Diminished curiosity in patients with probable Alzheimer's disease as measured by exploratory eye movements

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Article abstract—Clinical accounts of Alzheimer's disease (AD) suggest that some patients exhibit markedly diminished curiosity and initiative early in the course of their illness. Such behavioral changes are extremely difficult to measure experimentally. We studied one aspect of curiosity by measuring exploratory eye movements in response to provocative visual stimuli in 12 patients with probable AD and 10 matched controls. Subjects viewed slides, each of which contained an incongruous or irregular figure paired with a congruous or regular one. Unlike controls, who spent significantly more time viewing the incongruous stimuli, AD patients distributed their viewing time equally and spent significantly less time than controls looking at the novel stimuli. Additionally, when presented with picture slides containing an unexpected element, AD patients exhibited diminished visual exploration overall and decreased attention to the incongruous part. Further analyses suggest that the results cannot be adequately explained by a general decline in cognition or by problems with ocular motility or directing visual attention. We conclude that AD patients exhibit diminished curiosity which can be measured by the study of exploratory eye movements.

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Research on the clinical symptoms of Alzheimer's disease (AD) has focused on the progressive deterioration of cognitive functions such as memory. Although changes in personality and behavior are often noted, they have not been studied as extensively.[1-5] Passivity, apathy, indifference, and diminished curiosity are commonly observed and contribute to serious disruption of daily living activities and interpersonal relationships. The few existing studies on this topic have relied primarily on surveys and interviews with family members or on clinical interviews and observations of patients.[2-5] The lack of objective and reliable measures of diminished curiosity, exploration, and motivation has limited the ability of researchers to adequately characterize, follow, and correlate these deficits with other aspects of the illness. This paper reports the results of an experimental investigation of curiosity and visual exploration in patients with dementia of the Alzheimer type using an objective methodology.

Visual attention is tightly linked to visual fixations and saccadic eye movements.[6-13] The close correspondence between direction of gaze and the allocation of visual attention enables eye movements to be used as an objective, physiologically based measure of directed attention. Normal subjects tend to focus a disproportionate amount of attention, as measured by looking time, on those aspects of the environment that are the most novel, unpredictable, or incongruous. Berlyne[14] conducted seminal studies on this topic. In one experiment,[14] young adults viewed pairs of slides for 10 seconds each. One member of the pair differed from the other in terms of irregularity of arrangement or shape, amount of visual material, heterogeneity of elements, or incongruity. Significantly more time was spent looking at the more novel or unusual stimuli. Berlyne interpreted these results as evidence of novelty-seeking behavior and the curiosity drive. Normal subjects exhibit similar behavior during picture-viewing tasks, concentrating their fixations on the unusual details or incongruous elements of a scene.[15-17]

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In the current study, we operationally defined curiosity as the preference for directing visual gaze to the more novel, unfamiliar, and irregular aspects of the visual environment and measured this phenomenon by recording exploratory eye movements in response to provocative visual stimuli. We hypothesized that in comparison with age-matched, nondemented controls, AD patients would exhibit diminished and abnormally distributed exploratory eye movements in response to novel or incongruous stimuli.

Methods. *Subjects.* There were two subject groups for this study. One consisted of patients with the diagnosis of probable Alzheimer's disease (PRAD) based on NINCDS criteria.[18] In accordance with these criteria, patients were excluded if they (1) suffered from medical conditions that could account for their dementing illness, (2) had evidence of infarction on CT, (3) had a Hachinski ischemic score[19] of greater than four, or (4) had clinical evidence of major depression as defined by DSM-III-R criteria.[20] Family members or friends of patients were recruited to serve as controls. The control group consisted of older subjects with no known diseases of the CNS (eg, documented strokes, tumor, seizures), normal results on a cognitive test battery (see below), and no evidence of impairment of daily life activities by history. Subjects were excluded if their pupils could not be discriminated by the eye movement equipment (eg, due to droopy eyelids, bifocals, cataracts, or pupils <2 mm). Subjects were also excluded if they could not participate in the calibration procedure. A total of 15 patients with PRAD and 13 age-matched controls were initially recruited for this study. Three patients with PRAD were lost because of inability to image their pupils or problems in data recording. Two potential controls were not included because of their poor performance on the cognitive test battery. Another potential control was excluded because of a history of strokes. The final number of subjects for this study was 12 patients with PRAD (five men and seven women) and 10 normal age-matched controls (three men and seven women). Subject numbers for individual experimental protocols varied slightly because of lost data due to data recording problems. There were no statistically significant differences between the two subject groups in terms of age (AD patients 73.1 ± 4.7 versus controls 71.0 ± 6.4), education (AD patients 13.4 years ± 2.3 versus controls 13.1 ± 4.5), or work experience. No subject was taking hypnotics, sedatives, or major tranquilizers. Medication use and medical illnesses in both groups were comparable.

