Spatial disorientation in Alzheimer’s
disease

The remembrance of things passed

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Abstract—Background: Patients with Alzheimer’s disease (AD) and many older adults become lost even in familiar surroundings. This is commonly attributed to memory impairment, but it may reflect impaired spatial cognition. Methods: The authors examined the role of memory, perceptual, and cognitive mechanisms in spatial disorientation by comparing the performance of normal young (YN), middle-aged (MA), older adult (OA), and AD subjects on neuropsychological and spatial orientation tests. Results: The tendency to become lost is shared by almost all patients with AD (93%) and some OA subjects (38%). This impairment is not related to memory impairment. Instead, it reflects an inability to link recognized scenes with locations in the environment. Conclusions: Spatial disorientation reflects the impaired linking of landmarks and routes that should be assessed in conjunction with routine memory testing in elderly patients.

Alzheimer’s disease (AD) presents with progressive memory loss and cognitive impairments.1,2 More than one-third of patients with AD have disabling visuospatial disorientation3–5 that interferes with safe driving and independent living.6 Spatial orientation relies on cues about location and

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self-motion. Location cues orient the observer by relating recognized landmarks to remembered positions in a cognitive map of the environment. Self-motion cues orient the observer by incrementally updating position relative to a starting point using path integration. Therefore, landmark orientation relies on remembered scenes in familiar environments, whereas path integration is independent of familiarity with the surroundings.7

Hippocampal involvement in patients with early stages of AD8 could impair landmark orientation by undermining the role of hippocampal place neurons in maintaining cognitive maps.8,10 This would force patients with AD to rely on path integration that may be maintained by parietal cortical integration of self-movement cues.11,12 Involvement of parietal cortex in the later stages of AD13 could impair path integration, leaving patients with AD without a viable orientation mechanism and causing spatial disorientation.

We have shown previously that patients with AD with spatial disorientation are unable to process the self-movement cues in optic flow,14 the global pattern of visual motion that supports orientation by path integration.15 We now examine the use of landmark orientation in patients with AD by assessing their ability to navigate in a familiar environment.

Methods. Research subjects. Four groups were studied: young normal adults (YN; n = 47; mean age ± SD = 23.5 ± 5.9 years), middle-aged adults (MA; n = 24; mean age = 51.8 ± 4.9 years), older adults (OA; n = 26; mean age = 73.0 ± 7.6 years), and patients with AD (AD; n = 14; mean age = 73.4 ± 5.9 years). There was no difference in age between the OA and AD groups. Mini-Mental State Examination (MMSE) scores were lower in the AD group (F(3,100) = 28.7, p < 0.0001; Tukey honestly significant difference (HSD), p < 0.0001): YN = 29.3 ± 1.1, MA = 29.7 ± 0.5, OA = 28.7 ± 1.4, and AD = 23.1 ± 0.3. This suggests that our patients with AD should be considered mildly impaired.

All subjects were free of neurologic, ophthalmic, and psychiatric illness other than the defining illness in the AD group. Corrected binocular visual acuity of 20/40 and an MMSE score >7 were required. Patients with AD were recruited from outpatient programs affiliated with the University of Rochester Medical Center and were diagnosed as meeting National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA) criteria for probable AD by a geriatric neurologist or psychiatrist who specialized in dementia.1 YN subjects were undergraduate or graduate students. The MA and OA groups consisted of volunteers from the community or AD patients’ spouses or caregivers.

Each subject gave informed consent at recruitment. The Institutional Human Subjects Review Board approved all procedures and protocols.

Spatial orientation testing. All tests were administered in the Visual Orientation Laboratory or in the lobby of the Strong Memorial Hospital, Rochester, NY. Testing was completed in two 90-minute sessions on two days as detailed below.

Basic visual function. All subjects underwent Snellen visual acuity testing to confirm binocular acuity of at least 20/40. Contrast sensitivity was tested at five spatial frequencies (0.5 to 18 cycles/°, Vistech Consultants, Inc., Dayton, OH). Contrast sensitivities were in the normal range for all groups. YN subjects performed better than the other three groups, but there were no significant differences among the three other groups.

