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Attentional Networks in Normal Aging and Alzheimer's Disease

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Abstract

By combining a flanker task and a cueing task into a single paradigm, we assessed the effects of orienting and alerting on conflict resolution, and explored how normal aging and Alzheimer's disease (AD) modulate these attentional functions. Orienting failed to enhance conflict resolution; alerting was most beneficial for trials without conflict, as if acting upon response criterion rather than upon information processing. Alerting cues were most effective in the elderly groups --healthy aging and AD. Conflict resolution was impaired only in AD. Orienting remained unchanged across groups. These findings provide evidence of different life-span developmental and clinical trajectories for each attentional network.

Keywords: Alzheimer's disease; executive processing; orienting; conflict resolution; alerting

Early stages of Alzheimer's disease (AD) are characterized by deficits in episodic memory, caused by medial-temporal lobe atrophy and neuronal loss in the basal forebrain cholinergic system (Kohler, Black, Sinden, Szekely, Kidron, Parker, Foster, Moscovitch, Winocur, Szalai, & Bronskill, 1998; Whitehouse, Price, Struble, Clark, Coyle, & DeLong, 1982). Although memory impairments are at the core of AD, over the last ten years evidence has accumulated for early deficits in attention (Baddeley, Baddeley, Bucks, & Wilcock, 2001; Rizzo, Anderson, Dawson, Myers, & Ball; for reviews, see Fernandez-Duque & Posner, 2001; Parasuraman, Greenwood, & Sunderland, 2002). Some of the brain areas most important for attention are hypometabolic in early AD, and attention is influenced by acetylcholine --which is decreased in AD (Davidson & Marrocco, 2000; Parasuraman, Greenwood, Haxby, & Grady, 1992). This has led some researchers to propose that memory problems in AD may stem in part from a cholinergic disruption of attention (Voytko, 1996).

The term 'attention' refers to many different cognitive abilities, such as orienting to sensory stimuli, maintaining the alert state, and orchestrating the computations needed to perform the complex tasks of daily life (Fernandez-Duque & Posner, 1997). Under this latter category are the abilities to switch between tasks, inhibit prepotent responses, and other skills sometimes referred to as 'executive functions' (Baddeley et al., 2001; Fernandez-Duque, Baird, & Posner, 2000). After reviewing the anatomical literature, Posner and Petersen (1990) proposed dividing the attentional system into three discrete anatomical networks: orienting, alerting, and executive. By emphasizing anatomical networks with specific computational functions, this model encouraged the development of neuroimaging and neuropsychological studies exploring dissociation and interactions among attentional processes. The model also shifted the emphasis from etiology to brain localization, arguing that different pathologies would lead to the same cognitive deficit if they affected the same brain area. This emphasis on anatomy further allowed for predictions on the role of different

neuromodulators, based on their unique patterns of cortical projections. These features of the model converged with evidence from AD research on cholinergic dysregulation and regional atrophy. As efforts for early treatment of AD become closer to reality, it becomes all the more important to fully understand the attentional deficits in AD, the interactions among the attentional networks, and the neurochemical substrates underlying them. The current study is a step in this direction.

Several studies have looked at the ways in which different components of attention are disrupted by AD. Most of the research has been devoted to the orienting network, after early reports revealed an orienting deficit in AD (Buck, Black, Behrmann, Caldwell, & Bronskill, 1997; Danckert, Maruff, Crowe, & Currie, 1998; Faust and Balota 1995; Festa-Martino, Ott, & Heindel, in press; Maruff & Currie, 1995; Oken, Kishiyama, Kaye, & Howieson, 1994; Parasuraman et al., 1992; Tales, Muir, Bayer, & Snowden, 2002). Some studies have further reported an orienting deficit in the re-scaling of the attentional focus (i.e., 'zoom-in' function) (Coslett, Stark, Rajaram, Saffran, 1995; Greenwood, Sunderland, Friz, & Parasuraman, 2002; Parasuraman, Greenwood, & Alexander, 2000). Other studies have explored executive functions such as inhibitory control and dual task performance (Baddeley et al., 2001; Spieler, Balota & Faust, 1996), partly motivated by the finding that healthy older adults are impaired in these functions (Hasher & Zacks, 1988; Mayr, 2001). Finally, other studies have investigated whether vigilance decrements and alerting effects are spared in AD and healthy aging (Baddeley, Cocchini, Della Sala, Logie, Spinnler, 1999; Berardi, Parasuraman, & Haxby, 2001; Festa-Martino et al., in press; Nebes & Brady, 1993, Tales, Muir, Bayer, Jones, & Snowden, 2002).

In contrast to the wealth of research probing individual attentional networks, there have been no assessments of the three networks within a single experimental paradigm. In some studies, separate tasks have been tested in the same group of patients, and patterns of correlations taken as

evidence for interactions among networks (Levinoff, 2002). This approach should be commended for its inclusiveness, but it requires a large number of subjects, and superficial differences across tasks may obscure the interpretation of the findings. A different approach is to design a task in which all three components can be assessed simultaneously. Recently, Posner and collaborators have developed such a paradigm, which they labeled Attentional Network Test (ANT), and tested it in normal young adults (Fan, McCandliss, Sommer, Raz, & Posner, 2002)

The ANT is a combination of Posner's covert orienting task and Eriksen's flanker task (Eriksen & Eriksen, 1974; Posner, 1980). In the covert orienting task, attention is cued to one side or another before the target appears. The reaction time difference between valid and invalid cue locations constitutes a measure of orienting. Other trials include a warning cue that provides temporal information about the target onset but no spatial information (neutral cue). These trials are compared to trials in which the target occurs without any warning (no cue). The difference in reaction time is a measure of alerting. Finally, Eriksen's flanker task displays a target flanked by distractors with information congruent or incongruent to the target. For example, in an incongruent trial, the target arrow may point to the left, with the flankering arrows pointing to the right. The difference in reaction time between congruent and incongruent trials provides a measure of conflict resolution, one of the functions of the executive network.

Insert Figure 1 here – the task

By combining the four types of cue (valid, invalid, neutral, no cue) with the two types of distractor (congruent, incongruent), our modified version of the ANT explored how alerting and orienting influence conflict resolution (see Figure 1).¹ We explored whether and how normal aging

and AD modulate these effects, and whether the patterns previously observed in young adults generalize to healthy aging and AD.

Results

Consistent with previous findings (Faust & Balota, 1997), patients with Alzheimer's disease had increased difficulties maintaining fixation, and made eye movements in a larger percentage of trials than age-matched controls, $t(24) = 3.3$, $p < .001$, (AD: $M = 9.6\%$, $SD = 7\%$, Range: 1.8%-23%; Healthy Elderly: $M = 2.9\%$, $SD = 2$, Range: 0 – 5.4%). Trials with eye movements were excluded from the analyses. Error trials and trials immediately following an error were further excluded from the RT analyses.

From the remaining trials, median RTs were calculated for each group (young, healthy elderly, AD), cue type (valid, invalid, neutral, no cue), and distractor type (congruent, incongruent) (see Table 2). To control for the possibility that differences in overall speed among groups influenced the absolute size of the effects, we also computed proportional scores. For each subject, the median RT in each condition was divided by the participant's overall RT (Faust & Balota, 1997). These transformed data yielded the same pattern of results, unless otherwise specified.