Eye movement equipment. Eye movement data for all experimental protocols in this study were collected using an Applied Science Laboratories Model 3000 video-based pupil center to corneal reflection system. In this system, the eye is illuminated with a filtered near-infrared light source. The pupil and corneal bright spot are imaged with a high-speed CCD camera sensitive in the near-infrared range. This illumination is neither visible nor dangerous to the subject. The subject's eye line-of-gaze is determined by the measurement of the center of the pupil with respect to the center of the corneal reflection. The system has an accuracy of ±0.75°. Linearity in the system is less than 10%. The system samples at a rate of 60 Hz, with a temporal resolution of 16 msec. The video detection and coordinate extraction technique for determining the eye's point-of-regard are fully described by Young and Sheena.[21] The system generates information on eye position as input to all further analysis. The viewing room in which subjects were seated measured 2.26 meters by 2.21 meters. The viewing distance was 1.5 meters from the stimulus screen. The total field of the slide screen subtended an angle of 29° horizontally and 22° vertically. The total field of the CRT screen subtended an angle of 19° horizontally and 14° vertically. No physical constraints or attachments were imposed on subjects while viewing the stimulus presentation. Calibration was accomplished employing a nine-point array and using the EYEPOS software supplied with the system. The eye tracking system employed allows calibration accuracy to remain extremely stable over the course of measurements.

Testing procedures. At the start of an experimental session, patients and family members who served as normal controls were briefed about the experiments, and informed consent was obtained. Information about patients was updated, and demographic and medical information was obtained from control subjects. Each session consisted of the collection of eye movement data during the experimental protocols and the administration of the cognitive tests and a bedside neuro-ophthalmologic examination. The sessions took approximately 2.5 hours for each pair of subjects and included two eye movement testing periods of approximately 20 minutes each and ample time for rest periods. The patient and control subject alternated between participation in experimental protocols and either rest periods or other testing (cognitive screening and neuro-ophthalmologic examination).

Mental state testing. All subjects were given the Information-Memory-Concentration (IMC) Subtests of the Blessed Dementia Scale[22] to assess the general severity of cognitive impairment of AD patients and to ensure that control subjects did not have cognitive deficits. Subjects recruited as age-matched controls were also given a cognitive test battery (Digit Span forward and backward,[23] the Stroop,[24] Controlled Word Fluency Test,[25] Judgment of Line Orientation,[26] Boston Naming Test,[27] and Three Words-Three Shapes Test of Memory[28]) to exclude those with abnormal cognitive profiles.

Clinical neuro-ophthalmologic examination. To test for elementary abnormalities of eye movement control that might influence performance on the experimental protocols, all subjects were given a bedside clinical neuro-ophthalmologic examination. It evaluated visual fields, pursuit movements, saccadic movements, and partial field optokinetic nystagmus.

Eye movement experiments. The subject was comfortably seated in the viewing room and a calibration procedure, which took a few minutes, was run to adjust the measurement system to each subject's eye. During the calibration procedure, the subject was instructed to fixate premapped locations on the screen (slide or CRT) while eye position was recorded. Eye calibration was periodically checked between protocols to ensure accuracy and stability of calibration. A second experimenter was present in the viewing room with all patients, but not with control subjects. He sat behind the patient and out of view. Three of the experimental protocols will be reported.

1. Curiosity Slides Task. Subjects were shown 10 slides that contained pairs of stimuli. These slides were a subset of the stimulus set used by Berlyne.[14] One stimulus was a line drawing of an irregular or incongruous figure and one a regular or congruous counterpart to that

figure (figure 1). Figures subtended a visual angle of approximately 7° × 7°, were well above threshold acuity levels, and were separated by 12° of visual angle. The incongruous figure appeared alternatively on the right or left side of the screen. Subjects were instructed to "look at the slides however you like." Slides were exposed for 12 seconds each, with a blank slide exposed for 1 second between all trials. Eye movements were recorded as subjects viewed each slide. This protocol took approximately 2 1/2 minutes.

