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Visuomotor Integration Is Compromised in Alzheimer's Disease Patients Reaching for Remembered Targets

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Key Words
Alzheimer's disease · Visuomotor transformation · Visuomotor ability

Abstract
This study examined the ability of neurologically healthy individuals and individuals with Alzheimer's disease (AD) to successfully complete procedures involving short-term spatial visuomotor memory tasks, and tasks involving increasingly complex visuomotor transformations. Participants made sliding finger movements over a clear touch-sensitive screen on two separate spatial planes (vertical and horizontal), to visually constant and remembered target positions. Significant main effects were observed between participant groups on reaction time and movement time measures. As well, significant changes in reaction time and movement time were observed within the patient group over the different of any experimental procedures. In addition, as task increased in complexity significant increases in errors were observed in the AD group. Overall, the results reveal that AD patients show substantial declines in their ability to process and integrate visual information to produce motor responses. Therefore, we believe that this psychophysical research provides further evidence that AD, even early stages of AD, can affect anatomical regions supporting vision for action.

Introduction

Reaching for a visual target in extrapersonal space requires a series of complex neural computations, commonly referred to as visuomotor transformations. Visuomotor transformations rely on our ability to successfully integrate visual information about hand and target position, which is then relayed to motor regions that control muscles and joint motion. This information can be updated, monitored and adjusted using visual feedback in order to reach the target [1–8]. When a task increases in visuomotor complexity, reliance on visual feedback increases. Complex skills refer to those skills requiring arbitrary associations, or 'nonstandard' mappings, where the goal of the movement is not in direct spatial alignment with the visual stimulus guiding it [9, 10]. In these more complex tasks, the successful integration of visual information is of paramount importance in generating effective motor responses. Individuals with certain disorders can struggle with the process of transforming visual stimuli into the appropriate motor commands. One such disorder not typically associated with limited visuomotor ability, but which has recently been shown to involve a number of impairments in processing visuomotor stimuli, is Alzheimer's disease (AD) [11–13].

To date, the majority of research examining AD has focused on cognitive and memory impairments [14–18].

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However, researchers have recently begun to identify other symptoms such as motor deficits [19–23], which can cause significant disruption in their ability to complete effective sensory-guided movements. In the past, visuomotor/motor dysfunction observed in AD patients was often dismissed as a causal factor of advancing age [24]. However, recent research has indicated that impaired visuomotor performance can be linked to AD deficits [13, 21, 22, 25, 26]. Psychophysical research exploring visuomotor ability in AD individuals has shown that even mild cognitive impairments can compromise their performance in producing effective motor response to visual stimuli [13, 19, 22, 23, 27]. These visuomotor performance impairments can occur even before early signs of initial cognitive impairments (i.e. memory disruptions) are observed [22]. Specifically, AD patients are compromised in their ability to sustain a planned reach to visual targets when visual feedback of the limb is limited, even if the targets remain visible [21, 28]. Other findings suggest that AD individuals have a limited ability to update preexisting or ongoing motor plans, leading to a reduction in visuomotor performance [13]. The capacity to sustain a motor plan or update an existing motor plan relies on the brain's ability to maintain an active role in generating successful responses.

Given the difficulties AD patients have in completing effective motor plans [13, 21], the removal of relevant visual information could result in deficits in reaching targets, not because of poor planning ability, but because of an individuals' inability to effectively access short-term spatial memory of target position, effectively diminishing the use of online feed forward control. One area known to be associated with the storing and responding to information related to the short-term spatial location of objects is the posterior parietal cortex (PPC) [29, 30]. In addition, anatomical research has also indicated that the PPC is one of the primary regions involved in visuomotor function. Recent fMRI research has shown significant overlap of active regions in the PPC during eye and pointing movements [31]. In addition, several additional neurophysiological and imaging studies have indicated that information regarding eye and hand position converge within the PPC [25, 32–35]. Interestingly, one of the primary anatomical areas noted to be affected by AD in the early stages of the disease are regions within the parietal cortex [36], as well as cortico-cortical connections to the frontal lobe [26, 36–38]. These regional deficits may cause early visuomotor disruptions before a significant area of perfusion is observed within cerebral regions primarily identified for cognitive/memory functioning.

In the present study, we compared the performance of AD patients and age-matched controls on eye-hand coordination tasks. Two primary questions were addressed: (1) Does a short-term visuomotor memory delay create greater psychophysical performance deficits in AD participants despite increased time to generate a motor plan? and (2) Can these deficits be further exaggerated with the added task of completing a complex (i.e. nonstandard) visuomotor transformation? Our aims were to characterize the nature of the relationship between these two types of complexity, and to assess movement planning versus movement performance in AD patients. These results will allow an indirect assessment of the contributions of different brain regions to distinct aspects of a reach to remembered targets under nonstandard mapping conditions, and the effect of AD on this process.

