neglect cannot be considered as a unitary, homogeneous entity. Several dissociations of performance have been described between the outcomes of neuropsychological tasks, whether clinical [31] or experimental [32]. It has proven difficult to find a clear
correspondence between behavioural dissociations and different lesion localizations, perhaps because clinical, low-definition images are often used, and the focus has mainly been on grey matter lesions (see below). As mentioned before, a possible source of (spurious) dissociations may result from patients learning to use compensatory strategies in a domain but not in another. This occurrence may be difficult or impossible to ascertain; functional dissociations with corresponding lesion differences (e.g. [24,31]) seem the best suited to substantiate claims for different underlying causes.

The possible mechanisms leading to neglect have fostered considerable debate during the last few decades. Several independent deficits, probably interacting with each other, may contribute to neglect signs. These may include deficits in orienting of spatial attention [33], in building or maintaining spatial representations [34], or in programming left-directed hand movements [35]. It is also possible, however, that some deficits have more weight than others in shaping patients’ behaviour. For example, deficits of spatial attention, such as an engagement of attention towards right-sided, nonneglected items as soon as the visual scene unfolds [1,32,36,37], may combine to produce overt neglect behaviour [1,35].

Lesional correlates
In keeping with the multifarious nature of their symptoms, patients with neglect often have relatively large lesions of the right hemisphere, which are likely to disrupt several functional modules. The precise localization of these lesions, however, still remains controversial. Neglect patients’ lesions, as detected by computerized tomography (CT) or MRI, often overlap on the inferior parietal lobule (IPL), at the junction with the temporal lobe [48]. Conflicting evidence, however, also indicates lesions of the middle and rostral parts of superior temporal gyrus (STG) [49,50], and tends to exclude a role for lesions of the temporoparietal junction [51]. Recent proposals have suggested that parietal or STG dysfunction may lead to different forms of neglect (respectively, personal/extrapersonal [49], or viewer-centred/stimulus centred [52]). The lesion overlap method, however, obviously lacks spatial resolution, may reflect differences in vascular territories rather than true functional architecture, and does not satisfactorily deal with multiple lesions [53,54]. Thus, other neuroimaging techniques have recently been applied to the study of the neural bases of neglect.

Transcranial magnetic stimulation (TMS) transiently disrupts the integrated activity of cortical networks in a relatively noninvasive fashion. TMS over the left hemisphere decreased left extinction and neglect in right brain-damaged patients [55]. Temporary inactivation of the middle/rostral portions of the STG produced nonlateralized impairments in visual search tasks [56]. In the same study, TMS stimulation of the central sectors of the STG did not modify judgments of the length of horizontal lines (Landmark task), in contrast to inactivation of the posterior parietal cortex, which provoked lateralized effects similar to those shown by patients with neglect on the same task.

Functional MRI has been employed to explore the neural correlates of subacute and recovered neglect [57]. Four weeks after a stroke, when performing a response time task to lateralized stimuli, neglect patients had decreased activation of structurally intact fronto-parietal regions in the right hemisphere (especially the intraparietal sulcus, the superior parietal lobe and the dorsolateral prefrontal cortex), coupled with robust activation of the homologous regions in the left hemisphere. Thirty-nine weeks after lesion onset, recovery of neglect signs was paralleled by the disappearance of the imbalance between the two superior parietal lobules. Thus, lesions of the right temporoparietal junction may determine a functional imbalance of the superior parietal lobules, which are structures important to attentional orienting, with consequent biased orienting towards right-sided objects. A promising implication of these results is the possibility to ameliorate left neglect by functionally inhibiting the left parietal lobe using TMS [55].

Temporary electrical inactivation of small brain region (~5 mm) stimuli can be performed during brain surgery to prevent postoperative deficits. Thiebaut de Schotten et al. [58] described the performance of two patients who bisected horizontal lines while being submitted to the surgical resection of low-grade gliomas. Patients deviated rightward upon inactivation of the supra-marginal gyrus (the rostral subdivision of IPL) and of the caudal part of the STG; however, bisection performance was accurate when more rostral portions of the STG or the frontal eye field were inactivated. These findings run counter to a strong version of the STG hypothesis [51], at least as far as line bisection is concerned. Importantly, however, the strongest deviations occurred in one patient upon
inactivation of a white-matter region in the depth of the IPL after most of the tumour had been removed. The course of long association fibres in the white matter of this particular patient was mapped in postoperative MRI scans using diffusion tensor MRI tractography (DT-MRI), a new technique capable of tracking white matter fibres [59]. The tract whose inactivation had brought about the maximal rightward deviation corresponded to the likely human homologous of the second branch of the superior longitudinal fasciculus [60]. This pathway connects the inferior and the superior parietal lobules, particularly the angular gyrus (BA 39), including the intraparietal sulcus (IPS), to the middle and superior frontal gyri (BA 9, 8, 46 and 6) [61]. The observation that functional fronto-parietal disconnection dramatically disrupted the symmetrical processing of the visual scene is consistent with many findings obtained in rodents, in nonhuman primates and in human stroke patients (see [54,62] for review). A more recent intraoperative stimulation study [63] confirmed the TMS findings reviewed above [56], by showing that electrical inactivation of the central STG during brain surgery produced nonlateralized impairments in visual search. These results [56,63] thus seem consistent with the possibility that regions of the right temporal lobe are important for visual recognition and memory [64], but their relevance to neglect remains unclear.

DT-MRI tractography can be used to track the long-range white matter pathways (Fig. 2) and then explore, in a standardized brain space, their relationships with the lesions found in stroke patients with standard, anatomical MRI. Thus, for the first time white matter pathways can be explored in detail in the living human brain, and the focus can shift from impairment of cortical modules to dysfunction of cortical networks [59]. A recent meta-analysis [62] of previous lesion overlapping studies demonstrated that the subcortical lesions of neglect patients invariably overlapped at or near the human homologues of superior longitudinal fasciculus (SLF) II and III. Disconnection between cortical modules may thus be a general mechanism of neglect [54]. This possibility is also consistent with the results of computer simulations of attention [65].

These results support models of neglect which postulate a dysfunction of large-scale right-hemisphere networks [66]. Parietal components of the network may determine the perceptual salience of extrapersonal objects; frontal components may be implicated in the production of an appropriate response to behaviourally relevant stimuli, in the online retention of spatial information, or in the focusing of attention on salient items through reciprocal connections to more posterior regions. The network approach may prove important for patient diagnosis because a particular form of white matter disconnection may have greater predictive value than the localization of grey matter lesions. The demonstration of anatomically intact but functionally inactivated areas may also open perspectives for treatments (whether pharmacological or

Figure 2 Three long-range fronto-caudal white matter pathways in the right hemisphere of the normal human brain, with their cortical projections

The arcuate fasciculus (AF) and the human homologues of the second and third branches of the superior longitudinal fasciculus (respectively, SLF II and III) are shown [61].
rehabilitative), aimed at restoring normal neural activity in these areas.

Although neglect commonly results from lesions in the territory of the middle cerebral artery, posterior cerebral artery strokes can also give rise to neglect signs. Also in these patients, the presence of neglect seems to correlate with inter and intrahemispheric disconnection [67]. Bird et al. [68] located the maximal lesion overlap on a white matter tract linking the parahippocampal gyrus to the angular gyrus, as tracked using DT-MRI of a normal individual.

Conclusion
Neglect remains a highly controversial topic, both concerning its mechanisms and its neural bases. Besides its clinical importance, its study has implications for our understanding of attention, consciousness, and perception. Research on the functional mechanisms appears to be moving from the description of dissociations in patients’ performance to the dissection of the possible component deficits and of their modes of interaction. New, high-resolution imaging techniques are providing evidence relevant to the debate on the anatomical bases of neglect, shifting the focus from the study of cortical modules to large-scale brain networks. A huge explanatory gap still separates the functional and the anatomical descriptions of neglect, but it is a gap which seems now to be narrowing at a fast pace.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:
• of special interest
•• of outstanding interest

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27 New, ingenious tests were used in this single case study to explore the mechanisms of imaginal neglect.
28 Due to problems with right brain damage. Neurology 2006; 67:1801–1808.
30 Neglect patients produced rightward-shifted medians of imagined numerical intervals, but not of nonnumerical intervals, such as those between letters or months.
34 New, ingenious tests were used in this single case study to explore the mechanisms of imaginal neglect.
37 Patients with imaginal neglect produced incomplete descriptions of a map of France, irrespective of the presence or absence of (task-unrelated) visual stimuli.
39 An intriguing report of REM asymmetries in a neglect patient, and of their relation to his dreams.
43 A systematic analysis of the component deficits of spatial orienting in 26 patients with right brain damage. The anatomical correlates of the deficits are also described, but only clinical images with limited resolution were available.
According to the authors, the precise combination of component deficits may vary between patients, and no single deficit needs to be crucial to neglect.


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68 Bird CM, Malhotra P, Parton A, et al. Visual neglect following right posterior cerebral artery infarction. J Neurol Neurosurg Psychiatry 2006; 77:1008–1012. This study on patients with infarcts in the territory of the right posterior cerebral artery indicated a possible disconnection correlate of neglect in white matter tracts running in the depth of the temporal lobe.
Brain networks of spatial awareness: Evidence from diffusion tensor imaging tractography

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Key words: Unilateral Neglect, Spatial Attention, Diffusion MRI

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Summary
Left unilateral neglect, a dramatic condition which impairs awareness of left-sided events, has been classically reported after right hemisphere cortical lesions involving the inferior parietal region. More recently, the involvement of long-range white matter tracts has been highlighted, consistent with the idea that awareness of events occurring in space depends on the coordinated activity of anatomically distributed brain regions. Damage to the superior longitudinal fasciculus (SLF), linking parietal to frontal cortical regions, or to the inferior longitudinal fasciculus (ILF), connecting occipital and temporal lobes, have been described in neglect patients. In this study four right-handed patients with right-hemisphere strokes were submitted to a high-definition anatomical MRI with diffusion tensor imaging (DTI) sequences and to a paper-and-pencil neglect battery. We used DTI tractography to visualize the SLF, the ILF and the inferior fronto-occipital fasciculus (IFOF), a pathway running in the depth of the temporal lobe, not hitherto associated with neglect. Two patients with cortical involvement of the inferior parietal and superior temporal regions, but intact and symmetrical fasciculi, showed no signs of neglect. The other two patients with signs of left neglect had superficial damage to the inferior parietal cortex and white matter damage involving the IFOF. These findings suggest that superficial damage to the inferior parietal cortex per se may not be sufficient to produce visual neglect. In some cases, a lesion to the direct connections between ventral occipital and frontal regions (i.e. IFOF) may contribute to the manifestation of neglect by impairing the top-down modulation of visual areas from frontal cortex.
Introduction

Left visual neglect is a frequent consequence of right hemisphere lesions, entailing a defective awareness for left-sided events. Lesions determining neglect often overlap on the temporoparietal junction (TPJ)\(^1,2\). Conflicting evidence, however, indicates lesions of more rostral parts of superior temporal gyrus (STG)\(^3,4\). Signs of neglect can also occur after lesions of the ventrolateral prefrontal cortex (VLPFC)\(^5\), of the medial temporal lobe\(^2\), of the occipital lobe and the corpus callosum\(^6\), or after damage to two major rostro-caudal brain pathways, the superior\(^7,8\) and inferior\(^9\) longitudinal fasciculi. Thus, rather than damage to single cortical modules, dysfunction of large cortical networks\(^10,11\) can be the crucial antecedent of neglect\(^7,8\),\(^12-14\).

Diffusion tensor imaging (DTI) tractography can be used to track the long-range white matter pathways\(^15\) and then explore, in a standardized brain space, their relationships with the lesions found in stroke patients with standard, anatomical MRI. A recent meta-analysis\(^13\) of previous lesion overlapping studies demonstrated that the subcortical lesions of neglect patients invariably overlapped at or near the SLF. Disconnection between cortical modules might thus be a general mechanism of neglect\(^12\). This possibility is also consistent with the results of monkey studies,\(^16,17\) rodent studies\(^18\) and of computer simulations of attention\(^19\). Here we describe four patients with strokes in the right hemisphere, two of whom showed signs of extrapersonal neglect on paper-and-pencil tests. We used DTI tractography to directly visualize the SLF, the ILF and the inferior fronto-occipital fasciculus (IFOF), a pathway running in the depth of the temporal lobe, not hitherto associated with neglect.

Methods

Four right-handed patients with right hemispheric vascular stroke gave written informed consent to participate to this study, which was approved by the ethics committee of the Hôtel-Dieu Hospital in Paris, France. Patients performed a paper-and-pencil neglect battery including tests of line bisection, target cancellation, identification of overlapping figures and the copy of a landscape drawing (See Table 1 and the supplementary material for demographic and clinical data). MRI data were acquired using echo-planar imaging at 1.5T and diffusion tensor imaging (DTI) was acquired using 36 independent directions (full details of the MRI and DTI acquisition and processing are available in the supplementary material). Fibre tracking of the superior longitudinal fasciculus (SLF), inferior longitudinal fasciculus (ILF) and the inferior fronto-occipital fasciculus (IFOF) was performed with Brainvisa 3.0.2 (http://brainvisa.info/), using a two-regions of interest (ROIs) approach\(^20\). The reconstructed tracts were displayed in 3D and the number of streamlines (a surrogate marker of tract volume) was counted for each fasciculus in both hemispheres (see Supplementary Material).
Table 1: Demographical and clinical data, with lesion location on structural MRI (see Supplementary Fig. 1)

<table>
<thead>
<tr>
<th>Case</th>
<th>Lesion location</th>
<th>Clinical diagnosis of neglect</th>
<th>Visual Field</th>
<th>Gender / age / education (years of schooling)</th>
<th>Onset of illness (days)</th>
<th>Line bisection (% deviation)</th>
<th>Line cancellation (max 30 / 30)</th>
<th>Bells cancellation (max 15 / 15)</th>
<th>Letter cancellation (max 30 / 30)</th>
<th>Overlapping figures (max 10 / 10)</th>
<th>Landscape drawing (max 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>pI, STG, IPL, pMTOG</td>
<td>NO</td>
<td>Normal</td>
<td>F / 45 / 14</td>
<td>9</td>
<td>-3.10</td>
<td>30 / 30</td>
<td>15 / 15</td>
<td>29 / 30</td>
<td>10 / 10</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>pI, TP, STG, MTG, ITG</td>
<td>NO</td>
<td>Normal</td>
<td>M / 60 / 14</td>
<td>5</td>
<td>+4.80</td>
<td>30 / 30</td>
<td>15 / 15</td>
<td>28 / 29</td>
<td>10 / 10</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>Subinsular and temporal stem WM, BG, CR, IPL</td>
<td>YES</td>
<td>LE</td>
<td>F / 59 / 10</td>
<td>9</td>
<td>+15.70*</td>
<td>29 / 30</td>
<td>0 / 6*</td>
<td>0 / 13*</td>
<td>6 / 10*</td>
<td>4.5*</td>
</tr>
<tr>
<td>4</td>
<td>IPL, SPL, precuneus, cuneus, MTOG, pITG</td>
<td>YES</td>
<td>LH</td>
<td>F / 80 / 17</td>
<td>729</td>
<td>+1.00</td>
<td>30 / 30</td>
<td>1 / 15*</td>
<td>9 / 28*</td>
<td>9 / 10*</td>
<td>3.5*</td>
</tr>
</tbody>
</table>

pI, posterior part of the insula; STG, superior temporal gyrus; MTG, middle temporal gyrus; ITG, inferior temporal gyrus; IPL, inferior parietal lobule; SPL, superior parietal lobule; pMTOG, posterior part of the middle temporo-occipital gyrus; TP, temporal pole; WM, white matter; BG, basal ganglia; CR, corona radiata; LE, left extinction; LH, left hemianopia. * Pathological score. For the line bisection test, the cumulated percentage of deviation from the true centre of all the lines was calculated, with rightward deviations carrying a positive sign and leftward deviations having a negative sign. For the cancellation tests and the overlapping figures test, the number of items cancelled (or identified) on each half of the page or of the central figure is reported. For the landscape copy, 2 points were assigned to the complete copy of the house and 1 point to the complete copy of each tree, 0.5 point were given to items whose only right half was copied, and 0 points to items completely omitted.
Results
Cases 1 and 2 demonstrated no signs of neglect on paper-and-pencil tests; cases 3 and 4 had signs of left neglect in more than three tests of the neglect battery (Table 1). Fig. 1 displays three-dimensional reconstructions of the lesions and DTI tractography (see also the supplementary material).
Case 1 displayed no signs of extinction or neglect on neuropsychological testing nine days after the onset of an ischemic stroke affecting both the inferior parietal and the superior temporal cortices, both of which has been considered as the crucial lesional correlate of neglect. The tractography reconstruction visualized bilaterally intact SLF, IFOF and ILF. Similarly, case 2 had no signs of extinction or neglect when assessed five days after clinical onset. The lesion involved the posterior part of the insula, the whole temporal pole and the superior, middle and inferior temporal gyri, including the temporo-parietal junction. Subcortical white matter was also affected, but long-range association tracts (SLF, IFOF and ILF) were intact.
Case 3 had left visual and tactile extinction and signs of severe left neglect with anosognosia. The lesion involved the subinsular and temporal stem white matter, the body of the caudate nucleus, the lenticular nucleus, the middle part of the corona radiata and the inferior parietal lobe with the underlying white matter. The tractography reconstruction showed intact ILF and SLF in both hemispheres, and complete absence of the right IFOF. At follow-up testing 34 and 41 days after clinical onset, case 3 still showed signs of left neglect (see Supplementary Material).
Case 4 had a right haemorrhagic occipital-parietal stroke. Two years after onset, she still had left hemiparesis and signs of left neglect. The lesion involved the inferior and superior parietal lobe with underlying white matter, the cuneus and precuneus, the middle temporo-occipital gyrus and the posterior part of the inferior temporal gyrus. The tractography reconstruction showed intact ILF and SLF and complete absence of the right IFOF.
Neither patient 1 nor 2 presented language deficits after stroke, which renders unlikely the possibility of them having an unusual pattern of hemispheric lateralization.
The 2-ROIs approach to tractography dissections allows dissecting long-range pathways, but it may underestimate the involvement of more superficial (U-shaped) fronto-parietal connections. Hence, we have overlapped the lesions of the four patients to probabilistic maps of fronto-parietal connections as derived from a normative dataset (see Supplementary Fig. 2). This analysis showed that in all four subjects the lesions extended into superficial fronto-parietal connections, sparing deep long range SLF fibres.

Discussion
We used DTI-tractography to show direct evidence of disconnection of major rostro-caudal white matter pathways in neglect patients with vascular lesions. Previous studies demonstrating white-matter disconnection in neglect patients had relied on anatomical or functional MRI, and inferred the localization of tract lesion either from general anatomical knowledge, or from DTI in normal subjects. Compared to previous attempts, the use of DTI tractography allowed us to identify more precisely the white matter pathways that were damaged in neglect patients. The present results suggest that (1) complete damage of the IFOF can be associated with chronic visual neglect, and (2) cortical lesions sparing the SLF and IFOF, but damaging at least part of IPL and STG, two areas previously indicated as the critical cortical loci for spatial awareness, do
not necessarily cause chronic visual neglect. The limited number of subjects in this study do not allow us to generalise from these preliminary findings to the all neglect patients; nevertheless, they do suggest that the neuroanatomical correlates of neglect may be more complex than previously thought and brings up important hypotheses on the role of direct connections between occipital and frontal lobes in spatial processing.

The involvement of the IFOF in left neglect has not been previously described. The IFOF connects the VLPFC and medial orbitofrontal cortex to the occipital lobe and represents the only direct connection between occipital and frontal lobes in humans. The inferior-lateral portion of the frontal lobe, a cortical end-station of the IFOF, has been frequently associated with frontal neglect. Lesions to the occipital origin of the IFOF have also described in left neglect. Finally, as the central part of the IFOF runs in the stem of the temporal lobe, it is possible to hypothesise an occipito-frontal disconnecting mechanism in those neglect patients with large lesions of the temporal lobe. It remains to be seen whether a lesion of the IFOF per se is sufficient to cause neglect, without involvement of other cortical and subcortical regions. In our patients the inferior parietal cortex and the underlying U-shaped fibres were affected, which is in keeping with previous evidence from monkey studies and human patients. However, the extension into the deep white matter of parietal lobes is a factor that has not been considered before and future studies in larger series should clarify the relationship between clinical manifestations of neglect and extension of white matter lesions to fronto-parietal connections.

Interestingly, we observed that the two patients with IFOF lesion show little asymmetry of performance on the line cancellation test (i.e. a test without distracters), whereas they omitted most contralateral targets on the bells and letter cancellation tests. In the latter tests a target/distracter discrimination is required, an additional factor that neglect patients with predominantly frontal lesion seem to find particularly difficult. IFOF disconnection may deafferent the ventral frontal cortex from more posterior sources of visual input, related, for example, to object identification. In the monkey, neuron populations in the lateral prefrontal cortex respond both to the location and to the identity of previously presented visual objects, thus allowing the integration of "what" and "where" information. Regions in the human VLPFC, which constitute a projection site for the IFOF, show lateral selectivity in the short-time retention of spatial information and may be important to resolve perceptual ambiguity. Damage to these regions in the right hemisphere may bias towards the right the mental reconstruction of a number line. Furthermore, the right VLPFC is a cortical endpoint of the ventral spatial attentional network, which is important for the response to previously unattended targets, and whose dysfunction leads to neglect behavior. The right VLPFC may represent a convergence zone of three streams of visual processing: (1) the occipito-temporal stream, dedicated to object processing, through the IFOF and the uncinate fasciculus; (2) the ventral parieto-frontal attentional network, presumably connected by the human homologue of the third branch of the SLF (described in the monkey by Schmahmann and Pandya) and (3) the dorsal parieto-frontal attentional network, linked by the human homologue of the second branch of the SLF.

In conclusion these preliminary findings suggest that neglect is a syndrome with a heterogeneous clinical presentation and complex anatomical correlates, where damage to fronto-parietal and possibly occipito-frontal connections may impair at different levels visuo-spatial processing.

Acknowledgments
We thank the patients for their cooperation and the staff of BrainVISA software (www.brainvisa.info) for technical support for image analysis.
Figure Legend

Figure 1: Three-dimensional anatomical reconstruction of the patients’ lesions and lateral views (right hemisphere, R; left hemisphere, L) of the DTI tractography of the SLF (in green), the ILF (in blue) and the IFOF (in red) for the four patients studied. For each hemisphere, the three fasciculi are displayed on a T1 sagittal native MRI slice in the anterior/posterior commissure referential.
References


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Looking while imagining
The influence of visual input on representational neglect
G. Rode, MD, PhD; P. Revol, PhD; Y. Rossetti, MD, PhD; D. Boisson, MD, PhD; and P. Bartolomeo, MD, PhD

Abstract—Background: Subjects with hemispatial neglect often exhibit representational neglect: a failure to report details from the left side of mentally visualized images. This failure could reflect impaired ability to generate the left side of the mental image, or it could reflect failure to explore the left side of a normally generated mental image. When subjects with hemispatial neglect look at pictures or drawings, their attention tends to be drawn to objects on the right side, thereby aggravating their failure to explore the left side. If representational neglect represents a failure to explore the left side of a normally generated mental visual image, then it should be improved by blindfolding, which removes the attention-catching right-sided stimuli. However, if representational neglect represents a failure to generate the left side of the mental visual image, then blindfolding should have little impact on reporting of details of the image. Methods: To determine which of these explanations is correct, we asked eight normal participants and eight brain-damaged patients with left representational neglect to imagine the map of France and to name as many towns as possible in 2 minutes. In different sessions, participants performed the task with eyes open or while blindfolded. Results: Normal participants mentioned more towns while blindfolded than with vision, thus suggesting a distracting effect of visual details on mental imagery. Patients with neglect, however, showed no appreciable effect of blindfolding on reporting of details from either side of mental images. Conclusion: Representational neglect may represent a failure to generate the left side of mental images.

Representational neglect has been ascribed to a failure to generate or maintain a normal representation of the contralesional side of mental images.1-3 Representational neglect is commonly assessed by requiring subjects to draw objects from memory4 or to name the towns or the countries on an imagined map.5,6 For example, when subjects with hemispatial neglect are asked to evoke mentally the map of France, they may omit to mention the towns located on the left part of the map,6,7 thus suggesting an amputation of the left part of their mental representation of space.3,8 An alternative explanation is that the mental image of contralesional space was not lacking, but rather that it was not adequately explored. This explanation is consistent with a hypothesis postulating that visual mental imagery involves some of the attentional-exploratory mechanisms that are employed in visual behavior,9,10 in particular, an inability to direct attention to areas of imagined space.3,11 The positive influence of head position,11 sensory manipulations4,12,13 and prismatic visuomotor adaptation4,15 (all of which might be expected to affect exploratory behavior but not the generation of a mental image) on representational neglect in a pure imaging task fits well with this explanation.

When patients with neglect were asked to perform a drawing from memory task,4,16-18 with or without blindfolding, left neglect was decreased and even eliminated by blindfolding. These results suggest that visual feedback may exacerbate representational neglect and support the hypothesis that engaging attention through visual input can influence the processing of visual imagery.10 However, even in the blindfolded state, such tasks incorporate a major intentional component that underlies the act of drawing itself as well as the ongoing dynamic process involved in repeatedly comparing what is imagined to have been drawn with the original mental image template. This intentional component could serve to normalize an originally defective visual mental image. Can the presence or absence of visual input influence representational neglect in a similar way in the absence of such an intentional component? The aim of the present study was to answer this question.

Editorial, see page 400
Methods. We studied eight right brain–damaged patients (six men, two women, mean age 55.6 ± 10.1 years) and eight age-matched healthy subjects (five men, three women; mean age 55.1 ± 7.5 years). All subjects were right-handed and gave informed consent. All the patients had been admitted to a neurologic rehabilitation unit for treatment of left hemiplegia. Clinical features and CT scan data are described in table 1. Rightward head and eye deviation were rated on a 4-point scale: score 0 = no deviation; score 1 = intermittent deviation; score 2 = mild deviation that the subject was able to overcome with verbal instruction; score 4 = severe deviation that the subject was unable to overcome even with verbal instruction. Anosognosia for motor impairment was assessed using 4-point scale.19

All the patients showed an extensive unilateral lesion. Etiology was always vascular, ischemic in six cases and hemorrhagic in the two other cases. None of subjects had impaired arousal, confusion, dementia, or psychiatric disorders. At the time of examination, 1 month post-onset, all patients showed a marked left-sided visuospatial neglect defined by several tests: a line bisection task,20 a line and star cancellation task,21,22 and reading a text and writing under dictation. All the patients also demonstrated left neglect on drawing from memory (a daisy and a clock) and on copying a daisy and a Gainotti drawing.23 At the time of testing, only three of eight subjects (N2, N5, and N8) showed mild anosognosia.

Each subject was asked to mentally visualize the map of France as if he or she could see the map in front of him or her in his or her mind in two conditions: with eyes closed or eyes open. To help participants, they were asked to remember the map of France that they had learned during their first school period or to remember the weather forecast map featured each on television or in the newspapers. Participants had to list all the towns that they remembered the weather forecast map featured each on television or in the newspapers. Participants had to list all the towns that they could “see” in 2 minutes.24 No instruction was given concerning the idea that performance relied on the exploration of an inner image. In patients with neglect, the named towns were placed on the right half of the map, which, however, looks like the right side of the map produced by healthy subjects. This suggests a fully spared representational deficit on the right side. However, the defective left half of the maps imagined by patients with hemispatial neglect suggests a left representational deficit (figure 1B). Notably, patients with neglect never named a town more than once, whatever its location.

In healthy subjects, mean total scores were 225 in the eyes-open condition and 259 in the eyes-closed condition, whereas in patients with neglect, the mean total scores were similar in both conditions (145 and 150). ANOVA revealed that the subject factor as well as the condition factor were significant (F1,7 = 9.31; and F1,7 = 12.36) because more towns were mentioned in eyes-closed condition (25.56 vs 23.13), and patients with neglect listed less towns than controls (18.44 vs 30.25).

Results. Individual data are summarized in table 2. Healthy subjects had symmetrical scores. For all patients, the left-sided score was less than the right-sided score in both conditions, thus suggesting a deficit in image generation. To estimate more accurately the location of named towns, they were placed on a tracing of a map of France (figure 1). In healthy subjects, the reported towns are distributed over the entire map and in aggregate they create a complete map of France (figure 1A). This is consistent with the idea that performance relied on the exploration of an inner image. In patients with neglect, the named towns were placed mainly on the right half of the map, which, however, looks like the right side of the map produced by healthy subjects. This suggests a fully spared representation on the right side. However, the defective left half of the maps imagined by patients with hemispatial neglect suggests a left representational deficit (figure 1B). Notably, patients with neglect never named a town more than once, whatever its location.

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In healthy subjects, the mean left- and right-sided scores were 11.13 and 10.88 in eyes the eyes-open condition and 11.38 and 12.38 in the blindfolded condition, whereas in patients with neglect, these scores were statistically different (2.50 and 12.50 in the eyes-open condition and 1.50 and 14.00 in blindfolded condition). ANOVA thus revealed no significant effect of condition or side \( (F_{1,11021} = 1) \) in healthy subjects. To check that blindfolding did not affect the evocation of towns located in the right part of the map, an additional ANOVA was performed on these items. No significant difference was found \( (F_{1,7} = 1.05) \).

In patients with neglect, three-way ANOVA revealed a significant side effect \( (F_{1,7} = 35.71) \) but no condition effect. Moreover, our data suggest that the blindfolded condition slightly reduced the left-sided total score (2.5 in the eyes-open condition and 1.50 in the blindfolded condition) and slightly increased right-sided total score (12.50 in the eyes-open condition and 14.00 in the blindfolded condition) in patients with neglect. However, these changes were marginal as no significant condition x side interaction was found \( (F_{1,7} = 1.67) \).

In healthy subjects, Kruskal-Wallis ANOVA did not reveal a significant condition-related difference \( (H_{1,407} = 0.15) \), suggesting that the distribution of responses was

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In patients with neglect, three-way ANOVA revealed a significant side effect \( (F_{1,7} = 35.71) \) but no condition effect. Moreover, our data suggest that the blindfolded condition slightly reduced the left-sided total score (2.5 in the eyes-open condition and 1.50 in the blindfolded condition) and slightly increased right-sided total score (12.50 in the eyes-open condition and 14.00 in the blindfolded condition) in patients with neglect. However, these changes were marginal as no significant condition x side interaction was found \( (F_{1,7} = 1.67) \).

In healthy subjects, Kruskal-Wallis ANOVA did not reveal a significant condition-related difference \( (H_{1,407} = 0.15) \), suggesting that the distribution of responses was

**Table 2** Left-sided, right-sided, and total scores of neglect patients (N1 to N8) and mean scores of healthy subjects in two conditions of evocation of the map of France (eyes open and eyes closed)

**Figure 1.** Mental evocation of map of France in eight healthy-subjects (A) and eight patients with neglect (B) with eyes open and eyes closed. Each circle indicates the location of named town on a tracing of the map (scale: 1/5,000,000; 1 cm = 50 km). For each town, the size of the circle reflects the number of repetitions for all healthy subjects and patients with neglect.
similar in the two conditions. In addition, the median was close to the vertical meridian line and did not differ significantly in the two conditions: (median = 0 (range −1,250 to 670), median test $\chi^2 = 0.35$) (figure 2). These results suggest a symmetrical exploration of the map by normal subjects. Moreover, for any given deviation from midline, the number of towns named by normal subjects was always higher than the number named by patients with neglect except for the single sector range: 200 to 400 (figure 2). In patients with neglect, there was also no significant condition-related difference (Kruskal-Wallis ANOVA $H_{1,286} = 0.07$). The median was shifted toward the right side in both conditions (median = 279.5 [range −1250 to 650] in the eyes-open condition and median = 277.5 [range −1250 to 651] in the blindfolded condition) (figure 2B).

Finally, comparison of normal subjects with patients with neglect revealed a significant shift of the distribution and the median in patients with neglect in both the eyes-open condition (Kruskal-Wallis ANOVA $H_{1,360} = 17.65$; median test $\chi^2 = 30.65$) and the blindfolded condition (Kruskal-Wallis ANOVA $H_{1,407} = 35.48$; median test $\chi^2 = 46.55$).

**Discussion.** We wondered whether visual input might increase representational neglect as it increases visual neglect. The performances of the healthy subjects on the imagery task clearly showed a symmetrical access to the geographic knowledge when they were required to build a visual image of the map, whatever the condition, suggesting that the suppression of vision did not affect this access. However, in the blindfolded condition, the total number of named towns increased. This suggests that the lack of visual information from the environment improved the mental evocation, perhaps because blindfolded subjects were distracted by “real” visual items. During the task, the whole of the map was scanned, as suggested by the topographic distribution of the towns, consistent with a similar result found in a previous study. The strategy of evocation appeared to rely on some kind of mental exploration, i.e., on an inner visual scanning.

The performance of patients clearly showed left representational neglect when they were asked to evoke mentally the map of France. Neglect affected the left side of the mental image, suggesting a distorted representation of the map, similar to that previously reported in a series of patients. In our patients, as in previous studies, the same side of space (left) was affected in both mental and physical (extrapersonal) spaces. A similar co-occurrence of representational neglect with visual neglect has been reported in other group studies. Nevertheless, dissociations between representational and visuospatial neglect have been reported: visuospatial neglect in the absence of representational neglect, representational neglect without visuospatial neglect, and even right-sided peripersonal and personal visuospatial neglect and left-sided representational neglect.

Our patients displayed a rightward inner exploration bias. In both the eyes-open and blindfolded conditions, the retrieval and generation from long-term memory of an inner image of the map did not succeed in providing topographic information about towns on the western part of the map, but yielded normal performance on the middle and eastern parts of the map. In a task requiring only visual imagery, visual input did not influence the mental representation of space. The present findings contrast with the effects of visual feedback and visual context demonstrated in visuomotor tasks, such as drawing from memory. For example, a study reported a patient with neglect who displayed object-centered neglect with the eyes open, which disappeared with the eyes closed.
formance was reported in three of the six patients with neglect. In this study, five subjects with neglect showed improved drawing symmetry when blindfolded, reflecting both an increase in the extent and the number of details on the left side of the drawing and a reduction of the extent of the right. These results suggest that the attentional capture exerted by the right-sided details of drawings that subjects were producing may be reduced in the absence of visual input, thus facilitating a leftward orienting of attention. However, no similar modification of performances was observed in our patients in a pure mental imagery task during suppression of vision. The left representational neglect remained unchanged as did the number and location of named towns on the right half of the map. These findings run counter to the prediction that “the suppression of visual guidance will dramatically reduce what looks like representational neglect.” It must, however, be noted that visual input was not relevant in our task, which involved pure visual imagery, whereas visual feedback regarding right-sided details involved in the drawing task was essential to performance of this task. Task-relevant visual details might be more effective in capturing patients’ attention. It may also be that visual input influences performance on spatial representation tasks only when these tasks involve a manual response, i.e., an interaction between neural processes supporting visual representation and action. Even in the blindfolded state, such tasks incorporate a major intentional component that underlies the act of drawing itself as well as the ongoing dynamic process involved in repeatedly comparing what is imagined to have been drawn with the original mental image template. This intentional component could serve to normalize an originally defective visual mental image.

A recent report of a patient with pure representational neglect and poor performance on a visuospatial working memory task suggested that the inability to build, activate, or explore the mental representation of left hemispace could result from a visuospatial working memory deficit. This account was explored in a recent study of 10 right-brain damaged patients with representational and very mild perceptual neglect. Patients were asked to recall immediately the names of objects presented in four-object visual displays that had been placed directly in front of them. They recalled many more right-sided than left-sided objects. This result could have been explained either by a failure of learning and generation of a visual image (working memory) of the objects in left hemispace or by failure to direct attention to left hemispace in the course of reporting what they remembered seeing. However, when the subjects were asked to recall the objects as they would appear when viewed from the opposite direction, their recall of objects in the left hemispace—now in the imagined right hemispace—did not improve, indicating impairment in their original learning of the objects in the left hemispace; if their deficit had been in directing attention, their performance in the imagined right hemispace would have been normal. In addition, their recall of objects in the right hemispace—now the imagined left hemispace—fell to the level of their original performance in the left hemispace. These results, in aggregate, are far more consistent with a working memory/image generation defect account of representational neglect than they are with a directed attention defect account. Our study provides further evidence in support of the working memory/image generation account through a task that did not require either learning of novel visual arrays or mental visualization from a different perspective. Furthermore, the fact that our subjects never repeated recalled cities in either condition suggests that they did not mentally “revisit” the same locations and thus had a hemispace-specific deficit and not a generalized deficit in visuospatial working memory.

References


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**NeuroImages**

**Pathologic startle following brainstem lesion**

G. Della Marea, MD, PhD; D. Restuccia, MD; P. Mariotti, MD; C. Armelisasso, MD; M.L. Vaccario, MD; C. Vollono, MD, Rome and Udine, Italy

The startle reflex is a motor response that originates in the lower brainstem. Abnormal symptomatic startle can be secondary to lesions in the startle pathway, involving brainstem and spinal cord. A 56-year-old woman developed an acute demyelinating lesion of unknown origin in medulla oblongata (figure, A–D), causing dizziness and bilateral sensory impairment with paresthesias. No tongue weakness, myoclonus, or symptoms of restless leg syndrome were present. When the symptoms remitted, she developed a severe symptomatic startle response. Pathologic startle was elicited by sensory—especially acoustic—stimuli (video, see the Neurology Web site at www.neurology.org). Startle was bilateral and the EMG burst duration, recorded with surface deltoid EMG, ranged from 500 to 1,200 msec. Startle was not responsive to pharmacologic treatment (benzodiazepines and carbamazepine) and was disabling for the patient.

Figure. MRI scans. An area of abnormal signal, probably of demyelinating origin, is evident in the upper medulla and pons. No other signal abnormalities are evident within the CNS; in particular, the cervical cord is spared (B).

