Eye tracking during a visual paired comparison task as a predictor of early dementia

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Abstract

The authors present profiles of performance on a behavioral task (Visual Paired Comparison) using infrared eye tracking that could potentially be useful in predicting the onset of Alzheimer's Disease. Delay intervals of 2 sec and 2 min were used between the initial viewing of a picture and when the picture was displayed alongside a novel picture. Eye-tracking revealed that at the 2 second delay, 6 mild cognitively impaired patients (MCI), 15 matched control subjects (NC), and 4 neurological control subject's with Parkinson's Disease (PD) performed comparably, i.e., viewed the novel picture greater than 71% of the time. When the delay increased to 2 minutes, MCI patients viewed the novel picture only 53% of the time ($p < .05$), while NC and PD remained above 70%. These findings are consistent with the idea that the MCI patients did not remember well which picture was recently viewed. These findings demonstrate the usefulness of this task for assessing normal as well as impaired memory function.

Keywords

mild cognitive impairment; Alzheimer's Disease; eye tracking; early diagnosis; visual paired comparison; preferential looking

Introduction

The diagnosis of mild cognitive impairment (MCI) refers to individuals who have memory loss but relatively preserved abilities in other cognitive areas (1). Unfortunately, this population appears to be at high risk for developing dementia, especially Alzheimer's Disease (AD) (2). A review of the literature suggests that the progression rate from MCI to AD is between 6 – 25% per year (3). Accordingly, patients with MCI are an important target for the development of research strategies that could lead to early diagnosis and possible prevention of dementia (4).

The memory impairment associated with MCI has been linked to structural changes beginning in the medial temporal lobe (5,6). In particular, structures in the medial temporal lobe, including the hippocampal region, together with the entorhinal, perirhinal, and parahippocampal cortices have been found to make up what is now referred to as the medial temporal lobe memory system. Damage to components of this system produce impairments in declarative memory, i.e. the ability to consciously recollect facts and events (7,8). These impairments in declarative memory give rise to the hallmark memory complaints made by AD patients and observed by their family members. However, given the lengthy prodromal phase of AD, which can last up to 7 to 10 years (9,10), many of the early memory changes that take place can go undetected until well into the course of the disease. Therefore, it will be critical to have available very sensitive memory tests in order to detect memory deficits as early in the disease process as possible.

A task that is proving to be highly sensitive to memory impairment is the visual paired-comparison (VPC) task (11). The VPC task is a recognition memory task that assesses the proportion of time an individual spends viewing a new picture compared to a picture they have previously seen, i.e. novelty preference. An important characteristic of normal individuals is that they tend to focus disproportionately more attention on those aspects of the environment that are the most novel (12-14). In regards to the VPC task, expected normal performance would presumably be characterized by more time spent looking at the new picture than the old one. By contrast, memory impaired performance might be characterized by looking times that were about equally distributed between the novel and familiar pictures, i.e. impaired declarative memory for what has already been viewed.

It has previously been demonstrated in three species, rats (15) humans (16,17) and monkeys (18,19), that lesions of the hippocampus produce impaired declarative memory and impaired performance on the VPC task. In monkeys, performance on the task was impaired even when 70 – 80% of the hippocampus was spared (19). Moreover, monkeys with hippocampal lesions performed relatively worse on the VPC task than on other tests of recognition memory when the same delay intervals were used. Therefore, the VPC task appears to be very sensitive to minimal damage to the hippocampus and ought to be especially useful in detecting impaired declarative memory in individuals with little detectable damage to the hippocampus, e.g. patients with MCI who are in the early stages of AD.

The VPC task also has many advantages over other memory measures. Unlike many declarative tasks that require extensive training, the VPC task requires little to no instruction. Additionally, the VPC task requires no language comprehension or production, as well as minimal motor output, hence its previous successful use with rodents (15), primates (19), infants (20) and adults (17,21). Therefore, the VPC task can be used with participants whose verbal and motor skills substantially vary. This is quite beneficial when assessing for cognitive deficits in individuals with varying educational backgrounds and intellectual capabilities.