Neuropsychological tests. The neuropsychological battery assessed general cognitive ability, spatial orientation, and verbal and nonverbal memory. The Money Road Map Test assesses topographic orientation in simulated route following by having subjects use a pencil to trace a predrawn path on a village map and report whether turns are to the traveler’s left or right.16 Two tests from the Wechsler Memory Scale–Revised (WMS-R) were used: the Figural Memory Test uses block patterns in an immediate visual recognition task; the Verbal Paired Associates Test I has an immediate and delayed recall subtest of memory for a list of word pairs.17 Categorical Name Retrieval, Facial Recognition, and Judgment of Line Orientation tests were also administered.18 The MMSE was used only to assign subjects to groups and would later be used to retrace the route and undergo testing related to it. Subjects were then pushed along the 1000-foot path over 4 minutes. No further cuing or discussion took place until the route was completed.

The hospital lobby was built several years ago, but some subjects had previous experience in this space. We recorded each subject’s reported number of such visits to assess the impact of remote experience. We counted the number of persons seen on each experimental excursion to assess the impact of traffic volume as a potential distractor. On completion of the route, 8 tests were administered to assess knowledge concerning the route; each subtest consisted of 10 questions. For some subtests, the map (layout) of the maze was presented, and subjects were oriented to the map with identification of the main information desk. The Video Recognition and Photo Location subtests, which use images, and the Video Location subtest, which uses video clips, were presented on a laptop computer with PowerPoint (Microsoft, Inc., Redmond, WA). These tests were administered in the order described below.

Route learning. To assess route learning based on the first presentation, the route was begun a second time immediately after completing the initial excursion. Subjects were wheeled to each of 10 choice points along the route and asked whether they had gone left, right, or straight at that point. Responses were recorded, and subjects were corrected to maintain the integrity of the route. In our later analyses, subjects who made one or more errors were categorized as having become lost on the route.

Free recall. Verbal memory of the test environment was evaluated immediately after the route-learning excursion. Subjects were given 1 minute to name as many objects or landmarks as they could recall from the trip. This test was scored as the total number of items up to a maximum of 10. Follow-up analysis assessed whether the order of recall matched the sequence in which items were encountered along the path.

Orientation relative to scenes from the test route was assessed while subjects were seated at the starting/finishing point. Subjects were shown pictures of 10 different objects or locations taken from the test route. They were asked to point in the direction of the location as if there were no walls between themselves and the target. Responses were scored as correct if they pointed in the correct general direction judged as being within 45° of the experimenter’s assignment of the correct direction using local cues. The picture presentation sequence was randomized.

Route drawing. The capacity to graphically represent survey knowledge of the route was assessed by a route-drawing task. After the subjects were moved to a quiet area adjacent to the test route, they were asked to draw the route one segment at a time. A drawn-to-scale outline of the lobby was provided; the main information desk was indicated; and subjects were asked to draw an “x” at the starting point. The next lobby outline included the correct starting point, and subjects were asked to draw a line from the starting point to show the first segment of the trip to the next choice point. This was done 10 times to complete the drawing of the entire route. Responses were considered correct when the line drawn was consistent with direction and approximate magnitude of that segment of the route test.

Landmark recall. To determine which landmarks were remembered as useful navigational cues, subjects were asked to name all objects or fixtures that were helpful in finding their way on the self-directed, second trip around the lobby. The number of objects listed, up to a maximum of 10, was used as the dependent measure.
Photograph recognition. To assess visual recognition of scenes from the route, 10 still photographs were presented—5 from the subject's view of the test path and 5 from the same height at remote public locations in the Medical Center. Subjects were asked to identify each photo as a scene from the test route or not. Responses were scored as correct, false positive, or false negative.

Photograph location. We evaluated each subject's ability to link scene snapshot visual recognition with route locations. To do so, we presented a different set of 10 photographs, all taken from the subject's view of the test path. Subjects were asked to identify each photo as a scene from the test route or not. Responses were scored as correct, false positive, or false negative.

Video location. We also evaluated subjects' ability to link moving video scene recognition with route locations. To do so, 10 short video clips taken from the subjects' view of the test path were presented. After each video clip, subjects were asked to draw an "x" on a blank map where the clip began and an arrow coming from the "x" showing where the rider was moving in the clip and where the clip ended. The clips could be viewed up to three times each. Responses were considered correct if the "x" was placed in the correct location and if the arrow indicated the correct direction.

Retesting. A random subset of subjects in each group (31 YN, 13 MA, 9 OA, and 5 AD) was retested on the entire navigational task within 48 hours of the initial test.