Methods

Participants

The performance of 10 control participants (5 male, 5 female, mean age 78.3 ± 3.5, mean years of education 9 ± 2.8, mean Mini-Mental State Exam, MMSE, score 29.40 ± 0.15) was compared to that of 10 patients with a diagnosis of probable AD (3 males, 7 females, mean age 79.6 ± 3.1, mean years of education 8.3 ± 4.4, mean MMSE score 22.50 ± 0.47). Control participants were recruited from the general community. Patient participants were recruited from a local hospital. Participants were excluded if they displayed, reported or if their medical records indicated any uncorrected visual disability or if any medical condition hindered their task performance (i.e. arthritis). Neither participant group had extensive computer experience. Participants signed a consent form outlining the procedures, approved by the York University Human Participants Ethics Committee, prior to participating in the experiment.

Procedure and Apparatus

A laptop computer was used in conjunction with a clear touch-sensitive screen (Keytec Magic Screen: Model KTMT-1315, sampling rate: 100 Hz). The laptop was aligned to the midsagittal plane, approximately 20–30 cm from the subject, the keyboard was approximately at waist height, and the monitor was tilted upward slightly. In conditions 1 ('vertical constant', VC) and 2 ('vertical memory', VM), the touch screen was placed directly over the monitor so that there was a complete spatial correspondence between cursor (cross-hair) representing the finger position on the touch screen and the actual finger movement (standard mapping, fig. 1a, b). In condition 3 ('horizontal memory', HM) the touch screen was placed horizontally in front of the laptop (fig. 1c).

Participants began a trial in the vertical constant condition by fixating on a central start location on the monitor with their eyes and touching the central target with their index finger, as indicated by the cursor on the monitor. All targets were 4 cm in diameter. The participants kept their finger within the central target for a variable time period (center hold time, 2,000 ± 500 ms). At

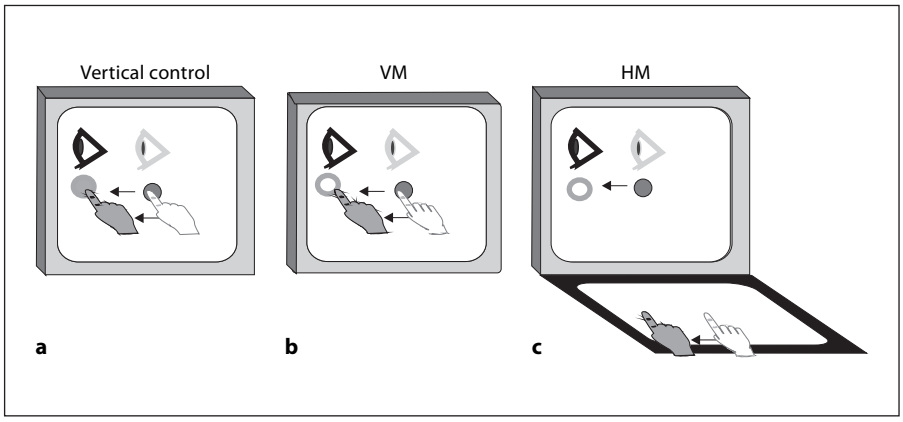

Fig. 1. Experimental conditions: display changes in target visibility (short-term memory task) and spatial changes in screen placement (standard to nonstandard visuomotor transformations). **a** Condition 1 reflects movements made to visible targets (denoted by closed circle) on vertical plane. **b** Condition 2 reflects vertical movements to cued targets (absence of visible target, open circle reflects cued position before movement). **c** Condition 3 displays horizontal movements made to cued targets (absence of a visible cue). Light eye and hand symbols state starting gaze directions and hand locations.

the end of the center hold time, the central target disappeared and one of four peripheral targets, arrayed around the central target at locations of 0, 90, 180, or 270° (0° being directly to the left, increasing angles are clockwise) were presented. The centers of the central and peripheral targets were 9.5 cm apart. The presentation of the peripheral target served as the 'go signal' for the VC condition. Participants then displaced the cursor (under their finger for this condition) by moving their finger to the target, and held the cursor at the peripheral target for 1,000 ms.

In the VM (fig. 1b) and HM (fig. 1c) conditions, participants were required to remember peripheral target positions and to make a movement to remembered target locations after a brief delay period. In addition, the HM tasks required that subjects make an added spatial transformation (i.e. change in spatial location of touch screen). VM and HM procedures included the same parameters as the VC condition. However, the procedure differed in that participants were presented with peripheral targets simultaneously when they touched the center target, and after 1,800 ms the peripheral target would extinguish. Participants were then instructed to wait in the center target location until the center target extinguished (2,200 ms) which was the 'go signal' to move to the remembered target location. After 7,000 ms from the trial start, the peripheral target would reappear to provide participants with feedback of their performance.

Five trials were presented to each of the four target positions in a randomized block design for each of the three conditions, for a total of 60 trials per subject. Participants were given explicit instructions on how to complete the trials in each condition, in addition to being instructed to move as quickly and accurately as possible. Also, participants were instructed to focus on the screen and cursor movement and not to look at their hand. A familiarization phase was conducted at the onset of each new condition to ensure that participants knew how to generate a successful response. Once participants demonstrated knowledge of how to perform a trial correctly, the familiarization phase was terminated and experimental testing began. The familiarization phase never exceeded 6 discrete trials. To limit the amount of task complexity, no stylus or tool (i.e. joystick or mouse) was used to displace the cursor. Procedure reminders were continually provided.