Performance on the VPC task can be analyzed in considerable detail when it is administered in conjunction with the use of non-invasive infrared eye tracking. Recent studies have taken

advantage of these new eye tracking techniques to examine eye movement patterns in patient populations with Alzheimer's Disease (13,22) and Parkinson's Disease (23). For example, Daffner and colleagues (13) demonstrated that patients with AD exhibited reduced curiosity for novel and irregular features of the visual environment and spent significantly less time looking at novel/provocative stimuli than normal controls. They suggested this behavior was reflective of disruption in neural pathways. Accordingly, the use of infrared eye tracking equipment with the VPC task to investigate memory performance in normal and memory impaired individuals could be revealing.

In the present study we have used the VPC task, combined with non-invasive eye tracking, to investigate the following possibilities: 1. Can the VPC task detect mild cognitive impairment in humans? 2. Is performance on the VPC task sensitive specifically to hippocampal damage? If true, neurologic patients without damage to the hippocampus (e.g. patients with Parkinson's Disease) should perform comparably to age-matched controls, and perform differently than MCI patients. 3. Can impaired performance exhibited by the MCI group on the VPC task be attributed to aspects of performance other than memory?

Methods and Materials

Participants

Three subject groups were assessed. Group MCI: Six subjects diagnosed with mild cognitive impairment (mean age = 70.0, SD = 8.1); Group PD: Four subjects with Parkinson's Disease (mean age = 63.8, SD = 6.4); Group NC: Fifteen normal elderly control subjects (mean age = 67.5, SD = 5.6). All participants were recruited from the Alzheimer's Disease Research Center at Emory University, Atlanta, Ga. Informed consent was obtained for each participant in accordance with the regulations of the Institutional Review Board at Emory University.

A detailed medical, social and family history was obtained from each subject. MCI and PD patients had caregivers or informants who could corroborate their history. Participants completed the five subtests of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) neuropsychological battery that included the following subtests: Animal Fluency, Boston Naming Test – 15 item (BNT-15), Mini-Mental Status Exam (MMSE), Word List Memory (WLM) and Constructional Praxis (CP). Additional neuropsychological tests included Trail-Making Tests Parts A and B (TMT-A, TMT-B), Digit Span subtest of the Wechsler Adult Intelligence Scale – Revised (WAIS-R), and the Clock Drawing Test (24). The Geriatric Depression Scale (GDS) was administered to assess for the presence of depressive symptomatology. Group demographic information and neuropsychological performance for the three groups are summarized in Table 1. MCI and PD patients also received a full neurological examination. Clinical diagnoses of MCI, PD, or NC were established following a standardized assessment and review by three clinicians, expert in evaluation and management of Geriatric Neurology patients. Clinical diagnosis of MCI required evidence of a decline in baseline function in memory and possibly additional cognitive domains, with the severity of symptoms or consequent functional limitations insufficient to meet DSM-III (R) criteria for Dementia. A diagnosis of PD was given if the participant fulfilled the criteria for PD according to the United Kingdom Parkinson's Disease Society Brain Bank clinical diagnostic criteria (25). Participants were classified as NC if they demonstrated no evidence of cognitive decline from baseline functioning based on their clinical interview and assessment. Exclusion criteria included a history of substance abuse or learning disability, dementia, neurological (e.g. stroke, tumor) or psychiatric illness. Because the VPC task involves visual memory, subjects were also excluded if: 1) the eye tracking equipment could not achieve proper pupil and corneal reflection due to physiological constraints or visual problems (e.g. droopy eyelid, cataracts, detached retinas, glaucoma, pupils too small [7 subjects]); and/or 2) they could not complete the calibration procedure (3 subjects).

Equipment and Stimuli

During the task, participants' eye movements were continuously recorded using an Applied Science Laboratories (ASL) Model 5000 remote pan/tilt camera system. A ring of filtered near-infrared LEDs illuminated the eye and a high-speed, near-infrared sensitive CCD camera captured the pupil and corneal reflection. The gaze angle was determined by the relative positions of corneal and pupil centers with an accuracy of ±0.75°. The system sampled at 60 Hz, with a temporal resolution of 16 ms and linearity less than 10%. The participants were seated approximately 26 inches from a 19-inch flat panel computer screen that displayed the stimuli. No physical constraints other than a chinrest were used with the participants. Calibration for each subject was accomplished using a nine-point array. Eye fixation and eye movement data were recorded with ASL EYEPOS software. All images were black and white, high contrast clipart images measuring 4.4 inches wide by 6.5 inches high. Unique pictures were used for each trial.

