Attentional Blink and Top-Down Directives in Alzheimer's Disease and Aging

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Abstract

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It is not well understood why patients with Alzheimer's disease (AD) have difficulty attending to relevant information in their environment. Deficits in top-down processing (such as difficulty using prior instruction or category identification to direct attention) or limitations in coping with rapid temporal demands maybe possible explanations for this impairment. This study was design to address attention deficits using the attentional blink paradigm that can dissociate top-down directives from rapid temporal demands. The attentional blink occurs when two stimuli (S1 and S2) are presented in rapid succession and the accurate identification of the second stimulus (S2) is reduced if it is presented very shortly after the first (S1).

The accuracy of S2 was compared in patients with AD, age-matched healthy controls and younger healthy controls. We hypothesized that aging would affect the ability to keep pace with rapid presentations, but patients with AD would have additional deficits in top-down directives.

Results showed that younger and older controls could utilize top-down instructions to improve their accuracy, but older controls could only improve their performance with sufficient time between stimuli presentation. This confirmed our hypothesis of age-related slowing. Accuracy in the AD group was lower overall than either healthy groups but importantly, performance was the same whether or not a priori instructions were provided. This supports our hypothesis that patients with AD are not able to utilize top-down directives. Results are discussed in the context of theories related to limited attentional resources and inhibition.

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Research Question

While most people are aware that the hallmark of Alzheimer’s disease (AD) is memory problems, many do not know that patients with AD also have attention problems even early in the course of the disease. The function of attention is to act as a gate for information that is constantly coming from both within ourselves and from our complex environment (Cohen, Sparling-Cohen, & O'Donnell, 1993). By selecting salient and important information, attention allocates limited resources and reduces the amount of information to be processed further, enabling us to respond appropriately to the demands of the situation. The world may be very confusing for patients with AD because of attentional deficits. Bombarded with important, as well as irrelevant information, patients with AD are unable to focus their resources to process only the necessary information to guide their behavior. As a result, they may be overwhelmed and have difficulty managing tasks such as grocery shopping, finding their way around once familiar places, and taking part in social events such as family gatherings.

This study sought to understand why patients with AD have problems paying attention to important information, while disregarding irrelevant information, in their environment. Researchers previously posited that patients with AD have difficulty directing attention based on goals and expectations (top-down processes) efficiently on selective attention tasks, relying instead on stimulus characteristics or bottom-up processes (Foldi, Schaefer, White, Johnson, Berger, Carney, & Macina, 2005), in part because of slow processing speed (Gao, Cheung, Chan, Chu, & Lee, 2013; Warkentin, Erikson, & Janciauskiene, 2008), inability to inhibit distracters (Amieva, Phillips, Della Sala, & Henry, 2004; Collette, Amieva, Adam, Hogge, Van der Linden, Fabrigoule, & Salmon, 2007), and impaired semantic (Harasty, Halliday, Xuereb, Croot, Bennett, & Hodges, 2001) or categorization skills (Au, Chan, & Chiu, 2003). The aim of this study is to understand why patients with AD cannot use prior directives to direct attention and limit irrelevant information. The attentional blink (will hence forth be written as blink) paradigm allows us to incorporate the role of top-down directives on the temporal aspect of attention without the confound of distracters in order to examine changes that occur with disease and age in groups of patients with AD, age-matched healthy controls, and healthy younger controls.

Literature Review

Alzheimer’s Disease (AD)

A brief summary of AD, including neurological changes associated with the disease, will be presented first followed by a review of how the areas affected by pathology are related to attentional impairments. AD is the most common cause of dementia, with one in eight people age 65 or older having AD (Alzheimer's Association, 2012). AD is a neurodegenerative disorder associated with cognitive deficits and social and functional impairment (Jack, Albert, Knopman, McKhann, Sperling, Carrillo, Thies, & Phelps, 2011; McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984). The onset of the disease is gradual with a course of continued cognitive decline. The most commonly used diagnostic criteria for AD were developed by (1) the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s disease and Related Disorders Association Work group (NINCDS-ADRDA, McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984), and (2) the Diagnostic and Statistical Manual of Mental Disorders-IV TR (DSM-IV TR, American Psychiatric Association, 2000). According to the DSM-IV TR, patients with AD have marked impairments in learning and memory with at least one additional cognitive dysfunction, such as aphasia, apraxia, agnosia, or executive dysfunction, which must be accompanied by functional impairment. The cognitive impairments are not due to delirium or other Axis I disorders. The NINCDS-ADRDA criteria (McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984) require documentation of a progressive dementia with impairment in at least two cognitive domains, including memory, language, visuospatial function, calculation, praxis, or executive function and the absence of delirium and other dementing disease. The cognitive impairments also need to result in functional impairment, such as inability to manage finance or do household chores. In 2011, the National Institute on

Aging (NIA) and the Alzheimer’s Association workgroups proposed an update to the diagnostic guidelines (Jack, Albert, Knopman, McKhann, Sperling, Carrillo, Thies, & Phelps, 2011), which included the addition of biomarkers for use in research settings only. However, in all three sets of guidelines, impairment in attention is not specifically mentioned despite evidence that it is prevalent in individuals with AD (Gorus, De Raedt, Lambert, Lemper, & Mets, 2006; Greenwood & Parasuraman, 1997; Perry & Hodges, 1999; Perry, Watson, & Hodges, 2000).

The neuropathological characteristics of AD include a greater presence of neurofibrillary tangles and neuritic plaques, especially in the cerebral cortex, than expected for age (Braak & Braak, 1991; Braskie, Klunder, Hayashi, Protas, Kepe, Miller, Huang, Barrio, Ercoli, Siddarth, Satyamurthy, Liu, Toga, Bookheimer, Small, & Thompson, 2010; Takashima, 2009). Other pathological changes in AD include reductions in synaptic density, loss of neurons, and granulovacuolar degeneration (Cummings & Cole, 2002). Cortical atrophy and neuronal loss occurs in the brainstem, basal forebrain, neocortical association cortex of the temporoparietal junction, frontal lobe neocortex, and the temporolimbic areas including the hippocampus, entorhinal cortex, and the corticomedial nuclear groups of the amygdale (Price, Ko, Wade, Tsou, McKeel, & Morris, 2001; Salat, Kaye, & Janowsky, 2001). Atrophy typically begins in the entorhinal cortex and spreads to the hippocampus, with resulting deficits in learning and retention of new information (Killiany, Hyman, Gomez-Isla, Moss, Kikinis, Jolesz, Tanzi, Jones, & Albert, 2002). Neuronal loss in the temporoparietal regions of the left hemisphere is associated with aphasia, neuronal loss in the temporoparietal regions of the right hemisphere is associated with impaired visuospatial abilities, and neuronal loss in the frontal lobe is associated with deficits in executive function (Braskie, Wilcox, Landau, O'Neil, Baker, Madison, Kluth, & Jagust, 2008). Additionally, neuronal loss in the nucleus basalis of Meynert of the forebrain and locus ceruleus and raphe nuclei of the brainstem leads to a reduction in cholinergic, noradrenergic, and serotonergic transmitters (Mendez & Cummings, 2003; Mufson, Ginsberg, Ikonomovic, & Dekosky, 2003).

The cholinergic system is affected during the early stage of AD as a result of cell loss in the nucleus basalis of Meynert (Cullen, Halliday, Double, Brooks, Creasey, & Broe, 1997; Davies & Maloney, 1976; Whitehouse, Price, Struble, Clark, Coyle, & Delon, 1982). The forebrain provides the major cholinergic innervations to the hippocampus, amygdala, and neocortex (Gu, 2002). Reduced levels of acetylcholine are associated with memory impairment (Ballard, Greig, Guillozet-Bongaarts, Enz, & Darvesh, 2005; Bartus, Dean, Beer, & Lippa, 1982) as well as deficits in arousal, attention and motivation, and behavior regulation (Bohnen, Kaufer, Hendrickson, Ivanco, Lopresti, Koeppe, Meltzer, Constantine, Davis, Mathis, Dekosky, & Moore, 2005; Gu, 2002). The cortical cholinergic system works to optimize how signals are processed in attention-demanding contexts (Sarter, Hasselmo, Bruno, & Givens, 2005). The link between acetylcholine and visual attention tasks has been documented through animal studies that associate higher levels of acetylcholine with demanding attention tasks and lower acetylcholine levels with poorer performance on these tasks (Balducci, Nurra, Pietropoli, Samanin, & Carli, 2003; Himmelheber, Sarter, & Bruno, 2000; Passetti, Dalley, O'Connell, Everitt, & Robbins, 2000). Research in patients with AD has also shown that cholinergic treatments such as galantamine and donepezil improve performance on simple and choice reaction time tasks and visual selective tasks (Foldi, White, & Schaefer, 2005; Galvin, Cornblatt, Newhouse, Ancoli-Israel, Wesnes, Williamson, Zhu, Sorra, & Amatniek, 2008; Vellas, Cunha, Gertz, De Deyn, Wesnes, Hammond, & Schwalen, 2005). Given that the cholinergic system is affected during the early stages of AD, it stands to reason that attention is also affected early in the course of the disease. In the following section, AD's effect on the different subtypes of attention will be reviewed.

Alzheimer's Disease and Attention

Although memory dysfunction is often the most prominent deficit in AD, impairment in visual attention is also well documented (Perry & Hodges, 1999) and present even during the early disease course (Baddeley, Baddeley, Bucks, & Wilcock, 2001; Perry, Watson, & Hodges, 2000). The notion that attention plays an important role in the operation of other cognitive functions is well established (James, 1890). The attentional system is comprised of subsystems that play different but interrelated functions (Fan & Posner, 2004; Posner & Petersen, 1990). Known attentional subsystems include arousal, alertness, sustained attention, orientation, divided attention, and selective attention.

Each subsystem has a different function and underlying neural substrate, and may be differentially affected by AD (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005; Fan, McCandliss, Sommer, Raz, & Posner, 2002). For example, arousal, or wakefulness, mediated by the reticular activating system (Kandel, Schwartz, & Jessell, 2000) is usually not compromised in AD until the late stages of the disease. Patients with AD generally have intact alertness and sustained attention during the early stages of the disease (Perry, Watson, & Hodges, 2000). Alertness consists of two states: phasic alertness, or voluntary receptivity for information, and tonic alertness, a continuous involuntary receptivity (Nebes & Brady, 1993). The network associated with alerting involves frontal and parietal regions of the right hemisphere (Jennings, Dagenbach, Engle, & Funke, 2007). Similar to tonic alertness, sustained attention involves maintaining effortful vigilance to detect stimuli over a period of time. Patients with AD only differ from healthy controls on tasks requiring longer periods of alertness and sustained attention

(Brazzelli, Cocchini, Dellasala, & Spinnler, 1994). This suggests that 1) shorter tasks are mediated by other structures associated with attention, such as thalamic structures, and relatively preserved in AD (Gainotti, Marra, & Villa, 2001), and 2) longer tasks require recruitment of additional cortical regions (Johannsen, Jakobsen, Bruhn, & Gjedde, 1999), which are compromised in AD.

Another type of attention is orienting, which refers to directing attention toward a stimulus, which requires disengaging attention from a stimulus or location, shifting attention, and reengaging attention to a new stimulus (Posner, 1980). Orientation can be overt or covert. Eye gaze is directed towards the stimulus in overt orienting, while in covert orienting, attention is shifted towards the stimulus even if eye gaze is not directed toward the stimulus. In valid covert orienting, a cue is presented prior to the onset of a stimulus to indicate the location of the stimulus, whereas in the invalid condition, the cue presented indicates an erroneous location of the upcoming stimulus (Posner & Petersen, 1990). The network associated with orienting includes frontal and parietal areas such as the superior parietal lobe and temporal-parietal junction (Jennings, Dagenbach, Engle, & Funke, 2007; Posner, Walker, Friedrich, & Rafal, 1987). Patients with AD are able to utilize spatial cues to improve their accuracy and speed in detecting a stimulus as effectively as healthy age-matched controls (Parasuraman, Greenwood, Haxby, & Grady, 1992). However, with invalid covert cues, patients with AD performed worse than controls (Greenwood, Parasuraman, & Haxby, 1993). Disengaging from an incorrect location, a process involved in invalid covert condition, is mediated by parietal and frontal cortical networks that are affected in the early stages of AD (Corbetta, Miezin, Shulman, & Petersen, 1993; Greenwood, Parasuraman, & Alexander, 1997). Valid covert conditions involve engaging and shifting, processes mediated by the superior colliculi and pulvinar, which are intact in AD. A separate theory posits that patients with AD have less total attentional capacity (Parasuraman, Greenwood, Haxby, & Grady, 1992) or limited access to attentional resources (Porter, Leonards, Wilcock, Haworth, Troscianko, & Tales, 2010; Sebastian, Menor, & Elosua, 2006). In invalid covert conditions, engagement to the erroneous location may usurp attentional resources, and the additional resources required to disengage, redirect, and engage a new location may not be available.

The next subtype of attention is divided attention, which involves the allocation of attention to at least two competing tasks or stimuli (Pashler, 1994; Pashler, 1998). The right prefrontal and parietal areas are associated with divided attention (Madden, Turkington, Provenzale, Hawk, Hoffman, & Coleman, 1997; Nestor, Parasuraman, Haxby, & Grady, 1991). Divided attention has been shown to be particularly vulnerable in AD, even during the early stages (Baddeley, Baddeley, Bucks, & Wilcock, 2001). In addition to impaired ability during the early stages of AD, Baddeley and colleagues (2001) found that performance on dual task conditions decreased with disease severity. Neuroimaging studies also have found differences between patients with AD and age-matched controls. In one study, participants were asked to discriminate between changes in frequency on visual and tactile stimuli (Johannsen, Jakobsen, Bruhn, & Gjedde, 1999). Patients with AD showed reduced cerebral blood flow patterns in the right frontal and subcortical areas compared to age-matched controls, though there were no significant differences in their responses. In another study (Nestor, Parasuraman, Haxby, & Grady, 1991), participants were presented with either a single reaction time task or a dual task with competing visual and auditory stimuli. Right frontal and parietal hypometabolism was observed in patients with AD during the dual task condition. In addition, patients with AD had slower reaction time compared to controls.

Finally, selective attention is considered to be one of the more demanding attentional tasks, requiring the coordination of several cognitive functions including search, detection, discrimination, and inhibition of irrelevant information and involves the frontoparietal network (Madden, 2007; Posner, 1987). Selection and preattentive mechanisms appear to be intact in AD, as patients are able to select targets that “pop out” among distracters that share no physical similarities (Greenwood, Parasuraman, & Alexander, 1997). However, patients with AD have more difficulty when the targets and distracters share physical characteristics (Foldi, Jutagir, Davidoff, & Gould, 1992; Foldi, Schaefer, White, Johnson, Berger, Carney, & Macina, 2005). Discrimination is generally spared in patients with AD, but is impaired when they are asked to perform the task in the context of a search (Foldi, Schaefer, White, Johnson, Berger, Carney, & Macina, 2005). Moreover, patients with AD may perform worse as the physical similarity among distracters increase. The researchers proposed that in AD, inhibition is impaired and top-down processing strategies become ineffective, such that individuals with AD have to rely on inefficient bottom-up strategies. One way to investigate this theory further is to utilize the blink paradigm, which is a type of selective attention task that incorporates the use of top-down directives along with the rapid demands of allocating attentional resources. A historical overview of the blink along with some of the major theories behind the phenomenon will be discussed in the next section.

Blink

When two events occur sequentially, the processing of the second event is compromised if the events occur temporally close together but gradually improves as the events appear further apart. In laboratory experiments, when two stimuli (S1 and S2) occur in rapid succession, identification or detection of the second target (S2) is reduced if it falls within a specific time window and temporally close to the presentation of the first target (S1) (Broadbent & Broadbent, 1987; Telford, 1931). This phenomenon has been investigated using the blink (Raymond, Shapiro, & Arnell, 1992) and psychological refractory period (Welford, 1952) paradigms, and is of interest because it allows researchers to examine the amount of information that can be processed within a fixed period of time. This temporal component of attention involves the time course it takes to direct attention to a stimulus and the length of time the stimulus continues to command attention (Egeth & Yantis, 1997). The early investigation of the psychological refractory period (Telford, 1931) was influenced by documented observations of the refractory phases in neurons, cardiac tissues, and skeletal muscles. Telford (1931) investigated the reduced ability to make a voluntary response following a previous response that occurred in close temporal proximity. This is thought to reflect the limited capacity of the human attention system. Although the blink and psychological refractory period are thought to stem from the same phenomenon, they have traditionally been investigated separately using different methodologies (Wong, 2002). Whereas the psychological refractory period is typically measured by the reaction time in detecting S2, the blink is usually examined through the accuracy of reporting S2.

The blink has typically been elicited using a rapid serial visual presentation (RSVP) where a stream of stimuli are presented in a central location and S1 and S2 (e.g., letters) are embedded among a series of distracters (e.g., numbers) (Shapiro, Raymond, & Arnell, 1994). However, the blink can also be elicited when S1 and S2 are displayed in different locations or presented in isolation without distracters (Duncan, Ward, & Shapiro, 1994). The number of distracters or intervening items presented between S1 and S2 are called lags. The number of lags varies from trial to trial within each experiment. In studies that do not utilize distracters, the onset time between S1 and S2 or stimulus onset asynchrony (SOA) are varied instead.

In most experiments, participants are instructed to report S1 and S2 at the end of each trial (Chun & Potter, 1995; Duncan, Ward, & Shapiro, 1994; Nieuwenstein, Chun, van der Lubbe, & Hooge, 2005; Raymond, Shapiro, & Arnell, 1992). As such, the dependent variable in these paradigms is the accuracy in reporting S2, with data presented as the percent correct. The reduced accuracy of S2 observed when the temporal separation between S1 and S2 is short is referred to as the blink deficit. One feature of the blink is *the extent of the deficit*, which is defined as the blink magnitude (Visser, Bischof, & Di Lollo, 1999) (Figure 1). Large blink magnitude represents lower accuracy and small magnitude represents better accuracy. A second feature of the blink is *the duration of the transient insensitivity to S2*. This time period is referred to as attentional dwell time (Figure 1) because it is thought to be the time when attention "dwells" on S1 (Duncan, Ward, & Shapiro, 1994; Hari, Valta, & Uutela, 1999). In healthy adults, dwell time typically lasts about 250-500 milliseconds (ms) after the onset of S1 (Theeuwes, Godijn, & Pratt, 2004). The time period immediately following the onset of S1 to around 250 ms does not typically show reduced S2 accuracy and is referred to as lag-1 sparing (Akyurek & Hommel, 2005). Although the blink is a robust phenomenon, its psychological mechanisms are not clearly understood. The following section will provide an overview of the major theories on the blink.

Theoretical Models of Attentional Blink

Attentional blink is a term analogous to the blink of the eye (Raymond, Shapiro, & Arnell, 1992). However, attentional blink is not a reflection of the limitation in the visual sensory system but rather of attentional mechanisms. According to Wong (2002), the blink paradigm involves several operational stages, including encoding, short-term memory consolidation, and retrieval, and the locus of the blink can occur in any one of the stages. A number of models have been proposed to account for the blink in healthy adults. Some of the major theories, including the *two-stage model* (Chun & Potter, 1995), *central interference model* (Jolicoeur, 1998), *retrieval interference model* (Shapiro, Raymond, & Arnell, 1994), *attentional dwell model* (Duncan et al., 1994), *dual interference model* (Wong, 2002), and *temporary loss of control model* (Di Lollo, Kawahara, Shahab Ghorashi, & Enns, 2005), will be reviewed in this paper (see Table 1).

Working memory serves a critical role in the blink. Working memory, a cognitive function that allows for the temporary storage and manipulation of information, is an important intermediary between perception and controlled actions (Baddeley, 1998). Baddeley's (2012) theory of a multi-component system of working memory is comprised of four components, the central executive, episodic buffer, phonological loop, and visuospatial sketchpad. The phonological loop holds and manipulates auditory and speech based information while the visuospatial sketchpad manipulates and temporarily maintains visual information as object representations. The episodic buffer acts as a buffer store that can hold multidimensional representations but is limited in capacity. The fourth component of working memory, the central executive is an attentional control system that has an important role in selective and divided attention (Baddeley, Baddeley, Bucks, & Wilcock, 2001). Working memory has been shown to decline with age (De Beni & Palladino, 2004; Salthouse, 1994) and is compromised in AD (Baddeley, Baddeley, Bucks, & Wilcock, 2001; Lim, Juh, Pae, Lee, Yoo, Ryu, Kwak, Lee, & Lee, 2008). The first two theories discussed, the *two-stage model* and the *central interference model*, map onto Baddeley's (2012) system of working memory.