Note that the VC and VM conditions, in which the subject was sliding his/her finger directly over the computer monitor, could be considered 'standard mapping'. In contrast, the HM condition required the use of nonstandard mapping rules for successful completion (i.e. to move the cursor up, required a forward motion on the screen). Therefore the HM condition had the greatest amount of dissociation between the visual stimulus and the required motor action. In addition, real-time continuous visual feedback from the cursor was available throughout the experiment. For the VC and VM conditions, however, this was a redundant form of feedback since the subjects' finger was aligned with the cursor. Lastly, subjects had full vision of their arm.

Data Analysis

Error Trials

In order to track a participant's ability to perform the task successfully, errors were monitored and recorded. An inability to complete a trial correctly could occur in several ways; (1) failure to touch the center target within 5,000 ms of its appearance, (2) failure to maintain position at the center target location prior to the go signal (peripheral target appearance in the VC condition, extinguishing of the central target in the VM and HM conditions), (3) leaving the center target less than 150 ms after the go signal, (4) leaving the center target more than 1,000 ms after the go signal. Also, the VC condition included two additional types of errors; (5) exceeding the maximum movement time (MT) to the outer target (7,000 ms) and (6) failure to maintain the cursor at peripheral target location for 1,000 ms. Error trials were not repeated.

Movement Timing

In the VC condition, the reaction time (RT) epoch began when the peripheral target was presented and ended at movement onset (see below). In the VM and HM conditions, the RT epoch began when the center target extinguished and ended at movement onset. For all conditions, participants who moved away from the center target location prematurely (before the target was extinguished) RT was not scored and the trial was scored as an error trial (see above). If subjects maintained center position (more than 150 ms) but delayed movement onset beyond 1,000 ms (VC condition) or 4,000 ms (memory conditions) after the go signal, this was scored as an error (type 4), and a new trial would be started. In the memory conditions, such a trial would also be included in the RT analysis, with an RT of 4,000 ms. The MT epoch for all conditions began from movement onset and ended at the first point at which

participant's finger slowed to below 10% peak velocity. For the VC condition, if participants moved past the outer target or did not reach the outer target within the allowed 7,000 ms following the go signal, MT was calculated as 7,000 ms, and the trial was also counted as an error trial. For conditions VM and HM, because participants were given a greater amount of time to reach a final position, no trials were scored as errors if participants were not able to reach the outer target location or if they slid their finger beyond the peripheral (remembered) target position.

Movement Trajectories

Individual movement paths were first low-pass Butterworth filtered at 10 Hz (filt function, Matlab, Mathworks Inc.). Movement onset and end points were automatically chosen as the point of 10% peak velocity for each trial individually, using a custom-written computer algorithm. Each point was verified visually to ensure that the end point chosen was the first point at which the movement slowed. For the VM and HM conditions, although full visual feedback of hand position was available throughout the trials, participants did not make corrective movements. This was likely because the procedure required them to move to a remembered position and therefore they had no feedback of the actual target location until the trial was completed. Directional errors were quantified. Trajectories were counted as directional errors if the first half of the trajectory went beyond $\pm 45°$ from the direction of the correct target.

Endpoint Analysis

Constant error (CE) (i.e. endpoint accuracy) was defined as the distance between the participant's mean movement end points for each target location (Σ x/n, Σ y/n) from the actual target position (defined by the x, y coordinates at the center of the target) and calculated for each of the four target positions. Variable error (VE) refers to the distance of endpoints of the individual's movements (σ^2) from his/her mean movements (i.e. movement precision).

Interpretation of MMSE Scores

To assess the level of cognitive ability of patients compared to control subjects, participants completed an MMSE. The MMSE is a standardized cognitive test for assessing mental state. The standard ratings are normally reported as the following: 25–29 is identified as questionable impairment, 20–25 mild impairment, 10–20 moderate impairment and 10 or less is considered severe impairment [15]. The role of the MMSE is to help determine the level of dementia an individual is experiencing.