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Impaired Orienting of Attention in Left Unilateral Neglect: A Componential Analysis

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Centre National de la Recherche Scientifique and Université René Descartes (Paris 5)

Sylvie Chokron
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Twenty-six patients suffering from damage to the right side of the brain, 19 of whom exhibited signs of left neglect, as well as 32 matched controls, ran 3 spatial cuing tasks. Patients were also tested with 2 cancellation tests, a line-bisection test, the copy of a complex drawing, and a visual extinction procedure. Results first showed correlations between extinction and cancellation tests performance on one hand, and between line bisection and copy on the other hand. Second, results demonstrated that an engagement deficit toward contralesional targets appeared to be the most striking feature of neglect, and the engagement score was correlated with the cancellation score and extinction. Most patients with neglect also presented a deficit in disengagement, a deficit of inhibition of return, and probably a deficit of alertness. Deficits in engagement and in disengagement, as well as poor scores in cancellation tests, seemed to be related with posterior cortical and subcortical lesions. Most important, even if an endogenous deficit (frequently related with a thalamic lesion) could aggravate the neglect behavior, neglect syndrome was mainly explained by a deficit of exogenous attention.

Keywords: spatial neglect, spatial cuing, right hemisphere brain damage, orienting of attention

Unilateral neglect is a relatively frequent and disabling disorder occurring after unilateral brain lesions, mainly in the right hemisphere. Patients with neglect syndrome may omit contralesional targets in cancellation tasks or left-sided details in copying tasks and may shift rightward the subjective center of horizontal lines. They typically show difficulties in orienting spatial selective attention toward the contralesional hemispace. A question remains as to the exact nature of the attentional deficit in neglect. Attention is not a unitary construct, and several components or elementary operations of spatial attention have been identified on the basis of the cuing paradigm developed by Posner and colleagues (Posner & Cohen, 1984; Posner, Walker, Friedrich, & Rafal, 1984). The main goal of the present study is to evaluate the relationship between these different attentional operations or components and unilateral neglect signs measured through paper-and-pencil tests.

Posner et al. (1984) tested patients with posterior parietal lesions and showed that, although detection of contralesional and ipsilesional targets evoked broadly similar response times (RTs), target detection in the contralesional hemifield was abnormally slowed when attention had previously been engaged on an invalid cue in the ipsilesional hemifield. The authors interpreted this deficit as a difficulty in disengaging attention from its current focus in order to move toward the contralesional direction. A disengage deficit has been demonstrated in patients with parietal lesions even when clinical signs of neglect or extinction were absent (Eglin, Driver, & Rafal, 1994; Friedrich, Egly, Rafal, & Beck, 1998; Friedrich & Margolin, 1993; Posner et al., 1984; Posner, Walker, Friedrich, & Rafal, 1987). However, the severity of the disengage deficit has been correlated with the severity of clinical neglect (Morrow & Ratcliff, 1988).

Such a disengage deficit could explain why contralesional omissions on cancellation tasks are reduced when targets are erased instead of marked (Eglin, Robertson, & Knight, 1989; Mark, Kooistra, & Heilman, 1988). If the presence of the rightmost marked targets renders difficult the disengagement operation, the hypothesis is that disengaging would be facilitated with deletion of these targets. A disengage deficit could also explain why some patients are able to correctly describe the drawing of a flower and...
notice the petals in the contralesional part, while forgetting these petals when asked to copy the flower (Ishiai, Seki, Koyama, & Yokota, 1996). The copying task supposedly enhances focusing of attention toward the rightmost details of the drawing, from which patients are slow to disengage (see also the differences in dealing with hierarchical stimuli as a function of the task; Marshall & Halligan, 1995a; Worthington & Young, 1996). Moreover, it has been found that suppressing the visual feedback (by drawing with eyes closed) frequently reduces neglect signs compared with drawing under visual control (Chokron, Colliot, & Bartolomeo, 2004; Mesulam, 2000). However, a deficit in the operation of disengaging attention cannot account for several aspects of neglect behavior, and it has been argued that other attentional deficits might be present in patients with neglect syndrome. Indeed, in cancellation tasks, most patients still show a nonnegligible amount of neglect even if rightmost targets have been erased (Mark et al., 1988). Also, if the disengage deficit can explain why patients have difficulties in processing contralesional targets once they have engaged on ipsilesional targets, the question remains of why patients with neglect syndrome usually start to explore the external world by rightmost stimuli.

Losier and Klein (2001), in a meta-analysis of several previously published spatial cuing studies in neglect, showed that responses to validly cued targets in the contralesional hemispace were significantly slower than responses to validly cued targets in the ipsilesional hemispace, although the fact is hardly mentioned in most of the individual studies. They concluded that patients with neglect syndrome present an engage deficit of attention toward contralesional targets, because patients did not fully benefit from contralesional cues. An abnormal orienting bias of attention toward the ipsilesional hemispace (lateral preference) could be an important component of neglect (Gainotti, D’Erme, & Bartolomeo, 1991; Kinsbourne, 1993; Lådavas, 1993; Mattingley, Bradshaw, Nettleton, & Bradshaw, 1994). Patients with neglect syndrome frequently start scanning from the right side of a spatial display (for example, in cancellation tasks; see Jalas, Lindell, Brunila, Tenovuo, & Hämäläinen, 2002), a fact easier to explain by an abnormal ipsilesional capture of attention or a bias in engaging attention than by a disengage deficit, even if motor-directional akinesia could also, at least partially, explain this phenomenon. Finally, the mere appearance on the computer screen of the peripheral boxes in which a target can appear elicits a shift of patients’ attention toward the rightmost box (D’Erme, Robertson, Bartolomeo, Daniele, & Gainotti, 1992), an experimental fact which is clearly in favor of an ipsilesional bias in engaging attention.

Another component of attention, inhibition of return (IOR), has also been implicated in neglect. In spatial cuing tasks using peripheral cues, RTs in valid trials are normally faster than RTs in invalid trials for short (less than 300 ms) stimulus onset asynchronies (SOAs), but the opposite pattern of results occurs for longer SOAs, with RTs being the slowest in valid trials, as if attention was inhibited from returning to previously explored objects (Maylor & Hickey, 1985; Posner & Cohen, 1984). An absence of IOR in the ipsilesional hemifield has been described in patients with neglect syndrome (Bartolomeo, Chokron, & Siéroff, 1999; Bartolomeo, Siéroff, Chokron, & Decaix, 2001) as well as in parietal patients without signs of neglect (Vivas, Humphreys, & Fuentes, 2003).

In summary, the orienting deficit in neglect could have at least three components: (a) a bias in engaging attention in favor of the ipsilesional hemispace, which would explain why patients process and respond to ipsilesional stimuli first even when stimuli are simultaneously presented in each hemispace; (b) a deficit in disengaging of attention, explaining why attention to contralesional stimuli is reduced when patients have engaged their attention on ipsilesional stimuli; (c) and a deficit of ipsilesional IOR, contributing to the favoring of ipsilesional “anchoring” of attention. A possibility is that the operations involved in neglect behavior are depending on the anatomical locus of the lesion. A distinction has been proposed with the disengage operation in the posterior parietal areas (Posner et al., 1984, 1987) or in the temporoparietal junction (Friedrich et al., 1998), the engagement operation in the pulvinar (Rafal & Posner, 1987), and the IOR in the superior colliculus (Posner, Choo, Rafal, & Vaughn, 1985).

Whatever the exact nature of the orienting component involved in neglect, most authors seem to agree with a deficit of exogenous attention rather than endogenous attention (Bartolomeo, Siéroff, Decaix, & Chokron, 2001; Gainotti, 1996; Lådavas, 1993; Lådavas, Carletti, & Gori, 1994; Luo, Anderson, & Caramazza, 1998; Natale, Posteraro, Prior, & Marzi, 2005; Smania et al., 1998). In other words, patients present difficulties in orienting when exogenous events capture their attention, but their voluntary orienting is more or less intact and can overcome the exogenous deficit under some conditions. The spatial cuing method is well suited to dissociate endogenous and exogenous orienting of attention, specifically by varying the proportion of valid and invalid trials (see e.g., Berger, Henik, & Rafal, 2005). The disengage deficit in patients with neglect syndrome has been described with different cuing procedures, but is usually stronger in experiments using peripheral cues and exogenous attention conditions (no predictive information of the cue, i.e., in experiments using as many invalid trials as valid trials) than in experiments using central or symbolic (arrows) cues and endogenous conditions, namely when the cue is informative because most of the trials are valid (Losier & Klein, 2001). The disengage cost can even be reversed to an advantage for left invalidly cued targets, if most cues predict that the target will occur on the opposite side (Bartolomeo, Siéroff, Decaix, & Chokron, 2001). In this case, patients may use preserved endogenous processes to orient forward after a right-sided cue and obtain relatively fast RTs to left invalidly cued targets. A predominant exogenous deficit in the neglect syndrome is also in agreement with brain imaging studies showing that exogenous orienting of spatial attention predominantly activates the right hemisphere in the ventral part of parietal and frontal regions overlapping those whose lesion provokes neglect (Corbetta & Shulman, 2002).

What is the relationship between performance in the spatial cuing task and performance in clinical neglect tests? Morrow and Ratcliff (1988), using an overall score of neglect with different tests, found a positive correlation between the disengage deficit and the severity of neglect. However, the exact relationship between each of the main neglect tests (cancellation, line bisection, copy) and the different component scores (disengagement, engagement, IOR) in the cuing task has not been established. Even if the different clinical tests of neglect are frequently disturbed in the same patients, dissociations have clearly been found, for example between cancellation and line bisection (Binder, Marshall, Lazar, Benjamin, & Mohr, 1992; Halligan & Marshall, 1992; Seki, 1996),
with most authors recognizing the composite nature of neglect. According to McGlinchey-Berroth et al. (1996), whether an individual will be impaired solely on one of these tests could not be predicted on the basis of lesion location. However, other authors have maintained that separable components of neglect may be associated with damage to discrete areas of the right hemisphere. Binder et al. (1992) found a relation between cancellation scores and frontal or deep lesions, on one hand, and between line bisection performance and posterior lesion on the other (see also Rorden, Fruhmann, Berger, & Karnath, 2006). Still, Marshall and Halligan (1995b) found the opposite pattern. We hypothesized that, if performance in one clinical test of neglect depends on the integrity of posterior areas in the brain, it should be correlated with elementary operations involved in orienting spatial attention, such as engagement or disengagement, the deficits of which follow posterior lesions.

Furthermore, authors frequently argue for some common underlying deficit in visual extinction and clinical neglect (see Driver & Vuilleumier, 2001). However, visual extinction has been found using different materials in left hemisphere lesions as well as in right hemisphere lesions, although neglect is prevalent following right hemisphere lesions (Friedland & Weinstein, 1977; Sié roff & Michel, 1987). Also, the lesion site may differ between extinction and neglect (Karnath, Himmelbach, & Küker, 2002; Vallar, Rusc oni, Bignamini, Geminiani, & Perani, 1994). The relationship between the extinction phenomenon and the deficits in the different components of attentional orienting or the deficits in paper-and-pencil neglect tests remains to be established.

In this study, we present the results of three cueing experiments using peripheral cues and the detection of simple targets in patients suffering from a right hemispheric lesion. These patients were distinguished by the presence or absence of symptoms associated with left neglect syndrome. The experiments differed only in the proportion of information given by the cue in each condition. In the first experiment, in which 50% were valid trials and 50% were invalid trials, the cue provided no information on the location of the target. Thus, RT differences between valid and invalid trials were supposedly caused by exogenous orienting of attention. The second experiment used informational cues (80% valid trials), and effects should have been at least partially caused by endogenous orienting of attention. Although central cues are typical in this type of experiment, we preferred to use the same peripheral cues as in the previous experiment, to make results comparable. In the third experiment, most trials were invalid: For example, a right cue was followed by a left target in 80% of the cases and by a right target in 20% of the cases only. Here, the endogenous component of orienting of attention consists of the ability to inhibit the attentional capture by the cue and to reorient attention from the location of the cue to the opposite location.

This study aims to evaluate the different components of attention (disengagement, engagement, and IOR) in three groups: those suffering from right brain damage with signs of neglect, those suffering from right brain damage without signs of neglect, and age-matched healthy participants. By comparing results between the three experiments, we determine the endogenous or exogenous nature of the deficits. Finally, we calculate correlations between scores evaluating the different components of attention and patients’ performance on clinical tests of neglect and of extinction.

Method

Participants

Twenty-six patients (13 men and 13 women) and 32 controls (13 men and 19 women) participated in the study. All participants were right-handed. Mean age was 63.96 years (SD = 13.09, range = 29–80) for patients and 60.19 (SD = 13.00, range = 39–81) for controls. Mean sociocultural level was 4.82 (SD = 1.85) for patients and 4.81 (SD = 1.47) for controls. Table 1 shows the demographic and clinical characteristics of patients. Figure 1 and Table 2 show the anatomical sites of the lesion for the 14 patients who had available MRI or CT scan.

Patients were selected on the basis of the lesion location in the right hemisphere and the absence of hemianopia (all patients had full visual field to confrontation within 30° of fixation). The study was carried out by following the guidelines of the Ethics Committee of the Cochin Hospital in Paris.

Clinical Tests

Unilateral neglect was assessed by means of a battery of paper-and-pencil neglect tests (Bartolomeo & Chokron, 1999a), including tasks of target cancellation, line bisection, and drawing copy. Only the 26 patients performed these tests.

Line bisection. Patients were asked to mark the middle of 8 lines of 1-mm width and of different lengths (6, 18, 10, 18, 6, 6, and 10 cm), arranged on the left, the middle, or the right part of a vertical A4 sheet of paper. Deviation from the true middle was measured in mm. Then, a line-bisection score of rightward deviation was calculated: The deviation from the middle was expressed as a percentage of half the length of the line. A positive score indicates a rightward deviation, whereas a negative one indicates a leftward deviation. Pathological left neglect scores correspond to rightward deviations superior to 11.1% (Bartolomeo & Chokron, 1999a).

Bells cancellation test (Gauthier, Dehaut, & Joanette, 1989). Patients were asked to circle 35 targets (black-ink drawings of bells) presented on an horizontal A4 sheet, among 280 distracters. Targets were presented in a pseudorandomized way and were equally distributed in seven columns. Only the targets of the three lateral columns were taken into consideration (15 targets each). The bells laterality score is the difference between the number of cancelled bells on the left and on the right. Positive scores indicate more omissions in the left half than in the right half. Scores superior to 2 are considered pathological (Rousseaux et al., 2001).

Albert cancellation test (Albert, 1973). Patients were asked to mark all 60 of the short lines randomly presented on a horizontal A4 sheet. The Albert laterality score is the difference between the number of cancelled lines on the left and on the right. Positive scores indicate more omissions in the left half than in the right half. Scores superior to 2 are considered pathological (Rousseaux et al., 2001).

Copy. Patients had to copy a scene on a horizontal A4 sheet (Gainotti, D’Erme, Monteleone, & Silveri, 1986). The total score is 6 points: 1 for the trees on the right (omission of the left half of
Table 1
Demographic and Clinical Characteristics of Patients

<table>
<thead>
<tr>
<th>Patients</th>
<th>Sex</th>
<th>Age</th>
<th>Sociocultural level</th>
<th>Onset of illness (days)</th>
<th>Hemiplegia</th>
<th>Anosognosia</th>
<th>Visual extinction</th>
<th>Neglect tests</th>
<th>Z score</th>
<th>Pathological neglect tests</th>
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<td>AD</td>
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<td>60</td>
<td>2</td>
<td>45</td>
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<td>N</td>
<td>13</td>
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<td>9</td>
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<td>BL</td>
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<td>67</td>
<td>3</td>
<td>92</td>
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<td>4</td>
</tr>
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<td>CB</td>
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<td>N</td>
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<td>4</td>
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<td>13</td>
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<td>3</td>
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<td>HC</td>
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<td>N</td>
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<td>11.8</td>
<td>0</td>
<td>0</td>
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<td>5</td>
<td>19</td>
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<td>N</td>
<td>18</td>
<td>16.9</td>
<td>5</td>
<td>9</td>
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<td>61</td>
<td>5</td>
<td>296</td>
<td>N</td>
<td>N</td>
<td>15</td>
<td>10.7</td>
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<td>7</td>
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<tr>
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<td>278</td>
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<td>16</td>
<td>8.8</td>
<td>6</td>
<td>5</td>
</tr>
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<td>12</td>
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<td>110</td>
<td>Y</td>
<td>N</td>
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<td>40</td>
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<td>M</td>
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<td>74</td>
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<tr>
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<td>3</td>
<td>50</td>
<td>Y</td>
<td>Y</td>
<td>18</td>
<td>8.4</td>
<td>15</td>
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<td>66</td>
<td>2</td>
<td>36</td>
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<td>N</td>
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<td>1.4</td>
<td>2</td>
<td>6</td>
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<tr>
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<td>M</td>
<td>73</td>
<td>4</td>
<td>66</td>
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<td>78</td>
<td>6</td>
<td>28</td>
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<td>280</td>
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<tr>
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<tr>
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<td>JC</td>
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<td>0</td>
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<tr>
<td>MH</td>
<td>M</td>
<td>68</td>
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<td>179</td>
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<td>0</td>
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<tr>
<td>SM</td>
<td>F</td>
<td>70</td>
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<td>32</td>
<td>Y</td>
<td>N</td>
<td>11</td>
<td>4.2</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Note. Pathological scores are in bold. M = male; F = female; Y = yes; N = no.

a tree = 0.5), 2 for the house (omission of a window, the door or a part of the roof = 0.5; omission of the left half of the house = 1), and 1 for the trees on the left. Scores are considered as pathological when superior or equal to 0.5.

Extinction. The presence of visual extinction was clinically tested by briefly wiggling fingers for 2 s in one or both visual fields. The examiner controlled central gaze fixation, and 36 trials were given in a fixed pseudorandom sequence including 18 unilateral trials (9 on each side) and 18 simultaneous bilateral trials. Extinction was considered as present when a patient failed at least once to report a contralosional stimulus during bilateral simultaneous presentation, while accurately detecting unilateral stimuli (Azouvi et al., 2002). An extinction score was calculated by the difference between correct detection on the right and on the left (maximum = 18) in the bilateral condition.

Response Time to Visual Targets

In all experiments, participants sat facing a computer monitor at a distance of approximately 50–60 cm. Stimulus presentation and response collection were controlled by the Psychlab software (Bub & Gum, 1995). The method was directly inspired from the method used by Posner et al. (1984).

Each trial began with the appearance of a horizontal display of three black unfilled square boxes on a white background. Each square box was 10 mm wide (approximately 1° of visual angle) and each side of the square was 0.35 mm thick. The distance between the boxes was 30 mm (approximately 3° of visual angle). Patients were instructed to fixate a black dot located in the central box (remaining present in the whole trial). Eye movements were observed by one of the experimenters, so that such trials could be discarded; however, discarded trials were not replaced by new trials. After 500 ms, a cue (thickening of the boxes by 0.7 mm) followed during 300 ms. The target (a black asterisk, 0.5° of visual angle in diameter) appeared in one of the peripheral boxes after a variable delay (SOA = 100, 500 or 1,000 ms) from the cue and remained visible until a response was made. The task was to press the space bar of the keyboard as quickly as possible with the index finger of the right hand as soon as the target appeared. Patients were instructed to respond exclusively to the target and not to the cue. The intertrial interval was 1,500 ms.

There were three cuing conditions. On valid trials, the target appeared at the same location as the cue, whereas on invalid trials the target appeared on the side opposite the cue. Before each experiment, participants were informed about the level of predictability of the cue. In Experiment 1, 50% of valid trials and 50% of invalid trials were presented (for a total of 252 trials, with three blocks of 84 trials each). In Experiment 2, 80% of valid trials and 20% of invalid trials were presented (for a total of 270 trials, with three blocks of 90 trials). In Experiment 3, 20% of valid trials and 80% of invalid trials were presented (for a total of 270 trials, with three blocks of 90 trials). Also, neutral trials were presented in separate blocks, with the neutral cue consisting of the thickening of the central
square box (for a total of 252 trials, with three blocks of 84 trials). Note, however, that this condition may not represent a true neutral condition in patients with neglect syndrome, as suggested by Posner et al. (1984; see results of Experiment 1 for further discussion). Blocks of trials, corresponding to the three experiments varying the percentage of valid and invalid trials and to the neutral condition, were presented in a counterbalanced way over three sessions separated by 1 or 2 days in patients and 1 hr in healthy controls. Rest periods were provided between each block of a session. Participants practiced the task (30 trials) before the data was collected while the experimenter observed to ascertain that the directions were understood and that the participant was not making eye movements.

Results

Analyses of Results

Clinical tests were analyzed by use of raw scores for copy and line bisection and the right–left difference for extinction and both cancellation tests (Albert, bells). Correlations were calculated between clinical tests themselves and between tests and elementary operations revealed by the cuing task. However, because more than half of the patients were at ceiling in the extinction and the copy tasks, an analysis considering only the failure or the success of these tests was conducted, and t tests were calculated when correlations were not significant. Because of the finding of a positive correlation between the disengage deficit and the severity of neglect using an overall score (Morrow & Ratcliff, 1988), an overall neglect score was calculated by converting and averaging scores of the four neglect tests and of extinction test to z scores.

In the cuing experiments, RTs exceeding the range of 150–5,000 ms were discarded from the analysis. For each experiment, median RTs were entered in a repeated-measures ANOVA, with group (patients with neglect, patients without neglect, healthy controls) as a between-factors variable, and field (left, right), cue type (valid, invalid, neutral) and SOA (100 ms, 500 ms, 1,000 ms) as within-factor variables.

We also tried to relate the neuroanatomical findings to the behavioral data. However, MRI or CT-scan was available for 14 patients only. Because of the diversity of the lesions presented by these patients (see Figure 1 and Table 2), multiple component analyses were not conclusive. Consequently, we chose to argue mainly on the basis of the dissociations between patients.
### Table 2

Anatomical Sites of the Lesions in Patients for Whom We Have Brain Imagery, and Pathological Scores for the Experiments and Clinical Tests

<table>
<thead>
<tr>
<th>Lesion sites, experiments, and clinical tests</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BL</td>
</tr>
<tr>
<td><strong>Lesion sites</strong></td>
<td></td>
</tr>
<tr>
<td>Frontal lobe</td>
<td></td>
</tr>
<tr>
<td>Lateral: rolandic region</td>
<td>++ + + ++</td>
</tr>
<tr>
<td>Operculum</td>
<td>++</td>
</tr>
<tr>
<td>Parietal lobe</td>
<td></td>
</tr>
<tr>
<td>Inferior</td>
<td>++ + +</td>
</tr>
<tr>
<td>Lateral</td>
<td>++ + +</td>
</tr>
<tr>
<td>Para-/supraventricular</td>
<td>++</td>
</tr>
<tr>
<td>Inferior gyrus (posterior)</td>
<td></td>
</tr>
<tr>
<td>Middle gyrus (posterior)</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Posterior to auditory region</td>
<td>++ + +</td>
</tr>
<tr>
<td>Auditory region</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Anterior to auditory region</td>
<td>++ + +</td>
</tr>
<tr>
<td>Middle gyrus (anterior)</td>
<td>+ + ++ +</td>
</tr>
<tr>
<td>Temporal lobe: mesial</td>
<td>++</td>
</tr>
<tr>
<td>Anterior (amygdala)</td>
<td></td>
</tr>
<tr>
<td>Posterior (hippocampus)</td>
<td>++</td>
</tr>
<tr>
<td>Occipital lobe</td>
<td></td>
</tr>
<tr>
<td>Mesial</td>
<td>++</td>
</tr>
<tr>
<td>Lateral: inferior</td>
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<tr>
<td>Paraventricular area</td>
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</tr>
<tr>
<td>Insula</td>
<td>++ + +</td>
</tr>
<tr>
<td>Subcortical</td>
<td></td>
</tr>
<tr>
<td>Head of caudate nucleus</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Body of caudate nucleus</td>
<td>++</td>
</tr>
<tr>
<td>Lenticular nucleus/internal capsule</td>
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</tr>
<tr>
<td>Thalamus: anterior part</td>
<td>++</td>
</tr>
<tr>
<td>Thalamus: posterior part</td>
<td>++</td>
</tr>
<tr>
<td>Thalamus: lateral part</td>
<td>+ + + +</td>
</tr>
</tbody>
</table>

### Experiments

<table>
<thead>
<tr>
<th>Experiments</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BL</td>
</tr>
<tr>
<td>Disengagement SOA 100</td>
<td>++ +</td>
</tr>
<tr>
<td>Disengagement SOA 500</td>
<td>++ +</td>
</tr>
<tr>
<td>Engagement SOA 100</td>
<td>++ +</td>
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<tr>
<td>Engagement SOA 500</td>
<td>++ +</td>
</tr>
<tr>
<td>Engagement SOA 1,000</td>
<td>++ +</td>
</tr>
<tr>
<td>Right IOR</td>
<td>++</td>
</tr>
<tr>
<td>Experiment 2</td>
<td></td>
</tr>
<tr>
<td>Disengagement SOA 100</td>
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<td>Engagement SOA 1,000</td>
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<td>Experiment 3</td>
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<tr>
<td>Inhibition of RVF cue</td>
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<tr>
<td>Reorienting of attention</td>
<td>POS</td>
</tr>
<tr>
<td>Bisection deviation</td>
<td></td>
</tr>
<tr>
<td>Bells score</td>
<td>+</td>
</tr>
<tr>
<td>Albert score</td>
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</tr>
<tr>
<td>Copy</td>
<td>+</td>
</tr>
<tr>
<td>Exinction</td>
<td>+</td>
</tr>
</tbody>
</table>

**Note.** The signs + or ++ indicate a lesion or a pathological score. In Experiment 3, “POS” indicates that patients were able to inhibit the right hemifield capture of attention or to efficiently reorient attention toward the left hemifield. SOA = stimulus onset asynchrony; IOR = inhibition of return; RVF = right visual field.
Results in Clinical Tests

Table 1 shows the performance of the patients on the neglect battery and on the test of visual extinction. Nineteen patients had at least one pathological score in neglect tests (cancellation, bisection, copy) and, consequently, were considered as suffering from neglect. They form the right brain damage group with neglect syndrome, or RBDN+ group. Seven patients with right brain damage had no pathological score on neglect tests. They form the RBDN− group.

We analyzed and compared the performance in the visual extinction task, two cancellation tests (Albert test, bells test), and the line-bisection and copy tasks in the 26 patients. As could be expected, performance on both cancellation tests (Albert and bells tests) was positively correlated ($r = .69, p < .01$). Also, the Albert test performance was correlated with extinction ($r = .60, p < .01$). However, neither the cancellation tests nor the extinction test correlated with the line-bisection task ($r = .37$ for the Albert test, $r = .06$ for the bells test, $r = .15$ of the extinction score). Finally, only the line-bisection test correlated with the copy task ($r = .58, p < .01$).

As can be seen in Tables 1 and 2, clear dissociations emerged between the different tests. Only 4 patients showed a deficit in all five clinical tests. The anatomical data were available for only two of them (MB2 and PB). Both of them revealed a lesion involving the inferior frontal and the superior part of anterior-middle temporal cortex, the anterior part of the capsulo-lenticular region. This result is consistent with recent data (Karnath, Frutmann Berger, Küker, & Rorden, 2004; Karnath, Himmelbach, & Rorden, 2002), even if the parietal lobe has also been incriminated in neglect syndrome and in extinction (see Doricchi & Tomaiuolo, 2003; Mort et al., 2003). Cases of neglect are frequently caused by lesions in different parts of the right hemisphere, the neglect syndrome being now considered as a deficit of a complex attentional network (Mesulam, 2000).

Seven patients presented a left extinction and a pathological score in one or two cancellation tests without a pathological rightward deviation in the line-bisection test (BL, DM, JD1, JD2, MB1, MS, and MV2). Five lesions involved the temporal lobe, three involved the parietal lobe, four involved the capsulo-lenticular region, and three involved the thalamus. Five other patients presented a deficit in at least one cancellation test but no extinction and no deficit in the bisection test. These patients had a lesser deficit on the cancellation tests than the previous patients. Scans were available for only three of them (DB, JL1, and JL2). One showed a parietal lesion and one showed a lesion of the temporal lobe; all patients also showed a thalamic lesion. Overall, only 3 of the patients presenting a deficit in cancellation tests (with or without extinction) and not in the bisection test had a lesion involving the frontal lobe (DB, JD2, and JL1).

Finally, three patients presented a clear rightward deviation in the line-bisection test without any deficit in any of the cancellation tests and without extinction. Unfortunately, no scan was available for these patients. Note, however, that the 2 patients showing a deficit in the line-bisection test (as well as in other tests), for whom we have precise anatomical data on the lesion site (MB2 and PB), seemed to present lesions including more anterior regions (lateral and posterior frontal areas, anterior part of the superior temporal gyrus, and anterior part of the capsulo-lenticular area).

In conclusion, these results are compatible with Marshall and Halligan’s (1995b) hypothesis of a relationship between cancellation deficit and posterior lesions (temporal and parietal lobes, posterior subcortical structures), and between line bisection deficit and more anterior lesions, although exceptions can be found.

Experiment 1

In Experiment 1, the ratio of valid and invalid conditions was 50:50. The peripheral cue occurred at the target location in only 50% of the trials, thus providing no useful information. With this type of experiment using noninformative cues, exogenous orienting of attention can be evaluated without much influence from endogenous components, at least when the differential effects of the cue are considered. Results for the three groups are presented in Figure 2.

Global RT analysis. All main effects were significant. The main effect of Group, $F(2, 55) = 29.46, MSE = 639E+03, p < .01$, reflected slower RTs for RBDN+ patients ($M = 833$ ms, $SE = 65$ ms) and for RBDN− patients ($M = 700$ ms, $SE = 86$ ms) than for the control group ($M = 424$ ms, $SE = 15$ ms). However, RTs were not significantly different between both groups of patients, $F(1, 55) = 2.57, MSE = 639E+03, ns$. This result is congruent with the usual finding of slowness following a right hemisphere lesion, a deficit, which could be related, at least partially, to a difficulty in being alerted by external events (Posner & Petersen, 1990).

There was a main effect of SOA, $F(2, 110) = 32.59, MSE = 20.8E+03, p < .01$, and the interaction of Group × SOA, $F(4, 110) = 3.84, MSE = 20.8E+03, p < .01$, reflected a stronger effect of the delay between the cue and the target (for difference between the shortest and the longest SOAs, $M = 135$ ms, $SE = 29$ ms) in RBDN+ patients than in controls ($M = 63$ ms, $SE = 10$ ms), with the difference obtained in RBDN− patients ($M = 103$ ms, $SE = 47$ ms) being intermediate. The stronger effect of SOA found in RBDN+ patients compared with other groups could simply be explained by the fact that RTs were slower in RBDN+ patients, leaving room for a strong improvement with SOA. In this case the effect should be stronger in slower left hemifield targets. However, the interaction of Group × Field × SOA was not significant, $F(4, 110) = 1.94, MSE = 13.7E+03, ns$. Another explanation is that patients with neglect syndrome present an additional deficit of alertness (Posner & Petersen, 1990; Robertson, 1993). In our procedure, the boxes in which the target was presented disappeared at the end of each trial and reappeared at the beginning of each trial, 500 ms before the appearance of the cue, which is different from the procedure used by Posner et al. (1984), in which the boxes were always present on the screen. A possibility is that in control participants, the first event (sudden appearance of the boxes) could summon a maximum of alert effect at a fast rate, and the effect of SOA after the cue would consequently be less visible. In RBDN+ patients, the alerting effect caused by the sudden boxes appearance was smaller (or slower), and alert could be additionally recruited by another following event, the cue (the visual cue can also act as an alerting device; Fernandez-Duque & Posner, 1997; Posner, 1978). If the difference in the SOA effect is actually due to a deficit in alertness in patients with neglect syndrome, it could explain why the effect did not interact with the hemifield, alertness being a change in the internal state indepen-
dent from orienting (Fernandez-Duque & Posner, 1997). A deficit in alertness should be found with right hemifield targets as well as with left hemifield targets.

The field effect, $F(1, 55) = 20.74$, $MSE = 182E+03$, $p < .01$, showed faster RTs for the right hemifield, but the interaction of Group × Field was also significant, $F(2, 55) = 16.27$, $MSE = 182E+03$, $p < .01$. Only the RBDN+ patients showed a field effect (in favor of right hemifield targets, $M = +338$ ms, $SE = 78$ ms), $F(1, 55) = 53.61$, $MSE = 182E+03$, $p < .01$, the difference between both hemifield being not significant in RBDN– patients ($M = +92$ ms, $SE = 62$ ms) and in controls ($M = +7$ ms, $SE = 3$ ms). Because of the small number of patients in the RBDN– group and their heterogeneity, results considering this group have to be taken cautiously. Still, it remains interesting that only the RBDN+ patients showed faster RTs for right hemifield targets than for left hemifield targets, even when global measures independent from validity effects were used.

Finally, the cue type was also significant, $F(2, 110) = 11.04$, $MSE = 29.2E+03$, $p < .01$. Of great interest is the significant interaction of Group × Field × Cue Type × SOA, $F(8,$

Figure 2.  Response times for the three groups in Experiment 1: RBDN+ patients (right brain damage with left neglect syndrome), RBDN– patients (without neglect syndrome), and controls.
220) = 6.04, MSE = 8.7E+03, p < .01. Further analysis explored the deficits in disengagement of attention, engagement of attention and IOR in neglect and found differences, which can clarify this interaction.

**Disengagement of attention.** An initial question is whether patients with neglect syndrome show a specific deficit in disengaging attention from right-sided ipsilesional stimuli before moving it toward left-sided contralateral stimuli. To measure a differential deficit of disengagement between hemifields, we calculated the difference between valid and invalid conditions in the left and in the right hemifield, then a disengage score (Losier & Klein, 2001; Morrow & Ratcliff, 1988), as follows: (left invalid – left valid) – (right invalid – right valid).

RBDN+ patients showed a larger disengagement effect for left hemifield targets (M = +319 ms, SE = 74 ms; M = +321 ms, SE = 106 ms, respectively) than for right hemifield targets (M = +101 ms, SE = 47 ms; M = +57 ms, SE = 35 ms, respectively) at the shortest (100 ms) SOA, \(F(1, 55) = 34.95, MSE = 6.5E+03, p < .01\), and at the 500-ms SOA, \(F(1, 55) = 19.17, MSE = 17.3E+03, p < .01\). The disengage score was +218 ms (SE = 57 ms) at the 100-ms SOA and +264 ms (SE = 103 ms) at the 500-ms SOA. RBDN− patients did not show a significant difference of disengagement between hemifields (for disengagement score at the 100 ms SOA, M = +32 ms, SE = 71 ms; at the 500-ms SOA, M = +53 ms, SE = 38 ms), and neither did controls (M = -2 ms, SE = 10 ms; M = -32 ms, SE = 10 ms). The asymmetry of disengagement was significantly larger in patients with neglect syndrome than in controls at the shortest 100-ms SOA, \(F(1, 55) = 22.38, MSE = 6.5E+03, p < .01\), as well as at the 500-ms SOA, \(F(1, 55) = 15.07, MSE = 17.3E+03, p < .01\), showing a clear disengage deficit. RBDN− patients did not differ from the control group at both these SOAs. The asymmetry of disengagement was also significantly larger in patients with neglect syndrome than in RBDN− patients at the 100-ms SOA, \(F(1, 55) = 8.63, MSE = 6.5E+03, p < .05\). Our results confirm the strong deficit in disengaging attention from an ipsilesional cue in patients with neglect syndrome in order to orient toward contralateral targets (Morrow & Ratcliff, 1988), specifically for short and medium SOAs (100 ms and 500 ms).

Note that an asymmetry for patients with neglect syndrome was also found when we considered the difference between valid and neutral conditions at both 100- and 500-ms SOAs (M = +233 ms, SE = 72 ms; M = +156 ms, SE = 59 ms, respectively), showing that neutral conditions using a cue in the central box can elicit a deficit in disengagement (Posner et al., 1984). In other words, the disengage difficulty of patients with neglect syndrome occurs whenever the cue is located to the right of the target, regardless of whether it occurs in the opposite ipsilesional hemifield (Posner et al., 1987).

Also, if patients with neglect syndrome showed a larger valid–invalid difference for left targets than for right targets as compared with controls, note that there was a tendency for a disengage deficit at the 100-ms SOA, even for right hemifield targets in RBDN+ patients (M = 101 ms, SE = 47 ms) compared with the control group (M = 35 ms, SE = 9 ms), \(F(1, 55) = 3.23, MSE = 8.05E+03, p = .078\).

To document the relationship between the contralateral disengage deficit and the severity of neglect, we compared scores obtained in neglect tests with the disengage score. Results from all 26 of the patients were entered in the analysis. The disengage score at the 100-ms SOA did not correlate with any of the clinical tests: Albert test \((r = .09)\), bells test \((r = .02)\), line-bisection task \((r = -.03)\), and copy task \((r = .03)\). Finally, no correlation was found between the disengage deficit and the overall neglect score \((r = .12)\). Similar results were obtained when only those 19 patients actually showing neglect were entered in the analysis. Morrow and Ratcliff (1988) found no correlation between the severity of neglect and the contralateral disengage deficit in left hemispheric patients \((n = 10)\), but a strong correlation in right hemispheric patients \((n = 12)\). Our results are in partial agreement with theirs. A stronger disengage deficit was found in RBDN+ patients than in RBDN− patients, showing that the disengage deficit is a rather specific feature of neglect, but its magnitude seems to have no specific relationship with the severity of neglect. This may be due to differences between our analysis and that of Morrow and Ratcliff. First, the number of patients in their study was only 12 (for the right hemispheric group). Second, they calculated an overall score of neglect, using performance on a letter-cancellation test, line-bisection test, and the copy of the Rey figure. Our measures are more precise in evaluating correlations with each of the different clinical tests, but they did not include the copy of the Rey figure. Third, their cuing procedure was slightly different from ours, because they used informative cues (75% valid trials with peripheral cues) and calculated correlations for the 50-ms SOA. We examine, in Experiment 2, whether the disengage deficit is correlated with clinical tests when cues are informative.

The disengage deficit has been called the *extinction-like* deficit (Posner et al., 1984), because the invalid condition (the cue on one side and the target on the other) resembles the typical extinction in which one stimulus is presented on each side of the fixation. In our study, no significant correlation occurred between the extinction score and the disengage score \((r = .26)\), perhaps because many patients were at ceiling on the extinction test. However, as expected, patients with extinction had a disengage deficit \((M = 281 ms, SE = 76 ms)\), which was significantly larger than that showed by patients without extinction \((M = 83 ms, SE = 59 ms)\) \(r(23) = 2.09, p < .05\).

