Right-side neglect in Alzheimer's disease

Article abstract—Unilateral neglect—the inability to pay attention to events occurring on one side of space—usually occurs for left-side events after focal right-hemisphere damage. We report a 73-year-old woman with probable AD and no evidence of focal brain lesions who showed signs of right-side neglect and extinction. Neglect was more severe after 1 year. Neuroimaging techniques demonstrated an asymmetry of cortical involvement, with cortical atrophy and hypoperfusion predominant in the left posterior regions. Unilateral neglect should be assessed systematically in AD.

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Unilateral neglect—the failure to orient or respond to contralesional (usually left side) visual stimuli—has only occasionally been studied in AD patients. Freedman and Dexter[1] studied 14 patients with dementia of cortical origin and found signs of neglect in 11 patients. Unexpectedly, half of the patients exhibited a pattern of right-side neglect. Unfortunately, none of the tests used was devised specifically to detect neglect. Using a neglect test battery, D'Erme et al.[2] found visuospatial disturbances lateralized mainly to the left hemispace in three patients with probable AD, with left neglect being a major source of cognitive impairment in one of them. Ishiai et al.[3] described a rightward deviation on line bisection, not accompanied by other left-neglect signs, in a patient with probable AD. In another study[4] of 15 AD patients, seven showed signs of left neglect and two showed signs of right neglect on a visual search task and a cancellation task, but none on line bisection.

We describe a patient with probable AD who showed signs of unilateral neglect for the right hemispace. These signs were consistent throughout several tasks and became more severe at a retest after 1 year.

Case report. A 73-year-old retired secretary with a high school education presented with memory impairment and spatiotemporal disorientation. She experienced difficulty finding her way in unfamiliar places and was often unable

Table *Patient's performance on tests of unilateral neglect during the two testing sessions*

Testing session	Line cancellation		Letter cancellation		Overlapping figures		Line bisection, % deviation*
	Left	Right	Left	Right	Left	Right	
Oct. 1996	30/30	29/30	20/30	10/30	10/10	7/10	+3
Nov. 1997	30/30	26/30	21/30	15/30	6/10	6/10	−9

* Mean percentage deviation of the subjective center (positive values, deviation toward the right side; negative values, deviation toward the left side).

to find the light switch on the wall, especially when it was on the right side. The patient met both the criteria of the National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association and of the Diagnostic and Statistical Manual of Mental Disorders–IV (code 290.0) for the diagnosis of probable AD.

Methods. The patient, who was alert and cooperative, was tested twice, with a 1-year interval between tests. On both occasions, the Mini-Mental State Examination (MMSE), the Wechsler Adult Intelligence Scale (WAIS) digit–symbol test, and a French version of the cognitive portion of the Alzheimer's Disease Assessment Scale (ADAS-cog)[5] were administered.

Visual and tactile extinction were assessed by administering single or double simultaneous stimuli in a fixed, random order.[6]

Tests for unilateral neglect included line and letter cancellation, in which stimuli were scattered on a horizontal A4 sheet; overlapping figure identification,[6] in which the patient had to identify five patterns of overlapping linear drawings of common objects, each pattern including a central object and a pair of objects depicted at each side; a line bisection test that consisted of three 62-mm, three 100-mm, and two 180-mm samples disposed horizontally on a vertical A4 sheet in a fixed, random order at different distances from the left margin of the sheet; and a requirement to copy a linear drawing representing a house and four trees, presented on a horizontal A4 sheet.

Initial assessment. The patient scored 19 on the MMSE, 7 on the WAIS digit–symbol test, and 43 on the ADAS-cog. She extinguished right-side stimuli in both the visual and the tactile modalities. On double simultaneous visual stimulation (18 stimuli for each side), she reported all the stimuli delivered on the left side, but only 10 right-side stimuli (Fisher's exact test, $p < 0.005$). Also on single stimulation (nine stimuli for each side), she failed twice to report right-side stimuli. The patient extinguished two right-side tactile stimuli of 12 double stimuli, but she reported correctly all single stimuli (six for each side).

Signs of right neglect were present on cancellation tests and on overlapping figure identification, but not on line bisection, for which performance was accurate (see the table). When copying the landscape drawing, she omitted the rightmost item (figure 1).

Second assessment. One year later, cognitive impairment had progressed. The patient scored 9 on the MMSE and 48 on the ADAS-cog (in which she left the drawing of the diamond open on the right side). The relative discrepancy of progression between MMSE and ADAS-cog resulted partly from a drop in performance on the MMSE reverse spelling subtest. She was now unable to perform the WAIS digit–symbol test.

The patient extinguished five right-side stimuli of 12 double-visual stimuli ($p < 0.05$) and five right-side stimuli of 18 double-tactile stimuli ($p < 0.05$).