Results

Performance Timing

We proposed that the AD patients tested here would experience difficulty integrating visual information in order to generate an appropriate reaching movement. We asked whether this difficulty would be evident for movement planning, movement execution, or both. A multivariate analysis between participant groups was performed for each experimental condition on both RT and MT measures. Overall, the AD patients took significantly longer to plan and make a movement than the control subjects. Results yielded a significant main effect of group for both RT and MT measures: RT ($F_{1, 59} = 15.43$, $p < 0.001$), MT ($F_{1, 59} = 18.92$, $p < 0.001$). As well, a significant main effect of condition for both MT and RT were also observed: RT ($F_{2, 59} = 12.73$, $p < 0.001$), MT ($F_{2, 59} = 12.11$, $p < 0.001$). A group $\times$ condition interaction effect was not observed. However, because a large mean increase was observed, particularly within the patient group, when an additional experimental procedure was added, further analysis was conducted to examine if these effects were indeed significant. A within-subject multivariate analysis for the control group displayed significant differences between all conditions for both RT and MT: RT ($F_{2, 29} = 6.19$, $p < 0.05$), MT ($F_{2, 29} = 7.18$, $p < 0.05$). A post-hoc analysis on the control group revealed only significant differences between the VC and HM conditions for both RT and MT ($p < 0.01$). Thus, control participants only displayed significant differences when they were required to employ nonstandard mapping to a remembered target location, the most complex task condition in the study. For the patient group, a within-subject multivariate analysis found significant differences between conditions for both RT and MT: RT ($F_{2, 29} = 7.64$, $p < 0.05$), MT ($F_{2, 29} = 6.05$, $p < 0.05$). A post-hoc analysis found longer RTs for the VC vs. VM conditions ($p < 0.05$) and the VC vs. HM conditions ($p < 0.01$). As well, significantly longer MTs were observed for VC vs. VM ($p < 0.05$) and VC vs. HM ($p < 0.01$).

Thus, regardless of the type of added task complexity (e.g. visually remembered targets, nonstandard mapping) patients struggled to complete the required task. Figure 2 displays the mean RT values for each group observed for each experimental condition. As figure 2 demonstrates, patients have great difficulty planning a motor response in a timely manner, especially when even one additional transformation is required. Figure 3 displays the mean MT values for each group in each experimental condition. As this figure shows, patients also struggled with timely execution of motor plans with added task complexity (i.e. short-term memory tasks and nonstandard mapping).

Note that overall, one can observe a steady increase in RT and MT for both patients and controls as the experimental conditions increased in difficulty, particularly in the HM condition (fig. 2, 3).

Task Completion Errors

Overall, there were substantial increases in errors for all participants when required to complete experimental

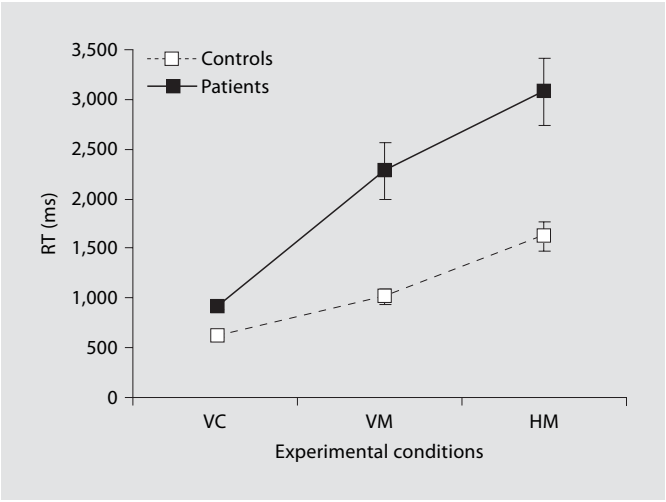

Fig. 2. RT results for all experimental conditions, VC, VM, and HM. Error bars represent standard error of the mean.

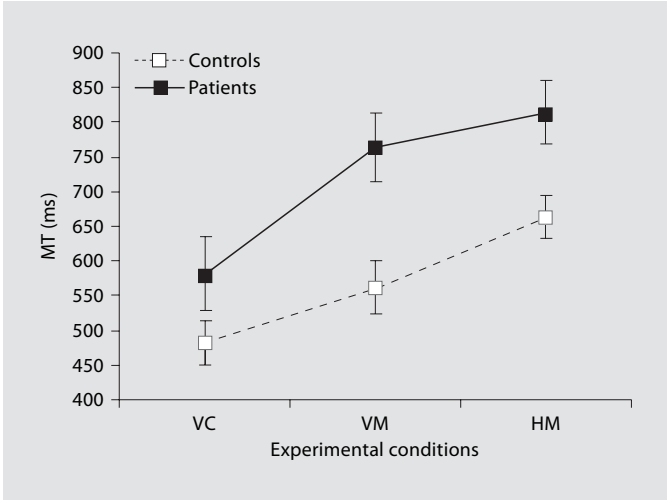

Fig. 3. MT results for all experimental conditions. VC, VM, and HM. Error bars represent standard error of the mean.