Fourteen of the 19 RBDN+ patients (3 of the 7 RBDN− patients) showed a valid–invalid difference for left hemifield targets at more than two standard deviations from the controls’ mean. Eleven of these patients showing a disengage deficit had brain imagery (see Table 2). Lesions involved various parts of the brain: parieto-occipital (BL, DB, and JD1), postero-temporal (JD1, JD2, and MB1), occipital (BL, JD1, and JD2), and subcortical (JD2, JL1, JL2, MB1, MB2, MS, MV2, and PB). Three patients with imagery did not present a disengage deficit (BN, DM, and MH); none of these patients had a large lesion in the parietal or the occipital lobe, and DM had a large temporal lesion. We found the same result when considering other patients for whom we had only the reports of their scan (AD, HL, and VG). So, apparently, a disengage deficit is most probable when the lesion involves the posterior part of the right hemisphere, including the parietal lobe, but a right parietal lesion is not necessary, and other lesions sparing the right posterior cortex can give rise to a disengage deficit.

Interestingly, 6 RBDN+ patients and 2 RBDN− patients showed a valid–invalid difference for right hemifield targets at more than two standard deviations from the controls’ mean. All 6
of the RBDN+ patients also had a deficit for left hemifield targets, and this left hemifield deficit was even stronger than the deficit for right hemifield targets in 4 patients. Among these 6 patients, 5 had a lesion including the lenticular capsule (JL1, MB2, MS, MV2, and PB) and 5 had a cortical lesion, including the frontal Rolandic areas (JL1, MB2, and PB), the anterior part of the temporal lobe (JL1, MB2, and PB), the mesial part of the temporal lobe (MV2), and the parieto-occipital areas (BL). Thus, lesions seem slightly more anterior in this group.

**Engagement of attention.** The engagement component of orienting was evaluated with the score (left valid) – (right valid), and the parieto-occipital areas (BL). Thus, lesions seem slightly (JL1, MB2, and PB), the mesial part of the parietal and the parieto-occipital areas (MV2), and the anterior part of the temporal lobe (JL2, MB1, and MH) did not present any engage deficit.

Eight of the 19 RBDN+ patients showed a significant engage deficit in the right hemifield at the 100-ms SOA condition (IOR) in the right hemifield did not correlate either with the overall neglect score (r = .09) or with any clinical test of neglect in the totality of patients: extinction (r = .18), Albert test (r = .12), bells test (r = .10), line-bisection task (r = -.09), and copy task (r = .01). Similar results were obtained when we considered only the 19 RBDN+ patients.

Eight of the 19 RBDN+ patients, but no patient without neglect, showed a right facilitation of return at more than two standard deviations compared with the controls’ mean. Lesions involved the temporal lobe in 3 patients (completely in DM, of the mesial part in MV2, and anterior in PB), and the mesial part of the parietal and occipital lobes in 1 patient (BL). Subcortical structures were also involved in 3 patients (DM, MV2, and PB).

In the left hemifield, the invalid minus valid difference at the 1,000-ms SOA was −105 ms (SE = 96 ms) for the RBDN+ patients, −22 ms (SE = 8 ms) for controls and +82 ms (SE = 40 ms) for RBDN− patients. However, there was no significant difference between groups, probably because of the large variance characterizing patients’ performance with left-sided targets (see Anderson, Mennemeier, & Chatterjee, 2000; Bartolomeo, 1997; Bartolomeo, Siéroff, Chokron, & Decaix, 2001).

**Experiment 2**

Experiment 1 has shown that left unilateral neglect can be related to a deficit in exogenous attention. The aim of Experiment 2 was, first, to evaluate the frequency of a deficit in endogenous attention in patients with neglect syndrome and, second, to evaluate whether a deficit in endogenous attention can aggravate neglect. In Experiment 2, the ratio between valid and invalid conditions was 80:20. The peripheral cue occurred at the target location in 80% of the trials, thus providing useful information to anticipate and move or shift attention in advance toward the location of the target. Both exogenous and endogenous orienting of attention should contribute the detection processes. Exogenous orienting should affect RTs for short SOAs, like in Experiment 1. Endogenous orienting should influence later processes, anticipation being usually present with SOAs superior to 300 ms (Müller & Findlay, 1988). Results of the three groups are presented in Figure 3.
Global RT analysis. All main effects were significant. The main effect of group, $F(2, 55) = 27.19$, $MSE = 680E+03$, $p < .01$, reflected, as in Experiment 1, slower overall RTs for RBDN patients ($M = 843$ ms, $SE = 69$ ms) and for RBDN− patients ($M = 676$ ms, $SE = 72$ ms) than for the control group ($M = 433$ ms, $SE = 15$ ms).

There was also a main effect of SOA, $F(2, 110) = 23.09$, $MSE = 22.4E+03$, $p < .01$, and the interaction Group × SOA, $F(4, 110) = 2.63$, $MSE = 22.4E+03$, $p < .05$, reflected a stronger effect of SOA (141 ms of difference between the short and the long SOAs, $SE = 33$ ms) in RBDN+ patients than in controls ($M = 64$ ms, $SE = 11$ ms) and in RBDN− patients ($M = 67$ ms, $SE = 25$ ms). However, as in Experiment 1, the interaction Group × Field × SOA was not significant, $F(4, 110) < 1$, $MSE = 19.5E+03$, ns.

The field effect, $F(1, 55) = 14.26$, $MSE = 224E+03$, $p < .01$, showed faster RTs for the right hemifield, but the interaction of Group × Field was also significant, $F(2, 55) = 13.48$, $MSE = 224E+03$, $p < .01$. Only RBDN+ patients showed a field effect (+336 ms in favor of the right hemifield, $SE = 89$ ms). $F(1,$
ORIENTING IN NEGLECT

55) = 42.92, $MSE = 224E+03$, $p < .01$, the difference between both hemifields being not significant in RBDN− patients ($M = +63$ ms, $SE = 35$ ms) and in controls ($M = +3$ ms, $SE = 3$ ms).

The effect of cue type was significant, $F(2, 110) = 21.57$, $MSE = 23.6E+03$, $p < .01$, and there was an interaction of Group $\times$ Cue Type, $F(4, 110) = 8.38$, $MSE = 23.6E+03$, $p < .01$. Valid trials showed the fastest RTs ($M = 566$ ms, $SE = 32$ ms), followed by neutral trials ($M = 584$ ms, $SE = 36$ ms) and by invalid trials ($M = 640$ ms, $SE = 40$ ms). RBDN+ patients showed a larger difference between valid and invalid trials ($M = 162$ ms, $SE = 39$ ms) than controls ($M = 19$ ms, $SE = 3$ ms), $F(1, 55) = 25.18$, $MSE = 29.3E+03$, $p < .01$, with the results of RBDN− patients being at an intermediate level ($M = 86$ ms, $SE = 17$ ms). Also, the difference between invalid and neutral trials was larger in RBDN+ patients ($M = 121$ ms, $SE = 33$ ms) than in controls ($M = 17$ ms, $SE = 3$ ms), $F(1, 55) = 15.71$, $MSE = 24.5E+03$, $p < .01$, RBDN− patients being at an intermediate level ($M = 60$ ms, $SE = 23$ ms). However, contrary to Experiment 1, neither the Group $\times$ Field $\times$ Cue Type $\times$ SOA nor the Group $\times$ Field $\times$ Cue Type interactions were significant, $F(8, 220) < 1$, $MSE = 21.3E+03$, $ns$; $F(4, 110) = 1.06$, $MSE = 23.0E+03$, $ms$, respectively. Theoretically relevant results were followed up by paired associations.

Disengagement of attention. At the shortest 100-ms SOA, the disengagement score was significantly larger for patients with neglect syndrome ($M = +178$ ms in favor of right hemifield targets, $SE = 122$ ms) than for controls ($M = -8$ ms, $SE = 13$ ms), $F(1, 55) = 4.23$, $MSE = 24.3E+03$, $p < .05$; the score of RBDN− patient was at an intermediary level ($M = +22$ ms, $SE = 40$ ms). None of the other SOAs showed differences in the disengagement score between groups. Thus, high predictability of the target location did not increase the disengage deficit, and even tended to reduce this deficit. The disengagement deficit in RBDN+ patients was numerically smaller in Experiment 2 ($M = 178$ ms, $SE = 122$ ms) than in Experiment 1 ($M = 218$ ms, $SE = 57$ ms), and occurred only for the 100-ms SOA. Therefore, the disengagement deficit obtained in Experiment 2 could be explained by the fact that our cues are peripheral and still call for exogenous attention at short SOAs. Losier and Klein (2001) have found, in their review, that the disengagement deficit in patients with neglect syndrome is frequently stronger in conditions of exogenous orienting of attention (peripheral cues) than in conditions of endogenous orienting of attention (symbolic central cues). Our results are in agreement with this meta-analysis and present the advantage of comparing exogenous and endogenous attention by using the same type (peripheral) of cue.

As expected, there was a positive correlation between the disengage score and the extinction score ($r = .51, p < .01$). However, no correlation with the clinical tests of neglect was obtained: Albert test ($r = .07$), bells test ($r = .34$), line-bisection task ($r = .25$), and copy task ($r = .12$).

Engagement of attention. At the 100-ms SOA, the engage score (valid difference between hemifields) was significantly larger in RBDN+ patients ($M = +241$ ms, $SE = 80$ ms) than in controls ($M = +12$ ms, $SE = 6$ ms), $F(1, 55) = 14.99$, $MSE = 20.8E+03$, $p < .01$, and only marginally different between RBDN+ patients and RBDN− patients ($M = +74$ ms, $SE = 41$ ms), $F(1, 55) = 3.43$, $MSE = 20.8E+03$, $p = .069$, RBDN− patients being not significantly different from controls. This engage score is numerically equivalent to the one obtained in Experiment 1. The engage score at the 500-ms SOA was significantly stronger in RBDN+ patients ($M = +289$ ms, $SE = 90$ ms) than in controls ($M = +3$ ms, $SE = 5$ ms), $F(1, 55) = 18.74$, $MSE = 25.9E+03$, $p < .01$, and RBDN− patients ($M = +29$ ms, $SE = 28$ ms), $F(1, 55) = 6.67$, $MSE = 25.9E+03$, $p < .05$. The engage score at the 1,000-ms SOA was also significantly stronger in RBDN+ patients ($M = +312$ ms, $SE = 105$ ms) than in controls ($M = +1$ ms, $SE = 8$ ms), $F(1, 55) = 16.30$, $MSE = 35.4E+03$, $p < .01$, and RBDN− patients ($M = +42$ ms, $SE = 41$ ms), $F(1, 55) = 5.27$, $MSE = 35.4E+03$, $p < .05$. Interestingly, the engage score of patients with neglect syndrome is numerically smaller at the longest SOA in Experiment 2 with informative cues than in Experiment 1 ($M = +403$ ms, $SE = 108$ ms) with noninformative cues.

As in Experiment 1, at the 100-ms SOA, the engage score correlated with extinction ($r = .41, p < .05$), but with none of the neglect scores, which is at variance with the results of Experiment 1: Albert test ($r = .26$), bells test ($r = .18$), line-bisection task ($r = .14$), copy task ($r = .28$), and overall neglect score ($r = .36$). This difference between Experiment 1 (noninformative cues) and Experiment 2 (informative cues) again suggests the predominance of exogenous impairments in left neglect. Still, at the 1,000-ms SOA, the engage score correlated with the Albert test ($r = .51, p < .01$), the Bells test ($r = .50, p < .01$), and the extinction score ($r = .44, p < .05$).

Because of the predictability of the cue, endogenous strategies can be produced to anticipate the side of the target. Despite this, with endogenous orienting of attention being slower than exogenous orienting, deficits of endogenous orienting should appear for long SOAs. A score of endogenous engagement and maintenance of attention toward the left hemifield was therefore calculated by use of the difference in the valid left condition between the shortest (100 ms) and the longest (1,000 ms) SOAs. A positive score indicates that subjects were faster at the long SOA.

The left endogenous score (+16 ms in RBDN+ patients, $SE = 77$ ms; +32 ms in RBDN− patients, $SE = 49$ ms; and +50 ms in controls, $SE = 12$ ms) was not significantly different between the three groups, $F(1, 55) < 1$ for each comparison, which militates against a deficit in endogenous attention in neglect syndrome. However, RBDN+ patients’ variability of performance was substantial, and 4 RBDN+ patients and 1 RBDN− patient showed a strong deficit in endogenous engaging and/or maintaining of attention in the left hemifield after a left hemifield cue. Among these patients, four had an available CT scan (BL, −221 ms; MB2, −248 ms; MS, −1,185 ms; and MV2, −155 ms). For all these patients, the lesion involved the thalamus and/or the capsulo-lenticular regions. These results are compatible with the role of the thalamus in engagement (Petersen, Robinson, & Morris, 1987; Rafal & Posner, 1987) and maintenance of attention (LaBerge, 1995; LaBerge & Buchsbaum, 1990). However, some patients showing a thalamic lesion, although partial, did not present a deficit in maintaining attention toward the left hemifield (JL1, +10 ms; JL2, +140 ms; and MH, +2 ms). Note also that 2 patients (BL, −221 ms, and JD1, +200 ms) clearly showed a lesion in the superior part of the parietal lobe (which has been included in an endogenous network of attention by Corbetta and Shulman, 2002, dorsal fronto-parietal network), although this did not include superior frontal areas. Only BL, whose lesion was also...
involving the thalamus, actually showed a deficit in endogenous orienting and/or attention maintenance.

The left endogenous score was not correlated with extinction ($r = -.18$), the line bisection task ($r = .16$), the copy task ($r = .21$), or the global neglect score ($r = -.21$), but was negatively correlated with both cancellation tests: Albert test ($r = -.42$, $p < .05$), bells test ($r = -.53$, $p < .01$). Patients with a deficit in endogenous attention toward the left hemifield showed the strongest deficit in these tests. This pattern of results suggests that, if neglect behavior is mainly related to an exogenous deficit, it can be aggravated by an additional deficit in endogenous attention. Indeed, only 2 of the 19 patients with neglect syndrome (AD and MM) presented an engage and/or a disengage deficit in Experiment 2 without any deficit in Experiment 1, thus showing a rather pure endogenous deficit.

**Experiment 3**

The aim of Experiment 3 was to evaluate the possibility of patients with or without neglect syndrome to endogenously reorient attention to the contralesional hemifield when the cue is located in the “good” ipsilesional hemifield. In Experiment 3, the ratio between valid and invalid conditions was 20:80. The target occurred at the location opposite the peripheral cue in 80% of the trials. Thus, participants could anticipate and shift attention in advance toward the location of the target. In Experiment 3, both exogenous and endogenous orienting of attention should contribute to the orienting process. At short SOAs, peripheral cues should capture attention, but this exogenous process might be endogenously inhibited because participants were expecting the target to occur at the opposite location. The endogenous component could also occur at longer SOAs and consists of reorienting attention from the invalid cue location toward the contralateral target location. Thus, in Experiment 3, we explored the endogenous ability of patients with neglect syndrome to inhibit ipsilesional capture of attention and to reorient attention toward contralesional targets. Results of the three groups are presented in Figure 4.

**Global RT analysis.** The main effect of group, $F(2, 55) = 28.32$, $MSE = 703E+03$, $p < .01$, reflected slower overall RTs for RBDN+ patients ($M = 858$ ms, $SE = 70$ ms) than for RBDN− patients ($M = 674$ ms, $SE = 74$ ms) and for RBDN− patients compared with the control group ($M = 431$ ms, $SE = 16$ ms).

There was a main effect of SOA, $F(2, 110) = 22.52$, $MSE = 24.0E+03$, $p < .01$, and the interaction of Group × SOA was only marginally significant, $F(4, 110) = 2.42$, $MSE = 24.0E+03$, $p = .053$. RBDN+ patients showed a 121-ms ($SE = 38$ ms) difference between the short and the long SOAs, 62 ms ($SE = 37$ ms) for RBDN− patients and 73 ms ($SE = 13$ ms) for controls. Once again, the interaction of Group × Field × SOA was not significant, $F(4, 110) = 1.70$, $MSE = 16.0E+03$, $ns$.

The field effect, $F(1, 55) = 19.98$, $MSE = 227E+03$, $p < .01$, showed faster RTs for the right hemifield, but the interaction of Group × Field was also significant, $F(2, 55) = 19.83$, $MSE = 227E+03$, $p < .01$. As in previous experiments, only RBDN+ patients showed a field effect ($M = +406$ ms in favor of the right hemifield, $SE = 88$ ms), $F(1, 55) = 62.12$, $MSE = 227E+03$, $p < .01$, the difference between both hemifield being not significant in RBDN− patients ($M = +71$ ms, $SE = 57$ ms) and in controls ($M = +1$ ms, $SE = 3$ ms).

Cue type was not significant, $F(2, 110) = 2.17$, $MSE = 28.7E+03$, $ns$, and neither were the interaction of Group × Cue Type, $F(4, 110) = 1.70$, $MSE = 28.7E+03$, $ns$, and the interaction of Group × Field × Cue Type × SOA, $F(8, 220) < 1$, $MSE = 15.1E+03$, $ns$. However, there was an interaction of Cue Type × SOA, $F(4, 220) = 2.48$, $MSE = 17.3E+03$, $p < .01$, because of the stronger improvement between the 100-ms and the 1,000-ms SOAs for invalid ($M = 116$ ms, $SE = 15$ ms) and neutral trials ($M = 104$ ms, $SE = 16$ ms) than for valid trials ($M = 43$ ms, $SE = 29$ ms). Finally, there was an interaction of Group × Field × Cue Type, $F(4, 110) = 3.75$, $MSE = 14.6E+03$, $p < .01$. The only significant differences between cue type conditions, independent from SOA, were found in RBDN+ patients. For left hemifield targets, there was a difference between valid and invalid trials in favor of invalid trials ($M = +90$ ms, $SE = 65$ ms; for comparison, $M = -36$ ms, $SE = 14$ ms, in RBDN− patients; $M = +21$ ms, $SE = 8$ ms, in controls), $F(1, 55) = 5.26$, $MSE = 232E+03$, $p < .05$. There was a difference between invalid and neutral trials in favor of neutral trials ($M = +50$ ms, $SE = 32$ ms; for comparison, $M = +19$ ms, $SE = 14$ ms, in RBDN− patients; $M = -13$ ms, $SE = 10$ ms, in controls), $F(1, 55) = 5.81$, $MSE = 70.1E+03$, $p < .01$. There was also a difference between valid and neutral trials ($M = +140$ ms, $SE = 58$ ms; for comparison, $M = -17$ ms, $SE = 59$ ms, in RBDN− patients; $M = +8$ ms, $SE = 10$ ms, in controls), $F(1, 55) = 14.86$, $MSE = 557E+03$, $p < .01$. For right hemifield targets, there was a difference between invalid and neutral trials only in RBDN+ patients (in favor of neutral trials, $M = +43$ ms, $SE = 27$ ms), $F(1, 55) = 5.80$, $MSE = 51.6E+03$, $p < .05$.

The triple interaction is mainly explained by a stronger left hemifield difference between valid and invalid conditions in patients with neglect syndrome than in other groups. Invalid trials gave faster RT than valid trials. However, this result cannot be entirely explained by an efficient endogenous reorienting of attention to the left hemifield, because the difference between Experiment 3 and Experiment 1 was a small gain in invalid trials (1.047 ms vs. 1.094 ms) in favor of an endogenous reorienting of attention, as well as a large cost in valid trials (1.137 ms vs. 916 ms). Patients with neglect syndrome were specifically slow in valid left trials in this experiment, certainly because a left cue indicating the frequent occurrence of a right target (80% invalid conditions) led to an endogenous orienting toward the right hemifield. When the cue was valid, patients had to shift the direction of attention and return to left locations. Most probably, this shifting in the direction of attention was difficult in patients with neglect syndrome.

**Disengagement and engagement.** In Experiment 3, there was no disengagement deficit for left hemifield targets in any group of patients at the 100-ms SOA, RTs being even faster in invalid trials (1.167 ms) than in valid trials (1.192 ms) in RBDN+ patients. A deficit in engaging attention at short SOA was found in RBDN+ patients ($M = +524$ ms, $SE = 133$ ms) but not in RBDN− patients ($M = +9$ ms, $SE = 49$ ms).

**Inhibition of right hemifield cue.** We were interested in the possibility for the patients with neglect syndrome to inhibit the location of the right hemifield cue when right targets rarely followed right cues, that is, to resist to right attentional capture.
We calculated the gain in RTs to invalid left targets (right cue), independently from SOA, between Experiment 1 and Experiment 3. This gain was 47 ms in RBDN+ patients (SE = 44 ms), 90 ms in RBDN− patients (SE = 37 ms), and 5 ms in controls (SE = 5 ms). Eight of the 19 RBDN+ patients and 5 of the 7 RBDN− patients showed a large gain (more than two standard deviations from controls’ mean), demonstrating an effective inhibition of right attentional capture. However, analyses of lesions in RBDN+ patients showing or not showing inhibition of right cues did not point to specific regions in the brain (see Table 2).

Reorienting of attention. To further examine the endogenous attention abilities in patients with neglect syndrome, we looked closely at their reorienting of spatial attention from a right cue toward a contralateral left target. Because endogenous control of attention is a slower process than exogenous orienting (Posner & Snyder, 1975), a comparison was made in left invalid targets at the longest SOA, between Experiment 1 and Experiment 3. A score of reorienting of attention was calculated as follows: \((\text{left invalid E1}) - (\text{left invalid E3})\) at the 1,000-ms SOA. RBDN+ patients showed a negative score \((M = -56 \text{ ms}, SE = 41 \text{ ms})\), demonstrating poor abilities in reorienting of
attention from ipsilesional right cue toward left contralesional targets. RBDN+ patients showed a positive score ($M = +86$ ms, $SE = 48$ ms) as well as controls ($M = +13$ ms, $SE = 8$ ms). Three RBDN+ patients and 4 RBDN− patients had a positive reorienting score more than two standard deviations away from controls’ mean, showing effective reorienting attention toward contralesional targets. Table 2 indicates patients presenting a deficit in reorienting of attention. Unfortunately, no anatomical conclusion could be drawn.

Discussion

The present study supports claims to the heterogeneous nature of left neglect, because we showed that neglect could be composed of dissociable deficits in several paper-and-pencil tests and in elementary operations, like engagement or disengagement of attention. However, in keeping with previous results, our findings also stress that an asymmetry of attentional engagement, with faster engagement for right-sided than for left-sided objects, is a major component deficit in left neglect. Also, our results clearly demonstrate that neglect is mainly explained by an exogenous deficit, even if a possible endogenous deficit could exacerbate neglect behavior.

Dissociations Among Paper-and-Pencil Tests

Results in the paper-and-pencil tests of neglect indicate that not every test is correlated with others. Even if spatial neglect is sometimes considered as a globally unitary syndrome, several authors have described dissociations, for example between performance on cancellation tests and the line-bisection test (Binder et al., 1992; Halligan & Marshall, 1992; McGlinchey-Berroth et al., 1996; Seki, 1996). Our results clearly confirm such dissociations. Although performances on both cancellation tests (Albert and bells tests) were unsurprisingly correlated, only 4 patients presented a deficit in both cancellation and line-bisection tests. Twelve patients showed a deficit in the cancellation tests only, and 3 patients showed a deficit in the line-bisection test only, an asymmetry, that has already been noted (Ferber & Karnath, 2001). Also, performance on the cancellation tests were correlated with extinction, in agreement with previous findings (McGlinchey-Berroth et al., 1996), and line bisection was correlated with copy, a correlation that has not been described in the literature.

Available CT scans tend to indicate that lesions are mainly posterior (including the parietal lobe, the temporal lobe, and the posterior part of subcortical structures) when a cancellation deficit exists, and more anterior (the anterior part of the temporal lobe, the frontal lobe, and the anterior part of the capsulo-lenticular region) in patients presenting, although not isolated to, a significant bias in line bisection, a result that is similar to the dichotomy proposed by Marshall and Halligan (1995b). Finally, all lesions of patients showing extinction involved the temporo-parietal region, in agreement with the findings of Karnath, Himmelbach, and Küker (2002).

The presence of double dissociations between cancellation tests and the line-bisection test rule out explanations due to the differential complexity of the task, even if those patients showing a deficit in the cancellation tests without deficit in the line-bisection test did not present the strongest cancellation deficit in our group of patients. The cognitive explanations for the cancellation–line-bisection dissociations are currently in debate. Marshall and Halligan (1995b) have argued that line bisection requires the computation of a midpoint that is not physically present in the stimulus array. Still, according to the results reported here, we also have to explain, first, why cancellation tests and extinction are correlated and, second, why line bisection and copy are correlated.

A motor involvement exists in cancellation tests and in line bisection (as well as in copy), but not in extinction, and cannot easily represent an explanation. A possibility is that the type of motor involvement differs between tasks. Even if cancellation tasks require a motor response, and the performance can be affected by a motor-directional akinnesia, the evaluation of the performance is not based on a fine analysis of the quality of the response (for example, a circle around the bell is counted as a correct response even if the circle is not perfect and complete). On the contrary, the motor response in copy or even in line-bisection tasks has to be much more precise.

Another explanation is that several objects are presented to the patient in the cancellation and extinction tests, whereas only one is presented in the bisection test, so that results in the different tests could differ according to the presence or absence of object- versus viewer-centered neglect (Chatterjee, 1994). The distribution of attention on several separated objects could play a role in cancellation and extinction tests. Conversely, in both copy and line-bisection tests, attention on individual objects could be involved. Although several objects were presented in our copy test, our score depended mostly on the left neglect of individual objects (Behrmann, 1994; Driver & Halligan, 1991; Gainotti, Messerli, & Tissot, 1972). Similarly, several lines were presented on the same sheet of paper in our line-bisection test; however, in this task, patients had to focus attention on each individual line. Riestra, Crucian, Burks, Womack, and Heilman (2001) have shown that patients had more difficulties in judging the similarity between the left and right segments when presented with a pre-bisected line than when presented with sequential, individual segments. If this result pleads in favor of an extinction-like phenomenon playing a role in line bisection bias, it can also be argued that left and right segments in a pre-bisected line can be considered as two parts of the same object and not two different objects, although the sequential individual segments could involve the processing of two different objects. It would be interesting to see whether patients exist with a stronger deficit in the sequential segments judgment task than in the pre-bisected judgment task, and whether such a deficit is correlated with other tests like the cancellation test.

Finally, only cancellation and extinction scores were correlated with scores obtained in the cuing task, specifically the engagement and the disengagement scores. As in these clinical tests, targets in the cuing task could appear in several (two) locations, these locations being marked by empty boxes, which were present during the whole trial. Possibly, good performance in these clinical tests and in our cuing task shares the need for the distribution of attention over several objects and for the orienting of attention between object locations.

Left Neglect and the Elementary Operations of Attention

Both groups of patients, distinguished by the presence or absence of neglect syndrome, were slower than controls in the cuing
experiments. However, only for patients with neglect syndrome were RTs to left hemifield targets systematically slower, in all three experiments, than RTs to right hemifield targets.

We first found some argument in favor of a deficit in phasic alertness in patients with neglect syndrome. They improved their RTs with SOA more than other groups, which can be caused by some slowness in the alerting effect of the sudden appearance of the boxes in the beginning of each trial. However, even if this result is in agreement with other results using physiological or reaction time data, we are careful about the conclusion of a deficit in phasic alertness in our patients, because our measure of alertness was quite indirect.

Most important, patients with left neglect syndrome clearly differ from controls and from patients suffering from right brain damage without neglect syndrome in terms of the effects of a spatial peripheral precue on the detection of a single target. Concerning the question of the locus of the cuing effect, there is evidence that location cuing does affect perceptual processing (Bonnel, Possamaï, & Schmitt, 1987; Müller & Humphreys, 1991). Cue could also have an effect on motor preparedness. However, most our patients did not produce any false alarm (responding to the cue instead of the target, specifically with long SOAs), and the total percentage of false alarms was less than 3%. Consequently, the results presented here, using a peripheral spatial cuing procedure, are indicative of which elementary operations of attention are specifically associated with left neglect syndrome.

Disengagement. In agreement with Morrow and Ratcliff (1988), there was a clear deficit in disengaging from ipsilesional stimuli in patients with neglect syndrome, and patients without neglect did not show a strong deficit in disengaging attention. Furthermore, in both Experiments 1 and 2, we found a close relationship between a disengage deficit and the extinction phenomenon (Posner et al., 1984). However, the disengage deficit in Experiment 1 (noninformative cues) as well as in Experiment 2 (informative cues) did not correlate with neglect severity, either measured by scores on individual paper-and-pencil tests or by a global neglect score, contrary to the study of Morrow and Ratcliff (1988). A possible explanation of this difference between our results and theirs is that these authors included the copy of the Rey figure. Impairment on this task frequently results from right hemispheric lesion, and left neglect could make it worse (Pillon, 1981; Rapport, Farchione, Dutra, Webster, & Charter, 1996). Despite this, our results suggest that other components of orienting of attention might be more closely related to left neglect clinical signs.

Concerning the lesion location, our results are compatible with the proposed relationship between disengaging of attention and posterior cortex (Egly et al., 1994; Friedrich et al., 1998; Friedrich & Margolin, 1993; Posner et al., 1984, 1987). Still, it is difficult to delimit a specific area for a deficit in disengaging of attention, for example concerning the superior parietal lobule, as proposed by Posner et al. (1984), or the tempo-parietal junction, as proposed by Friedrich et al. (1998). The analysis of morphological data may not be sufficient to the comprehension of the pathophysiology of neglect. All our patients were tested less than 1 year after the ictus and, for 17 of them, less than 3 months. Lesions could therefore be accompanied by diaschisis effects within an attentional neural network, as suggested by several authors (e.g., Demeurisse, Hublet, Paternot, Colson, & Serniclaes, 1997). Also, subcortical lesions could provoke a disconnection of some cortical areas. Accordingly, some lesions not involving the tempo-parietal junction or the superior parietal lobule could still be accompanied by a disengage deficit.

Finally, a nonnegligible number of patients with neglect syndrome suffering from a right hemisphere lesion showed a disengage deficit in both hemifields, a result in agreement with the clinical fact that some patients with neglect syndrome have difficulties even in the right hemispace (see Bartolomeo & Chokron, 1999b). This result cannot be totally explained, at least in our patients, by a tendency to compensate for the contralateral neglect, because all patients showing a disengage deficit in the right hemifield showed an even stronger disengage deficit in the left hemifield. Such a bilateral deficit in orienting of attention is compatible with evidence from other methods, showing that the right hemisphere processors play a role in orienting of attention in both hemifields or hemispaces (Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000; Heilman & Van der Abell, 1980; Mesulam, 1981; Perry & Zeki, 2000). However, another possibility is that some diaschisis effect occurred in the left parietal lobe, a phenomenon that has been described with acute right parietal lesion (Perani, Vallar, Paulesu, Alberoni, & Fazio, 1993). The fact that lesions provoking a bilateral disengage deficit seem more anterior than lesions provoking a unilateral disengage deficit does not allow us to conclude in favor of one or the other explanation.

Engagement. In their review, Losier and Klein (2001) wrote that

patients with posterior, right-hemisphere damage responded significantly more slowly to validly cued targets in the contralesional than ipsilesional hemispace. Although this pattern is present in each of the five studies contributing to this analysis, in no case did the authors indicate whether the trend was significant. (p. 9)

In the present study, the patients with neglect syndrome showed a strong difference between left and right engagement of attention compared with controls, which is in agreement with Losier and Klein’s meta-analysis. Is it really a deficit in engaging of attention? In principle, this could be ascertained by a comparison between valid and neutral conditions (absence of benefit in valid condition). However, the definition of a neutral condition in cuing procedures is always problematic (Jonides & Mack, 1984), and all the more so in patients with neglect syndrome, for whom neutral cues occurring in the central box can act as invalid cues for left targets (Posner et al., 1984). A possibility is that the difference between left and right valid conditions could be caused by a low-level sensory deficit. Patients suffering from an acuity deficit in the left hemifield should be slower for left targets compared with right targets even if this target is validly cued. Two issues militate against this hypothesis. First, according to our inclusion criteria, none of our patients suffered from left hemianopia. Second, the left–right difference for valid targets was obtained even with relatively long SOAs, which should have permitted compensation for a visual sensory deficit without engage deficit.

We not only were able, like Losier and Klein (2001), to conclude that a deficit in engaging attention toward contralesional targets is frequent in neglect, but we also found that the engage deficit was correlated with the deficit in the cancellation tests and the overall neglect score (at least in Experiment 1). Our findings
confirm the pervasive nature of a left-sided engage deficit in left neglect (D’Erme et al., 1992; Gainotti et al., 1991).

Results also indicate that patients who present a visual extinction not only have difficulty disengaging attention from ipsilesional stimuli but also have a strong deficit in engaging attention toward left contralesional stimuli. This result is important because relating the extinction phenomenon solely to a deficit in disengaging from ipsilesional stimuli does not explain why patients prefer to report ipsilesional targets first (unless we consider that their attention was strongly engaged on the fixation item).

Anatomically, the engage deficit seems related to posterior cortical and subcortical lesions, like the deficit in cancellation tests. However, here again it remains difficult to point to a specific locus. Only studies of patients with a longer delay from the ictus could give more precise information on the anatomical locus of the elementary operations.

Even if we were unable to delimit different anatomical loci for disengage and engage deficits, double dissociations clearly exist. According to several theories, orienting of attention could be explained by an imbalance between hemispheres (Farah, 1994; Kinsbourne, 1993). A unilateral lesion should provoke a bias in orienting of attention toward ipsilesional targets. Such theories explain why patients with neglect syndrome have a contralesional deficit even in valid conditions, but they predict that the contralesional deficit should be stronger in the invalid condition, because the invalid cues would reinforce the bias in favor of ipsilesional targets. Such theories do not predict dissociations between deficits in engaging of attention and deficits in disengaging of attention. An engage deficit should always been accompanied by a disengage deficit. Cohen, Romero, Farah, and Servan-Schreiber (1994) have argued that the difficulty in disengaging attention can be interpreted as an emergent property of interactions among the remaining parts of the system, without the need to invoke a specific disengager. Contrary to this prediction, we found instances of engage deficit without disengage deficits, as well as the opposite dissociation, showing that these elementary operations are produced by different anatomical processors, in agreement with Posner’s theory (Posner et al., 1984).

IOR. In addition to attentional engagement and disengagement, other components of attention were also impaired in our patients with neglect syndrome. We found a clear deficit of IOR in the ipsilesional hemifield of patients with neglect syndrome, even replaced by a facilitation, but not in patients suffering from a right brain damage without neglect, confirming previous results (Bartolomeo et al., 1999; Bartolomeo, Siéroff, Decaix, & Chokron, 2001). The absence of IOR, or even the facilitation of return in the ipsilesional hemifield could explain why patients with neglect syndrome repeatedly process ipsilesional targets (Bartolomeo et al., 1999). In our patients, right facilitation of return was correlated with the left target disengage score. Thus, a strong possibility is that facilitation of return is the consequence of a difficulty in disengaging attention from right hemifield locations.

Exogenous Versus Endogenous Deficit

Our results clearly support the hypothesis of a deficit in exogenous orienting of attention in the neglect syndrome (Bartolomeo, Siéroff, Decaix, & Chokron, 2001; Gainotti, 1996; Ladavas et al., 1994; Luo et al., 1998; Natale et al., 2005). A substantial deficit in endogenous orienting in patients with neglect syndrome would have led to a stronger left–right RT asymmetry in Experiment 2 (80% valid cues) than in Experiment 1 (noninformative cues), which was not observed. On the contrary, the disengage deficit was stronger with noninformative cues (Experiment 1) than with informative cues (Experiment 2) and was found only with short SOAs between the cue and the target (100 ms and 500 ms in Experiment 1; 100 ms in Experiment 2), thus confirming the results of the meta-analysis of Losier and Klein (2001). Moreover, the engage deficit was correlated with different clinical tests of neglect in Experiment 1, but less systematically so in Experiment 2. This result is important because most (but not all) studies exploring orienting in patients with neglect syndrome have used informative cues.

Corbetta and Shulman (2002) have developed a model of attention in which a ventral network in the parietal (temporo-parietal junction) and frontal lobes sustains exogenous orienting, and a dorsal parieto-frontal network sustains endogenous orienting. Most of our patients showed lesions in the ventral network and showed signs of deficits in exogenous orienting.

As seen in Experiment 2, few patients presented a clear deficit in endogenous engagement and/or maintaining of attention in the left hemifield (and only 2 out of the 19 patients with neglect syndrome showed an apparently pure endogenous deficit). These patients also presented more severe signs of left neglect. Thus, even if neglect is mainly explained by a deficit in exogenous orienting of attention, it is not surprising that an additional deficit in endogenous orienting could aggravate the neglect behavior. We found that those patients with an endogenous deficit suffered mainly from thalamic lesions, in agreement with the role of the thalamus in endogenous orienting of attention (LaBerge & Buchsbaum, 1990; Petersen et al., 1987; Rafal & Posner, 1987). Only 2 of our patients suffered from a lesion in the superior part of the parietal lobe (thus in the posterior part of the dorsal network of Corbetta & Shulman, 2002), but only 1, also showing a thalamic lesion, presented a deficit in endogenous orienting.

Finally, contrary to Experiments 1 and 2, patients with neglect syndrome did not present a disengage deficit in Experiment 3, in which 80% of the trials were invalid. Two issues may account for this dissociation. First, RTs to left valid trials were slower than in the other experiments, possibly because left cues incited patients to orient towards the right, and the few cases in which a left target actually occurred after a left cue engendered a disproportionate cost in RT, because patients had to shift the direction of attention. Second, patients with neglect syndrome showed, as did other groups, the possibility of inhibiting the capture of attention from right ipsilesional cues. The possibility of endogenously inhibiting the attentional capture exerted by right-sided objects is also consistent with a substantial sparing of endogenous processes in left neglect. Still, most of our patients with neglect syndrome did not present the possibility of developing an efficient endogenous reorienting of attention toward contralesional targets, even when ipsilesional cues were most probably followed by contralesional targets (Experiment 3). This result is different from that obtained by Bartolomeo, Siéroff, Decaix, and Chokron (2001) in a study using a similar methodology. A possible explanation underlying this difference is that patients in the present study had fewer trials per block than in the study by Bartolomeo, Siéroff, Decaix, and Chokron.
(2001), and the time to build and develop endogenous strategies of leftward reorienting might have been insufficient. Regardless, it is difficult to ascertain that a problem in reorienting of attention from an ipsilesional right cue to a contralesional left target is caused by a deficit in endogenous orienting. Because of the fact that patients may have an exogenous bias in attention toward the right hemisphere and a difficulty in disengaging of attention, reorienting should be more difficult to operate even when the endogenous mechanisms are not deteriorated. More studies are necessary, varying the number of trials in a block and using longer delays (greater than 1,000 ms) in order to better evaluate endogenous reorienting in patients with neglect syndrome, but our results suggest that the endogenous inhibition of right hemifield capture of attention is easier than the efficient reorienting of attention toward left hemifield in patients with neglect syndrome.

