

Visual attention impairments in Alzheimer's disease

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Article abstract—*Background:* Impaired attention can hinder information processing at multiple levels and may explain aspects of functional decline in aging and dementia. Impairments of attention in early AD may contribute to performance reductions in other cognitive domains, including memory and executive functions. *Method:* The authors analyzed the scores on a battery of tests of attention and cognitive abilities in 64 older individuals: 42 with mild AD and 22 control subjects without dementia. The authors tested the hypotheses that patients with AD would have impairments of visual attention, and that these impairments would correlate with dysfunction in other key cognitive domains. *Results:* Patients with AD performed significantly worse than control subjects on measures of sustained attention, divided attention, selective attention, and visual processing speed. The differences were not due to differences in age, education, or basic visual function. Strong relationships were identified between reduced attention skills and overall cognitive impairment. *Conclusions:* Deterioration of attention abilities occurs in early stages of AD, and likely contributes to functional decline in these patients. More routine assessment of visual attention deficits could give a more accurate measure of functionally useful perception in patients with AD who show normal visual acuity and visual fields, perhaps providing useful clues to diagnosis and staging. **Key words:** AD—Visual attention—Speed of processing—Visual cortex.

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The human CNS codes, stores, retrieves, modifies, and acts upon information, using attention to allocate limited processing capacity to these tasks. Age-related neurologic diseases disrupt these functions with debilitating effects, as in AD, the most common cause of abnormal cognitive decline in older adults.¹ Failure of memory (coding, storage, and retrieval) is often emphasized as a lapidary defect in early AD.² Yet attention abilities and speed of processing also deteriorate in aging and AD.^{3–5} This can diminish information processed from each glance, shrink the useful field of view,³ and hinder performance of tasks that require visual search (e.g., reading, finding a face in a crowd, or operating a motor vehicle).^{3,6,7} It can also increase risk of injury at work, from falls, or in vehicular crashes.^{8,9} Deficits of attention in early AD may also contribute to performance reductions in other cognitive domains including memory and executive functions,¹⁰ provide information relevant to diagnosis and management of dementia, and even comprise a core feature of AD.¹¹ For these reasons, we analyzed attention and cognitive profiles of 64 older individuals: 42 with mild AD and 22 without dementia. We tested the hypotheses that AD causes impairments of visual attention and that these impairments correlate with the level of dysfunction in other key cognitive domains.

Method. *Subjects.* Forty-two volunteers with AD (mean [SD] age, 71.8 [8.4] years; education, 13.2 [3.2] years) were

recruited from the Alzheimer's Disease Research Center in the Department of Neurology. The diagnosis of probable AD was based on standard National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) Work Group criteria.¹² All participants with AD were living at home, able to attend to personal needs (e.g., feeding and dressing), and most were either still driving or had just quit. The average Clinical Dementia Rating score was 0.68, consistent with mild dementia.

Twenty-two participants without dementia (age, 71.9 ± 6.7 years; education, 14.3 ± 3.0 years) were also studied. This group participated in the same screening protocols as participants with AD. The control subjects were independent, community-dwelling older individuals with no active health problems, and were not recruited from patients who sought evaluation for memory complaints. They were fully oriented, capable of self-care, able to solve everyday problems, maintain home, manage financial affairs, and function at usual levels in customary activities such as shopping, automobile driving, hobbies, and social encounters. These participants did not meet standard criteria for possible AD. The 1.1 year difference in education levels between groups was not significant (Wilcoxon two-sample test).

Each subject was interviewed and examined to assess for neurologic, psychiatric, or ophthalmologic problems. They completed the General Health Questionnaire as well as questionnaires on visual health and alcohol consumption. Alcoholism and depression were exclusion criteria. No subject had diabetes, renal or hepatic disease, significant

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hypertension, macular degeneration, untreated cataract requiring surgery, ocular motor paralysis, congenital amblyopia, or hereditary color blindness. One subject with AD had glaucoma that had been successfully treated, and none had features suggesting a visual variant of AD.