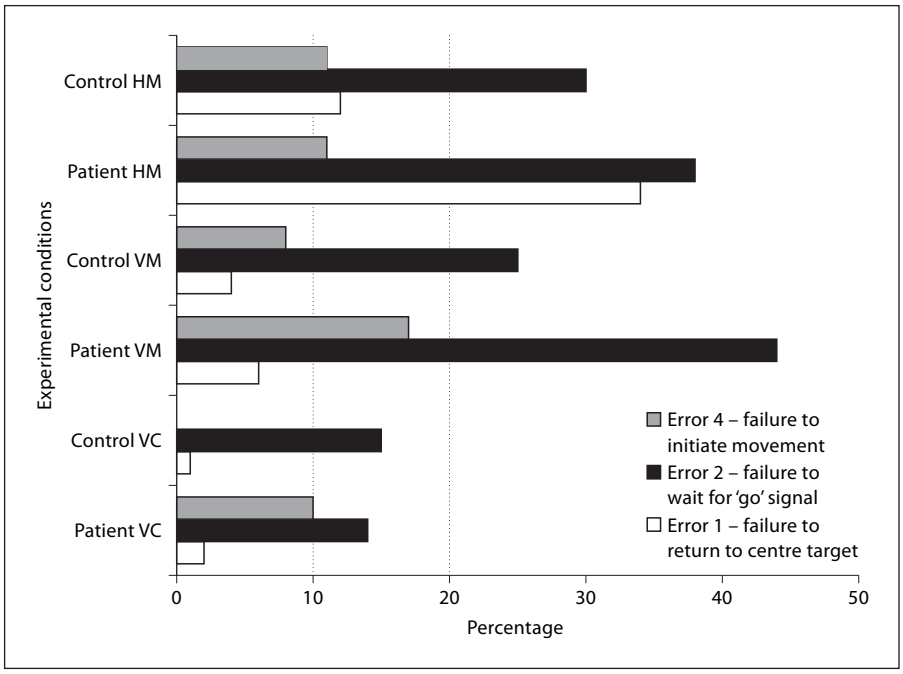

Fig. 4. Percentage of errors displayed by experimental condition (VC, VM, HM) and type of error for each participant group.

conditions with a memory component (i.e. both VM or HM), or when the mapping between the visual target and the required motor output became increasingly disassociated (i.e. HM condition). Figure 4 displays percentage of error, by the type of errors committed in both participant groups. The majority of errors were of types 1, 2, and 4, and thus will be the main focus of the error analysis. Only two type 3 errors were committed, and there were no type 5 or 6 errors in the VC condition. To review, type 1 errors indicated that the participants had difficulty returning to center target after finishing a previous trial. Type 2 errors occurred when individuals did not wait for the 'go' signal before moving, suggesting that they had difficulty inhibiting their movements. Type 4 errors were errors that oc-

curred when individuals had problems initiating a response following the 'go' signal. We believe that these errors indicate difficulty in processing and integrating visually identified target locations and generating the appropriate motor response. Most subjects predominantly had difficulty inhibiting responses to target locations, as demonstrated by a large number of type 2 errors (fig. 4).

Across all error types analyzed and all conditions, patients (error totals, VC: 51, VM: 133, HM: 166) were markedly reduced in their ability to perform the tasks as successfully as their control counterparts (error totals, VC: 33, VM: 76, HM: 108). An independent t test found a significant difference in the number of errors between the two groups for both the VM [$t(38) = -2.52$, $p < 0.05$] and HM [$t(38) = -2.24$, $p < 0.05$] conditions. As values indicate, tasks that included both elements of task complexity presented greater difficulty for our patient participants than for the control participants.

Errors in the initial directions of movement were also analyzed to identify subjects who did not have difficulty initiating responses, but instead chose inappropriate directions (i.e. participants who missed the cued target location). Trials were summed to reflect the number of movements to the wrong target locations in the 'remembered target' conditions (i.e. VM and HM). Directional error results indicate that as soon as experimental procedures were introduced, incorrect directional responses increased substantially in the patient group (patient total directional error, VM: 23, HM: 41). However, the control group errors remained relatively stable across conditions (control total directional error, VM: 7, HM: 8), indicating that maintaining object location in short-term memory was more difficult for the patient group compared to the control group, and became increasingly difficult with the added element of the nonstandard task.

Hand Path Formation

Variability in hand path trajectories increased for both groups when completing movements to remembered target locations in either the vertical or horizontal plane. Both these tasks required moving the cursor to the appropriate target location without constant visual feedback of the targets (VM) and with the added complexity of navigating the cursor on a different spatial plane (HM). As displayed in figure 5, our patient group had substantially increased deviation in their hand path trajectories compared to the control group, particularly when completing experimental conditions.

Overall, both groups displayed greater difficulty moving to the targets under memory and nonstandard mapping conditions relative to the VC condition. However, as the trajectories show in figure 5, on many trials patient participants often made small, incomplete movements and had few completed trials to target positions, particularly on the VM and HM condition (fig. 5b, c). As well, many patients had difficulty not only maintaining the ability to move to remembered target locations but they also had problems relating the cursor position to their hand position (HM). It is readily apparent that while the control participants were able to perform the experimental procedures relatively well, the patient's movements increasingly deteriorated; on many occasions they could only complete a very few number of trials (and in some cases, no trials), despite constant feedback/reminders about task procedure.

Endpoint Variability

An analysis of average endpoint displacement was conducted using a CE measurement for all experimental conditions, in all target positions, as well as both within and between population samples.