2. Incongruous Picture Slides Task. Subjects were shown two slides of photographs of scenes that contained unexpected or incongruous elements. The "horse slide," subtending a visual angle of 22° (vertical) × 17° (horizontal), depicted a man sitting on a horse that appears to have no hind legs (figure 2A). The "lion slide," subtending an angle of 22° (vertical) × 26° (horizontal), showed a classroom of children that had a lion on one of the desks (figure 2B). The slides were exposed for 15 seconds each and subjects were instructed to "look at the pictures however you like." Eye movements were recorded as subjects viewed the slides. This protocol took less than 1 minute.

3. Saccade to Target Task. This protocol tested the ability of subjects to allocate attention throughout the visual field and direct gaze to randomly occurring events. It also provided information about the capacity of subjects to make saccades between stimuli separated in space, one prerequisite for successful performance on the Curiosity Slides. Subjects were asked to fixate a cross that appeared in the center of the screen and remained visible throughout all of the trials. At randomly timed intervals (2.5 seconds ± 0.5 seconds) a target ball, subtending a visual angle of 0.5° and well above threshold acuity level, appeared in random order in one of the four corners of the CRT screen 10° from the center of the fixation cross and remained visible for 550 msec. Subjects were instructed to look directly at the ball when it appeared and when it disappeared to look back at the cross until another ball appeared. Prior to data collection, subjects were given 10 practice trials. All verbal instructions were supplemented by showing each step in the sequence individually. The experimental task ran for 1 minute, which provided approximately 10 trials for each quadrant. Eye movements were recorded throughout. Correct trials were defined as those in which the direction of the initial saccade was toward the appropriate quadrant (ie, where the ball appeared) and the target was fixated prior to its disappearance. Incorrect trials included those in which no attempt was made, the first saccade was toward an inappropriate quadrant, or the latency of saccade initiation was so long that subjects never fixated the target. Saccade latency was defined as the difference between the fixation end time of the fixation that began prior to the target onset, and the target onset time.

Data analysis. For each experimental protocol, the visual field was divided into several areas of interest (AOIs). For the Curiosity Slides, the AOIs were 9° × 9° boxes drawn around the congruous and incongruous stimuli. For the Incongruous Picture Slides, the AOIs were boxes of varying dimensions drawn around major elements of the picture. Six AOIs were drawn for each Incongruous Picture Slide, which included one AOI surrounding the incongruous element (figures 2B and 3).

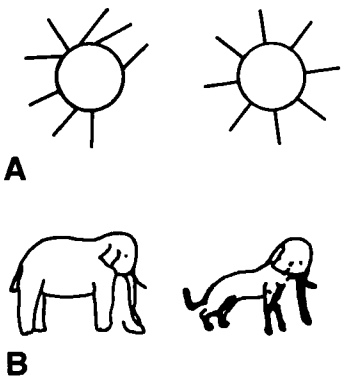

Figure 1. Two examples from the Curiosity Slides Task. One stimulus differs from the other in terms of (A) irregularity of arrangement and (B) incongruity of parts. (Reproduced from Berlyne,[14] public domain.)

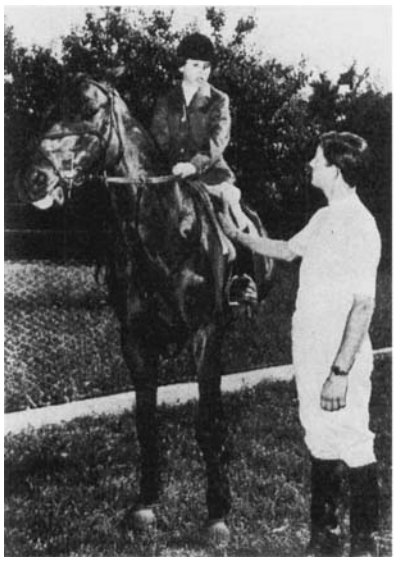

Figure 2. Incongruous Picture Slides. (A) The horse appears to have no hind legs, and (B) a lion appears in a classroom of children. Superimposed upon B is a display of six areas of interest (AOIs), which includes one AOI surrounding the incongruous element (arrow). (A: photograph by Michael C. Kotch, United States Army, 8/18/58, public domain. B: photograph by A.Y. Owen, 12/3/51, Life Magazine © Time-Warner Inc., reproduced with permission.)