There were no differences (Wilcoxon two-sample test) between participants with AD and participants without dementia in corrected static visual acuity measured using Sloan letters: at near range using a standard Snellen card (20/27.4 [11.8] versus 20/26.6 [8.4]; $p = 0.68$) and at far range using a wall chart (20/27.7 [16.7] versus 20/26.1 [10.3]; $p = 0.91$). Contrast sensitivity as measured using a Pelli Chart was slightly lower for the AD group (1.75 [0.22] versus 1.84 [0.21]; $p = 0.027$).

Of 64 participants, 35 were men (54.7%) and 29 women (45.3%); of 42 with AD, 25 were men (59.5%) and 17 women (40.5%); and of the 22 control subjects, 10 were men (45.5%) and 12 women (54.5%). The relationship between gender and disease among participants was nonsignificant (Fisher's exact test). Informed consent was obtained in accord with institutional guidelines at The University of Iowa.

Cognitive assessment. All subjects participated in a battery of nine standardized neuropsychological tests assessing a range of cognitive functions.¹³ All tests were administered by trained technicians blind to experimental hypotheses. The battery included:

- 1) Temporal Orientation (TO). Identify the current date, day of week, and time of day. Deviation from the correct answer is quantified.
- 2) Wechsler Adult Intelligence Survey-Revised (WAIS-R) Information (INFO). Answer questions from one's fund of general knowledge (e.g., history, geography).
- 3) WAIS-R Digit Span (DIGIT). First, repeat aurally presented digit strings of increasing length, placing demands on immediate memory. In the second part, the digits are repeated in reverse order, placing demands on working memory.
- 4) WAIS-R Block Design (BLOCK). Under a time constraint, analyze a visual display and reproduce a pattern with blocks.
- 5) Complex Figure Test-Copy (CFT). Using paper and pencil, copy a complex geometric figure. This places demands on visuospatial and visuoconstructional abilities.
- 6) Benton Visual Retention Test-Revised (BVRT). View simple geometric figures for 10 seconds, then draw those figures after they are removed from sight. The figures become increasingly complex, placing demands on immediate visual memory and working memory.
- 7) Controlled Oral Word Association (COWA). Generate as many words as possible in a brief period of time in response to a specific letter cue. This places demands on language, memory, executive functions, and speed of processing.
- 8) Facial Recognition Test (FRT). With no time constraints, match complex visual stimuli (black and white images of partially masked unfamiliar faces) in the context of highly similar foils. This places demands on perceptual discrimination ability.
- 9) Trail Making Test (TMT), Parts A and B. Part A: draw a continuous line sequentially connecting the numbers 1 to 25, which are in a random array on a page. Part B: draw a continuous line alternating between numbers

and letters (e.g., 1—A—2—B, etc.). These tasks place demands on visual search, speed of processing, and divided attention.

A composite score was developed to gauge overall cognitive ability. Each of nine tests from the neuropsychological assessment battery (all variables listed in the table, except TMT-A) were rescaled into standard t scores with mean = 50 and SD = 10. These nine standardized scores were then summed into a composite variable called ADSTAT. Lower ADSTAT scores indicated worse cognitive status.

Assessment of visual attention. All subjects completed a set of tasks dependent on visual attention to make simple detection or discrimination responses. These tasks were designed to place minimal demands on higher cognitive functions (e.g., memory, language, and executive functioning).

Useful field of view. Useful field of view (UFOV) was assessed with the Visual Attention Analyzer, Model 2000 (Visual Resources, Inc., Chicago, IL). This microprocessor-based instrument uses three subtests that provide a reliable measure of UFOV size expressed in terms of percent reduction (0% to 90%) of a maximum 35° radius field.⁸ Subtest 1 assesses speed of processing (SP) through identifying the stimulus duration corresponding to the 75% correct identification of a visual target (the silhouette of a car or a truck) presented at fixation. Subtest 2 assesses divided attention (DA) and requires identification of the central target as well as localization of a peripheral target presented simultaneously at three eccentricities (10°, 20°, and 30°). Subtest 3 assesses selective attention (SA) ability and requires these same two responses (also at different stimulus durations); however, the peripheral target is embedded among distractors (triangles). All three subtests are presented on a large video monitor at a viewing distance of 23.5 cm. Targets are presented at high contrast (99%), and subtended 5.1° × 3.2°. For subtest 1, we noted the minimum duration that subjects could perform the task with 75% correct identification. For subtests 2 and 3, the best fitting line reflecting the relationship between eccentricity and localization errors was computed for each test duration. UFOV size was defined as the eccentricity at which a subject could localize the peripheral target 50% of the time. Performance in the subtests was combined to arrive at three scores representing the extent of difficulty with regard to SP, DA, and SA. These scores ranged from 0 (no problem) to 30 (great difficulty). Deficits in each of these abilities have been shown to be additive in their effect on UFOV size.⁸ To summarize UFOV performance, the three scores were combined to yield a score between 0 and 90 that represents percent reduction of a maximum 35° radius field.