Two-Stage Model

The *two-stage model* (Chun & Potter, 1995) posits that the recognition process involves two stages: a perceptual encoding stage and a short-term consolidation stage. In the perceptual encoding stage, visual features of a stimulus are constructed into a short-lived perceptual representation that can be processed further (Potter, 1993). In the short-term consolidation stage, the temporary perceptual representation is transformed and consolidated into a more durable working memory representation (Chun & Potter, 1995). The consolidation process is thought to be relatively slow and draws upon attentional resources. As such, consolidation of S1 may still be ongoing when S2 is presented. Because S1 and S2 can only be processed serially, a bottleneck is created and the processing of S2 is delayed as S1 is being consolidated. Thus, the representation of S2 may be lost or subjected to the interference of distracters before it is consolidated in short-term memory, thereby decreasing the likelihood that it would be reported. In support of the role of working memory in blink, Colzato and colleagues (2007) found that individuals with better working memory had smaller blink deficits. Participants' ability to solve simple mathematical problems while remembering words to recall later was negatively correlated with their blink magnitude.

Central Interference Model

The *central interference model* proposed by Jolicoeur (1998) is similar to the *two-stage model* in that it too assumes a bottleneck and that the processing of S1 and S2 occurs in a serial fashion such that the processing of S1 delays that of S2. However, this model posits that the locus of the bottleneck can occur in one or two stages, the consolidation (Dell'Acqua, Jolicoeur, Luria, & Pluchino, 2009) or the response selection stage (Jolicoeur, 1998). In Jolicoeur's original experiment, participants were instructed to either report S1 and S2 at the end of the trial, make an immediate button press when they detect S1 and S2, or make both an immediate manual response to the targets and report them at the end of the trial. In conditions where an immediate response was required, a larger blink deficit was observed compared to conditions that only required identification at the end of the trial. Furthermore, in conditions requiring immediate responses, faster reaction time was correlated with a smaller blink magnitude and shorter dwell time. These results indicate that by manipulating what was required in the response selection stage of processing, the size and duration of the blink is affected. This suggests that the processing of S1 at any stage can postpone the short-term consolidation of S2 (Arnell & Jolicoeur, 1999; Crebolder, Jolicoeur, & McIlwaine, 2002) and that the mechanism underlying blink is similar to that of the psychological refractory period (Jolicoeur, 1998). Although the theory posits that the mechanism of blink is similar to the psychological refractory period, the methodology used in this experiment (i.e., measuring reaction time), is commonly used in psychological refractory period paradigms. As a result, this methodology may have elicited mechanisms of the psychological refractory period as well as those of the blink.

Retrieval Interference Model

While the *two-stage model* and the *central interference model* proposed that blink occurs before S2 enters short term memory, the *retrieval interference model* (Shapiro, Raymond, & Arnell, 1994) hypothesized a late-selection account of the blink. The theory posits that the blink occurs after S1 and S2 enter short term memory such that the retrieval of S2 from short term memory is compromised by the interference of other items in short term memory, including S1 and distracters. Participants, in different conditions, detected or identified targets that consisted of either a white letter, black letter, white dots, or a gap of time in which no stimuli was presented. A blink deficit occurred only in conditions where S2 was an object (i.e., letters or dots). When S2 was a temporal gap, a blink deficit did not occur. When S1, S2, and distracters were physically similar to each other (i.e., S2 was an object) either by category or color, competition for retrieval arose. On the other hand, when S2 was different from S1 and the distracters (i.e., S2 was a temporal gap), there was better retrieval of S2. Because the degree of similarity between the targets and distracters influenced performance on S2, Shapiro and colleagues (1994) theorized that the blink was the result of a retrieval failure from short term memory. If the blink simply occurred because of processing difficulties before S1, S2, and distracters entered short term memory, similarity between the stimuli should not have played a role in eliciting a blink (Visser, Davis, & Ohan, 2009). The role of physical similarity among stimuli was also observed in other paradigms, including selective search, where greater physical similarities led to slower search and greater error rates (Foldi, Schaefer, White, Johnson, Berger, Carney, & Macina, 2005; Schialfa, Esau, & Joffe, 1998).

Attentional Dwell Model

The *attentional dwell model* by Duncan, Ward, and Shapiro (1994) proposes that the processing of S1 and S2 occurs in parallel as opposed to serially as put forth by the *two-stage model* and *central interference model*. Although the targets are processed in parallel, the ongoing processing of S1 interferes with the processing of S2 because it competes for a limited pool of attentional resources. Duncan and colleagues (1994) used a different presentation (four boxes surrounding a central fixation point) than is typically used in blink paradigms. In their experiment, a number was used as S1 and a letter was used as S2. First, a number (S1) was presented along the horizontal axis (i.e., either left or right of a central fixation point), and was followed by a mask. Then, a letter (S2) was presented along the vertical axis (i.e., either top or bottom of a central fixation point), and was also followed by a mask. The SOAs between S1 and

S2 were varied from trial to trial with no distracters presented in between. There were three conditions in the experiment. In one condition, participants were instructed to report only one target, a number, and ignore the letter in the vertical location. In another condition, participants reported only the letter and ignored the number in the horizontal location. In the third condition, participants reported both targets (the number and the letter). The typical blink deficit was elicited when participants were instructed to report both S1 and S2, with S2 showing reduced accuracy when the SOA was short. In the report one stimulus condition, when participants reported either a number or letter, their accuracy was good regardless of SOA and whether the target to be attended to was a S1 or S2.

Duncan et al. (1994) concluded that the blink occurs because more objects to be attended to placed greater demands on capacity. In the report both stimuli condition, the processing demands of S1 occupy resources for a few hundred milliseconds, leaving fewer resources to be allocated to the encoding of S2. In the report one stimulus conditions, participants only need to attend to one target, which places less demand on capacity. Perry and Hodges (2003) used the same paradigm to investigate the role of instructions in the context of top-down directives.

Dual Interference Model

In a study examining both the psychological refractory period and the blink, Wong (2002) concluded that while the psychological refractory period is the result of a central bottleneck, the blink is caused by two mechanisms. By incorporating earlier theories, the *dual interference model* suggested both a central bottleneck (Jolicoeur, 1998) and limited processing capacity (Duncan, Ward, & Shapiro, 1994). The author proposed that impairment due to limited capacity occurred in the perceptual encoding stage while the central bottleneck occurred after perceptual encoding but before response selection. In line with the *two-stage model* (Chun &

Potter, 1995) and the *central interference model* (Jolicoeur, 1998), Wong (2002) suggested that the locus of the bottleneck was in the consolidation stage. Like Jolicoeur (1998), Wong (2002) utilized both the psychological refractory period and blink methodologies by examining speed and accuracy. As such, the same criticisms may hold true for this experiment in that the mechanisms involved in the psychological refractory period were elicited along with those of the blink.

Temporary Loss of Control Model

The final blink theory to be reviewed is the *temporary loss of control model* (Di Lollo, Kawahara, Shahab Ghorashi, & Enns, 2005), which proposes that top-down control is temporarily suspended during blink. Top-down mechanisms are goal-directed and based upon task demands and directions (Desimone & Duncan, 1995). Bottom-up mechanisms refer to stimulus driven mechanisms that depend on properties of the stimulus, including color and other visual features of the stimulus (Wolfe, 1998). In this theory (Di Lollo, Kawahara, Shahab Ghorashi, & Enns, 2005), top-down control, originating from the executive control system, configures the sensory system to filter in S1 and exclude distracters. While processing S1, signals from top-down mechanisms are interrupted. The filter template set up by the executive control system becomes open to influence by bottom-up input from the distracters. As a result, the filter template may be changed so that S2 no longer matches the template and selection of S2 becomes difficult.

Findings from a study by Kawahara et al. (2006) supported the theory of a temporary loss of control during the blink. The authors found that identification of S2 was not impaired if the distracters presented in between S1 and S2 were from the same category as the two targets. The authors theorized that if the targets and distracters were from the same category, the distracters did not change the filter template, allowing for accurate S2 identification. However, a study that investigated top-down control through the use of spatial cues to indicate the location of S2 disputed this theory (Zhang, Shao, Nieuwenstein, & Zhou, 2008). Findings indicated that presenting spatial cues aided S2 identification even when the cues and S2 fell within the dwell time interval. The researchers suggested that individuals were able to utilize top-down control for target selection even during the blink.

A study conducted by Dux and Marois (2008) suggested that the blink is in part due to the failure to suppress the distracters in the stream of stimuli presented among S1 and S2. In this study, participants were primed with a distracter preceding S2 with similar physical characteristics. Theoretically, participants who were able to suppress distracters would have more difficulty identifying S2 when it was subsequently presented. Indeed, there was a correlation between the ability to suppress distracters and blink magnitude. Findings from these studies (Dux & Marois, 2008; Hommel & Akyurek, 2005) indicate that the working memory account of the blink may be too simplistic. Rather, the interaction between working memory capacity and other ongoing processes, including inhibition and strategic allocation, may better explain the phenomenon.

The theories summarized above provided a brief overview of some of the major theories involving blink mechanisms. Though no consistent findings have emerged, some processes, including working memory, inhibition, and top-down control, appear to play important roles in the phenomenon. However, their exact contribution to the blink and the relationship they have with each other remain unclear. Our study may be able to elucidate some of the mechanisms involved in the blink through dissociating top-down processes with temporal demands and by comparing the effects of AD with that of normal aging.

Neural Correlates of Attentional Blink

Some studies have attempted to examine the neural correlates of the blink using functional magnetic resonance imaging (fMRI) in healthy young adults. Marois et al.'s study (2000) manipulated the blink magnitude by introducing a high interference condition, which contained a distracter immediately following S1, and a low interference condition, which did not include a distracter after S1. The high interference condition showed reduced S2 accuracy and increased activation in the right intraparietal and lateral frontal cortex compared to the low interference condition. However, these results may be attributed to the effects of the distracters and not just to the blink phenomenon alone. Marcantoni and colleagues' study (2003) presented S2 either during the dwell time window (i.e., 300 ms) or after the dwell time window (i.e., 700 ms). When S2 was presented during the dwell time window, increased activation was observed in the inferotemporal, lateral frontal, left posterior parietal, and occipital cortex compared to when S2 was presented outside of the dwell time window. Using a similar paradigm, Kranczioch and colleagues (2005) found that the lateral frontal and parietal areas showed increased activation when S2 was detected in conditions when S2 was presented during the dwell time window than compared to when S2 was missed. When S2 was missed, increased activation in the occipitotemporal region was observed. The researchers included an additional condition where S2 was not presented at all. Increased activation was found in the parietal, inferior frontal, superior frontal, and anterior cingulate cortex when S2 was presented but not reported than compared to when S2 was not presented at all. This finding lent support to theories which postulated that S2 is processed to some extent but does not reach awareness due to poor working memory consolidation, inhibition of distracters, or top-down control (Chun & Potter, 1995; Di Lollo, Kawahara, Shahab Ghorashi, & Enns, 2005; Duncan, Ward, & Shapiro, 1994; Jolicoeur, 1998; Shapiro, Raymond, & Arnell, 1994). In all, these findings suggest that the frontoparietal areas are involved with the blink because increased activation is associated with explicit perception of S2 during the blink interval. Implications for AD will be discussed in the following sections.

Alzheimer's disease and Attentional Blink

To date, few studies have used the blink as a way to investigate the attentional limitations of patients with AD. One study, conducted by Kavcic and Duffy (2003), found a prolonged dwell time and greater blink magnitude in patients with AD compared to age-matched healthy controls. The researchers suggested that impairments in working memory and inhibitory feedback may be involved in the exacerbated blink deficit found in patients with AD. In addition, unlike age-matched controls, patients with AD made errors identifying S1 even when they were able to accurately identify S2. Errors in reporting S1 depended on the number of lags (greater number of lags result in longer time interval) between the presentations of S1 and S2. More errors occurred in S1 when the two targets appeared closer together, which the authors termed "attentional masking." The researchers suggested that S2 permanently blocked or masked the recall of S1, which had to be reported after both stimuli were presented. Attentional masking was correlated with immediate and delayed verbal memory scores while the blink was not. The combination of the blink and attentional masking suggest that patients with AD have severe temporal limitations in their attention.

Using the methodology put forth by Duncan and colleagues (1994), Perry and Hodges (Perry & Hodges, 2003) examined the blink and its relationship with top-down mechanisms in controls and patients with Mild Cognitive Impairment (MCI) who later progressed to AD. MCI is conceptualized as a predementia phase of AD in which the there is a concern for change in cognition and the degree of cognitive impairment is not normal for age (Albert, DeKosky, Dickson, Dubois, Feldman, Fox, Gamst, Holtzman, Jagust, Petersen, Snyder, Carrillo, Thies, & Phelps, 2011). Patients with MCI do not meet the criteria for dementia by virtue of their intact activities of daily living (Albert, DeKosky, Dickson, Dubois, Feldman, Fox, Gamst, Holtzman, Jagust, Petersen, Snyder, Carrillo, Thies, & Phelps, 2011; Petersen & Negash, 2007; Petersen, Stevens, Ganguli, Tangalos, Cummings, & Dekosky, 2001). Patients with MCI are thought to have the prodromal syndrome of AD and eventually progress to meet criteria for AD (Jicha, Parisi, Dickson, Johnson, Cha, Ivnik, Tangalos, Boeve, Knopman, Braak, & Petersen, 2006). In a MRI study examining patterns of atrophy in different subtypes of MCI, Whitwell and colleagues (2007) found that patients with MCI showed gray matter loss predominantly in the medial and inferior temporal lobes when compared to age-matched controls. Patients with MCI involving multiple domains had additional loss in the posterior temporal lobe, parietal association cortex, posterior cingulate, and medial frontal lobe. In a later study, Whitwell and colleagues (2008) compared patterns of atrophy in patients with MCI who progressed to AD within 18 months and patients with MCI whose diagnoses remained stable for three years. Patients who progressed to AD showed greater gray matter loss in the medial and inferior temporal lobes, temporoparietal cortex, anterior and posterior cingulate, precuneus, and the frontal lobes. These patterns of atrophy are consistent with those found in AD and as a result, attentional functions may be impacted.

One study investigated simple, divided, and selective attention in patients with MCI using choice-reaction time tasks (Okonkwo, Wadley, Ball, Vance, & Crowe, 2008). In the simple attention condition, participants were asked to identify a centrally presented stimulus. The divided attention condition included the identification of a central stimulus and the localization of a peripheral stimulus. The final condition, selective attention, was similar to the divided attention condition with the addition of distracters in the visual display. Participants with MCI performed significantly slower on the divided attention condition compared to controls. However, their performance did not differ from controls on the simple and selective attention conditions. Another study examined orientation in MCI and controls found that both groups performed similarly on the covert orienting task (Bagurdes, Mesulam, Gitelman, Weintraub, & Small, 2008). Finally, a study looking at the efficacy of cholinergic treatment with galantamine in patients with MCI after seven days found improvement in learning and delayed recall on a list learning task and in a visuospatial task but not in other cognitive functions including attention (Gron, Brandenburg, Wunderlich, & Riepe, 2006). Attention, in this study, was investigated using a motor speed task, a detection task where participants responded when they saw a visual stimulus, and a divided attention task where they had to respond to auditory stimuli while they were presented simultaneously with visual stimuli.

Utilizing the blink paradigm to examine blink and its relationship with top-down mechanisms, Perry and Hodges (2003) found that both the MCI and control groups exhibited the expected blink deficit when both stimuli had to be identified. When participants were instructed to ignore one of the stimuli from a specified location, identification of S2 was not compromised in the control group. On the other hand, the MCI group showed attenuated identification of S2 due to the interference of S1 from the unattended location. These findings indicate that patients with MCI were not able to utilize top-down control to complete the task in the same way as age-matched controls and that frontal functioning, including top-down processing, is impaired early in AD and in patients with MCI (Perry & Hodges, 1999). The authors suggested that there is a dissociation between dwell time and top-down control and that these two aspects of attention are subserved by different neural systems, with top-down control mediated by circuits in the prefrontal cortex (Desimone & Duncan, 1995; Kastner & Ungerleider, 2000).

These findings indicate that top-down deficits are present very early in the course of the disease, during the prodromal phase of AD before patients meet criteria for diagnosis. Therefore, it stands to reason that top-down deficits will also be present in AD. However, the role that age plays in phenomenon is unclear. In order to understand the changes that occur in the early disease course, we need to understand the changes that occur in healthy aging. The following section will review age-related changes in attention.

Aging

Cognitive functioning changes with age (Ballesteros, Nilsson, & Lemaire, 2009) though not all cognitive functions decline with age (Salthouse, 2009). According to Hedden and Gabrieli (2004), overlearned materials such as vocabulary and semantic knowledge, and automatic processes such as phonological storage, implicit memory, recognition memory, and emotional processing show minimal to no decline. Other functions, such as processing speed, working memory, episodic memory, spatial ability, and reasoning are thought to decline with age (Park, Lautenschlager, Hedden, Davidson, Smith, & Smith, 2002; Schaie, 1993; Zelinski & Burnight, 1997). Based on these findings, we believe that the blink, with its speed and information processing demands, should be vulnerable to age-related decline.

Neuroimaging also support behavioral findings. A documented change is lower white and gray matter volume in older adults as compared to younger adults (Resnick, Pham, Kraut, Zonderman, & Davatzikos, 2003). Similar to changes in cognitive function, the aging of white matter and grey matter do not change uniformly in healthy older adults (Hedden & Gabrieli, 2004). Anterior regions show greater decline than posterior regions (Raz, Lindenberger, Rodrigue, Kennedy, Head, Williamson, Dahle, Gerstorf, & Acker, 2005), with the frontostriatial system, which consists of connections between frontal lobes and the basal ganglia, exhibiting the greatest reduction (Gunning-Dixon, Head, McQuain, Acker, & Raz, 1998; Raz, Gunning-Dixon, Head, Rodrigue, Williamson, & Acker, 2004; Tisserand, Pruessner, Sanz Arigita, van Boxtel, Evans, Jolles, & Uylings, 2002). In addition to volumetric changes, neurotransmitters undergo decline in the prefrontal cortex and striatum (Braskie, Wilcox, Landau, O'Neil, Baker, Madison, Kluth, & Jagust, 2008; Wang, Volkow, Logan, Fowler, Schlyer, MacGregor, Hitzemann, Gur, & Wolf, 1995). Age-related reduction in dopamine and serotonin receptors have been associated with poorer performance on tasks of motor speed, mental flexibility, and response inhibition (Volkow, Ding, Fowler, Wang, Logan, Gatley, Hitzemann, Smith, Fields, & Gur, 1996; Volkow, Fowler, Wang, Logan, Schlyer, MacGregor, Hitzemann, & Wolf, 1994; Volkow, Gur, Wang, Fowler, Moberg, Ding, Hitzemann, Smith, & Logan, 1998; Wang, Volkow, Logan, Fowler, Schlyer, MacGregor, Hitzemann, Gur, & Wolf, 1995). Loss of white matter tract integrity in the prefrontal cortex and anterior corpus callosum has been observed using diffusion tensor imaging (Bennett, Madden, Vaidya, Howard, & Howard, 2010; Chen, Li, & Hindmarsh, 2001; Guttmann, Jolesz, Kikinis, Killiany, Moss, Sandor, & Albert, 1998). Reduced frontal white matter integrity is associated with a decline in processing speed, immediate and delayed memory, and executive functions (Gunning-Dixon & Raz, 2000). These age-related changes in cognition and brain structure suggest that attention also undergoes age-related change.

Aging and Attention

Visual attention has been shown to decline with age (Birren & Fisher, 1995; Levitt, Fugelsang, & Crossley, 2006; Rabbitt, 1979; Salthouse, 1996). Slower reaction time in older adults is found on attentional tasks such as alerting (Jennings, Dagenbach, Engle, & Funke, 2007), covert orienting (Greenwood, Parasuraman, & Alexander, 1997), divided attention (Madden, Turkington, Provenzale, Hawk, Hoffman, & Coleman, 1997) or dual tasks (Verhaeghen, Steitz, Sliwinski, & Cerella, 2003), and selective attention (Madden, 2007; Madden & Langley, 2003; Pesce, Guidetti, Baldari, Tessitore, & Capranica, 2005). Using a psychological refractory period paradigm to investigate dual tasks, Allen and colleagues (2002; 1998) found that older adults had a disproportionate amount of slowing at short SOAs. However, given that the attentional system is distributed throughout the brain and aging differentially affects different parts of the brain at various ages, examining attentional changes across the life-span can further elucidate age-related changes to attention and underlying brain mechanisms.

Aging and Blink

The blink has typically been studied in college-age adults, and only a handful of studies have investigated age-related changes in blink (Georgiou-Karistianis, Tang, Vardy, Sheppard, Evans, Wilson, Gardner, Farrow, & Bradshaw, 2007; Lahar, Isaak, & McArthur, 2001; Maciokas & Crognale, 2003). In one of these studies, Lahar and colleagues (2001) found that the blink magnitude was greater among older adults aged 62 to 77 than in younger adults aged 17 to 30. The researchers also observed that the blink deficit varied among individuals. This led them to classify individuals as either “deep blinkers” (i.e., those with large blink magnitude) or “shallow blinkers” (i.e., those with small blink magnitude). There were significantly more deep blinkers in the older group than in the younger group.

