# DISORIENTATION IN ALZHEIMER DISEASE:
# ALLOCENTRIC AND EGOCENTRIC MECHANISMS

by

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# Abstract

SPATIAL DISORIENTATION IN ALZHEIMER DISEASE:
EGOCENTRIC AND ALLOCENTRIC MECHANISMS

by

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**Introduction:** Spatial disorientation is a common symptom of Alzheimer Disease (AD). The cognitive mechanisms of this difficulty have not been explored in this population. It is unclear which commonly used standard measures of neuropsychological function are more predictive of the risk of getting lost or disoriented. Ability to use allocentric and egocentric reference frames in AD has received little attention in research. We hypothesized that patients with AD will be more impaired on tasks of allocentric function than egocentric function and that this impairment will be more pronounced in AD sample compared to the healthy age-matched controls. Relative contributions of allocentric and egocentric functions to reports of orientation and wayfinding ability were explored. **Method:** Thirty-five participants (22 controls, 13 AD) were assessed with computer-based Allocentric-Egocentric Test, standardized measures of attention and executive function, and a self-report (controls) or caregiver-report (AD group) measure of daily wayfinding ability. **Results:** Participants with AD performed significantly worse than age-matched controls on all spatial tasks. Once the effects of interference that confounded performance on the Egocentric-I condition were controlled for (Egocentric-NI condition), participants with AD were more affected on the allocentric than the egocentric task.

Participants with AD performed significantly worse on the allocentric task than age-matched controls, but performance on the egocentric task (Egocentric-NI) was not significantly different between the groups. Neuropsychological data revealed that attention and executive function together were highly predictive of all tests of spatial function regardless of frame of reference. However, only attention alone contributed significantly to the models on both egocentric tasks, and not on allocentric task. Executive function alone did not contribute significantly to any of the models. Performance on the allocentric and the two types of egocentric tasks together was highly predictive of reports of daily wayfinding ability, but none of these alone contributed significantly to the model. **Conclusions:** Allocentric functioning is differentially affected by the AD process compared to the egocentric functioning. Attention, but not executive function, is an important cognitive mechanism of egocentric, but not allocentric orientation. In our sample, ability to use either frame of reference alone did not explain daily wayfinding ability.

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# Introduction

## Early Studies

The early knowledge about the mechanisms of spatial orientation stems from the study of neurological disorders. Russell Brain's (1941) comprehensive historical review of the disorders of disorientation noted that earlier cases considered spatial disorientation an artifact of dysfunctions of visual perception and integration, such as visual agnosia. Brain noted that in the latter decades of the 19th to early 20th century, European neurologists such as Hughlings Jackson, Wilbrand, Wendenburg, and von Stauffenberg noticed that some patients who had difficulty localizing an object they had seen, judging the relative distances between two objects, dressing themselves, or distinguishing their right from left hand, did not demonstrate visual perceptual impairments. This discrepancy suggested that visual agnosia did not account for all the cases of spatial disorientation (Brain, 1941). Over the decades multiple case studies described patients with diversely localized lesions who had a broad variety of disorders of spatial orientation. This led to the notion that some core features of the disorder could be taxonomically organized. In addition to these early accounts, large numbers of patients from WWII with brain injury due to focal gunshot wounds became available for systematic inquiry into the neural mechanisms of cognition and behavior. These data generated the conceptual framework that spatial dysfunction could be divided into two main categories: body orientation (egocentric) and orientation in the extrapersonal (allocentric) space (Semmes, Weinstein, Ghent, & Teuber, 1963). Importantly, the behavioral findings (Semmes, Weinstein, Ghent, & Teuber, 1955; Semmes, et al., 1963; Weinstein, Semmes, Ghent, & Teuber, 1956) also revealed a partial dissociation in neural mechanisms underlying the two systems of spatial coding: patients with injuries to the anterior regions of the left hemisphere were more likely to suffer from impairments in egocentric (personal) orientation, whereas those with right posterior lesions exhibited difficulties performing tasks of allocentric (extra-personal) orientation. This structural dichotomy was only partial, because lesions in the left posterior regions also resulted in the marked decrement in the performance on both types of tasks (Semmes, et al., 1963). Nevertheless, the dichotomy has since been supported by behavioral and neurobiological data using both animal and human paradigms, and persists throughout our current conceptual framework in the study of spatial orientation.

## Current Conceptual Frameworks

Some disagreement regarding the relative contributions of egocentric versus allocentric frames of reference to the human ability to orient and navigate our environment still exists. However, there is a general agreement that the two frames of reference are distinct from one another. Proponents of the *disorientation model* emphasize the relative importance of the egocentric processes that rely on constant updating of self and object location in an effortful, on-line process, allow for a flexible way to arrive at many new destinations via unfamiliar routes (R. Wang & Spelke, 2002; R. F. Wang & Spelke, 2000) and to recognize spatial scenes despite constant changes in vantage points as the positions of the gaze, head, and trunk change are altered all the time as the organism navigates the environment (Nakatani, Pollatsek, & Johnson, 2002; Shelton & McNamara, 1997; Shelton & McNamara, 2001). Nevertheless, when the organism's ability to use egocentric cues is disrupted by several rotations, it must rely on the use of external or allocentric cues to reorient itself (R. Wang & Spelke, 2002) and to locate the object of search (Lee, Shusterman, & Spelke, 2006).

Proponents of the *two-system model* (Burgess, 2006) propose that both transient, body-to-object, egocentric associations and the more stable, object-to-object, allocentric representations co-exist and complement each other (Burgess, Becker, King, & O'Keefe, 2001; Easton & Sholl, 1995; Waller & Hodgson, 2006). The cooperation of the allocentric and the egocentric reference frames is necessary whenever one navigates following a geographic map: the map provides the allocentric cues, but when one has to make a turn, the decision is based on the egocentric body coordinates (Gugerty & Brooks, 2004). Further, performance on the three navigational tasks (route finding, object localization, and identifying object location) becomes significantly less accurate and the latency of response much greater when the two spatial reference frames are misaligned (Gugerty & Brooks, 2001, 2004). Such misalignment may occur, for example, when the street grid of the map (allocentric coordinate) is not aligned with the top of the map (egocentric coordinate; Gugerty & Brooks, 2004).

The mechanisms of cooperation between the two reference frames are not well understood.  However, earlier studies suggest that the allocentric information is coded as a large-scale stable map of the environment (O'Keefe & Nadel, 1978). In novel situations such representation would be quite crude as there is no existing map, and the organism will more likely rely on the on-line egocentric mechanisms until it learns the environment and the allocentric representations of this environment become more refined thereby allowing for the use of the stable cognitive map with greater accuracy (Burgess, 2006; Mou, McNamara, Rump, & Xiao, 2006; Waller & Hodgson, 2006).

## Neural Substrates of the Allocentric and the Egocentric Mechanisms

The role of the medial temporal lobes in processing of the allocentric spatial information has been extensively researched. The seminal findings that neurons in the rat’s hippocampus were activated in response to a particular location, suggested the presence of a neural representation of a stable cognitive map of the animal’s spatial environment (O'Keefe &

Dostrovsky, 1971; O'Keefe & Nadel, 1978). Induced hypoactivity of glucocorticoid receptors in the hippocampi of mice resulted in the selective disruption of the allocentric but not the egocentric learning (Steckler, Weis, Sauvage, Mederer, & Holsboer, 1999). Other animal paradigms showed that destruction of posterior parietal cortices (DiMattia & Kesner, 1988; King & Corwin, 1992) resulted in the allocentric disorientation. Recent fMRI studies with healthy human participants revealed the partially overlapping neural networks differentially activated by the allocentric and the egocentric reference frames: allocentric judgments activated parieto-temporal regions whereas egocentric judgments activated parieto-frontal network (Committeri et al., 2004; Galati et al., 2000; Galati, Pelle, Berthoz, & Committeri, 2010; Gramann, Muller, Schonebeck, & Debus, 2006; Neggers, Van der Lubbe, Ramsey, & Postma, 2006).

The interaction and cooperation between the two spatial frames of reference appear to have underlying neural representations as well. Save and Poucet (2000) proposed that parietal cortices integrate visual, sensory, and proprioceptive environmental inputs coded into the egocentric representations and then, via neuronal projections to the hippocampus, are involved in the conversion from the egocentric to the allocentric representations.

In summary, animal and human studies generally agree on the relative importance of both parietal and medial temporal areas for the intact allocentric orientation and the parieto-frontal connections for the egocentric orientation.

### Relationship to the AD pathology.

Impairment of spatial navigation function is highly prevalent among the patients with AD (Monacelli, Cushman, Kavcic, & Duffy, 2003; Teri, Borson, Kiyak, & Yamagishi, 1989). Regions of the brain underlying the allocentric orientation system considerably overlap with those affected by the AD pathology. Early medial temporal lobe pathology (Braak, de Vos, Jansen, Bratzke, & Braak, 1998) with later progression to parietal and frontal cortices (Braak & Braak, 1996) in the course of AD have been well-documented in literature. The disease gradually invades the association areas of neocortex through the intermediate stages, and finally destroys connections between the medial temporal regions and neocortex as well as those between the sensory association areas and prefrontal cortices in the final stages (Braak, Rub, Schultz, & Del Tredici, 2006). Further, decreased right posterior hippocampal and parietal volumes in patients with AD are associated with increased instances of becoming lost and poor performance on the task of allocentric spatial processing, such as identifying location on a map (deIpolyi, Rankin, Mucke, Miller, & Gorno-Tempini, 2007). Limited data from the virtual reality-based paradigms (Cushman, Stein, & Duffy, 2008) and the real-life navigation tasks (Hort et al., 2007; Laczo et al., 2010) point in direction of early vulnerability of the allocentric spatial processing to the AD pathology.

Further support for the early loss of the allocentric orientation as a result of the AD process comes from the animal paradigms. A study using knock-out mice with AD-associated hAPP genes (deIpolyi et al., 2008) revealed that wildtype (genetically unaltered) mice typically rely on the allocentric strategies when solving the maze tasks, whereas mice expressing AD genes begin relying on the egocentric strategies early in the progression of the disease. This may be interpreted as an early compensatory mechanism where reliance on the hippocampally-based allocentric strategy compromised by the disease pathology would be inefficient (deIpolyi, et al., 2008).

### Relationship to normal aging.

Normal aging is associated with a number of changes in the neural mechanisms supporting allocentric and egocentric reference frames. Hippocampus and the hippocampal formation, critical in the conversion of the egocentric to the allocentric representations of the environment (O'Keefe & Nadel, 1978) are diminished during the early aging (Moffat, Elkins, & Resnick, 2006). Neurobiological data (Moffat, et al., 2006) show reduced activation of parieto-temporal neural circuits, underlying allocentric spatial representations (Galati, et al., 2000; Gramann, et al., 2006; Zaehle et al., 2007) in healthy elderly as compared with younger adults.

Involvement of frontal lobes in processing the egocentric information has been well documented (Galati, et al., 2000; Semmes, et al., 1963; Zaehle, et al., 2007). Extensive data also exist showing subclinical white matter changes and gray matter atrophy preferentially affecting the frontal lobes and consequently disrupting the frontostriatal circuit in the healthy elderly (Hedden & Gabrieli, 2004; Pfefferbaum, Adalsteinsson, & Sullivan, 2005).

As neurobiological substrates underlying both allocentric and egocentric spatial reference systems show vulnerability in normal aging, some healthy older adults experience episodes of becoming lost. According to one study, 38% of normal older adult participants, as opposed to 93% of participants with dementia of Alzheimer’s type, experienced such episodes (Monacelli, et al., 2003). Brain plasticity allows most healthy older adults to maintain intact navigation and orientation abilities. Recent studies confirm that normal aging brain is quite plastic, such that in advanced age, in absence of the disease, more areas of the brain tend to be recruited to compensate for reduced activation of primary areas associated with any given function (Cabeza, Anderson, Locantore, & McIntosh, 2002; Greenwood, 2007). Some heterogeneity in brain plasticity has been demonstrated in normal aging, as some elderly engaged larger areas of the brain during the cognitive tasks, whereas others relied on the same areas as the young adults (Cabeza, et al., 2002). Reduced efficiency of brain activation could be an additional explanation why some normal older adults experience episodes of disorientation whereas the majority do not, but this too has yet to be tested. In summary, healthy older adults have several areas of brain-related change that put spatial orientation in jeopardy. The effects alone, however, are not sufficient to cause disorientation, and comprehensive comparisons to healthy younger adults have yet to be performed.

Animal (Begega et al., 2001; Milgram et al., 2002) and human (Moffat, et al., 2006) paradigms show that aged animals and humans performed as well as the younger adults on tasks requiring navigation based on egocentric cues, but performed worse on tasks of allocentric navigation. In comparison to younger adults, healthy older adults demonstrate reduced ability to form cognitive maps as measured by a virtual reality water maze task (Moffat & Resnick, 2002). In that study, normal older adults exhibited more variability in performing the virtual water maze task, spent less time in the vicinity of the platform, showed reduced appreciation for the geometric cues of the room, and preferred more proximal rather than distal allocentric cues when navigating the maze. Behavioral data from the developmental studies confirm that allocentric spatial representations arise later than egocentric representations in early development (Learmonth, Newcombe, & Huttenlocher, 2001), and are diminished in normal aging (Moffat & Resnick, 2002).

### Attention and Executive Function in AD and Normal Aging

Attentional dysfunction in AD has been extensively reported (Baddeley, Baddeley, Bucks, & Wilcock, 2001; Foldi et al., 2005; Perry & Hodges, 1999) and aside from memory, is one of the earliest cognitive domains to be affected by the AD process (Grady et al., 1988; Perry & Hodges, 1999). More specifically, selective (Levinoff, Li, Murtha, & Chertkow, 2004; Redel et al., 2010), focused (Levinoff, Saumier, & Chertkow, 2005), and divided attention (Baddeley, et al., 2001) deficits associated with AD are well-known.

Attention (Madden, 2007) and processing speed (Finkel, Reynolds, McArdle, & Pedersen, 2007) decline with age in the absence of the disease process. Normal aging is also associated with the detrimental effect of increased cognitive load (i.e., performing two or more tasks at the same time) on cognitive performance (Baddeley, et al., 2001; Logie, Della, MacPherson, & Cooper, 2007; Verhaeghen & Cerella, 2002). This decrement is particularly notable with regard to performance on motor tasks such as walking (Harley, Wilkie, & Wann, 2009).

The domain of executive function encompasses a broad range of cognitive constructs. Executive impairments have been found even in the early stages of the AD (Baudic et al., 2006). Working memory (Baddeley, Bressi, Della, Logie, & Spinnler, 1991) has been found susceptible to the AD process. A recent study of attention and executive function in normal aging and participants with AD (Coubard et al., 2011) found that normally aging controls exhibited more specific attentional and executive deficits such as response inhibition, switching attention when the shift was made unpredictable (i.e., not all trials of the task involved set-shifting), and readiness for the unpredictable set-shift, whereas participants with AD exhibited a broader, less-specific range of attentional and executive dysfunction.

## Significance and Rationale

Although spatial disorientation is a one of the most common symptoms of the AD, not all patients exhibit such deficit. The clinicians are not able to predict which patients are at higher risk for becoming lost or disoriented based on typical paper-and-pencil neuropsychological tests (Habib & Sirigu, 1987; McCarthy, Evans, & Hodges, 1996). Such prediction would be crucial to informing the caregivers as to the optimal balance of the safety and the autonomy of the patient, thereby improving the quality of life for both patients and their caregivers.

The cognitive mechanisms of spatial disorientation in AD have been understudied and consequently poorly understood. Declines in attention and executive function associated with the normal aging (Coubard, et al., 2011; Madden, 2007)and with AD (Baddeley, et al., 2001; Coubard, et al., 2011; Foldi, et al., 2005) have been documented in literature, but their contributions to the ability to use allocentric and/or egocentric environmental cues have not been explored to date either in the healthy elderly or in AD population.

Limited data regarding allocentric and egocentric spatial processing in AD exist, but these studies utilized virtual reality or real-life navigation tasks which engage multiple cognitive mechanisms that are difficult to parse out. The current study used a simpler, experimental measure designed to better isolate utilization of allocentric and egocentric frames of reference.