Starry Night Task. The Starry Night Task tests a subject's ability to detect transient on and off signals presented to both hemifields.¹⁴ Performance depends on the observer's visual sensory function and ability over time to sustain visual attention across a spatial array.¹⁵ Target events comprise the onset or offset of a small (0.44 mm) white light target presented against a black background at maximal contrast on a 14-inch (diagonal) monitor. The target is embedded among many identical and spatially random distractor elements, creating a display that resembles a starry night. The observer is seated 30 cm from the monitor. To start the procedure, the observer fixates on a

small cross, located in the center of the monitor. A trial begins after the observer indicates that he or she is ready. Each trial consists of 200 consecutive target events. These events occur one at a time, at unpredictable intervals and locations throughout the display. Observers are asked to respond as quickly as possible to these events by pressing a key. This response triggers a computer clock to determine reaction time (RT) and the accuracy of the responses. The Starry Night display contains 1000 elements (stars). The occurrence of on and off events is unpredictable to the observer and is designed to keep the total number of elements in the display within ± 3 elements during each trial. Each trial lasts approximately 5 to 10 minutes, depending on the response pattern of the observer. Any response between 100 and 2000 msec after an event is regarded as a hit. If there is no response within 2000 msec it is regarded as a miss. Any response following a hit or miss in the absence of a new event is a false positive (FP). Any response within 100 msec after an event is also a FP response and was probably initiated prior to the sensory event. Signal detection theory is used to analyze the pattern of responses.¹⁶ The true sensitivity measure (d') provides the most reliable index of observer accuracy, independent of his or her bias to respond. The d' measure assesses the difference between the probability that an observer will report an event given signal-plus-noise (present in the environment and in the nervous system) versus noise alone. The higher the d' measure, the greater the ability to detect signal. d' is derived from the percent correct (hits) and percent FP responses.¹⁶

Relationships between attention and cognition. To test relationships between attention and cognitive deficits, we calculated Spearman correlation coefficients (r_s) between scores on the attention tasks (UFOV and Starry Night scores) and overall cognitive ability indexed by ADSTAT scores, as well as individual scores from the cognitive battery. Receiver-operator characteristic (ROC) curves were calculated to test the ability of attention measures on the UFOV and Starry Night tests to discriminate between participants with and without AD.¹⁷ ROC curves represent the relationship between proportions of hits (i.e., diagnosing AD in individuals who meet NINCDS criteria for probable AD) and FP results (diagnosing AD in those who do not meet criteria for probable AD) for a range of criterion levels. The FP rate, hit rate (sensitivity), specificity ($1 - \text{FP}$) and d' were calculated at each criterion level.

Results. Cognitive assessment. The AD group performed worse than the control subjects on all indices ($p = 0.017$ for DIGIT, $p < 0.001$ for all others) and showed lower group means and greater variability of performance, as anticipated, on a battery of tasks sensitive to cognitive decline in AD. Most scores fell within the range of mild to moderate impairment (table). As expected, the group with AD achieved poorer ADSTAT scores (group mean [SD] 416.3 [61.1] in the AD group versus 507.1 [30.0] in the control group; $p < 0.001$). The difference remained after adjustment for education (using a two-way analysis of variance [ANOVA]; $p < 0.001$).