In another study examining age-related blink differences, Maciokas and Crognale (2003) devised a single task condition in which participants were instructed to ignore S1 and report S2 only and a dual task condition in which participants reported both S1 and S2. The magnitude of the blink deficit was larger in older adults (aged 64 to 79) than in younger adults (aged 23 to 43) in the dual task condition. Interestingly, during the single task condition, older adults were not able to utilize top-down instructions to ignore the first stimulus like younger adults. Not only were older adults unable to take advantage of top-down directives to mitigate the blink effect, S1 captured their attentional resources involuntarily through bottom-up mechanisms (Folk, Remington, & Johnson, 1992; Whiting, Madden, & Babcock, 2007) and impaired their performance in identifying S2. In a third study, Georgiou-Karistianis and colleagues (2007) utilized a life-span approach to examine blink differences in individuals aged 18 to 82. The researchers found that age was correlated with a longer dwell time and larger blink magnitude. In addition, blink deficits improved from ages18 to 40 and were followed by subsequent decline after age 40. This pattern is similar to the milestones observed in frontal lobe development using neuropsychological (Salthouse, 2009) and imaging studies (Bartzokis, Beckson, Lu, Nuechterlein, Edwards, & Mintz, 2001; Bartzokis, Cummings, Sultzer, Henderson, Nuechterlein, & Mintz, 2003), which led Georgiou-Karistianis and colleagues (2007) to suggest that age-related changes in blink were due to a decline in inhibitory processes.

A number of theories have been suggested to explain these age-related differences, including generalized slowing (Birren & Fisher, 1995), distraction from other stimuli (Hasher, Stoltzfus, Zacks, & Rypma, 1991), or decreased top-down efficiency (Whiting, Madden, & Babcock, 2007). One possibility is that overall slowing makes adults more vulnerable to lapses during attention tasks, particularly during shorter SOAs. Hartley and Little (1999) proposed that age-related slowing affects all stages of processing and slower processing speed has been consistently found in older adults (Salthouse, 2009). However, this would not explain the exacerbated slowing when S1 and S2 appear closer together in time.

Lending support to the inhibitory theory, Lahar and colleagues (2001) also proposed that the larger blink found in older adults was due to older adults' difficulty inhibiting distracters. In their study, older adults were more likely than younger adults to make intrusion errors by reporting distracters when trying to identify S2. Older adults' poorer ability to inhibit irrelevant information has also been demonstrated in negative priming and Stroop paradigms (Bugg, DeLosh, Davalos, & Davis, 2007; McDowd & Oseas-Kreger, 1991). In the negative priming paradigm, participants are instructed to respond to a target and ignore a distracter. If a target in one trial had been a distracter in a previous trial, identification of the target will be slower because that target had been inhibited in the preceding trial. This effect is attenuated in older adults, suggesting that older adults do not inhibit the distracters in the first trial as well as younger adults (McDowd & Oseas-Kreger, 1991). In the Stroop paradigm, participants identify the color of the ink words are printed in while they inhibit reading of the words. When the color of the ink and the word are incongruent (e.g., word "blue" is printed in red print), older adults are disproportionately slower than younger adults (Bugg, DeLosh, Davalos, & Davis, 2007). These results also suggest an age-related deficit in inhibitory control. In addition, Rissman et al. (2009) suggested that impairment in the top-down inhibition of irrelevant information underlies the deficits in working memory found in aging.

In support of a top-down efficiency explanation of age-related difference in the blink, frontally mediated functions, such as executive function and top-down control, are more vulnerable in older adults (Gazzaley & D'Esposito, 2007; Greenwood, 2007; Wecker, Kramer, Wisniewski, Delis, & Kaplan, 2000; West, 1996). In the typical blink paradigm, both stimuli have to be reported (Chun & Potter, 1995; Raymond, Shapiro, & Arnell, 1992). However, in a modified paradigm, directive instructions can be given such that participants attend to only one of two the stimuli (Maciokas & Crognale, 2003; Perry & Hodges, 2003). This ‘top-down’ directive can minimize the magnitude of the blink. However, top-down directives are thought to draw on frontal processes, which are vulnerable in aging (Gazzaley & D'Esposito, 2007; Gazzaley, Rissman, Cooney, Rutman, Seibert, Clapp, & D'Esposito, 2007). As a result, older adults are disproportionately impacted by the blink due to decreased top-down efficiency. The studies reviewed above suggest that the temporal aspect of attention may be impacted early in the aging process.

Thus far, there has been no study linking age-related changes in the blink and changes that occur in AD. The studies reviewed above indicate that changes occur early, around middle age in normal aging and early during the course of AD. From a clinical view, the early presence of an exacerbated blink deficit in aging and disease suggests that the blink may be an early and sensitive indicator of disease and changes in the disease. This leads to questions about how age-related changes differ from that which occurs in disease and if the mechanisms underlying the changes differ as well.

The results from studies by Maciokas and Crognale (2003) and Perry and Hodges (2003) implicate the role of top-down processes in the changes observed in the blink. However, several questions remain unanswered. The paradigm used by Perry and Hodges (2003) disclosed to participants spatial information about the to-be-searched alphanumeric item with information about the only possible axis for each target type. Thus, if a participant were instructed to search for a letter, the participant only had to search the horizontal axis. Should S1 appear as a number on the vertical axis, the participant already knew to avoid this input from the veritable axis and await S2 on one of the two possible horizontal locations. This strategy benefits accuracy for S2, and may be an explanation as to why there is no blink for controls. Therefore, it is unclear whether the difference found between MCI and control groups was a difficulty developing a strategy (frontal), appreciating the differences of each alphanumeric category (semantic grouping), maintaining the multiple possible cues (memory), or truly having difficulty allocating attentional resources to reduce the blink. Maciokas and Crognale's study (2003) included a top-down condition where participants were instructed to ignore S1 and to report only S2. Poorer peformance by older adults was attributed to the fact that S1 involuntarily captured their attentional resources, thus, using bottom-up processing mechanisms (Folk, Remington, & Johnson, 1992; Whiting, Madden, & Babcock, 2007). Another interpretation, however, may be secondary to the design of the RSVP paradigm. Specifically, in the RSVP paradigm, participants are presented with S1, S2, as well as multiple intervening sequential distracters. The traditional interpretation is that poor S2 accuracy is a result of attentional capture of S1; however, it may also be that the distracters themselves capture attention, use available resources, and thus mitigate the ability to process S2.

Aims and Hypotheses

This study sought to understand whether differences in the blink emanated from top-down processes per se (prior instruction or category identification), or from the temporal demands of rapid decision presented in a modified paradigm of that used by Duncan and colleagues (1994) and Perry and Hodges (2003). The paradigm presentation we utilized had two notable characteristics. First, it does not have intervening distracters, which would remove the confound of attentional capture of distracters versus S1. Second, it does not include a priori information about location, which would require participants to perceive both S1 and S2, thus enabling the examination of efficient allocation of attention resources in younger and older healthy controls (HC) as well as patients with AD.

Aim 1: To examine attentional decline in aging and Alzheimer's disease.

Hypotheses:

1A. The blink magnitude, as measured by differences in accuracy at the shortest SOA, would be smaller in the Younger HC group compared to Older HC group, who in turn, would have a less pronounced magnitude than in patients with AD.

1B. The dwell time or duration of the blink will be shorter in the Younger HC than the Older HC group, who would have a less prolonged dwell time than in patients with AD. This would be measured by reduced S2 accuracy at the shorter SOAs such that there would be an interaction between group and SOA.

Aim 2: To understand whether deficits in the blink are due to difficulties with top-down processes or coping with rapid temporal demands.

Hypotheses:

2A. The Younger and Older HC groups would take advantage of a priori instructions, as measured by having better accuracy under conditions with a priori instructions (Report-One Stimulus) than in the condition without a priori instructions (Report-Both Stimuli), while patients with AD would not be able to benefit. The performance in patients with AD would not differ whether or not they were given a priori instructions.

2B. While both Younger and Older HC groups would benefit from top-down instructions, they would differ in their ability such that under rapid temporal demands (or high temporal load), the Older HC group would not be able to utilize the instructions.

Experiment 1: Pilot

Methods

The objective of the pilot experiment was to reproduce the blink effect using a simplified procedure modified from that used by Duncan, Ward, and Shapiro (1994) and Perry and Hodge (2003). The purpose of the modification was to ensure that the task could be applicable to patients with diagnosed AD who were more impaired relative to participants with Mild Cognitive Impairment (MCI) than was used in the study by Perry and Hodges. In their search experiment, the investigator provided four squares surrounding a central fixation point on the screen. They gave participants multiple top-down instructions to detect and identify the targeted alphanumeric characters including information about the targets' color, locations in which they would appear, and alphanumeric type (e.g., the white numbers are to be presented on the vertical axis and black letters are to be presented on the horizontal axis). We believed that was too much information, which in turn made significant demands on memory. This would disadvantage patients with AD known to have more severe memory deficits than patients with MCI (Albert, DeKosky, Dickson, Dubois, Feldman, Fox, Gamst, Holtzman, Jagust, Petersen, Snyder, Carrillo, Thies, & Phelps, 2011; Petersen & Negash, 2007). As we were not interested in examining the amnestic demands of the task but rather wanted to focus on the attentional demands, we therefore omitted these pieces of information.

There were two major goals of the Pilot Experiment. The first objective was to test that all vertical and horizontal positions of the stimulus display showed equal accuracy. The second goal was to demonstrate that the blink effect could be elicited with simpler instructions such that the patients with AD would be more likely to understand and maintain instruction set. Thus, the experiment incorporated only the top-down instruction of alphanumeric type because patients with AD have impaired categorization skills (Au, Chan, & Chiu, 2003). In sum, the pilot experiment attempted to validate the simplified experimental procedure and demonstrate that the stimulus display could produce the blink effect in young healthy controls.

Participants

Twenty Queens College students (N = 20) taking Psychology 101 course participated in this experiment and received class credit for their participation. Inclusion criteria were normal or corrected-to-normal vision and exclusion criteria included current or past history of psychiatric disorders including depression, anxiety, alcohol abuse, or history of neurological illness. Demographic characteristics for this sample are presented in Table 2. Prior to initiating the experiment, it was approved by the Institutional Review Board of Queens College, City University of New York.

Stimuli and Procedure

Calibration task: The first step of the experiment was to calibrate individualized stimulus exposure durations such that each participant performed at ≥ 85% accuracy, similar to the procedures of Perry and Hodges (2003). This ensured that participants had sufficient time to perceive and accurately identify the stimulus. The duration time obtained was used for the participant's subsequent trials in the Blink task.

Each trial consisted of four consecutive black screens (Figure 2), with a central red fixation point surrounded by four white boxes on the vertical and horizontal axes. A single stimulus consisting of a randomly selected number (i.e., 2, 4, 6, 7, or 9) or letter (i.e., A, D, F, K, or P) was displayed randomly in one of the four locations at different exposure times as described below. The stimulus was followed by a mask in the same location. The alphanumeric characters were chosen because they are physically dissimilar from one another to avoid perceptual confusion. The stimulus display subtended a 4.2^{o} visual angle at a fixed viewing distance of 50 centimeters and was presented on a 2.01 GHz, 960 MB RAM PC computer and a 13½” monitor with a refresh rate of 75 Hz.

Participants were instructed to fixate on the central red point and verbally report each alphanumeric character as it appeared. Correct and incorrect responses were recorded by the examiner. Optimal stimulus exposure durations were determined using an adapted “up-and-down” trial method (Dixon, 1965; Dixon & Mood, 1948; Wetherill & Leviltt, 1965), where the initial stimulus was presented for 240 ms and a participant’s correct response decreased the subsequent stimulus duration by 26 ms, while an incorrect response increased the duration by 26 ms. The shortest optimal exposure time was determined when six consecutive accurate responses at the same stimulus duration were obtained and that they achieved at least 85% accuracy at that duration, estimating the lowest presentation duration at which the participant could accurately identify alphanumeric stimuli. As a result, the total number of trials varied for each individual and concluded when optimal exposure time was determined. This calibrated duration time was applied to all of the participant’s subsequent experimental trials.

Blink task: Immediately following the Calibration task, participants completed the Blink task. The same stimulus display was used presenting *two* sequential stimuli (S1 and S2). S1 and S2 appeared in two different boxes (Figure 3). The two stimuli consisted of one randomly selected number (i.e., 2, 3, 5, 6, or 9) and one randomly selected letter (i.e., A, D, E, N, or R). The interval times between when the two stimuli appeared (stimulus onset asynchrony, SOA) were also randomized for each trial. The SOA intervals (133, 266, 399, 532, or 655 ms) were chosen to capture the typical blink duration of 250 to 500 ms (Theeuwes, Godijn, & Pratt, 2004) as well as when accuracy should asymptote. The specific time intervals were set due to the refresh rate of the computer monitor. Each of the stimuli (i.e., S1 and S2) was presented for the established calibrated stimulus durations determined during the Calibration task, and were followed by a mask.

There were three i*nstruction* conditions, two of which include a priori information (1. Report-Number and 2. Report-Letter), and one condition which does not include information (3. Report-Both Stimuli). In the Report-Number condition, participants were instructed to report only the number of the two stimuli presented, while in the Report-Letter condition only the letter. In these conditions, the target stimulus could either be the first stimulus (S1) presented or the second stimulus (S2) presented. These two instructions directed participants' attention to the target by providing a priori information about the target's alphanumeric category, thus providing top-down directives. In contrast, in Report-Both Stimuli condition required participants to report both stimuli (i.e., the number *and* the letter), thus not providing any a priori information.

There were three possible *spatial configuration*s in which S1 and S2 could appear: 1) in any two of the four locations (4-configuration: left, right, above, and below the central fixation point), 2) only on the horizontal axis (H-Configuration: left and right of the central fixation), or 3) only on the vertical axis (V-Configuration: above and below the central fixation).

The three instruction and three spatial configuration conditions yielded nine blocks. Administration of the blocks was counterbalanced but blocks containing the Report-Number and Report-Letter instructions were administered before blocks with Report-Both instruction. The blocks were administered in sequence. Each block consisted of 40 trials, which resulted in a total of 360 trials per participant. Five practice trails proceeded each block. Participants' verbal responses were recorded by the examiner.

Data Analysis

First, to validate the modified stimulus display, analyses were conducted to examine response accuracy of each of the four locations (top, bottom, left, and right). Data from the Report-Number and the Report-Letter instruction conditions were combined into a Report-One Stimulus variable. Two separate, repeated measures analysis of variance (ANOVAs) were performed on data from the Report-One Stimulus and Report-Both Stimuli instruction conditions with the location of the stimulus (4 levels: left, right, top, and, bottom) as the within variable and response accuracy as the dependent variable. These analyses were conducted across all SOAs and spatial configurations.

Second, to validate the simplified experimental procedure and verify that the blink phenomenon could be demonstrated, a 2 x 2 x 5 repeated measures ANOVA was performed, with instruction condition (2 levels: Report-One Stimulus and Report-Both Stimuli), presentation (2 levels: S1 and S2), and SOA (5 levels: 133 ms, 266 ms, 399 ms, 532 ms, and 665 ms) as the within measure variables and response accuracy as the dependent variable.

Huynh-Feldt corrections were used in cases of violations of sphericity. The Fisher’s Least Significant Difference (LSD) test was used in post hoc analyses. Significance was set at $p \leq .05$ for all analyses.

Results

Individualized calibrated stimulus exposure durations averaged 40.57 ms (SD = 0.95, range 26.6 – 66.5 ms) for the 20 participants.

There was a significant accuracy difference in identifying stimuli in each of the four locations on the Report-One Stimulus instruction, *F*(1.86, 53.63) = 4.31, $p = .023$, partial $\eta^2 = .19$. Post hoc analysis showed significantly lower accuracy of stimuli appearing beneath the central fixation (79% accuracy) compared to above (89%, $p = .008$), left (89%, $p = .009$), or right (91%, $p = .002$) of the central fixation, the latter three were not significantly different from each other. Similar results were also found in the Report-Both Stimuli condition, *F*(2.13, 56.16) = 11.64, $p < .001$, partial $\eta^2 = .38$, with worse accuracy (75%) for stimuli presented beneath the central fixation compared to above (83%, $p < .001$), left (85%, $p < .001$), or right (87%, $p < .001$) of the central fixation, the latter three were not significantly different from each other. These findings indicated that the identification of stimuli appearing in the location beneath the fixation point was significantly less accurate than those in the other locations and suggested that spatial configurations that include the bottom location should not be used.

Following these results, a 2 x 2 x 5 repeated measures ANOVA was conducted to validate that the blink phenomenon could be elicited with both stimuli presented on only the horizontal axis (H-Configuration). Results showed a main effect of presentation order, *F*(1,19) = 8.54, $p = .009$, partial $\eta^2 = .31$. Stimuli presented first (S1) were more accurate than stimuli presented second (S2). There was also a main effect of SOA, *F*(4,76) = 14.61, $p < .001$, partial $\eta^2 = .44$. Post hoc tests showed an increase in accuracy with better performance at the longer SOA intervals (i.e., 399, 532, and 665 ms) than at the two shorter SOA intervals (i.e., 133 and 266 ms), $p < .001$ for all comparisons. Finally, the blink effect was demonstrated in the presentation order x SOA interaction, *F*(4, 76) = 13.42, $p < .001$, partial $\eta^2 = .41$. The accuracy of items presented first (S1) did not differ across the different SOA but items presented second (S2) were less accurate at the short SOA intervals (i.e., 133 ms and 266 ms), $p < .05$ for all comparisons. The main effect of instruction was not significant indicating that accuracy under each of the instruction conditions did not differ.

Summary: Pilot Experiment

We modified an existing experimental procedure used by Duncan, Ward, and Shapiro (1994) and Perry and Hodges (2003). This was done to address our concern that participants in our AD group would have difficulty comprehending complex instruction unlike those with MCI in Perry and Hodges's study (2003). The two objectives of the Pilot Experiment using young healthy participants were to test that all vertical and horizontal positions showed equal accuracy and to demonstrate that the blink effect could be elicited with simpler instructions. The first result indicated that of the four possible locations where a stimulus could be presented, it was significantly more difficult to identify stimuli presented beneath the central fixation point than at any of the other three locations (i,e., above, to the left, or right of the fixation point). Our finding is supported by previous literature on altitudinal pseudoneglect (McCourt & Olafson, 1997), where healthy controls often demonstrate an upward bias when asked to bisect vertical lines (Suavansri, Falchook, Williamson, & Heilman, 2012). Although our paradigm is not a bisection task, the bias toward the upper half of space can explain our results. Therefore, we determined that the bottom location should not be used in any subsequent experiment, thereby omitting the vertical axis and leaving only the horizontal axis for stimulus presentations.

A second result of the Pilot Experiment verified that the blink effect was easily elicited in conditions with or without a priori instruction using alphanumeric stimuli presented only on the horizontal axis. Thus, our modification of the Duncan et al.'s paradigm (1994) was validated and we were confident it could be administered to patients with AD in the primary experiment.

Experiment 2: Main Experiment

Methods

Participants

Eighty-six participants (N=86), comprising of three groups: 1) patients with AD, 2) Older Healthy Control (HC), and 3)Younger Healthy Control (HC), were included in this study. The AD group consisted of twenty-seven (n=27) participants with AD who were recruited from the Memory and Cognitive Disorders Center and the Division of Geriatrics at Winthrop University Hospital. A diagnosis of AD (McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984) was made by members from Neuropsychology, Geriatrics, Neurology, and Neuroradiology services. Other inclusion criteria for the AD group included a Mini Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) score of greater than 15/30, and normal or corrected-to-normal bilateral vision. Exclusion criteria: Participants with current or prior use of cholinesterase inhibitors, other primary neurological conditions (e.g., history of significant cerebrovascular accident, Parkinson’s, and Huntington’s disease), psychiatric disorders (e.g., Schizophrenia, Major Depressive Disorder, or Bipolar Disorder), and visual deficits that would interfere with the participant’s ability to engage in experimental procedures (e.g., macular degeneration).

HCs were stratified by age into two groups: Younger (n=24) and Older (n=35). Demographic characteristics are presented in Table 3. Participants in both HC groups (Younger and Older) were recruited from Queens College, Queens College Psychology 101 subject pool, and senior centers in the local geographic area and received either course credit or monetary compensation for their participation. Inclusion criteria included normal or corrected-to-normal bilateral vision, and an MMSE (Folstein, Folstein, & McHugh, 1975) score greater than or equal to 26/30 (Monsch, Foldi, Ermini-Funfschilling, Berres, Taylor, Seifritz, Stahelin, & Spiegel, 1995). To ensure that participants were not demented, individuals over 55 years old had an additional inclusion criterion, Dementia Rating Scale-2 (DRS-2) (Mattis, 2005) score of greater than or equal to 135/144 (Salmon, Thomas, Pay, Booth, Hofstetter, Thal, & Katzman, 2002) (see Table 4). Exclusion criteria included past verbal history of neurological (e.g., head trauma, stroke, or a diagnosis of Alzheimer's, Parkinson's, or Huntington's disease) or psychiatric disease (e.g., depression, schizophrenia, or alcohol abuse).