Insert Table 1 here – Median RTs & error rates

Error data were analyzed following the same approach as RT data. We analyzed the raw error data, and also the arcsine-transformed error rates which reduced the skewness of the distribution and minimized the effect of outliers (Winer, 1971). We report the analysis on the raw error data, but the transformed data yielded a similar pattern of results, unless otherwise noted.

First, we assessed the effects of aging by comparing young and healthy elderly subjects. Later, we assessed the effects of Alzheimer's disease by comparing patients and healthy elderly subjects.

Effects of Normal Aging

A mixed analysis of variance included Cue Type (valid, invalid, neutral, no cue) and Distractor Type (congruent, incongruent) as within-subject factors, and Group (young, healthy elderly) as a between-subjects factor.

Congruency Effect and Aging

The RT analysis revealed a main effect of age, $F(1, 24) = 50, p < .0001$, and a main effect of distractor type, $F(1, 24) = 121, p < .0001$, but no interaction, $F(1, 24) = .29, ns$. As expected, elderly healthy adults were slower than young subjects, and responses were slower when the distractors provided information incongruent with the target. However, the cost of conflict did not increase with age (see Figure 2). In fact, when overall speed was taken into account by analyzing the proportional scores, older adults exhibited a smaller congruency effect than young adults [Group by Distractor Type interaction for the proportional scores: $F(1, 24) = 5.8, p < .03$]. Possibly, the general slowness with which older adults responded afforded them more time to resolve conflict information, thus decreasing the congruency RT effect. The error data support this interpretation: only young adults were sensitive to the congruency effect and made increased errors to incongruent trials, as revealed by simple effects exploring the distractor type by group interaction, $F(1, 24) = 9.9, p < .001$.

Insert Figure 2 here – Three Main Effects

The RT analysis also showed a main effect of cue, $F(3, 72) = 40, p < .0001$, which interacted with distractor type, $F(3, 72) = 7.2, p < .001$. Similar findings were obtained in the error data [cue main effect: $F(3, 72) = 3.5, p < .02$, cue by distractor interaction, $F(3, 72) = 5.5, p < .05$]. To further explore these effects of cue type, post-hoc analyses of variance were conducted. The first set of analyses assessed the alerting effect by comparing neutral vs. no cue trials, and the second set assessed the validity effect by comparing valid vs. invalid trials. We discuss these analyses in turn.

Alerting effect

The first post-hoc analysis explored the alerting effect, by comparing trials with a spatially neutral cue and trials with no cue. Other factors were Group (young, healthy elderly) and Distractor type (congruent, incongruent).

Alerting and Aging. As expected, the RT analysis revealed faster response times to targets preceded by a neutral cue than to targets occurring without a cue, $F(1, 24) = 55, p < .0001$. More interestingly, this alerting effect interacted with age, being most beneficial for older subjects, as revealed by simple effects that followed the interaction, $F(1, 24) = 10., p < .004$ (simple effects: $p < .05$) (see Figure 2). A possible interpretation is that older adults had difficulty sustaining attention in the absence of an external cue, and therefore were disproportionately slow in no cue trials. Alternatively, older adults might have adopted a more conservative response criterion overall, thus giving more room for the alerting cue to exercise its effect. The error data revealed no age differences in the effectiveness of the warning cue, $F(1, 24) = .1, ns$

Alerting and Conflict Resolution. The alerting RT effect interacted with the type of distractor, $F(1, 24) = 8, p < .01$, being least effective for incongruent trials. In other words, subjects benefited most from a cue announcing the imminent occurrence of a target the when target and distractor were congruent, and conflict resolution was not required (see Figure 3). This finding is

consistent with previous claims that the alertness acts by shifting the response criterion, rather than by truly enhancing information processing (Fan et al., 2002; Posner, 1978; Prinzmetal, Hansen, & Park, submitted). Also consistent with this hypothesis, the error data revealed an interaction between alertness and congruency, $F(1, 24) = 3.8, p < .06$. More specifically, alerting cues led to an increased number of errors for incongruent trials, probably by triggering a motor response before conflict was resolved in such trials.

Insert Figure 3 here –Alerting & Congruency

Validity Effect

The second post-hoc analysis explored the effect of spatially informative cues by comparing valid and invalid cues. Other factors included Group (young, healthy elderly), and distractor type (congruent, incongruent).

Spatial Attention and Aging: As expected, RTs were faster when the target appeared at the cued location, $F(1, 24) = 50, p < .0001$. This validity effect was similar for young and older adults, with no interaction between validity and age, $F(1, 24) = .7, ns$ (see Figure 2). However, the error data did reveal an interaction, $F(1, 24) = 6, p < .02$, and simple effects showed a validity effect for older adults but not for young adults.

Insert Figure 4 here –Validity & Congruency

Spatial Attention and Conflict Resolution: The valid cue did not reduce the cost of incongruent distractors. In fact, valid trials sometimes elicited a larger congruency effect than invalid

ones, as revealed by a 3-way interaction among cue type, distractor type, and group, $F(1, 24) = 6, p < .02$. Post-hoc analyses to this 3-way interaction revealed that, for young adults, cue type and distractor type did not interact, $F(1, 12) = .1, ns$, but for older adults valid cues led to larger congruency effects than invalid cues, $F(1, 12) = 8.6, p < .01$ (see Figure 4). The error analysis revealed a larger congruency effect for valid than for invalid trials for both groups, $F(1, 24) = 13, p < .001$. These data argue against a beneficial effect of spatial cueing on conflict resolution in paradigms such as this.

Effects of Alzheimer's Disease

Data from patients with Alzheimer's disease were analyzed using the same approach described above. Thus, a mixed analysis of variance included Cue Type (valid, invalid, neutral, no cue) and distractor type (congruent, incongruent) as within-subject factors, and Group (AD, healthy elderly) as the between-subjects factor.

Congruency Effect and Alzheimer's Disease

The RT analysis revealed a main effect of group, $F(1, 24) = 10.9, p < .003$, and a main effect of congruency, $F(1, 24) = 128, p < .0001$. As expected, patients with AD were slower than their age-matched controls, and responses were slower when the distractors provided information that conflicted with the target. Most importantly, there was an interaction between distractor type and group, $F(1, 24) = 7.7, p < .01$, so that the cost of an incongruent distractor was larger for patients with AD than for the age-matched controls (see Figure 2). This finding suggests that patients with AD had greater difficulty resolving conflict. The interpretation, however, is qualified by the overall group differences in RTs. When overall speed was taken into account by analyzing the proportional scores, the congruency effect for AD patients was not significantly different than for age-matched healthy adults, although with a trend in the right direction, $F(1, 24) = 2.4, p < .13$. Consistent with a

true deficit in conflict resolution in AD, the error data revealed a strong trend for interaction between distractor type and group, $F(1, 24) = 3.8, p < .06$. In other words, accuracy was disproportionately affected by incongruent trials in the AD group.