The current study focused on the distinction between the *egocentric* and *allocentric* representations of the environment (see Klatzky, 1998) and the differential contribution of these two types of representation to disorientation in Alzheimer's disease (AD). *Egocentric* representation defines the position of objects in one's environment in relation to one's own body or position of parts of the body (i.e., retina, head, or trunk). *Allocentric* representation refers to the position of the objects in the environment with regard to other objects, independent of one's body. The current experiment was designed to examine whether differential changes in the allocentric and the egocentric frames of reference related to the AD process were predictive of the changes in daily orientation ability.

As in previously described paradigms (Galati, et al., 2000), this experiment used a two-component stimulus consisting of the vertical red line (target) and the horizontal gray bar purported to provide allocentric cues in the allocentric condition. However, we hypothesized that the presence of the horizontal gray bar continued to provide allocentric cues even when the instruction was given to use only egocentric cues (i.e., the position of the red vertical line in relationship to one’s own midline). As we hypothesized that the interference would exist between the allocentric and the egocentric cues when the two-component stimulus is presented, we called the egocentric condition with the two-component stimulus Egocentric-Interference (Egocentric-I). However, to be able to directly contrast and compare the egocentric condition to the allocentric condition by changing only the instruction, we opted to retain this condition despite the possible interference effects. Unlike other paradigms, we introduced a condition, in which only the vertical red line appeared, thereby creating a purely egocentric condition. We proposed that introducing a one-component stimulus would eliminate any potential interference between the reference frames and therefore called the second egocentric condition Egocentric-No Interference (Egocentric-NI).

## Aims and Hypotheses

**Aim 1**: to determine whether patients with AD are more affected on spatial tasks (the allocentric and the egocentric ones) more than healthy elderly controls (HEC). We hypothesized that:

Hypothesis1. patients with AD would be more impaired overall than age-matched controls on all spatial measures.

**Aim 2**: to determine whether allocentric and/or egocentric spatial processing systems are differentially impaired in patients with AD compared to the age-matched controls. We hypothesized that:

Hypothesis 2a. the allocentric spatial processing would be more vulnerable to the disease process than the egocentric because brain mechanisms underlying the allocentric system are most likely affected. As such, performance on the allocentric condition would be more impaired than on both egocentric conditions in patients with AD.

Hypothesis 2b. As the one-component stimulus on the Egocentric-NI condition eliminated the potential interference inherent in a task in which a two-component stimulus was presented (Egocentric-I), Egocentric-NI condition will be easier than the Egocentric-I or Allocentric condition. Allocentric condition would be the most difficult for both groups. However, participants with the AD would be disproportionately affected on the Allocentric condition.

**Aim 3:** to determine whether objective measures of spatial processing are related to measures of attention and executive function. We hypothesized that:

Hypothesis 3a. composite scores of neuropsychological measures of attention and executive function would equally predict performance on measures of allocentric and egocentric processing.

Hypothesis 3b. the above prediction would be true of egocentric tasks with (Egocentric-I) and without (Egocentric-NI) the interference.

**Aim 4**: to determine whether there is a relationship between reports of getting lost and the objective measures of allocentric and egocentric spatial processing systems.

Hypothesis 4a. We hypothesized that performance on measures of the allocentric spatial processing would be more predictive on caregiver (for the participants in the AD group) or self-report (for the HEC group) of wayfinding ability as measured by Algase Wayfinding Effectiveness Scale. As predicted by Hypothesis 2, egocentric processing is expected to be relatively preserved in participants with AD and as such may not have an impact on daily functioning in the early stages of dementia.

# Method

## Participants

Thirty-five participants were recruited and assigned to two groups: healthy elderly controls (HEC; N =22) and Alzheimer's disease (AD; N = 13). Demographic characteristics of the sample are summarized in Table 1. Participants were selected from volunteers in the longitudinal study of memory disorders and aging conducted by Alzheimer's Disease Research Center (ADRC), Taub Institute for Research on Alzheimer's Disease and the Aging Brain, of Columbia University.

**AD Group Inclusion/Exclusion Criteria.** Participants in the AD group were at least 65 years of age on the day of participation in the experiment, had an established diagnosis of probable AD, have received Clinical Dementia Rating Scale (CDR) Global Score ≥ 1, Folstein Mini-Mental State Examination (MMSE) score of 15-26, and demonstrated capacity to provide consent.

A clinical consensus diagnosis of Alzheimer's disease was based on a decision by a collaborative team of neurologists, neuropsychologists, and psychiatrists. Consensus diagnosis was in part based on the findings from a comprehensive neuropsychological battery[1] in addition to neurological examination, laboratory findings, and neuroimaging data.

Exclusionary criteria were the evidence of focal infarcts > 1 cm in size on brain imaging, an episode of unexplained loss of consciousness, or a diagnosis of dementia of etiology other than AD.

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[1] Comprehensive neuropsychological battery included Folstein Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975), Buschke Selective Reminding Test (Buschke & Fuld, 1974), Boston Naming Test (Goodglass & Kaplan, 1983), Controlled Oral Word Association Test (CFL; Benton, Sivan, Hamsher, Varney, & Spreen, 1994), Boston Diagnostic Aphasia Examination Category Fluency Test (Animals; Goodglass & Kaplan, 1983), Trail Making Test (Trails A and B; Reitan, 1958), and Rosen Drawing Test (Rosen, 1981).

### HEC Group Inclusion/Exclusion Criteria.

Participants were at least 65 years of age on the day of participation in the experiment, had no history of memory or other cognitive complaints, received a CDR = 0, and had MMSE ≥ 27.

HEC participants previously participated in Columbia University ADRC studies, were found by the clinical consensus team to have no evidence of neurodegenerative disease or cognitive changes, and gave their permission to be contacted for other studies.

Participants were excluded if they met any of the exclusion criteria for AD group, reported a history of memory or cognitive complaints, had a past history of loss of consciousness > 30 minutes in duration, and/or exhibited clinically significant impairment on standardized tests of cognitive functioning.

## Measures

### Allocentric-Egocentric test (AET).

The AET (Galati, et al., 2000; Neggers, et al., 2006) is an experimental, computer-based measure of allocentric (extra-body) and egocentric (body-based) spatial orientation. The task was modified to accommodate the needs of the aging and cognitively impaired population and to better fit the objectives and hypotheses of this study.

There were three conditions in the task: Allocentric, Egocentric-I, and Egocentric-NI (see Figure 1).

In the Allocentric condition, the stimulus consisted of a red vertical line and a gray horizontal bar. The red line could be placed at different points along the gray horizontal bar (see Figures 1 and 2). The gray horizontal bar could also be displaced to the right or left of the middle of the computer screen (see Figure 2). Participants were asked to decide whether the red vertical line appeared to the left or right of the midpoint of the gray horizontal bar, and press a corresponding right or left button as quickly as possible.

In the Egocentric-I condition, participants were again presented with the red vertical line and the gray horizontal bar (see Figures 1 and 2). The gray horizontal bar was still present but not relevant to the task. Participants were asked to decide whether the red vertical line was to the left or right of their body's midline, corresponding to the midline of the screen, and respond by pressing the corresponding right or left button (see Figure 1).

The Egocentric-NI condition was added as a control measure for the possible interference effects between the cues provided by the red vertical line and the gray horizontal bar. The stimulus consisted of only the red vertical line (see Figure 1). The instruction was identical to the Egocentric-I condition, such that the participants were asked to respond whether the red vertical line was to the right or left of their body's midline.

Stimuli in all three conditions were presented against black background. The gray horizontal bar subtended 1.06°[2] by 9.02° visual angle. The red vertical line subtended 6.04° by 1.06° visual angle. The gray horizontal bar was displaced in relationship to the middle of the screen with 4 levels of displacement subtending -1.82°, and -2.42°, + 2.42°, +1.82° visual angle, where the negative values indicated displacement to the left, and the positive values indicate displacement to the right of the center of the screen (see Figure 2). The red vertical line was displaced in relationship to the middle of the gray horizontal bar with 4 levels of displacement

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[2] Degrees of visual angle were calculated using the following formula:

$\Theta = \tan^{-1}$ (physical size in cm/ viewing distance in cm), where viewing distance = 50 cm.

subtending -0.45°, -0.91°, +0.91°, + 0.45° visual angle (see Figure 2). Each of the three conditions of the task consisted of 16 combinations of the red vertical line and the gray horizontal bar (see Figure 2) which from this point on in the manuscript is referred to as a “position” of the stimulus. The positions were differentiated by the direction (right or left) and level of displacement of a) red vertical line in relationship to the gray horizontal bar and b) gray horizontal bar in relationship to the middle of the screen. Combinations in which the middle of the gray horizontal bar coincided with the middle of the screen were excluded to avoid ambiguity. Stimuli in which the red vertical line coincided with the middle of the screen were also excluded so that participant could make a left or right judgment in the Egocentric-I and the Egocentric-NI conditions.

### Neuropsychological Measures.

A portion of neuropsychological testing data was accessed retroactively from participants’ ADRC records and datasets and included the following measures:

<u>Clinical Dementia Rating Scale</u> (Morris, 1993). The CDR is a 5-point scale used to describe six domains of cognitive and functional performance: Memory, Orientation, Judgment and Problem Solving, Home and Hobbies, Community Affairs, and Personal Care. Information is obtained through a semi-structured interview of the patient and a reliable informant.

<u>Folstein Mini-Mental State Examination</u> (Folstein, et al., 1975). The MMSE is a 30-point question-and-answer, paper-and-pencil clinical tool designed and widely used to briefly assess global cognitive functioning, including orientation, attention, drawing ability, language, and calculation.

<u>Wechsler Adult Intelligence Scale-3rd revision: Digit Span subtest</u> (The Psychological Corporation, 1997a). The WAIS-III is a widely used, standardized test of general, verbal, and

non-verbal intelligence. The Digit Span subtest was designed to measure individual's attention span and working memory capacity. Participants are asked to repeat verbatim orally presented strings of numbers of increasing length.

Trail Making Test, A and B (Reitan, 1958). The TMT is a paper-and-pencil measure of attention, processing speed, and mental flexibility, which has been standardized for use in people ages 15-89. Participants were asked to connect circles with a pen or a pencil.

In addition, the following standardized measures were administered during the study session:

Spatial Span--Wechsler Memory Scale-3rd revision (The Psychological Corporation, 1997b) The WMS-III is an extensively used, well-normed and standardized tool designed to assess various aspects of memory functioning in individuals 16-89 years of age. The Spatial Span subtest is a measure of spatial attention span and working memory capacity, during which an examiner tapped on a sequence of numbered blocks and a participant was asked to repeat these spatial sequences as demonstrated (in Spatial Span Forward) or in reverse order (Spatial Span backward).

Cancellation Tasks (Sano, Rosen, & Mayeux, 1984). The Cancellation tasks are paper-and-pencil measures of selective attention. Participants were presented with two separate letter-sized sheets of paper: one pre-printed with an array of various shapes and the other, with an array of letter triads. They were asked to find and cross out all shapes or letter triads identical to a target shape or letter triad printed on top of the page as quickly as they can.

Algase Wayfinding Effectiveness Scale (Algase WES; Algase et al., 2007). This is a 30-item 5-point Likert scale questionnaire used to describe individual's real-life spatial orientation and wayfinding ability. Caregivers of participants in AD group completed Algase WES caregiver-report version, by checking the appropriate boxes for each of the 30 items. Items were assigned scores ranging from 1 (unable or never) to 5 (always), with higher score indicating better level of functioning, so that the lowest possible total score was 30 and the highest 150. The scale yielded 4 subscale scores: complex wayfinding goals (CWG), analytic strategies (AS), global strategies (GS), and simple wayfinding goals (SWG). Participants in the control group completed self-report version of the Algase WES in the same manner.

Composite scores for the domains of attention and executive function were computed as follows. Z-score distributions were generated for each participant for the neuropsychological measures of attention (Digit Span Forward maximum length, Spatial Span Forward maximum length, Trails A time, and Shape Cancellations total number of omission errors) and executive function (Digit Span Backward maximum length, Spatial Span Backward maximum length, Trails B time). A single domain score was then computed for each of the above as follows:

Attention = (z-score Digit Span Forward + z-score Spatial Span Forward + z-score Trails A time + z-score Shape Cancellations omissions) / 4

Executive = (z-score Digit Span Backward + z-score Spatial Span Backward + z- score Trails B time) / 3

The following measures described above were used as dependent variables: Allocentric-Egocentric computer test, Attention composite, Working Memory/Executive composite, and Algase WES.

## Procedure

Institutional Review Boards of New York State Psychiatric Institute and Queens College of the City University of New York (CUNY) approved the study. All participants gave a written informed consent in accordance with the current ethical standards as defined in Ethical Principles of Psychologists and Code of Conduct (American Psychological, 2002). Prior to being asked to participate, prospective participants in the dementia group received an independent assessment of their capacity to consent to a research study. Only those deemed capable to provide such consent on their own behalf were asked to take part in the experiment. Upon completion of the study session, each participant received a one-time monetary compensation of $15.

During the study session, participants completed the AET, Spatial Span, and Cancellation Tasks. The remainder of neuropsychological data was retroactively accessed from the ADRC files and database. A reliable informer (whenever possible, a primary caregiver) completed the Algase WES for the participants in the AD group. Participants in the control group completed a self-report version of the same questionnaire.

AET Procedure. The AET was administered using an IBM-compatible laptop computer with a 14-inch monitor with the resolution of 1024 X 768 pixels and refresh rate of 75 Hz. Participants were seated 50 cm away from the computer screen with their body midline aligned with the center of the screen. Responses were made by pressing one of the two buttons on the Ergodex® DX1TM Input System, an 8 X 10 inch pad connected to the computer and aligned with participant's midline, so that one button was on the participant's right and the other was on the left.

Each trial contained 4 screens (see Figure 3). In screen 1, a fixation pattern consisting of four stars forming a square field, was presented at the beginning of each trial for the duration of 1000 ms and the participants were instructed to fixate their gaze on the pattern. Fixation screen was followed by a black screen presented for the duration of 500 ms (screen 2), followed by the presentation of one of the sixteen positions of stimuli (screen 3). Participants were encouraged to respond as quickly as they could without making an error. As soon as they made their response, the stimulus disappeared and was replaced by a black screen (screen 4) for the duration of 500 ms. If they did not respond, the stimulus stayed on the screen for the maximum of 4500 ms followed by screen 4.

The inter-trial interval was 500 ms. Both response time (RT in milliseconds) and accuracy of response (correct = 1, wrong = -1, missed = 0) were recorded for each trial. There were a total of 96 trials per condition, such that each of 16 types of stimuli was randomly presented 6 times. Missed trials were randomly replaced within each condition of 96 trials. Therefore, for some participants the number of trials per condition was greater than 96, but no greater than 112, as each type of missed trial was only replaced once per condition.

Data from the AET yielded a total of 9953 trials. Anticipatory responses, defined as responses that were made within < 100 ms, were removed. Eight trials including such responses were eliminated from the analyses, resulting in 9945 trials. There were no significant group differences in terms of the number of anticipatory responses ($\chi^2$ = 4.41; *p* = .059). Z-score distributions were then generated for the RT data for each subject across the conditions and stimuli positions. One hundred ninety-four (194) outlier trials, defined as responses more than 3 standard deviations away from the mean reaction time (RT; -3 > zRT > +3) were eliminated. Significant group differences were observed between the groups, as the participants in the HEC group made significantly greater number of outlier responses than participants in the AD group ($\chi^2$ = 187.11, *p* = .00). The remaining 9751 trials were used for data analyses.

To ensure adequate effect sizes, given a small sample size, accuracy and RT data generated by the AET were combined in three different ways. The original 16 stimulus positions were combined based on one of three principles. (1) 4 levels of the position of the red vertical line relative to the body midline, such that the red line was presented to the "distal" left, “central” left, “central” right, and “distal” right of the body midline (see Figure 2). (2) 4 levels of the position of the red vertical line relative to the center of the horizontal bar, such that the red line could be presented to the “distal” left, “central” left, “central” right, and “distal” right of the middle of the gray horizontal bar (see Figure 2). (3) Sometimes the red line could be close to the body midline (central), but far (distal) from the midline of the gray horizontal bar (conflict). Also, the red vertical line could be distal to the body midline and distal to the midline of the horizontal bar (no conflict). This resulted in 2 levels (‘conflict’ or ‘no-conflict’) of distal vs. central position. The third set of analyses was based on the presence or absence of such conflicts.