The three groups did not differ in education (Table 3) or estimated IQ (Table 4). Differences in ethnicity and gender were due to greater diversity among the participants in the Younger HC group and AD group. The AD group had lower MMSE scores than the Younger and Older HC groups and lower DRS-2 scores than the Older HC group. The study was approved by the Institutional Review Boards of Queens College, City University of New York and Winthrop University Hospital, Mineola, New York. All participants provided written informed consent prior to participation. The consenting process for participants with AD was witnessed by family members, who also provided written consent.

Stimuli and Procedure

Each participant received a Calibration task to establish their individualized stimulus duration followed by an administration of the Blink task. The same stimuli and procedures described in the Pilot Experiment were used for the calibration trials of this experiment. For the Blink task, only the Horizontal configuration was used, where stimuli were presented to the left and right of the fixation point. The three instruction conditions: 1) Report-Number, 2) Report-Letter, and 3) Report-Both Stimuli were the same as described in the Pilot Experiment. Administration of the first two instruction conditions was counterbalanced and the third instruction condition was always administered last. The three instruction blocks were administered in sequence. Each block consisted of 40 trials, which resulted in a total of 120 trials per participant. Five practice trials preceded each of the instruction blocks. In addition, participants with AD completed an exercise with paper printouts of the computer presentation prior to the practice trials. The examiner recorded the participants' verbal responses.

Data Analysis

Aim 1: To examine attentional decline in aging and AD.

Hypotheses:

1A. The blink magnitude, as measured by differences in accuracy at the shortest SOA, would be smaller in the Younger HC group compared to Older HC group, who in turn, would have a less pronounced magnitude than in patients with AD.

1B. The dwell time or duration of the blink will be shorter in the Younger HC than the Older HC group, who would have a less prolonged dwell time than in patients with AD. This would be measured by reduced S2 accuracy at the shorter SOAs such that there would be an interaction between group and SOA.

Analysis: To test the two hypotheses, a 3 x 5 repeated measures ANOVA with group (Younger HC, Older HC, and AD) as the between-subjects factor and SOA (5 levels: 133, 266, 399, 532, 665 ms) as the within-subjects factor and percent accuracy of S2 as the dependent variable was performed. The accuracy of S2 was analyzed only in trials where S1 was correctly identified (Figure 4) to ensure that performance on S2 was due to the blink (Kavcic & Duffy, 2003).

Aim 2: To understand whether deficits in the blink are due to difficulties with top-down processes or coping with rapid temporal demands.

Hypotheses:

2A. The Younger and Older HC groups would take advantage of a priori instructions, as measured by having better accuracy under conditions with a priori instructions (Report-One Stimulus) than in the condition without a priori instructions (Report-Both Stimuli), while patients with AD would not be able to benefit. The performance in patients with AD would not differ whether or not they were given a priori instructions.

2B. While both Younger and Older HC groups would benefit from top-down instructions, they would differ in their ability such that under rapid temporal demands (or high temporal load), the Older HC group would not be able to utilize the instructions.

Analysis: To test the two hypotheses, a 3 x 2 x 5 mixed-model ANOVA with Group (3 levels: Younger HC, Older HC, and AD) as the between factor, Instruction (2 levels: Report-One Stimulus and Report-Both Stimuli) and SOA (5 levels: 133, 266, 399, 532, and 665 ms) as the within measure factors, and percent accuracy of S2 as the dependent variable was performed. The accuracy of S2 was analyzed in all trials to compare and equate the two conditions (Figure 5 and 6) because in the Report-One Stimulus condition, identification of S1 was not required, thus accuracy of S1 could not be determined.

Huynh-Feldt corrections were used in cases of violations of sphericity. The Fisher’s Least Significant Difference (LSD) test was used in post hoc analyses. Significance was set at $p \leq .05$ for all analyses.

Exploratory analyses were performed on errors in order to investigate why patients with AD would have difficulty. Inaccurate responses were categorized into four types of errors: 1) reported the other stimulus that appeared but not the target stimulus (“reported non-target stimulus”), 2) gave a response that was the same alphanumeric category as the target stimulus, 3) reported a character that was not presented in the trial and of a different alphanumeric category than the target stimulus, and 4) reported that they did not see the target stimulus or gave no response. Differences between the groups for each of the errors, under each Instruction condition, were tested at each SOA. An examination of the standardized skewness coefficients and standardized kurtosis coefficients revealed deviations from normality. Because the error data were not normally distributed, the Kruskal-Wallis Test was utilized.

Results

In examining the calibrated stimulus duration exposure times, Younger HC (56.53 ms, SD = 28.08) required shorter stimulus duration than the Older HC (102.98 ms, SD = 40.97) and AD groups (121.18 ms, SD = 62.96), $F(2, 83) = 13.09$, $p < .001$. The Older HC and AD groups did not differ in duration time.

Hypotheses 1A & 1B: Results yielded only a main effect of SOA, $F(3.07, 255.03) = 70.45$, $p < .001$, partial $\eta^2 = .46$. Post hoc analyses showed that SOAs 133, 266, and 399 ms were different from each other (p < .05 for all comparisons) but 532 and 665 ms SOAs were not different from each other, indicating improved accuracy with increased SOA. There was no main effect of Group or Group X SOA interaction (Figure 7). These results suggest that the three groups did not differ in their blink magnitude or their dwell time. Of note, there was a Group difference ($F(2, 83) = 6.05$, $p < .01$, partial $\eta^2 = .13$) in the amount of trials excluded from this analysis because the Younger HCs (8% inaccuracy) made significantly fewer errors than patients with AD (18% inaccuracy) and the Older HC group (14% inaccuracy), who were not different from each other.

Hypotheses 2A & 2B: Two main effects were found. The first was a main effect of Group, $F(2, 83) = 4.83$, $p = .01$, partial $\eta^2 = .10$, where the AD group’s overall performance (73% accuracy) was less accurate than both the Younger HC (85%, p = .003) and the Older HC groups (80%, p = .05). There was also a main effect of SOA, $F(3.39, 281.40) = 110.33$, $p < .001$, partial $\eta^2 = .57$, with differences between all SOAs ($p < .001$). There was no main effect of Instruction. There was an interaction between Group and Instruction, $F(2, 83) = 4.96$, $p = .009$, partial $\eta^2 = .11$ (Figure 8). Post hoc test showed that the Older HC group was more accurate during the Report-One Stimulus instruction than the Report-Both Stimuli instruction (83% vs.

77%, $p = .001$). Performance in the Younger HC (86% vs. 83%) and AD groups (72% vs. 75%) did not differ in the two different instruction conditions ($p = .19$ and $p = .18$, respectively). An interaction between SOA and instruction was found $F(3.73, 309.31) = 2.75$, $p = .03$, partial $\eta^2 = .57$ with better accuracy during the Report-One Stimulus instruction condition at the 266 ms SOA. The interaction between Group and SOA was not significant.

A 3-way interaction of Group, Instruction, and SOA was also significant, $F(7.45, 309.31) = 2.02$, $p = .05$, partial $\eta^2 = .046$ (see Figure 9). First, looking at the effects of a priori instruction, post hoc tests showed that in the Young HC group, performance between the two instruction conditions differed only at the shortest SOA (133 ms), with better accuracy with the Report-One Stimulus Instruction (67%) than the Report-Both Stimuli Instruction (58%, $p < .001$). This suggested that the Younger HC had better accuracy with Report-One Stimulus Instruction but only at the shortest SOA (133 ms). The Older HC group had better performance with Report-One Stimulus instructions at the 266 (83% vs. 70%, $p < .001$) and 399 ms (87% vs. 77%, $p < .001$) SOAs. These results indicated that the Older HC had better accuracy with Report-One Stimulus Instructions at the 266 and 399 ms SOAs but not at the shortest SOA (133 ms). With the AD group, performances between the two instructions only differed at the 133 ms SOA ($p < .001$), but with better accuracy with the Report-Both Stimuli instruction (50% vs. 60%), which was in contrast to the Younger and Older HC groups.

Error analyses were conducted to explore possible explanations for the different performances of each group under the two different instruction conditions. First, it was determined that all participants understood the task instructions and gave only one response to the Report-One Stimulus instruction and gave two responses to the Report-Both Stimuli instruction. In the Report-One Stimulus instruction condition, there was a group difference in the "reported non-target stimulus" error (Table 5) during the 133 ms ($X(2)^2 = 9.06$, $p = .01$), 266 ms ($X(2)^2 = 6.71$, $p = .04$), 399 ms ($X(2)^2 = 6.71$, $p = .04$), and 532 ms ($X(2)^2 = 6.71$, $p = .04$) SOAs. Pair-wise post hoc test using the Mann-Whitney U Test revealed that the AD group made more "reported non-target stimulus" errors than the Older HC group. The Younger HC group was not different from the Older HC or AD groups. Groups also differed on the "no response" error (Table 6) during the 266 ms ($X(2)^2 = 9.25$, $p = .01$), 399 ms ($X(2)^2 = 9.11$, $p = .01$), and 532 ms ($X(2)^2 = 7.29$, $p = .03$) SOAs with the AD group making more of this type of error than both of the HC groups. The groups did not differ on "same alphanumeric as the target" or "different category and not presented in trial" errors (Table 7 and Table 8). These results indicated that with Report-One Stimulus instruction, the AD group was more likely to either report the non-target stimulus (S1) even when they were instructed not to do so, or could not identify the stimuli all together.

Follow up analyses were conducted to examine whether the alphanumeric type of the target had an effect on performance. Accuracy scores were analyzed using two separate 3 X 2 repeated measures ANOVA with Group (3 levels: Younger HC, Older HC, and AD) as the between factor, Target Type (2 levels: Numbers and Letter) as the within factor, and percent accuracy of S2 on all trials as the dependent variable for both the Report-One Stimulus and the Report-Both Stimuli Instructions. There was a significant difference in target type for the Report-One Stimulus Instruction, $F(1, 83) = 4.01$, $p = .05$, partial $\eta^2 = .05$, with better accuracy for numeric stimuli (82%) compared to letter stimuli (80%). With the Report-Both Stimuli Instructions, $F(1, 83) = 13.07$, $p = .001$, partial $\eta^2 = .136$, accuracy for letter stimuli (80%) was better than numeric stimuli (76%). However, there was no significant Group X Target Type interaction, indicating that the target type did not influence performance differently among the three groups.

Discussion

Summary

This study sought to understand why patients with AD have difficulty attending to relevant information in their environment. Their deficits may emanate from difficulties in top-down processing or they may stem from trouble coping with rapid temporal demands in real life situations. The current study addressed these questions utilizing the attentional blink paradigm, which offers a way to dissociate top-down directives from rapid temporal demands. We examined the blink performance in patients with AD, older age-matched healthy controls, and younger healthy controls, hypothesizing that 1) aging would affect the ability to keep pace with rapid presentations such that dwell time would be longer in older than in younger participants, and 2) patients with AD would have additional deficits in top-down guidance, particularly under the duress of load. Our first finding did not support our prediction in that there was no age difference in either blink magnitude or dwell time. However, our second finding did support our prediction. We demonstrated that patients with AD, compared to either control group, did have deficits when given top-down, a priori instructions: while the younger and older healthy controls were able to take advantage of instructions that directed their attention to the category of the imminent target, patients with AD did not avail themselves of this a priori information. They performed the same whether or not they were given the category (letter or number) of to-be-identified alphanumeric character. An additional new finding to the literature was how attentional load affected performance, particularly in patients with AD who are especially susceptible to simultaneous attentional demands. Not only did patients with AD have deficits utilizing a priori information, but the additional attentional demand of higher load (i.e., requiring faster decision making) put them at a greater disadvantage than controls. To date, this is the first study to examine how age-related changes of the blink differ from that which occurs in disease. Together, these data provide important implications for attentional demands in patients with AD and can help to explain why they have such difficulty attending to information in their daily activities.

Our first aim addressed attentional decline in aging and in AD. We hypothesized that the blink magnitude (Hypotheses 1A) and dwell time (Hypotheses 1B) would be smaller in younger compared to older controls, who in turn, would have a less pronounced magnitude and shorter dwell time than in patients with AD. To assess this, we evaluated the accuracy of S2 when instructions required that both S1 and S2 be reported. In agreement with the methodology used in many blink studies (Hommel & Akyurek, 2005; Kavcic & Duffy, 2003; Nieuwenstein, 2006; Sessa, Luria, Verleger, & Dell'Acqua, 2007), we only analyzed trials in which S1 was correctly identified as a way to confirm that S1 had indeed been processed. While all three groups exhibited a blink, the overall findings did not show age- or disease-group differences in either blink magnitude or dwell time (Figure 7). Our results are in contrast to previous studies which did find larger blink magnitudes (Lahar, Isaak, & McArthur, 2001; Maciokas & Crognale, 2003) and longer dwell times by older compared to younger adults (Georgiou-Karistianis, Tang, Vardy, Sheppard, Evans, Wilson, Gardner, Farrow, & Bradshaw, 2007; Maciokas & Crognale, 2003) as well as a prolonged dwell time and greater blink magnitude in patients with AD compared to age-matched healthy controls (Kavcic & Duffy, 2003; Peters, Ergis, Gauthier, Dieudonne, Verny, Jolicoeur, & Belleville, 2012). Unlike ours, all of these other studies used the RSVP paradigm to elicit the blink, which serially presents the two targets as well as multiple intervening sequential distracters. Even though both paradigms elicit a blink, one explanation may be that the RSVP paradigm not only requires accurate S1 and S2 identification, but also inhibition of the distracters. That is, participants are seeing the distracter stimuli, but are supposed to ignore them and only report the relevant target stimuli. In contrast, participants in our study did not have to inhibit any intervening distracters and hence, the older control group as well as the patients with AD (who were age-matched) could respond like younger controls. Supporting this explanation, Lahar and colleagues (2001) used an RSVP paradigm and found that older adults were more likely than younger adults to report distracters when trying to identify S2, because of the older adults' difficulty inhibiting distracters. In contrast, Dux et al. (2008) showed that young adults exhibited a negative correlation, where better ability to suppress distracters was associated with smaller blink magnitude (i.e. better accuracy). An explanation of the poor ability to inhibit irrelevant information in older adults is related to decline in orbitofrontal functioning (Lamar & Resnick, 2004) and is a known phenomenon demonstrated in other paradigms such as negative priming (McDowd & Oseas-Kreger, 1991) and the Stroop (Bugg, DeLosh, Davalos, & Davis, 2007). Similarly, Rissman et al. (2009) suggested that impairment in the top-down inhibition of irrelevant information underlies the deficits in working memory found in aging. Colzato et al. (2007) investigated working memory in young participants doing a blink task: their 'working memory' task required them to solve mathematical operations while remembering words for later recall. Findings suggested that poor working memory skill was associated with larger blink magnitude (i.e. worse accuracy). Working memory is central to two major theories of the blink, the two-stage model (Chun & Potter, 1995) and the central interference model (Jolicoeur, 1998). As S1 and S2 are thought to be processed in a serial fashion, the bottleneck created leaves S2 vulnerable to decay or interference by distracters before it can be processed in working memory. Importantly, our experimental paradigm removes the influence of working memory, because without the intervening distracters and without their interference, older adults and even patients with AD achieve comparable processing of rapid consecutive stimuli. Therefore, our paradigm raises the possibility that greater blink magnitude (i.e., lower accuracy) or longer dwell time (i.e., longer time to recoup) previously found in older adults compared to younger adults may have been due to deficits in working memory and not blink per se.

The second aim sought to understand whether deficits in the blink were due to difficulties with top-down processes, coping with rapid temporal demands, or both. Would a priori instructions facilitate identification of the target by guiding a participant to attend to the category of that target stimulus? Based on prior findings of impaired selective search in AD (Foldi, Schaefer, White, Johnson, Berger, Carney, & Macina, 2005), we hypothesized that younger and older controls should be able to benefit from such instructions, whereas patients with AD would have great difficulty: that is, their accuracy performance would not differ whether or not they were given instructions (Hypothesis 2A). To test this hypothesis, all trials were included in the analysis to equate trials with and without instruction. Overall, participants with AD were less accurate than either young ($p < .01$) or older participants ($p = .04$), who were not different from one another. But more importantly, the interaction between Group x Instruction interaction ($p = .009$) partially supported our hypothesis. Both control groups performed better when they were given a priori instructions compared to conditions without such instructions, although only the older group was significantly more accurate with instructions ($p = .001$) (see Figure 8). This finding corroborates studies using the RSVP paradigms, which also found that guiding attention to the imminent target by using visual alerting cues (Nieuwenstein, Chun, van der Lubbe, & Hooge, 2005) or instructions that helped participants anticipate when the targets would appear (Martens & Johnson, 2005; Shen & Alain, 2012) facilitated more efficient allocation of resources and, reduced the dwell time or magnitude of the blink. In contrast, as predicted, the AD group did not benefit from prior instructions, and both conditions were equal (*p* = .18).

We also hypothesized that the control groups could not only benefit from top-down instructions by ameliorating the depth and length of their blink, but also that the effects of high temporal demands (load) would impinge on their performance differently (Hypothesis 2B) such that young participants could recoup more quickly than older participants, who in turn would be less vulnerable to speed of presentation than the patients with AD. Results revealed that the Younger HC group showed an effect of instruction at the shortest SOA (133 ms); that is, younger participants availed themselves of the top-down instructions particularly when the attentional load was high. The Older HC group also showed an effect of the instruction at varying load, but they only had better accuracy with instructions at the 266 and 399 ms SOAs, but not at the shortest 133 ms SOA. While previous research has shown top-down deficiencies among older adults as a function of load in the blink paradigm (Maciokas & Crognale, 2003), our current results refine these finding. Specifically, our Older HC group *was* able to utilize top-down directives, but *only* if given sufficient time; if not given sufficient time (i.e., at 133 ms SOA), no amount of prior knowledge seemed to help their performance. However, given a bit more time (i.e., 266 and 399 ms) the older participants behaved like their younger counterparts, availed themselves of the information, and identified the target stimulus better with than without the a priori directive. Top-down directives are thought to draw on frontally mediated functions, and could be vulnerable in aging (Gazzaley & D'Esposito, 2007; Gazzaley, Rissman, Cooney, Rutman, Seibert, Clapp, & D'Esposito, 2007; Greenwood, 2007). But, similar to the findings of our study, Whiting et al. (2007) also suggested that older adults *were* able to utilize top-down information like younger adults, but only in cases when there were no additional demands on their attentional resources. In their study, increased ‘attentional load’ was defined by increasing the number of top-down strategies participants had to maintain, which the authors proposed conflicted with resource-dependent components of attention. In our study increased load was achieved by increasing the temporal demands during which one has to make a decision. Thus, consonant with theories of slower processing speed in aging (Salthouse, 2009), our finding suggests that older controls can utilize top-down instructions to improve their accuracy, but only if it within the realm of their available resources and given sufficient time to do so.

Regardless of the load (SOA), the AD group showed no difference with or without instruction. But, interestingly, at the highest load (i.e., SOA 133 ms) there was a paradoxical phenomenon where they actually had better accuracy *without* than *with* prior instructions (Figure 9, panel 3). Perhaps, this suggested that the instructions could even hinder their performance when attentional demand/load was high – i.e. too much information.

The reasons patients with AD had difficulty with a priori instructions were explored in an error analysis, comparing their error performance to that of the other control groups. This analysis was restricted to trials where S2 was incorrect and top-down instructions were given. We posited that the reasons that patients with AD did not benefit from instructions was that it required knowledge of and/or access to the alphanumeric category, that is, semantic information. As category identification is impaired in AD (Au, Chan, & Chiu, 2003), this task would therefore be difficult, particularly when the temporal demands were high at the shorter SOA. Note, that it was not the case that participants were simply unable to do the top-down task: patients with AD understood and remembered the task instructions, as evidenced by the fact that they correctly gave only one response to the Report-One Stimulus instructions and gave two responses to the Report-Both Stimuli instruction. Moreover, they had greater than 80% accuracy at the long

SOAs (532 and 655 ms) indicating that they were able to understand and perform the task when the temporal demand was low. Therefore, we do not believe that the AD group had difficulty in trials with a priori instructions simply because of instruction complexity or deficits in language and memory.