In conclusion, our findings point out the importance of adapting the rehabilitation of neglect to these various attentional impairments. Rehabilitation should thus include not only the classic reorientation of attention towards the contralesional hemifield but also a reduction of the rightward attraction of attention in the ipsilesional hemifield. In addition, it appears that the attentional training should take into account the clear dissociation between exogenous versus endogenous orientation of attention observed in most patients with left neglect syndrome.

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Négligence spatiale unilatérale : une conséquence dramatique mais souvent négligée des lésions de l’hémisphère droit

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RÉSUMÉ


Mots-clés : Négligence spatiale unilatérale • Neuroanatomie • Théories cognitives • Modélisation • Rééducation

SUMMARY

Unilateral spatial neglect: a dramatic but often neglected consequence of right hemisphere damage.


Introduction. Unilateral Spatial Neglect (USN) is a common consequence of right brain damage. In the most severe cases, behavioral signs of USN can last several years and compromise patients’ autonomy and social rehabilitation. These clinical facts stress the need for reliable procedures of diagnosis and rehabilitation. State of the art. The last 3 decades have witnessed an explosion of studies on USN, which raises issues related to complex cognitive activities such as mental representation, spatial attention and consciousness. USN is probably a heterogeneous syndrome, but some of its underlying mechanisms might be understood as an association of disorders of spatial attention. A bias of automatic orienting towards right-sided objects seems typical of left USN. Afterwards, patients find it difficult to disengage their attention in order to explore the rest of the visual scene. Neglected objects are sometimes processed in an “implicit” way. Perspectives. The development of behavioural paradigms and of neuroimaging techniques and their application to the study of USN has advanced our understanding of the functional mechanisms of attention and spatial awareness, as well as of their neural bases. A number of new procedures for rehabilitation have recently been proposed. Conclusion. The present review describes the clinical presentation of USN, its anatomical basis and some of possible accounts of different aspects of neglect behavior. Results of computer simulations and of rehabilitation techniques are also presented with implications for the functioning of normal neurocognitive systems.

Keywords: Unilateral spatial neglect • Neuroanatomy • Attention • Simulation • Rehabilitation

INTRODUCTION

La Négligence Spatiale Unilatérale (NSU) est un syndrome neurologique se manifestant fréquemment après une lésion de l’hémisphère cérébral non dominant pour le langage (voir pour revue Bartolomeo et Chokron, 2001). On estime qu’environ 85 p. 100 des patients porteurs d’une lésion hémisphérique droite présentent en phase subaiguë des signes de NSU qui détermineront dans 36 p. 100 des cas une NSU modérée à sévère (Azouvi et al., 2002). Ce syndrome est caractérisé par une difficulté voire une impossibilité à détecter, s’orienter vers et identifier des événements situés dans l’hémispace gauche, indépendamment de la présence d’un déficit sensoriel ou moteur élémentaire.
(Heilman et Valenstein, 1979). Les patients se comportent comme si la partie gauche de leur espace corporel et/ou extra-corporel n’existait plus.

Le syndrome de NSU a donné lieu à de nombreuses recherches depuis ces 30 dernières années et reste à l’origine de nombreux débats encore actuellement tant sur le plan théorique que sur le plan neuroanatomique.

L’intérêt pour la NSU provient des questions théoriques qu’elle pose sur des activités cognitives aussi complexes que la représentation mentale, l’attention et la conscience de l’espace et sur leurs localisations et fonctionnement dans le cerveau.

Sur le plan de la santé publique, la NSU pose des problèmes importants, du fait qu’elle aggrave le handicap en gênant la rééducation motrice (Appelros et al., 2002 ; Denes et al., 1982 ; Jehkonen et al., 2000). La réhabilitation sociale de ces patients est également compromise, du fait de la réduction d’autonomie déterminée par la NSU (par exemple, ces patients ne peuvent pas conduire une voiture).

La compréhension des mécanismes de la NSU est importante pour fournir aux cliniciens des outils adaptés de diagnostic et de traitement (rééducation). La recherche sur la NSU peut en outre contribuer à une meilleure compréhension des mécanismes cérébraux du traitement de l’espace et des corrélats neuronaux de la conscience perceptive.

DESCRIPTION CLINIQUE

En phase aiguë, les patients négligents présentent typiquement une déviation de la tête et des yeux vers la droite et ne peuvent prêter attention aux événements du côté gauche. Ils ne peuvent pas conduire leur NSU dans la vie quotidienne et dans les tests alors que d’autres patients sont également compromise, du fait de la réduction d’autonomie déterminée par la NSU (par exemple, ces patients ne peuvent pas conduire une voiture).

La compréhension des mécanismes de la NSU est importante pour fournir aux cliniciens des outils adaptés de diagnostic et de traitement (rééducation). La recherche sur la NSU peut en outre contribuer à une meilleure compréhension des mécanismes cérébraux du traitement de l’espace et des corrélats neuronaux de la conscience perceptive.

Mise en évidence de la NSU dans les tests neuropsychologiques

Parfois, les patients ne présentent pas de signes cliniques évidents de NSU en phase subaiguë, et la NSU peut donc passer inaperçue si on ne fait pas de tests spécifiques sur lesquels repose le diagnostic. Ces tests standardisés sont simples (papier/crayon) et peuvent être administrés au lit du patient, en prenant garde de maintenir centrée la feuille de test par rapport au tronc du patient. Deux batteries validées sont souvent utilisées pour évaluer la NSU : La Behavioural Inattention Test comportant une série de tests conventionnels et neuf tests dits « comportementaux » (Halligan et al., 1991a) et la Batterie d’Évaluation de la Négligence Spatiale Unilatérale du GEREN, de langue française, validée sur une population de 206 patients permettant une évaluation à la fois du niveau de déficit, mais également de ses conséquences fonctionnelles (Azouvi et al., 2002 ; pour les données normatives, voir Rousseaux et al., 2001). Cette batterie comporte des tests visuo-peceptifs (cf. par exemple le test des figures enchevêtrées), visuo-graphiques (cf. par exemple la copie de dessin) ainsi que l’échelle Catherine Bergego (ECB), questionnaire en 10 items d’auto-évaluation de la NSU par le patient et par le thérapeute, permettant ainsi d’apprécier l’importance de l’anosognosie associée à la NSU (Bergego et al., 1995).

COPIE DE DESSIN (Gainotti et al., 1972)

Les patients négligents omettent ou distordent les éléments situés sur la gauche de la feuille (NSU centrée sur la scène, ou « scene-based »). Certains patients présentent un phénomène de NSU centrée sur l’objet (« object-based ») dans laquelle tous les éléments sont présents mais la partie gauche d’un item peut être manquante (Gainotti et al., 1972 ; Marshhall et Halligan, 1993 ; Walker, 1995) (Fig. 2). Enfin, certains patients peuvent aussi déplacer certains éléments situés à gauche sur le modèle du côté droit lors de la copie (allochirie : Critchley, 1953 ; Halligan et al., 1992).

TESTS DE BARRAGE

Les patients doivent cocher ou entourer des traits (Albert, 1973) (Fig. 3), des lettres (Mesulam, 1985) (Fig. 4), des formes (Gauthier et al., 1989 ; Halligan et Marshall, 1991a) (Fig. 5). En général, ils débutent l’exploration du côté droit et omettent les éléments situés à gauche.
Bissection de lignes

Quand on demande aux patients d’indiquer le milieu de lignes horizontales de différentes longueurs, ils dévient vers la droite le milieu subjectif (Schenkenberg et al., 1980) particulièrement pour les lignes longues. Paradoxalement, le milieu subjectif des lignes courtes est dévié à gauche (« cross-over effect », Marshall et Halligan, 1989) (Fig. 6).

Figures enchevêtrées (Gainotti et al., 1991)

Les patients doivent dénommer différents dessins d’objets qui sont en partie superposés (2 à gauche, 1 central et 2 à droite) (Fig. 7). Certains patients omettent les items de gauche, ou font des erreurs de reconnaissance en se focalisant sur les détails de droite des objets situés dans l’espace gauche. Souvent, même sans omission, on observe quand même une nette tendance des patients à dénommer en premier les items situés à droite.

Du fait que la NSU peut se manifester dans l’espace représentationnel, d’autres épreuves en permettent une évaluation plus spécifique : comme par exemple, les dessins de mémoire ou les épreuves reposant sur l’évocation mentale d’un espace, notamment l’évocation mentale de la carte de France (Rode et al., 1995 ; pour une revue des différents types d’épreuves d’évaluation voir Gainotti et al., 1989).

BASES NEUROANATOMIQUES DE LA NSU

Cortex pariétal

Brain (1941) a le premier souligné l’importance des régions pariétales postérieures à l’origine du tableau d’agnosie spatiale unilatérale. Par la suite, Hécaen et al. (1956) ont montré, dans une étude radio-anatomique, l’importance de la région pariéto-occipito-temporale droite à l’origine du syndrome apraxo-agnosique (chez des patients ayant subi une exérèse chirurgicale de cette région du fait d’une épilepsie rebelle). Cette région a par la suite été confirmée sur une population plus importante de 179 patients (Hécaen et al., 1972) ainsi que par les premières études en imagerie cérébrale par Heilman et al. (1983a) et par Vallar et Perani (1986). La NSU est retrouvée le plus fréquemment après lésion dulobe pariétal inférieur, plus particulièrement dans sa portion à la jonction avec le lobe temporal et plus rarement la portion dorso-latérale du lobe frontal de l’hémisphère droit (voir pour revue Vallar, 2001).
Le sillon intrapariétal sépare le lobule pariétal supérieur (dont la lésion engendrerait plutôt des comportements de type ataxie optique : Perenin et Vighetto, 1988) et le lobule pariétal inférieur (dont la lésion engendrerait des comportements de NSU : Jeannerod et al., 1994, et des difficultés de manipulation d’objets : Binkofski et al., 1999). De nombreuses aires ont été identifiées dans le sillon intrapariétal chez le singe (LIP : aire intrapariétale latérale ; AIP : aire intrapariétale antérieure ; MIP : aire intrapariétale médiane ; VIP : aire intrapariétale ventrale). L’implication du LIP dans la conscience visuo-spatiale gauche a été postulée chez l’homme (Marshall et al., 2002 ; Vallar, 2001) à partir notamment des travaux réalisés sur le singe chez qui les neurones du LIP sont dévolus à une représentation de saillance des objets ayant une pertinence pour le comportement de l’animal et dont l’activité est corrélée aux déplacements de l’attention dans l’espace dans des tâches requérant la détection perceptrice ou la mémoire spatiale (Gottlieb, 2002 ; Gottlieb et al., 1998). Ils sont également impliqués dans les mouvements de saccades du fait des projections massives avec les colliculi supérieurs et le champ oculo-moteur frontal. Le rôle de ces neurones pourrait également expliquer que des traitements comme la stimulation calorique vestibulaire ou la vibration des muscles pourraient également expliquer que des traitements comme la NSU puisse se manifester simultanément par rapport à ces cadres (Driver et Mattingley, 1998 ; Gottlieb, 2002 ; Pouget et Driver, 2000).

Ce rôle intégratif multi-modal du cortex pariétal est favorisé par la présence de nombreux neurones ayant des champs récepteurs bimodaux (auditivo-visuel au niveau du LIP et plutôt visuo-tactile au niveau du VIP), ce qui pourrait expliquer que la NSU puisse concerner plusieurs modalités sensorielles. De plus, les fortes connexions du lobe pariétal avec les systèmes moteurs, pré-moteurs ainsi que les aires extra-striées lui confèrent un rôle clé pour une orientation motrice et perceptive coordonnées vers des cibles.

Cette localisation pariétale a été précisée par la suite à partir d’études utilisant la méthode de superpositions de lésions (Bates et al., 2003 ; Frank et al., 1997 ; Rorden et Karnath, 2004) au gyrus angulaire et à la partie médiane du lobe temporal (Mort et al., 2003). Cette dernière région, assez inattendue, reste cohérente avec les résultats en imagerie fonctionnelle qui rapportent une activation de cette aire temporale lors de l’encodage d’une localisation spatiale ou de la récupération en mémoire de cette localisation (Epstein et al., 1999).

Autres localisations moins fréquentes

Des cas de NSU ont été rapportés également après des lésions dans différents territoires perfusés par l’artère cérébrale moyenne : le lobe frontal inférieur (Husain et Kennard, 1997) ; les ganglions de la base (Damasio et al., 1980 ; Ferro et al., 1987 ; Heaton et al., 1982 ; Karnath et al., 2002a ; Karnath et al., 2005) ; le thalamus (Cambier et al., 1980 ; Rafal et Posner, 1987 ; Schott et al., 1981 ; Watson et Heilman, 1979) ; le gyrus cingulaire, bien que de façon rare (Heilman et al., 1983b) du fait de son implication dans des tâches de déplacements de l’attention, d’exploration oculomotrice et de recherche manuelle chez les sujets normaux (Gitelman et al., 1999 ; Kim et al., 1999 ; Nobre et al., 1997).

Des cas de NSU après accident vasculaire touchant l’artère cérébrale postérieure ont également été rapportés, notamment lorsque des régions plus antérieures du lobe occipital sont également lésées (Cals et al., 2002 ; Doricchi et Angelelli, 1999).

Enfin, certaines études ont valorisé plutôt les lésions touchant le gyrus temporal supérieur (GTS) droit du moins chez les patients n’ayant pas d’hémianopsie latérale homonyme gauche associée. Ce résultat suggère que cette région, comparable à son homologue gauche dévolue au langage, soit responsable de la conscience de l’espace chez l’homme (Karnath et al., 2001 ; Karnath et al., 2002b ; Karnath et al., 2004a ; Karnath et al., 2004b) d’autant qu’elle reçoit de nombreuses afférences multimodales sensorielles (Jones et Powell, 1970). Le GTS est également connecté à un réseau anatomoque cortico-sous-cortical avec le putamen, le noyau caudé et le pulvinar qui, quand ils sont lésés, génèrent aussi...
le syndrome d’hémignéligence mais le rôle d’une lésion du cortex temporal supérieur dans la NSU est contesté par d’autres études (Doricchi et Tomaiuolo, 2003 ; Hommet et al., 2004 ; Marshall et al., 2002 ; Mort et al., 2003 ; Thiebaut de Schotten et al., 2005).

**Fibres de la substance blanche : une issue possible du débat**

En effet, il semble qu’une combinaison de lésions du cortex pariétal inférieur à des disconnexions sous-corticales pariétocorticale (Doricchi et Tomaiuolo, 2003 ; Gaffan et Hornak, 1997) ou à la fois pariétocorticales et pariétocorticale (Leibovitch et al., 1998) soient les causes les plus fréquentes d’observation du syndrome de NSU. Chez le singe, Gaffan et Hornak (1997) ont observé une NSU plus sévère avec des lésions incluant la substance blanche qu’avec des lésions confinées à la substance grise. Déjà Geschwind, en 1965, avait proposé que la NSU puisse résulter d’une disconnexion entre les aires visuelles et somatosensorielles hémisphériques droite, et l’hémisphère gauche, dominant pour le langage.

Certaines études ont confirmé l’implication de la substance blanche sous-corticale dans le déterminisme du comportement d’hémignéligence en rapportant des cas de patients porteurs de lésions touchant les fibres inter-hémisphériques du corps calleux (Heilman et Adams, 2003 ; Ishiai et al., 2001 ; Kashiwagi et al., 1990). Cependant, plus récemment, il semble qu’une lésion des fibres d’association intra-hémisphériques soit principalement invoquée (Doricchi et Tomaiuolo, 2003 ; Mort et al., 2003). Elle concerne des fibres d’association pariétocorticale dénommées en fonction des études comme le faisceau longitudinal supérieur droit (Doricchi et Tomaiuolo, 2003) qui interconnecte le lobule pariétal inférieur au gyrus frontal inférieur et au gyrus temporal supérieur (Catani et al., 2005 ; Catani et al., 2002) ou le faisceau occipito-frontal supérieur droit, une autre voie de communication pariétocorticale (Nieuwenhuys et al., 1988 ; Thiebaut de Schotten et al., 2005). Thiebaut de Schotten et al. (2005) ont mesuré les erreurs de déviation vers la droite dans une tâche de bisection de lignes au cours de stimulations électriques (inactivations transitoires) lors de la résolution d’un glisier chez deux patients gauchers (l’un situé sur la partie caudale du lobe temporal droit, l’autre sur le lobe pariétal inférieur droit). Diverses régions corticales et sous-corticales dans la substance blanche ont été stimulées afin de minimiser les dégâts de l’exérèse. L’inactivation de deux structures corticales déterminait une déviation : il s’agissait du gyrus supra-marginal (la partie antérieure du lobule pariétal inférieur) et de la partie caudale du GTS. En revanche, l’inactivation d’une partie plus antérieure du GTS ainsi que du champ oculomoteur frontal, ne provoquait pas de déviation significative. Toutefois, les déviations les plus massives (de l’ordre de 30 p. 100 de la longueur de l’hémisegment de droite de la ligne) étaient observées lors de l’inactivation de la substance blanche au fond du lobule pariétal inférieur. Grâce à une technique ino-
Cette capacité du cerveau à produire des images mentales permet la création de nouvelles représentations, essentielle à la mise en œuvre des processus cognitifs les plus complexes. En élaborant des images mentales nous pouvons créer des cartes représentationnelles, attribuant une dimension spatiale aux objets — dimension qui peut être sélectivement endommagée dans la NSU. Parmi les premières descriptions de patients présentant un déficit au niveau des représentations spatiales, on trouve Bisiach et Luzzatti (1978) qui ont introduit le terme de NSU représentationnelle. Ces deux auteurs demandent à leurs patients de décrire une place familière, la place de la Cathédrale à Milan (Piazza del Duomo, Fig. 8), selon deux perspectives diamétralement opposées.

Pour chaque point de vue, les patients rapportent les items situés à droite et peu d’items, voire aucun, à gauche. Selon Bisiach et Luzzatti, ce comportement reflèterait l’existence d’une représentation spatiale analogique et symétrique dans le cerveau. Dans la NSU, les patients pourraient perdre la moitié gauche d’une représentation cognitive de l’espace. D’autres auteurs proposent en revanche que le déficit ne se situerait pas au niveau de la représentation mais plutôt au niveau de l’exploration de cette représentation (Bartolomeo et al., 2005). La carte mentale serait intacte, mais les patients ne seraient pas capables d’explorer la partie gauche de leurs images mentales.

Suite aux descriptions de Bisiach et Luzzatti, de nombreux cas de dissociation entre NSU représentationnelle et perceptive ont été rapportés (Beshin et al., 2000 ; Guariglia et al., 1993 ; Ortigue et al., 2001). La question est alors de savoir si la NSU représentationnelle est une entité à part entière ou si elle fait partie intégrante de la NSU perceptive.

Guariglia et al. (1993) rapportent le cas d’un patient qui ne montre pas de signe de NSU personnelle, extra personnelle ou péri personnelle, mais présente de sévères problèmes dans la récupération d’items du côté gauche (des deux points de vue opposés) de places familières. Ce patient a des performances normales pour les tâches requérant la génération et la manipulation d’images d’objets. Beshin et al. (2000) rapportent le cas remarquable d’un patient présentant une sévère NSU personnelle droite ainsi qu’une NSU perceptive droite, alors qu’une NSU représentationnelle se manifeste du côté gauche. Ortigue et al. (2001) décrivent également le cas d’une NSU représentationnelle, sans NSU perceptive.


Un cas semble aller à l’encontre de la position de Bartolomeo et al. (1994, 2005) : Beshin et al. (1997) rapportent un patient avec un large infarctus pariétal droit sans signe évident de NSU perceptive immédiatement après l’accident vasculaire cérébral mais présentant une NSU limitée à l’imagerie visuelle. L’altération est extrêmement sévère lorsque le patient est évalué par la description de places familières et de la carte d’Italie. Le cas de NSU représentationnelle pure décrit par Ortigue et al. (2001) semble également être en contradiction avec cette hypothèse, puisque le patient manifeste une NSU représentationnelle apparentément isolée en phase aiguë.

L’un des problèmes de la mise en évidence de la NSU représentationnelle pourrait être dû à la non spécificité et sensibilité des épreuves. En effet, de nombreux tests utilisés pour évaluer un déficit perceptif sont standardisés et permettent un consensus dans l’interprétation des résultats, alors que les principales épreuves évaluant un déficit représentationnel font appel aux processus d’évocation, en demandant aux patients de décrire de mémoire des lieux familiers. Plusieurs points sont critiquables : 1) malgré l’instruction de s’imaginer la scène « comme si elle se trouvait devant leurs yeux », les patients peuvent simplement produire une liste d’items provenant de leur mémoire sémantique verbale ; d’ailleurs, il semble que le déficit ne soit observable que si une composante spatiale est en jeu. Della Sala et al. (2004) ont mis en évidence des troubles de la mémoire de travail.
visuo-spatiale dans la NSU représentationnelle. Quant à Rode et al. (2004), ils montrent clairement chez un patient présentant une NSU représentationnelle gauche durable que le déficit n’est présent que dans la condition où il doit imaginer mentalement l’espace à explorer mais disparaît dans la condition où il doit évoquer le nom de villes sans consigne d’imagination. 2) Ce type d’épreuve est influencé par le niveau socio-culturel, ce qui implique une importante variabilité inter et intra individuelle. Afin de pallier à ces critiques, récemment Bartolomeo et al. (2005) ont créé une tâche géographique sur la carte de France basée sur des temps de réaction et permettant ainsi une mesure plus contrôlée de l’imagerie mentale. Cette étude montre que seuls deux patients présentent une NSU représentationnelle en plus d’une NSU perceptive. Les patients étaient capables d’imaginer des items à gauche mais ils présentaient un ralentissement du temps de réponse pour ces mêmes items par rapport aux items de droite. La dissociation entre les temps de réponse et la précision de la réponse suggère que le côté gauche de leur carte mentale n’est pas perdu, mais seulement « exploré » moins efficacement.

D’autres types de test permettant d’évaluer l’imagerie mentale sont les épreuves papier/crayon. Il est demandé aux patients de réaliser des dessins de mémoire. Les deux patients décrits par Bisiach et Luzzatti (1978) présentaient également une NSU gauche lors de la réalisation de dessins. Cependant, le feedback visuel présent dans ces tâches papier/crayon influence l’expression de la NSU. Ainsi, en comparant les performances de patients lors de la réalisation de dessins de mémoire les yeux ouverts versus fermés, Chedru (1976) puis Anderson (1993) remarquent alors que les patients omettent moins de détails à gauche dans la condition « yeux fermés ». D’autres auteurs (Chokron et al., 2004 ; Halligan et Marshall, 1994) confirment ces résultats : les dessins réalisés avec les yeux fermés permettraient l’évaluation réelle de l’imagerie mentale alors que la présence d’un feedback visuel dans la condition « yeux ouverts » accentuerait les signes de NSU (Fig. 9 et 10). Lorsque les patients commencent à dessiner à droite, leur attention est capturée par ces éléments déjà présents et empêche l’exploration vers le côté gauche (Chokron et al., 2004).

La NSU représentationnelle reste à l’heure actuelle un déficit d’interprétation difficile et constitue un défi à la fois pour la rééducation des patients et pour une meilleure compréhension des liens qui existent entre l’imagerie mentale et la perception visuelle.

**NSU et orientation de l’attention**

Les théories attentionnelles de la NSU reposent sur des observations cliniques basiques comme la présence de l’attraction magnétique » du regard vers le côté ipsilésionnel (le fait que ces patients tendent à regarder vers la droite dès qu’une scène visuelle se présente à leurs yeux, Gainotti et al., 1991) et l’impossibilité apparente des stimuli présentés du côté opposé à la lésion cérébrale à capturer l’attention des patients. Il existe de nombreux résultats indiquant que la NSU résulte d’une association de plusieurs désordres de l’orientation de l’attention dans l’espace (Bartolomeo et Chokron, 2002 ; Heilman et Van Den Abell, 1980 ; Mesulam, 1981).

**Modèles anatomo-cliniques de l’attention spatiale**

La NSU est plus fréquente, plus sévère et plus durable après une lésion touchant l’hémisphère droit qu’après une lésion touchant l’hémisphère gauche (Beis et al., 2004 ; Stone et al., 1991). Cette asymétrie a encouragé l’émergence de modèles anatomo-cliniques du contrôle de l’orientation de l’attention par les hémisphères cérébraux et a été également reproduite par certains modèles mathématiques de simulation du comportement héminégligent.

Le modèle de Heilman (Heilman et Valenstein, 1979 ; Heilman et al., 1985 ; Heilman et al., 1983b ; Heilman et al., 1981)
1993) suppose que chaque hémisphère cérébral contrôle les niveaux attentionnel et intentionnel de l’hémispace controlatéral avec toutefois une compétence supplémentaire de l’hémisphère droit pour activer les systèmes attentionnels droit et gauche alors que l’hémisphère gauche ne pourrait activer que le système attentionnel controlatéral. Le niveau attentionnel et le niveau intentionnel mettraient en jeu des réseaux distincts : 1) un réseau postérieur qui gérerait l’attention spatiale via le thalamus qui filtre les informations sensorielles vers le cortex et les régions associatives, et 2) un réseau antérieur qui gererait l’intention via des boucles cortico-sous-corticales passant par le thalamus et les noyaux gris centraux. Une lésion hémisphérique gauche ne déterminerait pas une NSU sévère puisque l’hémisphère droit serait capable de compenser en partie l’orientation de l’attention vers la droite alors que l’hémisphère gauche ne pourrait pas prendre le relais en cas de lésion hémisphérique droite pour orienter l’attention vers la gauche.


Le modèle de Mesulam (Mesulam, 1981, 2002) suppose un circuit attentionnel impliquant trois régions interconnectées. Ces régions sont sous l’influence d’un système réticulé ascendant activateur permettant un niveau d’éveil et de vigilance suffisants et sont connectées à la fois à des structures sous-corticales comme le colliculus supérieur, le pulvinar et le striatum mais aussi à un ensemble d’aires situées dans le cortex pré-moteur, pré-frontal latéral, orbito-frontal, temporal latéral supérieur, para-hippocampique et insulaire. Mesulam décrit 1) un composant parietal postérieur (comprenant le sillon intra-pariétal, une partie des lobules pariétal supérieur, inférieur et temporo-médial supérieur) permettant la création d’une représentation mentale dynamique d’événements saillants dans des coordonnées multiples et le calcul des stratégies de mouvements attentionnels ; 2) le composant frontal centré sur le champ oculomoteur frontal, les cortex pré-moteur et préfrontal permettant la conversion de plans et d’intentions en séquences motrices qui dirigent le foyer attentionnel ; 3) le gyrus cingulaire permettant l’identification de la pertinence motivationnelle des stimuli. Mesulam ajoute également une dominance de l’hémisphère droit pour contrôler bilatéralement la distribution attentionnelle alors que l’hémisphère gauche n’aurait de compétence que pour un contrôle controlatéral et postule que le volume et l’activité des aires dévouées aux processus attentionnels soient plus importants dans l’hémisphère droit que dans l’hémisphère gauche.

**BASES NEURALES DE L’ATTENTION**

De nombreuses études mettent en évidence la ségrégation des aires cérébrales sous-tendant les différentes fonctions attentionnelles et leur réseau en imagerie fonctionnelle (Fig. 11), (Corbetta et Shulman, 2002). La préparation et l’application d’une sélection « top down » (dépendante des attentes du sujet) des stimuli et des réponses incluent une partie du cortex intrapariétal et le cortex frontal supérieur (notamment le champ oculomoteur frontal) : ce système dorsal, bilatéral, correspondrait à l’orientation volontaire de l’attention. Un autre système, ventral et latéralisé du côté droit, est impliqué dans une sélection « bottom up » (guidée par le stimulus). Il inclut le cortex temporo-pariétal et le cortex frontal inférieur (Corbetta et Shulman, 2002). Ce second système, automatique, est spécialisé dans la détection des stimuli pertinents pour le comportement, particulièrement quand ils sont saillants ou inattendus. Les aires cérébrales de ce réseau ventral recouvrent en majorité les régions corticales qui, quand elles sont lésées, provoquent le syndrome de NSU (Corbetta et Shulman, 2002).

**ATTENTION EXOGÈNE VERSUS ENDOGÈNE ET NSU**

Le modèle de Posner (Posner, 1980 ; Posner et Petersen, 1990), issu de la psychologie cognitive, spécifie trois processus essentiels à la mise en jeu de l’orientation de l’attention visuo-spatiale qui peuvent être étudiés au moyen du paradigme d’indication spatiale (Posner, 1984 ; Posner et Petersen, 1990 ; Posner et al., 1982 ; Posner et al., 1984). Trois carrés sont placés au centre de l’écran : un au milieu, un à gauche et un à droite. La consigne donnée au sujet est de détecter le plus rapidement possible une cible (ex : une astérisque) qui apparaît dans l’un des deux carrés latéraux. Des indices (épaississement du contour d’un carré périphérique, ou flèche centrale indiquant un des carrés latéraux) peuvent être présentés avant l’apparition de la cible. On distingue des indices valides, qui indiquent le bon côté d’apparition de la cible, et des indices non valides qui indiquent le carré opposé (Fig. 12).

La proportion des indices valides et non valides peut être manipulée : soit les indices ne sont pas informatifs car la cible apparaîtra autant de fois du même côté que du côté opposé (condition 50-50 p. 100), soit le sujet a tout intérêt à traiter la localisation de l’indice car elle lui indiquera dans la majorité des essais la localisation de la cible (condition 80-20 p. 100). Le temps entre l’apparition de l’indice et celle de la cible peut être plus ou moins long (par ex., de 150 à 1 000 ms). Ce paradigme permet de séparer les processus...
d’orientation automatique de l’attention (attention exogène) des processus d’orientation volontaire (attention endogène) : en effet, dans la condition avec indices non informatifs, le sujet n’a pas d’intérêt particulier à traiter volontairement l’indice alors que si les indices sont informatifs, le sujet doit engager volontairement son attention sur l’indice pour répondre plus rapidement à la cible. En réalité dans cette dernière condition, la mise en jeu exogène de l’attention n’est pas totalement absente du simple fait de l’apparition des carrés et de l’indice, mais elle atteint son maximum au bout de 150-200 ms de délai indice/cible ; après ce délai, l’attention exogène est supplantée par l’attention endogène, liée aux stratégies du sujet et qui demande donc plus de temps pour se mettre en place. Chez les patients, plusieurs études montrent que l’attention endogène vers le côté négligé est relativement préservée, bien que ralentie (Bartolomeo et Chokron, 2002 ; Bartolomeo et al., 2001) alors que l’orientation exogène est gravement perturbée, ce qui a pour effet l’absence de capture automatique de l’attention du côté négligé (Bartolomeo et al., 1999 ; Natale et al., 2005). Selon les travaux de Posner et al., l’engagement de l’attention vers une localisation spatiale dépendrait du pulvinar alors que le mouvement de l’attention vers un nouvel emplacement dépendrait du colliculus supérieur. De plus, les patients négligents présentent un déficit de désengagement à droite (le désengagement de l’attention serait sous-tendu par le lobe pariétal postérieur) : une fois leur attention engagée sur une cible du côté non négligé (à droite), ils montrent des difficultés de réorientation de l’attention vers la gauche (Bartolomeo et Chokron, 2002 ; Bartolomeo et al., 2001 ; Posner et al., 1984).

Ce déficit d’orientation automatique vers le côté négligé pourrait expliquer les comportements de déviation en bissection chez ces patients non pas comme le résultat d’une compression de l’espace vers la droite (Halligan et Marshall, 1991b) mais plutôt comme la conséquence d’un déséquilibre attentionnel automatique (Bartolomeo et al., 2004). En effet, Bartolomeo et al. (2004) ont montré que les patients ne deviennent pas la droite que lorsqu’il existe des stimuli distracteurs ipsilésionnels alors que leurs performances ne diffèrent pas de celles des témoins lorsqu’aucun stimulus n’est présent dans l’hémiespace droit. En effet, les stimuli ipsilésionnels attirent automatiquement l’attention vers l’hémiespace droit indépendamment de leur pertinence pour la tâche (Corben et al., 2001) en augmentant ainsi le déséquilibre attentionnel en défaveur de l’hémiespace gauche (Bartolomeo et al., 2004).

Au vu de la correspondance entre les aires dévolues à l’attention exogène et les régions lésées causant la NSU et à l’instar des données cognitives, il semble essentiel de considérer le déficit d’orientation automatique de l’attention à gauche chez ces patients comme l’un des facteurs principaux causant le syndrome de NSU.

Les troubles de l’attention sélective spatiale ne sont pas exclusifs dans la NSU puisqu’il existe également des troubles de l’attention sélective non latéralisés (« attentional blink », Husain et al., 1997). Chez les sujets normaux, la capacité à détecter un second objet apparaissant moins de 400 ms après la présentation d’un premier objet est altérée. Chez

Fig. 11. – Régions cérébrales activés lors de tâches impliquant l’orientation endogène (blanc) ou exogène (pointillés gris) de l’attention (d’après Corbetta et Shulman, 2002). Le réseau exogène est latéralisé à droite.

Cerebral regions activated by tasks involving endogenous (white) or exogenous (in gray dotted-line) orientation of attention (from Corbetta and Shulman, 2002).

Fig. 12. – Illustration du paradigme de Posner et al. (1984). Après avoir fixé le carré central, un indice (épaississement du contour) apparaît dans un des carrés latéraux pour une durée variable de temps. Ensuite apparait une cible (astérisque) dans le même carré que l’indice (condition valide) ou dans le carré opposé (condition non valide). Le sujet doit appuyer le plus rapidement possible sur un bouton dès qu’il voit la cible.

Design of a cued reaction time task (Posner et al., 1984). Each trial began with the appearance of the three boxes for 500 ms with a fixation point in the central box. Then the cue (brief brightening of the contour of one of the boxes) followed during 300 ms. The target (asterisk) appeared at a variable stimulus onset asynchrony (SOA) from the cue and remained visible until a response was made. The target (asterisk) could appear in the box previously cued (valid condition) or in the opposite box (invalide condition). Participants are asked to maintain fixation on the fixation point and to respond to the target as quickly and accurately as possible, by pressing the space bar.

M. URBANSKI et coll.
les patients négligents, ce temps est multiplié par trois, ce qui démontre que le déficit d’orientation de l’attention dans la NSU n’est pas uniquement spatial mais également temporel. D’autre part, il existe également des troubles de l’attention soutenue (Hjaltason et al., 1996 ; Robertson et al., 1995), un déficit fréquent de la mémoire de travail visuo-spatiale (Della Sala et al., 2004) ainsi qu’un déficit de remapping spatial du fait du dysfonctionnement du lobe pariétal qui conduit à des difficultés à guider les saccades à travers l’espace après qu’un objet à droite ou à gauche ait été fixé (Husain et Rorden, 2003 ; Husain et al., 2001 ; Pisella et Mattingley, 2004). L’association de ces différents troubles dans la NSU est importante à prendre en considération pour la compréhension du syndrome et les bases futures de rééducation.

NSU et conscience

Les patients négligents semblent se comporter comme si une partie du monde n’existait plus. Cependant, dans certains cas, on a pu mettre en évidence des signes de « connaissement implicite » des stimuli négligés (voir par exemple : Berti et Rizzolatti, 1992 ; Marshall et Halligan, 1988 ; Volpe et al., 1979). Certains patients semblent même capables d’éviter des obstacles qu’ils assurent ne pas voir (McIntosh et al., 2004a ; McIntosh et al., 2004b).

En 1988, Marshall et Halligan ont décrit une patiente qui était incapable de décrire la différence entre deux dessins de maisons identiques, sauf que dans l’un des deux des flammes sortaient de la partie gauche de la maison (Fig. 13), mais préférait la maison sans flamme quand on lui demandait dans laquelle elle préférerait vivre.

De même, malgré l’incapacité des patients à identifier de manière explicite les mots ou les images présents dans leur hémichamp négligé, la performance de certains d’entre eux s’améliore considérablement lorsqu’on leur demande de porter des jugements ou d’identifier par choix forcés les cibles présentées dans le champ négligé (D’Erme et al., 1993).

Des signes semblables de « perception implicite » peuvent se retrouver dans les tâches de localisation de cibles latéralisées (gauche ou droite) ou bilatérales (gauche et droite). Dans une étude menée chez des sujets négligents et des sujets sains, Marzi et al. (1996) ont montré que les 2 groupes de sujets répondaient plus rapidement quand les cibles étaient présentes des deux cotés par rapport à quand elles étaient présentées en condition unilatérale (« redundancy target effect »). Cet effet est présent chez les patients aussi bien dans les essais où leur perception des 2 cibles était correcte que dans les essais où ils avaient négligé la cible de gauche. Néanmoins, une autre étude a montré que des patients négligents étaient aussi lents à détecter les cibles en condition unilatérale gauche qu’en condition bilatérale (Vuilleumier et Rafal, 1999).

Un traitement implicite a été observé également lors des paradigmes d’amorçage dont l’amorce, non perçue consciemment, a un effet sur le traitement du stimulus suivant. Quand deux images, par exemple, sont présentées simultanément à droite et à gauche du champ visuel, les patients négligents nient voir celle de gauche et aucune perception ne semble se réaliser. Cependant, si on leur demande de réaliser une tâche de catégorisation ou de décision lexicale sur un mot central lié sémantiquement ou non à l’image qui le précède (l’amorce), le même effet d’amorçage présent chez les normaux peut se produire chez les patients : ils répondent mieux et plus vite à la cible quand celle-ci est précédée par une autre image de la même catégorie (ex : une rose et une marguerite). Cet effet — dit d’amorçage, est présent, voire supérieur (Schweinberger et Stief, 2001), quand l’amorce n’est pas perçue consciemment par le patient (Berti et Rizzolatti, 1992 ; Ládavas et al., 1993 ; McGlinchey-Berroth et al., 1993) Ces études d’amorçage chez les patients négligents suggèrent donc fortement un traitement inconscient de l’image du niveau perceptif jusqu’au très haut niveau du traitement sémantique (McGlinchey-Berroth et al., 1993).