Data from the Egocentric-NI condition were not included Analyses (2) and (3) above, as the gray horizontal bar was absent.

All statistical analyses were performed using PASW Statistics version 18.0 software.

### Design and Data Analysis.

To determine whether egocentric and allocentric spatial processing systems are differentially affected in patients with AD, a 2 (Group: AD, HEC) by 3(Condition: Allocentric, Egocentric-I, Egocentric-NI) by 4 (Stimulus Position :distal left, central left, central right, and distal right) mixed factorial Analysis of Variance (ANOVA) was performed, where Group, Condition, and Stimulus Position were independent variables and RT or accuracy (percent of correct responses) were dependent variables.

To determine the relationship between performance on the objective measures of allocentric and egocentric spatial processing, as measured by the AET and the self- or caregiver report of participants’ wayfinding ability (Algase WES), linear regression analyses were performed using RT or accuracy on AET as independent variables and Algase WES Total Score as a dependent variable.

To determine the relationship between objective measures of allocentric and egocentric spatial processing and domains of attention and working memory/executive function, two linear regression analyses were performed using Attention and Working Memory/Executive composite scores as calculated above as independent variables and RT or accuracy on AET as dependent variables.

Repeated measures ANOVAs were performed to determine whether allocentric and egocentric processing (AET) are differentially affected in participants assigned to AD group and whether participants in AD group performed worse on tasks of allocentric and egocentric processing compared to age-matched controls.  Six separate repeated measures ANOVAs were performed, such that for each of the three aforementioned groupings of data (i.e. body midline, gray horizontal bar midline, and “conflict/no-conflict”) there were two analyses: one using accuracy as dependent variable and another using RT as dependent variable.  Repeated measures analyses revealed that only grouping data by position of vertical bar in relationship to body midline produced significant results, with neither of the other two adding new information to these results. Thus, only data combined by body midline were used in further regression analyses, reported in the Results, and discussed.  These data are summarized in Table 4 (see Appendices B and C for Supplemental Tables and Figures on the two remaining groupings of data).

# Results

## Main Analyses

**Hypothesis 1:** Participants with AD would be more impaired than the HEC participants on the Alocentric, the Egocentric-I, and the Egocentric-NI conditions.

Two 2 x 3 x 4 repeated measures ANOVAs with Group (AD, HEC), Condition (Allocentric, Egocentric-I, Egocentric-NI), and Stimulus Position (Distal Left, Central Left, Central Right, and Distal Right) as independent variables and RT or accuracy of response as dependent variables were computed. The results of both ANOVAs supported the a priori prediction that participants with AD would perform significantly worse than participants in the HEC group, as measured by main effect of group (see Table 4).

RT.

There was a significant main effect of group, $F$ (1, 31) = 9.877, $p$ = .004, $\eta_p^2$ = .242. Participants with AD ($M$ = 978.21; $SD$ = 276.25) responded significantly slower than participants in HEC group ($M$ = 673.37; $SD$ = 271.66) on the Allocentric, Egocentric-I, and Egocentric-NI trials (see Table 4b).

Accuracy.

Participants with AD ($M$ = .90; $SD$ = .07) responded significantly less accurately than participants in HEC group ($M$ = .97, $SD$ = .07) on all Allocentric, Egocentric-I, and Egocentric-NI trials, as evidenced by significant main effect of group, $F$ (1, 33) = 7.213, $p$ = 0.011, $\eta_p^2$= .179 (see Table 4a).

**Hypothesis 2:** The allocentric spatial processing would be more affected than egocentric processing in participants with AD.

Two 2 x 3 x 4 repeated measures ANOVAs with Group (AD, HEC), Condition (Allocentric, Egocentric-I, Egocentric-NI), and Stimulus Position (Distal Left, Central Left, Central Right, and Distal Right) as independent variables and RT or the accuracy of response as dependent variables were computed. The results of these ANOVAs revealed that RT data supported the a priori prediction that the allocentric spatial processing would be more affected than the egocentric in participants with AD and the accuracy data showed a trend in the expected direction, as measured by condition by group interaction effect (see Table 4; Figure 4).

RT.

There was a significant Condition by Group interaction, F(2, 62) = 3.370, p = .041, ηp2 = .098 (see Table 4b and Figure 4b). Post-hoc analyses (LSD) revealed that while the HEC participants took significantly longer to respond on the Allocentric than the Egocentric-I trials, (p = 0.005) and on Egocentric-NI trials, (p = 0.000), there was no difference in performance between the Egocentric-I and the Egocentric-NI condition. In contrast, participants with the AD did not differ significantly on the Allocentric and the Egocentric-I conditions, but required significantly less time to respond on a the Egocentric-NI trials as compared to both Allocentric (p = .000) and Egocentric-I (p = 0.000) conditions. Participants with the AD performed significantly worse than the HEC participants on the Allocentric (p = .002) and Egocentric-I (p = .001), but not Egocentric-NI (p = .143) conditions.

Accuracy.

The Condition by Group interaction showed a trend, $F(2, 66) = 2.691$, $p < .075$, $\eta_p^2 = .075$. The decrement in performance on Egocentric-I as compared to the Allocentric and the Egocentric-NI condition was much greater in the AD group than in the HEC group (see Table 4a; Figure 4a). Post-hoc testing revealed that participants with the AD performed significantly worse than the HEC participants on the Allocentric (*p* =.042) and Egocentric-I (*p* = .002), but not Egocentric-NI (*p* = .644) condition.

**Hypothesis 3:** The performance on the neuropsychological tests of attention, working memory and executive functioning would be predictive of performance on measures of the allocentric and the egocentric processing

RT.

Three forced entry linear regression analyses were performed with RT as the dependent variable and the composite Attention and Executive scores as predictor variables. The results detailed below are summarized in Table 5.

Allocentric: The overall model was significant, *F* (2, 31) = 5.812, *p* = .008 with both predictors explaining 28.6 % of the variance ($R^2$ = .286). Neither attention (β = -.295, *p* = .250), nor executive function score (β = -.271, *p* = .289) contributed significantly to the model.

Egocentric-I: The overall model was significant, *F* (2, 31) = 10.170, *p* = .000, with both predictors together explaining 41.2% of the variance ($R^2$ = .412). The attention composite significantly predicted performance on computerized measures of allocentric processing (β = -.653, *p* = .008), whereas the executive functioning composite did not (β = -.014, *p* = .953).

Egocentric-NI: The overall model was significant, *F* (2, 31) = 5.593, *p* = .009, with both predictors together explaining 27.8% of the variance ($R^2$ = .278). The attention composite significantly predicted performance on computerized measures of the allocentric processing (β = -.584, *p* = .028), whereas the executive functioning composite did not (β = .075, *p* = .769).

In summary, measures of attention were predictive of the RT on the two egocentric conditions, whereas the executive functioning measure was not predictive of performance on any of the three conditions.

Accuracy.

The forced entry linear regression analyses were performed with accuracy of performance used as the dependent variable in the following three regression analyses, using the composite attention and executive functioning scores as predictors. The data described below are summarized in Table 5.

<u>Allocentric:</u> The results of the regression indicated that the overall model was significant, *F* (2, 31) = 9.215, *p* = .001 and explained 38.9% of the variance ($R^2$ = .389). Attention composite score alone significantly predicted accuracy of performance on this condition (β = .799, *p* = .002), but the executive function composite alone did not contribute significantly to the model (β = -.322, *p* = .290).

<u>Egocentric-I</u>: The overall model was significant, *F* (2, 31) = 7.022, *p* = .003, with the two predictors together explaining 32.6% of the variance ($R^2$ = .326). Attention composite score alone significantly predicted accuracy of performance on this condition (β = .710, *p* = .007), but the executive function composite alone did not contribute significantly to the model (β = -.194, *p* = .433).

<u>Egocentric-NI</u>: The overall model was significant, *F* (2, 31) = 4.323, *p* = .023, with the two predictors together explaining 23% of the variance ($R^2$ = .230). Attention composite score alone significantly predicted accuracy of performance on this condition (β = .717, *p* = .010), but the executive function composite alone did not contribute significantly to the model (β = -.388, *p* = .148).

Overall, models using combined measures of attention and executive functioning were significantly predictive of accuracy on all three conditions. However, only the attention composite alone contributed significantly to these models whereas the executive composite alone did not.

**Hypothesis 4:** The performance on objective measures of allocentric and egocentric functioning would be predictive of caregiver reports of wayfinding ability as measured by Algase WES Total Score.

The forced entry linear regression analysis was performed to investigate whether the RT or the accuracy of performance on the Allocentric, the Egocentric-I, and the Egocentric-NI conditions of the AET (predictors) would predict the caregiver reports of wayfinding ability as measured by the total score of Algase WES (dependent variable).

RT.

The overall model was significant $F$ (3, 33) = 3.319, $p$ = .033. RT on all three conditions together (Allocentric, Egocentric-I, and Egocentric-NI) explained 24.9% of the variance ($R^2$ = .249), but RT on any one of these conditions alone did not contribute significantly to the model.

Accuracy.

The overall model was significant F (3, 33) = 4.437, p = .011. Accuracy of performance on all three conditions of the AET together explained 30.7% of the variance (R2 = .307), but accuracy of performance on any one of these conditions alone did not contribute significantly to the model.

### Exploratory analyses

Additional exploratory analyses were conducted to examine properties of Allocentric-Egocentric Test and Algase Wayfinding Effectiveness Scale.

### Allocentric-Egocentric Test.

RT: Data combined by position of the red vertical line in relationship to body midline.

A repeated measured ANOVA with Group (AD, HEC), Condition (Allocentric, Egocentric-I, Egocentric-NI), and Stimulus Position (Distal Left, Central Left, Central Right, and Distal Right) as independent variables was computed with RT as a dependent variable. Mauchly's test indicated that the assumption of sphericity was violated for the Condition by Stimulus Position interaction, $\chi^2(20) = 117.302$, $p < .000$. Therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\varepsilon = .410$). Data detailed below are summarized in Table 4b.

Results showed a significant main effect of Condition, $F(2, 62) = 24.996$, $p < .000$, $\eta_p^2 = .446$ (see Appendix C, Supplemental Figure 1b). Post-hoc analyses using LSD procedure revealed that participants responded significantly slower on the Allocentric ($M = 916.315$, $SD = 391.167$) as compared to the Egocentric-I ($M = 798.391$, $SD = 377.346$, $p < .005$) and the Egocentric-NI conditions ($M = 623.183$, $SD = 193.485$, $p < .000$). Further, participants responded significantly slower on the Egocentric-I condition as compared to the Egocentric-NI condition ( $p < .000$).

Results showed a significant main effect of Stimulus Position, $F(3, 93) = 23.590$, $p < .000$, $\eta_p^2 = .432$ (see Appendix C, Supplemental Figure 2b). Post-hoc analyses using LSD procedure revealed that participants responded significantly slower on trials, in which the red vertical line was positioned to the central left ($M = 854.387$, $SD = 366.969$) as compared to those in which it was positioned to the distal left ($M = 700.233$, $SD = 222.331$, $p < .000$) and the distal right ($M = 716.892$, $SD = 293.997$, $p < .000$). Similarly, participants responded significantly slower on trials in which the red vertical line was positioned to the central right ($M = 857.477$, *SD* = 335.071) as compared to those in which it appeared to the distal left ($p < .000$) and to the distal right ($p < .000$). No significant differences in RT were found between trials in which the red vertical line was centrally located and those in which it was distally located.

Results showed a significant Condition by Stimulus Position interaction, $F(2.463, 76.348) = 5.0612$, $p < .005$, $\eta_p^2 = .140$. Post-hoc analyses using LSD procedure revealed that for the stimuli in which the red vertical line was located to the distal left of the body midline, participants responded most slowly on the Allocentric condition, which was significantly different than RT on the Egocentric-I ($p < .000$) and the Egocentric-NI conditions ($p < .000$). Further, RTs on these trials in the Egocentric-I condition were significantly slower than RTs on the same trials on the Egocentric-NI condition ($p < .000$). For the stimuli in which the red vertical line was located to the central left of the body midline, participants also responded most slowly on the Allocentric condition, which was significantly slower than RT on the Egocentric-I ($p < .011$) and the Egocentric-NI conditions ($p < .000$). Further, RTs on these trials in the Egocentric-I condition were also significantly slower than RTs on the same trials on the Egocentric-NI condition ($p < .000$). For the stimuli in which the red vertical line was located to the distal right of body midline, participants responded equally slowly on the Allocentric and the Egocentric-I conditions, but both were significantly slower than RTs on the Egocentric-NI condition ($p <.000$ and $p < .000$ respectively). For the stimulus positions in which the red vertical line was positioned to the distal right of body midline, RTs were slowest on the Allocentric condition, which was significantly slower than RTs on the Egocentric-I ($p < .000$) and the Egocentric-NI conditions ($p < .000$). In addition, RTs on these trials in the Egocentric-I condition were also significantly slower than RTs on the same trials on the Egocentric-NI condition ($p < .035$).

Accuracy: Data combined by position of the red vertical line in relationship to the body midline.

A repeated measures ANOVA with Group (AD, HEC), Condition (Allocentric, Egocentric-I, Egocentric-NI), and Stimulus Position (Distal Left, Central Left, Central Right, and Distal Right) as independent variables was computed with accuracy of response as the dependent variable. Mauchly's test indicated that the assumption of sphericity was violated for the main effects of Condition, $\chi^2(2) = 12.613$, $p < .002$, and Stimulus Position $\chi^2(5) = 20.428$, $p < .001$, as well as Condition by Stimulus Position interaction, $\chi^2(20) = 187.84$, $p < .000$. Therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\varepsilon = .754$ for the main effect of Condition and $\varepsilon = .764$ for the main effect of Stimulus Position; $\varepsilon = .481$ for the Condition by Stimulus Position interaction). Data described below are summarized in Table 4a.

Results showed significant effect of Condition, $F(1.509, 49.783) = 11.846$, $p < .000$, $\eta_p^2 = .264$ (see Appendix C, Supplemental Figure 1a). Post-hoc analysis using LSD procedure revealed that the accuracy of performance was significantly lower on the Egocentric-I condition ($M = .890$, $SD = .148$) as compared to the Allocentric condition ($M = .961$, $SD = .091$, $p < .001$) and as compared to the Egocentric-NI condition ($M = .976$, $SD = .062$, $p < .000$). Difference between accuracy on the Allocentric and the Egocentric-NI conditions was not significant.

Results showed significant effect of Stimulus Position, $F(2.293, 75.684) = 15.211$, $p < .000$, $\eta_p^2 = .316$ (see Appendix C, Supplemental Figure 2a). Post-hoc analysis using LSD procedure revealed that accuracy of performance was significantly lower on trials where the red vertical line appeared to the central left of the body midline ($M = .910$, $SD = .121$) as compared to the distal left ($M = .988$, $SD = .024$, $p < .000$) and the distal right ($M = .978$, $SD = .082$, $p < .001$). In addition, this analysis revealed that accuracy of performance was significantly lower on trials where the red vertical line appeared to the central right of the body midline ($M = .894$, *SD*

= .152) as compared to the distal right (*M* = .978, *SD* = .082, $p < .000$) and the distal left (*M* = .988, *SD* = .024, $p < .000$). Difference in accuracy of performance on trials where the red vertical line appeared to the distal left as compared to the distal right of the body midline was not significant.

Results showed significant Stimulus Position by Group interaction, $F(3, 99) = 3.398$, $p < .021$, $\eta_p^2 = .093$ (see Appendix C, Supplemental Figure 3a). Post-hoc analysis using LSD procedure revealed that the decrement in accuracy of performance on trials where the red vertical line was located to the central left (p < .004) and the central right of the body midline ($p < .001$) was more significant in the AD group as compared to the HEC group. The differences in accuracy of performance on trials in which the red vertical line was positioned to the distal left or the distal right of the body midline were not significant between the two groups.