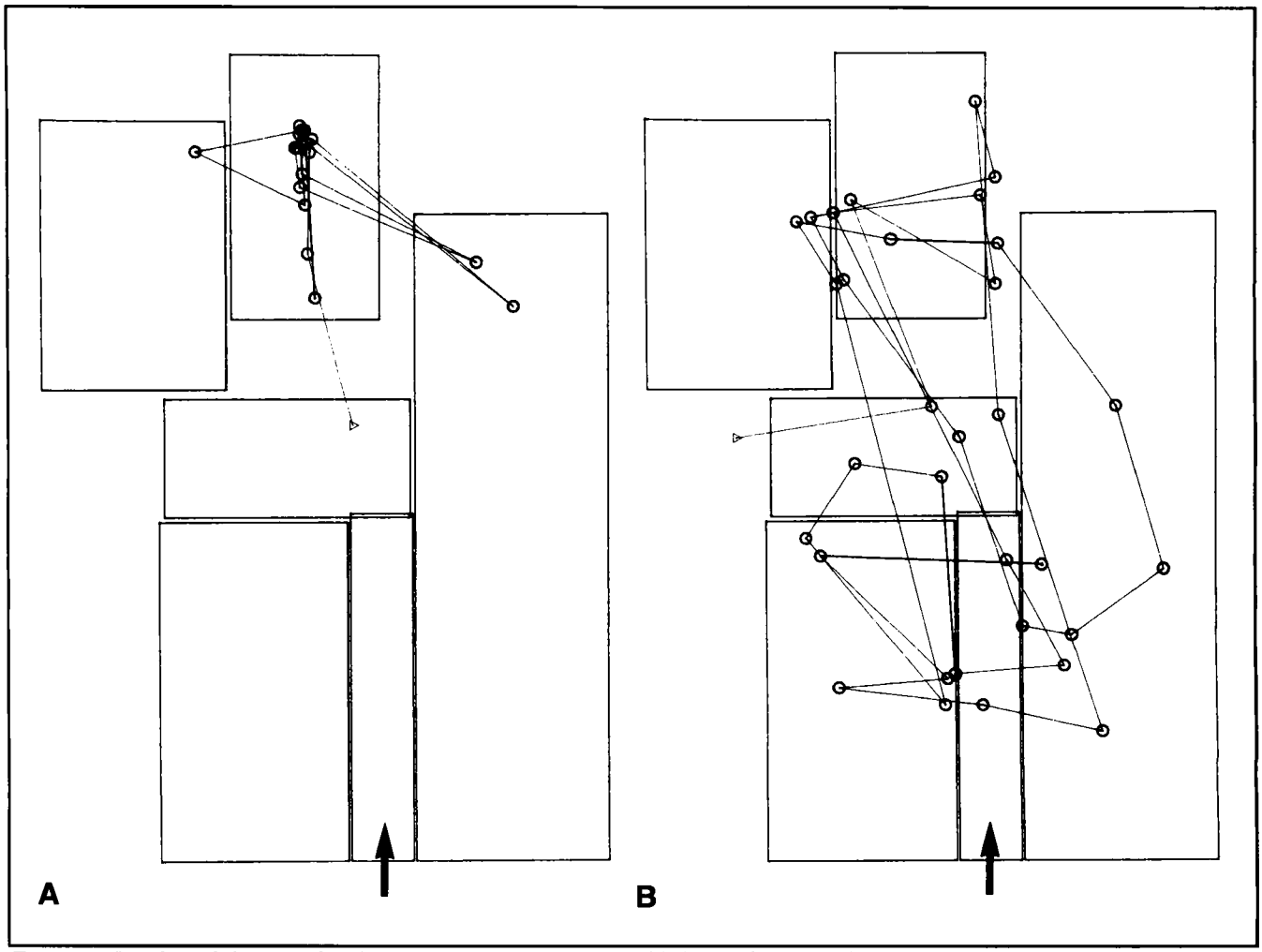

Figure 3. Display of the six AOIs for the Incongruous Picture Slide involving the horse, which includes one AOI surrounding the incongruous element (arrow). (A) An example of a scan path from an AD patient (number 2) revealing very limited visual exploration, which contrasts sharply with (B) an example of a scan path from a normal control (number 9).

For the Saccade to Target Task, a 1.5° × 1.5° box was drawn around the location of the target ball in each of four quadrants and around the center cross.