Les dissociations entre traitement explicite et implicite du stimulus négligé ne semblent toutefois être présentes que chez une minorité des patients. Pour la plupart des patients négligents, la destinée du stimulus négligé semble être l’oubli complet (D’Erme et al., 1993).

Souvent les patients négligents ne sont pas conscients de leur déficits moteur, sensoriels ou cognitifs (anosognosie : Babinski, 1914 et 1918). Il est important de lever l’anosognosie pour l’efficacité de la rééducation. Ce déficit de conscience peut également concerner l’hémicorps gauche des patients (hémiasomatognosie, qui est associée à l’anosognosie dans le syndrome d’Anton-Babinski) et entraîner des chutes ou des contusions lorsque les patients se cognent sur les obstacles situés du côté gauche. On assiste parfois même à des phénomènes de rejet, de déni d’appartenance de leur jambe ou de leur main gauche (misoplégie : Critchley, 1974). L’anosognosie pour l’hémiplégie semble associée
aux lésions des aires prémotorices (BA 6 et BA 44), de l’aire motrice BA 4 et du cortex somatosensoriel de l’hémisphère droit (Berti et al., 2005).

MODÈLES SIMULATIFS DE LA NSU

Aujourd’hui, grâce aux progrès de l’informatique et de la robotique, il est possible de construire des systèmes artificiels (simulés ou physiques) qui réussissent à reproduire, au moins pour certains aspects, le comportement humain et animal.

Cette méthodologie, dont l’esprit pourrait être traduit par l’expression « construire pour comprendre », dispose d’un grand potentiel théorique, parce que la construction d’un modèle d’un certain phénomène permet de vérifier sa capacité explicative.

Au contraire, dans l’étude des phénomènes naturels, il semble que trop souvent on se comporte comme les enfants qui, pour comprendre comment un jeu fonctionne, le démontent en petits morceaux et, à la fin, se retrouvent avec un tas de parties inutilisables.

Les simulations sont des théories interprétatives des phénomènes naturels formulées sous forme de programme (Parisi, 2001). Ce nouveau type d’investigation offre une série d’avantages non négligeables : exprimer une théorie comme un programme oblige tout d’abord à la définir quantitativement, clairement, explicitement et de manière univoque, sans quoi il est impossible que le programme fonctionne. La simulation permet ensuite de vérifier que les prédictions du chercheur résultent effectivement de sa théorie, car le programme qui représente la théorie doit contenir tous les mécanismes et les facteurs qui devraient expliquer un certain phénomène. Quand on fait tourner le logiciel, il est possible de vérifier si les phénomènes étudiés sont effectivement produits par l’action des mécanismes supposés.

Dans l’étude des déficits attentionnels de la NSU, cela se traduit par la nécessité de définir clairement et explicitement les hypothèses sur les fonctions normales et pathologiques des mécanismes de l’attention spatiale.

Les simulations constituent en outre des laboratoires virtuels dans lesquels il est possible d’avoir un contrôle très élevé sur la manipulation des variables et d’étudier dans un cadre expérimental des phénomènes qui, pour plusieurs raisons, n’y entrent pas facilement.

Pendant les dix dernières années, divers modèles simulatifs ont été proposés afin d’explorer la NSU. Ces derniers sont fondés essentiellement sur des modèles connexionnistes et implémentés à partir de réseaux de neurones artificiels.

Reproduction mathématique de certains signes de NSU

Cohen et al. (1994) ont pu obtenir le déficit de désengagement des patients négligents après avoir provoqué une lésion dans leur modèle reproduisant les effets attentionnels normaux de l’interaction et de la compétition entre les représentations de diverses zones de l’espace. Ainsi, le déficit de désengagement peut être interprété comme une propriété émergente de l’interaction des diverses parties du système sans qu’il soit nécessaire de postuler l’existence d’un module cérébral spécifique (« disengager »).

Mozer et collaborateurs (Mozer, 2002 ; Mozer et Behrmann, 1990 ; Mozer et al., 1997) ont utilisé un modèle connexionniste formé par des structures de haut et de bas niveau pour l’attention spatiale et la reconnaissance des objets bi-dimensionnels. À l’aide de lésions graduelles effectuées sur les connexions « bottom-up » qui relieaient une rétine artificielle à une couche « attentionnelle », plusieurs comportements associés à la NSU ont pu être reproduits, comme la dyslexie et la déviation à droite dans la bissection de lignes.

Pouget et Sejnowski (1997) ont implanté l’hypothèse selon laquelle les neurones pariétaux calculent la fonction de base des variables d’input dans un modèle computationnel (Pouget et Sejnowski, 2001). Leur modèle effectue des transformations sensori-motrices où la réponse du neurone pariétal est approchée avec le produit d’une fonction de Gauss de la position de la rétine et une fonction sigmoïde de la position de l’œil. En produisant des lésions sur ce modèle, les auteurs ont réussi à reproduire des déficits semblables à ceux observés chez les patients négligents.

Reproduction de l’asymétrie en faveur de l’hémisphère droit dans la NSU

Anderson (1996 et 1999) a proposé un modèle dans lequel la représentation des zones controlatérales et ipsilatérales de l’espace est différente dans chacun des hémisphères et, en particulier, que l’hémisphère droit intervient bi-latéralement alors que l’hémisphère gauche intervient en premier lieu dans l’hémispace droit. La contribution totale des deux hémisphères à la représentation neurale générale de l’espace n’est pas égale. En effet, la carte pariétale gauche est composée d’un nombre moins grand d’unités que la droite. Lorsqu’on le lève, ce modèle reproduit la déviation à droite dans la bissection de lignes tout comme la dyslexie de la NSU.


Di Ferdinando et al. (sous presse) ont comparé les différentes théories de la NSU dans une étude de simulation, afin de vérifier leur plausibilité théorique respective. Ils montrent que les asymétries sont expliquées plus précisément par l’hypothèse d’une dominance de l’hémisphère droit pour les représentations spatiales de l’espace.

Perspectives : les réseaux écologiques

La modélisation des déficits neuropsychologiques et du fonctionnement physiologique à travers la définition et la lésion de modèles connexionnistes se dirige désormais vers l’utilisation de « réseaux écologiques » (Di Ferdinando, don-
nées personnelles). Dans ces modèles, appartenant au cadre de la Vie Artificielle (Langton, 1989), non seulement le cerveau et le système nerveux peuvent être simulés, mais aussi les caractéristiques physiques d’un corps qui agit dans un milieu physique et dont les caractéristiques ne sont pas définies a priori mais émergent de l’interaction entre l’organisme et le milieu. Ce résultat est obtenu grâce à l’emploi d’un algorithme d’apprentissage non supervisé, l’algorithme génétique (Mitchell, 1997), s’inspirant de critères évolutifs. Bien que les réseaux de neurones et l’algorithme génétique ne soient que des représentations très schématiques du cerveau et de l’évolution, l’utilisation conjointe de ces deux méthodologies permet de reproduire des caractéristiques essentielles des organismes vivants, et présentent un pas supplémentaire dans la direction de la plausibilité des modèles simulatifs en neuropsychologie.

**PRATIQUES RÉÉDUCATIVES DANS LA NSU**

Malgré la possibilité dans la plupart des cas pour les patients de compenser leurs déficits initiaux, d’autres présentent une chronicité de leur NSU qui les handicapent. Pendant les 30 dernières années, de nombreuses recherches ont montré que certaines stimulations expérimentales pouvaient produire une rémission transitoire des signes de la NSU.

**Les techniques « top-down »**

Elles entraînent les patients à porter leur attention vers le côté négligé en stimulant les processus d’exploration visuo-spatiale (suivre le mouvement d’une lumière par exemple). Mais si elles permettent d’améliorer le niveau de conscience du déficit et la capacité à maintenir volontairement l’attention du côté controlésionnel, elles ne permettent pas toujours une généralisation aux activités de la vie quotidienne ni aux autres tâches (Gouvier et al., 1987 ; Weinberg et al., 1977). Il est donc nécessaire d’augmenter le nombre de tâches sur lesquelles entraîner le patient, en particulier ajouter des tâches écologiques, et ce sur une période de temps assez longue. Par exemple, Pizzamiglio et al. (Pizzamiglio et al., 1992) ont utilisé un traitement de 40 séances de réadaptation basé sur 4 procédures principales. Ces tâches utilisaient 1) un scanning visuo-spatial, 2) des tâches de lecture et copie de matériel verbal, 3) une copie de projets ou de matrices de points et 4) une description de figures. Tous les patients ont montré une amélioration de la symptomatologie aussi bien sur des tests visuo-spataux que sur une échelle fonctionnelle d’évaluation de la NSU (Zoccolotti et Judica, 1991). De même, Lladavas et al. (1994) ont entraîné des patients à diriger l’attention vers l’espace controlésionnel en utilisant des indices informatifs permettant de prédire la localisation de la cible, ce qui a permis à ces patients d’améliorer leur exploration vers la gauche. Malheureusement, ces procédures requièrent une bonne conscience du déficit alors que les patients négligents sont souvent anosognosiques.

**Les techniques « bottom-up »**

Elles ne requièrent ni un niveau élevé de conscience du déficit, ni un contrôle volontaire de l’attention vers la gauche (Frassinetti et al., 2002). Elles utilisent des stimulations sensorielles pour rehausser la saillance et la représentation de l’hémispace gauche, en se basant sur le rôle intégratif multi-modal du cortex pariétal postérieur. Ces techniques sont des processus passifs, dont la durée des effets bénéfiques sur les signes de NSU est confinée à la durée approximative des modifications sensorielles ; ainsi l’amélioration reste très limitée dans le temps et tend à disparaître dès que la manipulation est interrompue.

**LA STIMULATION VESTIBULAIRE CALORIQUE (SVC)**

Cette technique consiste à provoquer une déviation du regard et de la tête du côté de l’oreille où l’on aura instillé de l’eau froide. On peut produire le même effet, avec une intensité moindre, en introduisant de l’eau chaude dans l’oreille controlatérale (Cappa et al., 1987 ; Rubens, 1985 ; Vallar et al., 1990). Rubens (1985) a testé l’effet de la SVC chez 18 patients négligents et a montré une réduction significative, bien que transitoire, des signes de NSU extracorporelle gauche évalués par un test de barrage de lignes et un test de lecture. Des études ultérieures ont prouvé l’effet, là encore transitoire, de la SVC sur d’autres manifestations de la NSU comme la NSU corporelle, la NSU représentationnelle ou sur des manifestations associées comme l’anosognosie ou le délire somatophrénique (Geminiani et Bottini, 1992 ; Rode et Perenin, 1994). Une des explications possibles est que cette technique facilite les mouvements oculaires vers la gauche (Chokron et Bartolomeo, 1999 ; Gainotti, 1993).

**LA STIMULATION OPTO-CINÉTIQUE (SOC)**

Les études chez les sujets normaux ont montré qu’une stimulation optocinétique vers la gauche ou la droite détermine une activation de l’aire V5 (MT, MST), du sillon intrapariétal supérieur et du putamen préférentiellement dans l’hémisphère droit (Dieterich et al., 1998). De plus, les singes chez qui on inactive l’aire MST montrent une difficulté à initier un nystagmus en direction de l’hémisphère lésé ainsi qu’une perturbation de la poursuite oculaire (Dürsteler et Wurtz, 1988).

La SOC utilise un arrière-plan se déplaçant vers la gauche de façon à orienter automatiquement l’attention des patients cérébrolésés droits du côté controlésionnel. Elle agit comme l’arrière-fond en mouvement d’une scène visuelle, induisant un réflexe qui permet au sujet normal de maintenir constante l’image rétinienne lorsque son corps est en mouvement ou que l’objet fixé visuellement se déplace, ou est présenté sur un fond en mouvement.

Cette technique permettrait d’améliorer la NSU du fait d’une réactivation indirecte de l’hémisphère droit lésé par l’utilisation des afférences provenant de l’hémisphère...
ganglions de la base chez des patients avec lésion cérébrale
une activation bilatérale de l’aire temporo-pariétale et des
ont montré qu’une stimulation vers la gauche produisait
des signes de NSU (les vibrations imprimées du côté droit
et de réduire ainsi les signes de NSU.

LA STIMULATION DU MEMBRE CONTRALÉSIONNEL
Cette technique se base sur l’observation que la NSU
diminue lorsque le patient utilise le membre gauche lors de
l’exécution des tests standards d’évaluation du déficit (Hal-
igan et al., 1991b). Robertson et al. (1992) ont montré
que cette technique permet de réduire la NSU dans la vie
quotidienne pendant plusieurs semaines après la fin de
la rééducation. Même la simple stimulation proprioceptive
de la main gauche permet d’améliorer le déplacement des
patients (Robertson et al., 1994). Récemment, Ladosavas
et al. (1997b) ont trouvé une amélioration dans une tâche
de recherche de stimuli visuels lorsque des mouvements passifs
de la main gauche étaient exécutés dans l’espace gauche
alors que des mouvements au centre ou à droite ou encore
exécutés avec la main droite ne permettaient pas d’observer
d’amélioration dans cette tâche. Ces effets peuvent se pro-
duire pour l’espace proche comme pour l’espace lointain
(Frassinetti et al., 2001).

L’ADAPTATION PRISMATIQUE (AP)
Cette nouvelle technique (Rossetti et al., 1998) permet
une amélioration des symptômes de NSU pour les tests
standards et les échelles fonctionnelles. Elle a de nombreux
avantages par rapport aux autres techniques de réhabilitation
de la NSU et ne demande qu’une courte période d’entrainem-
ment pour produire des effets bénéfiques durables (Frassinetti
et al., 2001). Elle ne requiert pas d’orientation volontaire
de l’attention vers le côté négligé comme pour les autres
techniques (Angeli et al., 2004). Cependant les recherches
n’ont pas encore permis une identification précise des pro-
cessus à l’origine des effets de l’AP, bien que les hypo-
thèses attentionnelles soient prépondérantes. Les patients
font des mouvements d’atteinte d’une cible visuelle avec
la main pendant et après avoir porté des prismes qui dévient
tout le champ visuel vers la droite. Pendant qu’ils portent
les prismes, ils apprennent ainsi à adapter leurs mouvements,
en corrigeant vers la gauche des mouvements déplacés à
droite par le système visuel (qui voit la cible plus à droite
par rapport à sa position réelle). Dans une première étude
faisant porter aux patients pendant 5 minutes des prismes
produisant une déviation visuelle de 10 degrés vers la droite,
Rossetti et al. (1998) ont observé une adaptation prismatique
chez tous les patients ainsi qu’un important « after-effect »,
consistant en l’amélioration de la NSU.

Des études suivantes ont rapporté des améliorations
considérables de la symptomatologie de la NSU suite à

intact (Kerkhoff et al., 1999). De plus, Brandt et al. (2000)
on ont montré qu’une stimulation vers la gauche produisait
une activation bilatérale de l’aire temporo-pariétale et des
ganglions de la base chez des patients avec lésion cérébrale
droite et hémianopsie contralatérale. Pizzamiglio et al. (1990)
on ont mené des études avec SOC chez des contrôles, des
patients avec NSU et hémianopsie et des patients avec NSU
sous hémianopsie qui devaient effectuer une tâche de bis-
section de lignes présentées sur un fond de points en mouve-
ment. Le mouvement horizontal du fond vers la droite ou
vers la gauche produisait un nystagmus optocinétique à une
vitesse stable et cohérente avec la direction du mouvement.
Chez tous les sujets, la SOC engendrait une déviation du
point subjectif de bissection, par rapport à la situation de
non mouvement. Le mouvement vers la gauche permet de
réduire l’erreur de bissection chez les patients négligents.
Concernant l’explication des bénéfices de cette méthode,
Gainotti (1993) souligne que la stimulation directe contra-
latéralement réoriente l’attention vers le côté négligé en
diminuant le biais ipsilésionnel. Vallar et al. (1995a) sou-
tiennent que les effets de la SOC ont des répercussions sur
la proprioception, ce qui permet d’activer des représentations
multimodales de l’espace personnel dans l’hémisphère
droit et de réduire ainsi les signes de NSU.

LA ROTATION GUIDÉE DU TRONC
Karnath et al. (1993) ont obtenu une réduction des signes
de NSU en imposant au tronc de patients négligents gauche
une rotation de 15° vers la gauche. Poursuivant cette
démarche, Wiart et al. (1997) ont associé une rééducation de
l’orientation visuelle à un travail sur l’orientation volontai-
re du tronc. Un corset qui solidarise la tête et le tronc du
sujet, sur lequel est fixé une tige horizontale, permet au
patient de pointer vers des figures colorées placées sur un
panneau placé devant lui (ce dispositif a été conçu par Bon
Saint Côme). Le sujet est contraint d’imprimer une rotation
axiale à son tronc sous le contrôle de la vue pour déplacer
latéralement le pointeur. Les figures du panneau sont reliées à
un système lumineux et sonore qui d’une part assure le bio-
feedback au contact du pointeur, et d’autre part permet au
rééducateur d’indiquer les formes au patient (indication).
Au cours de 20 séances d’une heure, des patients ont été entraînés
to repérer et atteindre les figures à l’aide de la tige métallique,
la tâche se complexifiant progressivement (augmentation
du déplacement vers la gauche et diminution de l’indication).
Les résultats obtenus aux tests visuo-graphiques (au début
du protocole, à la fin puis un mois après) ont permis de montrer
un effet positif qui peut rester stable après un mois et est
transposable à une échelle d’indépendance fonctionnelle.

LA VIBRATION DES MUSCLES DE LA NUQUE
et la STIMULATION ÉLECTRIQUE TRANSCUTANÉE
Karnath et al. (1993) ont appliqué des vibrations mécani-
quées transcutanées sur les muscles du côté gauche de la
nuque de patients négligents gauches, pendant une tâche de
détention visuelle latéralisée et ont observé une réduction
des signes de NSU (les vibrations imprimées du côté droit
et n’aggravant pas les signes de NSU gauche). Vallar et al.
(1995b) ont utilisé ces stimulations sur la nuque et la main
de patients négligents et ont obtenu une amélioration des
résultats des patients à des tests de barrage de lettres ; Guar-
glia et al. (1998) ont obtenu avec cette procédure une amélio-
ration de la NSU représentationnelle. Schindler et al. (2002)
on ont montré un effet bénéfique et durable de cette méthode
associée à une rééducation de l’exploration visuelle par
rapport à une rééducation par entraînement de l’explora-
tion visuelle seule.

M. URBANSKI et coll.
CONCLUSION

Ces techniques offrent des perspectives de prise en charge de la NSU, qui malgré sa fréquence, peut passer inaperçue et reste souvent mésestimée au niveau de ses conséquences sur le plan de la santé publique. Sur le plan théorique, une meilleure compréhension du syndrome permettra de proposer des modèles plus adaptés du fonctionnement normal de la conscience de l’espace, des processus d’imagination mentale et de l’attention visuo-spatiale. Sur le plan neuro-anatomique, le débat commence à se ré solder grâce aux nouvelles techniques d’imagerie (notamment IRM en tenseur anatomique, le débat commence à se résoudre grâce aux nouvelles techniques d’imagerie (notamment IRM en tenseur de diffusion), éventuellement couplées à la stimulation électrique intra-opératoire, qui permettent de commencer à envisager la NSU comme une pathologie des réseaux pariéto-frontaux hémisphériques droits impliqués dans l’attention et la conscience de l’espace.

RÉFÉRENCES


M. URBANSKI et coll.
Experimental remission of unilateral spatial neglect

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Abstract

Over the past several decades a growing amount of research has focused on the possibility of transiently reducing left neglect signs in right brain-damaged patients by using vestibular and/or visuo-proprioceptive stimulations. Here we review seminal papers dealing with these visuo-vestibulo-proprioceptive stimulations in normal controls, right brain-damaged (RBD) patients, and animals. We discuss these data in terms of clinical implications but also with regards to theoretical frameworks commonly used to explain the unilateral neglect syndrome. We undermine the effect of these stimulations on the position of the egocentric reference and extend the notion that the positive effects of these stimulation techniques may stem from a reorientation of attention towards the neglected side of space or from a recalibration of sensori-motor correlations. We conclude this review with discussing the possible interaction between experimental rehabilitation, models of neglect and basic spatial cognition research.

Contents

1. Introduction ........................................................................................................... 3128
2. Caloric vestibular stimulation ........................................................................................ 3129
   2.1. CVS in normal controls ........................................................................................ 3129
   2.2. CVS and rehabilitation in RBD patients ................................................................. 3129
   2.3. Neurophysiological correlates of CVS ..................................................................... 3133
3. Optokinetic stimulation ............................................................................................... 3133
   3.1. OKS in normal controls ........................................................................................ 3133
   3.2. OKS and rehabilitation in RBD patients ................................................................. 3133
   3.3. Neurophysiological correlates of OKS .................................................................... 3134
4. Trunk rotation ............................................................................................................ 3135
   4.1. TR in normal controls ............................................................................................ 3135
   4.2. TR in RBD patients .............................................................................................. 3135
5. Transcutaneous mechanical muscle vibration ..................................................................... 3135
   5.1. TMV in normal controls ....................................................................................... 3135
   5.2. TMV and rehabilitation in RBD patients ................................................................. 3136
6. Transcutaneous electrical neural stimulation in RBD patients ..................................................... 3136
7. Limb activation in RBD patients ..................................................................................... 3136

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1. Introduction

Unilateral spatial neglect (USN) is a failure to report, respond, or orient to stimuli that are presented contralateral to a brain lesion, provided that this failure is not due to elementary sensory or motor disorders (Heilman & Valenstein, 1979). Symptoms of this bias range from a slowing in leftward responding to a complete lack of awareness of one half of space, at which point patients behave as if that half of the world does not exist (Fig. 1). A left neglect syndrome is most commonly observed in right brain-damaged patients and is often dramatic enough to constitute a major handicap (Heilman & Valenstein, 1979). Symptoms of this bias range from a slowing in leftward responding to a complete lack of awareness of one half of space, at which point patients behave as if that half of the world does not exist (Fig. 1). A left neglect syndrome is most commonly observed in right brain-damaged patients and is often dramatic enough to constitute a major handicap (Heilman & Valenstein, 1979). These patients often get lost in familiar environments, repeatedly bump into objects on their left side, and, as a result, often hurt themselves (Bartolomeo & Chokron, 2001).

Over the last few years a number of behavioural experimental remediation techniques have been developed to treat left neglect symptoms in right brain-damaged (RBD) patients. These techniques include training patients in visual (Pizzamiglio et al., 1992; Seron & Tissot, 1973; Weinberg et al., 1977; Wiart et al., 1997) and tactile (Weinberg et al., 1979) exploration, to enhance a voluntary, endogenous orientation of attention towards the left neglect hemispace, and suppressing visual feedback to reduce the pathological rightward attraction of attention (Chokron, Colliot, & Bartolomeo, 2004; Smania, Bazoli, Piva, & Guidetti, 1997). Although these procedures have shown some success in laboratory settings, they often fail to generalize to real-life environments (Heilman, Watson, & Valenstein, 1997).

Recently, a number of visual, vestibular and/or proprioceptive stimulation techniques have been developed (Karnath, 1994, 1995, 1996; Karnath, Christ, & Hartje, 1993; Karnath, Schenkel, & Fischer, 1991; Pizzamiglio, Frasca, Guariglia, Incoccia, & Antonucci, 1990; Robertson & North, 1992, 1993; Vallar, Antonucci, Guariglia, & Pizzamiglio, 1993; Vallar, Bottini, Rusconi, & Sterzi, 1993; Vallar, Guariglia, Magnotti, & Pizzamiglio, 1995; Vallar et al., 1995b; Vallar, Sterzi, Bottini, Cappa, & Rusconi, 1990) to treat left neglect. These techniques have been shown to induce transient reductions in left neglect signs during visuo-spatial and imagery tasks involving both extra-personal and personal space. These visuo-vestibulo-proprioceptive stimulation techniques include caloric vestibular stimulation (CVS), optokinetic stimulation (OKS), vibration of neck muscles on the left side, leftward trunk rotation, transcutaneous electrical stimulation (TES) of the left hand or neck muscles, limb activation, and prismatic adaptation (PA). There is some evidence to suggest that these techniques reduce symptoms of anosognosia and somatopsychia (Rode et al., 1992) as well as enhance auto-correction and awareness (Rubens, 1985).

A number of studies have demonstrated that vestibulo-proprioceptive stimulations can affect the position of one’s egocentric reference, which is a hypothetical frame of reference used in everyday life to localize objects with respect to one’s trunk (see Karnath, 1997; Perenin, 1997 for review). It has been suggested that the spatial bias observed in left neglect patients following a right-sided lesion stems from a rightward deviation of this egocentric frame of reference (Fig. 2). Such a rightward shift would eliminate one’s awareness of all objects that occur beyond the left boundary of the shifted or skewed reference frame. This hypothesis has led to a commonly held view that the left neglect syndrome is a disturbance of one’s egocentric frame of reference and that vestibulo-proprioceptive stimulations reduce the leftward neglect by restoring a normally oriented spatial frame of reference (Karnath, 1997; Karnath & Dieterich, 2006). However, more recent studies have repeatedly shown that there is no significant correlation between
the position of this egocentric reference and the presence and severity of left neglect signs (see Chokron, 2003 for review and discussion). In light of this, Gainotti (1993, 1996) has proposed an alternative hypothesis which suggests that the positive effects of vestibulo-proprioceptive stimulation stem from a reorientation of attention towards the neglected side of space rather than a restoration of one’s egocentric frame of reference.

Given the profound implications of these stimulation techniques for the remediation of neglect and for elucidating the neural mechanisms and processes underlying spatial cognition, each of the vestibulo-proprioceptive stimulation techniques mentioned above will be critically evaluated in the current review. First, each technique will be presented in terms of the aims, procedures, and main findings of relevant studies that include normal subjects and/or right brain-damaged patients. In addition, Table 1 summarizes the most relevant papers for each technique in terms of population, stimulation and effects. We will engage in a general discussion that will critically examine the theoretical construct that has been most commonly used to interpret the palliative although transient effects of vestibulo-proprioceptive stimulations (CVS, OKS, trunk rotation, neck muscles vibration) are seen to reduce left neglect behaviour by transiently restoring a sub-normal position of the ER (indicated by the arrow).

2. Caloric vestibular stimulation (CVS)

2.1. CVS in normal controls

CVS is a routine diagnostic technique used by neurologists to assess vestibulo-proprioceptive functioning. The technique involves the irrigation of the ear canal with either cold or warm water. In normal individuals, the application of cold water to the ear canal produces a vestibulo-ocular reflex in which the slow phase of the nystagmus moves toward the stimulated ear. Head turning is also induced in the same direction as the slow phase of the nystagmus. These automatic responses are mediated by way of vestibulo-spinal activity. The same effect is obtained only in the reverse direction by applying warm water to the opposite side.

2.2. CVS and rehabilitation in RBD patients

The link between parietal lesions and vestibular defects has been known for a long time. In 1951, Hécaen and coworkers (1951) first reported the existence of a vestibulo-ocular bias in the direction opposite to the side of a brain lesion. In addition, when blindfolded, patients suffering from a right parieto-occipital lesion were unable to maintain their arms in position while pointing straight ahead. Instead, the arms of the patients tended to drift toward the ipsilesional side. When CVS was applied to the right labyrinths of these patients, an asymmetrical vestibulo-ocular response was elicited. That is, the slow phase of the caloric nystagmus was stronger when it moved in the same direction as that of the ipsilesional arm drift. The authors also reported on a series of 14 parietal lesion cases following head trauma. A large proportion of these patients presented segmental deviations (e.g., arm drift and Romberg sign), directed as a rule toward the side of the lesion. The authors interpreted these data as reflecting impaired function of the inputs from the vestibular nucleus to the cortex. They reasoned that the lack of integration of vestibular inputs at the cortical level would result in the visuoconstructive deficits observed after right-sided parietal lesions. These deficits would manifest themselves in the misperception of spatial coordinates (Hécaen et al., 1951). This hypothesis has been confirmed via numerous animal lesion studies (see Jeannerod & Biguer, 1987).

The relationship between CVS and neglect was first suggested by Silberpfennig (1949) who observed improvements in reading words during the occurrence of vestibular nystagmus, when the slow component moved to the left, in a right frontal lobe tumor patient with right-sided deviation of gaze. More recently, Marshall and Maynard (1983) also reported improvements of leftward gaze after weekly administrations of left cold caloric irrigation in a patient who demonstrated a fixed gaze deviation to the right several months after suffering from a right hemi-
<table>
<thead>
<tr>
<th>Reference</th>
<th>Treatment</th>
<th>Procedure</th>
<th>Duration of treatment</th>
<th>Population</th>
<th>Time post-injury</th>
<th>Interval between stimulation and post-test</th>
<th>Absence of effect negative effect (increasing the spatial bias in N+ patients or inducing a spatial bias in controls)</th>
<th>Positive effects (reducing the spatial bias in N+ patients)</th>
<th>Long lasting effects (&gt;1 h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubens (1985) [case study]</td>
<td>CVS</td>
<td>Cold left ear CVS for 1 min followed 30 min after by warm right ear CVS for 1 min and the reverse the next day</td>
<td>One session</td>
<td>Eighteen RBD LN+, five healthy young controls</td>
<td>In the first 2 weeks post-stroke</td>
<td>Before, immediately after, 5 min later, 4-7 days later (for seven patients retested on the line crossing-test)</td>
<td>Left warm-water and right cold-water CVS showed no effect on RBD LN+</td>
<td>Left cold-water and right warm-water stimulation improved, gaze in all RBD LN+. Visual neglect in all RBD LN+ measured by cross line, reading, point and count people around him. Greater improvement after left cold-water than right warm-water stimulation</td>
<td>Return to baseline after 5 min delay Improvement in the line crossing test for the seven patients retested 4-7 days after treatment Informal observation showed improvement after 1 day delay on anosognosia, logorhea Return to baseline few days or few weeks after</td>
</tr>
<tr>
<td>Rode et al. (1992) [case study]</td>
<td>CVS</td>
<td>Cold (20°C) left ear colonic stimulation for 1 min</td>
<td>Two sessions (48 h interval)</td>
<td>One RBD LN+</td>
<td>Six months post-stroke</td>
<td>Before, immediately after, 1 day after the first stimulation and 2 days after the second one</td>
<td>No effects on: hemianesthesia, hemianopia</td>
<td>Motor deficit: hemiplegia for the left leg, head and gaze deviation, detection of auditory stimuli, visual neglect: line crossing test and detection of visual stimuli, personal neglect, anosognosia, somatoparaphrenia, logorhea Representational neglect (mentally evocation of the map of France and name as many towns as possible in 2 min)</td>
<td>Return to baseline few days or few weeks after</td>
</tr>
<tr>
<td>Rode &amp; Perenin (1994) [statistical analysis]</td>
<td>CVS</td>
<td>Cold (20°C) left ear CVS for 30 s</td>
<td>One session</td>
<td>Eight RBD LN+, six healthy age-matched controls</td>
<td>Between 3 weeks and 4 months post-onset</td>
<td>Before, immediately after</td>
<td></td>
<td>Spatial bias (40 cm line bisection task) during left OKS</td>
<td></td>
</tr>
<tr>
<td>Pizzamiglio et al. (1990) [statistical analysis]</td>
<td>OKS</td>
<td>Horizontal background of luminous dots fixed (baseline condition) or moving leftward vs. rightward at a speed of 50 cm/s</td>
<td>One session</td>
<td>Ten RBD LN+, 10 RBD LN, 10 healthy age-matched controls</td>
<td>Up to several month post-onset</td>
<td>During stimulation</td>
<td>Negative effect on spatial bias (40 cm line bisection task) during right OKS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vallar et al. (1993a) [statistical analysis]</td>
<td>OKS</td>
<td>Vertical background of luminous dots fixed (baseline condition) or moving leftward vs. rightward at a speed of 45° (s⁻¹)</td>
<td>One session</td>
<td>Ten RBD LN+, 10 RBD LN, 10 healthy age-matched controls</td>
<td>Up to several month post-onset</td>
<td>During stimulation</td>
<td>–</td>
<td>Position sense of both arms was improved during left OKS and deteriorated during right OKS</td>
<td></td>
</tr>
<tr>
<td>Bisiach et al. (1996) [statistical analysis]</td>
<td>OKS</td>
<td>Background of alternating yellow and blue vertical stripes fixed (baseline condition) or moving leftward vs. rightward at a speed of 13° (s⁻¹)</td>
<td>One session</td>
<td>Ten RBD left neglect patients, 10 RBD patients without neglect</td>
<td>From one to 93 months post-onset</td>
<td>During stimulation</td>
<td>Right OKS deteriorated performance level in line bisection test. Left OKS deteriorated performance level of task requiring to set both endpoint of the line only the midpoint was shown</td>
<td>Left OKS induced a leftward bias in line bisection test (reducing the rightward bias of RBD LN+)</td>
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<td>Kerkhoff, Keller, Ritter &amp; Manipad (2006) [statistical analysis]</td>
<td>R-OKS</td>
<td>Background of leftward moving dots at a speed of 7.5–50° (s⁻¹) vs. visual scanning training (VST)</td>
<td>Five sessions (8 days)</td>
<td>Five RBD LN+ (R-OKS), five RBD LN+ (VST)</td>
<td>&gt;2 months post-onset</td>
<td>Before and after stimulation</td>
<td>R-OKS induced an improvement in line bisection (perceptual and visuo-motor), digit cancellation, visual size distortion and reading, VST induced an improvement in visuo-motor line bisection only Improvement 2 weeks later</td>
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<td>Kumath et al. (1991) [statistical analysis]</td>
<td>Trunk orientation</td>
<td>Either both head and trunk were centred (baseline condition) or either the head or the trunk was turned 15° to the left vs. to the right (four test conditions)</td>
<td>One session</td>
<td>Four RBD LN patients, 4 LBD patients without neglect, 13 healthy controls</td>
<td>From 20 days to 21 months post-onset</td>
<td>During stimulation</td>
<td>Turning the trunk to the right or turning the head to the right or the left did not affect reaction time of ocular saccades in response to stimuli displayed in the left hemifield Turning the trunk to the left holding the orientation of all others axes constant induced a left deviation on straight ahead pointing task while turning the trunk to the right induced a right deviation in healthy controls</td>
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<td>Chokron &amp; Imbert (1995) [statistical analysis]</td>
<td>Trunk orientation</td>
<td>Either both head and trunk were centred (control group: baseline condition) or the trunk was turned 15° to the left vs. to the right (two exp. groups)</td>
<td>One session</td>
<td>Thirty healthy controls, 1 RBD LN+</td>
<td>During stimulation</td>
<td>Turning the trunk to the left holding the orientation of all others axes constant induced a left deviation on straight ahead pointing task while turning the trunk to the right induced a right deviation in RBD LN+</td>
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<tr>
<td>Taylor &amp; McCluskey (1991) [statistical analysis]</td>
<td>Neck muscles vibration</td>
<td>Vibration (100Hz) of the posterior muscles of the neck (applied below the left occiput just lateral to the spine)</td>
<td>One session</td>
<td>Nine healthy controls</td>
<td>During stimulation</td>
<td>Illusory displacement of a visual target consciously reported, Illusory alteration of head posture (non reported consciously except one participant)</td>
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<td>Study</td>
<td>Condition</td>
<td>Group</td>
<td>Duration</td>
<td>Outcome</td>
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<tr>
<td>Kamath et al. (1993)</td>
<td>Neck muscle vibration (NMV) and TENS</td>
<td>Four RBD LN+</td>
<td>From 3 days to 43 months</td>
<td>No effects for both control groups. For RBD LN+, turning the trunk to the right or vibrating the right posterior neck muscles induced no effects.</td>
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<td>Rossetti et al. (1998)</td>
<td>PA Pointing task for about 3 min during exposure to neutral goggle (control group) or to a rightward vs. leftward 10° optical shift of the visual field (two exp. groups)</td>
<td>Sixteen RBD LN+, healthy controls</td>
<td>Between 3 weeks and 14 months post-onset</td>
<td>No adaptation in the group submitted to the leftward shift of the visual field.</td>
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<td>Colent et al. (2000)</td>
<td>PA Pointing task for about 20 min during exposure to a rightward vs. leftward 15° optical shift of the visual field (two exp. groups)</td>
<td>Fourteen healthy controls</td>
<td>Before (baseline condition), immediately after</td>
<td>Rightward or leftward prismatic adaptation did not show effects on visuomotor bisection task, Rightward prismatic adaptation did not show effects on perceptual bisection task.</td>
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<td>Girardi et al. (2004)</td>
<td>PA Pointing task for about 20 min during exposure to a leftward 15° optical shift of the visual field</td>
<td>Eleven healthy controls (in exp 1), 12 healthy controls (in exp 2)</td>
<td>Before (baseline condition), immediately after</td>
<td>Induction of rightward bias in visual circle centring task, rightward bias in haptic circle centring task, rightward bias in visual proprioceptive pointing task, rightward bias in visual straight-ahead estimation task.</td>
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<td>Frassinetti et al. (2002)</td>
<td>PA Pointing task for about 15 min during exposure to a rightward 10° optical shift of the visual field vs. no treatment (control group)</td>
<td>Thirteen RBD LN+ (seven in exp. group and six in control group)</td>
<td>From 3 to 27 months post-onset</td>
<td>No significant effect on fluff test (find and remove paper pieces attached to their clothes on the left part of their body). No improvement for one patient who showed no adaption effect.</td>
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<td>Rode et al. (2001)</td>
<td>PA Pointing task for about 3 min during exposure to rightward 10° optical shift of the visual field</td>
<td>Two RBD LN+, two healthy controls</td>
<td>One month post-onset</td>
<td>No effects for healthy controls on mental imagery.</td>
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<td>Angelii et al. (2004)</td>
<td>PA Pointing task for about 15 min during exposure to neutral goggle (control group) or to rightward 10° optical shift of the visual field (exp. group)</td>
<td>Thirteen RBD LN+ (eight in exp. group and five in control group)</td>
<td>From 2 to 72 months post-onset</td>
<td>Improvement on: behavioural Inattention Test (Wilson, Cockburn, &amp; Halligan, 1987), bell cancellation, neglect dyslexia. Room description test (name items seen in the room for 2 min) and objects reaching tests (touch and name all the objects on a table for 2 min) Improvement for NL patients on: drawing a daisy from memory, Represenatational neglect: mental evocation of the France map and name as towns as possible in 2 min. Leftward shift in pointing task. Improvement on: neglect dyslexia: decrease of reading errors, Leftward shift of the landing position the first ocular saccade, increase of the ocular fixation time on the left part of words and decrease of the ocular fixation time on the right part of words.</td>
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**Note:**
- **NMV:** neck muscle vibration, **TENS:** transcutaneous electrical neck stimulation.
- **CVS:** caloric vestibular stimulation, **OKS:** optokinetic stimulation, **ROKS:** repetitive optokinetic stimulation, **PA:** prismatic adaptation, **RBD LN+:** right brain-damaged patients with left neglect (LN−: without left neglect), **LBD:** left brain-damaged patients, **exp.:** experiment.
sphere stroke. This CVS regime resulted in a permanent ability to look to the left and thus to compensate for a left homonymous hemianopia.