A univariate analysis revealed no differences in CE between subject groups on the VC condition. Therefore, both sample groups for the VC condition (control mean 1.36 ± 0.1, patients mean 2.04 ± 0.2) reach a fairly similar endpoint position for each target location, when targets remain visible throughout trials. A univariate analysis of endpoint displacement errors across all target locations for VM and HM displayed significant differences between the two groups; VM ($F_{1, 161} = 37.50$, $p < 0.01$), HM ($F_{1, 100} = 30.45$, $p < 0.01$). A within-group analysis on CE was conducted using independent t tests. Results display a significant and consistent increase in values across all conditions for the patient group, VC (mean 2.04 ± 0.2) vs. VM (mean 3.48 ± 0.28): [$t(160) = 3.485$, $p < 0.01$], VM vs. HM (mean 5.14 ± 0.46): [$t(71) = -2.05$, $p < 0.05$]. For the control group, no significant differences were observed between VC (mean 1.36 ± 0.1) and VM (mean 1.41 ± 0.18); however, VM was significantly different from HM (mean 2.29 ± 0.23), [$t(196) = -4.67$, $p < 0.01$]. As can be observed in figure 6, the mean displacement distance from actual target locations to mean endpoint position increased substantially across conditions in the patient group compared to the control group.

A univariate analysis revealed significant differences in VE between subject groups on all experimental conditions ($F_{1, 134} = 31.55$, $p < 0.01$). Patients displayed consistently greater variability in their endpoint precision (2.0, 3.1, and 3.8 cm versus 1.2, 1.2, and 1.4 cm for controls in the VC, VM, and HM conditions, respectively).

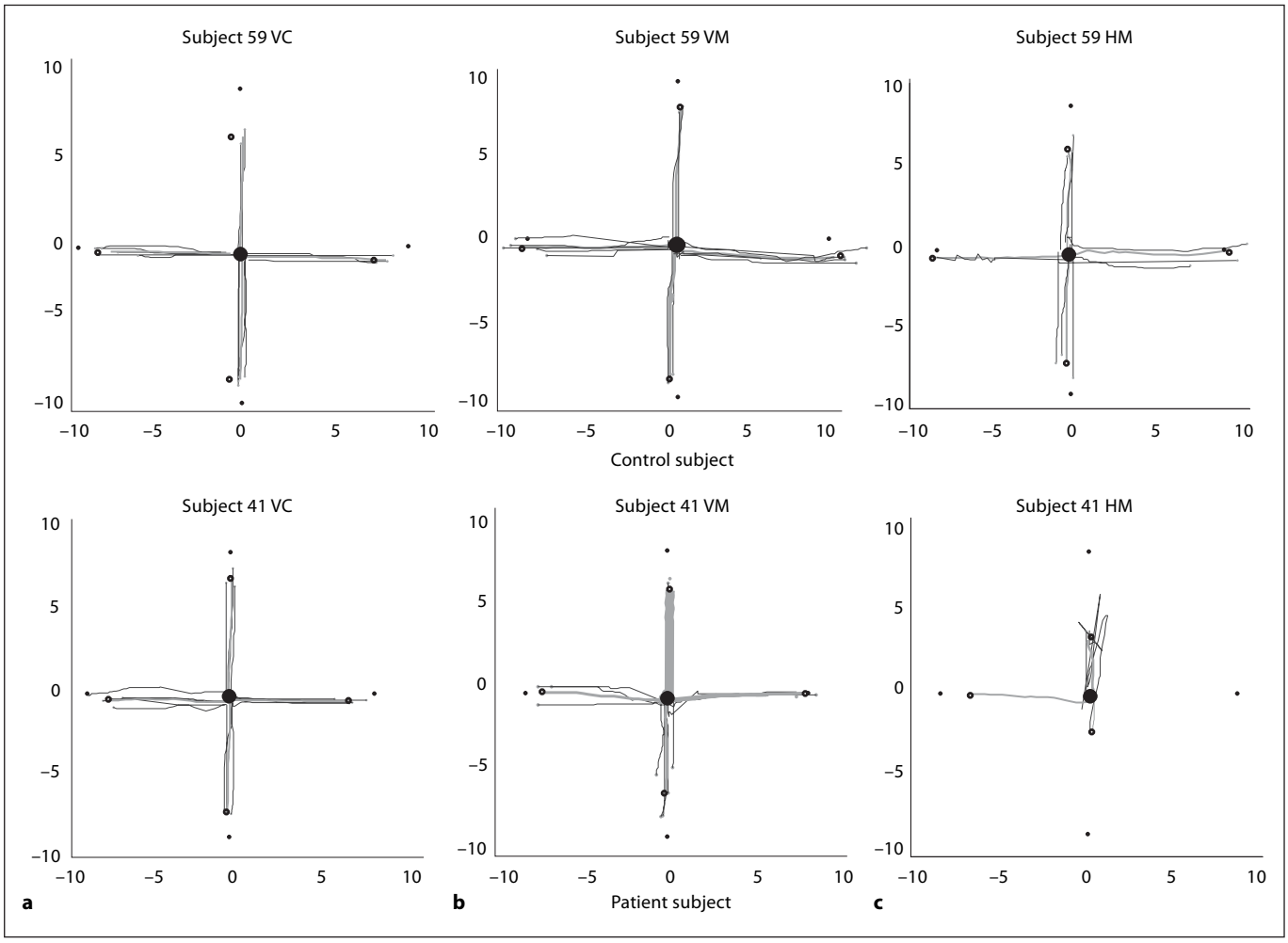

Fig. 5. Trajectory results for one subject representative of each group. Thick lines indicate mean movement trajectory, and thin lines display raw movement trajectories. Open circles represent mean movement position for subjects. Large inner circle represents home target position and outer small circles represent target positions. Trajectory values are in centimeters.