Results showed significant Condition by Stimulus Position interaction, $F\ (2.884, 95.182) = 8.752$, $p < .000$, $\eta_p^2 = .210$. Post-hoc analysis using LSD procedure revealed that accuracy of performance was not significantly different on all types of stimuli on the Allocentric and the Egocentric-NI conditions, but on the Egocentric-I condition, there was a significant decrement in accuracy of performance on trials, in which the red vertical line was located to the central left as compared to performance on same trials on the Allocentric ($p < .000$) and the Egocentric-NI ($p < .000$) conditions. Also, there was a significant decrement in accuracy of performance on trials where the red vertical line was located to the central right as compared to performance on same trials on the Allocentric ($p < .000$) and the Egocentric-NI ($p < .000$) conditions.

Results showed significant Group by Condition by Stimulus Position interaction, $F(6, 198) = 2.1497$, $p < .049$, $\eta_p^2 = .061$ (see Appendix C, Supplemental Figure 4a). Post-hoc analyses using LSD procedure revealed that accuracy of performance was not significantly different across three conditions (Allocentric, Egocentric-I, Egocentric-NI) on trials where the red vertical line was located to the distal left or right of the body midline for both groups (AD, HEC). Further, no significant difference between groups was found in accuracy of performance on the Egocentric-NI condition for trials in which the red vertical line was positioned to the central left or central right of the body. In contrast, significant differences were found between the groups on the Allocentric condition for the stimulus positions in which the red vertical line was placed to the central left ($p < .043$) and to the central right ($p < .025$) of body midline. Significant differences were found between the groups on the Egocentric-I condition for the stimulus positions in which the red vertical line was positioned to the central left ($p < .000$) and central right ($p < .000$) of the body midline. Further, decrement in accuracy observed on trials with the centrally located red vertical line as compared to the distally located red vertical line was more pronounced in the AD group.

RT: data combined by conflict/ no-conflict.

A repeated measured ANOVA with Group (AD, HEC), Condition (Allocentric, Egocentric-I), and Stimulus Position (Conflict, No-Conflict) as independent variables was computed with RT as a dependent variable (see Appendix B, Supplemental Table 2).

The results revealed a significant main effect of Condition, $F(1, 33) = 12.509$, $p < .001$, $\eta_p^2 = .275$ (see Appendix C, Supplemental Figure 5b). Post-hoc analysis using LSD procedure revealed that RT on the Allocentric condition ($M = 907.448$, $SD = 373.855$) was significantly longer than that on the Egocentric-I condition ($M = 749.950$, $SD = 320.392$, $p < .001$).

The results revealed a significant main effect of Stimulus Type $F(1, 33) = 12.800$, $p < .001$, $\eta_p^2 = .279$ (see Appendix C, Supplemental Figure 6b). Post-hoc analysis using LSD procedure revealed that the RT on trials in which there was a conflict between the position of the red vertical line and the instruction (*M* = 849.649, *SD* = 337.050) was significantly longer than on trials in which no such conflict was present (*M* = 817.749, *SD* = 320.013, $p < .005$).

The results revealed a significant Condition by Stimulus Position interaction, *F*(1, 33) = 12.232, $p < .001$, $\eta_p^2 = .270$ (see Appendix C, Supplemental Figure 9b). Post-hoc analysis using LSD procedure revealed that the presence of conflict between perceptual cues and instruction did not significantly impact performance on the Allocentric trials. In contrast, participants took significantly longer to respond on conflict trials of the Egocentric-I condition (*M* = 834.644, *SD* = 320.977) as compared to non-conflict trials (*M* = 761.042, *SD* = 286.226, $p < .000$).

Accuracy: data combined by conflict/ no-conflict.

A repeated measures ANOVA with Group (AD, HEC), Condition (Allocentric, Egocentric-I), and Stimulus Position (Conflict, No-Conflict) as independent variables was computed with accuracy as a dependent variable (see Appendix B, Supplemental Table 2a).

The results revealed a significant main effect of Condition, *F*(1, 33) = 8.5895, $p < .006$, $\eta_p^2 = .207$ (see Appendix C, Supplemental Figure 5a). Post-hoc analysis using LSD procedure revealed that accuracy of response on the Egocentric-I condition (*M* = .893, *SD* = .147) was significantly worse than that on the Allocentric condition (*M* = .962, *SD* = .091, $p < .009$).

The results revealed a significant main effect of Stimulus Position *F*(1, 33) = 9.0506, $p < .005$, $\eta_p^2 = .215$ (see Appendix C, Supplemental Figure 6a). Post-hoc analysis using LSD procedure revealed that accuracy of response on the trials in which there was a conflict between the position of the red vertical line and the instruction (*M* = .916, *SD* = .111) was significantly lower than on trials in which no such conflict was present (*M* = .939, *SD* = .089, $p < .005$).

The results revealed a significant Condition by Stimulus Position interaction, F(1, 33) = 24.643, p < .000, ηp2 = .428 (see Appendix C, Supplemental Figure 8a). Post-hoc analysis using

LSD procedure revealed that the presence of conflict between perceptual cues and instruction did not significantly affect accuracy of response on the Allocentric condition. In contrast, the presence of such conflict resulted in significantly lower accuracy on the Egocentric-I condition ($p < .000$).

Additional analysis was conducted to explore the effects of condition order on participants' performance. There were no significant condition order effects either on RT (F (2, 66) = .6708, *p* = .515) or accuracy data (*F* (2, 66) = 1.0609, *p* = .352).

Further, to examine the effect of age on RT, we divided both HEC and AD samples into 3 age groups: 65-74, 75-84, and 85 and older. A one-way ANOVA was computed for each sample (HEC, AD), with Age group as the independent variable and the RT on each of the three conditions of the AET (Allocentric, Egocentric-I, and Egocentric-NI) as the dependent variable. In the HEC sample, the results revealed no significant effect of age on the RT on the Allocentric, *F* (2, 21) = 1.615, *p* = .225; the Egocentric-I, *F* (2, 21) = .902, *p* = .422, or the Egocentric-NI condition, *F* (2, 21) = .523, *p* = .601. Similarly, in the AD sample, there was no significant effect of age on the RT on the Allocentric, *F* (2, 12) = .413, *p* = .672; the Egocentric-I, *F* (2, 12) = .767, *p* = .490; or the Egocentric-NI condition, *F* (2, 12) = .308, *p* = .742. When the data were not divided by group membership to examine the effects of Age on the RT across the entire sample, there were still no significant effects of age on the RT, but there was a trend on the Allocentric, *F* (2, 34) = 2.540, *p* = .095, and the Egocentric-I condition, *F* (2, 34) = 2.607, *p* = .089. On the Allocentric condition, participants 85 years of age and older exhibited the longest mean RT (*M* = 1089.94, *SD* = 477.53), followed by the participants ages 75-84 (*M* = 982.16, *SD* = 450.09), and the participants ages 65-74 having the shortest mean RTs (*M* = 756.43, *SD* = 141.76). Similarly, on the Egocentric-I condition, participants in the oldest age group exhibited the longest mean

RTs (*M* = 959.63, *SD* = 472.28), followed by participants in the 75-84 age group (*M* = 783.06, *SD* = 305.21), and participants in the youngest age group, ages 65-74 exhibiting the shortest mean RTs (*M* = 644.63, *SD* = 193.30). There was no significant effect of age on the mean RT on the Egocentric-NI condition, *F* (2, 34) = 1.867, *p* = .171.

**Algase WES.**

A one way ANOVA was computed to examine the effect of group (AD, HEC) on the caregiver/self-report of wayfinding ability in daily life, as measured by Algase WES Total Score. The results revealed a significant effect of group, *F*(1, 33) = 51.029, *p* < .000 on wayfinding score. Post-hoc analysis using LSD procedure revealed that participants in the AD group were rated much lower on the measure of wayfinding ability in daily life (*M* = 86.54, *SD* = 18.406) compared to the HEC participants (*M* = 122.45, *SD* = 11.446).

Accuracy and RT.

Exploratory analyses showed that accuracy data were quite variable and approached the ceiling effect. Further, significant negative correlations were found between the accuracy and the RT data on the Allocentric (*r* = -.714, *p* = .006), the Egocentric-I (*r* = -.562, *p* = .000), and the Egocentric-NI (*r* = -.345, *p* = .042) conditions. Namely, the lower the percent of accurate responses, the longer the mean RT was. As both reduced accuracy and increased mean RT are indicative of poorer performance, both indices were in agreement and, therefore, for the purpose of clarity the less variable, more reliable data (mean RT) were used to discuss the results.

## Discussion

The purpose of the study was to examine the allocentric and the egocentric mechanisms of spatial disorientation in Alzheimer's disease.

The sparse extant studies of the allocentric and the egocentric mechanisms of AD relied on virtual reality (Cushman, et al., 2008) or real-life navigation tasks (deIpolyi, et al., 2007), which are more ecologically valid, but performance on these tasks likely involves multiple cognitive mechanisms that would be difficult to parse out. Further, more complex virtual reality and real-life navigation paradigms may be difficult to learn for the patients with AD, who have a well-documented memory impairment. We used a simpler experimental measure of the allocentric and the egocentric functioning that used abstract geometric stimuli and allowed for the examination of participants' abilities to use allocentric versus egocentric spatial cues in relative isolation from other cognitive demands and one another.

Hypotheses 1 and 2 examined the differences in performance between the AD and the HEC groups on the Allocentric-Egocentric Test. The test had three conditions: the Allocentric, the Egocentric (Egocentric-I) and the Egocentric-no-interference (Egocentric-NI), where the Egocentric-NI was the modification of the Egocentric condition (see Figure 1).

In the first hypothesis, we predicted that participants with AD would perform worse than the age-matched controls on both allocentric and egocentric tasks. Our findings supported this hypothesis, as AD participants were significantly slower on all three conditions. These findings corroborate literature to date, which shows that patients diagnosed with AD consistently perform worse on both allocentric and egocentric types of spatial orientation and navigation tasks (Hort, et al., 2007; Laczo et al., 2009) compared to the age-matched controls.

The second aim was to examine whether allocentric and egocentric functions are affected differentially in the AD sample as compared to the HEC sample. We had hypothesized that a) the performance on the Allocentric condition would be significantly more impaired than performance on either Egocentric-I and Egocentric-NI conditions in the AD, but not in the HEC group; b) the participants in the AD group will perform significantly worse on the Allocentric condition, but not on the Egocentric-I or Egocentric-NI condition as compared to the HEC participants; and c) that eliminating the interference between the two components of the stimulus (i.e. the red vertical line and the gray horizontal bar) through introduction of a one-component stimulus (the red line alone) would result in the relative improvement in performance on the Egocentric-NI condition as compared to both Allocentric and Egocentric-I conditions in both groups. The initial analysis did not support our hypotheses, as performance on the Allocentric condition was not significantly worse than on the Egocentric-I condition in the AD group, but it was in the HEC group. However, exploratory analyses revealed that the presence of the two-component stimulus negatively impacted performance on the Egocentric-I but not on the Allocentric condition regardless of the group status (see Figure 14b). We propose that the presence of the two-component stimulus resulted in a conflict between the two spatial frames of reference, such that, for example, in the Egocentric-I condition, the participant may be instructed to use the egocentric spatial cues (i.e. is something to the right or left of your midline) but may not be able to disregard the allocentric cues automatically provided by the presence of the second component of the stimulus (the gray horizontal bar). Alternatively, when asked to respond to the red vertical line, participants may have been unable to disregard the presence of and consequently responded to the irrelevant component of the stimulus (i.e., gray horizontal bar), thereby placing additional attentional demand upon the participants. We also propose that patients with AD are particularly sensitive to the presence of such conflict, which made the Allocentric and the Egocentric-I conditions equally difficult for this population. In fact, presentation of a one-component stimulus resulted in the significant improvement in the ability to use egocentric cues in the AD sample (Mean RT Egocentric-NI < Egocentric-I), but not in the HEC sample. This finding supports the idea that HEC participants are not as susceptible to the presence of such conflict, caused by the presence of the two items, as the participants with AD. Further, when the stimulus was composed of a single item, participants with AD performed significantly better on the egocentric task rather the allocentric one (Mean RT Allocentric > Egocentric-NI), which supported our original hypothesis and is in agreement with literature to date.

Participants in the AD group were significantly slower on the Allocentric condition compared to the HEC group, but the groups' performance was equal on the Egocentric-NI condition, supporting our hypothesis that the ability to use egocentric cues is not affected by the AD process, but ability to process allocentric cues is.  It may be argued that our findings are secondary to generalized slowing, as other studies suggest that patients with AD exhibit general motor slowing as compared to the healthy elderly (Kluger et al., 2008) and therefore, an overall reduction in motor speed could have resulted in comparatively longer mean RT for the AD participants.  However, all three conditions involved identical motor task (i.e. pressing on the button as fast as possible). Although we did not specifically examine pure motor speed in our sample, the absence of significant differences in the mean RT on the Egocentric-NI condition suggests that reduction in motor speed alone in AD group does not explain the differences we found between the groups.

We found that even for the HEC sample, the tasks requiring the use of the allocentric cues were more difficult than the ones with the egocentric ones. Early developmental literature (Learmonth, et al., 2001; Lew, Bremner, & Lefkovitch, 2000) suggests that the ability to use allocentric cues arises later in childhood. Our findings may be indicative of the lifespan changes in differential ability to use allocentric versus egocentric environmental cues, with possible loss of the allocentric abilities as a result of normal aging. Further research with a younger control group would be necessary to confirm such hypothesis. In addition, we learned that the presentation of a two-component stimulus significantly affected reaction times of the participants in the AD group, such that they were significantly slower on the Egocentric-I as compared to Egocentric-NI condition. Such phenomenon was not observed in the HEC group. A number of mechanisms could explain such differential decrement in this group. AD is associated with deficits in divided attention (Baddeley, et al., 2001; Perry & Hodges, 1999), and participants' attention may well have been divided between two lines comprising the stimulus. Further, although the target line was vertical and the non-target line was horizontal in our study, similarity in shape between the target and the non-target may have played a role. Additionally, each of the components (red vertical line and gray horizontal line) may have provided discrepant spatial cues to the participants, which may have resulted in undue interference between the allocentric and the egocentric reference frames.

Our third aim was to examine the relationship between the objective measures of spatial processing and the cognitive constructs of attention and executive function. We hypothesized that attention and executive function together would be predictive of performance on measures of both allocentric and egocentric processing and would contribute equally to each model. Our data partially supported this hypothesis, as both indices of attention and executive function together were significantly predictive of performance on all three conditions of the Allocentric-Egocentric Test (see Table 7). However, the index of attention significantly contributed to the models on the Egocentric-I and Egocentric-NI conditions, but not on the Allocentric condition. The significant contribution of the attention to the performance on egocentric tasks fits well with the hypothesis that egocentric spatial processing involves primarily an ongoing, on-line processing of the spatial representations around a person (R. Wang & Spelke, 2002) and require significant attentional resources. In contrast, the more stable allocentric representations may be less dependent on attention and more dependent on other higher order cognitive domains. Although we expected executive function to be one of these domains, our data did not support that. This may be due to the fact that executive function is not a unitary construct and subsumes many higher order functions under its umbrella. It is possible that the neuropsychological tasks we chose to calculate the executive function index did not tap into the executive components involved in the allocentric spatial processing. Therefore, the specific executive components of allocentric orientation are yet to be elucidated in future research.

Our fourth and last aim was to examine the relationship between the objective measures of spatial processing and the reports of getting lost in familiar and unfamiliar environments. We proposed that measures of the allocentric and the egocentric function would be predictive of caregiver reports and that performance on the allocentric and the egocentric components of the Allocentric-Egocentric Task (Allocentric, Egocentric-I, and Egocentric-NI conditions) would equally contribute to the model. Our data supported our hypothesis in that performance on all three conditions of the task together predicted a significant amount of variance on the caregiver reports of getting lost. However, neither condition alone significantly contributed to the model. These data are in line with the existing data suggesting that we integrate information from both allocentric and egocentric frame of reference to navigate in our environment (Gugerty & Brooks, 2004; Maguire, Burgess, & O'Keefe, 1999; Save & Poucet, 2000). Our sample was too small to examine this model separately for the AD and the HEC groups. Future research with sufficient sample size is warranted to examine whether differences exist in these two samples with regard to relative contribution of the allocentric and the egocentric mechanisms to the reports of daily navigational ability.