Data analysis. The total score on all eight subtests (maximum score = 80) was used as a dependent measure of spatial orientation. We assessed the reliability of the spatial orientation test using retesting within 72 hours, its internal consistency by deriving an alpha coefficient, and its construct validity by principal components analysis. Dependent measures from the neuropsychological testing included the Money Road Map (maximum = 32), WMS-R Figural Memory (maximum = 10), Verbal Immediate

Figure 1. Group performance on the spatial orientation test. (Center) Total scores for each subject group. The older adult (OA) group showed significantly poorer performance than the normal young (YN) or middle-aged (MA) groups. The Alzheimer's disease (AD) group showed significantly poorer performance than all other groups. (A through H) Subtest scores for each group are arranged clockwise in order of decreasing magnitude of the correlation (r) between that subtest score and the total score. All subtests showed significant correlations with the total score, reflecting their coherence in testing spatial orientation. Asterisks indicate group differences (Tukey honestly significant difference, p < 0.05). Y = young normal; M = middle age; O = older adult; A = AD.
Figure 2. Error analysis of two subtests in which subjects showed different types of errors. (A) Errors on the Video Location subtest were classified as to whether the subject chose an incorrect location that had similar or dissimilar architectural geometry as that depicted in the video clip. Older adult (OA) and Alzheimer’s disease (AD) subjects made significantly more errors in which they chose location with dissimilar architectural geometry. (B) Errors on the Photo Recognition subtest were classified as false-positive responses (incorrectly attributing a scene to the test route, plotted here) or false-negative responses (failing to recognize a scene from the test route, not shown). AD subjects made significantly more false-positive errors. Y = young normal; M = middle age; O = older adult; A = AD.

Results. Spatial disorientation in aging and AD. Spatial orientation was substantially impaired in the OA and AD groups. There were differences between the groups on the spatial orientation test (F(3,100) = 63.75; p < 0.0001). Total scores were lower in the AD group than in all other groups (post hoc Tukey HSD, p < 0.001), and the OA group scored lower than the YN and MA groups (Tukey HSD, p ≤ 0.001) (figure 1, center).

Previous experience in the test environment, measured as each subject’s reported number of visits, did not have a significant effect (ANCOVA F(1,97) = 3.77; p = 0.055) and did not alter group effects (ANCOVA F(3,97) = 56.15; p < 0.0001). Likewise, pedestrian traffic volume in the test environment, measured as the number of persons seen by the experimenter during the excursion, did not have an effect (ANCOVA F(1,93) = 2.51; p = 0.116) and did not alter group effects (ANCOVA F(3,93) = 56.40; p < 0.0001).

All eight subtests were significantly correlated with the total score in the order depicted in figure 1. The subtests that were most highly correlated with the total score were Photo Location and Video Location, both tests of the capacity to indicate the map location of a scene from the test route. Step-wise regression showed that the Photo Location subtest alone could explain a great deal of the variance in the total scores (R² = 0.78; p < 0.0001).

The OA and AD groups had Photo Location and Video Location impairments. The OA group performed poorer than the YN and MA groups on Photo Location (p = 0.023) and Video Location (p = 0.0005) but not on other subtests. The AD group performed poorer than the YN and MA groups on all subtests (p < 0.003). Therefore, subtest scores reveal visuospatial impairments in the OA and AD groups and additional impairments in the AD group.

Similar errors in aging and AD. Subject groups used different strategies to formulate their responses, making different types of errors on the Video Location and Photo Recognition subtests. Video Location errors were classified as to whether the architectural geometry depicted in the video clip was similar to that of the selected map location (e.g., corner for corner vs straight hallway for corner). OA
Table Group neuropsychological profiles

<table>
<thead>
<tr>
<th>Neuropsychological measure (Max. score)</th>
<th>Subject group (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>YN (42)</td>
</tr>
<tr>
<td>Money road map (32)</td>
<td>30.4 ± 2.6</td>
</tr>
<tr>
<td>Line orientation (30)</td>
<td>26.4 ± 4.1</td>
</tr>
<tr>
<td>Figural memory (10)</td>
<td>8.0 ± 1.4</td>
</tr>
<tr>
<td>Verbal immediate (24)</td>
<td>20.6 ± 3.0</td>
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<tr>
<td>Verbal delayed (8)</td>
<td>7.7 ± 0.8</td>
</tr>
<tr>
<td>Animal name retrieval</td>
<td>23.6 ± 4.7</td>
</tr>
<tr>
<td>Facial recognition (56)</td>
<td>47.6 ± 4.1</td>
</tr>
</tbody>
</table>

* Indicates difference between OA and AD groups (p < .01).