The primary analysis also showed a main effect of cue, $F(3, 72) = 30, p < .0001$, which interacted with congruency, $F(3, 72) = 5, p < .002$. The error data revealed the same interaction, $F(3, 72) = 3.4, p < .02$. To further explore these effects, two post-hoc analyses of variance were conducted. The first set of analyses assessed the alerting effect by comparing neutral and no cue trials, and the second set assessed the validity effect by comparing valid and invalid trials. We discuss these analyses in turn.

Alerting Effect

The first post-hoc analysis explored the alerting effect, by comparing trials with a spatially neutral cue and trials with no cue. This analysis also explored whether the alerting effect was altered in AD, and whether alerting interacted with conflict resolution as suggested by previous analyses. For this, Group (AD, healthy elderly) and Distractor type (congruent, incongruent) were also included as factors in the analysis of variance.

Alerting and AD: The RT analysis revealed that neutral cues speeded up response times relative to trials with no cue, $F(1, 24) = 27, p < .0001$. The benefit provided by a warning was similar for patients and controls, with no interaction between alertness and group, $F(1, 24) = .4, ns$ (see Figure 2). The same was true for the error data, $F(1, 24) = .1, ns$.

Alerting and Conflict Resolution: The RT data revealed that neutral cues were more effective for trials in which the distracting information was congruent to the target than in trials with incongruent distractors, $F(1, 24) = 10.7, p < .003$ (see Figure 3). This result replicates the findings from young adults, and suggests that the alerting effect acted upon the response criterion rather than

enhancing information processing. Consistent with this view, alert trials increased the number of errors to incongruent trials, $F(1, 24) = 4, p < .05$.

Validity Effects

The second post-hoc analysis explored the effect of spatially informative cues by comparing valid and invalid cues. To explore whether the validity effect was altered in AD, and whether valid trials enhanced conflict resolution, the post-hoc analysis also included Group (AD, healthy elderly) and Distractor type (congruent, incongruent).

Spatial Attention and AD: This analysis revealed the standard validity effect, $F(1, 24) = 41, p < .0001$. The validity effect was as large in AD patients as it was in age-matched controls, and there was no interaction, $F(1, 24) = .1, ns$ (see Figure 2). The error data revealed a main validity effect, $F(1, 24), p < .05$, and a non-significant trend toward interaction with pathology, $F(1, 24) = 3.5, p < .07$, in that healthy elderly subjects, but not AD patients, benefited from valid cues.

Spatial Attention and Conflict Resolution: There was no interaction between validity and type of distractor. Thus, spatial attention was ineffective in reducing the RT cost of conflict resolution, $F(1, 24) = 1.6, ns$ (see Figure 4). Furthermore, the error data revealed a larger congruency effect for valid trials than for invalid ones, $F(1, 24) = 5.1, p < .04$. Similar to the data from young adults, the findings from this analysis argue against a role of spatial attention in conflict resolution when target and distractors occur inside the attentional focus.

General Discussion

The pattern of interactions and dissociation among the three attentional networks replicated previous findings in young adults, generalizing them to healthy aging and AD (Fan et al., 2002; Fernandez-Duque, in preparation). In particular, the presence of a spatially neutral cue increased the congruency effect, and the presence of a valid cue was ineffective in reducing the cost of

incongruent information. We discuss these findings first. Later we address group differences in the size of the alerting, congruency, and validity effects.

Interactions and Dissociations among Attentional Networks Common to all three Groups

It might be expected that a more alert state would enhance conflict resolution. If so, the increased congruency effect in alert trials would come as a surprise. However, that interaction is consistent with previous findings (Fan et al., 2002; Fernandez-Duque, in preparation) and with a theory of alertness proposed by Posner in 1978. That theory argues that warning signals do not enhance information processing, but rather act by shifting the response criterion. As a consequence, warning signals lead to hasty decisions and fast responses with incomplete information. Thus, the theory predicts an increased number of errors following a warning cue, particularly in incongruent trials, a prediction fulfilled in our study. The claim that alerting acts by automatically shifting response criterion also receives support from ERP studies. Data in such studies show that alertness modulates late components such as the P300, but does not enhance earlier, perceptual components, such as the P1 and the N1 (Griffin, Miniussi, & Nobre, 2002).

The lack of interaction between validity and congruency may come as a surprise too, as it might be expected that focused attention should help resolve conflict. However, previous studies have shown that spatial cueing does not affect congruency in the Stroop task (Shalev & Algom, 2000; Baldo, Shimamura, & Prinzmetal, 1998), the spatial compatibility task (Ro, Machado, Kanwisher, & Rafal, 2002), nor the flanker task (Fernandez-Duque, in preparation). In all these tasks, target and distractor occur in the same location or in very close proximity. As a consequence, when spatial attention is focused on the target, it is also focused on the distractor, and when a target appears at an unattended location so does the distractor. Therefore, the design of those paradigms biases spatial attention to enhance both target and distractor, leaving conflict unresolved. Consistent

with this interpretation, when target and distractors are dissociated in space, or attention is focused only on the target, the congruency effect is greatly reduced by orienting (Fernandez-Duque, in preparation, LaBerge, Brown, Carter, Bash, & Hartley, 1991; Van der Lubbe & Keuss, 2001). These behavioral studies converge with evidence from single neuron recording in primates, which shows that attention is most efficient when only the target is inside the neuron's receptive field (Desimone & Duncan, 1995).

Group Differences in Orienting, Alerting, and Congruency

All three groups of subjects showed the same pattern of interactions and dissociations, which is evidence of continuity in the networks' trajectory through healthy aging and disease. On the other hand, the magnitude of the effects was different among groups.

The group differences in effect size cannot be fully explained by a single general factor, such as increased slowness by healthy aging and disease. While overall RTs slowed down with healthy aging as well as with AD, the alerting effect became larger only with age, the congruency effect became larger only with pathology, and the validity effect remained unchanged. This pattern of results points to the existence of three distinct, albeit interactive, networks of attention: alerting, orienting, and conflict resolution.

Alerting. The alerting effect increased with age, but not with AD. A possible interpretation of this finding is that older adults had difficulty sustaining attention, and therefore benefited most from an external cue. However, this explanation is not supported by the literature on vigilance and aging. Under low cognitive demands, sustained attention is normal in healthy aging (Berardi, Parasuraman, & Haxby, 2001), and a similar pattern of brain activation is observed for older and young adults (Johansen, Jakobsen, Bruhn, & Gjedde, 1999).

A second, and more likely interpretation of the increased alerting effect proposes that older adults had normal sustained attention but adopted a more conservative criterion of response. The adoption of a more conservative response criterion by older adults is supported by the error data, which showed a congruency effect for young subjects but not for healthy elderly subjects, as if older adults were allowing more time for resolving conflict. It is also consistent with studies on metacognition, which demonstrate that older adults and AD patients, unlike younger subjects, tend to underestimate their accuracy when predicting their performance in a conflict resolution task (Fernandez-Duque & Black, in preparation a). By adopting an overall conservative criterion, older adults in both the healthy elderly and the AD groups stand to benefit most from a shift toward a liberal response criterion brought about by the alerting cue. In contrast, young adults with overall liberal response criteria cannot afford to accelerate their responses after a warning signal because it would entail an increased risk of error, particularly when distractors are incongruent.