The results of the current study suggest that ability to rely on the allocentric cues is diminished in patients with AD but their ability to use egocentric cues may remain intact until later in the progression of the disease process. Such knowledge may help clinicians inform the caregivers as to the environmental modifications to be put in place to achieve the optimal balance of autonomy and safety for the individual patient. For example, a patient with impaired allocentric, but intact egocentric ability may be able to navigate safely on their own if directions allow them to navigate solely using position of landmarks in relationship to their body (e.g., at the corner turn to your left, walk two blocks then walk to your right). In addition, given our findings of a significant relationship between attention and the egocentric orientation, significant attentional impairment on the neuropsychological evaluation may help clinicians identify those individuals at increased risk of becoming lost or disoriented and therefore require increased levels of supervision when traveling. In these patients, reduced attention will compromise their already inefficient orientation ability, as they have to rely on only one frame of reference (egocentric) and the one that places significant attentional demands on the individual at that. Also, given the attentional demands of navigating via use of egocentric cues alone, the patients should be instructed in minimizing distractions as much as they can when navigating unaccompanied, such as not talking on the phone or listening to music.

## Limitations

There were several limitations in our study. We selected and subsequently adjusted the Allocentric-Egocentric Test, originally created and described by Galati et al (2000), in order to accommodate the diminished skills of participants with AD. One limitation of the task is that it may have been too easy as evidenced by the high accuracy rates in both groups. In addition, the task only required the use of proximal allocentric cues. In many real life instances, allocentricity is determined by objects that are not necessarily in our proximal view. For instance, navigating to a room outside one's immediate view would require understanding where the room is in relationship to another distal place in space. Finding one's way requires even more conceptual organization, not only what is in the immediate view. Moreover, in real life tasks, places or objects contain a meaningful semantic component. For example, one may need to consider the location of the bedroom in relationship to the living room, or the cup on the table in relationship to the sugar bowl. These semantic cues amend the otherwise simplified feature recognition used in this study.

Another limitation was the small number of available participants with AD who met all inclusion/exclusion criteria, which in turn limited the number of predictors allowable in the regression analyses. Small sample size also prevented us from examining separate models of the relationship between the allocentric and egocentric orientation ability and cognition for the AD sample and the HEC sample. Participants in the AD group were in the relatively early clinical stage of disease (CDR = 1.0) as patients in more advanced stages would have had considerable difficulty learning the task secondary to greater memory impairment. This restriction in range of disease severity limited our ability to examine relationship between progression of neurodegenerative process and loss of allocentric and egocentric spatial processing ability as well as the range of deficits found on these tasks.

Lastly, the absence of the younger control group prevented us from examining the developmental changes in the allocentric and the egocentric spatial processing associated with normal aging.

# Appendix A

<u>Algase Wayfinding Effectiveness Scale</u>*

<u>Instructions:</u> Check the box that describes the participant best. <u>Scoring</u>: 1=Never/Unable; 2=Sometimes; 3= Often; 4=Always

| | Never/Unable | Sometimes | Often | Always |
|---|---|---|---|---|
| 1.Can find way to distant and unfamiliar places | _________ | _______ | ______ | _____ |
| 2.Can find way to near and unfamiliar places | ________ | _______ | ______ | _____ |
| 3.Can find way to distant places if route and destination are familiar | ________ | _______ | ______ | _____ |
| 4.Can generate alternative routes of comparable efficiency to common destinations | _______ | _______ | ______ | _____ |
| 5.Can compensate for forced detour when traveling to familiar destinations | _______ | _______ | ______ | _____ |
| 6.Can detect when “off course” to an unfamiliar location | _______ | _______ | ______ | _____ |
| 7.Can detect when “off course” to a familiar location | _______ | _______ | ______ | _____ |
| 8.Can find way to near places when route and destination are familiar | _______ | _______ | ______ | _____ |
| 9.Can find way to unfamiliar places around the area of residence | _______ | _______ | ______ | _____ |
| 10.Can compensate without assistance once off course to an unfamiliar location | _______ | _______ | ______ | _____ |
| 11. Overall, has a good sense of direction | _______ | _______ | ______ | _____ |
| 12. Locations an unfamiliar location by circling in on it | _______ | _______ | ______ | _____ |
| 13. Relies on maps when heading to a familiar location | _______ | _______ | ______ | _____ |
| 14. Relies on maps when heading to an unfamiliar location | _______ | _______ | ______ | _____ |
| 15. Relies on landmarks when traveling to an unfamiliar location | _______ | _______ | ______ | _____ |
| 16. Prefers route in cardinal sings when getting directions to a new location | _______ | _______ | ______ | _____ |
| 17. Finds way about in a mall or museum by accessing directory | _______ | _______ | ______ | _____ |
| 18. Prefers distance estimates in terms of miles or blocks when traveling to a new location | _______ | _______ | ______ | _____ |
| 19. Relies on landmarks when traveling to a familiar location | _______ | _______ | ______ | _____ |
| 20. Locates lost items in the home by retracing steps | ________ | _______ | ______ | _____ |
| 21. Locates lost items in the home by systematically searching each room | ________ | _______ | ______ | _____ |
| 22. Prefers route in terms of landmarks when obtaining directions to a new location | _______ | _______ | ______ | _____ |
| 23. Prefers route in terms of left-right when obtaining directions to a new destination | ________ | _______ | ______ | _____ |
| 24. Uses organizers, such as key hooks, to place often used items | _______ | _______ | ______ | _____ |
| 25.Ascribes to saying: a place for everything and everything in its place | _______ | _______ | ______ | _____ |
| 26.Can find way through own home with eyes closed | _______ | _______ | ______ | _____ |
| 27.Can locate any familiar room in one’s home | _______ | _______ | ______ | _____ |
| 28.Can locate any unfamiliar room in one’s home | _______ | _______ | ______ | _____ |
| 29.Can find way around the area of residence if route and destination are familiar | _______ | _______ | ______ | _____ |
| 30.Locates lost items by asking help of others | _______ | _______ | ______ | _____ |

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** Algase, et al. (2007). Initial psychometric evaluation of the Wayfinding Effectiveness Scale. Western Journal of Nursing Research, 29, 1015-1032.*

# Appendix B: Supplemental Tables

**Supplemental Table 1**. ANOVA Tables for the Allocentric-Egocentric Test Data Grouped by the Relative Position of the Red Line to the Horizontal Gray Bar

1a. Accuracy

| **Effect** | **SS** | **df** | **MS** | **F** | ***p*** | **$\eta_p^2$** |
|---|---|---|---|---|---|---|
| Group | .599 | 1 | .599 | 9.745 | **.000** | .991 |
| Condition | .366 | 1 | .366 | 8.638 | **.006** | .207 |
| Position | .008 | 3 | .003 | .559 | .643 | .017 |
| Group by Condition | .036 | 1 | .036 | .841 | .366 | .025 |
| Group by Position | .003 | 3 | .001 | .187 | .904 | .006 |
| Condition by Position | .078 | 3 | .026 | 4.206 | **.008** | .113 |
| Group by Condition by Position | .017 | 3 | .055 | .890 | .449 | .026 |

1b. Reaction Time

| **Effect** | **SS** | **df** | **MS** | **F** | ***p*** | **$\eta_p^2$** |
|---|---|---|---|---|---|---|
| Group | 6157380 | 1 | 6157380 | 8.513 | **.006** | .205 |
| Condition | 1771663 | 1 | 1771663 | 15.274 | **.000** | .316 |
| Position | 970667 | 3 | 323556 | 11.602 | **.000** | .260 |
| Group by Condition | 7212 | 1 | 7212 | .062 | .804 | .002 |
| Group by Position | 114335 | 3 | 38112 | 1.367 | .257 | .040 |
| Condition by Position | 1152619 | 3 | 384206 | 18.503 | **.000** | .359 |
| Group by Condition by Position | 70821 | 3 | 23607 | 1.137 | .338 | .033 |

**Supplemental Table 2.** ANOVA Tables for the Allocentric-Egocentric Test Data Grouped by the Presence or Absence of Conflict Between the Instructions and the Relative Position of the Red Line

2a. Accuracy

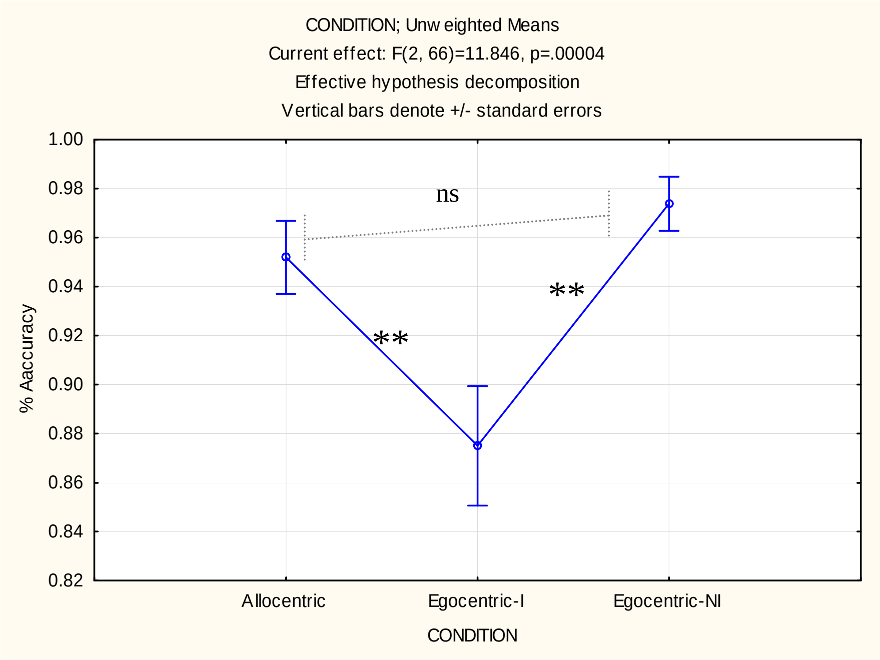
| **Effect** | **SS** | **df** | **MS** | **F** | ***p*** | **$\eta_p^2$** |
|---|---|---|---|---|---|---|
| Group | .306 | 1 | .306 | 10.005 | **.003** | .233 |
| Condition | .182 | 1 | .182 | 8.589 | **.006** | .207 |
| Position | .018 | 1 | .018 | 9.051 | **.005** | .215 |
| Group by Condition | .018 | 1 | .018 | .864 | .359 | .026 |
| Group by Position | .0004 | 1 | .0004 | .191 | .665 | .006 |
| Condition by Position | .025 | 1 | .025 | 24.643 | **.000** | .428 |
| Group by Condition by Position | .001 | 1 | .001 | .803 | .377 | .024 |

2b. Reaction Time

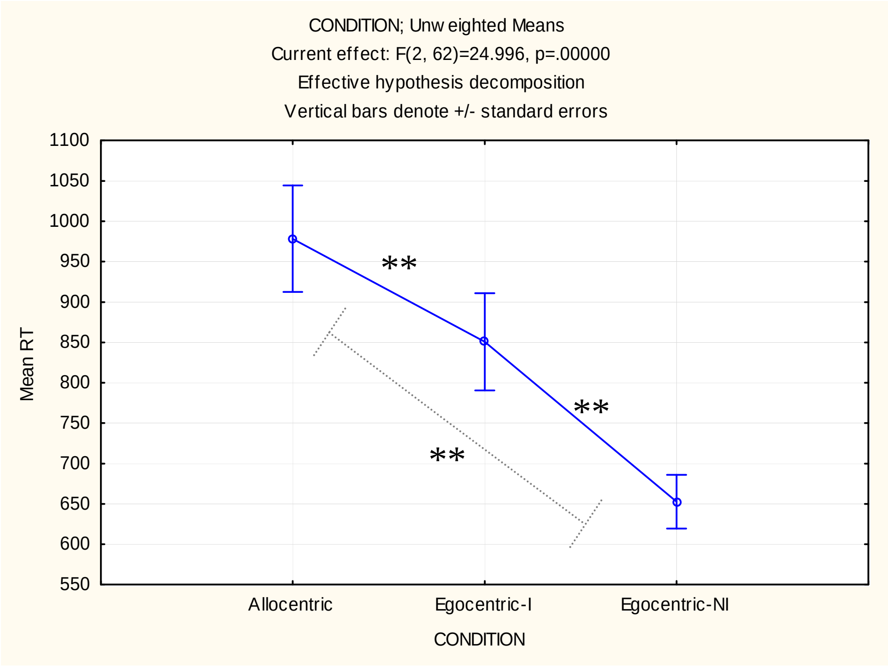
| **Effect** | **SS** | **df** | **MS** | **F** | ***p*** | **$\eta_p^2$** |
|---|---|---|---|---|---|---|
| Group | 3010492 | 1 | 3010492 | 8.578 | **.006** | .206 |
| Condition | 732991 | 1 | 732991 | 12.800 | **.001** | .279 |
| Position | 36217 | 1 | 36217 | 12.510 | **.001** | .275 |
| Group by Condition | 2509 | 1 | 2509 | .044 | .835 | .001 |
| Group by Position | 951 | 1 | 951 | .329 | .570 | .010 |
| Condition by Position | 53122 | 1 | 53122 | 12.232 | **.001** | .270 |
| Group by Condition by Position | 11717 | 1 | 11717 | 2.698 | .110 | .076 |

# Appendix C: Supplemental Figures

1a.

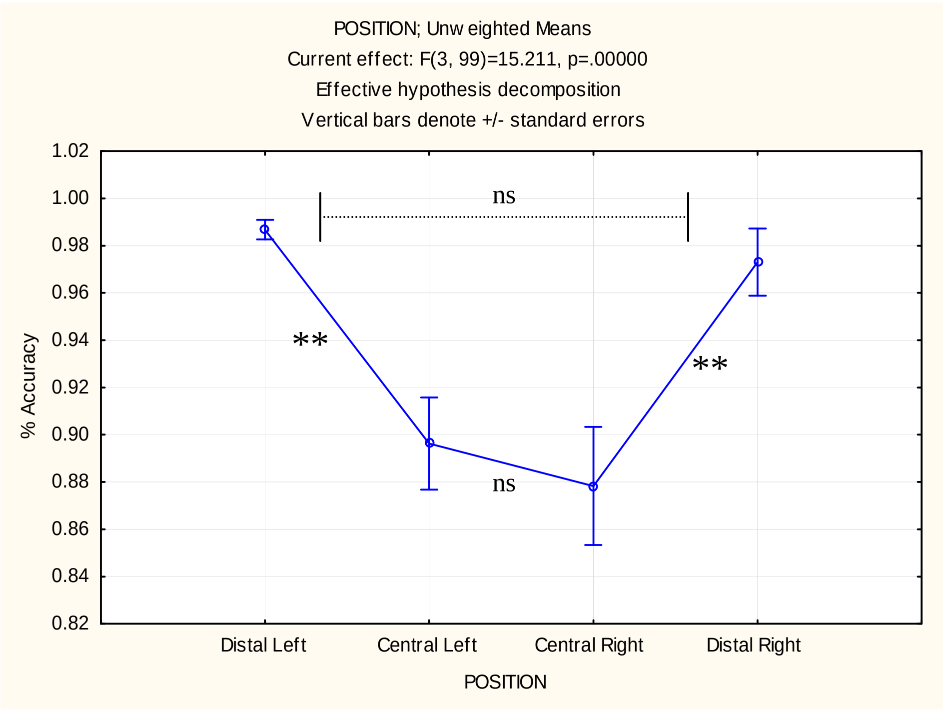


1b.