Procedure

Participants were brought into the testing room and seated comfortably in front of the monitor and their heads positioned within the chinrest to maintain their head/viewing position. Prior to presentation of the VPC task, a 9-point calibration procedure was completed. This was accomplished by having the subject fixate nine points at known locations on the computer monitor. The experimenter adjusted the calibration until the subject's fixations accurately mapped onto the calibration points on the screen. This calibration procedure enabled the eye tracking system to accurately compute the subject's gaze position on the computer monitor. Next, participants were informed that images would begin to appear on the computer screen. They were simply instructed that they should look at the images "as if watching television." During the calibration and the test phase, the subjects eye fixations and eye movements were recorded and stored for later analyses.

The entire testing procedure lasted approximately 25 - 30 minutes, including the calibration session. For the VPC task, subjects were administered four blocks of five trials (delay order: 2-minute delay, 2-second delay, 2-second delay, 2-minute delay) for a total of 20 trials. Each trial consisted of two phases; a familiarization phase followed by a test phase. During the familiarization phase, two identical pictures were presented side-by-side on the monitor for five seconds. The monitor then went dark for a delay interval of either two seconds or two minutes. Then, in the test phase, two pictures were again presented side-by-side for five seconds. One of the images was identical to the image presented during the familiarization phase and the other was a novel image. The side of presentation of the novel picture was selected pseudorandomly and it was presented equally often on the left or right side of the monitor screen. After the test phase of the trial, the monitor was darkened for 20 seconds until the beginning of the next trial. In order to ensure subject attention for test trials that had two-minute delays, the experimenter verbally alerted all subjects that there was "approximately ten seconds before the next pair of images."

Data Analysis

Eye fixation and eye movement data for each participant were extracted and analyzed off-line using ASL EYENAL software. A fixation was defined as a point of gaze continually remaining within 1° of visual angle for a period of 100 msec or more. For the data analysis in the current study, the fixations analyzed occurred within two designated areas of interest (AOIs): the area of the novel image, and the area of the familiar image. Fixations outside the two areas were not included in the present analysis.

Eye tracking data were characterized using three measures: (1) total looking time (i.e. the total sum of the duration for all fixations); (2) total number of fixations (i.e. the total number of

fixations that met the ≥ 100 msec criterion); and (3) percent looking time on novel image. For each measure, we calculated the median of the ten trials at each delay interval (2-sec, 2-min) for each subject. Finally, each measure was analyzed using a separate 3×2 repeated measures ANOVA, with group (MCI, PD, NC) as the between-subjects factor and delay (2-seconds, 2-minutes) as the within-subjects factor. All post-hoc pairwise comparisons were performed using the Tukey-Kramer test at α = .05 (two-tailed).

Results

Demographics and global cognitive status

Analyses revealed there were no significant differences among the three subject groups in age, education, or global cognitive functioning as measured by several of the tests used by the CERAD, as well as the Trail Making Test, Digit Span, Clock Drawing, and the Geriatric depression Scale (all p's > .05). *).* However, the MCI group was impaired on both the Word List Memory Total and the Word List Memory Delayed Recall measures compared to the NC group (p's < .01). The MCI group was also impaired relative to both the NC (p < .01) and PD (p < .05) groups on a visuo-construction task as measured by the CP copy measure. On the delayed recall version of this task the MCI group performed worse than the PD group (p < .05). No significant group differences in performance on any other neuropsychological measures were detected (all p's > .05). Results are summarized in Table 1.

Familiarization phase: Total looking time and total number of fixations

During the familiarization phase, subjects were presented with two identical stimuli for 5 seconds prior to a 2-second or 2-minute delay. For total looking time (Table 2), the effects of group (F (2,22) = 1.55, p = .24), delay (F (1,22) = 1.73, p = .20) and group by delay interaction (F (2,22) = 1.09, p = .35) were nonsignificant, suggesting that the three groups did not differ in the overall amount of time they spent looking at the familiarization images prior to either delay. Similarly, for the total number of fixations i.e., looking at either of the two identical stimuli, during the familiarization phase (Table 2), the effects of group (F (2,22) =1.26, p = .30), delay (F (1,22) = 0.04, p = .85), and group by delay interaction (F (2,22) = 0.22, p = .80) were nonsignificant. These results indicate that all three groups made a similar number of fixations during the familiarization phase.