Congruency. Unlike the alerting effect, the congruency effect did not increase with age, but it did increase with AD. Although this effect might be explained by an overall slowness in response, the error data also showed the same pattern. Together, these findings argue for a deficit in conflict resolution, consistent with the AD literature showing impairment in Stroop and anti-saccade tasks (Currie, Ramsden, McArthur, & Maruff, 1991; Danckert et al., 1998; Spieler et al., 1996). On the other hand, the deficit observed in our study was small. Conflict resolution is only one of many components of executive attention, and it seems likely that other executive functions would be even more disrupted by AD than conflict resolution. For example, early AD patients are severely impaired in dual tasking and set switching (Baddeley et al., 2001). An important question for future research is whether the executive functions most impaired in AD are also the ones most dependent on working memory. For example, conflict resolution, which was mildly impaired in our study, seems

unaffected by working memory demands in young adults performing a task similar to the present one (Fernandez-Duque, submitted). In contrast, set switching and vigilance decrements are heavily dependent on memory load (Parasuraman, 1976; Fernandez-Duque, submitted), and early AD patients are particularly susceptible to those memory load modulations (Baddeley et al., 1999; Fernandez-Duque & Black, in preparation b).

Validity. The validity effect was mostly unaffected in healthy elderly subjects, consistent with previous findings showing that healthy aging spares automatic orienting, and produces only modest effects in voluntary attention (Greenwood, Parasuraman, & Haxby, 1993; Hartley, Kieley, Slabach, 1990). This result is also consistent with ERP studies showing, in older adults, a normal enhancement of P1/N1 components, an electrophysiological marker of attention (Curran, Hills, Patterson, & Strauss, 2001).

The validity effect also was mostly unaffected by AD. This was a departure from previous studies, which showed impaired orienting in AD (Buck et al., 1997; Festa-Martino et al., in press; Parasuraman et al., 1992). However, the orienting deficit in AD is not a universal finding and when found is qualified by many factors, including the type of cue (central, peripheral), the type of task (detection, discrimination), the cue-target delay, and the severity of the disease. In fact, much of the research in AD and attention over the last ten years has been devoted to disentangling the pattern of interactions among these variables.

Our study tested patients at a very early stage of the disease, unlike most of the other clinical studies, in which patients at more advanced stages were included (Buck et al., 1997; Parasuraman et al., 1992; Oken et al., 1994; but see Festa-Martino et al., in press). Thus, disease severity may explain in part why our study yielded non-significant differences in orienting. However, disease severity alone is an unlikely explanation, as significant orienting deficits have been reported in

asymptomatic subjects who are at genetic risk for AD (Greenwood et al., 2002). These are subjects who perform normally in standard neuropsychological tests, but carry the E4 allele of the apolipoprotein E, a genetic risk factor for AD. The validity effect in carriers of the E4-allele is 20 ms larger than in subjects carrying alleles unrelated to AD. This finding suggests that mild deficits in orienting can be observed at very early stages of the disease.

There are other several candidate reasons why validity was normal for AD patients in the present study. One possibility is that our patients had an orienting deficit that was masked by our choice of peripheral cueing. We chose peripheral cueing rather than central cueing as an attempt to reduce cognitive load, minimize eye movements, and effectively manipulate the orienting system.² Although orienting deficits in AD have sometimes been reported for peripheral cueing (Buck, et al., 1997; Festa-Martino et al., in press), the AD deficit is most evident with central cues for the voluntary allocation of attention. When automatic and voluntary orienting are pitted against each other in a task in which the target usually appears opposite to the cue, AD patients have trouble overriding the automatic cueing to take advantage of the probability information (Maruff & Currie, 1995; Danckert et al., 1998). Also, the automatic re-orienting of attention is preserved at early stages of the disease, as revealed by normal inhibition of return (Faust and Balota 1995; Danckert et al., 1998). Thus, it is possible that the absence of abnormal validity effects in the current study was due to the use of peripheral cueing.

Unlike most studies of covert orienting, the current study required vertical shifts of attention rather than horizontal ones. There are well known hemispheric asymmetries in the orienting system of healthy adults (Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000), stroke patients (Rafal, 1998), and AD patients (Buck et al., 1997; Parasuraman et al., 1992; Maruff, Malone, & Currie, 1995). Thus, it is conceivable that vertical shifts of attention will exhibit a different profile in normal

development and pathology than horizontal shifts (but see Buck et al., 1997). Also, stimuli in our task were larger than in most tasks in which a cueing or a flanker paradigm is used. Larger stimuli were necessary for minimizing eye movements and maximizing discrimination in peripheral vision, but it had the unintended consequence of easing perceptual discrimination, thus reducing the need for attention. It is possible that a more difficult discrimination task would have revealed group differences in orienting.

Methods

Participants: Patients with AD were recruited through the Cognitive Neurology Unit at Sunnybrook and Women's Health Science Centre in Toronto, where the project received approval from the Research Ethics Board. Age-matched normal controls were recruited from a pool of healthy community elderly volunteers at the same Cognitive Neurology Unit and at Baycrest Centre for Geriatric Care. The group of young adults consisted of thirteen undergraduate students at University of Toronto, who participated in the task for course credit, with a mean age of 19.8 (SD=1.3). Consent for participation in the study was obtained from all subjects, as well as from the patients' caregivers. All subjects had normal or corrected-to-normal vision.

All patients met criteria for probable Alzheimer's Disease (AD), as established by the workgroup of the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) (McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984). As part of the standard work-up of AD, brain imaging was obtained in all the patients. This included a measure of regional cerebral blood flow using Single-Photon Emission Computed Tomography (SPECT), as well as an MRI (n=11) or a CT whenever MRI was contraindicated (n=1). Only patients with mild dementia were selected (MMSE ≥ 20). Nine of the 13 patients were treated with cholinergic agents for at least 80 days before testing.

A full neuropsychological battery was used to characterize the deficits of the AD patients. All thirteen patients and eight age-matched control subjects completed general neuropsychological testing. The other five age-matched control subjects completed a subset of tests (MMSE, the digit span task, the verbal fluency tasks) performing within normal levels. Table 1 shows the results of the neuropsychological tests. As expected, the AD group was impaired relative to the normal controls in most domains.

Insert Table 2 here – Demographics, Neuropsychology

Participant Selection. Data from 13 subjects in each group were included in the analyses. Data from other four patients were excluded from the analyses because they did not meet some of the following criteria: overall accuracy better than 75%, less than 20% of trials with eye movements, and at least 10 trials per cell from which to compute the median RT. Two other patients were unable to reach criterion in the practice trials, and therefore did not participate in the actual test.

Equipment: Stimuli were displayed on a 19-inch monitor set to a screen resolution of 1024 x 768 pixels. Data were collected via the keyboard of a Dell computer equipped with a Pentium III processor and Windows 98. The timing of stimulus display and data collection were managed using E-prime, a commercial experiment application.