The findings of the error analyses (see Tables 5 & 6) indicated that when asked to identify S2 with a priori instruction, the AD group reported the other non-target stimulus (i.e., S1) more frequently than older controls at all SOAs with the exception of the longest SOA (655 ms). Another type of error made by patients with AD was not responding (omission error), and they did so more than either of the control groups. These results suggested that patients with AD could have missed the target or report the non-target stimulus (S1) even when they were instructed not to do so. This error analysis leads to two possible explanations. One, is that patients with AD have difficulty making alphanumeric categorizations and cannot process S2 quickly enough, or that the attentional capture or ‘pull’ of S1 is overwhelming despite instructions not to attend to it. Data from our current study does not allow us to discern between the two explanations, and future research is warranted.

Our results lend support to and refine some of the existing models of blink. Since the time the blink phenomenon was first reported (Broadbent & Broadbent, 1987), a number of models have been proposed to account for the blink in healthy adults. Limited-processing capacity models (Chun & Potter, 1995; Dehaene, Sergent, & Changeux, 2003; Duncan, Ward, & Shapiro, 1994; Jolicoeur, 1998; Jolicoeur & Dell'Acqua, 1998; Visser, 2007) hypothesize that there is competition for attentional resources between the two targets leading to lesser allocation to process of S2. Other models center on the suppression or inhibition of stimuli that occur after S1 (Olivers & Meeter, 2008) or the inability to filter distracters from the targets (Di Lollo, Kawahara, Shahab Ghorashi, & Enns, 2005). Based on a review of the theoretical models, Dux and Marois (2009) posited that in an RSVP paradigm, all stimuli are processed perceptually and conceptually with their semantic information. As a function of task instruction (e.g., information of the target), distracters have to be inhibited, and both targets, which receive attentional enhancement, then compete with each other for higher processing, including episodic registration (Wyble, Bowman, & Nieuwenstein, 2009), working memory encoding, and response selection (Jolicoeur, 1998). The allocation of resources to process of S1 leads to fewer resources available to inhibit distracters or to enhance S2, resulting in poorer S2 identification. In all cases, limitations of available resources reduce the probability that S2 will be identified correctly.

In our paradigm, which does not include intervening distracters, we posit that competition for attentional resources as described in limited-processing capacity models (Chun & Potter, 1995; Dehaene, Sergent, & Changeux, 2003; Duncan, Ward, & Shapiro, 1994; Jolicoeur & Dell'Acqua, 1998) best explains the data. That is, there is a bottleneck for higher processing, such as working memory and response selection, so that S1 and S2 are processed serially. We propose that our data is best explained by the bottleneck created as a result of overallocation of limited resources, and top-down directives could offer strategic allocation of the resources to reduce the dwell time. That is, if attentional resources are limited (e.g., older more limited than younger participants), top-down directives help allocate resources efficiently, and this was especially seen in the improvement by both groups (albeit at different SOA). This idea is consistent with Colzato and colleagues (2007) who stated that the bottleneck proposed by Chun and Potter (1995) is not structural, which would indicate a depletion of attentional resources altogether, but functional in nature. Colzato et al. (2007) hypothesized that the overallocation of resources may be involuntary and a result of attentional capture by the stimulus through bottom-up processes (Folk, Remington, & Johnson, 1992)—i.e., the attentional ‘capture’ and interference of S1. The ‘functional’ bottleneck is also exhibited in other studies showing the “lag-1 sparing” effect (Potter, Chun, Banks, & Muckenhoupt, 1998). Lag-1 sparing occurs when S2 is presented as the first lag, that is, the presentation of S1 is immediately followed by S2 without any intervening item. In these trials, the accuracy in identifying S2 is as good as when S2 appears long after the presentation of S1 and beyond the typical dwell time window. This phenomenon occurs because both stimuli are processed as a single event and have access to the same attentional resources (Akyurek & Hommel, 2005). The ability to process both stimuli suggests that attentional resources may not be as limited as once thought, but that the system can process at least two stimuli if resources are allocated efficiently. In contrast, the patients with AD could not use any top-down instruction, and without this mechanism, patients have to give all stimuli equal allocation, even if they were told not to do so. They, therefore, have to inefficiently allocate most attentional resources to S1at the expense of identifying S2. In sum, our study suggests that the blink stems from the overallocation of limited resources and could be ameliorated by top-down directives, but only by individuals who could utilize the information. Those who cannot, namely patients with AD, are hugely disadvantaged as they treat all information equally to the point of overwhelming their attentional capacity.

Clinical Implications

Patients’ inability to use top-down information to select and attend to important stimuli in the environment has significant clinical implications. Patients with AD are likely to be easily overwhelmed in their daily routines, a phenomenon frequently seen in their activities of daily living (Kaplan, 2011). Precisely because they have difficulty filtering out and attending to what is important and what is not important in their environment, they have to attend to everything.

Moreover, they may not be able to use verbal instructions and directions given by their caregivers to help them even if they appear to understand or remember them. Instead, they are drawn to physically salient stimuli that capture their attention.

The translation of our findings to everyday concepts is important in helping clinicians provide better training to caregivers and family members to understand limitations and care for patients with AD. The concept of attentional load and the inability to process more than one stimulus quickly suggests that caregivers should limit the amount of instructions given to patients to only one piece of information at a time. Secondly, the inability to use top-down directives suggests that patients with AD may not be able to use prior information or instructions to help them, especially in situations requiring rapid processing and decision making such as driving.

Limitations and Implications for Future Research

This study had several limitations that should be noted. First, the cross-sectional design of our study was subject to possible cohort effects with regard to comfort with technology. Younger adults are more likely to be experienced with using rapid responses in computer use or in computer games, what we have dubbed the ‘Nintendo effect’. Other studies showed that individuals who play video games have faster reaction times (Dye, Green, & Bavelier, 2009), performed better on tasks of selective attention (Krishnan, Kang, Sperling, & Srinivasan, 2013), and could better distinguish whether simple visual and auditory stimuli occurred at the same moment or slightly offset in time to determine the temporal sequence of the stimuli (Donohue, Woldorff, & Mitroff, 2010). While we did not screen for prior use of technology in our cohorts, these recent findings suggest that such a variable may be indicated as a possible covariate in future studies.

A second limitation of the study is the many post hoc pairwise comparisons conducted with Fisher's LSD throughout the study. While a more conservative post hoc test, such as the Scheffé Test, could have been used to control for multiple testing, we chose the Fisher's LSD procedure given the small effect size and small sample size. Future studies with larger samples should be able to accommodate this limitation.

Another limitation of this study is the limited racial diversity in our participants, particularly among the AD groups, which may reduce the generalizability of our results. This is a common problem among other research studies (Galvao, 2011; Rabinowitz & Gallagher-Thompson, 2010; Sood & Stahl, 2011). Despite federal mandates to increase recruitment in minority populations, minority participation remains low (Corbie-Smith, Moody-Ayers, & Thrasher, 2004). There has been no study to date that looked at racial or ethnic differences in attention or top-down processes. One of the major consequences of the under-representation of ethnic minorities in research is the lack of information about normal cognitive and disease processes applicable to minority populations. This is especially important because the prevalence of AD is higher among African Americans and Hispanics than in non-Hispanic whites (Chin, Negash, & Hamilton, 2011). Moreover, Latinos have an earlier age of onset of AD, more cognitive impairment, and greater severity of cognitive impairment (Livney, Clark, Karlawish, Cartmell, Negron, Nunez, Xie, Entenza-Cabrera, Vega, & Arnold, 2011). Future studies will need to continue the effort to increase minority participation and increase generalizability.

Despite these limitations, the study was able to document the interaction of age and disease on attentional deficits in AD. This study is an initial attempt to emphasize that the combination of limited attentional resources and deficits in top-down processing affects performance, particularly in patients with AD. Further investigation is needed to determine whether patients with AD’s difficulty using top-down directives stems from deficits in making alphanumeric/semantic categorizations or the involuntary attentional capture of the first stimulus, which we were not able to do in this experiment. Understanding this should help us tailor ways to better deliver information to patients with AD.

Table 1. *Major Theoretical Models of Attentional Blink*

Model	Source of the Blink
Two-Stage Model (Chun & Potter, 1995)	Limited capacity, bottleneck at working memory consolidation stage
Central Interference Model (Jolicoeur, 1998)	Limited capacity, bottleneck at working memory consolidation and response selection stages
Retrieval Interference Model (Shapiro et al., 1994)	Failure to retrieve from short-term memory
Attentional Dwell Model (Duncan et al., 1994)	Limited capacity, but processing occurs in parallel
Dual Interference Model (Wong, 2002)	Limited capacity at perceptual stage and bottleneck at working memory consolidation stage
Temporary Loss of Control Model (Di Lollo et al., 2005)	Top-down control suspended, which leads to difficulty selecting S2

Table 2. *Demographic characteristics for Pilot Experiment:*

	N=20 Mean	 SD
Age (years)	20	2.99
Education - years	13.95	1.19
MMSE*	28.65	0.93
Gender	25% male	

*Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975)

Table 3. *Demographic characteristics for Main Experiment*

	Younger HC n=24	Older HC n=35	AD n=27	Statistic	*p*
Age – years Range	41.42 (11.7) 25 – 59	78.23 (7.4) 62 – 89	79.44 (7.0) 58-88		
Education-years	15.38 (2.1)	14.23 (2.5)	14.15 (3.9)	*F(*2, 83) = 1.41	.25
Ethnicity % Caucasian	62.5%	97.1%	100%	$\chi^2(2) = 21.81$	<.00
Gender % Female	62.5%	82.9%	55.6%	$\chi^2(2) = 5.85$	.05

Table 4. *Neuropsychological Tests for Main Experiment*

	Younger HC n=24	Older HC n=35	AD n=27	Statistic	*p*
MMSE	28.88 (0.9)	28.71 (1.3)	24.00 (3.8)	$F(2, 83) = 39.61$	<.00
DRS-2*		139.29 (3.8)	121.85 (10.2)	$t(60) = 24.58$	<.00
NAART** Estimated Full Scaled IQ	106.42 (8.1)	109.50 (7.6)	106.96 (8.8)	$F(2, 81)^+ = 1.26$	.29

* Dementia Rating Scale-2 (Mattis, 2005)
** North American Adult Reading Test (Uttl, 2002)

$^+$ Two participants did not complete the NAART because they were not fluent in English

Table 5. *Kruskal-Wallis Test for “Non-Target Stimulus” Errors*

SOA	Statistic	*p*
133 ms	$\chi^2(2) = 9.06$	.01
266 ms	$\chi^2(2) = 6.71$	.03
399 ms	$\chi^2(2) = 6.71$	.03
532 ms	$\chi^2(2) = 6.71$	.03
655 ms	$\chi^2(2) = 4.42$	.11

Table 6. *Kruskal-Wallis Test for "No Response" Errors*

SOA	Statistic	*p*
133 ms	$\chi^2(2) = 5.25$	.07
266 ms	$\chi^2(2) = 9.25$	.01
399 ms	$\chi^2(2) = 9.11$	.01
532 ms	$\chi^2(2) = 7.29$	.03
655 ms	$\chi^2(2) = 5.68$	.06

Table 7. *Kruskal-Wallis Test for “Same Alphanumeric Category” Errors*

SOA	Statistic	*p*
133 ms	$\chi^2(2) = 3.33$	.19
266 ms	$\chi^2(2) = 1.11$	.57
399 ms	$\chi^2(2) = 0.95$	.62
532 ms	$\chi^2(2) = 0.70$	.71
655 ms	$\chi^2(2) = 1.80$	.41

Table 8. *Kruskal-Wallis Test for "Different Category and Not Present in Trial" Errors*

SOA	Statistic	*p*
133 ms	No errors made	
266 ms	$\chi^2(2) = 2.19$	.34
399 ms	No errors made	
532 ms	No errors made	
655 ms	No errors made	

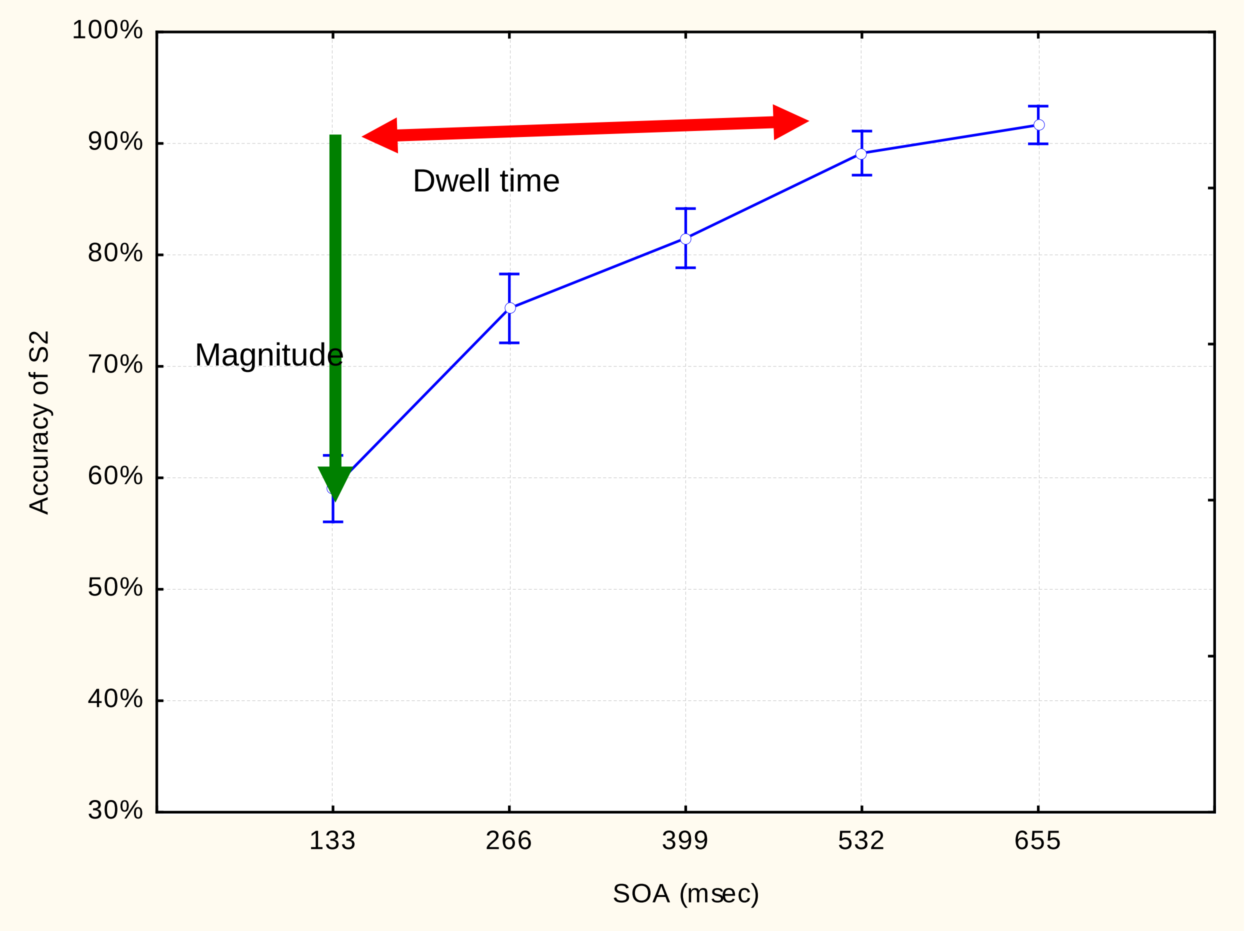

Figure 1. Blink magnitude and dwell time

Blink magnitude refers to the percent inaccuracy of S2 at the shortest SOA. Dwell time is the duration of the blink or transient time before S2 asymptotes.

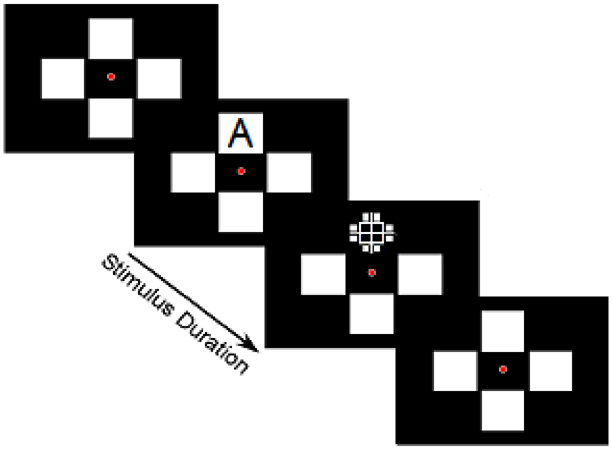

Figure 2. *Calibration task*

Event sequence involved a number or letter appearing in one of the four white squares surrounding a central red fixation point followed by a mask after the specific stimulus duration. The whole stimulus picture subtended 4.2^o; for clarity the designs are made larger.

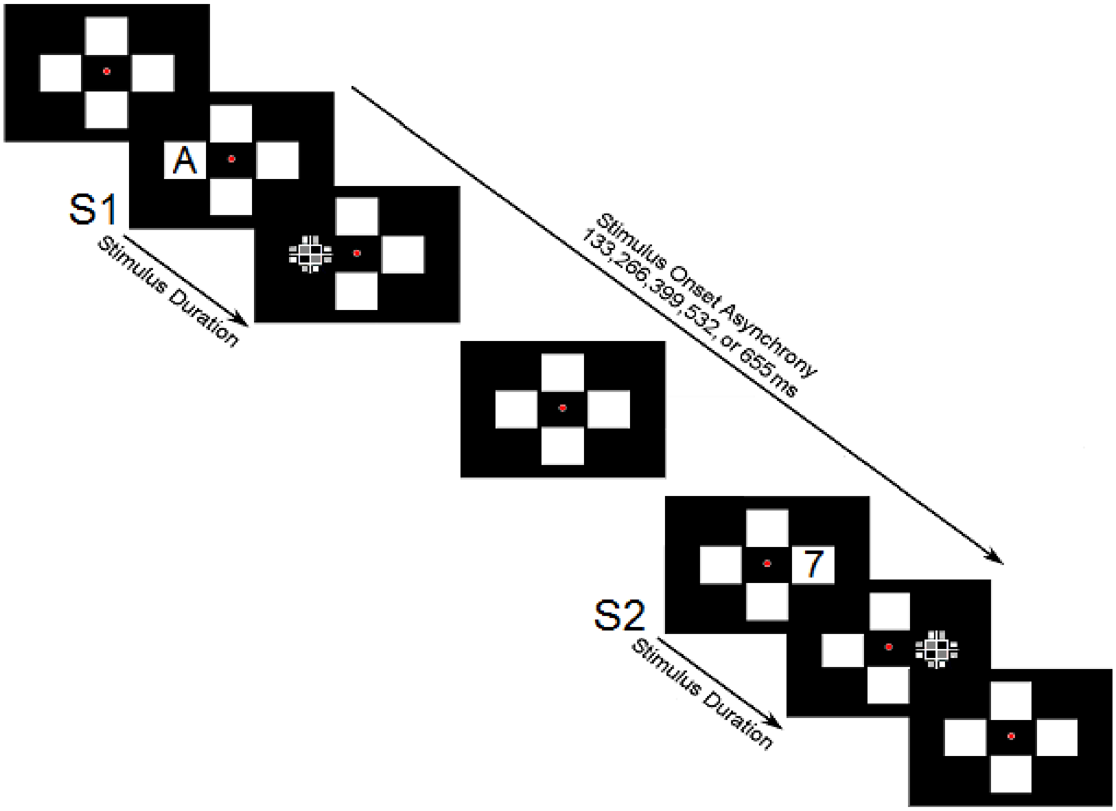

Figure 3. *Blink task*

With the same display design as the calibration task, two consecutive alphanumeric stimuli (S1 and S2) were separated by a 133, 266, 399, 532, or 655 ms interval. S1 could be either a number while S2 is a letter or vise versa. Stimulus duration of S1 and S2 were obtained from individualized calibration time from the previous task. The three spatial configurations in which S1 and S2 appeared in respect to the central red dot could either be horizontal only (H-Configuration), vertical only (V-Configuration), or any two of the four locations which includes H-Configuration and V-Configuration (4-Configuration). H-Configuration is shown above.