All raw eye position data were recorded in binary files for processing and analysis. Processing of raw eye position data yielded eye movement fixation files that contained information on number of fixations, mean fixation duration, and saccade amplitudes for each experimental protocol. Dependent variables for the experiments consisted of number and mean duration of fixations, mean saccade amplitude, latency of saccade initiation, and percent dwell time with respect to the predefined AOIs.

For the Curiosity Slides, the main dependent variable was the amount of dwell time, expressed as a percent of total viewing time subjects spent fixating the AOIs surrounding the incongruous stimuli, congruous stimuli, or neither stimuli (designated "other"). Within-group differences on the mean percent dwell time spent on the incongruous versus congruous stimuli, and between-group differences on the mean percent dwell time spent on the stimuli were analyzed using a Mann-Whitney U test. For the Incongruous Picture Slides Task, a Moses test was used to determine if there were group differences for eye movement patterns with respect to the designated AOIs. On the Saccade to Target Task, a Mann-Whitney U test was employed to determine if there were group differences in terms of percent correct trials, mean saccade latency and amplitude for correct trials, and number of hypometric and hypermetric saccades in correct trials. A number of correlation analyses were run, using Kendall's tau, to determine whether there were significant correlations between subjects' performance on various tasks (eg, the Curiosity Slides versus the Blessed Dementia Scale, and the Curiosity Slides versus the Saccade to Target Task).

Results. Data for individual subjects are summarized in table 1.

Mental status scores. On the IMC Subtests of the Blessed Dementia Scale, AD patients had a mean score of 11 ± 7.1, which was significantly worse than the nondemented age-matched controls (mean score, 0.90 ± 0.88; $p < 0.001$).

Clinical neuro-ophthalmologic examination. The clinical neuro-ophthalmologic examination did not reveal any major abnormalities in the patient or

Table 1. Summary of the data for each subject

Subjects	Age	BDS	MPDT-incong CS	MPDT-cong CS	MPDT-other CS	No. AOIs horse IPS	No. AOIs lion IPS	% CT STT
AD 1	75	13	43	40	17	5	5	61
AD 2	70	7	18	31	52	4	4	61
AD 3	71	25	51	36	14	5	—	32
AD 4	68	6	52	27	20	6	5	50
AD 5	81	18	54	34	12	4	4	45
AD 6	75	22	33	46	21	4	3	—
AD 7	74	6	50	35	15	5	4	82
AD 8	68	5	50	40	10	4	4	57
AD 9	76	7	—	—	—	4	4	42
AD 10	81	23	26	27	47	4	2	—
AD 11	70	3	33	36	30	6	—	—
AD 12	68	18	46	38	15	6	4	33
CNL 1	70	0	51	39	10	—	4	82
CNL 2	72	1	52	41	8	5	5	86
CNL 3	72	2	42	47	11	6	4	81
CNL 4	85	2	48	34	18	6	5	68
CNL 5	60	0	—	—	—	2	5	46
CNL 6	67	0	49	36	15	5	5	43
CNL 7	69	0	50	36	13	—	4	84
CNL 8	69	1	56	38	5	6	5	67
CNL 9	75	1	61	33	5	6	6	71
CNL 10	70	2	48	40	12	5	4	23

BDS Information-Memory-Concentration Subtest of the Blessed Dementia Scale (0-37).
MPDT-incong CS Mean percent dwell time on incongruous stimuli on the Curiosity Slides Task.
MPDT-cong CS Mean percent dwell time on congruous stimuli on the Curiosity Slides Task.
MPDT-other CS Mean percent dwell time on neither type of stimulus.
No. AOIs-horse Number of areas of interest fixated on the Incongruous Picture Slide of the horse (0-6).
No. AOIs-lion Number of areas of interest fixated on the Incongruous Picture Slide of the lion (0-6).
% CT STT Percent correct trials on the Saccade to Target Task.
AD Alzheimer's disease patients.
CNL Matched control subjects.

control groups. All subjects had full visual fields to confrontation. Their performance on partial field optokinetic nystagmus testing was unremarkable in both the horizontal and vertical directions. Several patients and one control exhibited mildly reduced upward gaze, a finding often associated with aging.[29,30] One patient had very mild breakdown of smooth pursuit movements, and another exhibited rare hypometric saccades.