Stimulus and design: The stimulus display is illustrated in Figure 1. The basic display was visible at all times and consisted of two black rectangular boxes and a black fixation cross, against a gray background. The boxes were centered horizontally on the monitor and displayed 3.5 cm (4° VA) above and below fixation, measured from the fixation cross to the center of the box. Each box was 12 cm wide and 2.2 cm high ($13.7^\circ \times 2.7^\circ$ VA), and the lines that form the box were 3 pixels wide.

In any given trial, a set of five black arrows was displayed inside one of the rectangular boxes. Each arrow measured 1.4 cm in length, with the arrow head measuring 1 cm in height (1.6° x 1.1° VA). Arrows were separated from each other by 1 mm. The central arrow constituted the target and the flanking arrows constituted the distractors. Target and distractors could point in the same direction (congruent trials) or in different directions (incongruent trials).

The attentional cue consisted of the brightening from black to white of one or two of the boxes. Depending on its relation to the 5-arrow display, the cue provided information that was spatially valid (same location), invalid (different location) or neutral (brightening of both boxes). There were also no cue trials, in which neither box brightened. Valid cues occurred in 50% of trials, and each of the other cue conditions (invalid, neutral, no cue) occurred in 16.7% of trials. The proportion of valid to invalid trials was 3 to 1, meaning that for trials in which spatial information was given, the validity of the cue was 75%.

Besides the congruency factor and the cue factor, we counterbalanced whether the target pointed left or right, and whether the arrows were displayed in the top or the bottom box. All possible combinations of this 2 x 4 x 2 x 2 design were represented in each block of 48 trials. There were five blocks, for a total of 240 trials.

Procedure: Subjects sat approximately 50 cm away from the screen, and used their left and right index fingers to press keys S and L on the keyboard. Eye movements were videotaped, and whenever an eye movement was detected online, subjects were reminded to keep fixation.

Each trial began with a cue and was followed by a target 500 ms later (for no-cue trials the cue event was invisible). Cue and target remained on display until response, or for a maximum of 5 seconds. Trials in which subjects were slower than 2000 ms were followed by visual feedback that read "too slow," for the first 1000 ms of the inter-trial interval. Inter-trial interval was randomized

between 1200 and 3000 ms. Each of the five blocks of 48 trials lasted approximately 3 minutes, and subjects were encouraged to take short breaks between blocks.

Instructions: Task instructions were read out loud and illustrated with computer displays. Subjects were told that it was “very important that you keep your eyes looking at the center cross and that you try to see the whole display without moving your eyes”.

To illustrate the congruency component, a 5-arrow display was presented in the top box, with the target arrow pointed to the right, and the distractors pointing to the left (i.e., an incongruent trial). Subjects were instructed that “the central arrow will indicate which key to press. In this example you should press right, because the central arrow points to the right”. The next three examples illustrated the remaining possible combinations between target direction (left, right) and distractor type (congruent, incongruent). Following the illustration, subjects completed four practice trials, one for each possible combination of target direction and distractor type. If any errors were made, the illustration and practice trials were repeated until the performance was flawless.

Next, the spatial component of the task was explained. A 5-arrow display was illustrated in the bottom box, and subjects were told that “in half of the trials, the arrows will appear in the bottom box. One of the boxes will light up, indicating where the arrows will most likely occur. For example...” Four examples of valid trials followed.

Next, the alerting component of the task was explained, by telling subjects that “sometimes the outline of both boxes will turn white, indicating no favorite location. The whitening of the outline will also inform you that the arrows will occur immediately.” These instructions were followed by two trials in which the spatially neutral cue was displayed.

Subjects were reminded once again to not move their eyes, and started 10 trials of practice. For practice trials no speed feedback was given, and subjects were encouraged to take as much time

as they needed to answer correctly. Subjects repeated practice blocks until they reached a criterion of 90% accuracy in a ten-trial block.

After practice, subjects completed five blocks of actual testing. For the actual test, subjects were instructed to respond as fast and accurately as possible, and were warned that speed feedback would follow abnormally slow responses. At the beginning of each block subjects were reminded to respond to the central arrow (i.e., the target) of the 5-arrow display.

Footnotes

1. The ANT, in its original version, does not include invalid trials, and the validity effect has to be estimated by comparing valid trials to trials with neutral cues. That design reduces the number of required trials, but does not assess the cost of disengaging attention from an invalid location. Previous studies suggest deficits in disengaging attention in Alzheimer's disease. Thus, we modified the original design to include invalid trials a third of the time that the cue provided spatial information.
2. In a pilot study, we found that AD patients made many more eye movements to central cues than to peripheral cues. We were also concerned that the cognitive demands would increase disproportionately in AD patients when asked to hold in mind further instructions about how to use the central cue.

Figure Captions

Figure 1. Figure 1 illustrates the experimental design. Five hundred milliseconds after the onset of the peripheral cue, target and distractors were displayed at the cued location (valid trials), or at the uncued location (invalid trials). Target and distractors pointed in the same direction (congruent trials) or in different directions (incongruent trials) for an equal number of trials. Spatial cues were predictive at a ratio of three to one (valid to invalid). There were also neutral trials, in which both locations were cued, and no cue trials.

Figure 2. The adult development and clinical trajectory of the three attentional networks. The figure illustrates the RT main effects of alerting ('no cue' trials minus 'neutral' trials), orienting ('invalid' trials minus 'valid' trials), and congruency ('incongruent' trials minus 'congruent' trials). The alerting effect increased with age, across both healthy aging and AD groups, while the congruency effect increased with AD but not with healthy aging. There were no significant modulations of the orienting network.

Figure 3. Interaction between Alerting and Conflict Resolution. The alerting cue increased the congruency effect in all three groups, with warning signals being most effective in trials with no conflict (i.e., congruent trials). Also illustrated by this figure, the alerting effect increased with age (i.e., healthy elderly and AD groups), and the congruency effect increased with pathology.

Figure 4. Orienting failed to enhance Conflict Resolution. For young adults and AD patients, the congruency effect was as large for valid as for invalid trials; for healthy older adults the congruency effect was larger for valid than for invalid trials. Also illustrated by this figure, the validity effect was unaffected by age or disease, and the congruency effect increased with pathology.