YN = young; MA = middle-aged; OA = older adult; AD = Alzheimer’s disease.

and AD subjects made more errors in which they matched video clips with dissimilar map locations, reflecting a failure to use the architectural information (ANOVA F(3,78) = 12.71; p < 0.0001) (figure 2A).

The OA and AD groups were aware of their difficulties in the task. The YN and MA subjects typically chose to view each video clip only once or twice (YN, 1.67 ± 0.36; MA, 1.75 ± 0.41), whereas the OA and AD groups chose repeated viewings of each video clip (OA, 2.01 ± 0.28; AD, 2.44 ± 0.36; maximum = 3) (F(3,68) = 13.94, p < 0.0001; Tukey HSD, p < 0.01; YN = MA < OA < AD).

Photo Recognition subtest errors were further classified as false-positive responses, in which the subject reported that the scene was part of the test route when it was not, and false-negative responses, in which the subject reported that the scene was not part of the test route when it was. There was a trend of increasing percentages of false-positive errors across subject groups (F(3,80) = 7.31, p < 0.0001; Tukey HSD, p < 0.03; YN = MA < OA < AD) (figure 2B). Therefore, OA and AD subjects have limited ability to distinguish between familiar and novel scenes, with patients with AD having a bias toward false recognition.

Getting lost in aging. We sought to understand why some people get lost on familiar routes by examining Route Learning errors in OA subjects. YN and MA subjects were not included because they did not get lost; they rarely made Route Learning errors (see figure 1E). Patients with AD made up to six Route Learning errors, but their diverse impairments obscure which deficits may cause them to get lost.

We classified the OA group into lost and not-lost subgroups based on whether subjects made at least one Route Learning error and would have been lost if not corrected. This criterion classified 38% of OA subjects (n = 10) as lost and 62% (n = 16) as not lost. The lost subjects showed poorer performance on the spatial orientation test than the not-lost subjects (ANOVA interaction F(6,144) = 4.27; p = 0.006). Differences (Bonferroni adjusted t-test, p < 0.007) were seen in all subtests except Free Recall and Landmark Recall, on which both subgroups did well, and Video Location, on which both subgroups did poorly (figure 3A).

The largest difference between the lost and not-lost OA subgroups was on the Photo Location subtest, which yielded the highest correlation with the lost/not-lost classification (r = −0.64; p < 0.0001). There were no differences between the lost and non-lost OA subgroups on any of the neuropsychological tests (ANOVA F(1,23) = 3.81; p = 0.063) (figure 3B). Therefore, getting lost was related to visuospatial skills rather than verbal memory about the route or other cognitive capacities.

Test reliability and validity. We examined the reliability and validity of spatial orientation test scores by studying the results of repeat testing and subtest correlations to determine reliability and by studying correlations with standard neuropsychological test scores to determine concurrent validity. Repeat spatial orientation testing was conducted 24 to 48 hours after the initial test in a subset of all subject groups to assess test reliability.

Retest reliability yielded a high correlation for total test scores when combining all groups (r = 0.90; p < 0.0001) equal to that of established tests (e.g., Judgment of Line Orientation). However, there were some group differences in retest correlation coefficients (YN: r = 0.82, p < 0.0001; MA: r = 0.76, p = 0.002; OA: r = 0.87, p = 0.003; AD: r = −0.11, p = 0.86). The high retest reliability of the YN, MA, and OA subjects attests to the stability of normal performance and the test. The low retest reliability of patients with AD suggests that they are inconsistent and impaired. Retest reliability for the subtests yielded correlations (p < 0.0001) that were greatest for Photo Location, Video Location, and Self-Orientation. Therefore, the subtests that were most strongly correlated with the total score were also the most consistent.

The internal consistency of the spatial orientation test was confirmed by an alpha coefficient of 0.86. Alphas >0.8 are considered psychometrically optimal and imply a unity of test content and good power to discriminate those with high vs low capacities. Significant group differences also attest to the test’s discriminative power.

Principal components analysis with varimax rotation was used to evaluate the underlying structure of spatial orientation capacities in normal subjects (YN, MA, and OA). A scree plot revealed that the two-factor solution is preferred. These two factors explained 57% of the variance. Factor 1 explained 42% of the variance with the highest loadings for Video Location (0.85) and Photo Location (0.83). Factor 2 explained 15% of the variance with the highest loading for Landmark Recall (0.85) and additional loading for Free Recall (0.57). This suggests that the total
spatial orientation scores combine spatial cognitive and verbal memory factors.