Curiosity Slides Task. On the Curiosity Slides Task, the control subjects looked at the incongruous stimuli significantly longer than the congruous stimuli (50.7% ± 5.5 versus 38.4% ± 4.1, $p < 0.01$). In contrast, AD patients spent approximately the same percent of time on the incongruous and congruous stimuli (41.5% ± 12.2 versus 35.5% ± 5.8, $p = 0.16$). AD patients spent significantly less time than controls looking at the incongruous stimuli ($p < 0.05$) (table 2). The two groups spent nearly the same percentage of time looking at the congruous stimuli. However, while the normal controls spent 10.8% (± 4.3) of time looking at neither type of stimulus, AD patients spent 23% (± 14.2), which was significantly greater ($p < 0.05$). There was no correlation between the AD patients' performance on the Curiosity Slides, as measured by mean percent dwell time devoted to the incongruous stimuli, and their scores on the IMC Subtest of the Blessed Dementia Scale (Kendall's tau = −0.018, z = 0.025, $p = 0.49$). To further study the relationship between concentration ability and the performance on the Curiosity Slides Task, a correlation analysis was run between performance on the Concentration Subtest of the Blessed Dementia Scale (0 to 6 points) and the Curiosity Slides Task, which yielded a Kendall's tau of −0.317 (z = 1.17, $p = 0.12$).

Incongruous Picture Slides Task. For the two Incongruous Picture Slides, the AD patients looked at significantly fewer AOIs than the control group ($p < 0.05$) (table 2). For the Incongruous Picture Slide involving the horse, the constricted visual exploration of AD patients resulted in 67% of them never even fixating the AOI surrounding the incongruous element (the apparently missing legs) as compared with 33% of the normal controls. The AD patients had significantly fewer and shorter fixations ($p < 0.05$) on the incongruous part. In contrast, the mean fixation durations across all AOIs combined were not significantly different between the two groups. Finally, the mean percent dwell time spent by AD patients on the incongruous element was less than the controls, but the difference only

Table 2. Data on the Curiosity Slides Task and the Incongruous Picture Slides Task

	AD patients		Controls		
	Mean	SD	Mean	SD	*p*
Curiosity slides					
% Dwell time on incongruous stimuli	41.5	12.2	50.7	5.5	<0.05
% Dwell time on congruous stimuli	35.5	5.8	38.4	4.1	NS
% Dwell time on other	23.0	14.2	10.8	4.3	<0.05
Incongruous Picture Slides					
Horse slide					
No. AOIs viewed	4.75	0.88	5.13	1.36	<0.05
% Dwell time on incongruous element	2.4	3.6	5.0	6.3	0.11
No. fixations on incongruous element	1.08	1.67	2.57	2.63	<0.05
Duration of fixations on incongruous element (msec)	123	168	211	184	<0.05
Duration of fixations overall (msec)	412	127	483	183	NS
Lion slide					
No. AOIs viewed	3.90	0.88	4.7	0.67	<0.05
% Dwell time on incongruous element	39.7	18.5	33.3	13.0	NS
No. fixations on incongruous element	10.4	4.16	9.55	3.39	NS
Duration of fixations on incongruous element (msec)	416	137	447	131	NS
Duration of fixations overall (msec)	407	127	395	57	NS

Curiosity slides: AD patients, N = 11; controls, N = 9.
Horse slide: AD patients, N = 12; controls, N = 10.
Lion slide: AD patients, N = 10; controls, N = 10.

approached significance ($p = 0.11$). (Figure 3 presents an example of the scan paths of an AD patient and a normal control.) No significant differences were found for the Incongruous Picture Slide involving the lion in terms of number and duration of fixations, mean percent dwell time on the incongruous element, or overall mean fixation duration. The lack of correspondence between the extent to which AD patients viewed the incongruous elements of the horse and lion slides probably is due to the difference in the way the elements of each scene were laid out. The "missing" hind legs of the horse were not preattentively discriminable and required active exploration to discover, which the AD patients failed to do. Although the lion was a figure incongruous to the classroom setting, it was centrally located, preattentively discriminable, and extremely difficult to miss. Even the patients who exhibited marked centration and minimal visual exploration were very likely to have their gaze fall upon the figure. In fact, it probably would have required active avoidance not to have fixated the lion.