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Table 2: Demographic and Neuropsychological Information

	Maximum Score	Aged-Matched	AD
Age	80	72.5 (5.7)	74.7 (6.7)
Years of education		14.3 (3.6)	14.1 (3.9)
MMSE	30	29.0 (0.5)	24.3 (2.5)*
DRS (Total)	144	141.4 (2.1)	122.9 (11.2) *
Attention	37	36.0 (0.7)	34.3 (2.0) ^
Initiation	37	36.4 (1.4)	31.3 (4.7) *
Praxis	6	5.7 (0.5)	5.3 (0.7)
Conceptualization	39	38.5 (1.0)	34.7 (3.7) *
Memory	25	25 (0.0)	17.3 (4.2) *
NART-R FS-IQ	n/a	117.5 (3.4)	107.3 (9.8) ^
Boston Naming	30	29.0 (1.2)	21 (5.8) *
Western Aphasia Battery			
Total		99.3 (0.6)	92.5 (4.2) *
Apraxia	60	59.4 (1.1)	59.7 (0.6)
Rey-Osterrieth	36	33.6 (1.5)	26.2 (6.1)*
Line Orientation Task	30	25.7 (3.7)	23.9 (3.4)
Visual memory immediate	41	32.6 (6.6)	19.9 (6.6)*
Visual memory Delayed	41	24.7 (7.5)	3.7 (5.7)*
Semantic Fluency	n/a	17.7 (2.0)	10.9 (4.5) *
Verbal Fluency (FAS)	n/a	45.5 (6.5)	30.3 (13.5) *
CVLT			
Acquisition (Trial 5)	16	10.6 (1.8)	5.8 (2.3)*
Short Delay Free Recall	16	8.9 (3.3)	1.8 (2.2)*
Short Delay Cued Recall	16	10.0 (2.5)	4.2 (2.6)*
Long Delay Free Recall	16	8.3 (3.3)	1.5 (2.0)*
Long Delay Cued Recall	16	9.4 (3.2)	3.4 (2.7)*
Forward digit span	12	9.6 (1.2)	8.3 (1.6)
Bacward digit span	12	7.8 (1.9)	6.1 (2.4)
Trails A	n/a	37.2 (9.6)	43.2 (12.7)
Trails B	n/a	78.7 (17.9)	180 (66.4)*
WCST Categories	6	3.5 (1.7)	2.3 (1.2)
WCST Correct	64	44.0 (6.5)	44.3 (6.5)
Raven's Progressive Matrices	36	34.1 (1.5)	25.9 (4.3)*

* $p < .01$; ^ $p < .05$. MMSE = Mini-Mental State Examination; DRS = Dementia Rating Scale; NART-R = National Adult Reading Scale-Revised; CVLT = California Verbal Learning Task; WCST = Wisconsin Card Sorting Task.

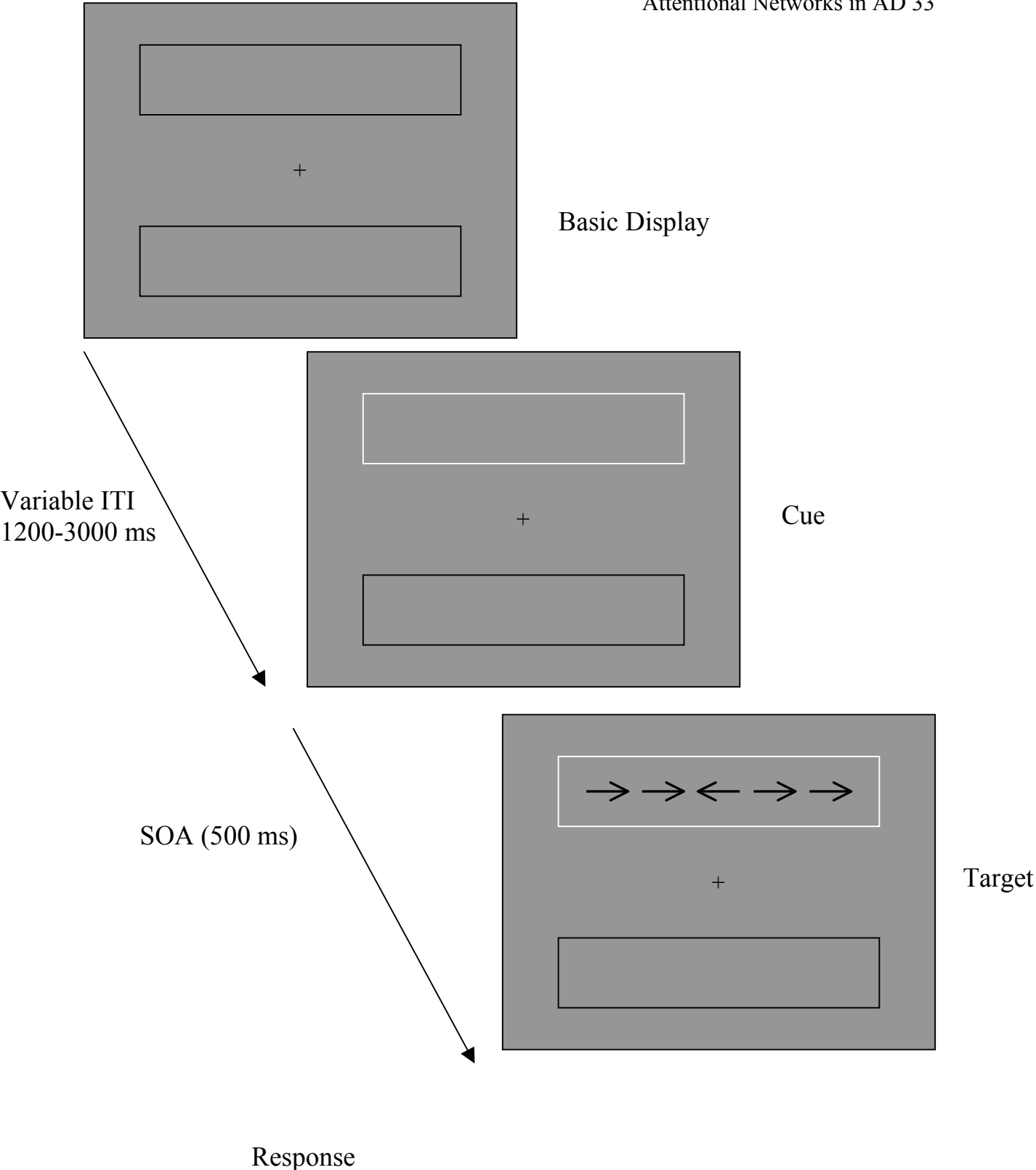
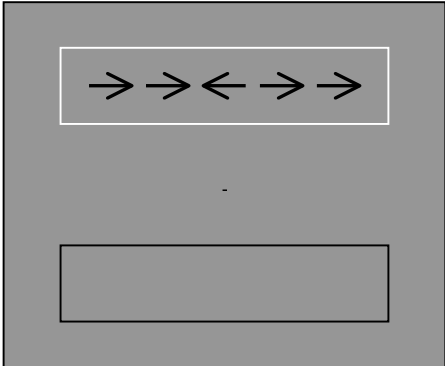
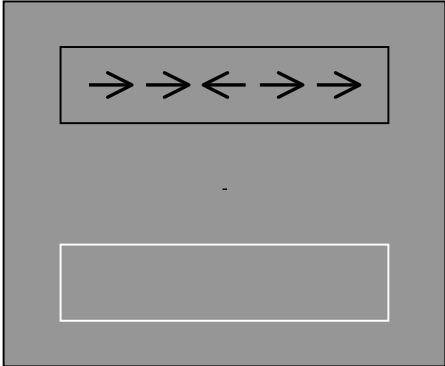