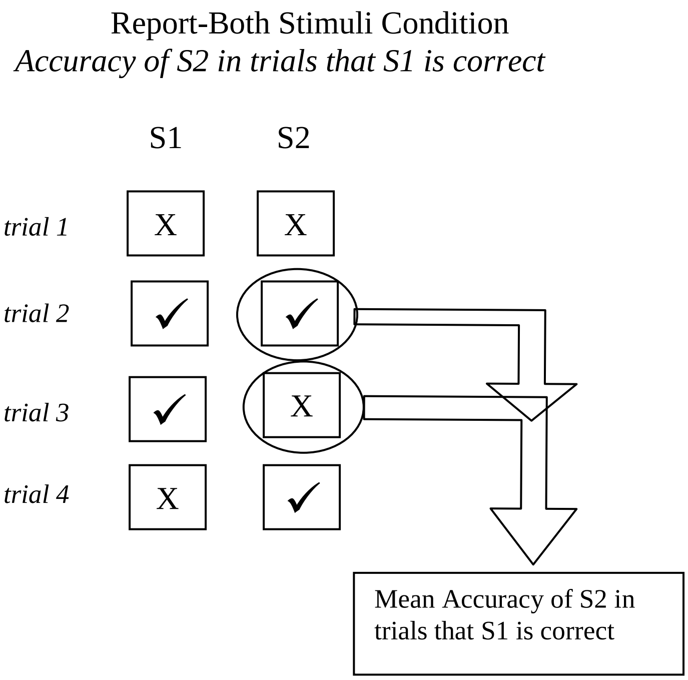

Figure 4. *Dependent variable of Hypotheses 1A and 1B*

Possible combinations of correct and incorrect responses to trials in the Report-Both Stimuli condition. X indicates incorrect responses from the participants, ✓ indicates correct responses. The dependent variable (mean accuracy of S2) is derived only from trials in which S1 are correct.

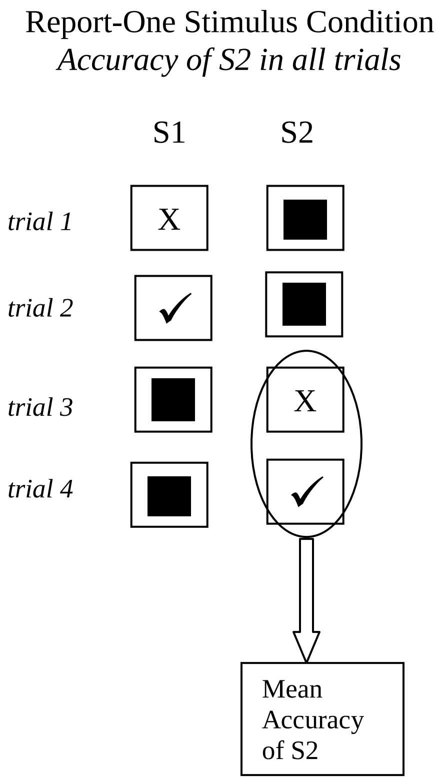
Report-One Stimulus Condition
Accuracy of S2 in all trials

Figure 5. *Dependent variable of Hypotheses 2A and 2B (Report-One Stimulus Condition)*

Possible combinations of correct and incorrect responses to trials in the Report-One Stimulus condition. X indicates incorrect responses from the participants, ✓ indicates correct responses. The dependent variable (mean accuracy of S2) is calculated from all trials in which there are S2 responses.

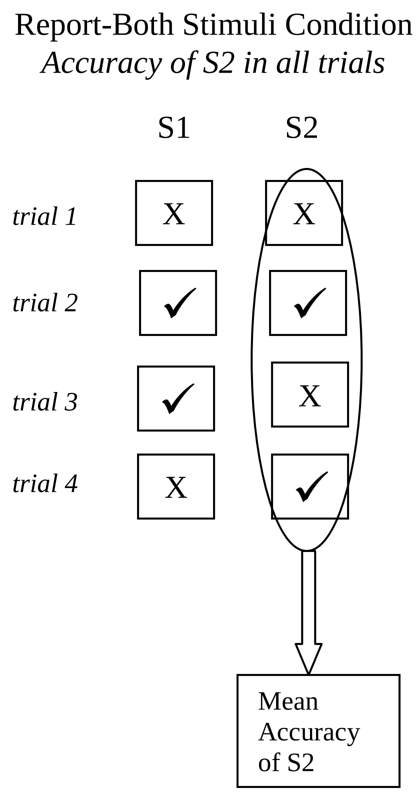

Figure 6. *Dependent variable of Hypotheses 2A and 2B (Report-Both Stimuli Condition)*

Possible combinations of correct and incorrect responses to trials in the Report-Both Stimuli condition. X indicates incorrect responses from the participants, ✓ indicates correct responses. The dependent variable (mean accuracy of S2) is derived from all trials.

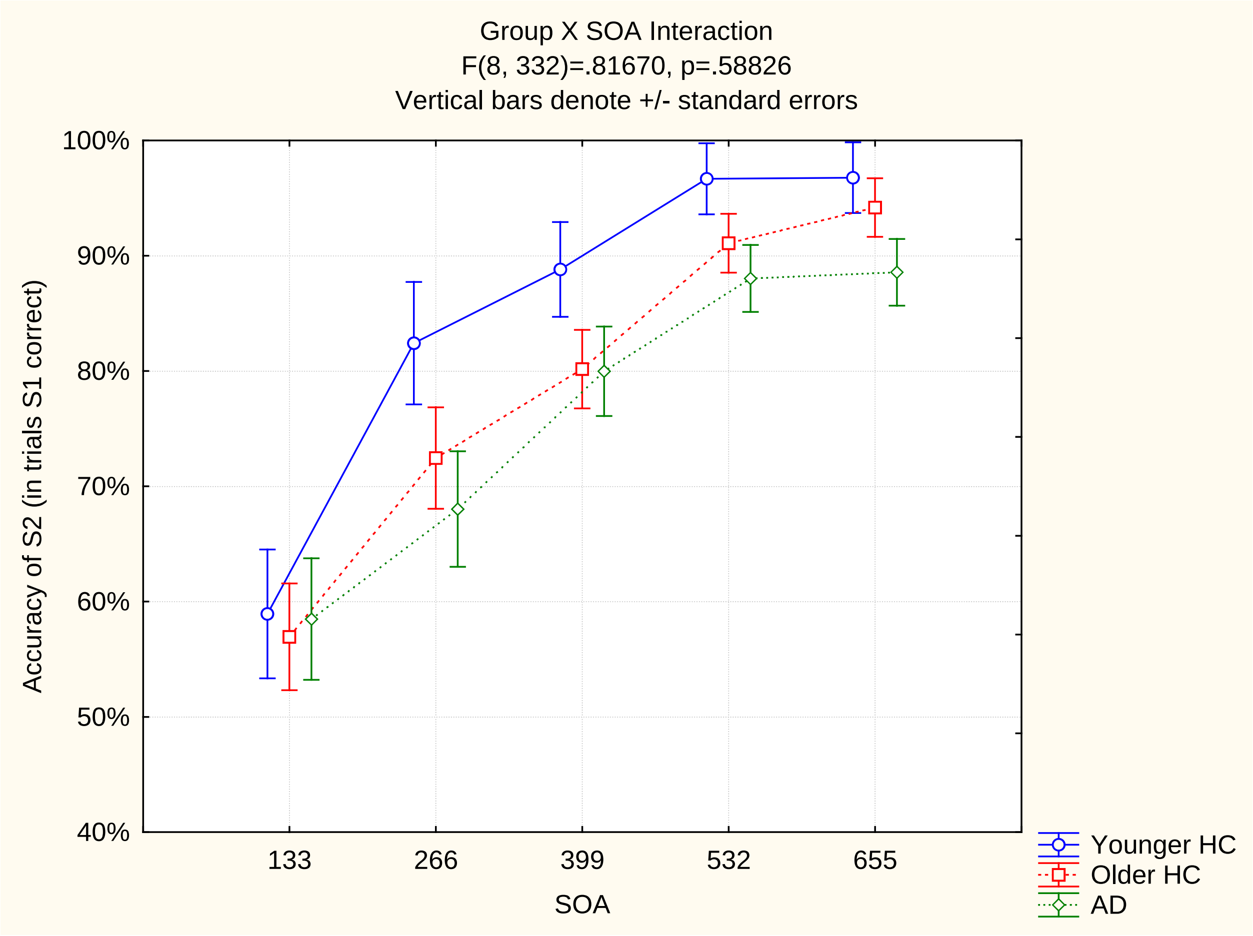

Figure 7. *Group X SOA Interaction*

Analysis to test hypotheses 1A and 1B using only trials in which S1 are correct
There are no significant results.

bars denote +/- standard error

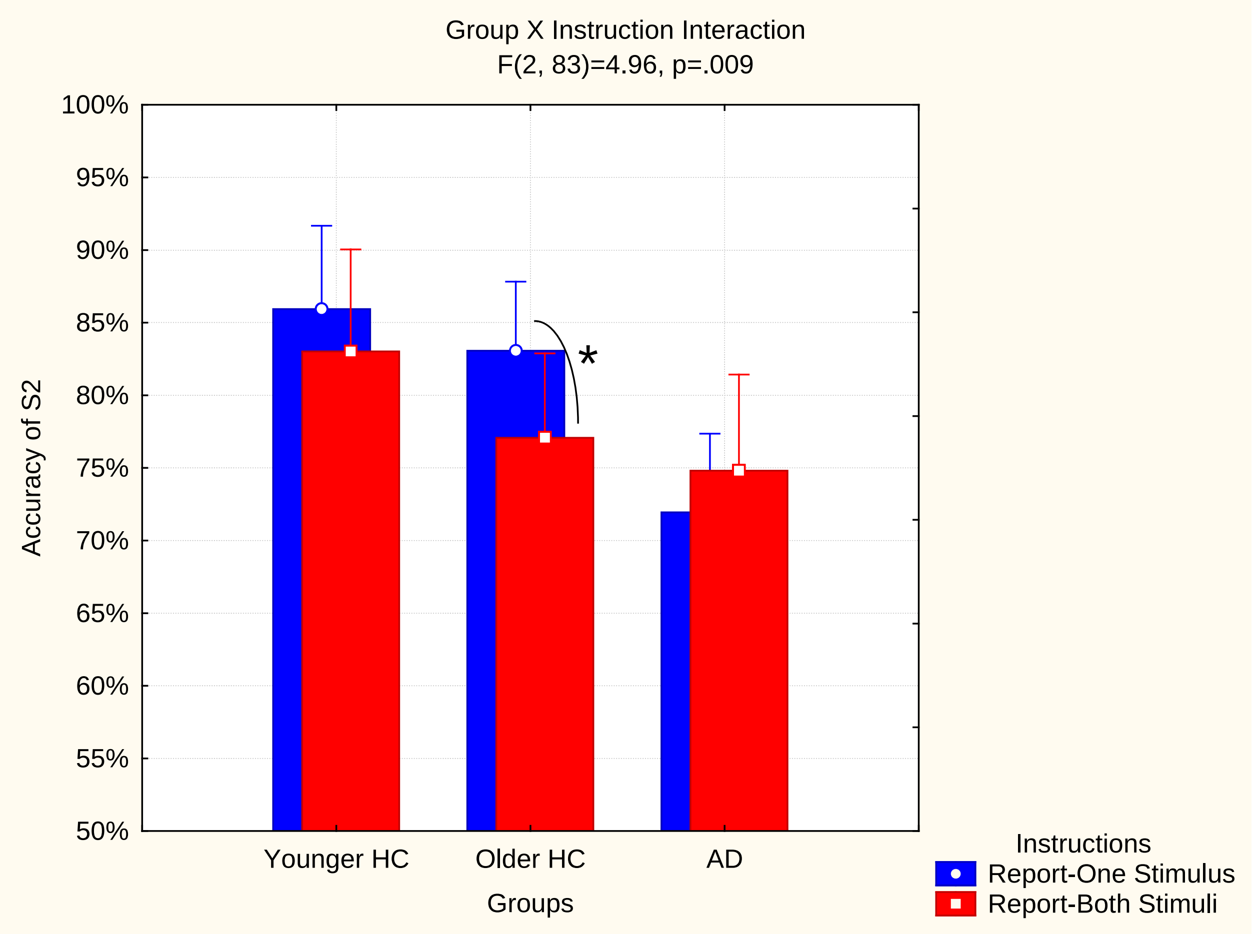

Figure 8. *Group X Instruction Interaction*

Analysis to test hypotheses 2A using all trials

* indicated p < .05
bars denote +/- standard error

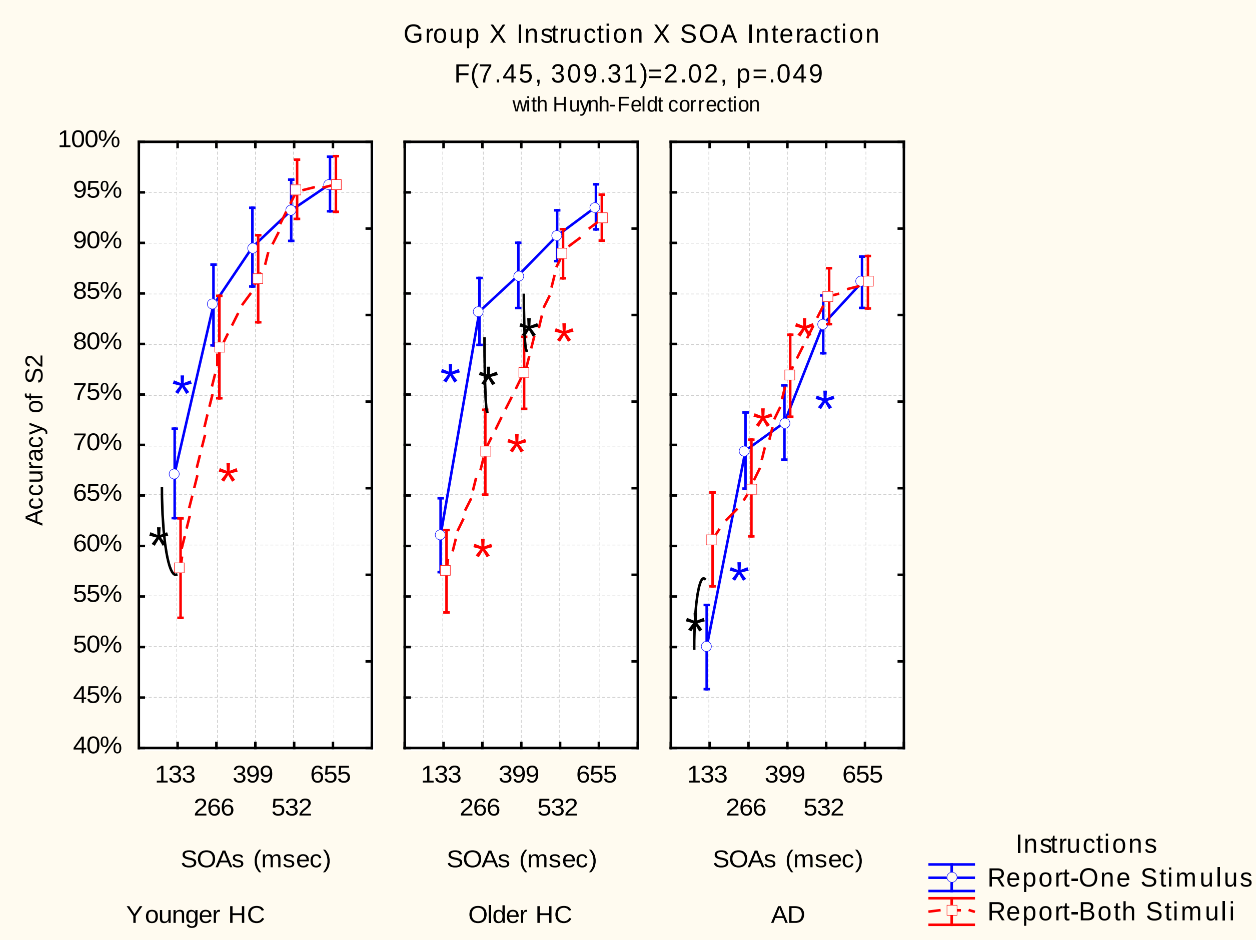

Figure 9. *Group X Instruction X SOA Interaction*

Analysis to test hypotheses 2A and 2B using all trials

* indicated p < .05
bars denote +/- standard error

References

Akyurek, E. G., & Hommel, B. (2005). Target integration and the attentional blink. *Acta Psychologica, 119*(3), 305-314. doi: 10.1016/j.actpsy.2005.02.006

Albert, M. S., DeKosky, S. T., Dickson, D., Dubois, B., Feldman, H. H., Fox, N. C., Gamst, A., Holtzman, D. M., Jagust, W. J., Petersen, R. C., Snyder, P. J., Carrillo, M. C., Thies, B., & Phelps, C. H. (2011). The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 7*(3), 270-279. doi: 10.1016/j.jalz.2011.03.008

Allen, P. A., Lien, M. C., Murphy, M. D., Sanders, R. E., Judge, K. S., & McCann, R. S. (2002). Age differences in overlapping-task performance: Evidence for efficient parallel processing in older adults. *Psychology and Aging, 17*(3), 505-519. doi: 10.1037/0882-7974.17.3.505

Allen, P. A., Smith, A. F., Vires-Collins, H., & Sperry, S. (1998). The psychological refractory period: Evidence for age differences in attentional time-sharing. *Psychology and Aging, 13*(2), 218-229. doi: 10.1037/0882-7974.13.2.218

Alzheimer's Association. (2012). 2012 Alzheimer's disease facts and figures. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 8*(2), 131-168. doi: 10.1016/j.jalz.2012.02.001

Amieva, H., Phillips, L. H., Della Sala, S., & Henry, J. D. (2004). Inhibitory functioning in Alzheimer's disease. *Brain, 127*(Pt 5), 949-964. doi: 10.1093/brain/awh045

Arnell, K. M., & Jolicoeur, P. (1999). The attentional blink across stimulus modalities: Evidence for central processing limitations. *Journal of Experimental Psychology: Human Perception and Performance, 25*(3), 630-648. doi: 10.1037/0096-1523.25.3.630

American Psychological Association. (2000). *Diagnostic and statistical manual of mental disorders : DSM-IV-TR* (4th ed.). Washington, DC: American Psychiatric Association.

Au, A., Chan, A. S., & Chiu, H. (2003). Conceptual organization in Alzheimer's dementia. *Journal of Clinical and Experimental Neuropsychology, 25*(6), 737-750. doi: 10.1076/jcen.25.6.737.16468

Baddeley, A. (1998). Working memory. *Comptes Rendus de lAcademie des Sciences Series III Sciences de la Vie, 321*(2-3), 167-173.

Baddeley, A. (2012). Working memory: theories, models, and controversies. *Annual Review of Psychology, 63*, 1-29. doi: 10.1146/annurev-psych-120710-100422

Baddeley, A. D., Baddeley, H. A., Bucks, R. S., & Wilcock, G. K. (2001). Attentional control in Alzheimer's disease. *Brain, 124*(Pt 8), 1492-1508. doi: 10.1071/AH970102

Bagurdes, L. A., Mesulam, M. M., Gitelman, D. R., Weintraub, S., & Small, D. M. (2008). Modulation of the spatial attention network by incentives in healthy aging and mild cognitive impairment. *Neuropsychologia, 46*(12), 2943-2948. doi: 10.1016/j.neuropsychologia.2008.06.005

Balducci, C., Nurra, M., Pietropoli, A., Samanin, R., & Carli, M. (2003). Reversal of visual attention dysfunction after AMPA lesions of the nucleus basalis magnocellularis (NBM) by the cholinesterase inhibitor donepezil and by a 5-HT1A receptor antagonist WAY 100635. *Psychopharmacology (Berl), 167*(1), 28-36. doi: 10.1007/s00213-002-1385-7

Ballard, C. G., Greig, N. H., Guillozet-Bongaarts, A. L., Enz, A., & Darvesh, S. (2005). Cholinesterases: roles in the brain during health and disease. *Current Alzheimer Research, 2*(3), 307-318. doi: 10.2174/1567205054367838

Ballesteros, S., Nilsson, L. G., & Lemaire, P. (2009). Ageing, cognition, and neuroscience: An introduction. *European Journal of Cognitive Psychology, 21*(2), 161-175. doi: 10.1080/09541440802598339

Bartus, R. T., Dean, R. L., Beer, B., & Lippa, A. S. (1982). The cholinergic hypothesis of geriatric memory dysfunction. *Science, 217*(4558), 408-414. doi: 10.1126/science.7046051

Bartzokis, G., Beckson, M., Lu, P. H., Nuechterlein, K. H., Edwards, N., & Mintz, J. (2001). Age-related changes in frontal and temporal lobe volumes in men: A magnetic resonance imaging study. *Archives of General Psychiatry, 58*(5), 461-465. doi: 10.1001/archpsyc.58.5.461

Bartzokis, G., Cummings, J. L., Sultzer, D., Henderson, V. W., Nuechterlein, K. H., & Mintz, J. (2003). White matter structural integrity in healthy aging adults and patients with Alzheimer disease: a magnetic resonance imaging study. *Archives of Neurology, 60*(3), 393-398. doi: 10.1001/archneur.60.3.393

Bennett, I. J., Madden, D. J., Vaidya, C. J., Howard, D. V., & Howard, J. H., Jr. (2010). Age-related differences in multiple measures of white matter integrity: A diffusion tensor imaging study of healthy aging. *Human Brain Mapping, 31*(3), 378-390. doi: 10.1002/hbm.20872

Birren, J. E., & Fisher, L. M. (1995). Aging and speed of behavior: Possible consequences for psychological functioning. *Annual Review of Psychology, 46*, 329-353. doi: 10.1146/annurev.ps.46.020195.001553

Bohnen, N. I., Kaufer, D. I., Hendrickson, R., Ivanco, L. S., Lopresti, B. J., Koeppe, R. A., Meltzer, C. C., Constantine, G., Davis, J. G., Mathis, C. A., Dekosky, S. T., & Moore, R.