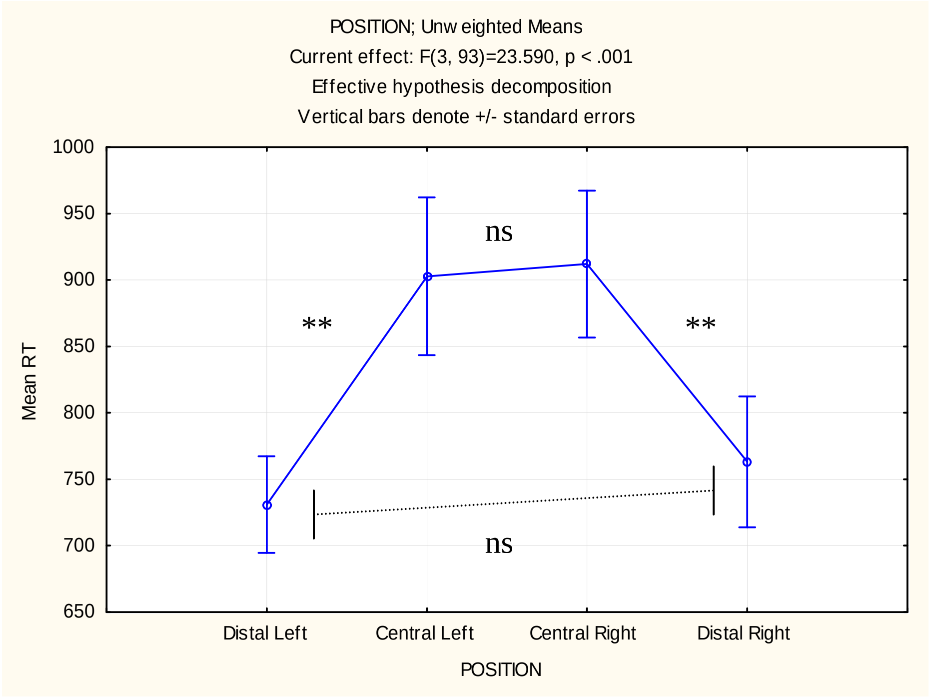


**Supplemental Figure 1.** Repeated measures ANOVA; main effect of condition. 1a) accuracy 1b) RT * p < .05 ** p < .01 ns = not significant

2a.

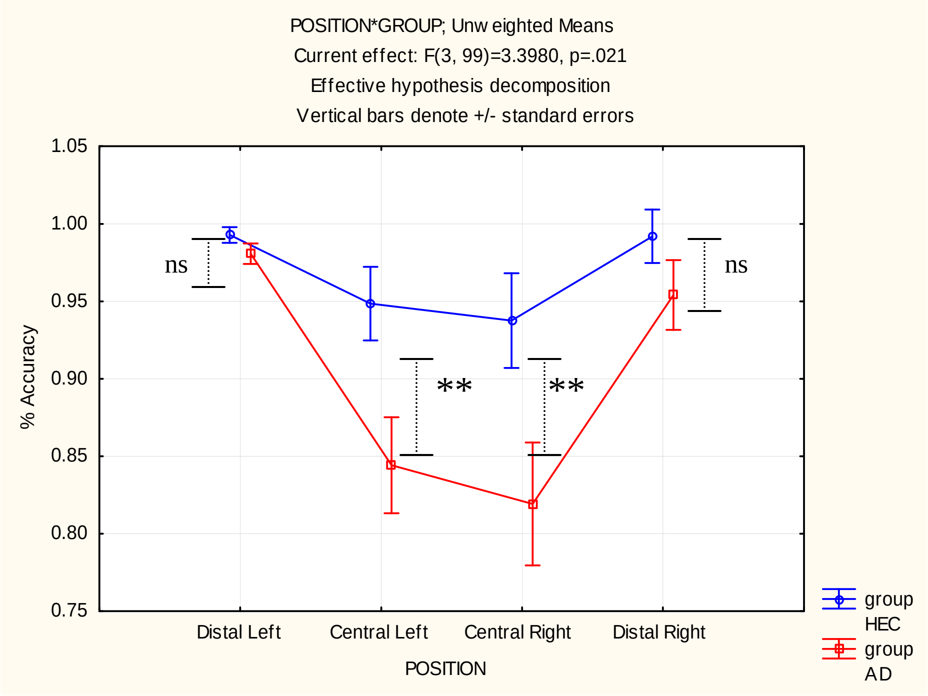


2b.

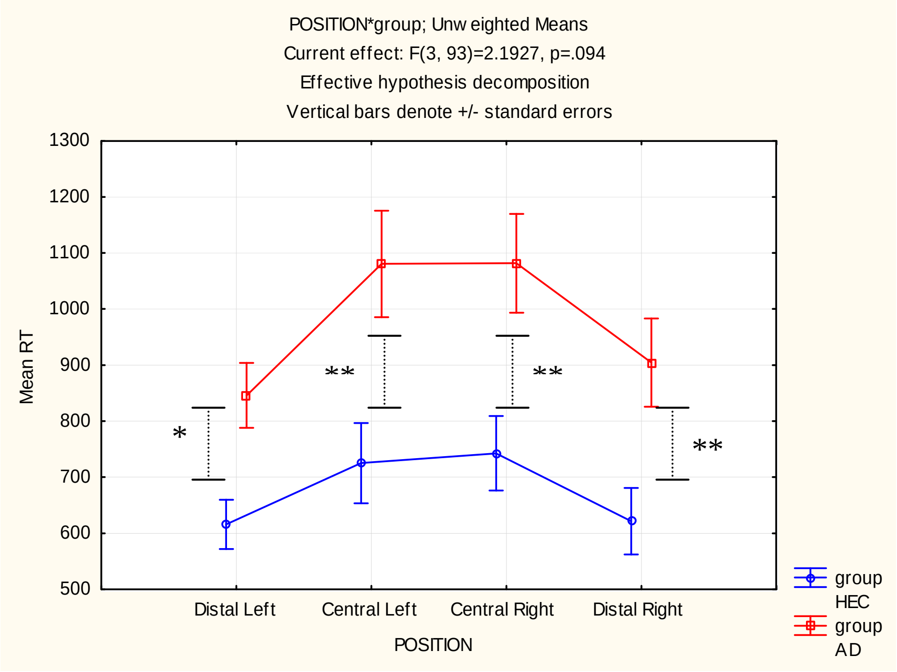


**Supplemental Figure 2.** Repeated measures ANOVA; main effect of Position; 2a) accuracy 2b) RT * $p < .05$ ** $p < .01$ ns = not significant

3a.

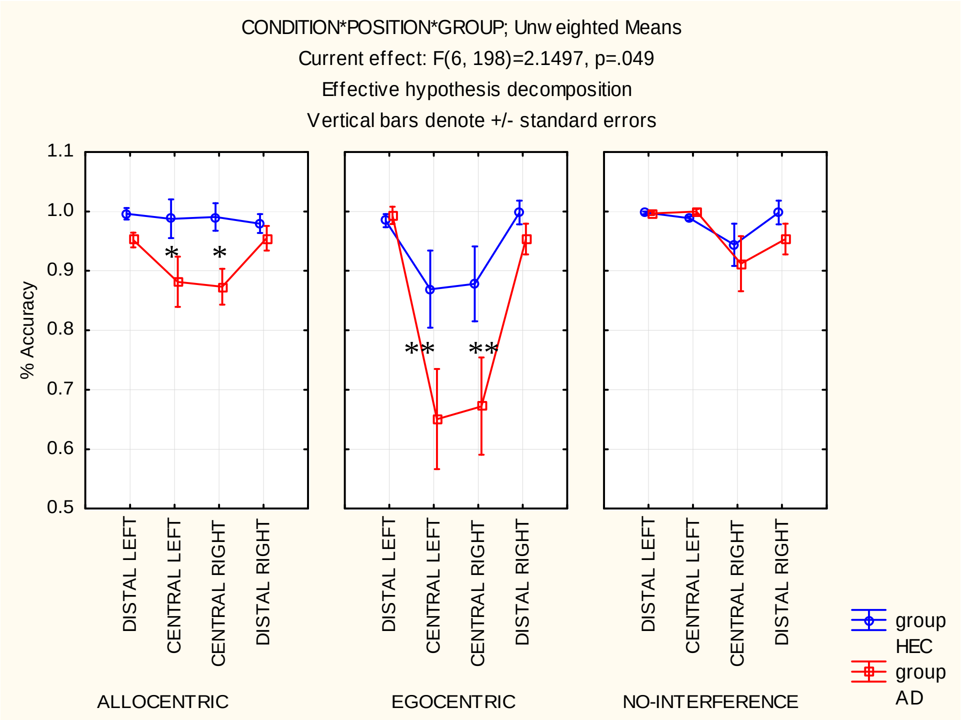


3b.

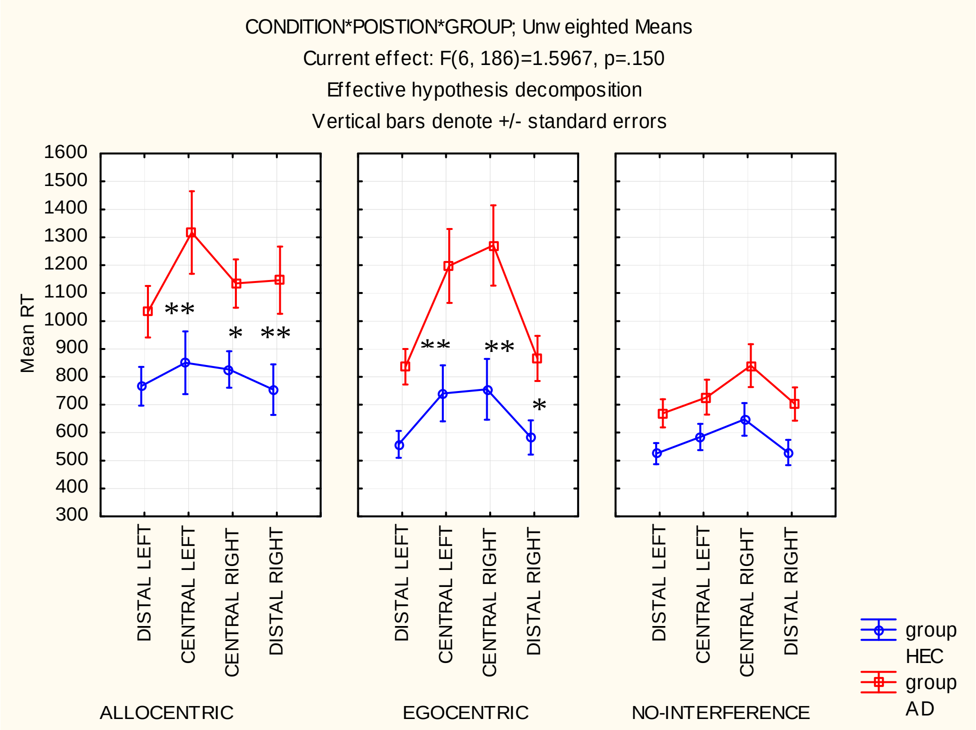


**Supplemental Figure 3.** Repeated measures ANOVA; Position by Group Interaction; 3a) accuracy 3b) RT; * *p* < .05 ** *p* < .01

4 a.

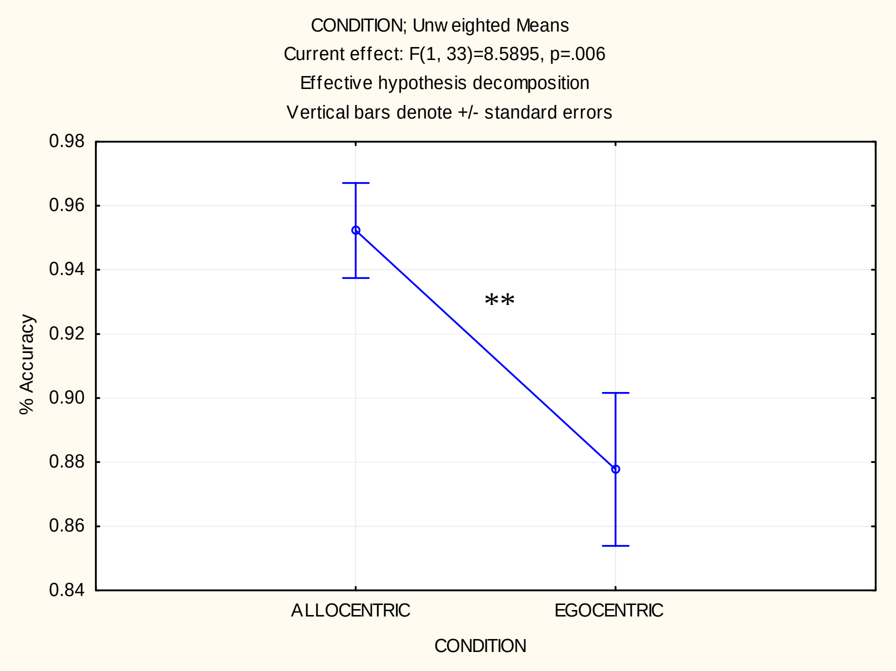


4b.

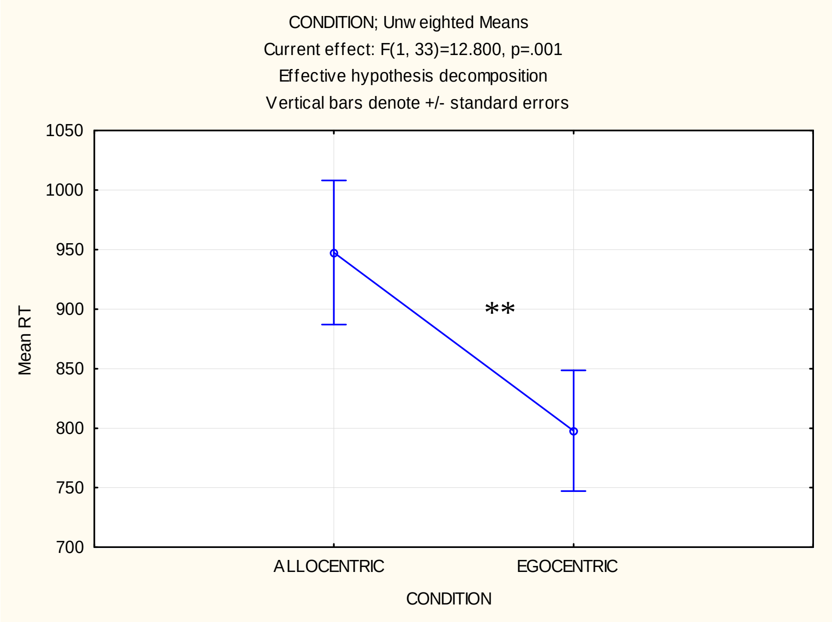


**Supplemental Figure 4:** Repeated measures ANOVA; Condition by Position by Group Interaction; 4a) accuracy 4b) RT; * *p* < .05 ** *p* < .01

5a.

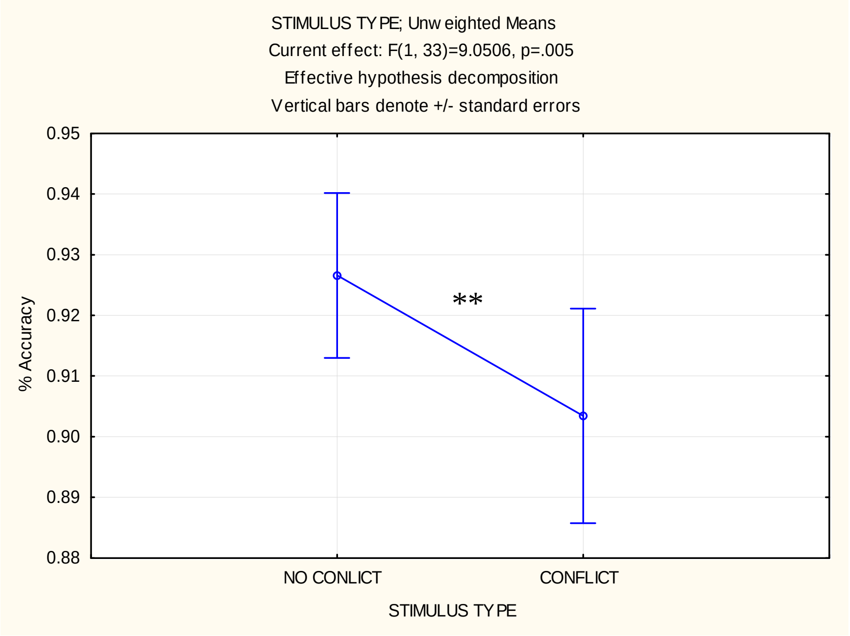


5b.