Test phase: Percent time looking at the novel image

During the test phase, subjects were presented with the original image from the familiarization phase together with a novel image for 5 seconds. The percent time looking at the novel image was the main measure of interest. There was a significant group by delay interaction (F (2,22) = 5.39, p = .012). For the 2-second delay, all three groups spent similar amounts of time looking at the novel image (71-76%; F (2,22) = 0.50, p = .61); Figure 1 and Table 2. However, for the 2-minute delay, the groups differed in their percent time looking at the novel stimulus (F (2,22) = 7.69, p =.003). Specifically, the MCI group spent only 53% of their total looking time viewing the novel image, compared to the PD group (71%) and the NC group (74%) (*p*'s < .05). The PD and NC groups did not differ from one another (*p* =.91).

Additional analyses revealed that impaired performance of the MCI group at the 2-minute delay could not be accounted for by group differences in the overall time spent looking at the images or by group differences in the overall number of fixations on the images. For total number of fixations (Table 2), the effects of group (F (2,22) = 0.81, p = .46), delay (F (1,22) = 0.09, p = .77) and group by delay interaction (F (2,22) =1.12, p = .34) were nonsignificant. This demonstrates that all three groups made similar numbers of fixations during the test phase. Furthermore, for total looking time the effects of group (F (2,22) = 2.03, p = .16), delay (F (1,22) = 0.16, p = .69), and group by delay interaction (F (2,22) = 0.72, p = .50) were also

nonsignificant. Therefore, groups did not differ in the amount of overall time spent looking at images during the test phase.

Discussion

The present study, to our knowledge, is the first to combine eye tracking together with a visual paired comparison (VPC) task of recognition memory. In the following sections we address the questions we raised in the Introduction.

1) Can the VPC task detect mild cognitive impairment in humans?

This work has demonstrated that patients diagnosed with MCI display impaired recognition memory performance compared to NC and PD groups. Specifically, all three groups demonstrated equivalent recognition memory performance (characterized by increased viewing time of the novel image relative to the familiar image) at the 2-sec delay. However, the MCI group showed a significant reduction in the amount of time they spent looking at the novel image when the delay interval was increased to two minutes (Figure 1). At the 2-min delay, NC and PD groups spent 74% and 71% (respectively) of the total looking time viewing the novel stimulus; obversely, they viewed the familiar image only 26 - 29 % of the total looking time. By contrast, the MCI group spent only 53% of the total looking time viewing the novel stimulus, and 47% of the total looking time viewing the familiar stimulus. Thus, the MCI group spent about equal amounts of time looking at both the novel and familiar images. These results suggest that the delay interval of 2 minutes sufficiently challenged the memory system so that the MCI subjects no longer remembered which image they had previously seen. Thus, the VPC task can successfully detect MCI in humans.

2. Is performance on the VPC task sensitive specifically to hippocampal damage?

The MCI group did not meet DSM-III criteria for dementia (Table 1). Instead, the MCI group evidenced a decline in memory function as measured by some of the tasks described in Table 1, and in particular by their selective deficit in performance on the 2-min delay portion of the VPC task, but not on the 2-sec delay portion of the task (the relevance of findings with the 2-sec delay is discussed below). Thus, one can ask whether there is evidence that links MCI impairment to disruption limited to the brain's memory systems, e.g., the medial temporal lobe (MTL) memory system (8), and the hippocampus in particular. There are cumulating data from work with animals as well as with humans suggesting that the impairment in the MCI group reported here is linked to hippocampal dysfunction. Specifically, the observed performance on the VPC task by the MCI group closely resembles performance on a similar VPC task administered to nonhuman primates who sustained lesions limited to the hippocampus (19). The monkeys with hippocampal lesions had a reduction in looking time at the novel stimulus as the delay interval on the VPC task was increased from 1 sec to 10 min (Figure 2). These monkeys had lesions of the hippocampus made by radiofrequency or by ibotenic acid. Similar to the MCI patients in the present study, monkeys with either RF or IBO lesions spent more time viewing the novel image on the VPC task when the delay interval was short (1 sec), with less time viewing the novel image as the delay interval increased. A similar pattern has also been observed in rats with hippocampal lesions (15). Other studies using memory impaired patients with damage limited to the hippocampus and similar tasks of recognition memory have also pointed to the importance of intact hippocampal function for successful performance (26). Thus, findings from work in humans, as well as monkeys, and rats all provide converging evidence that impairment on the VPC task reflects memory problems associated with hippocampal dysfunction.