Y. (2005). Degree of inhibition of cortical acetylcholinesterase activity and cognitive effects by donepezil treatment in Alzheimer's disease. *Journal of Neurology, Neurosurgery, and Psychiatry, 76*(3), 315-319. doi: 10.1136/jnnp.2004.038729

Braak, H., & Braak, E. (1991). Neuropathological stageing of Alzheimer-related changes. *Acta Neuropathologica, 82*(4), 239-259. doi: 10.1007/BF00308809

Braskie, M. N., Klunder, A. D., Hayashi, K. M., Protas, H., Kepe, V., Miller, K. J., Huang, S. C., Barrio, J. R., Ercoli, L. M., Siddarth, P., Satyamurthy, N., Liu, J., Toga, A. W., Bookheimer, S. Y., Small, G. W., & Thompson, P. M. (2010). Plaque and tangle imaging and cognition in normal aging and Alzheimer's disease. *Neurobiology of Aging, 31*(10), 1669-1678. doi: 10.1016/j.neurobiolaging.2008.09.012

Braskie, M. N., Wilcox, C. E., Landau, S. M., O'Neil, J. P., Baker, S. L., Madison, C. M., Kluth, J. T., & Jagust, W. J. (2008). Relationship of striatal dopamine synthesis capacity to age and cognition. *The Journal of Neuroscience, 28*(52), 14320-14328. doi: 10.1523/JNEUROSCI.3729-08.2008

Brazzelli, M., Cocchini, G., Dellasala, S., & Spinnler, H. (1994). Alzheimer Patients Show a Sensitivity Decrement over Time on a Tonic Alertness Task. *Journal of Clinical and Experimental Neuropsychology, 16*(6), 851-860. doi: 10.1080/01688639408402698

Broadbent, D. E., & Broadbent, M. H. (1987). From detection to identification: Response to multiple targets in rapid serial visual presentation. *Perception and Psychophysics, 42*(2), 105-113. doi: 10.3758/BF03210498

Bugg, J. M., DeLosh, E. L., Davalos, D. B., & Davis, H. P. (2007). Age differences in Stroop interference: Contributions of general slowing and task-specific deficits. *Neuropsychology, Development, and Cognition.Section B, Aging, Neuropsychology and Cognition, 14*(2), 155-167. doi: 10.1080/138255891007065

Chen, Z. G., Li, T. Q., & Hindmarsh, T. (2001). Diffusion tensor trace mapping in normal adult brain using single-shot EPI technique. A methodological study of the aging brain. *Acta Radiologica, 42*(5), 447-458. doi: 10.1080/028418501127347160

Chin, A. L., Negash, S., & Hamilton, R. (2011). Diversity and disparity in dementia: the impact of ethnoracial differences in Alzheimer disease. *Alzheimer Disease and Associated Disorders, 25*(3), 187-195. doi: 10.1097/WAD.0b013e318211c6c9

Chun, M. M., & Potter, M. C. (1995). A two-stage model for multiple target detection in rapid serial visual presentation. *Journal of Experimental Psychology.Human Perception and Performance, 21*(1), 109-127. doi: 10.1037/0096-1523.21.1.109

Cohen, R. A., Sparling-Cohen, Y. A., & O'Donnell, B. F. (1993). *The neuropsychology of attention*. New York: Plenum Press.

Collette, F., Amieva, H., Adam, S., Hogge, M., Van der Linden, M., Fabrigoule, C., & Salmon, E. (2007). Comparison of inhibitory functioning in mild Alzheimer's disease and frontotemporal dementia. *Cortex, 43*(7), 866-874.

Colzato, L. S., Spape, M. M. A., Pannebakker, M. M., & Hommel, B. (2007). Working memory and the attentional blink: Blink size is predicted by individual differences in operation span. *Psychonomic Bulletin & Review, 14*(6), 1051-1057. doi: 10.3758/Bf03193090

Corbetta, M., Miezin, F. M., Shulman, G. L., & Petersen, S. E. (1993). A PET study of visuospatial attention. *The Journal of Neuroscience, 13*(3), 1202-1226.

Corbie-Smith, G., Moody-Ayers, S., & Thrasher, A. D. (2004). Closing the circle between minority inclusion in research and health disparities. *Archives of Internal Medicine, 164*(13), 1362-1364.

Crebolder, J. M., Jolicoeur, P., & McIlwaine, J. D. (2002). Loci of signal probability effects and of the attentional blink bottleneck. *Journal of Experimental Psychology: Human Perception and Performance, 28*(3), 695-716. doi: 10.1037/0096-1523.28.3.695

Cullen, K. M., Halliday, G. M., Double, K. L., Brooks, W. S., Creasey, H., & Broe, G. A. (1997). Cell loss in the nucleus basalis is related to regional cortical atrophy in Alzheimer's disease. *Neuroscience, 78*(3), 641-652. doi: 10.1016/S0306-4522(96)00569-6

Cummings, J. L., & Cole, G. (2002). Alzheimer disease. *JAMA: The Journal of the American Medical Association, 287*(18), 2335-2338. doi: 10.1001/jama.287.18.2335

Davies, P., & Maloney, A. J. (1976). Selective loss of central cholinergic neurons in Alzheimer's disease. *Lancet, 2*(8000), 1403.

De Beni, R., & Palladino, P. (2004). Decline in working memory updating through ageing: Intrusion error analyses. *Memory, 12*(1), 75-89. doi: 10.1080/09658210244000568

Dehaene, S., Sergent, C., & Changeux, J. P. (2003). A neuronal network model linking subjective reports and objective physiological data during conscious perception. *Proceedings of the National Academy of Sciences of the United States of America, 100*(14), 8520-8525. doi: 10.1073/pnas.1332574100

Dell'Acqua, R., Jolicoeur, P., Luria, R., & Pluchino, P. (2009). Reevaluating encoding-capacity limitations as a cause of the attentional blink. *Journal of Experimental Psychology: Human Perception and Performance, 35*(2), 338-351. doi: 10.1037/A0013555

Desimone, R., & Duncan, J. (1995). Neural mechanisms of selective visual attention. *Annual Review of Neuroscience, 18*, 193-222. doi: 10.1146/annurev.ne.18.030195.001205

Di Lollo, V., Kawahara, J., Shahab Ghorashi, S. M., & Enns, J. T. (2005). The attentional blink: Resource depletion or temporary loss of control? *Psychological Research, 69*(3), 191-200. doi: 10.1007/s00426-004-0173-x

Dixon, W. J. (1965). The up-and-down method for small samples. *Journal of the American Statistical Association, 60*, 967-968.

Dixon, W. J., & Mood, A. M. (1948). A method for obtaining and analyzing sensitivity data. *Journal of the American Statistical Association, 43,* 109-126.

Donohue, S. E., Woldorff, M. G., & Mitroff, S. R. (2010). Video game players show more precise multisensory temporal processing abilities. *Attention, Perception & Psychophysics, 72*(4), 1120-1129. doi: 10.3758/APP.72.4.1120

Duncan, J., Ward, R., & Shapiro, K. (1994). Direct measurement of attentional dwell time in human vision. *Nature, 369*(6478), 313-315. doi: 10.1038/369313a0

Dux, P. E., & Marois, R. (2008). Distractor inhibition predicts individual differences in the attentional blink. *PLoS One., 3*(10), e3330. doi: 10.1371/journal.pone.0003330

Dux, P. E., & Marois, R. (2009). The attentional blink: a review of data and theory. *Attentions, Perception& Psychophysics, 71*(8), 1683-1700. doi: 10.3758/APP.71.8.1683

Dye, M. W., Green, C. S., & Bavelier, D. (2009). Increasing Speed of Processing With Action Video Games. *Current Directions in Psychological Science, 18*(6), 321-326. doi: 10.1111/j.1467-8721.2009.01660.

Egeth, H. E., & Yantis, S. (1997). Visual attention: control, representation, and time course. *Annual Review of Psychology, 48*, 269-297. doi: 10.1146/annurev.psych.48.1.269

Fan, J., McCandliss, B. D., Fossella, J., Flombaum, J. I., & Posner, M. I. (2005). The activation of attentional networks. *Neuroimage, 26*(2), 471-479. doi: 10.1016/j.neuroimage.2005.02.004

Fan, J., McCandliss, B. D., Sommer, T., Raz, A., & Posner, M. I. (2002). Testing the efficiency and independence of attentional networks. *Journal of Cognitive Neuroscience, 14*(3), 340-347. doi: 10.1162/089892902317361886

Fan, J., & Posner, M. (2004). Human attentional networks. *Psychiatrische Praxis, 31 Suppl 2,* S210-S214. doi: 10.1055/s-2004-828484

Foldi, N. S., Jutagir, R., Davidoff, D., & Gould, T. (1992). Selective attention skills in Alzheimer's disease: Performance on graded cancellation tests varying in density and complexity. *Journal of Gerontology, 47*(3), 146-153.

Foldi, N. S., Schaefer, L. A., White, R. E., Johnson, R., Jr., Berger, J. T., Carney, M. T., & Macina, L. O. (2005). Effects of graded levels of physical similarity and density on visual selective attention in patients with Alzheimer's disease. *Neuropsychology, 19*(1), 5-17. doi: 10.1037/0894-4105.19.1.5

Foldi, N. S., White, R. E., & Schaefer, L. A. (2005). Detecting effects of donepezil on visual selective attention using signal detection parameters in Alzheimer's disease. *International Journal of Geriatric Psychiatry, 20*(5), 485-488. doi: 10.1002/Gps.1319

Folk, C., Remington, R., & Johnson, J. (1992). Attentional capture by color and onset singletons in search tasks. *Journal of Experimental Psychology: Human Perception and Performance, 18*, 1030-1044.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-Mental State: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189-198.

Gainotti, G., Marra, C., & Villa, G. (2001). A double dissociation between accuracy and time of execution on attentional tasks in Alzheimer's disease and multi-infarct dementia. *Brain, 124*(4), 731-738. doi: 10.1093/brain/124.4.731

Galvao, M. (2011). Underrepresentation of minorities in clinical trials: a current problem with escalating future implications. *Heart Lung, 40*(5), 391-392. doi: 10.1016/j.hrtlng.2011.05.006

Galvin, J. E., Cornblatt, B., Newhouse, P., Ancoli-Israel, S., Wesnes, K., Williamson, D., Zhu, Y., Sorra, K., & Amatniek, J. (2008). Effects of galantamine on measures of attention: results from 2 clinical trials in Alzheimer disease patients with comparisons to donepezil. *Alzheimer Disease and Associated Disorders, 22*(1), 30-38. doi: 10.1097/WAD.0b013e3181630b81

Gao, J. L., Cheung, R. T., Chan, Y. S., Chu, L. W., & Lee, T. M. (2013). Increased prospective memory interference in normal and pathological aging: different roles of motor and verbal processing speed. *Neuropsychology, Development, and Cognition. Section B, Aging, Neuropsychology and Cognition, 20*(1), 80-100. doi: 10.1080/13825585.2012.672948

Gazzaley, A., & D'Esposito, M. (2007). Top-down modulation and normal aging. *Annals of the New York Academy of Sciences, 1097*, 67-83. doi: 10.1196/annals.1379.010

Gazzaley, A., Rissman, J., Cooney, J., Rutman, A., Seibert, T., Clapp, W., & D'Esposito, M. (2007). Functional interactions between prefrontal and visual association cortex contribute to top-down modulation of visual processing. *Cerebral Cortex, 17*, I125-I135. doi: 10.1093/cercor/bhm113

Georgiou-Karistianis, N., Tang, J., Vardy, Y., Sheppard, D., Evans, N., Wilson, M., Gardner, B., Farrow, M., & Bradshaw, J. (2007). Progressive age-related changes in the attentional blink paradigm. *Neuropsychology, Development, and Cognition.Section B, Aging, Neuropsychology and Cognition, 14*(3), 213-226. doi: 10.1080/13825580500320681

Gorus, E., De Raedt, R., Lambert, M., Lemper, J. C., & Mets, T. (2006). Attentional processes discriminate between patients with mild Alzheimer's disease and cognitively healthy elderly. *International Psychogeriatrics, 18*(3), 539-549. doi: 10.1017/S1041610205002723

Greenwood, P. M. (2007). Functional plasticity in cognitive aging: Review and hypothesis. *Neuropsychology, 21*(6), 657-673. doi: 10.1037/0894-4105.21.6.657

Greenwood, P. M., & Parasuraman, R. (1997). Attention in aging and Alzheimer's disease. In J. A. Burack & J. T. Enns (Eds.), *Attention, development and psychopathology* (pp. 289-317). New York: The Guilford Press.

Greenwood, P. M., Parasuraman, R., & Alexander, G. E. (1997). Controlling the focus of spatial attention during visual search: Effects of advanced aging and Alzheimer disease. *Neuropsychology, 11*(1), 3-12.

Greenwood, P. M., Parasuraman, R., & Haxby, J. V. (1993). Changes in visuospatial attention over the adult lifespan. *Neuropsychologia, 31*(5), 471-485.

Gron, G., Brandenburg, I., Wunderlich, A. P., & Riepe, M. W. (2006). Inhibition of hippocampal function in mild cognitive impairment: Targeting the cholinergic hypothesis. *Neurobiology of Aging, 27*(1), 78-87. doi: 10.1016/j.neurobiolaging.2004.12.005

Gu, Q. (2002). Neuromodulatory transmitter systems in the cortex and their role in cortical plasticity. *Neuroscience, 111*(4), 815-835. doi: 10.1016/S0306-4522(02)00026-X

Gunning-Dixon, F. M., Head, D., McQuain, J., Acker, J. D., & Raz, N. (1998). Differential aging of the human striatum: A prospective MR imaging study. *American Journal of Neuroradiology, 19*(8), 1501-1507.

Gunning-Dixon, F. M., & Raz, N. (2000). The cognitive correlates of white matter abnormalities in normal aging: A quantitative review. *Neuropsychology, 14*(2), 224-232.

Guttmann, C. R., Jolesz, F. A., Kikinis, R., Killiany, R. J., Moss, M. B., Sandor, T., & Albert, M. S. (1998). White matter changes with normal aging. *Neurology, 50*(4), 972-978.

Harasty, J. A., Halliday, G. M., Xuereb, J., Croot, K., Bennett, H., & Hodges, J. R. (2001). Cortical degeneration associated with phonologic and semantic language impairments in AD. *Neurology, 56*(7), 944-950.

Hari, R., Valta, M., & Uutela, K. (1999). Prolonged attentional dwell time in dyslexic adults. *Neuroscience Letters, 271*(3), 202-204.

Hartley, A. A., & Little, D. M. (1999). Age-related differences and similarities in dual-task interference. *Journal of Experimental Psychology.General, 128*(4), 416-449.

Hasher, L., Stoltzfus, E. R., Zacks, R. T., & Rypma, B. (1991). Age and inhibition. *Journal of Experimental Psychology.Learning, Memory, and Cognition, 17*(1), 163-169.

Hedden, T., & Gabrieli, J. D. E. (2004). Insights into the ageing mind: A view from cognitive neuroscience. *Nature Reviews Neuroscience, 5*(2), 87-U12. doi: 10.1038/Nrn1323

Himmelheber, A. M., Sarter, M., & Bruno, J. P. (2000). Increases in cortical acetylcholine release during sustained attention performance in rats. *Brain Research.Cognitive Brain Research, 9*(3), 313-325.

Hommel, B., & Akyurek, E. G. (2005). Lag-1 sparing in the attentional blink: Benefits and costs of integrating two events into a single episode. *Quarterly Journal of Experimental Psychology.Section A: Human Experimental Psychology, 58*(8), 1415-1433. doi: 10.1080/02724980443000647

Jack, C. R., Jr., Albert, M. S., Knopman, D. S., McKhann, G. M., Sperling, R. A., Carrillo, M. C., Thies, B., & Phelps, C. H. (2011). Introduction to the recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia, 7*(3), 257-262. doi: 10.1016/j.jalz.2011.03.004

James, W. (1890). *Principles of psychology*. New York: Holt.

Jennings, J. M., Dagenbach, D., Engle, C. M., & Funke, L. J. (2007). Age-related changes and the attention network task: An examination of alerting, orienting, and executive function. *Neuropsychology, Development, and Cognition.Section B, Aging, Neuropsychology and Cognition, 14*(4), 353-369. doi: 10.1080/13825580600788837

Jicha, G. A., Parisi, J. E., Dickson, D. W., Johnson, K., Cha, R., Ivnik, R. J., Tangalos, E. G., Boeve, B. F., Knopman, D. S., Braak, H., & Petersen, R. C. (2006). Neuropathologic outcome of mild cognitive impairment following progression to clinical dementia. *Archives of Neurology, 63*(5), 674-681. doi: 10.1001/archneur.63.5.674

Johannsen, P., Jakobsen, J., Bruhn, P., & Gjedde, A. (1999). Cortical responses to sustained and divided attention in Alzheimer's disease. *Neuroimage, 10*(3 Pt 1), 269-281. doi: 10.1006/nimg.1999.0475

Jolicoeur, P. (1998). Modulation of the attentional blink by on-line response selection: Evidence from speeded and unspeeded task1 decisions. *Memory and Cognition, 26*(5), 1014-1032.

Jolicoeur, P., & Dell'Acqua, R. (1998). The demonstration of short-term consolidation. *Cogn Psychol, 36*(2), 138-202. doi: 10.1006/cogp.1998.0684

Kandel, E. R., Schwartz, J. H., & Jessell, T. M. (2000). *Principal of neural science* (Vol. 4th). New York: McGraw-Hill.

Kaplan, L. (2011). *The relationship among attention, daily behavior and disease severity in patients with Alzheimer's disease.* (Ph.D. Dissertation), City University of New York, Ann Arbor. Retrieved from http://eresources.library.mssm.edu:2048/login?url=http://eresources.library.mssm.edu:9738/docview/857080113?accountid=41157 Available from ProQuest Dissertations & Theses Full Text (3443938)

Kastner, S., & Ungerleider, L. G. (2000). Mechanisms of visual attention in the human cortex. *Annual Review of Neuroscience, 23,* 315-341. doi: 10.1146/annurev.neuro.23.1.315

Kavcic, V., & Duffy, C. J. (2003). Attentional dynamics and visual perception: mechanisms of spatial disorientation in Alzheimer's disease. *Brain, 126*(Pt 5), 1173-1181.

Kawahara, J. I., Kumada, T., & Di Lollo, V. (2006). The attentional blink is governed by a temporary loss of control. *Psychonomic Bulletin & Review, 13*(5), 886-890. doi: 10.3758/Bf03194014

Killiany, R. J., Hyman, B. T., Gomez-Isla, T., Moss, M. B., Kikinis, R., Jolesz, F., Tanzi, R., Jones, K., & Albert, M. S. (2002). MRI measures of entorhinal cortex vs hippocampus in preclinical AD. *Neurology, 58*(8), 1188-1196.

Kranczioch, C., Debener, S., Schwarzbach, J., Goebel, R., & Engel, A. K. (2005). Neural correlates of conscious perception in the attentional blink. *Neuroimage, 24*(3), 704-714. doi: 10.1016/j.neuroimage.2004.09.024

Krishnan, L., Kang, A., Sperling, G., & Srinivasan, R. (2013). Neural strategies for selective attention distinguish fast-action video game players. *Brain Topography, 26*(1), 83-97. doi: 10.1007/s10548-012-0232-3

Lahar, C. J., Isaak, M. I., & McArthur, A. D. (2001). Age difference in the magnitude of the attentional blink. *Aging Neuropsychology and Cognition, 8*(2), 149-159.

Lamar, M., & Resnick, S. M. (2004). Aging and prefrontal functions: dissociating orbitofrontal and dorsolateral abilities. *Neurobiology of Aging, 25*(4), 553-558. doi: 10.1016/j.neurobiolaging.2003.06.005

Levitt, T., Fugelsang, J., & Crossley, M. (2006). Processing speed, attentional capacity, and age-related memory change. *Experimental Aging Research, 32*(3), 263-295. doi: 10.1080/03610730600699118

Lim, H. K., Juh, R., Pae, C. U., Lee, B. T., Yoo, S. S., Ryu, S. H., Kwak, K. R., Lee, C., & Lee, C. U. (2008). Altered verbal working memory process in patients with Alzheimer's disease: an fMRI investigation. *Neuropsychobiology, 57*(4), 181-187. doi: 10.1159/000147471

Livney, M. G., Clark, C. M., Karlawish, J. H., Cartmell, S., Negron, M., Nunez, J., Xie, S. X., Entenza-Cabrera, F., Vega, I. E., & Arnold, S. E. (2011). Ethnoracial differences in the clinical characteristics of Alzheimer's disease at initial presentation at an urban Alzheimer's disease center. *The American Journal of Geriatric Psychiatry: Official Journal of the American Association for Geriatric Psychiatry, 19*(5), 430-439. doi: 10.1097/JGP.0b013e3181f7d881

Maciokas, J. B., & Crognale, M. A. (2003). Cognitive and attentional changes with age: Evidence from attentional blink deficits. *Experimental Aging Research, 29*(2), 137-153. doi: 10.1080/03610730303715

Madden, D. (2007). Aging and visual attention. *Current Directions in Psychological Science, 16*(2), 70-74. doi: 10.1111/j.1467-8721.2007.00478.x

Madden, D., & Langley, L. (2003). Age-related changes in selective attention and perceptual load during visual search. *Psychology and Aging, 18*(1), 54-67.