Assessment of visual attention. Useful field of view. The group with AD showed more than twice the total UFOV loss (UFOVTOT) compared with control subjects (69.9% [22.2%] versus 31.9% loss [9.3%]; $p < 0.001$, Wilcoxon two-sample test). This included worse performance

Table Cognitive test scores

Test variable	Alzheimer group		Control group	
	Median	Mean (SD)	Median	Mean (SD)
TO	-1.5	-17.2 (32.7)	0.0	-0.09 (0.29)
INFO	9.0	8.8 (3.5)	12.0	11.9 (2.2)
COWA	29.5	31.4 (13.0)	42.5	41.5 (9.0)
DIGIT	9.0	8.9 (3.5)	10.0	10.5 (1.9)
CFT	23.0	21.6 (8.9)	32.0	30.7 (3.8)
BVRT	3.0	2.9 (1.8)	7.0	6.5 (1.8)
FRT	39.5	40.2 (6.9)	47.0	47.3 (3.5)
BLOCK	7.0	7.0 (3.5)	12.0	12.3 (2.0)
TMT-A	3.0	4.2 (3.3)	7.0	6.7 (2.9)
TMT-B	1.0	3.3 (3.1)	8.0	8.6 (3.8)

TO = temporal orientation; INFO = Wechsler Adult Intelligence Survey (WAIS-R) Information; COWA = Controlled Oral Word Association; DIGIT = WAIS-R digit span; CFT = complex figure test; BVRT = Benton Visual Retention Test; FRT = facial recognition test; BLOCK = WAIS-R Block Design; TMT = Trail Making Test.

on the SP (17.5 [13.3] versus 1.6 [4.7]), DA (23.1 [9.6] versus 5.0 [6.0]), and SA (29.4 [1.9] versus 25.3 [4.1]) subscores ($p < 0.001$, Wilcoxon two-sample test, all cases).

Starry Night Task. Participants with AD showed lower true sensitivity than control subjects on the Starry Night Task ($d' = 0.53$ [1.62] versus 1.97 [1.20]; $p < 0.001$, Wilcoxon two-sample test). Observers with AD also had longer RT for hits (541.6 [203.6] msec versus 498.0 [113.3] msec), but this was not significant ($p = 0.105$, Wilcoxon two-sample test). AD subjects also tended to make more FP responses (21.8 [28.4] versus 7.0 [10.4]; $p = 0.044$, Wilcoxon two-sample test). Reduced true sensitivity (d') on the Starry Night Task correlated with UFOVTOT ($r_s = -0.58$) ($p < 0.001$).

Given recent case reports of hemispheric asymmetries in attention in AD,¹⁸ we analyzed performance by hemifield. In the group with AD, mean d' in the right and left hemifields were similar (0.59 [1.57] versus 0.63 [1.49]), as in the control group (2.23 [1.08] versus 2.14 [1.25]). In the AD group, mean RTs in the left and right hemifields were also similar (488.9 [210.9] msec versus 494.8 [205.6] msec), resembling the pattern in control subjects (493.8 [112.7] msec versus 484.7 [85.1] msec). These data show no predilection in AD for degeneration in a specific hemisphere, but do exclude asymmetric degeneration in one hemisphere or the other. For this reason we calculated absolute value of the differences in performance between hemifields as a percentage of the overall performance. For RT, the group with AD showed a 13.1% asymmetry, whereas control subjects showed a 7.1% asymmetry. For d' , the AD group showed a 51.4% asymmetry, compared with only 15.5% for control subjects ($p = 0.032$, Wilcoxon two-sample test). Much of the asymmetry in the AD group was due to a single participant, who performed poorly in both hemifields. The mean percentage asymmetry for d' in the AD group dropped to 22.7% when Subject 32 was excluded. No subject showed evidence of hemineglect on clinical assessment or on neuropsychological tests we administered

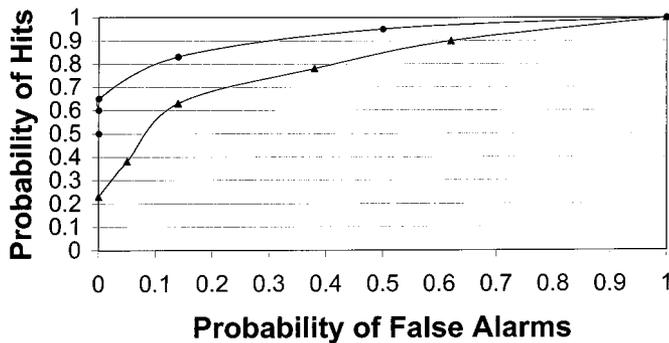


Figure. Prediction of AD diagnosis. Receiver-operator characteristic curves were plotted to test the ability of attention measures to discriminate between research participants with and without AD (see text). ▲ = Starry Night Task; ● = useful field of view.

that can be affected by visual neglect (CFT, FRT, BVRT, BLOCK, TMT-B).