A question arises whether the VPC task is sensitive specifically to medial temporal lobe damage in MCI or whether patients with other neurologic conditions, not specifically involving the

medial temporal lobe, would show impaired performance as well. In the present study, we addressed this question by assessing patients with PD as well as patients with MCI. PD is characterized by degeneration of dopaminergic neurons in the substantia nigra resulting in a depletion of dopamine. This depletion results in an abnormal motor behavior (e.g. resting tremor, rigidity, and akinesia) observed in this patient population (27,28). The cognitive profiles of PD patients can be heterogeneous and are frequently dominated by deficits in executive functioning (e.g. multi-tasking, planning, use of feedback) and visuospatial/ visuoconstructional difficulties (29-31). While memory impairment can occur in patients with PD (32,33), these memory deficits are not attributed to an insidious disease process occurring in the medial temporal lobe. In the current study, recognition memory performance was unaffected by the presumed subcortical damage associated with the PD group, suggesting that the VPC task is more selective to medial temporal lobe dysfunction (but see Whittington et al, 2000 [32] for a meta-analysis of recognition impairment in Parkinson's Disease). These results lend support to the possibility of utilizing the VPC task as an early diagnostic measure since it appears to be specifically sensitive to memory impairment. However, further longitudinal studies will need to be performed to investigate the use of the VPC task in this capacity.

At the time of the present study, only one of the six MCI subjects had undergone magnetic resonance imaging (MRI) scanning. This patient was impaired in all of the tasks that the MCI group was impaired on in Table 1. Additionally, this patient's performance on the VPC task was 62% at the 2-min delay, a score that was worse than all but one control subject. In the MCI subject, an MRI examination without gadolinium was performed according to a standard department (Neurology) protocol on a 3T magnet (Siemens Magneton Trio). Axial gradient-echo images for susceptibility were also performed. The clinical report, based on reviews of the images, indicated scattered foci of T2 prolongation in the periventricular and subcortical white matter of both hemispheres. Additionally, slight prominence of the sulci, cisterns, and ventricles, consistent with mild diffuse volume loss was noted. There was no evidence of acute territorial infarction, hemorrhage, mass, mass-effect or midline shift. The major intracranial vascular flow-voids also were reported as intact. Importantly, there was no reported evidence of abnormalities in the hippocampal region or in adjacent cortical regions of the medial temporal lobe. While the evidence is sparse, the MRI findings from this case raise the possibility that impaired performance on the VPC task by patients with MCI might precede detectable structural changes in the hippocampus and the medial temporal lobe region. If true, sensitive behavioral tasks like the VPC task combined with infrared eyetracking might serve as predictive biomarkers for underlying but as yet undetectable brain pathology or regional brain dysfunction, e.g., vascular subcortical pathology.

3. Can the impaired performance exhibited by the MCI group on the VPC task be attributed to aspects of performance other than memory?

It is possible that the differences in performance between the MCI and the NC groups on the 2-min delay portion of the VPC task could occur for reasons other than memory impairment on the part of the MCI group. Several possibilities include differences between the MCI and the NC groups in global cognitive status and demographics, or differences in attentional, motivational, and perceptual functions. However, as shown in Table 1, the groups were equivalent on cognitive status, age and education. Nor can the results be explained by group differences in attentional, motivational, or perceptual abilities since all groups performed equivalently at the 2-sec delay. Analyses revealed that all three groups were equivalent in the total amount of time they viewed the pictures during either phase, indicating all three groups were similarly able to attend to and accurately perceive the stimuli. Additionally, the number of fixations that met criteria for analyses cannot account for the observed group differences because the number of fixations that met criteria was not different for any group. Thus, the two groups performed quite similarly in all important ways that might have provided evidence for

a competing hypothesis to that of impaired memory in the MCI group. Accordingly, the idea that the MCI group's impaired performance on the 2-min delay portion of the task resulted from impaired memory remains compelling.