The overlapping figure identification was rendered difficult by the emergence of a concurrent object agnosia, which also impaired performance on the left side. On line bisection she showed a 9% leftward displacement of the subjective center, a result at 2 SDs from age-matched control subjects' performance on the same test.[7] A cumulative laterality score,[7] taking into account overlapping figure identification, line cancellation, and line bisection, deviated by 2 SDs from control subjects' performance on the first assessment and by more than 5 SDs on the second assessment, thus showing an overall worsening of neglect. When copying the landscape drawing, she only drew the leftmost item and the left halves of two other items, omitting completely the items lying on the right half of the sheet (see figure 1).

Neuroimaging studies. At the time of the second neuropsychological assessment, MRI revealed an asymmetric corticosubcortical atrophy, predominant in the left posterior regions. No focal brain lesions were demonstrated. Hexylmethylpropylene amineoxine ^{99}Tc SPECT showed a global reduction of regional cerebral blood flow in the left hemisphere compared with the right, most important in the left temporal and parieto-occipital regions (figure 2).

Discussion. This patient with probable AD showed signs of right unilateral neglect consistent

Figure 1. Copy of the landscape drawing during the first (A) and the second (B) neuropsychological assessment.

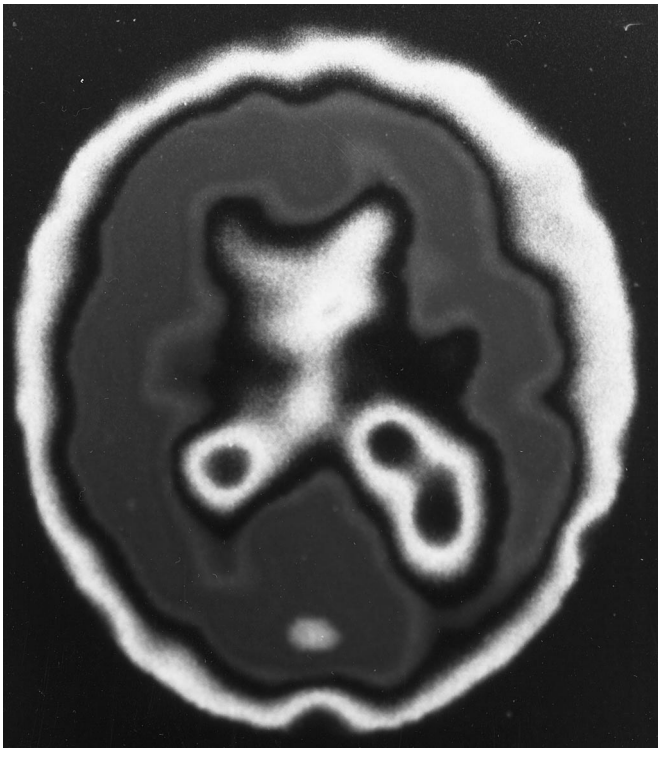

Figure 2. Hexylmethylpropylene amineoxine ^{99}Tc SPECT showing reduced regional cerebral blood flow in the posterior regions of the left hemisphere (right side of figure).

across several visuospatial tests. Signs of cognitive impairment and neglect progressed over time, suggesting a causal relation between AD and neglect.

In groups of patients with unilateral focal brain lesion, left neglect is much more frequent than right neglect. For example, using a neglect battery similar to that employed in the current study, Bartolomeo et al.[7] found signs of contralesional neglect in 17 of 30 right–brain-damaged patients (57%), but only in 2 of 30 left–brain-damaged patients (7%). To account for this asymmetry, the opponent processor model,[8] which posits that each hemisphere shifts attention toward the contralateral hemispace by inhibiting the other hemisphere, argues that in normal subjects there is a tendency for rightward orienting supported by the left hemisphere; right-hemisphere lesions determine left neglect by exaggerating this physiologic bias. Thus, only extensive left-hemisphere lesions in the absence of right-hemisphere lesions should produce right neglect, because only in these conditions can the weaker right-hemisphere processor prevail and shift attention leftward. Alternative views are that the right hemisphere can attend to both hemispaces, whereas the left hemisphere is only concerned with the right hemispace[9,10]; or that the right hemisphere is more involved with automatic, or bottom-up, forms of attentional orienting (which are typically biased in neglect), whereas the left hemisphere is more concerned in volitional, or top-down, orienting.[6] In contrast to the opponent processor model, both these hypotheses predict that right neglect should emerge mainly when extensive left-hemisphere lesions coexist with a (partial) right-hemisphere impairment. In a letter cancellation test, patients with bilateral lesions were more likely to show right neglect than patients with left unilateral lesions.[10] Our current findings—of right neglect in a patient with bilateral brain damage with greater involvement of the left hemisphere—are consistent with this evidence. Signs of right neglect might emerge relatively often in degenerative diseases with this pattern of asymmetric brain atrophy, thus explaining the frequent occurrence of right neglect in studies with demented patients.[1,4]

Our observation joins other reports[2-4] to suggest that unilateral neglect should be assessed systematically in AD. This assessment would contribute to determine more precisely the pattern of cognitive impairment in each patient and to identify patients at risk for spatial disorientation and wandering.

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