The first systematic research on the relationship between unilateral spatial neglect and CVS was conducted by Rubens (1985). Rubens, along with others (Chain, Leblanc, Chedru, & Lhermitte, 1979; Hécaen, 1962; Hécaen et al., 1951; Heilman & Valenstein, 1979) noted that, in the acute phase of visual neglect, patients tend to overtly look and turn away from the defective hemispatial field. Based on this observation, Rubens set out to test if USN is due, at least in part, to a [ipsilesional] bias of gaze and postural turning. He reasoned that, if this were so, then CVS could be used to force eye deviation and past-pointing in the direction opposite to the pathologically acquired bias and hence may reduce signs of visual neglect. Rubens tested this hypothesis on 18 patients suffering from left-sided visual neglect during the acute phase (i.e., during the first 2 weeks) following a right-hemisphere stroke. Rubens monitored a number of measures, including the patient’s direction of gaze, their capacity to point to and count people standing around the bed, their ability to read and visually cross lines placed at the patient’s bedside, immediately before, during, and immediately after CVS treatment. Moreover, Rubens systematically tested all the possible treatment conditions of CVS (i.e., caloric stimulation was carried out with 20 ml of warm versus cold water on both sides). The order in which the different conditions were administered was counterbalanced across subjects. Results demonstrated a significant improvement on the part of all patients who had a brisk vestibulo-ocular response in their ability to direct their gaze to the left side of space and in their performance on all tests of neglect. The improvement occurred more quickly and was more intense with left ice water than with right warm water stimulation. Unfortunately, within a 5 min post-stimulation period, gaze direction and signs of neglect returned to pre-stimulation levels. Rubens also noted some other intriguing behavioural changes. In the prestimulation period, all the neglect patients began their visual exploration of space at the extreme right, working from right-to-left, and then stopping at, or short of, the midline. During slow phase nystagmus to the left, 14 of the 17 patients changed direction and proceeded from left-to-right as they carried out the task. Ice water stimulation seemed to produce discomfort in all patients even when the left ear was stimulated, but most patients could not say why they were uncomfortable. Immediately after ice water irrigation, all patients seemed more alert, more attentive than before, and performed more quickly on a line crossing task. Patients also became more aware of what they were doing, checking their performance more often. Only a few patients experienced vertigo, oscilloscopia, or some other types of movement related sensation, even during brisk nystagmus.

A number of more recent studies have also investigated CVS as it relates to left unilateral neglect following right brain-damage. Using 20 and 60 ml of ice water, respectively, applied only to the left ear, Cappa, Sterzi, Vallar, and Bisiach (1987) and Rode et al. (1992), demonstrated that following CVS right brain-damaged patients experienced a significant decrease of anosognosia, somatoparaphrenic delusions, and left-sided personal neglect. These studies were the first to investigate the effects of CVS on long-term neglect related phenomena (e.g., anosognosia) that went beyond contralesional visuo-spatial impairments (Rode et al., 1992).

These effects of CVS on tasks that do not involve visuo-spatial control were confirmed by Geminiani and Bottini (1992) and Rode and Perenin (1994) using tasks that require representational imagery (i.e., creating a mental image of a familiar scene). Earlier studies (see Bartolomeo & Chokron, 2001, and Chokron et al., 2004b for review) had demonstrated that the neglect syndrome also extends to visuo-spatial imagery, such that patients with leftward neglect were unable to verbally report on landmarks that occurred to their left while they visualized themselves walking through a highly familiar area of their hometown. Using a similar task Geminiani and Bottini (1992) and Rode and Perenin (1994) showed that applying ice water to the left ear significantly reduced left neglect on a visuo-spatial imagery task in which subjects had to verbally describe the Piazza del Duomo and the map of France.

In addition, in a series of studies, Vallar and colleagues (Vallar et al., 1990, 1993b; Vallar, Guariglia, & Rusconi, 1997) were able to demonstrate that left somatosensory deficits like hemianesthesia or left tactile extinction following stroke can also be improved by left CVS. Along the same lines, Bisiach, Rusconi, and Vallar (1991), investigated the effects of vestibular stimulation on somatoparaphrenic delusion in a patient suffering from a fronto-temporo-parietal infarction located in the right hemisphere. The authors were able to demonstrate a transitory remission of the patient’s delusional belief that was consistently observed immediately after unilateral vestibular activation obtained by means of cold-water irrigation of the left (contralelional) ear. This positive effect of CVS on somatosensory deficits led the authors to suggest that these deficits may also be manifestations of the neglect syndrome that could also be sensitive to CVS.

Together, studies investigating CVS have provided strong evidence to suggest that this technique represents an effective way to ameliorate, although only transiently, contralesional visuo-spatial deficits that apply to extrapersonal, personal or representational space and also to somatosensory deficits. Interestingly, the positive effects of CVS on somatosensory impairment imply that these deficits may also be, at least in part, attentional (i.e., part of the neglect syndrome) rather than perceptual-motor (i.e., manifestations of primary sensory or motor impairment) in nature. As we will further discuss in the last section, the positive effects of CVS on non-visual manifestations in left neglect patients, such as somatoparaphrenic delusion or somatosensory deficits challenge any explanation restricted to an enlargement of visual orientation to the left hemispace due to the nystagmus.

1 Anosognosia refers to the patient’s lack of awareness of his own deficit. The somatoparaphrenic delusion refers to a misrepresentation of the left half of the body. For example, when asked to point to their left arm with their right hand, left neglect patients commonly answer that their left arm is gone or outside of the examination room. Personal neglect corresponds to neglect behaviour for the left half of the patient’s body or personal space. Patients suffering from left personal neglect usually do not attend (i.e., shave) the left half of their face.
2.3. Neurophysiological correlates of CVS

On the basis of neurophysiological studies, in monkeys and humans, several cortical projection areas for vestibular afferents, that are thought to mediate CVS, have been proposed. A number of studies using monkeys have all implicated the parietal lobe as being the primary projection area of vestibular inputs (Buttner & Buettner, 1978; Ödkvist, Schwarz, Fredrickson, & Hassler, 1974; Schwarz & Fredrickson, 1971). For example, cortical vestibular projections were studied by measuring single cortical neuronal activity (Buttner & Buettner, 1978) and evoked potentials (Fredrickson, Scheid, Figge, & Kornhuber, 1966; Schwarz & Fredrickson, 1971) following electrical stimulation of the vestibular nerve. These studies suggested that a cortical projection from the vestibular nerve is located in area 2 of the parietal lobe. On the other hand, using evoked potentials, Ödkvist and co-workers (1974) found cortical activation of area 3 in the parietal lobe, again following vestibular nerve stimulation. Some monkey studies have also reported a vestibular projection to the retrosinusual cortex (parieto-insular-vestibular cortex: PIVC) (Akbarian, Grusser, & Guldin, 1993) in which the PIVC neurons behave like polymodal vestibular units. It should be noted that the primary vestibular area and the retro-insular cortex have been implicated as playing a critical role in orienting one’s head in space (Akbarian et al., 1993; Fredrickson et al., 1966).

In contrast to the animal studies cited above, Penfield and Jasper (1954) found that electrical stimulation of the superior temporal gyrus in humans evoked a “true” vestibular sensation. Friberg et colleagues in 1985 (Friberg, Olsen, Roland, Paulson, & Lassen, 1985) examined regional cerebral blood flow (Xenon-33 method) in normal human subjects during CVS. In this study, the authors estimated that the location of the primary vestibular cortical area to be a little above and posterior to the auditory cortex within the temporal lobe, but bordering on the parietal lobe. Moreover, the same location was confirmed in all individuals, irrespective of the hemisphere examined.

Using positron emission tomography, (PET), Bottini et al. (1994) measured regional cerebral perfusion in humans with various vestibular stimulation techniques in order to map the central vestibular projections and to investigate the cerebral basis of spatial disorientation. The tempo-parietal cortex, the insula, the putamen, and the anterior cingulate cortex were found to be the cerebral projections of the vestibular system in humans. In addition, by using fMRI during CVS, Suzuki et al. (2001) found that vestibular stimulation increased neural activity in the intraparietal cortex. Notably, vestibular stimulation with cold water in the right ear induced activation of the same anatomical structures activated by cold vestibular stimulation in the left ear, but in the opposite hemisphere. Along those lines, using fMRI during vestibular stimulation in healthy subjects, Dieterich and co-workers (Dieterich et al., 2003) showed an asymmetric pattern of activation across the hemispheres. Cortical activation during CVS seems to be dependent upon three factors: the subject’s handedness, the side of the stimulated ear and the direction of the induced vestibular symptoms. As a matter of fact, these authors demonstrated that activation was stronger in the non-dominant hemisphere, in the hemisphere ipsilateral to the stimulated ear, and in the hemisphere ipsilateral to the fast phase of the vestibulo-caloric nystagmus.

3. Optokinetic stimulation (OKS)

3.1. OKS in normal controls

The vestibular system may be viewed as a sensor of head accelerations that cannot detect motion at constant velocity, and thus requires supplementary visual information (Brandt and Dieterich, 1999). Visual perception of self-motion induced by large-field optokinetic stimulation is thus essential. Vestibular stimuli invariably lead to the sensation of body motion. Stimuli of visual motion, however, can always have two perceptual interpretations: either self-motion or object-motion. The subject who observes moving stimuli may perceive himself as being stationary in space (egocentric motion perception) or the actually moving surroundings as being stable while he is being moved (exocentric motion perception). Visual self-motion can be perceived while gazing at moving clouds or a train moving on the adjacent track in a train station. Vestibular information about motion is elicited only through acceleration or deceleration; it ceases when the cupulae within the semicircular canals or the otoliths have returned to their resting position during constant velocity (see for review, Brandt and Dieterich, 1999). Our perception of self-motion during constant-velocity car motion is completely dependent on optokinetically inducedvection. In natural settings, the vestibulo-oculo reflex (VOR) is functionally and synergistically coupled with the optokinetic response (OKR). This interaction favours gaze stabilisation on visual targets during head–body rotation. As we will describe below, optokinetic stimulation (OKS) induces the VOR which can be used either for clinical purpose, in order to assess vestibulo-propiroceptive functioning or as presented here as an experimental technique.

The technique involves the presentation of a visual moving stimulus (i.e., background moving in a given direction across the screen) which triggers a nystagmus in which the slow phase is coherent with the movement of the triggering stimulus and the quick phase reverts eyes to the initial point of fixation (Howard & Ohmi, 1984). In normal individuals, the function of this reflex is to maintain a constant image of the moving stimulus on the retina as the stimulus moves though external space. In contrast to CVS, OKS evokes a continuous (tonic) signal from the retina rather than a phasic labyrinthine signal. For this reason, OKS effects do not decay after 20–30’s, as is the case with with vestibular reflexes, but can be generated over long periods of time.

3.2. OKS and rehabilitation in RBD patients

The first study to examine the effects of OKS in RBD patients was conducted by Pizzamiglio and co-workers (1990). These authors sought to investigate the possibility of inducing a shift in the spatial coordinates of normal individuals and in brain-
damaged subjects without neglect, as well as, realigning the spatial coordinates of neglect patients (i.e., correcting their spatial bias), by exposing them to OKS. Pizzamiglio and co-workers measured the displacement of the subjective midpoint produced by a moving background while subjects conducted a line bisection task in which they were asked to simply mark the midpoint of a visually presented line. Their results can be summarized as follows. First, OKS entailed a displacement of the subjective midpoint in the same direction as the moving background. This effect was observed for all subject groups for both directions of movement. The presence of a focal brain lesion without neglect did not increase or modify the OKS effect from that observed in normal subjects. In contrast, neglect patients were more susceptible than normal and brain-damaged (without neglect) subjects to the influence of the OKS. Also, in neglect patients, the displacement toward the right side tended to be greater than the displacement toward the left side. Further, these data also showed that those neglect patients who demonstrated greater impairment in space exploration, as assessed by the degree of error in the line bisection task without movement, also were more susceptible to the influence of OKS in displacing their subjective midpoint in either direction.

In the Pizzamiglio study, 13 out of the 33 neglect patients were re-tested after 1 week. Results demonstrated that the effect of OKS on line bisection remained constant in most of the neglect cases. The correlation between the results of the two test sessions was 0.85 for the rightward and 0.64 for the leftward OKS conditions.

In a subsequent series of studies, Pizzamiglio et al. (1990) and Vallar and colleagues (Vallar et al., 1993a; Vallar et al., 1995a), examined the effects of OKS on position sense in right brain-damaged patients with left neglect (RBDN+ patients), right brain-damaged patients without left neglect (RBDN− patients), and left brain-damaged patients without neglect (LBD patients). Results from these studies (Vallar et al., 1993a; Vallar et al., 1995a) showed that OKS did affect the position sense of only the RBDN+ group. Moreover, position sense errors were directional in that movement in the leftward direction improved accuracy, while movement in the rightward direction brought about a major decline in performance. Vallar and co-workers concluded that in patients with neglect, the disorder of position sense is produced at least in part by a shift of the egocentric reference system into the ipsilesional side of space.

Karnath (1996) also examined the effects of OKS on pathological perception of body position in space. Three patients with right hemisphere damage and unilateral neglect were asked to direct a laser pointer to the position which they felt falling exactly “straight ahead of their body’s orientation”. Results demonstrated that without stimulation all three patients localized the sagittal midplane of their bodies markedly to the right of the objective midpoint. However, while undergoing OKS, the subjective horizontal displacement of the sagittal midplane was reduced only when the stimulus moved to the left. Performance worsened with rightward movement.

Although the above cited studies all demonstrate a transient reduction of neglect due to OKS, Bisiach, Pizzamiglio, Nico, and Antonucci (1996) suggested that the effect of OKS may simply reflect a temporary suppression or mitigation of neglect symptoms without restoring the underlying spatial representation of the patients (i.e., restoring the neural circuits involved to a normal functional level). They addressed this question by requiring RBD patients with and without left neglect to execute a modified line bisection task during leftward or rightward OKS. Based on the midpoint of an imaginary line with a specific horizontal length, subjects were required to mark the imaginary line’s endpoints. During rightward movement, left neglect patients most frequently misplaced the end-points leftwards. When the task was executed during leftward OKS, the disproportion increased instead of vanishing. In addition, confirming previous findings (Pizzamiglio et al., 1990), neglect patients were abnormally susceptible to OKS whatever its direction, as compared to patients without neglect.

Based on the positive but transient effects of OKS above-mentioned, Kerkhoff (2001) and Kerkhoff et al. (2006) tested if repetitive OKS (R-OKS) could provide long term positive effects in RBD patients with left unilateral neglect. The authors described a multimodal (visual and auditory) improvement after five sessions of OKS (45 min each) delivered in a period of 2 weeks and this improvement was found to be stable after a 2-weeks follow-up. In the more recent study (Kerkhoff et al., 2006) the improvement after R-OKS was found to be more efficient than conventional visual scanning training using static visual displays.

3.3. Neurophysiological correlates of OKS

A number of studies have investigated the neurophysiological basis of OKS in both monkeys and humans. Using a single cell recording technique, Kawano (Kawano & Sasaki, 1984; Kawano, Sasaki, & Yamashita, 1984) has conducted a series of studies in macaques that have demonstrated that area 7a contains neurons that fire selectively in response to OKS, but not during smooth pursuit eye movements. Further a number of studies in monkey have also demonstrated that visual areas MT and MST in the superior temporal sulcus, which are commonly known to be involved in visual motion processing, show an enhancement of activity for both OKS and smooth pursuit eye movements (Dürsteler & Wurtz, 1988; Komatsu & Wurtz, 1988a, 1988b; Newsome, Wurtz, & Komatsu, 1988). In primates, it has been shown that unilateral lesions of the inferior parietal lobule (IPL) and peristriate cortex produce a significant reduction of the speed of the ipsilesional optokinetic slow phase nystagmus (Lynch & McLaren, 1983). Human studies of OKS have also revealed that parietal lesions, particularly when they extend into white matter regions, impair the slow phase of the optokinetic nystagmus in the ipsilesional direction. The ipsilesional optokinetic nystagmus impairment was associated with normal voluntary and reflex saccades (Baloh, Yee, & Honrubia, 1980). Similarly, Incoccia and colleagues (Incoccia, Doricchi,
Galati, & Pizzamiglio, 1995) found that left neglect patients with right brain damage centred around area 37 and with partial extension of the lesion to areas 19, 39, and the underlying white matter, also suffered an impairment of the optokinetic slow phase nystagmus. In addition to the slow phase component, these patients also demonstrated a reduction in the amplitude and speed of the quick phase component. Together with the animal studies cited above, these human data suggest that parietal damage results primarily in a reduction of the optokinetic slow phase nystagmus which is directed ipsilaterally to the lesion (Lynch & McLaren, 1983).

Using fMRI, Boileau et al. (2002) investigated the overlap of activity between optokinetic stimulation and a task of midline computation. Results confirmed that the right posterior parietal and frontal cortices were involved in both tasks (p < 0.0001). In the same vein, Bense et al. (2006), recently used fMRI to investigate (1) whether stimulus direction-dependent effects can be found, especially in the cortical eye fields, and (2) whether there is a hemispheric dominance of ocular motor areas. In a group of 15 healthy subjects, optokinetic nystagmus in rightward and lefward directions was visually elicited and statistically compared with the control condition (stationary target) and with each other. Direction-dependent differences were not found in the cortical eye fields, but an asymmetry of activation occurred in paramedian visual cortex areas, and there were stronger activations in the hemisphere contralateral to the slow optokinetic nystagmus phase (purdue). Furthermore, and contrasting with the preponderance of left neglect after right hemisphere damage, no hemispheric dominance for optokinetic nystagmus processing was found in right-handed volunteers.

4. Trunk rotation (TR)

4.1. TR in normal controls

Trunk rotation has been proposed as another method by which one’s egocentric reference frame can be displaced in normals or transiently realigned in neglect patients while performing various visuo-spatial tasks (Bradshaw, Nettleton, Pierson, Wilson, & Nathan, 1987; Chokron & Imbert, 1995). The use of trunk rotation for this purpose is based on the notion first proposed by Ventre, Flandrin, and Jeannerod (1984) that external objects in space are represented within the organism in terms of an internal egocentric reference frame that is aligned along the midline or longitudinal axis of the body. It is thought that this egocentric reference frame, superimposed on the mid-sagittal plane, divides the corporeal and extrcorporeal spaces into left and right hemispaces (Jeannerod, 1988; Jeannerod & Biguer, 1987). Chokron and Imbert (1995) and Chokron, Colliot, Atzeni, Bartolomeo, and Ohlmann (2004a)by asking normal subjects to point straight ahead while blindfolded have confirmed that the orientation of the trunk in space divides our normal space into egocentric “left” and “right” and may thus determine the “neglected” contralateral space. In these studies the authors imposed a leftward or rightward trunk rotation while the head remained fixed and found that normal subjects pointed in the orientation of the trunk position, with a relatively good accuracy.

4.2. TR in RBD patients

To evaluate the effects of trunk rotation with respect to displacements in the egocentric reference frame commonly observed in neglect patients, Karnath et al. (1991) manipulated trunk relative to the head positions of right brain-damaged patients with neglect (RBDN+) while studying saccadic reaction times (SRT). Their aim was to examine whether the midline of the trunk and/or head serves as a plane for dividing space into a “right” and “left” sector, and thus forms the basis for the neglected controlateral vs. normal ipsilateral side of neglect patients. This study was conducted among four RBDN+, four left brain-damaged (LBD) patients, and 13 normals. The subject’s trunk and head were either rotated together or the trunk was rotated 15° to the left or right relative to the position of the head. Alternatively, the subject’s head could be deviated 15° left or right relative to the trunk. Results of the study demonstrated that when head, trunk, and visual fields were aligned and corresponded to the middle of the projection screen, SRTs were longer in the left visual field (LVF) compared to right visual field (RVF). However, the LVF deficit could be compensated for by solely turning the trunk of the patients to the left while holding the orientation of the head and visual fields (aligned and corresponding to the middle of the projection screen). In contrast, turning the head to the left side relative to the trunk did not compensate for the LVF deficit. Moreover, LBDs and normal controls did not show the compensatory effects of trunk rotation on SRT. This study demonstrates that in left neglect patients the trunk position in space may determine the boundaries of the neglected field. This confirms that USN may be defined in egocentric coordinates.

5. Transcutaneous mechanical muscle vibration (TMV)

5.1. TMV in normal controls

An organism’s ability to execute coordinated movements requires that ongoing information about muscle length be transmitted to the vestibulo-proprioceptive system. In normals, precise information about muscle length is signaled via the discharge rate of muscle spindle afferents. Moreover, when a muscle or its tendon are made to vibrate, the afferent discharge of the muscle spindle increases. While this increased firing rate is interpreted by the proprioceptive system as a lengthening of the muscle, muscle length actually remains constant. Thus, in normal subjects, transcutaneous mechanical muscle vibration (TMV) produces illusory sensations of the position and shape of body parts (Goodwin, McCloskey, & Matthews, 1972; Lackner & Levine 1979). Moreover, Lackner (1988) was able to show that a visual target attached to a fixed limb also appears to move when the limb muscles are vibrated. Similarly, when left neck muscles are vibrated, normal subjects experience illusions of rightward displacement and movement of visually presented targets (Biguer, Donaldson, Hein, & Jeannerod, 1988; Taylor & McCloskey, 1991). Under such conditions, normal subjects also show a leftward displacement of their subjective midline when asked to stop the displacement of a point in
front of their subjective straight ahead (Karnath et al., 1993). However, Rorden, Karnath, and Driver (2001) demonstrated that this egocentric deviation was not associated to a bias in covert orienting of attention in normal subjects, which argues against explanations of neglect solely in terms of a pathological misperception of body orientation as we will further discuss.

5.2. TMV and rehabilitation in RBD patients

Based on the illusory effects of neck muscle vibration observed in normals (see above), some authors have proposed that this illusional effect may reflect a displacement of one’s egocentric visuo-spatial frame of reference. More specifically, it was hypothesized that similar to the stimulation techniques already discussed, left neck muscle vibration should improve left visuo-spatial neglect in RBD patients displacing the egocentric coordinates leftward. Such a leftward displacement during vibration would run counter to the rightward pathological displacement of these egocentric coordinates following a right hemisphere lesion (Karnath et al., 1993; Vallar et al., 1995b).

Based on the transcutaneous muscle vibration findings (see above), Karnath and co-workers (1991) reasoned that the compensatory effects of deviating the trunk (i.e., 15° to the left) relative to head/eye position on left-sided saccadic reaction times in RBDs with neglect (see above) were due to the fact that turning the trunk under these test conditions led to a lengthening of left posterior neck muscles. Moreover, they reasoned that if this hypothesis is correct, then it should be possible to induce a remission of neglect not only by turning the trunk relative to the head to the contralateral side, but also by vibrating the contralateral posterior neck muscles, since both of these conditions would induce the same afferent signal. Karnath et al. (1993) tested this hypothesis in 3 RBDLN+ patients, 5 LBD patients and 15 non brain-damaged dermatological patients.

The procedure used in this study was the same as the one described above (Karnath et al., 1991), only in addition to trunk orientation, they tested the effect of left and right neck muscle vibration, and compared each experimental condition to three control conditions: baseline (no vibration, no rotation), left hand vibration, and turning the head 15° to the left. Posterior neck muscles were vibrated during a visuo-spatial detection task. In terms of the RBDN+ patients, results demonstrated an improvement in the neglect patients’ performance, both while turning the trunk and vibrating left neck muscle, that seemed independent of the presence of a conscious illusion of movement and displacement of the visual stimuli. Although the compensatory effect of the vibration could be seen in all three patients, only one reported a visual illusion. Curiously, there was no worsening of the deficit in left neglect patients either when the trunk was rotated to the right or when right neck muscles were vibrated. According to these authors, these findings indicate that trunk rotation and neck muscle vibration may act on left neglect signs by manipulating the position of the egocentric reference via proprioceptive inputs.

6. Transcutaneous electrical neural stimulation in RBD patients (TENS)

In the same vein, Vallar et al. (1995b) tested the effect of transcutaneous electrical neural stimulation (TENS) on left neglect signs. This stimulation technique provides a somatosensory input to the vestibulo-proprioceptive system. The main clinical application of TENS has been for pain relief, and suggestions have been made that this effect involves the stimulation of larger myelinated cutaneous afferent fibres (α and β), and local spinal non-opiate mediated mechanism (Tardy-Gervet, Gilhodes, & Roll, 1989). Vallar et al. (1995b) hypothesized that if TENS provides proprioceptive inputs through large diameter afferents, then similar to transcutaneous mechanical vibration, this form of stimulation should positively affect left neglect. Fourteen RBDN+ patients performed a letter cancellation task while applying transcutaneous electrical stimulation to neck muscles. Thirteen patients improved when the left neck muscle was stimulated, even when head movements were prevented by a chin-rest. Conversely, stimulation of the right neck had no positive effect, rather it worsened exploratory performance in nine patients. Moreover, in contrast to the findings of Karnath (1995) using muscle vibration, stimulation of both the left hand and the left neck, had comparable positive effects on visuo-spatial hemineglect.

In a subsequent study, Vallar et al. (1997) tested the effect of TENS on contralesional tactile perception deficits, in 10 RBD patients and 4 LBD patients. Transient somatosensory improvement was noted after stimulating contralesional neck in all RBD patients, both with and without left somatosensory neglect, and in one LBD patient with right somatosensory neglect. In three LBD patients without neglect, the treatment had no detectable effects. In one RBD patient, stimulation of the ipsilesional neck temporarily worsened the somatosensory deficit.

This pattern of positive results is similar to that found in patients with hemineglect by using vestibular and optokinetic stimulations producing a nystagmus with leftward slow phase. Also, the finding that stimulation of the right side of the neck tends to worsen exploratory performance agrees with the results of studies using vestibular and optokinetic stimulations bringing about a nystagmus with a rightward slow phase. Unfortunately, unlike above-mentioned stimulations but like prismatic adaptation, we will not present the neurophysiological correlates of this stimulation which remain unclear.

7. Limb activation in RBD patients

Twenty years ago, Joannee, Brouchn, Gauthier, and Samson (1984, 1986), demonstrated that when using the left hand in manual pointing, left neglect patients exhibited better performance than when using the right hand. Subsequently, Robertson and co-workers (Robertson & North, 1992, 1993; Robertson, North, and Geggie, 1992) also showed that left neglect patients can be ameliorated during active movements of the contralesional limb in the contralesional hemispace. More specifically, the most beneficial effect was obtained when moving left fingers in the left hemispace without any visual feedback. These findings argue
in favour of the close link between visual attention and motor function and confirm Rizzolatti’s premotor theory of neglect. Spatial attention would not be a supramodal function controlling the whole brain but rather a modular function present in several independent circuits. According to this theory and in agreement with Robertson’s findings, activating the premotor circuits of the damaged hemisphere may in some way facilitate the sensory cells connected with them, and hence improve perception in the neglected hemisphere. Many of the stimulations presented here share in common this close link between motricity (gaze, limb activation, visuo-motor adaptation) and attention, for this reason we will further develop this point in the discussion section.

8. Prismatic adaptation (PA)

8.1. PA in normals

It is possible to optically alter the surrounding visual field by asking subjects to wear goggles fitted with wide-field, prismatic lenses creating an optical shift (usually about 10°). Exposure to such an optical alteration of the visual field is known to produce an initial disorganization of visuo-motor behaviour. This disorganisation can be assessed by asking subjects to perform a coordination task, e.g., target pointing. Usually, when people perform this kind of task while wearing prismatic lenses, the pointing error is initially large but quickly declines because of visuo-motor adaptation (Redding & Wallace, 1996). One major compensatory effect of short-term prismatic exposure is a shift of the egocentric reference which can be demonstrated by asking subjects to point straight-ahead in an open loop (Rossetti et al., 1998). Colent, Pisella, Bernieri, Rode, and Rossetti (2000) employed this protocol on 14 normal subjects which were divided in 2 groups in order to test opposite prismatic shifts of visual field on perceptual and visuo-motor bisection tasks. Results indicated a rightward deviation of the subjective middle in visual line bisection following prism adaptation to leftward optical shift. In addition, no bias was produced after rightward prismatic shift adaptation despite explicit measures of after-effects. Given the leftward specificity of visuo-motor adaptation and the perceptual predominance of these effects, the authors concluded that this directional shift mimics the spatial bias observed on left neglect patients. These results were subsequently confirmed by Michel et al. (2003) and prompted Girardi, McIntosh, Michel, Vallar, & Rossetti (2004) to extend this result to spatial haptic judgements. They assessed the subjective centre estimation of haptically explored circles on 11 normal subjects before and after exposure to leftward optical shift of field. Performances indicated rightward deviation suggesting that prismatic adaptation may affect sensori-motor level as well as higher levels of spatial representation. Using a landmark task with normal participants, Berberovic and Mattingley (2003) also confirmed the presence of a rightward bias in peripersonal space following leftward prismatic adaptation and a leftward deviation of the subjective sagittal midline whereas the right shift prismatic adaptation did not produce any deviation of the perceptual estimation of the centre of line. According to the authors, these results suggest that both straight-head pointing and landmark judgments were performed using different frames of reference which would be differentially affected by prismatic treatment. Finally, exploring eye movements during emotional expression judgments, Ferber and Murray (2005) showed that prismatic adaptation produces a bias in the pattern of oculomotor exploration of a scene in healthy participants. This bias occurred toward the right hemisphere without affecting the leftward perceptual bias in judgements about happy/neural chimeric faces. The authors thus assumed that a change in the oculo-motor pattern of exploration can occur in the absence of any change in higher cognitive spatial representations.

8.2. PA in RBD patients

Given that adaptation to a visual distortion can provide an efficient way to stimulate neural structures responsible for the transformation of sensory motor coordinates, the aim of Rossetti et al. (1998) was to investigate the effect of prismatic adaptation on left neglect signs. After exposition to wedge-prisms that shifted the optical field 10° to the right, left neglect patients were improved in a straight ahead pointing task and on classical neuropsychological tests (copying test, line cancellation, line bisection test). Unlike the short-lived remission induced by both CVS and OKS, this improvement lasted for at least 2 h after prisms removal. More recently, it has even been shown that these benefits may persist over a period ranging from 4 days (Pisella, Rode, Farne, Boisson, & Rossetti, 2002) to 5 weeks (Frassinetti, Angeli, Meneghelo, Avanzi, & Ladavas, 2002) which is the longest lasting effect observed among all the experimental stimulations presented here.

A positive feature of this method was large gains compared to the brief period of visuomotor adaptation. For instance, Rossetti et al. (1998) registered immediately after treatment benefits corresponding to about 7° leftward shift in straight head pointing, thus correcting the initial rightward shift. Since this seminal study, an increasingly important amount of research had focused on this visuomotor adaptation procedure regarding its possible implications on neglect recovery and understanding its therapeutic effects. An important consideration was the direction-specific effect of prismatic adaptation: beneficial effects were only observed following adaptations to rightward visual shift and not for leftward ones (Rossetti et al., 1998; Tilikete et al., 2001). In addition, prism exposure had shown regression of neglect signs only when adaptation to lateral deviation of visual field (confirmed by explicit measures of after effects) was obtained. Recently, Vallar, Zilli, Gandola, & Bottini, (2006) tested the effects of prism adaptation on omission errors, on rightward perseveration and on other graphic productions in a line cancellation task in nine right brain-damaged patients with left unilateral spatial neglect. In this study, prism adaptation improved both neglect, as indexed by omission errors, and perseveration behaviour, up to a delay of 60 min.

Effects of prismatic adaptation are not limited to clinical measures of neglect. In a recent study, Tilikete et al. (2001) have shown that improvement extends to postural control, such that the lateral displacement of centre of pressure measured by pos-
On the other hand, Rode, Rossetti, and Boisson (2001) generalized the effects of prism exposure over mental imagery. Two RBD patients with left unilateral neglect were asked to name towns during mental map exploration. Immediately after adaptation treatment, results revealed an increasing number of towns located on the left part of the map, but these effects did not last up to 24 h after prismatic adaptation. In addition, eye movements were not controlled and it was thus impossible to assess the effect of a possible leftward ocular exploration while performing the task. As we will further develop in the discussion section, given the fact that visual parameters such as visual feedback or eye position have been shown to influence the exploration of mental representations (Anderson, 1993; Chokron et al., 2004a; Chokron et al., 2004b), one cannot exclude that the positive effect of PA even in representational tasks is not linked to the compensatory leftward gaze deviation pattern (see Serino et al., 2006 for discussion).

McIntosh, Rossetti, and Milner (2002) assessed non-visual components of neglect in order to address the assumption that higher levels of spatial representations may be affected by adaptation treatment. They reported a single case study of a severe case of left neglect with 9-months chronicity. Results confirmed beneficial effects of treatment across many visuo-spatial tests of neglect, like star cancellation, scene copying and line bisection as well as in haptic spatial judgements. Indeed, when the patient was asked to estimate the centre of a haptically explored circle, a decrease of the rightward lateral deviation was observed 2 h post-treatment. These findings were confirmed and extended by Maravita et al. (2003). These authors have demonstrated a decrease in tactile extinction during bilateral stimulation following a 10-min period of visuomotor adaptation to 20° rightward shift of the visual field. More recently, Angeli, Benassi, and Ladavas (2004) have tested the effect of prismatic adaptation to the ipsilesional oculo-motor bias exhibited by some left neglect patients. The eye movements patterns of eight left neglect patients were recorded during reading. Results indicated a decrease of neglect dyslexia signs, with a reduction of reading errors after prismatic adaptation, as well as a positive effect on oculo-motor patterns during reading. According to the authors, the reduction of the oculo-motor bias observed in left neglect patients may stimulate low-order visuo-motor processes which may, in turn, induce a reorganization of higher-order spatial processes. Along the same lines, Serino and co-workers (2006) recently investigated the positive effects of PA on left neglect signs in conjunction with eye movement analysis. These authors found a significant correlation between leftward oculo-motor deviation produced by PA and recovery of neglect. As a matter of fact, they observed that in left neglect patients, the greater the leftward deviation of the first saccade, the greater the improvement in visuo-spatial tasks. According to Serino et al. (2006), the increase in amplitude of the first leftward saccade obtained after PA produced also a shifting of visual attention towards the left side of the visual field.

However, using the same prismatic exposure procedure with a left neglect patient, Ferber, Danckert, Joannis, Goltz, & Goodale (2003) failed to report any improvement in explicit detection of stimuli located in the contralesional space, despite a dramatic increasing of leftward eye fixations after prismatic adaptation. Although significant improvements were reported in the bells and the letter cancellation tests, this case study revealed the persistence of a rightward perceptual bias in emotional expression judgement of chimerical faces following successful adaptation to visual shift.

The fact that prismatic adaptation does not increase perceptual awareness in the neglected hemisphere favors the hypothesis that visuomotor adaptation may improve selective spatial judgments but probably does not restore the whole spatial representation. The link between gaze direction and neglect remission during all experimental stimulations described in this review will be further addressed in the discussion section.

8.3. Neurophysiological correlates of PA

Luauté et al. (2005) designed a positron emission tomography (PET) study in five neglect patients after a prism exposure period to investigate the neuroanatomical substrate of PA. Results showed a strong implication of the cerebellum probably linked to the realignment of the neuroanatomical substrate of PA. Results showed a strong implication of the cerebellum probably linked to the remission during all experimental stimulations described in this review will be further addressed in the discussion section.

9. Use of multiple stimulation techniques

Based on previous studies showing remission of left neglect symptoms after vestibular, proprioceptive and optokinetic stimulation, Karnath (1994) hypothesized that the afferent information obtained from visual, vestibular and proprioceptive signals are combined and elaborated into an egocentric, body-centred, visuo-spatial frame of reference. To test this hypothesis, Karnath conducted a series of experiments using RBDN+, LBD, and non-brain-damaged control subjects to investigate the effects of both neck muscles proprioception and CVS on the expected shift of the egocentric reference. Normal subjects were asked to actively direct a laser point towards the position of their subjective straight ahead (active visual straight ahead task) while patients had to stop the displacement of a pointer directed by the experimenter in front of their subjective sagittal middle (passive visual straight ahead task). The procedures for the stimulations were the same as in previous studies. For RBDN+ patients, as

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3 The procedures for the stimulations were the same as in previous studies: vibration of posterior neck (100 Hz), and 30 ml of cold water in the left ear during 1 min for the CVS. In the "vibration condition" the testing procedure started as soon as the subject had a clear illusion of target movement. CVS induced a brisk nystagmus in all subjects, with the slow phase towards the left side. The two baseline conditions consisted in no stimulation at all, respectively in the light
The neglect patients’ spontaneous horizontal displacement of sagittal midline to the right could be compensated for by either neck muscles vibration or by left CVS. With both types of stimulation, the subjective body orientation lay close to the objective position and to the judgements observed for the control groups in “baseline” condition, with no additional stimulation. Vibration of the right neck muscles led to a transient worsening of the ipsilesional displacement of subjective body orientation in two out of three neglect patients.

When neck muscle vibration and vestibular stimulation were combined and were simultaneously applied on the left side, the shift of the neglect patients’ subjective body orientation to the left further increased compared with the deviation observed when any of the stimulations was applied in isolation.

Moreover, when the left-sided vestibular stimulation was combined with the vibration of the posterior neck muscles on the right side, the effects neutralized each other. Again, only in the neglect patient who reported no apparent movement of the stationary target when vibrated on the right, left-sided vestibular stimulation had no additional effect on the subjective body orientation. It is likely that there was a displacement of the subjective body orientation to the left as was seen with exclusive left-sided vestibular stimulation.

10. General discussion

The different stimulations presented here have fostered various explanations going from an improvement of ocular movements paralleled by the presence of nystagmus to a restoration of the space representation or a facilitation in orienting spatial attention to the left hemispace.