Figure 1 part A

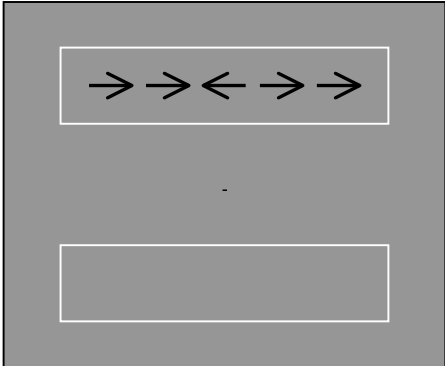
Types of Cue



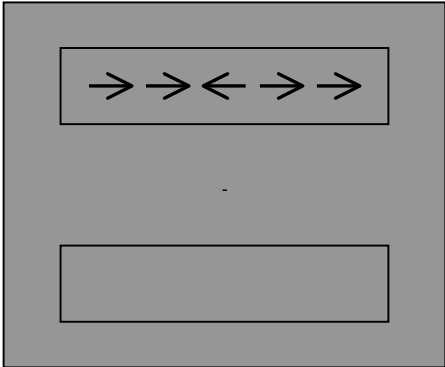
Valid



Invalid

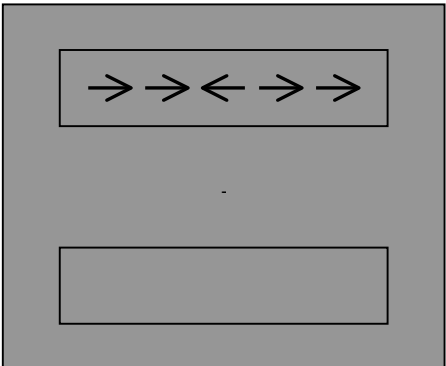


Neutral

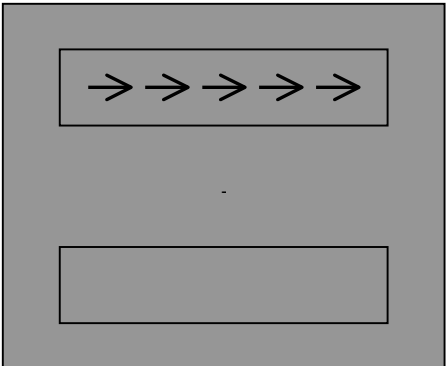


No Cue

Types of Target



Invalid



Congruent

Figure 1 part B

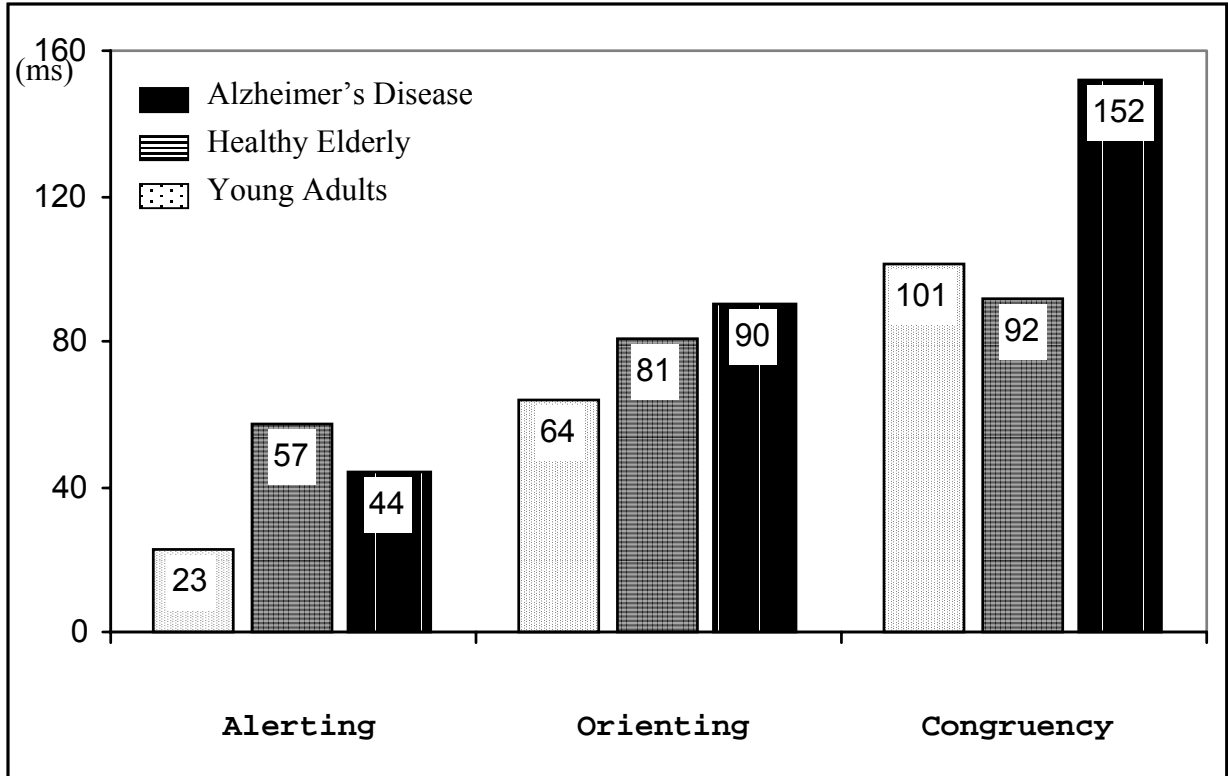


Figure 2

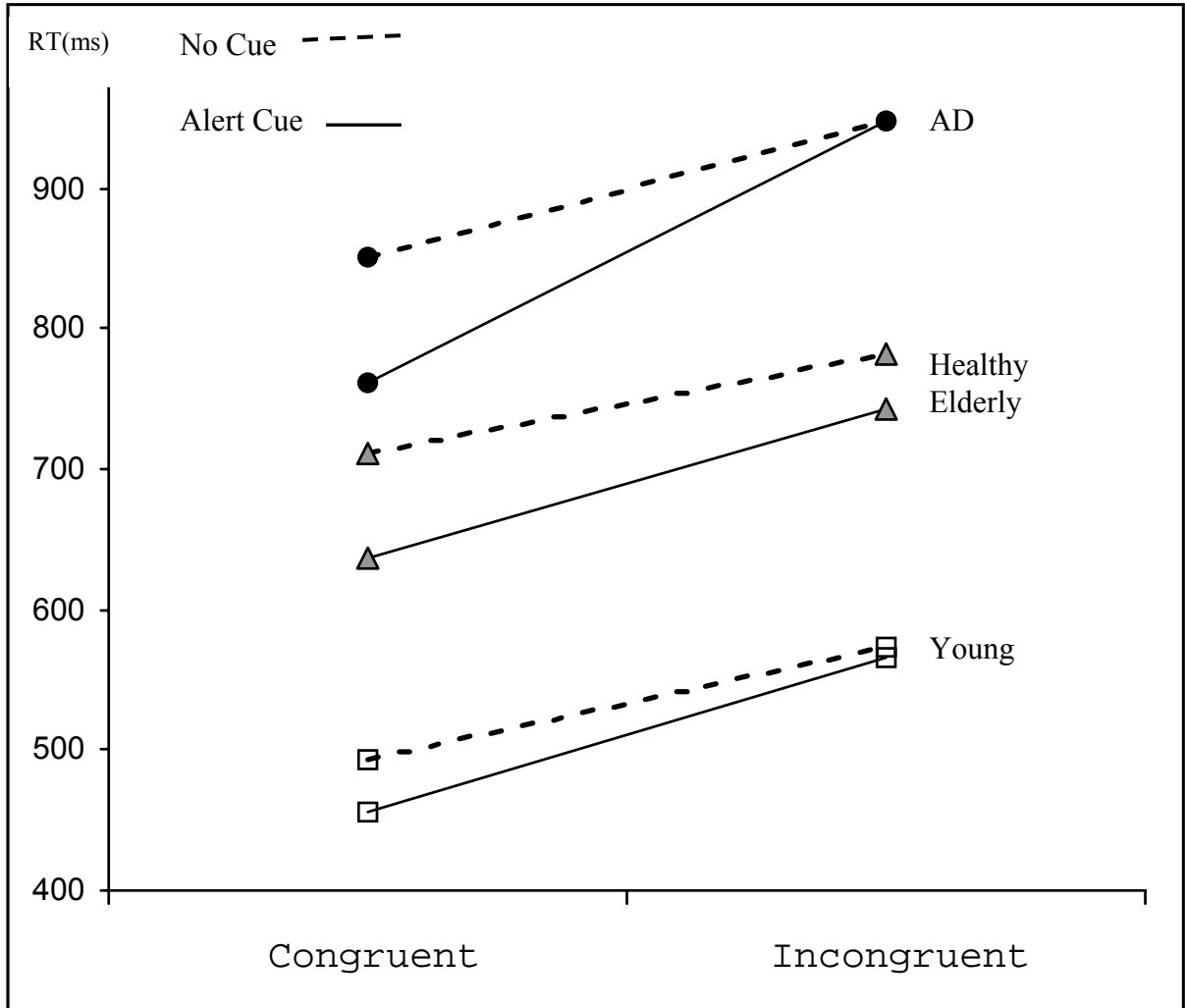


Figure 3

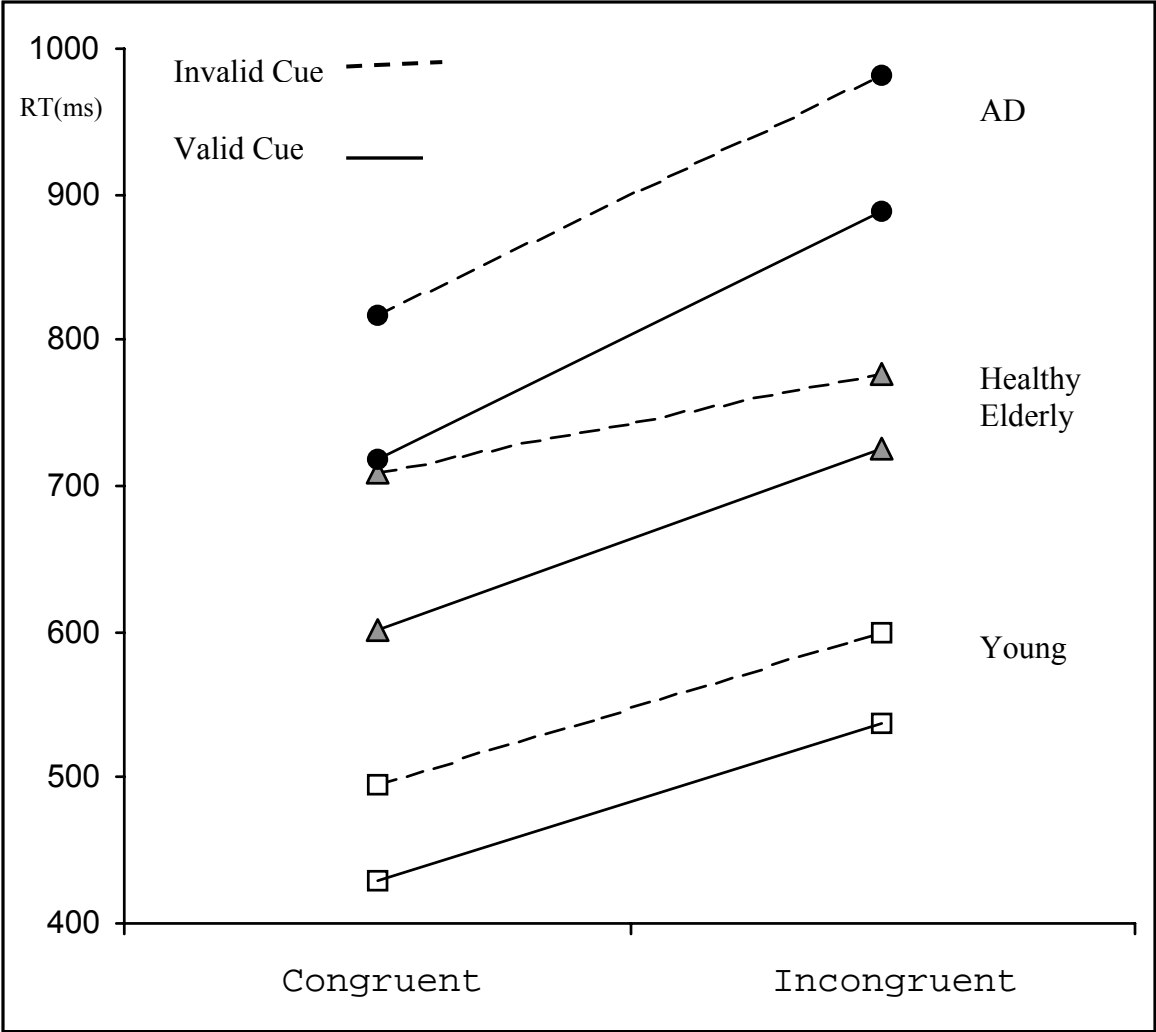


Figure 4.

Table 1-MedianRTs & Error Rates

	Alert		No Cue		Valid		Invalid	
	Congruent	Incongruent	Congruent	Incongruent	Congruent	Incongruent	Congruent	Incongruent
Young	455(47)	566(39)	493(46)	574(40)	429(44)	538(40)	495(53)	600(52)
Elderly	637(110)	743(87)	712(105)	782(101)	601(87)	726(88)	710(132)	777(79)
AD	761(160)	948(164)	851(131)	947(180)	729(137)	889(149)	817(143)	982(156)

	Alert		No Cue		Valid		Invalid	
	Congruent	Incongruent	Congruent	Incongruent	Congruent	Incongruent	Congruent	Incongruent
Young	1.9(3.3)	8.1(8.8)	1.2 (3.0)	5.5(6.1)	0.4(1.4)	7.6(6.3)	1.5(3.1)	6.2(6.3)
Elderly	0.4(1.4)	4.2(5.2)	1.6(2.5)	0.8(1.8)	0.2(0.6)	2.4(2.5)	7.1(7.2)	2.4(3.5)
AD	3.6(7.5)	9.3(13.0)	2.8(4.0)	7.2(12.6)	2.2(3.2)	8.3(9.2)	2.8(4.1)	8.5(9.7)