Madden, D., Turkington, T., Provenzale, J., Hawk, T., Hoffman, J., & Coleman, R. (1997). Selective and divided visual attention: Age-related changes in regional cerebral blood flow measured by H215O PET. *Human Brain Mapping, 5*(6), 389-409.

Marcantoni, W. S., Lepage, M., Beaudoin, G., Bourgouin, P., & Richer, F. (2003). Neural correlates of dual task interference in rapid visual streams: an fMRI study. *Brain and Cognition, 53*(2), 318-321.

Marois, R., Chun, M. M., & Gore, J. (2000). Neural correlates of the attentional blink. *Neuron, 28*(1), 299-308.

Martens, S., & Johnson, A. (2005). Timing attention: cuing target onset interval attenuates the attentional blink. *Memory & Cognition, 33*(2), 234-240.

Mattis, S. (2005). *Dementia Rating Scale-2*. Lutz, FL: Psychological Assessment Resources, Inc.

McCourt, M. E., & Olafson, C. (1997). Cognitive and perceptual influences on visual line bisection: psychophysical and chronometric analyses of pseudoneglect. *Neuropsychologia, 35*(3), 369-380.

McDowd, J. M., & Oseas-Kreger, D. M. (1991). Aging, inhibitory processes, and negative priming. *Journal of Gerontology, 46*(6), 340-345.

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology, 34*(7), 939-944.

Mendez, M., & Cummings, J. (2003). Alzheimer's disease. In M. Mendez & J. Cummings (Eds.), *Dementia: A clinical approach* (Vol. 3rd, pp. 67-119). Philadelphia: Elsevier.

Monsch, A. U., Foldi, N. S., Ermini-Funfschilling, D. E., Berres, M., Taylor, K. I., Seifritz, E., Stahelin, H. B., & Spiegel, R. (1995). Improving the diagnostic accuracy of the Mini-Mental State Examination. *Acta Neurologica Scandinavica, 92*(2), 145-150.

Mufson, E. J., Ginsberg, S. D., Ikonomovic, M. D., & Dekosky, S. T. (2003). Human cholinergic basal forebrain: chemoanatomy and neurologic dysfunction. *Journal of Chemical Neuroanatomy, 26*(4), 233-242.

Nebes, R. D., & Brady, C. B. (1993). Phasic and tonic alertness in Alzheimer's disease. *Cortex, 29*(1), 77-90.

Nestor, P. G., Parasuraman, R., Haxby, J. V., & Grady, C. L. (1991). Divided attention and metabolic brain dysfunction in mild dementia of the Alzheimer's type. *Neuropsychologia, 29*(5), 379-387.

Nieuwenstein, M. R. (2006). Top-down controlled, delayed selection in the attentional blink. *Journal of Experimental Psychology. Human Perception and Performance, 32*(4), 973-985. doi: 10.1037/0096-1523.32.4.973

Nieuwenstein, M. R., Chun, M. M., van der Lubbe, R. H. J., & Hooge, I. T. C. (2005). Delayed attentional engagement in the attentional blink. *Journal of Experimental Psychology: Human Perception and Performance, 31*(6), 1463-1475. doi: 10.1037/0096-1523.31.6.1463

Okonkwo, O. C., Wadley, V. G., Ball, K., Vance, D. E., & Crowe, M. (2008). Dissociations in Visual Attention Deficits among Persons with Mild Cognitive Impairment. *Aging, Neuropsychology, and Cognition, 15*(4), 492-505. doi: 10.1080/13825580701844414

Olivers, C. N., & Meeter, M. (2008). A boost and bounce theory of temporal attention. *Psychol Rev, 115*(4), 836-863. doi: 2008-14936-012 [pii]10.1037/a0013395

Parasuraman, R., Greenwood, P. M., Haxby, J. V., & Grady, C. L. (1992). Visuospatial attention in dementia of the Alzheimer type. *Brain, 115 (Pt 3),* 711-733.

Park, D. C., Lautenschlager, G., Hedden, T., Davidson, N. S., Smith, A. D., & Smith, P. K. (2002). Models of visuospatial and verbal memory across the adult life span. *Psychology and Aging, 17*(2), 299-320.

Pashler, H. (1994). Dual-task interference in simple tasks: Data and theory. *Psychological Bulletin, 116*(2), 220-244.

Pashler, H. E. (1998). *The psychology of attention*. Cambridge, MA: MIT Press.

Passetti, F., Dalley, J. W., O'Connell, M. T., Everitt, B. J., & Robbins, T. W. (2000). Increased acetylcholine release in the rat medial prefrontal cortex during performance of a visual attentional task. *European Journal of Neuroscience, 12*(8), 3051-3058.

Perry, R. J., & Hodges, J. R. (1999). Attention and executive deficits in Alzheimer's disease. A critical review. *Brain, 122 (Pt 3)*, 383-404.

Perry, R. J., & Hodges, J. R. (2003). Dissociation between top-down attentional control and the time course of visual attention as measured by attentional dwell time in patients with mild cognitive impairment. *European Journal of Neuroscience, 18*(2), 221-226. doi: 10.1046/j.1460-9568.2003.02754.x

Perry, R. J., Watson, P., & Hodges, J. R. (2000). The nature and staging of attention dysfunction in early (minimal and mild) Alzheimer's disease: Relationship to episodic and semantic memory impairment. *Neuropsychologia, 38*(3), 252-271.

Pesce, C., Guidetti, L., Baldari, C., Tessitore, A., & Capranica, L. (2005). Effects of aging on visual attentional focusing. *Gerontology, 51*(4), 266-276. doi: 10.1159/000085123

Peters, F., Ergis, A. M., Gauthier, S., Dieudonne, B., Verny, M., Jolicoeur, P., & Belleville, S. (2012). Abnormal temporal dynamics of visual attention in Alzheimer's disease and in dementia with Lewy bodies. *Neurobiology of Aging, 33*(5), 1012 e1011-1010. doi: 10.1016/j.neurobiolaging.2011.10.019

Petersen, R. C., & Negash, S. (2007). Mild cognitive impairment: An overview. *CNS Spectrums, 45*, 53.

Petersen, R. C., Stevens, J. C., Ganguli, M., Tangalos, E. G., Cummings, J. L., & Dekosky, S. T. (2001). Practice parameter: Early detection of dementia: Mild cognitive impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology, 56*(9), 1133-1142.

Porter, G., Leonards, U., Wilcock, G., Haworth, J., Troscianko, T., & Tales, A. (2010). New insights into feature and conjunction search: II. Evidence from Alzheimer's disease. *Cortex, 46*(5), 637-649. doi: 10.1016/j.cortex.2009.04.014

Posner, M. I. (1980). Orienting of attention. *Quarterly Journal of Experimental Psychology, 32*(1), 3-25.

Posner, M. I. (1987). Cognitive neuropsychology and the problem of selective attention. *Electroencephalography and Clinical Neurophysiology.Supplement, 39*, 313-316.

Posner, M. I., & Petersen, S. E. (1990). The attention system of the human brain. *Annual Reviews: Neuroscience, 13*, 25-42. doi: 10.1146/annurev.ne.13.030190.000325

Posner, M. I., Walker, J. A., Friedrich, F. A., & Rafal, R. D. (1987). How do the parietal lobes direct covert attention? *Neuropsychologia, 25*(1A), 135-145.

Potter, M. (1993). Very short-term conceptual memory. *Memory and Cognition, 21*(2), 156-161. doi: 10.3758/Bf03202727

Potter, M., Chun, M., Banks, B., & Muckenhoupt, M. (1998). Two attentional deficits in serial target search: The visual attentional blink and an amondal task-switch deficit. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 25*, 979-992.

Price, J. L., Ko, A. I., Wade, M. J., Tsou, S. K., McKeel, D. W., & Morris, J. C. (2001). Neuron number in the entorhinal cortex and CA1 in preclinical Alzheimer disease. *Archives of Neurology, 58*(9), 1395-1402.

Rabbitt, P. (1979). How old and young subjects monitor and control responses for accuracy and speed. *British Journal of Psychology, 70*(2), 305-311.

Rabinowitz, Y. G., & Gallagher-Thompson, D. (2010). Recruitment and retention of ethnic minority elders into clinical research. *Alzheimer Disease and Associated Disorders, 24 Suppl*, S35-41.

Raymond, J. E., Shapiro, K. L., & Arnell, K. M. (1992). Temporary suppression of visual processing in an RSVP task: An attentional blink? *Journal of Experimental Psychology.Human Perception and Performance, 18*(3), 849-860.

Raz, N., Gunning-Dixon, F., Head, D., Rodrigue, K. M., Williamson, A., & Acker, J. D. (2004). Aging, sexual dimorphism, and hemispheric asymmetry of the cerebral cortex: Replicability of regional differences in volume. *Neurobiology of Aging, 25*(3), 377-396. doi: 10.1016/S0197-4580(03)00118-0

Raz, N., Lindenberger, U., Rodrigue, K. M., Kennedy, K. M., Head, D., Williamson, A., Dahle, C., Gerstorf, D., & Acker, J. D. (2005). Regional brain changes in aging healthy adults: General trends, individual differences and modifiers. *Cerebral Cortex, 15*(11), 1676-1689. doi: 10.1093/cercor/bhi044

Resnick, S. M., Pham, D. L., Kraut, M. A., Zonderman, A. B., & Davatzikos, C. (2003). Longitudinal magnetic resonance imaging studies of older adults: A shrinking brain. *The Journal of Neuroscience, 23*(8), 3295-3301.

Rissman, J., Gazzaley, A., & D'Esposito, M. (2009). The effect of non-visual working memory load on top-down modulation of visual processing. *Neuropsychologia, 47*(7), 1637-1646. doi: 10.1016/j.neuropsychologia.2009.01.036

Salat, D. H., Kaye, J. A., & Janowsky, J. S. (2001). Selective preservation and degeneration within the prefrontal cortex in aging and Alzheimer disease. *Archives of Neurology, 58*(9), 1403-1408. doi: 10.1001/archneur.58.9.1403

Salmon, D. P., Thomas, R. G., Pay, M. M., Booth, A., Hofstetter, C. R., Thal, L. J., & Katzman, R. (2002). Alzheimer's disease can be accurately diagnosed in very mildly impaired individuals. *Neurology, 59*(7), 1022-1028.

Salthouse, T. A. (1994). The aging of working memory. *Neuropsychology, 8*(4), 535-543.

Salthouse, T. A. (1996). The processing-speed theory of adult age differences in cognition. *Psychological Review, 103*(3), 403-428.

Salthouse, T. A. (2009). When does age-related cognitive decline begin? *Neurobiology of Aging, 30*(4), 507-514. doi: 10.1016/j.neurobiolaging.2008.09.023

Sarter, M., Hasselmo, M. E., Bruno, J. P., & Givens, B. (2005). Unraveling the attentional functions of cortical cholinergic inputs: interactions between signal-driven and cognitive modulation of signal detection. *Brain Research Reviews, 48*(1), 98-111. doi: 10.1016/j.brainresrev.2004.08.006

Schaie, K. W. (1993). The Seattle Longitudinal Study: A thirty-five-year inquiry of adult intellectual development. *Zeitschrift für Gerontologie, 26*(3), 129-137.

Schialfa, C. T., Esau, S. P., & Joffe, K. M. (1998). Age, target-distractor similarity, and visual search. *Experimental Aging Research, 24*(4), 337-358.

Sebastian, M. V., Menor, J., & Elosua, M. R. (2006). Attentional dysfunction of the central executive in AD: evidence from dual task and perseveration errors. *Cortex, 42*(7), 1015-1020. doi: 10.1016/S0010-9452(08)70207-7

Sessa, P., Luria, R., Verleger, R., & Dell'Acqua, R. (2007). P3 latency shifts in the attentional blink: Further evidence for second target processing postponement. *Brain Research, 1137*, 131-139. doi: DOI: 10.1016/j.brainres.2006.12.066

Shapiro, K. L., Raymond, J. E., & Arnell, K. M. (1994). Attention to visual pattern information produces the attentional blink in rapid serial visual presentation. *Journal of Experimental Psychology: Human Perception and Performance, 20*(2), 357-371. doi: 10.1037/0096-1523.20.2.357

Shen, D., & Alain, C. (2012). Implicit temporal expectation attenuates auditory attentional blink. *PLoS One, 7*(4), e36031. doi: 10.1371/journal.pone.0036031

Sood, J. R., & Stahl, S. M. (2011). Community engagement and the resource centers for minority aging research. *The Gerontologist, 51*(Suppl 1), S5-7. doi: 10.1093/geront/gnr036

Suavansri, K., Falchook, A. D., Williamson, J. B., & Heilman, K. M. (2012). Right up there: hemispatial and hand asymmetries of altitudinal pseudoneglect. *Brain and Cognition, 79*(3), 216-220. doi: 10.1016/j.bandc.2012.03.003

Takashima, A. (2009). Amyloid-beta, tau, and dementia. *Journal of Alzheimer's Disease, 17*(4), 729-736. doi: 10.3233/JAD-2009-1090

Telford, C. W. (1931). The refractory phase of voluntary and associative responses. *Journal of Experimental Psychology, 14*(1), 1-36.

Theeuwes, J., Godijn, R., & Pratt, J. (2004). A new estimation of the duration of attentional dwell time. *Psychonomic Bulletin and Review, 11*(1), 60-64. doi: 10.3758/BF03206461

Tisserand, D. J., Pruessner, J. C., Sanz Arigita, E. J., van Boxtel, M. P., Evans, A. C., Jolles, J., & Uylings, H. B. (2002). Regional frontal cortical volumes decrease differentially in aging: An MRI study to compare volumetric approaches and voxel-based morphometry. *Neuroimage, 17*(2), 657-669. doi: 10.1006/nimg.2002.1173

Uttl, B. (2002). North American Adult Reading Test: Age norms, reliability, and validity. *Journal of Clinical Psychology, 24*(8), 1123-1137.

Vellas, B., Cunha, L., Gertz, H. J., De Deyn, P. P., Wesnes, K., Hammond, G., & Schwalen, S. (2005). Early onset effects of galantamine treatment on attention in patients with Alzheimer's disease. *Current Medical Research and Opinion, 21*(9), 1423-1429. doi: 10.1185/030079905X61884

Verhaeghen, P., Steitz, D. W., Sliwinski, M. J., & Cerella, J. (2003). Aging and dual-task performance: A meta-analysis. *Psychology and Aging, 18*(3), 443-460. doi: 10.1037/0882-7974.18.3.443

Visser, T. A. (2007). Masking T1 difficulty: processing time and the atenional blink. *Journal of Experumental Psychology: Human Perception and Performance, 33*(2), 285-297. doi: 10.1037/0096-1523.33.2.285

Visser, T. A., Davis, C., & Ohan, J. L. (2009). When similarity leads to sparing: probing mechanisms underlying the attentional blink. *Psychological Research, 73*(3), 327-335. doi: 10.1007/s00426-008-0155-5

Visser, T. A. W., Bischof, W. F., & Di Lollo, V. (1999). Attentional switching in spatial and nonspatial domains: Evidence from the attentional blink. *Psychological Bulletin, 125*(4), 458-469. doi: 10.1037//0033-2909.125.4.458

Volkow, N. D., Ding, Y. S., Fowler, J. S., Wang, G. J., Logan, J., Gatley, S. J., Hitzemann, R., Smith, G., Fields, S. D., & Gur, R. (1996). Dopamine transporters decrease with age. *Journal of Nuclear Medicine, 37*(4), 554-559.

Volkow, N. D., Fowler, J. S., Wang, G. J., Logan, J., Schlyer, D., MacGregor, R., Hitzemann, R., & Wolf, A. P. (1994). Decreased dopamine transporters with age in health human subjects. *Annals of Neurology, 36*(2), 237-239. doi: 10.1002/ana.410360218

Volkow, N. D., Gur, R. C., Wang, G. J., Fowler, J. S., Moberg, P. J., Ding, Y. S., Hitzemann, R., Smith, G., & Logan, J. (1998). Association between decline in brain dopamine activity with age and cognitive and motor impairment in healthy individuals. *American Journal of Psychiatry, 155*(3), 344-349.

Wang, G. J., Volkow, N. D., Logan, J., Fowler, J. S., Schlyer, D., MacGregor, R. R., Hitzemann, R. J., Gur, R. C., & Wolf, A. P. (1995). Evaluation of age-related changes in serotonin 5-HT2 and dopamine D2 receptor availability in healthy human subjects. *Life Sciences, 56*(14), L249-L253. doi: 10.1016/0024-3205(95)00066-F

Warkentin, S., Erikson, C., & Janciauskiene, S. (2008). rCBF pathology in Alzheimer's disease is associated with slow processing speed. *Neuropsychologia, 46*(5), 1193-1200. doi: 10.1016/j.neuropsychologia.2007.08.029

Wecker, N. S., Kramer, J. H., Wisniewski, A., Delis, D. C., & Kaplan, E. (2000). Age effects on executive ability. *Neuropsychology, 14*(3), 409-414. doi: 10.1037/0894-4105.14.3.409

Welford, A. T. (1952). The 'psychological refractory period' and the timing of high-speed performance: A review and a theory. *The British Journal of Psychology, 44*, 2-19.

West, R. (1996). An application of prefrontal cortex function theory to cognitive aging. *Psychological Bulletin, 120*(2), 272-292. doi: 10.1037/0033-2909.120.2.272

Wetherill, G. B., & Leviltt, H. (1965). Sequential estimation of points on a psychometric function. *British Journal of Mathematical and Statistical Psychology, 18*, 1-10.

Whitehouse, P. J., Price, D. L., Struble, R. G., Clark, A. W., Coyle, J. T., & Delon, M. R. (1982). Alzheimer's disease and senile dementia: loss of neurons in the basal forebrain. *Science, 215*(4537), 1237-1239. doi: 10.1126/science.7058341

Whiting, W. L., Madden, D. J., & Babcock, K. J. (2007). Overriding age differences in attentional capture with top-down processing. *Psychology and Aging, 22*(2), 223-232. doi: 10.1037/0882-7974.22.2.223

Whitwell, J. L., Petersen, R. C., Negash, S., Weigand, S. D., Kantarci, K., Ivnik, R. J., Knopman, D. S., Boeve, B. F., Smith, G. E., & Jack, C. R., Jr. (2007). Patterns of atrophy differ among specific subtypes of mild cognitive impairment. *Archives of Neurology, 64*(8), 1130-1138. doi: 10.1001/archneur.64.8.1130

Whitwell, J. L., Shiung, M. M., Przybelski, S. A., Weigand, S. D., Knopman, D. S., Boeve, B. F., Petersen, R. C., & Jack, C. R., Jr. (2008). MRI patterns of atrophy associated with progression to AD in amnestic mild cognitive impairment. *Neurology, 70*(7), 512-520. doi: 10.1212/01.wnl.0000280575.77437.a2

Wolfe, J. M. (1998). Visual search. In H. Pashler (Ed.), *Attention* (pp. 13-73). Hove England: Psychology Press/Erlbaum (UK) Taylor & Francis.

Wong, K. F. E. (2002). The relationship between attentional blink and psychological refractory period. *Journal of Experimental Psychology: Human Perception and Performance, 28*(1), 54-71. doi: 10.1037//0096-1523.28.1.54

Wyble, B., Bowman, H., & Nieuwenstein, M. (2009). The attentional blink provides episodic distinctiveness: sparing at a cost. *Journal of Experimental Psychology: Human Perception and Performance, 35*(3), 787-807. doi: 10.1037/a0013902

Zelinski, E. M., & Burnight, K. P. (1997). Sixteen-year longitudinal and time lag changes in memory and cognition in older adults. *Psychology and Aging, 12*(3), 503-513. doi: 10.1037/0882-7974.12.3.503

Zhang, D., Shao, L., Nieuwenstein, M., & Zhou, X. (2008). Top-down control is not lost in the attentional blink: Evidence from intact endogenous cueing. *Experimental Brain Research, 185*(2), 287-295. doi: 10.1007/s00221-007-1153-3