Table 3. Performance on the Saccade to Target Task

	AD patients		Controls		
	Mean	SD	Mean	SD	*p*
% Correct trials*	51.4	15.8	65.1	21.1	<0.05
Saccade latency for correct trials (msec)	353	71	265	60	<0.01
Saccade amplitude for correct trials (degrees)	9.82	0.50	9.96	0.46	NS
% Hypometric saccades for correct trials	18.4	10.7	16.0	9.7	NS
% Hypermetric saccades for correct trials	5.0	1.0	6.2	4.4	NS

*A correct trial is defined as one in which the direction of the initial saccade was toward the appropriate quadrant (where the target ball appeared) and the target was fixated before its disappearance.

Saccade to Target Task. AD patients had only 51.4% (± 15.8) correct trials on the Saccade to Target Task, as defined by those trials in which the initial direction of the saccade was toward the appropriate quadrant and the AOI surrounding the target was fixated prior to the target's disappearance. This performance was significantly worse than the normal controls, who had 65.1% (± 21.1) correct trials ($p < 0.05$) (table 3). On the correct trials, AD patients exhibited a mean latency of 353 msec (±71) before initiating saccades, which was significantly longer than the 265 msec (±60) latency of the normal controls ($p < 0.01$). However, for correct trials, there were no significant differences between the two groups on the mean saccade amplitude or the percentage of trials in which saccades were hypometric or hypermetric. There was no significant correlation between performance of AD patients on the Saccade to Target Task, as measured by mean percent correct trials, and performance on the Curiosity Slides, as measured by mean percent dwell time on the incongruous stimuli (tau = −0.370, z = 1.13, $p = 0.13$). Similarly, there was no significant correlation between performance on the Saccade to Target Task and performance on the Incongruous Picture Slides, as measured by the number of AOIs fixated (horse slide: tau = −0.099, z = 0.226, $p = 0.41$; lion slide: tau = 0.166, z = 0.335, $p = 0.37$).

Discussion. Studies of exploratory eye movements in AD patients during the performance of tasks designed to provoke curiosity in nondemented

adults reveal the following: (1) When presented with pairs of visual stimuli differing in the regularity of their elements or in their degree of incongruity, AD patients distributed their looking time almost equally between the two kinds of stimuli and spent less time than controls looking at the novel stimuli. (2) When presented with picture slides containing an unexpected element, AD patients exhibited diminished overall exploration of the visual array as well as decreased attention to the incongruous part. (3) In response to unpredictable targets presented in the periphery, AD patients had fewer correct trials than control subjects, but there was no significant correlation between performance on this task and the others measuring visual exploratory activity. (4) There was no significant correlation between visual exploratory behavior and the severity of the dementia as measured by the Blessed Dementia Scale.

"Curiosity" is a term used to designate a set of hypothetical mechanisms that serve to orient or attract an organism to novel stimuli. Curiosity as manifested in this drive toward novelty has been demonstrated in a variety of studies on healthy rats, monkeys, and humans.[31-35] This drive is central to survival and adaptive behavior.[14,31,33,35] Its most elementary expression includes the detection of novelty through the orienting response and the habituation of neural reactions to repetitive stimuli. More complex dimensions involve the active seeking of varied perceptual and conceptual experiences. Curiosity has been highlighted as a key factor in the psychological development of children and in the engagement of adults with their social and physical environments.[31,33,35] Previous research employing Berlyne's paradigm to study curiosity has been limited to young adults.[14] Our study is the first reported investigation of this phenomenon in an older population and has demonstrated that, like young adults, nondemented older subjects show a strong preference for looking at the novel, irregular, or incongruous stimuli.

Some of the behavioral and personality changes associated with AD may reflect a diminished tendency to seek novel and varied stimulation. Clinical descriptions and results of survey data on AD patients emphasize the development of passivity, apathy, and indifference. Patients often withdraw from their environment, and interests and activities become increasingly restricted. These behavioral changes are notoriously difficult to measure. Cognitive test batteries do not address these behavioral features nor do they assess curiosity drive or novelty-seeking behavior. The few existing studies of such behavioral changes have relied on interviews with the patient or caregiver or on data derived from inventories completed by appropriate informants.[2-5] These methods have limitations, as inventory items are descriptive, not operationally defined, and very dependent on the subjective views of the caregiver.