Relationships between attention and cognition. Strong relationships were found between attention scores and overall cognitive ability, compatible with our hypothesis. ADSTAT was strongly correlated with UFOVTOT ($r_s = -0.82$), SP ($r_s = -0.75$), DA ($r_s = -0.76$), and SA ($r_s = -0.61$) (despite a floor effect on the SA variable). Thus, the size of UFOV decreases in conjunction with overall cognitive decline in AD due to reductions in SP, DA, and SA. Similarly, overall cognitive ability was strongly correlated ($r_s = 0.60$) with true sensitivity (d') on the Starry Night Task ($r_s = 0.60$), and moderately correlated with FP results ($r_s = -0.36$).

The low level of correlation between ADSTAT and RT on the Starry Night Task ($r_s = -0.25$; $p = 0.052$) contrasted with the high correlation between ADSTAT and SP from the UFOV task. SP depends on perceptual processing speed independent of motor speed whereas RT on the Starry Night Task depends on motor speed. Relative preservation of motor function in mild to moderate AD could explain the lack of correlation between RT on the Starry Night Task and overall cognitive decline.

Correlation between d' and RT ($r_s = -0.31$) on the Starry Night Task indicates that true accuracy (d') increases as RT decreases ($p = 0.014$). The correlation, albeit significant, was not strong, perhaps because reduced attention resources in AD interfere with control of speed-accuracy trade-off.

The UFOVTOT, SP, and DA results were moderately to strongly correlated with deficits in tasks that place high demands on processing of visual information (CFT, FRT, BVRT, BLOCK, TMT-B; $r_s = -0.63$ to -0.83 ; $p < 0.001$, all cases). SA was correlated with deficits in the same tasks ($r_s = -0.46$ to -0.66 ; $p < 0.001$) as was impairment of d' on the Starry Night Task ($r_s = 0.43$ to 0.60 ; $p < 0.001$).

Receiver-operator characteristic curves were plotted to test the ability of attention measures to discriminate between research participants with and without AD for a range of criterion levels. The levels tested for UFOVTOT and the Starry Night Task (the true sensitivity measure) included the mean and values 0.5 SD and 1 SD above and below the mean to provide five criterion levels for each variable (figure). The best balance between sensitivity and

specificity (0.83, 0.86) for discriminating between mild and no dementia was found for UFOVTOT of 43.4 (mean -0.5 SD). The d' value for each variable (true sensitivity for discriminating AD versus no AD calculated using signal detection theory) was 2.03 for UFOVTOT and 1.23 for the Starry Night Task.

Recall that contrast sensitivity was slightly lower in the AD group. After adjusting for contrast sensitivity by using a multiple logistic regression model, UFOVTOT ($p = 0.001$) and the Starry Night Task d' ($p = 0.015$) were still predictive of AD status.

Discussion. We found that mild AD was characterized by impairments of visual attention and processing speed, in line with our hypothesis. Several aspects of attention were affected, including DA and SA as measured on the UFOV task, and sustained attention as measured on the Starry Night Task. Performance on these tasks depends upon automatic processes (fast or parallel, involuntary and unavailable to introspection) and controlled processes (slow or serial, deliberate and capacity demanding).¹⁹ Disturbance of these basic mechanisms of attention may affect performance in other cognitive domains. Indeed, we find that reduced attention skills in AD strongly correlate with specific cognitive deficits (e.g., memory, decision making, higher visual functions) and with overall cognitive ability. We cannot exclude the possibility that decreased cognitive ability may contribute to reduced performance on attention tests. However, the nonvisual attentive cognitive demands of these tasks are minimal, and participants with AD performed similarly to normal subjects on tests of basic visual function with comparable demands on language and memory. Also, attention measures still predicted AD status after corrections for small differences in contrast sensitivity.