Note that for patients the VE increased steadily with an increase in task difficulty. This was not found for control subjects, who had quite consistent VEs across task conditions, thus their precision remained unaffected (illustrated by SEM bars on fig. 6). This result is further supported by an independent t test comparing all successful trials. It showed that for the control participants there was no significant difference between any of the experimental conditions. Patients, however, had significant differences when either a memory delay [VC vs. VM, $t(154) = 40.72$, $p < 0.001$], or a spatial location change [VC vs. HM, $t(154) = 5.392$, $p < 0.001$] was introduced. There was no significant difference in VE between the VM and HM conditions. Thus, patients had difficulty in making

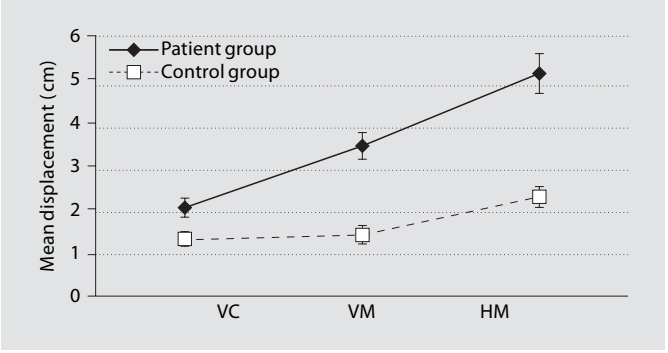

Fig. 6. Results for CE as represented for each experimental condition (VC, VM, and HM) and for each participant group. SEM bars reflect variable error.

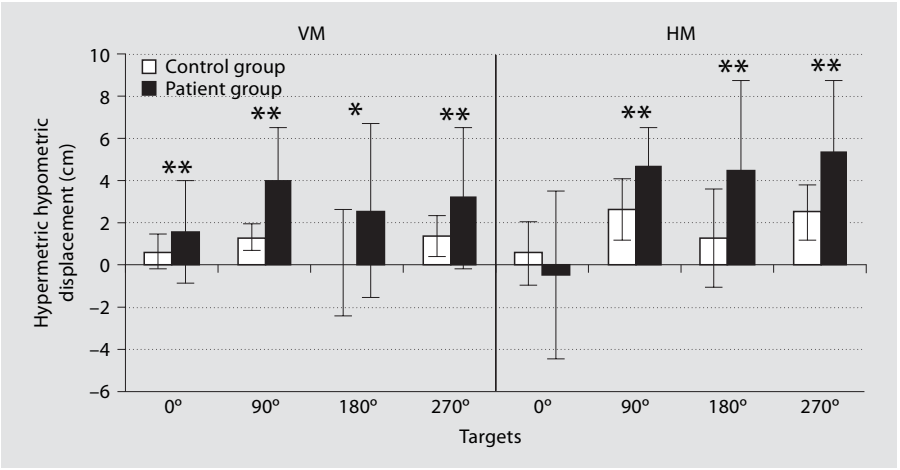

Fig. 7. Results reflect mean end position of pointing movements for participant group, for each target location for the VM and HM experimental procedures. Asterisks represent significant differences * $p < 0.05$; ** $p < 0.001$; error bars represent standard error of the mean.

precise movements with the introduction of any complexity, but these deficits were not additive. To characterize the spatial aspect of the movement variability, CE values were plotted. Figure 7 displays hypometric and hypermetric values by target location for each participant group based on VM and HM conditions. CEs for both groups were hypometric (positive scores represent hypometric responses) for the majority of target locations for conditions VM and HM. However, for target 0° on the HM condition, the patient result may have occurred due to patients completing less than three successful trials. Between-group analysis for experimental procedures VM and HM for all target locations (with the exception of target 1, HM) revealed that the errors made by the patient group were significantly different from their control counterparts (one-way ANOVA $p < 0.01$, except for target 3 VM, $p < 0.05$).

Discussion

Planning and Execution of Visuomotor Tasks

The experiments conducted in this research show that tasks requiring short-term motor memory and nonstandard mapping transformations disrupt the ability to effectively complete visuomotor tasks in both patients and controls, but these deficits are more profound in AD patients. In the VC condition we found that, overall, AD subjects had results similar to the age-matched controls, particularly in their ability to maintain straight-line trajectories to target locations. As well, for this condition participants all had relatively similar CE, thus they were equally successful in making accurate movements to target locations when targets remained visible and when transformations were standard, although with increased variability in the patient group. However, a difference between groups was observed in the timing results; a significant difference was observed in their RTs and MTs. This result suggests that AD patients take longer to identify/locate and plan a movement to target locations even when the targets remain visible. Also, once a decision is made and motor commands are generated, the AD sample requires more time to execute the plan. These RT and MT results support the contention that AD individuals display early signs of cognitive deficits that could be attributed to an inability of cortical networks to communicate effectively to plan timely motor responses. Reduced activation in these parietofrontal cortical networks [37, 39, 40] may underlie the compromised performance observed here. Such networks are required for both simple [29, 39, 41, 42] and more complex visuomotor tasks [37, 39, 40].