An additional point of importance involves the benefit derived from combining infrared eye tracking with the VPC task. Infrared eye tracking research is becoming distinguished in its diagnostic role (13,22,32). As used in the present study, eyetracking provided objective and quantitative evidence of each subject's visual, attentional, and memory processes. Moreover, the eye movement data were acquired in an unobtrusive, noninvasive manner and provided on-line measures as well as data-based storage of information for later analyses. Additionally, eyetracking allowed for a number of potentially informative and sensitive measures in addition to a simple novel stimulus viewing-time measure. Thus, two additional parameters we measured, i.e., overall viewing time, and number of fixations, helped to eliminate the possibility that the impaired performance by the MCI group could have been attributed to other than mnemonic dysfunction. Additional measures not examined in this paper (e.g. saccade length and latency, pupil diameter, inter-fixation durations, etc.) might also be of potential help in gaining more understanding of the perceptual, as well as encoding and retrieval processes during stimuli presentation and recognition, thus providing more insight into the nature of normal and impaired memory.

Conclusion

The results from the current study demonstrate that the VPC task combined with eye tracking technology can be used successfully with normal elderly adults and with elderly neurologic patients. Additionally, eye-tracking performance on the VPC task can be used to detect mild memory impairments associated with MCI. Moreover, VPC performance, as measured by percent time viewing the novel stimulus, appears to be selective to declarative memory impairment reflective of medial temporal lobe dysfunction since patients with subcortical damage performed comparable to control subjects. Finally, the recording of eye tracking performance during a VPC task has the potential to be an effective screening tool. With further investigation, it could potentially be used as a diagnostic measure and to maximize early therapeutic intervention (34,35).