As we will see, it is difficult both to reconcile any of these hypotheses with what we already know from the body of work on unilateral neglect, and to find an explanation that fits all the reported effects of stimulations. However, we attempt to discuss the different hypotheses that had been proposed (see also Kerkhoff, 2003; Redding and Wallace, 2006; Rossetti and Rode, 2002 for reviews) and propose a new explanation in terms of a restoration of sensori-motor correlations.

10.1. Experimental stimulation as a means to restore space representation in left USN patients

After the seminal study of Rubens (1985), most of the authors testing the effect of experimental stimulations on left USN refer to a particular model of neglect relying on Jeannerod and co-workers’ experimental work (Jeannerod & Biguer, 1987, 1989; Ventre & Faugier-Grimaud, 1986; Ventre et al., 1984).

On the basis of neurophysiological data, Ventre et al. (Ventre & Faugier-Grimaud, 1986; Ventre et al., 1984) hypothesized that a body reference that allows a reconstruction of body position in space with respect to external objects is built as an internal representation of body midline or longitudinal axis. In keeping with Jeannerod and Biguer (1987, 1989) this internal representation of the sagittal axis would be the egocentric reference (ER) segmenting body and space in two halves: a left and a right hemispace. The position of the ER is conceived as an equilibrium position between information arising from both sides of space, that guides actions directed towards those sides. This position is thus assumed to be a result of symmetric activity of associative neural structures. Unilateral lesions of these structures are supposed to produce a permanently asymmetric activity, inducing in turn a displacement of the egocentric coordinates to a new position located in the ipsilesional hemispace, thus provoking contralesional neglect (Fig. 1).

For most of the authors using stimulations in neglect patients, the appropriate stimulation may modify the pattern of sensory input on which the internal representation of the body is constructed. This, in turns, would lead to a temporary displacement of the egocentric representation towards the contralesional side. The stimulation therefore, by running counter to the unbalancing effect of the lesion, restores at least in part the appropriate correspondence with the somatotopic representation (Fig. 2). Patients become then temporarily aware of otherwise neglected stimuli delivered to the affected side. This model implies three distinct assertions. Firstly, it takes for granted the existence of an ipsilesional deviation of the egocentric reference in left USN patients. Secondly, this deviation is seen as the cause of the neglect behaviour. Thirdly, the stimulation is only seen as a means to restore the position of the reference. If some physiological and clinical evidence appears to support these assertions, other experimental findings have not. As we have seen before, the vestibular system is a component part of cerebral circuits including cortical and sub-cortical structures. Its main cortical projections are directed to the parietal cortex (Fredrickson et al., 1966) which in turn has efferent projections to the vestibular nuclei in the brainstem (Ventre & Faugier-Grimaud, 1986). According to these anatomical data, the vestibular system could be involved in maintaining orientation in egocentric space (Karnath & Dieterich, 2006).

In addition, some neurophysiological studies suggest that the cortical projection area of the vestibular system is a posterior-superior temporal region. This area is adjacent to the infero-posterior parietal cortex which is frequently damaged in patients with contralateral hemineglect (Stein, 1989; Vallar & Perani, 1986).

Concerning experimental studies among neglect patients, a constant “directional” error which would fit the hypothesis of an ipsilesional deviation of the egocentric reference has been described by various authors. Heilman et al. (1983) reported in five left neglect patients a large deviation of the subjective straight-ahead to the right ipsilesional hemispace. This was replicated by Karnath (1994) and Karnath et al. (1991) and Chokron and Imbert (1995). Along the same lines Chokron and Bartolomeo (1999) showed that in left brain-damaged patients...
there is a correlation between the position of the egocentric reference and the presence and severity of right neglect signs (Chokron & Bartolomeo, 1999).

But there is also clinical evidence of a significant deviation of the egocentric reference in non-neglect patients suffering from hemianopia (Fuchs, 1920), ataxia (Perenin, 1997), or primary motor deficit (Chokron & Bartolomeo, 1997). Moreover, it was recently shown that unlike left brain-damaged patients, there is no significant correlation between left neglect signs and either the presence or the side of a deviation of the egocentric reference position (Bartolomeo & Chokron, 1999; Chokron & Bartolomeo, 1997). We thus recently concluded that the position of the egocentric reference plays no crucial role in the behavioural consequences of spatial bias induced by right-hemisphere lesions (Bartolomeo & Chokron, 1999; Chokron, 2003). In addition, the fact that left neglect signs may arise in other frames of reference than the egocentric one (Behrmann & Moscovich, 1994; Driver & Halligan, 1991; Reuter-Lorenz, Drain, & Hardy-Morais, 1996; Tipper & Behrmann, 1996) as well as the presence of revisiting behaviour in the right, ipsilesional hemispace (Pisella & Mattingley, 2004) also contradict the egocentric reference hypothesis.

However, a deviation of the egocentric reference may follow the presence of an extensive parietal lesion (Chokron & Bartolomeo, 1999; Hasselbach & Butter, 1997).

If there is no systematic and specific deviation of the position of the egocentric reference in left neglect patients, the positive effect of the above-cited stimulations cannot stem from a restoration of the egocentric frame of reference.

Bisiach et al. (1996) showed that OKS does not restore space representation in neglect. The authors thus proposed that manipulations such as OKS may remove neglect without normalizing the representational medium itself. In the same way, we showed that left-to-right scanning of a to-be-bisected line may induce a pathological leftward deviation of the subjective middle in neglect patients, thus reversing their left neglect behaviour without reducing it (Chokron, Bartolomeo, Perenin, Helft, & Imbert, 1998). Along those lines, given the fact that these stimulations induce a directional bias of either the gaze, the trunk or the left arm towards the left neglected hemispace, one could propose that the positive effects are simply resulting from this motor and proprioceptive orientation towards or in the left hemispace.

10.2. Experimental stimulation as a means to reduce lateral gaze bias and directional hypokinesia in left USN patients

As we have seen before, the first description of a positive effect of a stimulation on left USN was reported by Rubens (1985) using CVS. The temporary remission of extrapersonal neglect signs after left cold or right warm stimulation, led him to hypothesize that most, if not all of the improvement of USN patients was clearly the result of the leftward eye movements permitted by the nystagmus. He thus proposed that this transient remission was mediated quasi-entirely through vestibulo-ocular and vestibulo-spinal mechanisms.

His other proposition was that CVS also acts on directional hypokinesia, the unwillingness to produce arm movements toward the contralesional hemispace (Heilman, Bowers, Coslett, Whelan, & Watson, 1985). According to Heilman et al. (1985, 1983) the cortico-limbic system is implicated in the maintenance of hemispheric arousal and readiness to respond towards the contralateral hemispatial field. The unilateral destruction of this system leads to directional hypokinesia and impaired attention to the contralateral hemispace. In line with this framework, Rubens (1985) proposed that the stimulation of the vestibular system, with its rich connections to the reticular system could have lightened general attention and diminished left-sided hypokinesia. This idea was also defended by Storrie-Baker, Segalowitz, Black, McLean, and Sullivan (1997) who showed that while during caloric stimulation both hemispheres increased in EEG activation, the right hemisphere increase is significantly greater, supporting an activation-arousal hypothesis of neglect (Heilman, Watson, & Valenstein, 1993). According to the subsequent studies that employed CVS in left neglect patients during non-visual tasks, Rubens’ low level explanation can only account for the remission of extrapersonal visual neglect. The positive effects obtained with CVS, OKS, neck muscle vibration and TENS (see above sections), on the remission of both personal, extrapersonal, representational neglect and somatosensory deficits led the respective authors, to propose an interpretation in terms of a higher-level effect of the experimental stimulation used on target position. However, as seen before, the effect of leftward gaze orientation consecutive to the nystagmus may be interpreted not only as a primary low-level effect, but also as a mechanism acting at a higher level of integration, such as the orientation of attention in space. This question was also addressed by Serino, Angeli, Frassinetti, and Ladavas (2006) who recently targeted the mechanisms underlying neglect recovery after prism adaptation. As above-mentioned, during the adaptation process under prism exposure, patients perform pointing movements to a visual target and receive visual feedback concerning the final position of the hand with respect to the target. In the very first trials patients show a rightward deviation when pointing to the visually perceived target. As explained by Serino et al. (2006), a possible strategy to adapt to the prismatic deviation consists in pointing to the side of the target by an amount sufficient to reduce the visual error. As proposed by the authors, since there is evidence that, during pointing, eye movements are yoked to hand movements and vice versa, it is possible to speculate that under prism exposure condition, due to this eye-hand coordination, the leftward deviation of hand movements could induce a leftward deviation of the oculo-motor system. This link is confirmed by the fact that the authors found a positive correlation between the first saccade deviation and the improvement in visuo-spatial tasks obtained at the end of the treatment. Thus after the treatment eye movements remain leftwardly oriented, at variance with the hand movement after effects that are known to vanish after few days (Farnè, Rossetti, Toniolo, & Ladavas, 2002). This dissociation might be explained by the fact that after the removal of the prisms, the leftward deviation of the oculo-motor system could enhance in neglect patients the detection of stimuli presented in the contralesional side of the space. Therefore, as above discussed, it is also possible to speculate that the increase in the amplitude of the first leftward saccade obtained
after PA produces also a shifting of visual attention towards the left side of the visual field, thus mediating the recovery of visual neglect. This hypothesis could also account for the improvement of neglect patients during representational tasks. As a matter of fact, it has been shown that rotating the eyes towards the left may improve the recall of left-sided items suggesting that the direction of eye movements can influence the formation or retrieval from spatial representations (Meador, Loring, Bowers & Heilman, 1987; and see for discussion, Chokron et al., 2004b).

In this way and as pointed by Serino et al. (2006), the positive effect of lateral gaze orientation towards the left hemispace by means of CVS, OKS or PA as well as the interpretation of left effect of lateral gaze orientation towards the left hemispace by Honore´, 1982). In these orientation of attention (Gainotti, 1993, 1996).

However, the general mechanism through which vestibular stimulation acts upon personal and extrapersonal neglect, anosognosia, and hemianesthesia might well consists in a contralesional stimulation which are not accompanied by ocular movements? This can explain the positive effects of the stimulations which induce a nystagmus what about the prismatic adaptation, the trunk rotation, the neck vibration or the transcutaneous electric stimulation which are not accompanied by ocular movements?

One could easily argue that these stimulations all include a sensory or motor stimulation occurring in the left hemispace that could be responsible for a left orientation of attention, similar to the effect of cueing procedures (Riddoch & Humphreys, 1983). While trunk rotation, neck muscle vibration and transcutaneous electric stimulation all comprise an explicit proprioceptive stimulation of the left corporeal hemispace, the prismatic adaptation is designed to force the patient to point leftward to a seen target. As several authors have shown, orienting left neglect patients’ attention to the left by using either visible or invisible cues (Mattingley, Pierson, Bradshaw, Phillips, & Bradshaw, 1993; Riddoch & Humphreys, 1983) as well as spatio-motor cues (Robertson & North, 1992) or using the movement of a background or of a stimulus as a cue (Chokron et al., 1998; Dunai, Bennett, Fotiades, Kritikos, & Castiello, 1999; Kerkhoff, Schindler, Keller, & Marquardt, 1999; Mattingley, Bradshaw, & Bradshaw, 1994) (even in the absence of optokinetic nystagmus) may reduce the amount of left neglect signs. In addition, it was recently demonstrated that rightward prismatic adaptation reduced both the rightward attentional bias and the disengage deficit in patients with right brain damage irrespective of the presence of neglect (Striemer & Danckert, 2007).

The hypothesis that visuo-vestibulo-proprioceptive stimulations act by re-orienting attention towards the leftward neglected hemispace is confirmed, as described below, by the presence of nonspecific positive effects when using these experimental stimulations.

10.4. Nonspecific effects of experimental stimulations

In his seminal paper, Rubens (1985) reported that left neglect patients appeared more ‘alert’ while carrying out tasks during ice-water stimulation. Along the same lines, several authors reported some nonspatial, positive effects of CVS, OKS and PA in brain-damaged patients, raising the question of both the nature and the specificity of these effects. Left cold CVS was thus found to be effective on both left and right hemianesthesia (Vallar et al., 1990; Bottini et al., 2005) and proposed by Ramachandran and McGeech (2007) for the treatment of apotemnophilia because of its positive effects on somatopaforia (Rode et al., 1992). In addition, an effect of vestibular stimulation on dichotic lexical decision performance was found by Schueli, Henn, and Brugger, (1999). These authors reported a shift of right ear advantage (REA) in right-handed men during a dichotic listening task with words and non-words as stimuli, using vestibular stimulation by

Neither Rubens (1985) nor the authors who have replicated and extended his findings have entirely attributed the observed remission of hemineglect to that of an improved capacity to explore visually the contralateral half-space.

Several lines of evidence, concerning both normal and brain-damaged patients, confirm that eye movements may orient the subject’s attention towards the appropriate part of space. This effect was shown in normal subjects in several tasks that are not under visual control: in dichotic listening both verbal (Gopher, 1973) and non-verbal (Larmande, Blanchard, Sintes, Belin, & Autret, 1984; Larmande, Elghozzi, Bigot, Sintes, & Autret, 1983) and in the detection of tactile stimuli (Honore´, 1982). In these experiments, the direction of eye movements towards the part of space stimulated improved both the subject’s performance and the reaction times, confirming the hypothesis of a link between the gaze direction and the spatial allocation of attention. Regarding brain-damaged patients, Larmande and Cambier (1981) showed that in patients with left tactile extinction the incidence of extinction decreased when the gaze was oriented towards the left half space and increased when it was directed to the right. On the other hand, two patients presenting a pathological rightward gaze deviation were submitted to a non verbal dichotic task (Belin, Perrier, Cambier, & Larmande, 1988) where conversely to normal subjects they showed a right ear advantage as if the right gaze deviation had oriented their attention to the right. In the same way, Meador et al. (1987) reported a patient with left neglect whose recall from memory of items located in the left hemispace improved when his head and eyes were physically directed toward the left. From the above-mentioned results, Gainotti (1994) concluded that the direction of eye movements leads to a corresponding spatial orienting of attention towards the corresponding parts of personal and extrapersonal space. If this hypothesis could also account for the improvement of neglect patients during representational tasks. As a matter of fact, Gainotti (1993, 1996) proposed that the facilitation of ocular movements towards the neglected half-space leads to a reduction of neglect and of related phenomena not only because it allows a better visual exploration of the neglected half-space but also because it automatically orients attention towards this space. This hypothesis was subsequently confirmed in various protocols including the Posner paradigms (see for review, Bartolomeo & Chokron, 2002) as well as drawing objects from memory (Chokron et al., 2004b).
using a rotating chair. There was a reliable REA for lexical decision accuracy in the baseline and right-to-left trials but not during left-to-right rotation. In this condition, whereas the performance of the right ear was not affected, there were more correct lexical decisions to left-ear targets. As we have discussed before, the authors interpreted this effect in terms of a leftward attentional shift induced by left-to-right rotation, and put together this effect and what is observed in left neglect patients with cold water in the left ear.

Along the same lines, Kerkhoff (2003), Kerkhoff (2003, 2006) demonstrated that the positive effect of repetitive OKS on left neglect patients was not restricted to the visual modality since both auditory neglect and neglect dyslexia were substantially improved and remained stable after a 2-week follow-up in all cases. These improvements were thus obtained in two different sensory modalities (vision and audition) which underlie the multimodal efficiency of OKS that was already documented with short-term optokinetic stimulation.

Apart from its positive effects on left neglect, PA had also been proved to rehabilitate patients suffering from a various range of deficits. As a matter of fact, RBD patients without left neglect signs were found to benefit from PA regarding their postural imbalance (Tilikete et al., 2001). Moreover, as above-described for CVS and R-OKS, PA was shown to affect performance in other modalities than vision such as haptic perception (Girardi et al., 2004; McIntosh et al., 2002) and audition (Maravita et al., 2003). These multimodal effects have been interpreted by the different authors as an indirect effect of PA on the central level of space representation. However, the fact that PA had been found to decrease visuo-constructive disorders in RBD patients (see Rode, Klos, Courtois-Jacquin, Rossetti, and Pisella, 2006 for review) suggests that PA does not act specifically on the ipsilesional bias characteristic of unilateral neglect but rehabilitates the visual functions more generally attributed to the right cortical hemisphere. More surprising is the recent study of Sumitani et al. (2007) among five patients with complex regional pain syndrome (CRPS). The patients adapted to prism adaptation could be a viable cognitive treatment for CRPS. Perhaps also other CRPS pathologic features, suggesting that prism adaptation realignment would substitute for dysfunctional positioning, but not sizing of a task-work space. This hypothesis is closed to the referential hypothesis of neglect above discussed, but these authors proposed in addition that ‘such amelioration of dysfunctional positioning may enable relearning strategic processes (calibration) perhaps, even partially restoring the ability to appropriately size the task-space’ (see Redding and Wallace, 2006, p. 16). This idea of a ‘recalibration’ of space decreasing neglect signs seems can be connected to the hypothesis of spatial remapping impairments in left neglect. Indeed, Pisella and Mattingley (2004) proposed that manifestations of neglect can be accounted for by spatial remapping impairments due to parietal dysfunction. According to their view, in normal subjects primary visual areas contain retinotopic maps that are renewed and overwritten at each new ocular fixation. These remapping processes are seen to operate in higher-level oculocentric visual maps of the parietal cortex thus ensuring visual integration of the successive retinal images over time and space, and create a constantly updated representation of stimulus locations in terms of distance and direction from the fovea. In left neglect patients, due to the right parietal lesion these processes would be deficient, generating thus deficits that could be interpreted in terms of a spatial remapping impairment within the left visual field following a saccade to a left-side target. According to the authors, proprioceptive information from head and body may influence the remapping mechanisms and in this way, visuo-proprioceptive stimulation such as prismatic adaptation could improve neglect by influencing the gain of the remapping mechanisms. But as the authors underline, information concerning the neural substrates of prismatic adaptation is still lacking to confirm this hypothesis.

Following the idea that sensori-motor contingencies influence visual awareness, O’Regan and Noe (2001) have recently proposed that visual consciousness is not the result of having built a detailed mental representation of the visual environment, but is nothing over and above the mastery of the laws which govern the sensorimotor contingencies associated with visual exploration. For example, our consciousness of the presence of an object on our left would principally result from our capacity to direct a saccade toward that object. There is no need to build a detailed mental representation of the visual environment, because the visual world is already outside there, each detail being immediately available for visual exploration. As a matter of fact, consideration of the neglect behaviour and of its rehabilitation with experimental stimulations bring substantial support

10.5. Experimental stimulation as a means to restore spatial remapping and sensori-motor correlations

Recently, Redding and Wallace (2006) reviewed the positive effects of prismatic adaptation and proposed an alternative hypothesis. Prism adaptation realignment would shift the egocentric coordinates of a sensory-motor reference frame, thereby bringing at least part of the neglected hemisphere into the dysfunctional task-work space. According to these authors, prism adaptation would substitute for dysfunctional positioning, but not sizing of a task-work space. This hypothesis is closed to the referential hypothesis of neglect above discussed, but these authors proposed in addition that ‘such amelioration of dysfunctional positioning may enable relearning strategic processes (calibration) perhaps, even partially restoring the ability to appropriately size the task-space’ (see Redding and Wallace, 2006, p. 16). This idea of a ‘recalibration’ of space decreasing neglect signs seems can be connected to the hypothesis of spatial remapping impairments in left neglect. Indeed, Pisella and Mattingley (2004) proposed that manifestations of neglect can be accounted for by spatial remapping impairments due to parietal dysfunction. According to their view, in normal subjects primary visual areas contain retinotopic maps that are renewed and overwritten at each new ocular fixation. These remapping processes are seen to operate in higher-level oculocentric visual maps of the parietal cortex thus ensuring visual integration of the successive retinal images over time and space, and create a constantly updated representation of stimulus locations in terms of distance and direction from the fovea. In left neglect patients, due to the right parietal lesion these processes would be deficient, generating thus deficits that could be interpreted in terms of a spatial remapping impairment within the left visual field following a saccade to a left-side target. According to the authors, proprioceptive information from head and body may influence the remapping mechanisms and in this way, visuo-proprioceptive stimulation such as prismatic adaptation could improve neglect by influencing the gain of the remapping mechanisms. But as the authors underline, information concerning the neural substrates of prismatic adaptation is still lacking to confirm this hypothesis.
to these notions. Much of the empirical evidence reviewed here suggests that a crucial mechanism leading to reduction of the spatial bias in neglect patients is the sensori-motor component of the experimental stimulation. Moreover, as repeatedly underlined in prismatic adaptation studies, the more the left neglect patients adapt to the prismatic deviation, the greater the improvement (see for discussion, Serino et al., 2006). Thus, in the same vein than O’Regan and Noe hypothesis, the positive effects of the different stimulations above-mentioned might be understood as temporarily restoring patients’ knowledge of sensorimotor contingencies associated with leftward orienting. It has indeed to be noted that all these experimental stimulations are both perceptual and motor in nature, and one could propose that they reduce neglect by providing new sensori-motor contingencies either by the visual or proprioceptive or vestibular disturbance they induce.

Contrary to the hypothesis of Redding and Wallace (2006) which states that a realignment of a sensory-motor reference frame accounts only for the effect of prismatic adaptation, our hypothesis is more about the effect of acquiring new sensori-motor rules in the left neglect hemisphere by adaptation to the perturbation induced by the vestibulo-proprioceptive stimulation, whatever its nature (all stimulations described in the present paper may elicit such effects). The positive effect of these stimulations could be seen as resulting from such ‘sensori-motor’ learning in the left hemisphere and could be interpreted either in terms of a compensation of the existing rightward bias or as an additional leftward bias that counterbalances the existing spatial bias in neglect. Indeed, as suggested by Girardi et al. (2004) on prismatic adaptation, transient modification of sensori-motor contingencies creates a temporary leftward spatial bias which compensates for the massive rightward bias of left neglect patients. Consistent with this hypothesis is the fact that healthy subjects do not show long-lasting effects of PA as compared to left neglect patients. For this reason, the decrease of left neglect signs after experimental stimulations could be interpreted as the result of a pathological, leftward sensori-motor bias created by the new sensori-motor contingencies generated by the vestibulo-proprioceptive stimulation. From a neuromotor perspective, this hypothesis is in accordance with the sensori-motor function of the right parietal cortex which has been extensively described by numerous authors (see for review Andersen et al., 1997; Grefkes and Fink, 2005). According to our hypothesis, if left neglect signs might be reduced by new sensori-motor contingencies, one could propose that unilateral spatial neglect is due to a kind of sensori-motor decorrelation. As proposed by Andersen et al. (1997), the role of the right posterior parietal cortex (PPC) is to perform sensory-motor transformations and an important aspect of this transformation process is to convert spatial information between several coordinates. The PPC thus represents an interface between sensory and motor areas where cognitive functions related to sensory-motor transformations such as attention, intention and selection of targets are performed. In this view, visuo-vestibulo-proprioceptive stimulations by both inducing a sensori-motor conflict and requiring an adaptation to it could give a chance to left neglect patients to recalibrate sensory-motor information in their left hemisphere, by learning a new relationship between perception (especially visual perception and proprioception) and action. Regarding this hypothesis, even if all stimulations described here can promote the acquisition of new sensori-motor rules by adaptation to the perturbation, PA could be the more effective stimulation (with long-lasting effects) because this stimulation requires an active adaptation to the induced deviation compared to other stimulations like CVS, OKS, TMV or TENS which induce a more passive adaptation. In turn, according to O’Regan and Noe (2001) this active adaptation (and, to a lesser extent, passive adaptation) to the imposed distortion could restore spatial awareness of the left hemispace by the way of a recalibration of the left hemispace. According to our present hypothesis, if these stimulations decrease left neglect signs by inducing a re-correlation of sensori-motor information in the left hemispace, one could propose that left neglect behaviour is the consequence of a sensori-motor decorrelation (or loss of sensori-motor rules) in the contralesional hemispace. From a neuromotor point of view, this sensori-motor decorrelation hypothesis of neglect is confirmed by recent studies showing that the disruption of a fronto-parietal network could be the determinant in the severity and recovery of left neglect signs (He et al., 2007; Thiebaut de Schotten et al., 2005).

Some studies using prismatic adaptation in normals (Colent et al., 2000; Michel et al., 2003) have shown some lateralized spatial bias in healthy participants. To confirm our present hypothesis, further experimental studies are needed to investigate the extent to which a lateralized sensori-motor decorrelation is able to induce a ‘neglectlike’ spatial bias in healthy subjects.

10.6. Conclusions and implications for future research

In this review different stimulations that have been reported to transiently reduce left neglect signs were discussed. The mechanisms by the way these stimulations act are still unknown, however the understanding of the processes implicated in their effects may be helpful in defining the levels of impairment in left neglect patients and in designing rehabilitation techniques with lasting positive effects. As pointed out by Kerkhoff and Rossetti (2006) and more recently by He et al. (2007), animal experiments, functional imaging studies and longitudinal outcome studies suggest that injured brains can change their function and connectivity, both on the behavioural and neural level, and both spontaneously (i.e. without intervention) as well as in response to specific treatments. However, many questions in this context still remain open. First of all, it would be interesting to understand what these stimulations share with other techniques that had also been reported to decrease left neglect signs such as cueing procedures (Riddoch & Humphreys, 1983), imposing a left-to-right visual scanning direction (Chokron et al., 1998; Mattingley et al., 1994; Reuter-Lorenz & Posner, 1990), imagery tasks (Smania et al., 1997) reducing the visual guidance (Chokron et al., 2004b; Hjaltason & Tegner, 1992) and using devices that supposedly reduce the ipsilesional colliculus activation (Butter & Kirsch, 1992). There might either be a link between these different effective stimulations or their diversity could simply reflect the heterogeneity of neglect signs (or neglect syndromes?) as dis-
ussed by several authors (Binder, Marshall, Lazar, Benjamin, and Mohr, 1992; Bartolomeo & Chokron, 2001; Chaterjee, 1998; Halligan & Marshall, 1992, 1994; Vallar, 1994). Moreover, as pointed out by Kerkhoff (2003), given the large cortical and subcortical network involved in spatial neglect, the search for multimodally effective treatments is probably a challenge for the future. In the same way, in addition to testing new therapeutic tools, researchers could also design longitudinal studies where long-lasting effects of experimental stimulations, as well as the natural course of the deficits, can be more thoroughly studied. Furthermore, the possibility of the better efficacy of certain treatments during acute stages of neglect versus in the chronic stage of neglect can be explored. Advances in anatomical knowledge are likely to inspire and guide the development of such studies. New neuroimaging techniques, such as diffusion tensor imaging, are now shifting the focus from the prevalent consideration of cortical modules, to that of large-scale brain networks and of their white matter connections (Catani, 2006). The network approach may prove particularly relevant for complex entities such as neglect and attention (Bartolomeo, Thiebaut de Schotten, & Doricchi, 2007; Thiebaut de Schotten et al., 2005). New experimental tools such as TMS will permit to refine this structural knowledge by studying the functional aspects of the explored networks (Fierro, Briginha, and Bisiach, 2006; Rounis, Yarrow, and Rothwell, 2007; Valerio-Cabre, Russimore, and Payne, 2006).

Finally, in order to elucidate how the experimental stimulations reviewed here lead to neglect remission, future research should also include experiments in which in addition to neglect patients, normal subjects are confronted with these stimulations, as well as patients suffering from a peripheral perceptual disorder (caused by a vestibular lesion for example). Therefore, attention should be paid to the brain-damaged patients who do not have any deviation of their subjective straight ahead position, (Chokron & Bartolomeo, 2000; Farne, Ponti, & Ladavas, 1998), patients in whom neglect signs arise in other frames of reference than the egocentric one (Behrmann & Moscovitch, 1998), patients in whom neglect signs arise in other frames of reference (Chokron & Bartolomeo, 2000; Farne, Ponti, & Ladavas, 1998), patients in whom neglect signs arise in other frames of reference such as the natural course of the deficits, can be more thoroughly studied. Furthermore, the possibility of the better efficacy of certain treatments during acute stages of neglect versus in the chronic stage of neglect can be explored. Advances in anatomical knowledge are likely to inspire and guide the development of such studies. New neuroimaging techniques, such as diffusion tensor imaging, are now shifting the focus from the prevalent consideration of cortical modules, to that of large-scale brain networks and of their white matter connections (Catani, 2006). The network approach may prove particularly relevant for complex entities such as neglect and attention (Bartolomeo, Thiebaut de Schotten, & Doricchi, 2007; Thiebaut de Schotten et al., 2005). New experimental tools such as TMS will permit to refine this structural knowledge by studying the functional aspects of the explored networks (Fierro, Briginha, and Bisiach, 2006; Rounis, Yarrow, and Rothwell, 2007; Valerio-Cabre, Russimore, and Payne, 2006).

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References


Neural correlates of primary and reflective consciousness of spatial orienting

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Abstract

Using functional magnetic resonance imaging, we asked participants to perform a visual target detection task with peripheral cues. In the first part of the experiment, cues were not predictive of the side of occurrence of the incoming target. In the second part of the experiment, unbeknownst to the participants, cues became 80\% predictive, thus inducing an endogenous orienting of spatial attention. Confirming previous results, in the second part response times (RTs) decreased for validly cued trials and increased for invalid trials. Half of the participants were subsequently able to correctly describe the cue–target relationships (‘verbalizers’), thus demonstrating reflective consciousness of endogenous orienting. Also non-verbalizer participants showed a similar RT pattern, indicating the occurrence of endogenous orienting without reflective consciousness. Both groups of participants showed fronto-parietal activity typically observed in spatial attention tasks. Verbalizers, in addition, demonstrated stronger activity in the anterior cingulate cortex (ACC), consistent with the proposed role of this structure in purposeful behaviour and in the monitoring of its consequences. The extensive pattern of connectivity of the ACC is ideally suited to integrate the activity of the large neural assemblies necessary for reflective consciousness to emerge.

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Keywords: Spatial attention; Response times; Consciousness

1. Introduction

Changes in brain functioning during cognitive activities may provide hints concerning the neural correlates of consciousness (see Rodriguez et al., 1999). In recent years, this idea has prompted an increasing interest for research on consciousness in cognitive neuroscience. Although it remains unclear how to establish precise causal relationships between brain events and subjective experience (Dalla Barba, 2002), patterns of neural activity which correlate in a lawful manner with the development of a determinate subjective experience can constrain models of consciousness, and may offer insights for developing rehabilitation strategies for brain-damaged patients.

The phenomenological tradition has often distinguished between primary and reflective forms of consciousness (see Bartolomeo & Dalla Barba, 2002; Marcel, 1988; Vermersch, 2000). Primary consciousness refers to the basic condition of being aware of something. This ability is shared by humans and animals with limited semantic capabilities and no true language (Edelman & Tononi, 2000). Humans are also capable of (presumably) higher-order forms of consciousness, which can involve linguistic abilities. In particular, reflective consciousness allows subjects to perceive and describe their own actions and thoughts. This distinction may help explaining apparently bizarre results from experimental psychology, such as the finding that people observing an array of letters for a very short time are well aware of having seen all the letters, but can name only a subset of them (Sperling, 1960). Thus, in Sperling’s words, “at the time of exposure, and for a few tenths of a second thereafter, observers have two or three times as much information available as they can later report” (Sperling, 1960, p. 26). In these cases, the short presentation time may have allowed participants to develop primary, or pre-reflective consciousness of
the letter identities, but may have prevented them from building more reflective forms of consciousness, necessary for accurate verbal report. In the words of Merleau-Ponty (1942), one can “live” forms of perception that one cannot speak about. Take, for example, someone who enters a room and feels an impression of disorder, only to later discover that this impression came from a crooked picture on the wall. Before discovering that, this person’s consciousness was “living things that it could not spell out,” and was thus a form of consciousness not immediately amenable to verbal description (Merleau-Ponty, 1942, p. 187). Also patterns of performance of brain-damaged patients, who may show a selective impairment for either variety of consciousness, may be consistent with the primary/reflective dichotomy (Bartolomeo & Dalla Barba, 2002). For example, patients may be intellectually aware of their deficits, thus showing intact reflective consciousness, but they are often unable to compensate for them in everyday life, when more primary processes are needed. Thus, the celebrated film director FF, who had left unilateral neglect after a right hemisphere stroke, jokingly asked to include his neglect condition in his calling card, but persisted in producing funny drawings lacking their left part (Cantagallo & Della Sala, 1998). In a similar way, despite being anosognosic for his memory impairment, an amnesic patient was nevertheless verbally aware of his incapacity to appreciate his disorder (Dalla Barba, Bartolomeo, Ergis, Boissé, & Bachoud-Lévi, 1999).

Cognitive neuroscientists have often focused on the study of primary consciousness, because reflective consciousness is related to meta-cognitive processes less amenable to an experimental approach (see, e.g., Crick, 1994; Edelman & Tononi, 2000). However, if one accepts participants’ verbal reports as a reliable behavioural correlate of their experiences (Merikle, Smilek, & Eastwood, 2001), then reflective consciousness may also be open to scientific investigation. The present study was aimed at exploring the neural correlates of a recently demonstrated dissociation between primary and reflective consciousness of orienting of spatial attention (Bartolomeo, Decaix, & Siéroff, 2007; Decaix, Siéroff, & Bartolomeo, 2002). Attention can be directed to an object in space either in a relatively automatic way (e.g., when a honking car attracts the attention of a pedestrian), or in a more voluntary mode (e.g., when the pedestrian monitors the traffic light waiting for the ‘go’ signal to appear). These two processes are often referred to as, respectively, exogenous and endogenous orienting (Posner, 1980). Exogenous orienting would be more automatic and unconscious than endogenous orienting, which is usually attributed to voluntary, strategic and conscious processes (Jonides, 1981; Posner & Snyder, 1975). As a consequence, exogenous orienting is often unavailable to verbal report. For example, subjects may be unable to report that their attention was captured by a peripheral visual stimulus, despite response time (RT) evidence that it was (Kettridge, Heywood, & Weiskrantz, 1999; McCormick, 1997).

The voluntary nature of endogenous orienting leads to the prediction that subjects should be able to verbally report its occurrence. However, the Kettridge et al. (1999) study provided evidence that predictive properties of cues can be exploited without subsequent verbal report. In one experiment in that study, peripheral cues were used which predicted target occurrence in a remote location. Their blindsight participant learned to exploit this contingency over a few hundred trials, despite being unable to describe the occurrence of the cues or the contingency. More recently, Decaix, Siéroff, and Bartolomeo (Bartolomeo, Decaix, et al., 2007; Decaix et al., 2002), used cue–target detection tasks (Posner, 1980), in which, unbeknownst to the participants, the predictive character of the cues varied during the course of the experiment. In the first section of the experiment, cues were not predictive of the future target location (50% “valid” trials, with targets appearing in the cued box, and 50% “invalid” trials, with targets occurring in the uncued box). In the second section, cues could be either predictive (80% valid trials) or, in a different experiment, counter-predictive (20% valid trials). Despite the fact that participants were not informed about the cue–target relationships, these influenced their RTs in the direction predicted by the development of endogenous expectations about the likely location of target occurrence. About half of the participants were subsequently able to correctly describe the cue–target relationships, and were labelled as ‘verbalizers’. Surprisingly, however, even the remaining participants, who were unable to produce an accurate verbal report of the task characteristics (‘non-verbalizers’),1 demonstrated similar validity effects, indicating analogous capacities of endogenous orienting. These results were interpreted as showing that pre-reflective forms of consciousness of the cue–target relationships need not give rise to reflective consciousness to exert their effects on performance.

In these experiments, the ability, shown by verbalizer participants, to describe the cue–target relationships was not associated with a dramatic improvement in performance as compared to non-verbalizers. This might suggest that the capacity to verbalize is a purely verbal epiphenomenon of the underlying processes, which could actually be the same in verbalizers and non-verbalizers. On the other hand, despite the lack of behavioural difference, the ability to verbalize might reflect a genuine difference in participants’ subjective experience. Functional neuroimaging seems particularly apt to explore the neural correlates of participants’ performance in this setting, because a single experiment with identical stimuli and procedure is used, and participants are split into two categories after having performed the experiment (see McIntosh, Rajah, & Lobaugh, 1999). The two alternative hypotheses outlined above generate different predictions concerning the neural correlates of participants’ performance. According to the verbal epiphenomenal hypothesis (same underlying processes in the two groups, plus verbal description in verbalizers), only language-related areas of the left hemisphere might be more active in verbalizers than in non-verbalizers. If, on the other hand, the ability to verbalize reflects a specific difference in participants’ subjective experience, then

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1 We prefer these descriptive labels to the less theoretically neutral “aware/unaware”, which would imply a total lack of awareness for participants unable to provide an accurate verbal description. See Bartolomeo, Decaix, et al. (2007) for further discussion.
different brain activation patterns are expected. For example, reflective consciousness might result from a wider broadcast of information through networks of distant brain regions (see Dehaene & Naccache, 2001; Edelman & Tononi, 2000), than is the case for direct consciousness. If so, structures important for integrating distant neural activities, e.g., the pre-frontal regions, might be more active for verbalizer than for non-verbalizer participants.

2. Methods

2.1. Participants

A total of 22 undergraduates from the Aachen University (mean age 25.7 years, S.D. = 4.1 years) took part in the experiments. All were right-handed and reported normal or corrected-to-normal vision. All participants were naive to the purpose of the experiment. They gave informed consent and were paid for participation in the fMRI study. The study was approved by the local Ethics Committee of the University Hospital, Rheinisch-Westfälische Technische Hochschule, Aachen.

2.2. Design and procedure

The task stimuli were presented via a head mounted video optical unit (VisuaStim XGA with eye tracker, Arrington Research Inc.). The virtual image displayed by the unit had a maximum size of 76.2 cm at 1.2 m distance; total field of view was 30°. Stimulus presentation and response collection were controlled by custom-made software. Three black empty square boxes, with each side subtending about 1.15° of visual angle, were displayed on a white background. The boxes were horizontally arranged, the central box being located at the centre of the screen. The central box contained a small black rectangular fixation point (about 0.1°). Distance between boxes was about 3°. Cues consisted of a 300-ms thickening (from 0.4° to 0.8°) of the contour of one box. The target was an asterisk about 5° in diameter, appearing inside one of the lateral boxes, at a retinal eccentricity of about 3.83°.