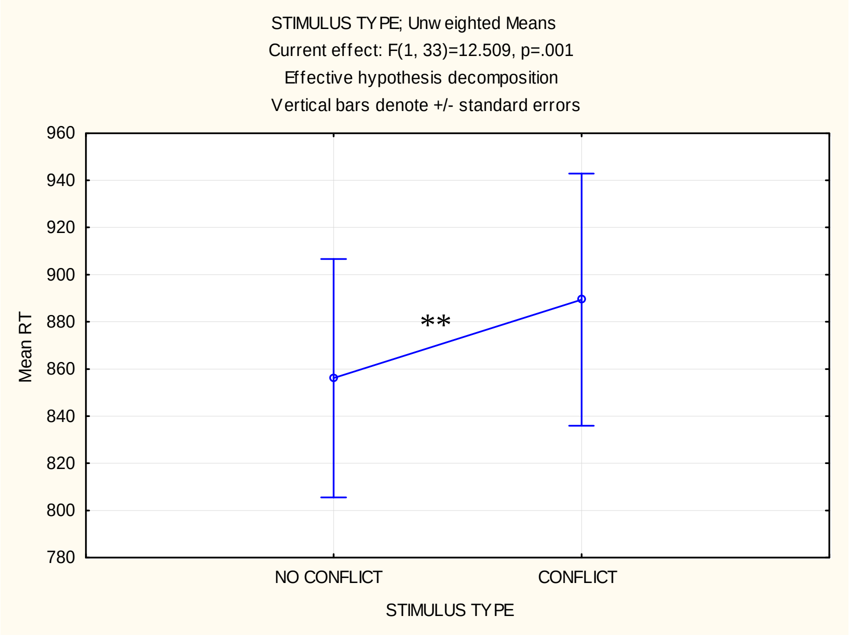


**Supplemental Figure 5.** Repeated measures ANOVA; data combined by conflict/ no conflict between position of red vertical line and instruction; Main effect of Condition; 5a) accuracy and 5b) RT; ** p <.01

6a.

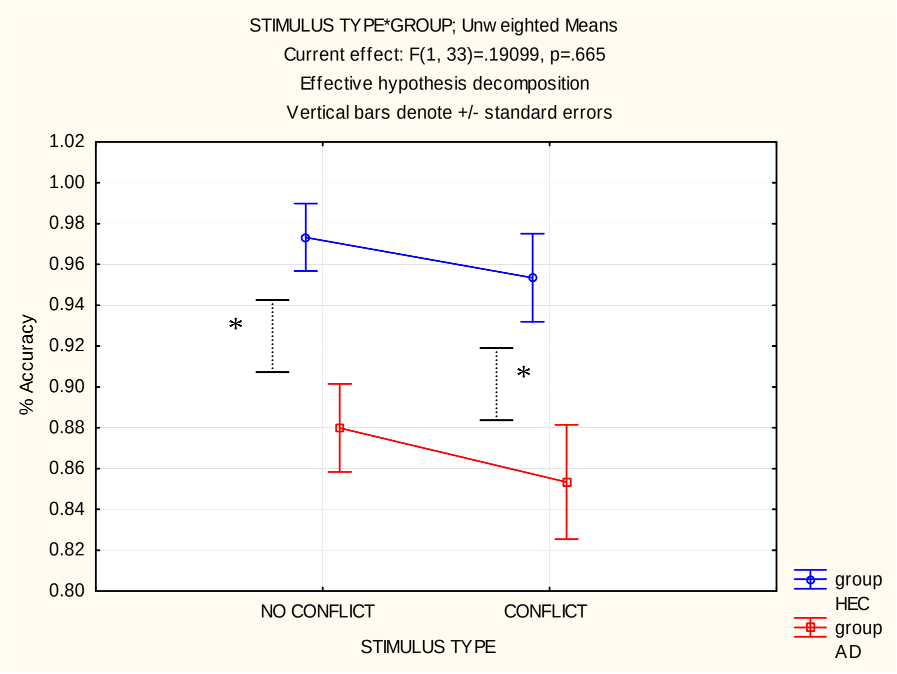


6b.

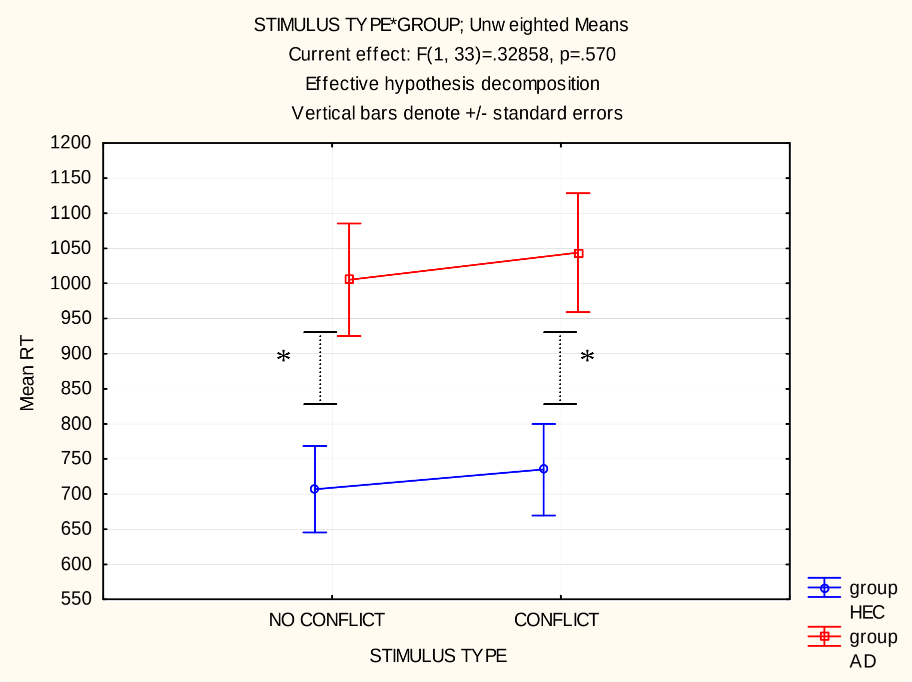


**Supplemental Figure 6.** Repeated measures ANOVA. Data combined by conflict/ no conflict between position of red vertical line and instruction; Main effect of Stimulus Position; 6a) accuracy 6b) RT; ** p < .01

7a.

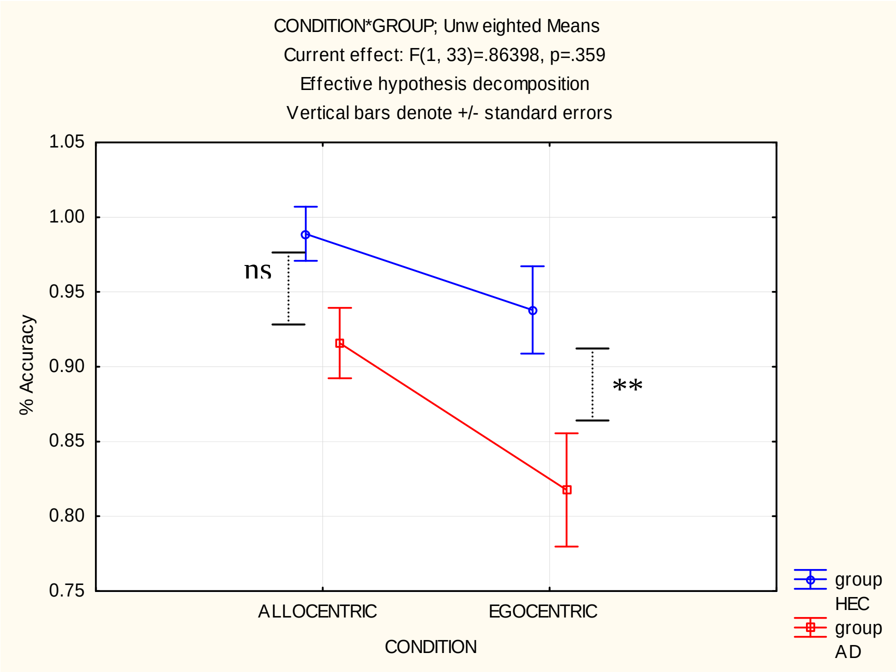


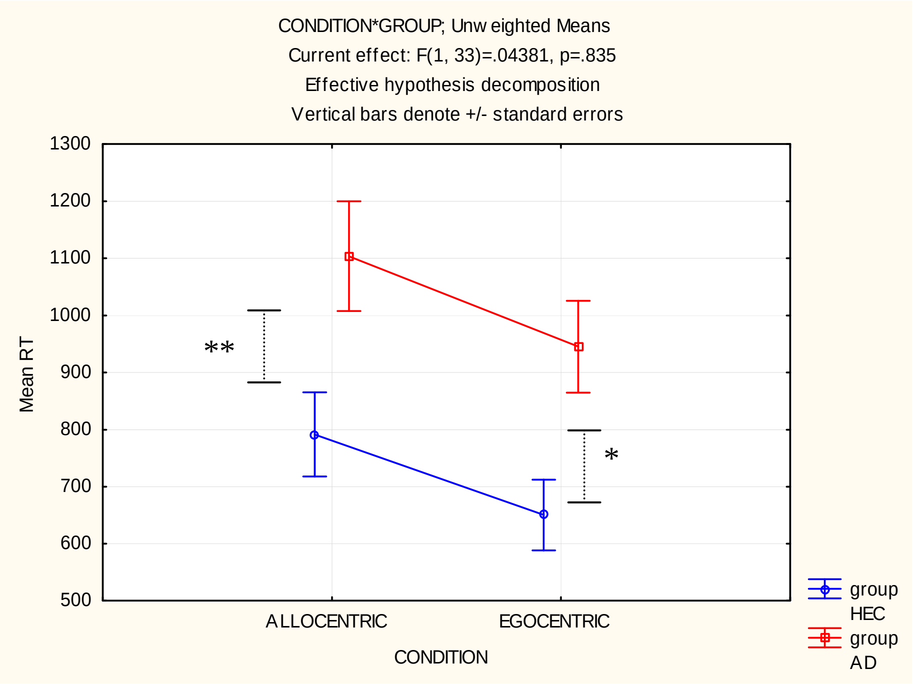
7b.



**Supplemental Figure 7**. Repeated measures ANOVA. Data combined by conflict/ no conflict between position of red vertical line and instruction; Stimulus Position by Group interaction (not significant); 7a) accuracy 7b) RT; * p < .05

8a.

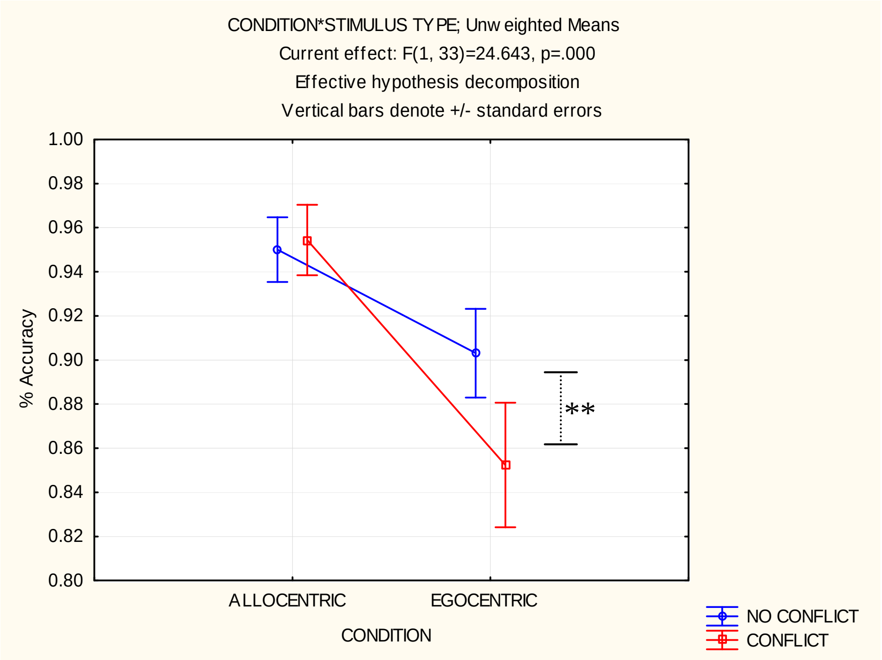




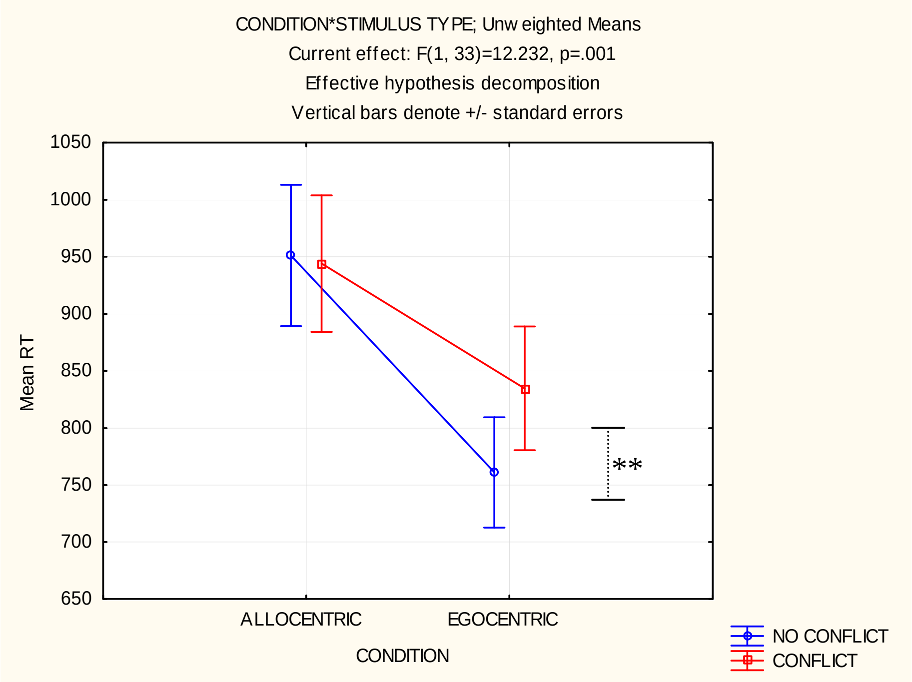
8b.

**Supplemental Figure 8**. Repeated measures ANOVA. Data combined by conflict/ no conflict between position of red vertical line and instruction; Condition by group Interaction (not significant); 8a) accuracy 8b) RT; * p < .05 ** p < .01

9a.



9b.



**Supplemental Figure 9**. Repeated measures ANOVA. Data combined by conflict/ no conflict between position of red vertical line and instruction; Condition by Stimulus Position Interaction; 9a) accuracy 9b) RT; ** p < .01; only significant results indicated.

**Table 1.** Characteristics of the sample

| | Healthy Elderly Controls (*n* = 22) | | Alzheimer's Disease (*n* = 13) | |
|---|---|---|---|---|
| | *M (SD)* | Min -Max | *M (SD)* | Min -Max |
| Age | 74.64 (8.07) | 65.00 – 94.00 | 78.43 (8.11) | 65.00 – 89.00 |
| Years of education | 15.64 (2.50) | 10.00 – 19.00 | 15.14 (3.88) | 6.00 – 20.00 |
| Mini-Mental State Examination (Maximum = 30) | 29.27 (0.77) | 27.00 – 30.00 | 23.64 (4.27) | 16.00 – 29.00 |
| Clinical Dementia Rating Scale (Sum of boxes) | 0.05 (0.15) | 0.00 – 0.50 | 4.79 (1.41) | 2.00 – 8.00 |

*Note.* Samples did not differ in terms of age or years of education, but differed significantly in their performance on the Folstein Mini-Mental State Examination *F* (1, 34) = 35.812, *p* = .000 and Clinical Dementia Rating Sum of Boxes score *F* (1, 34) = 235.513, *p* = .000).