James²⁰ explained that attention is “taking possession by the mind, in clear and vivid form, one out of what seem several simultaneously possible objects or trains of thought. Focalization, concentration, of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others . . .” Degeneration of such mechanisms can have wide-ranging effects on cognitive functions (or “psychical” functions, as Ricksher and Jung²¹ inferred in 11 “senile dementia” cases). Aspects of attention at risk for decline in AD include orienting (disengaging, moving or shifting, and engaging attention),²² focusing (selecting critical information from a broader field for further processing), and sustaining (related to vigilance).²³ These aspects of attention affect all manner of basic tasks from visual search to object recognition to working memory.²⁴ Effects of brain injury on these diverse factors of attention can be interpreted within three broad categories: 1) arousal or alertness and sustained attention; 2) selective attention (the ability to set priorities to make use of limited sensory capacity); and 3) energetic aspects of attention, including ef-

fort, resource allocation (as in divided attention tasks), and SP.²⁵

Slowed SP can hinder information processing at multiple levels and help account for some aspects of cognitive decline with advancing age.²⁶ These effects increase with task complexity²⁶ and are probably amplified in AD. In this study, slowed processing speed was evident in the poorer performance of the AD group on the time-dependent aspects of the UFOV task. Strong relationships were found between these variables and overall cognitive ability.

Orienting of attention has been assessed by asking subjects to respond to visual targets under the influence of predictive cues.⁴ The cost of misleading cues, interpreted in a serial processing scheme, depends on ability to disengage, move, and engage the focus or “spotlight” of attention between miscued and proper locations.²² This cost in AD is high, indicating defective orienting of attention⁴ due to changes in a “posterior attention system”²⁵ that also affects eye⁷ and limb control.²⁷ In this study, impairments of orienting of attention probably contributed to defects on subtests 2 and 3 of the UFOV tasks, in which participants had to orient to peripheral targets presented at unpredictable locations in the context of DA and SA tasks.

Sustained attention is thought to depend on mechanisms of “tonic alertness” that are sensitive to diurnal changes in systemic steroid levels, fatigue, depression, drugs, and the functioning of an autonomic arousal system comprising the reticular activating system (including midbrain, limbic structures, and hypothalamus).²⁵ Damage to these areas could affect sustained attention in early stages, and general arousal and appetitive functions in end stages of AD. In this study, we found a defect of sustained attention affecting ability to detect brief phasic events (stimulus onset or offset) on the Starry Night Task. This defect includes reduced true sensitivity (d') to events, and increased numbers of FP responses. FP responses could be due to increased “noise” in the degenerating nervous system of individuals diagnosed with AD, and less ability to separate signal from noise to make accurate perceptual decisions.²⁸

Reports of asymmetric impairment of visual attention in AD suggest greater involvement in one hemisphere^{18,29} due to impaired disengagement of attention³⁰ or an “attentional grasp reflex.”³¹ The latter mechanism was invoked to explain behaviors in Balint’s syndrome, a condition later described in some cases of AD³² with posterior cortical atrophy. Our data suggest that the large asymmetries reported in some cases of AD are uncommon.

Attention abilities are not uniformly affected in AD. Recent studies, including ours, show that patients with mild AD generally have impairments of processing speed, detection of stimuli in peripheral locations, DA, shifting attention between stimulus features, and disengagement of attention. Yet, compared with control subjects without dementia, patients with mild AD can show similar engagement of

attention,^{4,5,33} shifting of attention to an expected location,⁴ single-feature search, and conjunction search.³⁴ They can perform adequately on tests of sustained attention when task demands are low²⁴ and show preserved inhibition and habituation (processes that contribute to selective attention).³⁵ Differences between patients with AD could reflect distribution of neurodegenerative changes in structures mediating aspects of attention.⁹

Findings from neuropathologic and metabolic studies of AD suggest that attention decline in mild AD might depend on multifocal degeneration in a cerebral network for attention that comprises occipital lobe, adjacent temporal and parietal areas, frontal lobe, and subcortical regions such as pulvinar.³⁶⁻³⁹ Visual attention deficits similar to those we found in AD are the most convincing impairments observed following experimental lesions of basal forebrain made with cholinergic excitotoxins; together with pharmacologic studies, these findings support a role for the basal forebrain-cortical cholinergic system in attention⁴⁰ and a rationale for disease-modifying treatment of visual attention deficits in AD.

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