The experimental methodology described in this report provides an objective measure of eye movements during visual exploration. Neurophysiological, psychophysical, and behavioral evidence converge to suggest that voluntary distribution of visual attention is tightly linked to visual fixation and saccadic eye movements.[6-13] Eye movements have therefore been used in the study of different aspects of directed attention, including responses to behaviorally relevant events in the periphery, scanning and exploratory strategies, and novelty-seeking behavior.[36-43]

The lack of a significant correlation between performance on the curiosity tasks and scores on the Blessed Dementia Scale implies that novelty-seeking behavior represents a distinct behavioral domain. The poor performance by AD patients cannot be adequately explained by a general deterioration in cognition involving faculties such as memory, concentration, or language. Two of the AD patients who performed most poorly on the Curiosity Slides exhibited only mild cognitive impairment as indicated by scores of 3 and 7 on the IMC Subtest of the Blessed Dementia Scale, in support of previous observations suggesting that in a subgroup of AD patients, the earliest symptoms may not be cognitive deficits (eg, amnesia) but diminished curiosity or disengagement from the environment.[2] The nearly equal distribution of dwell time expended by AD patients on the incongruous and congruous stimuli also argues against the hypothesis that they were overwhelmed by an inability to make sense of novel stimuli and therefore actively avoided them.

Impairment of elementary aspects of ocular motility cannot adequately account for the findings of the present study. The clinical neuro-ophthalmologic examination did not detect any major abnormalities in extraocular movements. There were no defects that could have prevented subjects from performing a task that involved looking at visual stimuli separated by 12° of visual angle (Curiosity Slides) or a picture slide with several AOIs (Incongruous Picture Slides). On the Saccade to Target Task, AD patients were able to direct their gaze to all four quadrants and they performed as well as controls on several measures of ocular motility including saccade amplitude and percent of trials exhibiting hypometria or hypermetria.

The few available studies on attention in AD have reported deficits.[44-48] The possible contribution of deficits in vigilance and shifts of attention to the AD patients' poor performance on the curiosity tasks needs further clarification. In the present study, on the Saccade to Target Task, which assessed these factors, AD patients had significantly fewer correct trials, but there was no significant correlation between performance on the Saccade to Target Task and performance on the Curiosity Slides Task. A lack of correlation between performance on the Curiosity Slides Task and the Concentration Subtest of the Blessed Dementia

Scale further suggests that other deficits in attentional tone (concentration or vigilance) cannot account for the findings. Also of note, patients with AD spent almost 80% of dwell time on either the congruous or incongruous stimuli, although these took up only a small proportion of the available space at which to look. This indicates that the visual fixations of the AD patients were not randomly distributed as might be expected if they were simply not attending to the task. We interpret the tendency of AD patients to spend more time than normal controls looking at neither of the two stimuli as further evidence that they are not as attracted to visual stimuli with higher information content.

In summary, neither dementia severity nor more elementary problems with ocular motility or visual attention seem to account for this study's major finding that AD patients attend to novel stimuli and explore their visual environment significantly less than nondemented controls. Such behavior deprives AD patients of a normal range of varied experiences and exposure to informative aspects of their environment. It is possible that AD patients have an impaired capacity to identify stimuli that are novel, complex, or incongruous, and thus may be relatively indifferent to them. Alternatively, AD patients may have a diminished novelty-seeking drive and therefore may not seek stimuli that are novel either perceptually or conceptually. These cognitive and motivational components of diminished curiosity may be linked, as the neural mechanisms that mediate the detection of novelty may also drive subjects toward it. Both components may be contributing to the apathy, loss of initiative, and diminished engagement noted in clinical accounts of AD.

Directed attention has been hypothesized to be controlled by an integrated cerebral network with three major cortical components: the posterior parietal lobe, frontal eye fields, and cingulate gyrus.[49-51] Although the neural substrate underlying novelty-seeking behavior is not as well established as for other aspects of directed attention, behavioral and electrophysiologic research in monkeys and humans has suggested that in addition to the three cortical components noted, there is an important role for temporal-limbic structures and prefrontal association cortex.[52-57] Recent work also has indicated that the basal forebrain responds to novelty, which then may modulate cortical responses.[58] All of these regions appear to be heavily involved in the distribution of pathology in AD.[59-64]

The results of our study need to be replicated with a larger sample size, expanded tests of visual attention and exploration, and more detailed neuropsychological study. The current study has demonstrated that the methodological approach of studying eye movements in response to provocative visual stimuli is a promising one for the investigation of deficits in directed attention, exploration, and curiosity that may underlie some of the cognitive, behavioral, and personality changes associated with Alzheimer's disease.

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