Short-Term Visuomotor Memory Processing

We predicted that AD individuals would experience great difficulty when confronted with a short-term memory task requiring a motor response. It has been shown by several researchers that motor performance deficits can often be observed in individuals with AD [21, 22, 43, 44]; however, an extensive search revealed no previous studies incorporating short-term visuomotor memory performance in individuals with AD. Visual short-term memory has been noted to rely on a network of brain regions including the PPC dorsal stream that are essential for retaining the location of stimuli that have just been perceived [45, 46]. In addition, an experiment examining short-term

memory reported that activation of PPC neurons was required to be successful in identifying the location of visually presented objects after a 2-second delay [29]. In another study, subjects that received transcranial magnetic stimulation over the PPC were disrupted in their performance of a task that required them to move their eyes to a location where an object was recently presented [47]. To further illustrate our point that AD dysfunction may be subserved by deficits within the PPC, we predicted that our short-term memory task would unmask visuomotor performance difficulties, similar to those that have been interpreted as AD planning deficits [21]. We believe that our results confirm this assumption.

AD patients showed a decline on all of our measures, reflecting the difficulty that they had in adapting to the memory task. Deficits in the parietal region can affect one's ability to maintain target position, which is an essential factor for successful completion of a visuomotor memory task. Thus, we believe that this substantially compromised visuomotor ability in AD patients may be related to a dysfunctional parietofrontal network generally, and a compromised parietal region more specifically.

Visuomotor Control in Nonstandard Mapping

The second major goal of this research involved examining the additive effect of a nonstandard mapping process (i.e. the HM condition) onto a short-term visuomotor memory procedure. Based on previous research tasks that involve nonstandard or standard mapping sensorimotor transformations, such procedures rely heavily on effective functioning of the PPC [13, 32, 33, 48]. As well, when tasks progressively increase in complexity (dissociation from standard mapping procedures) the result is identifiable increases in activity within the PPC [34, 49, 50]. The inability to perform such tasks (i.e. nonstandard mapping procedures) can be connected to regional deficits/lesions within the parietal region [51–54], thus creating deficits in signal transmission throughout brain networks supporting vision for action. If increased activity is observed in the PPC when a task increases in complexity, then adding a nonstandard mapping to a task that is already eliciting ineffective responses due to parietal lobe dysfunction (here, a short-term visuomotor memory) should result in a further decrease in performance. Indeed, we showed that the AD group experienced greater difficulty (reflected by increased RT and failed trials) and larger performance deficits (reflected by an increased MT and trajectory deterioration) compared to our control group, particularly as the task increased in complexity. These data support previous anatomical and neuroimaging research suggesting that the PPC is one of the primary regions affected early on in the course of AD [14, 36, 55, 56]. Overall, it is readily apparent that individuals affected by AD find the additional 'load' (i.e. parietofrontal network processing) of completing a nonstandard visuomotor transformation in addition to a memory task to be very taxing, and in many cases this resulted in a complete breakdown in the ability to successfully complete these trials at all. These results support our previous research [13] and indicate that nonstandard transformations are not only substantially more difficult for AD individuals to complete, but they have a cumulative/additive effect on performance ability when subjects are already engaged in a 'parietal' lobe task.

Conclusion

We postulate that individuals with AD will undoubtedly display an inability to process and respond to visual information that contains short-term memory components. As well, nonstandard transformations remain a difficult task for AD individuals to perform and can cause further disruption in visuomotor processing tasks that they may currently be engaged in. We believe that this research provides further psychophysical evidence supporting the hypothesis that the PPC plays a functional role in processing visuomotor information, and that the functional deficits experienced by AD patients may be due, in part, to a deterioration of this region and subsequently creating deficits in its ability to communicate to other cerebral regions intimately tied to supporting visually guided movements. These types of visuomotor dysfunctions may provide insight into disease onset, existence, and progression. In addition, based on these results we need to be aware that when presenting information to AD individuals, we should consider the fact that they have difficulty storing information and generating visuomotor responses effectively; therefore, information needs to be continuously available and should be presented in a standard (rather than nonstandard) format to reduce error responses. For example, when driving, people with AD may display difficulty responding to nonstandard tasks, such as when to use the brake or the gas, responding to arbitrary cues (i.e. traffic lights), and remembering the location of pedestrians or other cars while making turns (i.e. short-memory for the location of objects). Therefore situations that contain these two elements can be exhaustive and potentially hazardous for individuals with AD.

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