Acknowledgements

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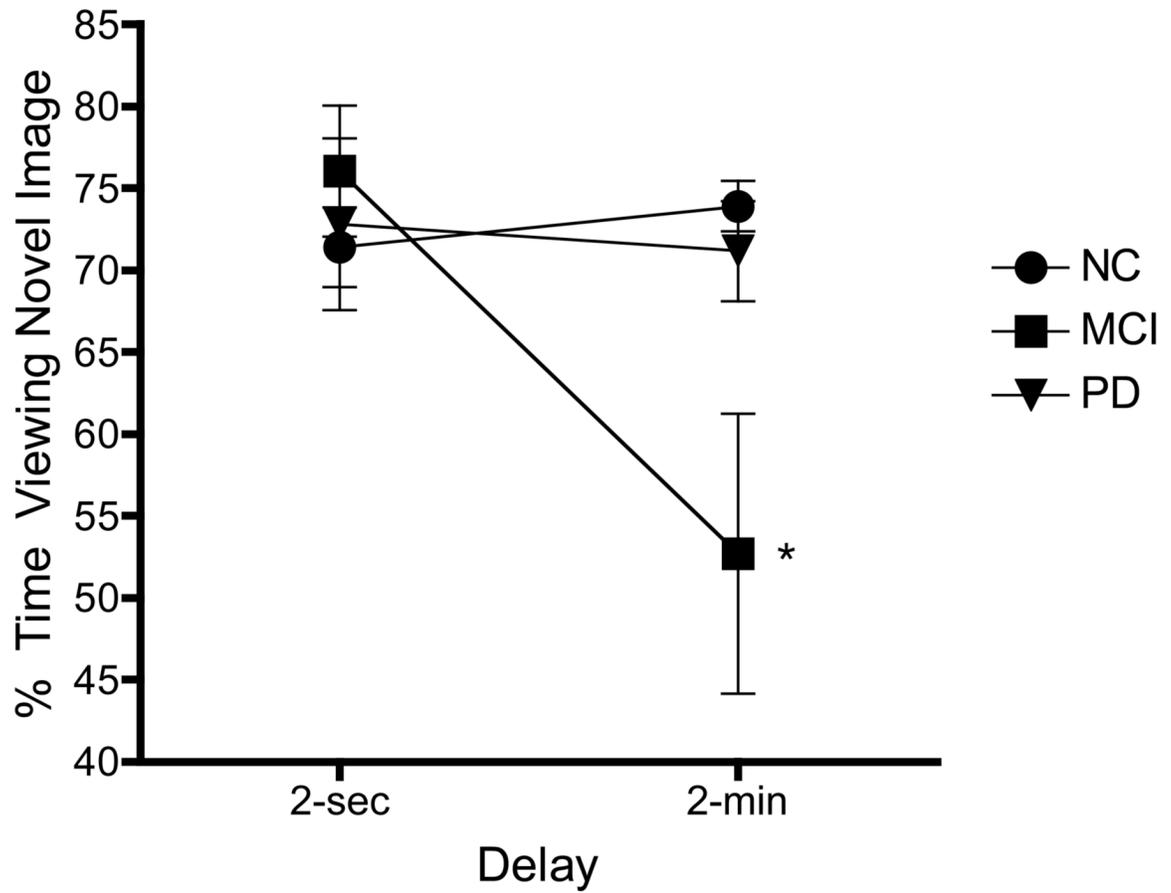
Figure 1.
Group differences in percent time looking at either the novel images at the 2-second and 2-minute delays (test phase). An asterisk indicates that the MCI group significantly differed ($p < .05$) from both NC and PD groups in the amount of time spent looking at the novel images at the 2-minute delay. Error bars reflect standard error.
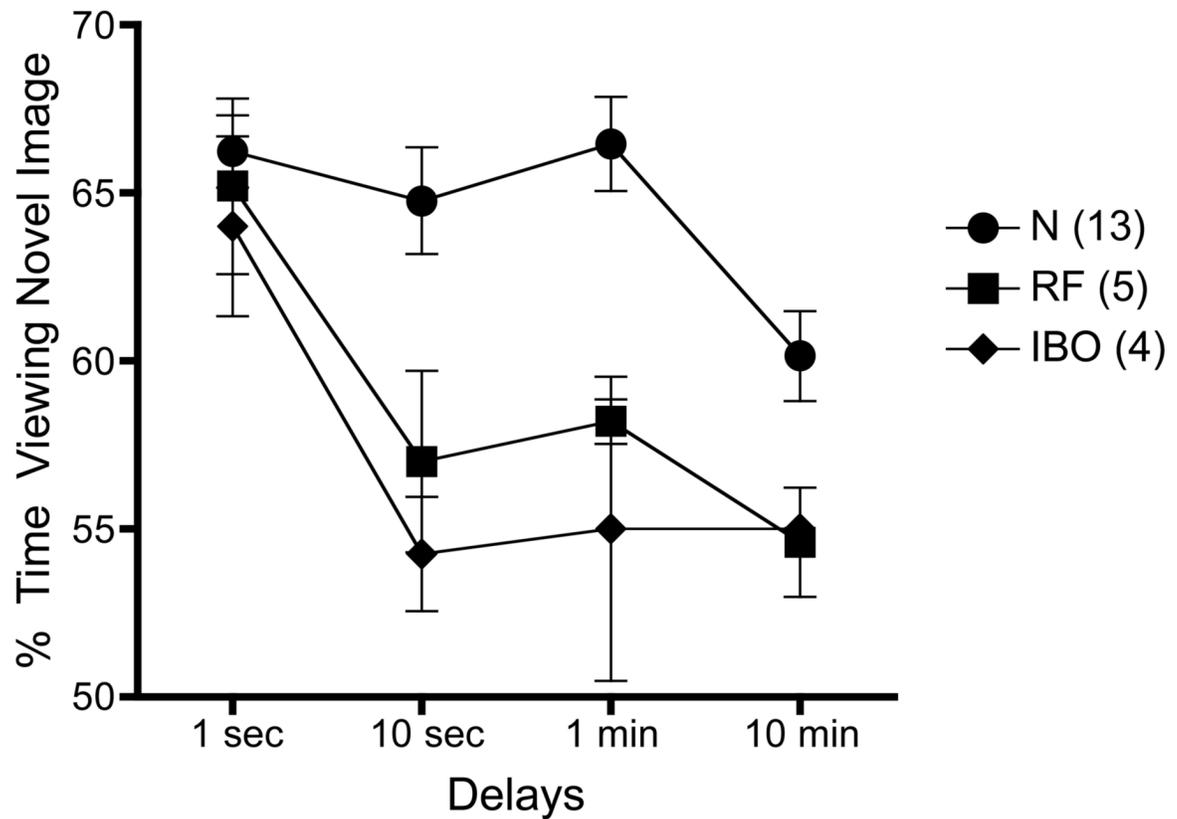
Figure 2.
Performance on the visual paired-comparison task by monkeys with lesions limited to the hippocampal region. In monkeys, performance on this task can be impaired even when 70% to 80% of the hippocampus is spared, either when the lesion is made by ibotenic acid or radio frequency. Parentheses indicate the number of monkeys in each group. N= normal; RF = lesion created by radio frequency; IBO = lesion created by ibotenic acid. Graph is adapted from Zola et al, 2000.