Each trial began with the appearance of the three placeholder boxes for 1000 ms. Then the cue followed for 300 ms. The target appeared at a variable stimulus-onset asynchrony (SOA; 600, 800 or 1000 ms) from the cue, and remained visible for 100 ms. Multiple SOAs were used, within a range in which endogenous effects are typically observed (Müller & Rabbit, 1989), in order to make the cue–target interval unpredictable and hence prevent participants from responding to the time of occurrence of the target, rather than to the target itself. The different SOAs were used in a pseudorandom order. A total of 900 ms after target offset was allowed for response. After an intertrial interval of 1000 ms, a new trial began. Participants were instructed to maintain fixation on the fixation point. The experiment was stopped whenever three or more violations of the fixation instruction were detected by the eye tracker device. Fixation was trained intensively with each subject off-line; as a consequence, no participant had to be excluded during the experiment. Participants were given a nonmagnetic custom-designed cylindrically shaped response key to respond to the target stimuli with the right hand. The key was held in the closed hand and had to be squeezed for a button press.

There was a total of 12 runs of 12 trials each. Runs were separated by rest intervals of 18.6 s. Following a previously described procedure (Bartolomeo, Decaix, et al., 2007; Decaix et al., 2002), the cues changed their informative content during the course of the experiment, unbeknownst to participants. In the first six runs, targets could appear with equal probability in the cued or in the uncued box, i.e., there were equal numbers of valid and invalid trials. In the last six runs, 80% of trials were valid and the remaining 20% were invalid. Trials within each run were presented in a previously randomized sequence. The same sequence of trials was used for all participants. This fixed order of presentation was inevitable in order to keep possible “awareness” effects, which could only be expected under the 80%-valid condition, equal across all participants.

Immediately before the experimental session, participants were orally given the following instructions: “You are going to see three boxes. Keep your gaze fixed on the central box and press this key every time you see an asterisk appear in one lateral box. Try to be as fast as possible. Before the asterisk appears, the contour of one lateral box will briefly become thicker. Do not pay attention to this occurrence and be sure to respond to the asterisk only”. Soon after completion of the fMRI session, participants were asked to answer a post-experiment questionnaire (inspired by Lambert, Naikar, McLahan, & Aitken, 1999). The questionnaire asked whether participants noticed any cue–target relationship, and, if yes, whether cues predicted most often the target location or the wrong location (see Appendix A for an English translation). Participants were also asked to rate their confidence in their judgment on a scale ranging from 1 (pure guess) to 6 (certainly the correct choice).

2.3. Magnetic resonance imaging

Functional images were acquired using a Philips NT Gyroscan 1.5 Tesla scanner with a standard bird-cage head coil designed for whole-brain volume echo planar imaging (EPI). The participants were rigidly fixated in the head coil using Velcro-straps and foam padding to minimise motion artefacts. Field homogeneity was optimised for each subject before each scan using an automatic shimming sequence. Thirty-four transversal slices were acquired with a susceptibility weighted multishot T2*-weighted gradient echo EPI sequence with a 3100-ms repetition time (TR), a time to echo (TE) of 50 ms and a flip angle (FA) of 90°. Slice thickness was 3.4 mm with no interslice gap. Voxel size was 4 mm × 4 mm × 4 mm. High-resolution proton density fast spin echo images (256 × 256 matrix, 250 mm × 250 mm FOV) were also obtained during the same scanning session to provide anatomical images for co-registration with the functional images. These anatomical scans were acquired with the following parameters: TR = 204 ms; TE = 14 ms; FA = 90°. All anatomical and functional slices were obtained in transaxial planes parallel to the AC-PC line.

Functional runs consisted of 216 images, acquired in 12 alternating rest-activation pairs. In a typical box-car design 6 images were obtained in each rest epoch followed by an activation epoch of 12 images. During rest periods, participants were asked to relax but to maintain fixation (only the central fixation box was presented). The total duration of activation and rest periods was fitted to the TR time (3100 ms), duration being a multiplicator of TR time. Thus, each activation phase lasted 37.2 s, each rest phase 18.6 s. Total time of the experiment was 669.6 s. The order of presentation of trials with different SOAs was pseudorandom. This provided variable TR-time intervals (jittering) across trials.

2.4. Imaging data analysis

The functional magnetic resonance imaging (fMRI) data were analysed using SPM2 software (Wellcome Department of Cognitive Neurology, London, UK) running under the MATLAB environment (Mathworks Inc., Sherborn, MA) (Friston, Frith, Turner, & Frackowiak, 1995; Friston, Holmes, Poline, Price, & Frith, 1996; Friston, Jezzard, & Turner, 1994; Friston et al., 1995; Worsley & Friston, 1995). All functional images were realigned to the first volume, co-registered to the anatomic images and then spatially normalized into a standardized neuroanatomical space (Talairach & Tournoix, 1988) using the MNI (Montreal Neurological Institute, Québec, Canada) template as a reference (Ashburner & Friston, 1999). The images were smoothed using an isotropic Gaussian kernel with a FWHM of 12 mm × 12 mm × 12 mm.

The functional data were analysed using the general linear model implemented in SPM2. Data of the 22 participants were averaged in a group analysis using the random effects model approach (second level analysis; Friston, Holmes, & Worsley, 1999). Statistical parametric maps (SPMs) were obtained and voxels were considered significant if their corresponding linear contrast values (compared to the rest periods) were significant at a level of p < 0.001 (uncorrected, cluster size k = 5 voxels). Additionally, for a comparison of the two subgroups differing with respect to awareness (see Section 3) two-sample t-tests were calculated both for the 80% and for the 80% minus 50% conditions, in order to compare the significant activations of the contrasts mentioned above between these two groups. Finally, a conjunction analysis was done for the 80% condition in order to reveal possible overlaps of activation patterns for the two groups. In order to take into account the lower statistical power of two-sample t-tests, for these analyses an uncorrected p < 0.01 was used.
3. Results

3.1. Behavioural results

The initial runs for each level of cue predictiveness (runs 1 and 7) were considered as practice and discarded from further analysis. The mean RT and S.D. were calculated for each participant, and RTs exceeding the range of 2.5 S.D.s around the participant’s mean were considered as outliers and discarded from further analysis. The trimming procedure resulted in the exclusion of less than 2% of responses. Mean RTs were entered in a repeated-measures analysis of variance (ANOVA), with group (verbalizers, non-verbalizers) as between-participants factor and section (first, 50% valid cues; second, 80% valid cues), cue (valid, invalid) and SOA (600, 800, 1000 ms) as within-participants factors.

Based on the results of the post-experiment questionnaire, participants were divided into two groups, which happened to be of equal size: those who responded correctly to the questionnaire, hereafter the verbalizer group (N = 11), and those who gave inaccurate responses, the non-verbalizer group (N = 11). Specifically, participants were characterized as verbalizers when they correctly described the cue–target relationship in question (2) (see Appendix A), ticked “possibly correct” or more in question (3), and chose the correct alternative in question (4). Question (5) was not taken into account because only few of the verbalizers could correctly classify the time. Interestingly, very similar figures (seven verbalizers and nine non-verbalizers) were obtained in a previous similar experiment, which employed a similar procedure with different participants and fewer trials in section 1 than in section 2 (Bartolomeo, Decaix, et al., 2007; Decaix et al., 2002, Experiment 1). The two groups had exactly the same mean confidence rating, 4.00 (range, 3–6). Thus, no participant rated his or her response as resulting from pure guess.

Behavioural responses were successfully recorded from 17 of 22 participants during fMRI data acquisition (for 4 verbalizers and 1 non-verbalizer some of the recordings were erroneous and thus their behavioural data had to be excluded from analysis; the fMRI results for these participants were, however, used in the fMRI analysis). Table 1 reports the results for the two groups. The effect of group did not reach significance, F(1, 15) = 2.52, p = 0.13. The tendency was toward verbalizers being 41 ms faster than non-verbalizers. Overall, valid trials evoked responses 18 ms slower than invalid trials, F(1, 15) = 7.52, p = 0.02. There was an effect of SOA, F(2, 30) = 26.70, p < 0.001, because RTs tended to speed up with increasing SOAs. Importantly, an interaction between condition and cue validity emerged, F(1, 15) = 20.36, p = 0.0004.

In the section with non-informative, 50% valid cues, RTs were faster for invalid trials (301 ms) than for valid trials (329 ms), consistent with a typical 28-ms inhibition of return (IOR; see Lupiáñez, Klein, & Bartolomeo, 2006; Posner & Cohen, 1984). In the 80% validity section, instead, valid trials evoked similar RTs (321 ms) as invalid trials (312 ms), as if an endogenous facilitation for validly cued targets offset IOR (Lupiáñez et al., 2004). No other effect or interaction reached significance.2

Planned comparisons showed that the section by validity interaction was statistically reliable both for verbalizers, F(1, 15) = 11.68, p = 0.004, and for non-verbalizers, F(1, 15) = 8.69, p = 0.01 (Fig. 1). Thus, participants unable to verbally report about the correct relationships between cues and targets were nevertheless able to employ these relationships to speed up their responses to validly cued targets in section 2. This pattern of results closely replicates the findings of the previous behavioural studies employing a similar paradigm (Bartolomeo, Decaix, et al., 2007; Decaix et al., 2002), and suggests that endogenous orienting processes may be unavailable to reflective consciousness and, consequently, to verbal report. The alternative possibility, namely a decrease of IOR from the first to the second section resulting from practice (see Weaver, Lupiáñez, & Watson, 1998), is highly unlikely, because practice-related reductions of IOR in detection tasks typically only occur after 200 or more trials (Lupiáñez, Weaver, Tipper, & Madrid, 2001). Moreover, this possibility was directly excluded by Bartolomeo, Decaix, et al. (2007, Experiment 2), who found unchanging IOR in an experiment similar to the present one, but with equal proportions of valid and invalid trials in both sections of the experiment.

Despite the similar performance of verbalizers and non-verbalizers on both sections of the experiment, there might be differences in the timing of the use of endogenous strategies in the two groups. For example, verbalizers might have employed the correct strategy earlier in the course of the second section than non-verbalizers. To check for this possibility, we split the data points of each section in an early period and a late period (N = 36 trials each). A further ANOVA was performed with group (verbalizers, non-verbalizers) as between-participants factor and section (first, 50% valid cues; second, 80% valid cues), cue (valid, invalid) and period (early, late) as within-participants factors.3 Once again, the group factor did not interact with any other factors (all Fs < 1), contrary to the timing hypothesis. An unexpected interaction emerged between

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2 In particular, the group x section x validity interaction did not approach significance, F < 1. This suggests that the effect of endogenous attention in Section 2 was not larger in verbalizers than in non-verbalizers.

3 We thank an anonymous reviewer for suggesting this analysis. RTs for the three SOAs were pooled together in order to obtain a sufficient number of data points.
section, period and validity, $F(1, 14) = 7.49, p = 0.02$, because in the early period of the second section there was a small but positive advantage for cued trials, which became a cost in the late period. However, the amount of the small cue validity effect in the early period of the 80% valid section was not larger for verbalizers (4 ms) than it was for non-verbalizers (8 ms).

3.2. Imaging results

Participants tended to show much stronger activations in the first section of the experiment (50% valid condition) compared to the second section (80% valid condition), which rendered any direct comparison between the conditions difficult. This effect could either result from practice decreasing the BOLD signal (Kelly & Garavan, 2005), or from some intrinsic difference between the two conditions. To adjudicate between these possibilities, three additional participants were tested with a similar procedure, except that the order of the sections was reversed; the experiment now started with the 80% valid condition and ended with the 50% condition. The additional participants again demonstrated stronger activation in the first half of the experiment compared to the second one, thus corroborating the practice hypothesis ($p = 0.001$, fixed effects analysis for complex contrasts 50% − 80% versus 80% − 50% across three subjects). The results (Fig. 2) showed an overall stronger activations when the 50% condition was subtracted from the 80% condition (Fig. 2(a)) than for the subtraction the other way round (80% − 50%, Fig. 2(b)).

To investigate the possible differences in brain activation between verbalizers and non-verbalizers, the participants were split according to the answers given to the post-experiment questionnaire, following the method used for the behavioural analysis; a second-level-analysis was done across all participants of each group for the 80% valid condition, which is specifically related to endogenous orienting processes ($p \leq 0.001$).

In order to compare the significant activations of the contrasts mentioned above between the two awareness groups, a two-sample $t$-test was calculated both for the 80% and for the 80% minus 50% conditions. Finally, a conjunction analysis was done for the 80% condition in order to reveal possible overlaps of activation patterns for the two groups. For each of these analyses an uncorrected $p \leq 0.01$ was chosen.

3.2.1. Verbalizers

Verbalizers showed bilateral activation in the inferior parietal lobule and right hemisphere (RH) activation in the superior parietal lobule, as well as activation in the precuneus of the left hemisphere (LH) (Table 2 and Fig. 3(a)). In the frontal cortex, there was mostly RH activation in the precentral and medial frontal cortex and in the rostral part of the anterior cingulate.
gyrus (see Picard & Strick, 1996). Besides a right inferior temporal gyrus and fusiform gyrus activation, there were foci in left subcortical areas (thalamus, putamen and caudate nucleus).

3.2.2. Non-verbalizers

Non-verbalizers revealed parietal activation in the right superior parietal lobule as well as a LH focus in the postcentral gyrus (Table 3, Fig. 3(b)). In the frontal cortex, there were bilateral activations in the superior and middle frontal gyrus, as well as a left cingulate gyrus activation. Furthermore, there was a right middle temporal and fusiform gyrus activation and a focus in the right caudate.

3.2.3. Verbalizers versus non-verbalizers

Two-sample t-tests were conducted to compare the activations of verbalizer and non-verbalizer participants within the different conditions (80% and 80% – 50% conditions). Brain areas showing significant increases of activation are presented below, listing all cortical regions comprising at least five voxels.

3.2.3.1. Verbalizers > non-verbalizers, 80% valid condition.

When compared to non-verbalizers, verbalizers showed stronger activation in the left superior parietal lobule, bilaterally in the rostral anterior cingulate cortex (ACC), middle temporal gyrus and fusiform gyrus, in the left inferior frontal and right precentral gyrus and in the left amygdala (Fig. 3(c), Table 4). The global maximum of the ACC activation was very close to the corpus callosum but the nearest grey matter activation was clearly referred to the ACC. An anatomical view of the right ACC activation is depicted in Fig. 3(f).

3.2.3.2. Non-verbalizers > verbalizers, 80% valid condition.

Non-verbalizers compared to verbalizers revealed stronger

Table 2

<table>
<thead>
<tr>
<th>Brain regions</th>
<th>BA approx.</th>
<th>Side</th>
<th>Cluster size</th>
<th>Talairach coordinates</th>
<th>z-Value</th>
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<td>Parietal cortex</td>
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<tr>
<td>Precuneus</td>
<td>7</td>
<td>L</td>
<td>76</td>
<td>(−28, −44, 46)</td>
<td>4.08</td>
</tr>
<tr>
<td>Inferior parietal lobule</td>
<td>40</td>
<td>L</td>
<td>5</td>
<td>(−55, −33, 31)</td>
<td>2.46</td>
</tr>
<tr>
<td>Inferior parietal lobule</td>
<td>40</td>
<td>R</td>
<td>86</td>
<td>(44, −37, 42)</td>
<td>3.71</td>
</tr>
<tr>
<td>Superior parietal lobule</td>
<td>7</td>
<td>R</td>
<td>12</td>
<td>(24, −67, 59)</td>
<td>3.08</td>
</tr>
<tr>
<td>Frontal cortex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precental gyrus</td>
<td>6</td>
<td>L</td>
<td>197</td>
<td>(−36, 1, 29)</td>
<td>3.75</td>
</tr>
<tr>
<td>Precental gyrus</td>
<td>9, 8, 6</td>
<td>R</td>
<td>180</td>
<td>(40, 13, 36)</td>
<td>3.74</td>
</tr>
<tr>
<td>Medial frontal gyrus</td>
<td>25</td>
<td>R</td>
<td>8</td>
<td>(12, 7, −17)</td>
<td>3.15</td>
</tr>
<tr>
<td>Anterior cingulate</td>
<td>24</td>
<td>R</td>
<td>8</td>
<td>(12, 17, 21)</td>
<td>3.03</td>
</tr>
<tr>
<td>Cingulate gyrus</td>
<td>32</td>
<td>R</td>
<td>5</td>
<td>(12, 21, 36)</td>
<td>2.88</td>
</tr>
<tr>
<td>Temporal cortex</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior temporal gyrus</td>
<td>37</td>
<td>R</td>
<td>41</td>
<td>(55, −55, −4)</td>
<td>3.05</td>
</tr>
<tr>
<td>Occipital cortex</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Fusiform gyrus</td>
<td>37</td>
<td>R</td>
<td>5</td>
<td>(28, −47, −11)</td>
<td>2.72</td>
</tr>
<tr>
<td>Subcortical areas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Ventral thalamus</em></td>
<td>–</td>
<td>L</td>
<td>13</td>
<td>(−16, −11, 12)</td>
<td>3.44</td>
</tr>
<tr>
<td>Lentiform nucleus, putamen</td>
<td>–</td>
<td>L</td>
<td>6</td>
<td>(−28, 4, −7)</td>
<td>2.84</td>
</tr>
<tr>
<td>Caudate, caudate body</td>
<td>–</td>
<td>L</td>
<td>31</td>
<td>(−16, 20, 14)</td>
<td>2.90</td>
</tr>
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</table>
activation only in bilateral inferior frontal gyri (Fig. 3(d), Table 5).

3.2.3.3 Conjunction analysis, verbalizers and non-verbalizers, 80% valid condition. A conjunction analysis was done for the 80% condition in order to reveal possible overlaps of activation patterns for the two groups. There was significant overlap in the right inferior parietal lobule, bilaterally in the middle frontal gyrus, in the right inferior and left superior frontal gyrus and in the right superior temporal gyrus (Fig. 3(e), Table 6).

3.2.3.4 Verbalizers > non-verbalizers, 80% − 50% valid conditions. In these complex contrasts, the 50% valid condition is subtracted from the 80% condition, so that only those activations reach significance that are activated in the 80% and not in
Table 3
Activation foci for non-verbalizers, 80% valid condition ($p \leq 0.001; k \geq 5$)

<table>
<thead>
<tr>
<th>Brain regions</th>
<th>BA approx.</th>
<th>Side</th>
<th>Cluster size</th>
<th>Talairach coordinates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>x</td>
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<tr>
<td>Parietal cortex</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postcentral gyrus</td>
<td>3, 1</td>
<td>L</td>
<td>41</td>
<td>−51</td>
</tr>
<tr>
<td>Superior parietal lobule</td>
<td>7</td>
<td>R</td>
<td>148</td>
<td>32</td>
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<tr>
<td>Frontal cortex</td>
<td></td>
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<tr>
<td>Superior frontal gyrus</td>
<td>6, 8</td>
<td>R</td>
<td>75</td>
<td>8</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>11, 10</td>
<td>R</td>
<td>60</td>
<td>44</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>9, 8, 46, 6</td>
<td>R</td>
<td>217</td>
<td>48</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>6</td>
<td>L</td>
<td>12</td>
<td>−28</td>
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<tr>
<td>Middle frontal gyrus</td>
<td>47, 10</td>
<td>L</td>
<td>11</td>
<td>−48</td>
</tr>
<tr>
<td>Cingulate gyrus</td>
<td>24</td>
<td>L</td>
<td>31</td>
<td>−20</td>
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<tr>
<td>Temporal cortex</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Claustrum</td>
<td>–</td>
<td>R</td>
<td>23</td>
<td>36</td>
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<tr>
<td>Middle temporal gyrus</td>
<td>39</td>
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<td>6</td>
<td>44</td>
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<td>Occipital cortex</td>
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<tr>
<td>Fusiform gyrus</td>
<td>37</td>
<td>R</td>
<td>5</td>
<td>28</td>
</tr>
<tr>
<td>Subcortical areas</td>
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<td></td>
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<tr>
<td>Caudate, caudate tail</td>
<td>–</td>
<td>R</td>
<td>8</td>
<td>36</td>
</tr>
</tbody>
</table>

Table 4
Activation foci for verbalizers > non-verbalizers, 80% valid (two-sample $t$-test, total $n = 22$, $p \leq 0.01; k \geq 5$)

<table>
<thead>
<tr>
<th>Brain regions</th>
<th>BA approx.</th>
<th>Side</th>
<th>Cluster size</th>
<th>Talairach coordinates</th>
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<tr>
<td>Superior parietal lobule</td>
<td>7</td>
<td>L</td>
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<tr>
<td>Frontal cortex</td>
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<td>Anterior cingulate</td>
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<td>R</td>
<td>11</td>
<td>12</td>
</tr>
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<td>Anterior cingulate</td>
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<td>7</td>
<td>−4</td>
</tr>
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<td>Precentral gyrus</td>
<td>4, 6</td>
<td>R</td>
<td>19</td>
<td>55</td>
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<tr>
<td>Inferior frontal gyrus</td>
<td>9</td>
<td>L</td>
<td>11</td>
<td>−40</td>
</tr>
<tr>
<td>Temporal cortex</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle temporal gyrus</td>
<td>19, 20, 39</td>
<td>R</td>
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<td>Middle temporal gyrus</td>
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<td>26</td>
<td>−28</td>
</tr>
<tr>
<td>Middle temporal gyrus</td>
<td>21, 37</td>
<td>L</td>
<td>8</td>
<td>−55</td>
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<tr>
<td>Middle temporal gyrus</td>
<td>39</td>
<td>R</td>
<td>10</td>
<td>48</td>
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<td>Occipital cortex</td>
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<tr>
<td>Fusiform gyrus</td>
<td>20, 36, 37</td>
<td>R</td>
<td>5</td>
<td>44</td>
</tr>
<tr>
<td>Fusiform gyrus</td>
<td>20, 37</td>
<td>R</td>
<td>6</td>
<td>51</td>
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<tr>
<td>Fusiform gyrus</td>
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<td>L</td>
<td>8</td>
<td>−40</td>
</tr>
<tr>
<td>Subcortical areas</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Uncus, amygdala</td>
<td>28</td>
<td>L</td>
<td>7</td>
<td>−20</td>
</tr>
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</table>

Table 5
Activation foci for non-verbalizers > verbalizers, 80% valid (two-sample $t$-test, total $n = 22$, $p \leq 0.01; k \geq 5$)

<table>
<thead>
<tr>
<th>Frontal cortex</th>
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<td>46</td>
<td>R</td>
<td>7</td>
<td>44</td>
</tr>
<tr>
<td>Inferior frontal gyrus</td>
<td>9</td>
<td>R</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Inferior frontal gyrus</td>
<td>13</td>
<td>L</td>
<td>7</td>
<td>−40</td>
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</table>
Table 6
Activation foci for the conjunction analysis verbalizers and non-verbalizers, 80% valid (two-sample t-test, total n = 22, \( p \leq 0.01; |z| \geq 5 \))

<table>
<thead>
<tr>
<th>Brain regions</th>
<th>BA approx.</th>
<th>Side</th>
<th>Cluster size</th>
<th>Talairach coordinates</th>
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</thead>
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<td>Parietal cortex</td>
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</tr>
<tr>
<td>Inferior parietal lobule</td>
<td>40</td>
<td>R</td>
<td>46</td>
<td>44</td>
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<tr>
<td>Frontal cortex</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>6</td>
<td>L</td>
<td>12</td>
<td>−40</td>
</tr>
<tr>
<td>Inferior frontal gyrus</td>
<td>9</td>
<td>R</td>
<td>40</td>
<td>48</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>6</td>
<td>R</td>
<td>7</td>
<td>40</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>6</td>
<td>L</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Temporal cortex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior temporal gyrus</td>
<td>22</td>
<td>R</td>
<td>6</td>
<td>59</td>
</tr>
</tbody>
</table>

The 50% condition. Thus, these contrasts only show the areas specific to the 80% valid condition.

Under this condition, verbalizers compared to non-verbalizers showed a significantly stronger activation in the right rostral section of the anterior cingulate gyrus, the left superior and inferior parietal lobules, the right brain stem and the right fusiform gyrus (\( p = 0.01 \), uncorrected, see Fig. 4(a) and Table 7). An anatomical view of the right ACC activation under the 80% minus 50% condition is presented in Fig. 4(c).

3.2.3.5. Non-verbalizers > verbalizers, 80% – 50% valid conditions. Non-verbalizers compared to verbalizers revealed significantly stronger activations in the right inferior frontal gyrus and in the right inferior parietal lobe but also (if less prominent) in the right middle and superior frontal and in the right inferior temporal gyrus (\( p = 0.01 \), uncorrected, see Fig. 4(b) and Table 8).

4. Discussion

Cue–target RT paradigms are widely used to explore the orienting of spatial attention and its disorders (Posner, 1980). Functional MRI studies using various implementations of these paradigms have demonstrated the activation of large distributed fronto-parietal networks (Corbetta & Shulman, 2002; Nobre, 2001; Rosen et al., 1999). The present study took a different approach, in which a cued detection task was used to explore different forms of awareness of the cue–target relationships, as assessed by a post-experiment questionnaire.
The current behavioural results closely replicate previous findings (Bartolomeo, Decaix, et al., 2007; Decaix et al., 2002), showing that when spatial cues change their informative value during the experiment, and become useful to predict the side of occurrence of the incoming targets, participants are able to adopt strategies of endogenous orienting of spatial attention. Importantly, we replicated the previous finding that endogenous orienting can occur independent of participants’ ability to subsequently describe their strategy. Only half of the participants were able to do so; however, there was no major difference in their RT pattern of results, consisting in an IOR pattern in the 50% valid condition, followed by longer RTs to invalidly cued targets and shorter RTs to validly cued ones in the 80% valid condition. Thus, both in the previous and in the present study, not only could participants who failed to report the changed contingency verbally nevertheless make use of the changed contingency, but their behaviour (as expressed in terms of cue effects on RTs) did not differ from that of the explicitly verbalising participants—they were not less effective than the verbalizers at using the changed contingency. Again consistent with the previous experiments, in the 80% valid condition valid cues did not produce faster RTs than invalid ones because valid peripheral cues, appearing, as they do, in the same location of subsequent targets, induce IOR—in other words a cost in responding to stimuli at a recently attended location (Berlucchi, Chelazzi, & Tassinari, 2000; Lupiáñez et al., 2004). Thus, IOR may cancel the effects of endogenous facilitation on RTs (Berlucchi et al., 2000; Lupiáñez et al., 2004).

The imaging results for the 80% condition (see Fig. 3) replicated the findings of previous neuroimaging studies demonstrating the implication of large fronto-parietal networks in orienting of spatial attention (Corbetta & Shulman, 2002; Nobre, 2001; Rosen et al., 1999) (see also Bartolomeo, Thiebaut de Schotten, & Doricchi, 2007; Doricchi & Tomaiuolo, 2003; Mesulam, 1999; Thiebaut de Schotten et al., 2005, for further supporting evidence from brain-damaged patients). When activity relative to the 50% condition was subtracted out, non-verbalizers compared to verbalizers continued to show fronto-parietal activity, particularly in right inferior frontal and inferior parietal regions (see Fig. 4(b)), corresponding to the ventral fronto-parietal network described by Corbetta and Shulman (2002), as important for responding to unexpected targets. This may suggest that non-verbalizers’ pre-reflective endogenous expectancies concerning the side of occurrence of the target in the 80% valid condition were somewhat less consistent than those developed by verbalizers. Non-verbalizers may have failed to expect the correct location of a larger number of targets as compared to verbalizers, with corresponding more frequent activation of the ventral attentional network.

### Table 7
Activation foci for verbalizers > non-verbalizers, 80% valid minus 50% valid (two-sample t-test, total $n=22$, $p \leq 0.01$; $k \geq 5$)

<table>
<thead>
<tr>
<th>Brain regions</th>
<th>BA approx.</th>
<th>Side</th>
<th>Cluster size</th>
<th>Talairach coordinates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Parietal cortex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior parietal lobule</td>
<td>7</td>
<td>L</td>
<td>10</td>
<td>−32</td>
</tr>
<tr>
<td>Inferior parietal lobule</td>
<td>40</td>
<td>L</td>
<td>5</td>
<td>−55</td>
</tr>
<tr>
<td>Frontal cortex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior cingulate gyrus</td>
<td>32</td>
<td>R</td>
<td>8</td>
<td>20</td>
</tr>
<tr>
<td>Occipital cortex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fusiform gyrus</td>
<td>37</td>
<td>R</td>
<td>5</td>
<td>28</td>
</tr>
<tr>
<td>Subcortical areas</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brainstem</td>
<td></td>
<td>R</td>
<td>7</td>
<td>8</td>
</tr>
</tbody>
</table>

### Table 8
Activation foci for non-verbalizers > verbalizers, 80% valid minus 50% valid (two-sample t-test, total $n=22$, $p = 0.01$; $k \geq 5$)

<table>
<thead>
<tr>
<th>Brain regions</th>
<th>BA approx.</th>
<th>Side</th>
<th>Cluster size</th>
<th>Talairach coordinates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
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<tr>
<td>Parietal cortex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior parietal lobule</td>
<td>39</td>
<td>R</td>
<td>5</td>
<td>55</td>
</tr>
<tr>
<td>Frontal cortex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior frontal gyrus</td>
<td>47</td>
<td>R</td>
<td>8</td>
<td>51</td>
</tr>
<tr>
<td>Middle frontal gyrus</td>
<td>9</td>
<td>R</td>
<td>5</td>
<td>36</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>10</td>
<td>R</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Temporal cortex</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior temporal gyrus</td>
<td>20</td>
<td>R</td>
<td>5</td>
<td>51</td>
</tr>
<tr>
<td>Insula</td>
<td>13</td>
<td>R</td>
<td>9</td>
<td>44</td>
</tr>
</tbody>
</table>
But what are the neural correlates of the ability to verbally report one’s orienting strategy? Verbalizer participants, in comparison with non-verbalizers, showed stronger activations in the anterior cingulate cortex (ACC) and in the superior parietal lobe as well as in the superior part of the brain stem (see Fig. 3(c) and Table 7). The most strict (while most conservative) result is the activation under the 80% − 50% condition, because differences in activations which might arise between verbalizers and non-verbalizers at the beginning of the experiment under the nonpredictive 50% condition are subtracted out. Both the pure 80% and the 80% − 50% condition, however, led to quite comparable results regarding the ACC. Although the coordinates differed slightly (x = 12, y = 17, z = 21 versus x = 20, y = 36, z = 17), the activation foci both lie within the right rostral section of the ACC, as defined by Picard and Strick (1996).4

This result is not consistent with the hypothesis that the ability to verbalize is merely epiphenomenal, which would have predicted activations in language-related areas (although the parietal activations in verbalizers are mainly in the left hemisphere, see Fig. 4(a) and Table 7). It suggests, instead, that verbalizers were able to describe the cue–target relationships because they had actively formulated hypotheses about these relationships during the second half of the experiment. A straightforward interpretation of the ACC activation in verbalizers may rest on the well-known role of this structure in cognitive control. Many studies have addressed the ACC as a centre for anticipation and preparation of attentional activity (LaBerge & Buchsbaum, 1990; Murtha, Chertkow, Beaugerard, Dixon, & Evans, 1996; Paus, 2001) but also for preparation of motor action (for a review and reinterpretation of ACC sections see Picard & Strick, 1996). ACC activity typically correlates with tasks requiring a voluntary action and the monitoring of its consequences (Walton, Devlin, & Rushworth, 2004). In a PET study, Paus, Petrides, Evans, and Meyer (1993) found an activation focus within 15 mm of the focus described here when participants endogenously generated saccades in response to central cues, after reversal of the previously practiced cue–target contingencies (x = 7, y = 27, z = 29 in the reversal minus overpractice subtraction). A nearby focus was activated when participants had to produce saccades away from a visual stimulus (x = 1, y = 10, z = 42 in the antisaccade minus prosaccade subtraction). In these two conditions, participants had to exert an endogenous control over their spatial orienting by actively contrasting automatic tendencies. Also evidence from patients with ACC lesions, who typically show abulia and lack of spontaneous activity (Laplane, Degos, Baulac, & Gray, 1981), is consistent with these proposals. Carter, Botvinick, and Cohen (1999) argued that the ACC is involved in executive processes and that it serves an evaluative function in executive control, rather than a strictly strategic function. A recent fMRI study with the attention network test (Fan, McCandliss, Sommer, Raz, & Posner, 2002) found ACC activation for the executive part of the task (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005).

Many studies revealed an involvement of the ACC in response conflict (e.g., in the Stroop task: Carter, Mintun, & Cohen, 1995; Pardo, Pardo, Janer, & Raichle, 1990; or in verb generation: Barch, Braver, Sabb, & Noll, 2000). Although some of these studies demonstrated right rostral ACC activations, they seemed more medial (x = 2 or 3) than our activations (x = 12 or 20). A similar consideration applies to the medial frontal activations related to erroneous responses (Hester, Foxe, Molholm, Shpaner, & Garavan, 2005, x = 3, y = 40, z = 20; Klein et al., 2007, x = −2, y = 30, z = 27). More importantly, although error awareness might well be considered as a special case of reflective consciousness, in both these studies error-related medial frontal activations were apparently unmodulated by error awareness, being present for both aware and unaware errors. Important methodological differences preclude a direct comparisons between these studies and ours; nevertheless, this discrepancy recommends prudence in interpreting our results merely in terms of error awareness.

More relevant to the present RT task, an important role of the ACC seems to be the modulation of arousal depending on task demands (Mottaghy et al., 2006; Sturm et al., 1999, 2004). In the present experiment, such an up-regulation of arousal seems to be behaviourally reflected by the nonsignificant tendency shown by verbalizer participants to respond faster than non-verbalizers, which was paralleled by an activation of the brain stem as a part of the arousal/alerting system. The role of the ACC in the control of arousal was further underlined by a review of PET studies focusing on this structure (Paus, Koski, Caramanos, & Westbury, 1998). The authors found that task difficulty was strongly correlated with activation peaks especially in the supracallosal part of the ACC, more difficult tasks possibly calling for an increased level of arousal and a higher activation of the brain stem catecholaminergic systems. The ACC cortical region is densely connected to the noradrenergic (Gaspar, Berger, Febvre, Vigny, & Henry, 1989) and cholinergic (Mesulam, Hersh, Mash, & Geula, 1992) subcortical systems involved in the regulation of arousal (see also Sarter, Givens, & Bruno, 2001).

Visual awareness is often considered to correlate with frontoparietal activity (Rees, Kreiman, & Koch, 2002). Stephan et al. (2003) showed enhanced coupling of the right ACC during visuospatial decisions. The present results are not inconsistent with these findings, because all participants were presumably well aware of the occurrence of cues and targets, independent of their capacity to subsequently describe the cue–target contingencies. This is reflected by the fact that both verbalizers and non-verbalizers showed fronto-parietal activation (see conjunction analysis, Table 6 and Fig. 3(e)), but only the verbalizers revealed stronger mostly right rostral ACC activity. One might surmise that ACC activation in verbalizers was a consequence of their being aware of the cue–target relationship, which in turn prompted them to control their behaviour (i.e., to explicitly expect the target at the cued location). According to this view, the right rostral ACC activation would be the neural correlate of this control. Alternatively, the “awareness” of the cue–target relationships could be nothing over and above the

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4 According to other classifications (e.g., Vogt et al., 2003), these ACC foci might have different cytoarchitecture and functions. The level of resolution and statistical power of the present contrasts are probably insufficient to settle the issue.
willed control of action. Monitoring systems might employ the
same neural resources that are responsible for the primary func-
tion that has to be monitored (see Berti et al., 2005). Cognitive
processing is increasingly seen as a set of active processes, rather
than passive representation of information. In particular, con-
sciousness, like locomotion, might be more related to intrinsic
neural activity than to sensory representations (Llinas, Ribary,
Contreras, & Pedrollo, 1998). According to another similar
proposal, experience is something the animal “enacts” as it
explores its environment (see also O’Regan & Noë, 2001; Varela,
Thompson, & Rosch, 1991). If so, the right rostral ACC activa-
tion might constitute the direct neural correlate of participants’
reflective consciousness.

The ACC, with its wide-ranging cortical and subcortical con-
nectivity, seems ideally suited to integrate the activity of different
neural assemblies, situated in brain regions far from one another.
This integration is likely to be a necessary condition for con-
sciousness to emerge (Dehaene & Naccache, 2001; Edelman &
Tononi, 2000). Reflective consciousness, indispensable to accu-
rate verbal report, might require an even broader long-distance
integration than primary consciousness, and may thus well cor-
relate with a comparatively higher activity of ACC, consistent
with the present results.

A crucial question for future research concerns the specific
conditions under which information gains access to the ACC for
wide neural broadcasting and consequent explicit knowledge.
Further questions are related to the potential of communica-
tion between these different forms of consciousness and to the
possibilities to influence it. It could be important, for example,
to render pre-reflective forms of consciousness more explicit,
in order to enhance learning abilities. On the other hand, the
availability of reflective forms of consciousness for use in every-
day life could help rehabilitation of neuropsychological deficits,
of which patients may be reflectively, but not directly aware
(Bartolomeo & Dalla Barba, 2002).

To conclude, we note that research on the cognitive neu-
roscience of consciousness faces peculiar problems (Petitot,
Varela, Pachoud, & Roy, 1999). In extreme synthesis, how can
a (third-person) scientific enterprise tell something about first-
person experience (Nagel, 1974)? According to Owen Flanagan
(2000), the scientific methods can be applied to the study of
consciousness by using converging evidence coming from (1)
experimental psychology, (2) phenomenology (as inferred by
participants’ reports of their experiences) and (3) neuroscience.
We believe that the present study, which combined these three
sources of evidence in the form of manual response times, verbal
reports and fMRI, provides a concrete, if preliminary, example
of such an integrated research approach.

Appendix A. Post-experiment questionnaire

1) During the experiment, you saw the frame of one of the
peripheral squares thicken for a short time. Did you notice
any relationship between thickening of the frame and the
asterisk appearing shortly after that?

Yes–no

2) If yes, please describe this relationship.

3) Please indicate how confident you are about the judgment
you just made by ticking one of the following options.

I believe my judgment was...

1. Just guesswork
2. Mainly guesswork
3. Possibly correct
4. Probably correct
5. Very probably correct
6. Certainly correct

[Displayed on a following page not visible to participants
until the first page was filled in]

4) To make sure we understand correctly your statement on the
preceding page, we have listed three statements about the
experiment below. Please tick the statement you consider to
be correct.

- There was no connection between the frame and asterisk.
- The asterisk appeared most of the time in the square whose
frame had thickened before.
- The asterisk appeared most of the time in the square whose
frame had not thickened before.

5) If there was a relationship, please indicate the time of the
experiment at which this relationship occurred by ticking
one of the following statements.

The relationship occurred:

- at the beginning of the experiment,
- in the middle of the experiment,
- at the end of the experiment.

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