We assessed the validity of the spatial orientation test by comparing it with standard neuropsychological tests. Neuropsychological tests showed group differences (MANOVA F(21,253) = 8.15; p < 0.0001) (table 1). Aging effects were evident in differences between YN and OA groups in the Road Map (p = 0.03), Figural Memory (p = 0.01), Immediate Verbal Memory (p = 0.001), Delayed Verbal Memory (p = 0.01), and Verbal Fluency (p = 0.04) tests. AD subjects performed worse than all other groups on all tests, with differences between the AD and OA groups on Figural Memory (p < 0.0001), Immediate Verbal Memory (p < 0.0001), Delayed Verbal Memory (p < 0.0001), and Verbal Fluency (p < 0.0001) tests. Therefore, patients with AD show some impairment in all domains, whereas OA subjects show smaller impairments on fewer tests.

Spatial orientation scores were strongly correlated with the results of the Judgment of Line Orientation test (subjects: r = 0.53, p < 0.0001; AD: r = 0.67, p < 0.02) and the Road Map test (subjects: r = 0.51, p < 0.0001; AD: r = 0.74, p < 0.004) in all groups. In normal subjects, but not in patients with AD, spatial orientation scores were also correlated with Figural Memory (r = 0.42, p < 0.0001) and Verbal Fluency (r = 0.27, p = 0.01). The consistently low scores of patients with AD on all memory and verbal tests undermined that correlation.

Therefore, the deficits that define AD limit these patients to spatial orientation strategies that are based on visual perceptual analyses. In contrast, normal subjects can use orientation strategies that place greater emphasis on memory and verbal mechanisms.

Discussion. We have developed a spatial orientation test based on real-world wayfinding that reveals deficits in OA and AD subjects with excellent retest reliability (r = 0.90).21 Factor analysis across the eight subtests identified two major components: the first pertained to wayfinding and landmark recognition, and the second pertained to verbal memory. This is consistent with evidence that separate spatial and verbal capacities are combined to influence spatial orientation and navigation.22-25

Age and AD affected spatial orientation: YN and MA groups performed well on all measures; the OA group showed significant impairments; and the AD group was more consistently and severely impaired. This is consistent with subtle cognitive deficits in OA subjects,26 which are more prominent in AD and relate to the tendency of patients with AD to become lost when navigating even in familiar surroundings.27 In contrast, verbal memory deficits were seen only in the AD group, possibly reflecting the role of such deficits in diagnosing AD.28

The OA and AD groups not only made similar numbers of spatial orientation errors but also made similar types of errors. In the Video Location subtest, the OA and AD subjects did not consider the architectural geometry depicted in the video clip and on the map, often mistaking corners for straight halls. This may reflect topographic imperception, consistent with visual processing deficits in AD and the topographagnosia commonly attributed to parietal or parietotemporal lesions.

The OA and AD subjects also made more false-positive Photo Recognition errors than the other groups, often misidentifying a scene from another place as being from the test route. This is consistent with previous reports of increased false recognition of photographs and video displays as a mild deficit in normal aging and a more severe impairment in dementia.33

These findings suggest that some OA subjects and most patients with AD have a visuospatial disorder that distinguishes them from YN, MA, and unaffected OA subjects. In this study, the main difference between spatially impaired OA subjects and patients with AD is that the patients with AD also show verbal memory impairments. OA subjects with isolated spatial deficits may have a spatial variant of mild cognitive impairment (MCI). Such monosymptomatic syndromes may identify patients who are at greater risk for developing AD and who may be good candidates for focused monitoring and possible treatment.35

Subjects who made at least one error on the Route Learning subtest were classified as having become lost during self-directed route following. Getting lost was most closely related to performance on the Photo Location subtest. In contrast, neuropsychological tests did not predict who might get lost.

Taken together, these studies identify our Photo Location, Video Location, and Self-Orientation subtests as having the strongest relationship to overall spatial orientation performance. These three subtests also are the most reliable in repeat testing and are closely related to getting lost. The lack of a relationship to memory impairment suggests that this is not the critical factor in spatial disorientation.

This is consistent with the relationship between impaired visual motion processing and ambulatory and vehicular navigation in AD, possibly reflecting posterior parietal cortical dysfunction in integrating multisensory cues about self-movement.37

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