Table 1

Group demographic information and neuropsychological performance scores

Measure	NC	MCI	PD	Tukey-Kramer [*]
Total N	15	6	4	
Age	67.5 (5.6)	70.0 (8.1)	63.8 (6.4)	ns.
Education	16.4 (2.3)	16.3 (2.7)	15.0 (2.6)	ns.
CERAD[a]				
Animal Fluency	20.9 (2.9)	16.2 (5.6)	17.0 (4.3)	ns.
Boston Naming Test −15	14.6 (.6)	14.0 (.9)	14.8 (.5)	ns.
Mini-Mental State Exam	29.1 (1.3)	27.5 (2.8)	29.0 (.8)	ns.
Word List Memory (WLM)				
WLM total	24.0 (4.5)	17.8 (1.9)	21.0 (1.7)	NC vs MCI p<.01
WLM delayed recall	8.1 (1.8)	5.2 (2.4)	7.3 (.5)	NC vs MCI p<.01
Constructional Praxis (CP)				
CP copy	10.9 (.3)	9.7 (1.5)	11.0 (0)	NC vs MCI p< .01 PD vs MCI p<.05
CP delayed recall	9.9 (2.1)	7.2 (3.8)	12.0 (1.4)	PD vs MCI p<.05
Trail Making Test (TMT)				
TMT- A	33.6 (15.7)	42.8 (16.1)	36.7 (8.0)	ns
TMT- B	74.8 (33.5)	93.7 (14.9)	59.3 (15.5)	ns
Digit Span Forwards	11.1 (2.0)	9.3 (2.2)	13 (2.0)	ns
Digit Span Backwards	8.1 (2.4)	6.8 (1.3)	7.0 (3.6)	ns
Clock Drawing Test	12.7 (.6)	12.7 (.5)	12.0 (1.7)	ns
Geriatric Depression Scale	2.4 (3.1)	3.0 (1.7)	2.7 (3.8)	ns

Note: The mean for each variable is given with SD in parentheses; ns. = ANOVA not significant,; no post-hoc tests were performed.

NC= normal control; MCI = mild cognitively impaired; PD = Parkinson's Disease

[*] If the ANOVA F was significant ($p < .05$), then the Tukey-Kramer post-hoc pair-wise comparisons were performed and p values are presented.

[a] Consortium to Establish a Registry for Alzheimer's Disease

Table 2

Mean and standard deviations for total number of fixations and total looking time during the familiarization and test phases

Eye tracking variables	NC	PD	MCI	Tukey-Kramer
Familiarization phase				
Total number of fixations				
2-second delay	10.53 (3.09)	11.00 (1.15)	8.83 (2.42)	ns
2-minute delay	10.77 (1.96)	10.25 (1.71)	9.00 (4.16)	ns
Total Looking Time (secs)				
2-second delay	2.85 (1.05)	3.37 (0.37)	2.46 (0.78)	ns
2-minute delay	2.90 (0.54)	2.76 (0.42)	2.27 (0.99)	ns
Test phase				
% Looking Time on Novel Stim.				
2-second delay	71.39 (9.47)	72.82 (10.50)	76.06 (9.78)	ns
2-minute delay	73.75 (5.82)	71.18 (6.10)	52.71 (20.90)	*
				NC vs MCI p< .01
				PD vs MCI p< .05
				NC vs PD ns
Total number of fixations				
2-second delay	10.83 (2.93)	10.50 (1.96)	8.42 (3.97)	ns
2-minute delay	10.50 (2.60)	10.00 (2.45)	9.75 (2.54)	ns
Total Looking Time (secs)				
2-second delay	3.03 (1.07)	3.52 (0.52)	2.24 (1.12)	ns
2-minute delay	3.06 (0.79)	3.35 (0.42)	2.58 (0.86)	ns

Note: The mean for each variable is given with standard deviations in parentheses NC = normal control; MCI = mild cognitive impairment; PD = Parkinson's Disease

No significant differences were detected between NC and PD (p = .85); ns = nonsignificant.

[*]
Tukey-Kramer post-hoc comparisons revealed significant differences between MCI and PD (p < .047), and MCI and NC (p < .002).