**Table 2.** Standard Neuropsychological Tasks

| | Healthy Elderly Controls (*n* = 22) | | Alzheimer's Disease (*n* = 13) | |
|---|---|---|---|---|
| | M(SD) | Min-Max | M(SD) | Min-Max |
| Digit Span Forward Length | 7.14 (.83) | 6-8 | 6.57 (1.22) | 4-8 |
| Digit Span Backward Length | 5.32 (1.21) | 4-7 | 4.07 (1.00) | 3-7 |
| Spatial Span Forward Length | 5.41 (.96) | 4-7 | 4.07 (1.14) | 3-6 |
| Spatial Span Backward Length | 4.55 (1.06) | 3-6 | 3.50 (1.02) | 2-5 |
| Shape Cancellation Time (sec) | 49.36 (11.05) | 22-72 | 87.57 (34.80) | 49-166 |
| Shape Cancellation Omissions | 4.09 (2.60) | 0-9 | 7.43 (2.79) | 2-11 |
| Trails A Time | 31.00 (12.23) | 15-55 | 59.36 (35.68) | 30-134 |
| Trails A Errors | .09 (.29) | 0-1 | .36 (.84) | 0-3 |
| Trails B Time | 77.32 (32.03) | 40-164 | 227.27(96.08) | 54-300 |
| Trails B Errors | .32 (.57) | 0-2 | 1.56 (1.42) | 0-4 |

**Table 3.** Descriptive Statistics for the Allocentric-Egocentric Test Data by Group and Condition

**Table 3a. Accuracy**

| | Healthy Elderly Controls (*n* = 22) | | Alzheimer's Disease (*n* = 13) | |
|---|---|---|---|---|
| Condition | *M (SD)* | Min - Max | *M (SD)* | Min - Max |
| Allocentric | .99 (.02) | .93 - 1.00 | .92 (.13) | .53 - 1.00 |
| Egocentric-I | .93 (.10) | .68 - 1.00 | .82 (.18) | .47 - 1.00 |
| Egocentric-NI | .98 (.03) | .86-1.00 | .97 (.10) | .65 – 1.00 |

**Table 3b. Reaction Time**

| | Healthy Elderly Controls (*n* = 22) | | Alzheimer's Disease (*n* = 13) | |
|---|---|---|---|---|
| Condition | *M (SD)* | Min -Max | *M (SD)* | Min –Max |
| Allocentric | 794.62 (203.23) | 583.22 – 1385.67 | 1122.26 (536.80) | 661.15 – 2394.24 |
| Egocentric-I | 658.91 (197.35) | 439.09 - 1068.88 | 1042.49 (491.20) | 529.05 – 1965.24 |
| Egocentric-NI | 567.49 (158.68) | 399.44 – 909.05 | 717.43 (216.10) | 447.48 – 1185.29 |

**Table 4.** ANOVA Tables for the Allocentric-Egocentric Test Data Grouped by Body Midline

**Table 4a. Accuracy**

| **Effect** | **SS** | **df** | **MS** | **F** | ***p*** | $\eta_p^2$ |
|---|---|---|---|---|---|---|
| Group | .456 | 1 | .456 | 7.213 | **.011** | .994 |
| Condition | .704 | 2 | .352 | 11.846 | **.000** | .264 |
| Position | .866 | 3 | .289 | 15.211 | **.000** | .316 |
| Group by Condition | .160 | 2 | .080 | 2.691 | .075 | .075 |
| Group by Position | .193 | 3 | .065 | 3.398 | **.021** | .093 |
| Condition by Position | .796 | 6 | .133 | 8.752 | **.000** | .210 |
| Group by Condition by Position | .196 | 6 | .033 | 2.150 | **.049** | .061 |

**Table 4b. Reaction Time**

| **Effect** | **SS** | **df** | **MS** | **F** | ***p*** | $\eta_p^2$ |
|---|---|---|---|---|---|---|
| Group | 8348578 | 1 | 8348578 | 9.877 | **.004** | .242 |
| Condition | 6579628 | 2 | 3289814 | 24.996 | **.000** | .446 |
| Position | 2410059 | 3 | 803353 | 23.590 | **.000** | .432 |
| Group by Condition | 887033 | 2 | 443517 | 3.370 | **.041** | .098 |
| Group by Position | 224022 | 3 | 74674 | 2.093 | .094 | .066 |
| Condition by Position | 980301 | 6 | 163384 | 5.061 | **.000** | .140 |
| Group by Condition by Position | 309264 | 6 | 51544 | 1.597 | .150 | .050 |

**Table 5.** Summary of the results of regression analyses.

| | | ALLOCENTRIC | EGOCENTRIC-I | EGOCENTRIC-NI |
|---|---|---|---|---|
| REACTION TIME | Whole Model | ** | ** | ** |
| | Attention | ns | ** | * |
| | Executive | ns | ns | ns |
| ACCURACY | Whole Model | ** | ** | * |
| | Attention | ** | ** | * |
| | Executive | ns | ns | ns |

*Note:* Forced entry linear regressions with reaction time or accuracy on the three conditions of the Allocentric-Egocentric Test (Allocentric, Egocentric-I, and Egocentric-NI) as dependent variables and the composite scores of Attention and Executive Function as predictors (independent variables); * $p< .05$ ** $p< .01$ ns = not significant

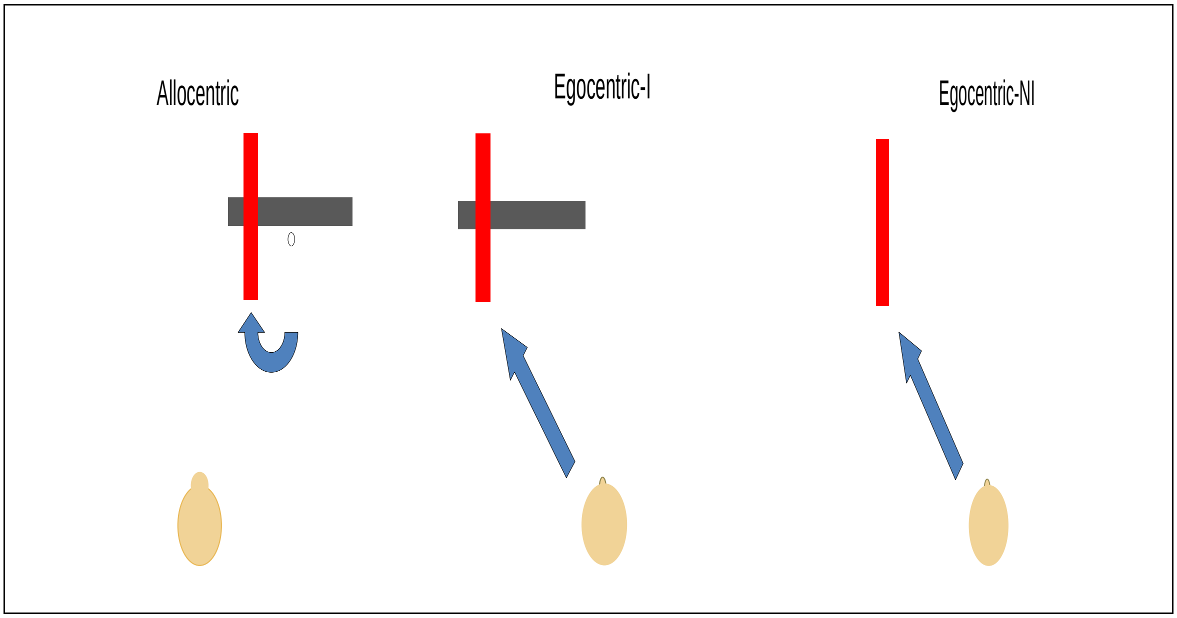
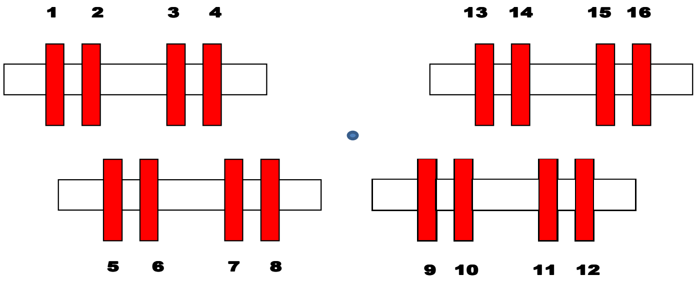


**Figure 1.**
Allocentric-Egocentric Test conditions: Allocentric, Egocentric-I; Egocentric-NI. The blue arrow indicates the instruction for each task: in Allocentric condition participants were asked to indicate whether the red line is to the right or left of the middle of the gray horizontal bar. The middle of the horizontal bar was not identified and the participants had to estimate it. In the Egocentric-I and the Egocentric-NI conditions the participants were asked to indicate whether the red line is to the right or left of their own midline.



| Red Vertical Bar Position in Relationship to Body Midline | | | |
|---|---|---|---|
| Distal Left | Central Left | Central Right | Distal Right |
| 1 2 5 6 | 3 4 7 8 | 9 10 13 14 | 11 12 15 16 |

**Figure 2.**
16 positions of vertical red line were reduced to 4 based on the relative position of the red vertical line to the body midline resulting in 4 positions: distal left, central left, central right, and distal right.

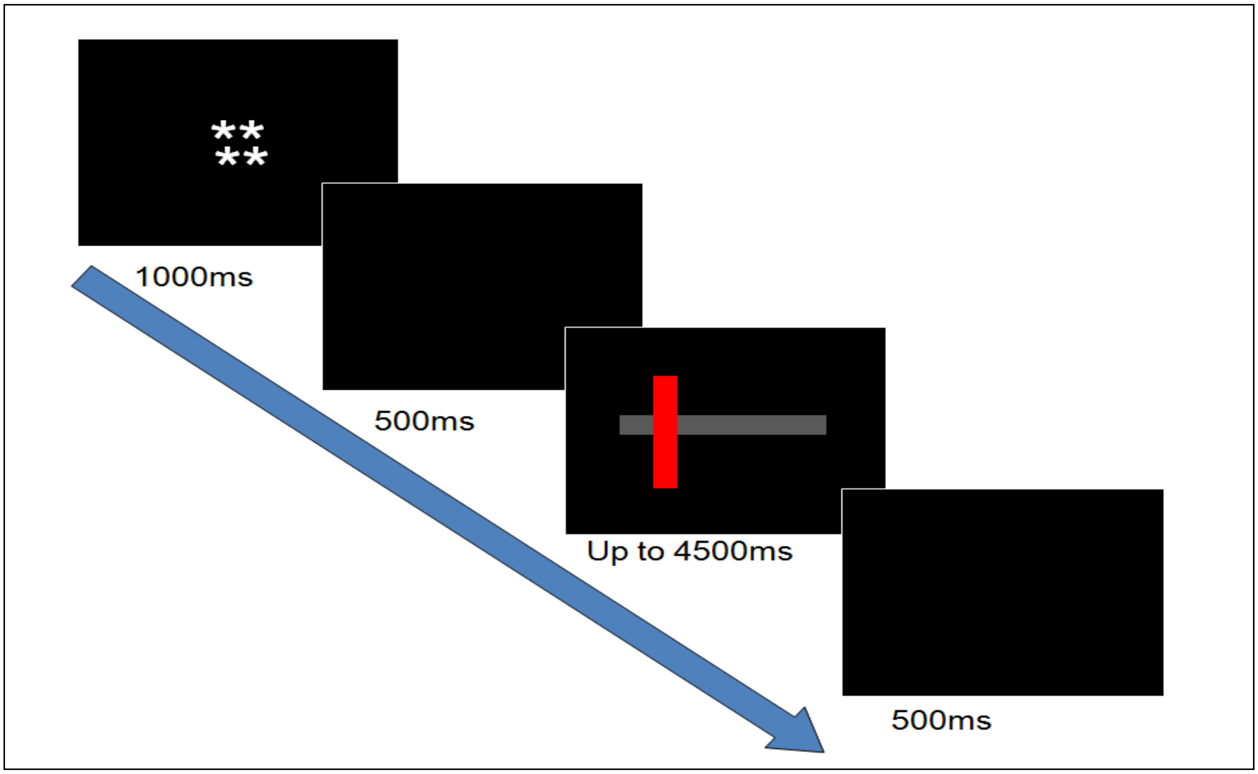
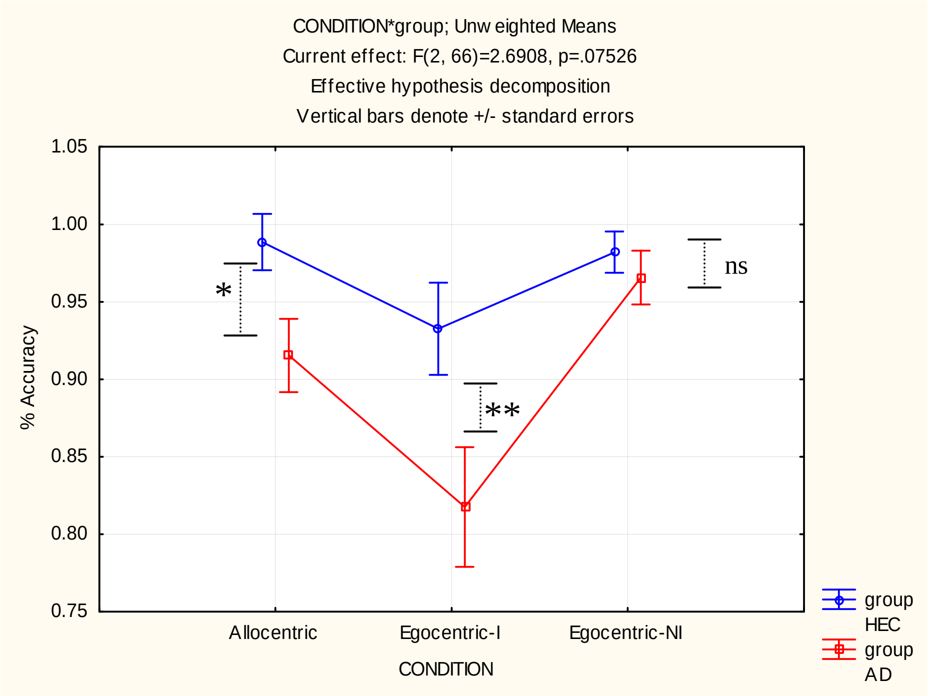


**Figure 3.**
The Allocentric-Egocentric Test. Each experimental trial was comprised of 4 screens. Screen 1: fixation pattern composed of four stars presented for 1000 milliseconds. Screen 2: Black screen presented for 500 milliseconds. Screen 3: The stimulus was presented and stayed until the participant made a response or up to 4500 milliseconds. Screen 4: Black screen for the 500 milliseconds.

4a.



4b.

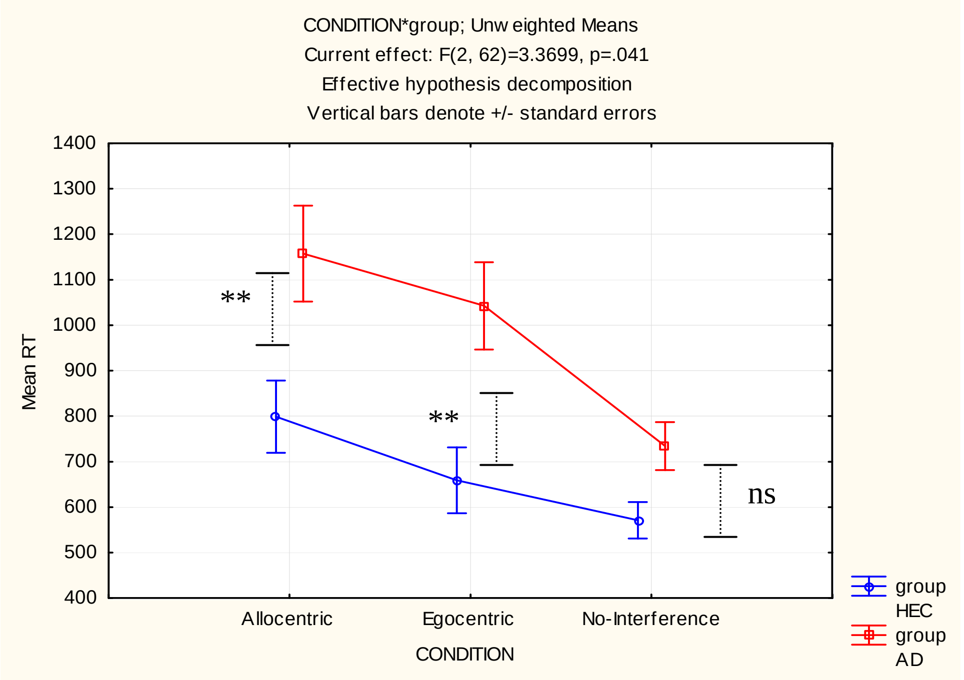


**Figure 4.**
Repeated measures ANOVA; Condition by Group Interaction; 4a) accuracy
4b) RT ; * p < .05 ** p < .01 ns = not significant

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