

Working Memory Deficits in Alzheimer's Disease

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ABSTRACT

Alzheimer's disease (AD) is a neurodegenerative disorder in which patients demonstrate cognitive deficits, especially deficiencies in long-term memory. However, working memory (WM) impairments can also be observed in Alzheimer's disease, yet they are not as clearly defined as other long-term memory deficits. Here, neuropsychological evidence regarding WM deficits in patients with AD is evaluated, utilizing the WM model proposed by Baddeley and Hitch. Impairments in the central executive component have been the most documented early WM impairments seen among AD patients. The phonological loop seems to remain intact in earlier stages of the disorder but impairments in the ability to temporarily maintain and internally rehearse verbal information progress with disease severity. Deficits in the visuospatial sketchpad have been observed among patients with AD, although more research is needed for further distinction of visual and spatial processing impairments. Finally, the inability to strategically organize and integrate multimodal information is characteristic of impairments associated with the episodic buffer in AD patients. Overall, this review demonstrates that WM deficits in AD differ depending on disease severity, making WM performance a potentially valuable clinical marker. By defining the WM deficits associated with AD, clinical distinctions are able to be made between AD and other memory-related disorders, which may allow for more comprehensive treatment plans and coping strategies for patients.

1 INTRODUCTION

Memory impairment is the most predominant cognitive deficit associated with Alzheimer's disease (AD). Patients with AD often experience a decline in episodic long-term memory performance at the earliest stages of the disease and further degeneration as the disease progresses (for a review see Huntley & Howard, 2010). However, AD patients do not only show impairments in the formation and storage of long-term memories, as deficits in working memory have also been observed (Collette et al., 1999). Working memory refers to the short-term storage and manipulation of information necessary for certain cognitive tasks (Baddeley, 1992). Everyday tasks such as the ability to comprehend speech, learn new information, and reason, all rely on working memory (Baddeley, 1992).

According to the model proposed by Baddeley & Hitch (1974), working memory can be further subdivided into three components: the central executive, phonological loop, and the visuospatial sketchpad. The central executive component of working memory operates as the attentional control unit and facilitates manipulation and control of information within working memory (Baddeley et al., 1991; Baddeley, 2000). The remaining components are subsidiary systems; the phonological loop maintains verbal information while the visuospatial sketchpad maintains visual and spatial information. Since the proposal of the 1974 model, a fourth component of the model, the episodic buffer, has been proposed, which serves as the binding element between episodic long-term memory and working memory (Baddeley, 2000). Although heterogeneity exists

among patients with AD, these individuals often demonstrate similar impairments on tasks assessing these subsystems of working memory.

The present paper will utilize the Baddeley and Hitch model of working memory (Baddeley, 2000) to discuss WM and executive control impairments observed in patients with Alzheimer's disease. Prior research has found impairments on a variety of tasks assessing attentional control in AD patients compared to young and elderly controls (e.g., Belleville, Chertkow, & Gauthier, 2007; Stopford et al., 2012), however, deficits in other components within the model are not yet clearly understood, as discrepancies are present in the literature. Impairments within these systems of working memory have also been observed during different stages of AD. Thus, recognizing when deficits occur may aid in early diagnosis. It is also important to identify the impairments associated with AD in particular, as this may provide distinctive markers to differentiate AD from other memory-related disorders.

2 THE CENTRAL EXECUTIVE

The central executive component of working memory is involved in performing executive functions such as focusing and inhibiting attention, sequential planning, switching and dividing attention, and monitoring and updating information that is held in mind (Baddeley, 1996). It serves as the attentional control unit and assists in the coordination of the subsidiary systems of the Baddeley and Hitch model (for a review see Huntley & Howard, 2010; Baddeley, 1996). Working memory impairments observed in patients with AD are typically associated with attentional issues controlled by the central executive component (Stopford et al., 2012). Tasks that have previously been used to assess central executive functioning include alphabet span tasks, Brown-Peterson paradigms, divided attention tasks, and the N-back task (for a review see Huntley & Howard, 2010; Collette et al., 1999; Belleville, Chertkow, & Gauthier, 2007).

Collette et al. (1999) examined central executive functioning in AD patients measuring performance on an α -span task and a dual-task paradigm. The α -span task first consisted of a typical word-span procedure but later required participants to recall information in serial order or in alphabetical order. Compared to elderly control participants, AD patients exhibited similar performance in serial recall but demonstrated greater impairment in alphabetical recall. Significant deficits observed in the alphabetical recall condition may be a result of the necessary utilization of multiple executive functions in this task, such as inhibiting the tendency to recall in serial order as well as updating WM and monitoring performance to ensure the correct sequencing of items (Collette et al., 1999). Utilization of executive functions for the α -span task differ from those required for the dual-task paradigm (Collette et al., 1999). Within the dual-task paradigm, participants viewed a trail of boxes on a piece of paper and were also read aloud various digit sequences. Participants were required to verbally repeat the digit sequences given while simultaneously responding to the boxes as quickly as possible by using a pencil to mark a cross on each in the trail. These

tasks assessed the ability to switch attention and coordinate verbal and motor systems. Compared to healthy controls, AD patients demonstrated a greater decrease in performance from the single to the dual-task condition, and overall performance for the dual-task paradigm was poorer for AD patients than control participants.

Similarly, Belleville, Chertkow, & Gauthier (2007) found severe impairments on tasks requiring attentional control in AD patients. An analogous design assessed participants with alphabetical recall and a dual-task paradigm. Patients with AD performed significantly worse in the alphabetical recall condition compared to the serial recall condition. To assess dual-task abilities, an adapted Brown-Peterson paradigm was utilized in which participants encoded consonants auditorily, followed by a delay in which a series of numbers were presented orally, prompting participants to provide the next number in the series by adding one to the last number given. Verbal memory was tested after the delay. Findings indicated that AD patients recalled fewer items, regardless of the amount of delay time, compared to control participants. Belleville, Chertkow, & Gauthier (2007) also utilized an adaptation of the Hayling task to examine inhibition abilities. This task consisted of an automatic condition, where participants produced a word that best completed a sentence read aloud, and an inhibition condition, in which participants completed the sentences presented with an entirely unrelated word. Patients with mild cognitive impairment (MCI), a preclinical stage of AD, and healthy control participants performed equally well on this task. However, patients with mild AD demonstrated significant impairments in the inhibition abilities required to generate an unrelated word.

Deficits in attentional abilities and executive functions seem to be apparent in the early stages of AD, and dual-task impairments have been recognized as a marker for the disorder (Belleville et al., 2007). Yet, several studies found no significant difference between minimal AD/MCI and control participants on divided attention paradigms (for a review see Huntley & Howard, 2010). Therefore, conflicting reports in how early these impairments occur in AD pose difficulties in detection and intervention during preclinical stages.

3 THE PHONOLOGICAL LOOP

The phonological loop assists with the maintenance of verbal information within working memory. It has been proposed to contain two subcomponents: the phonological short-term store (PSS) and articulatory rehearsal mechanism (ARM) (for a review see Huntley & Howard, 2010; Baddeley, 2000). The PSS serves as a storage unit for verbal information which fades after a few seconds. Evidence for this functional component can be characterized by the phonological similarity effect (PSE) in which memory span is greater when presented with words that are phonologically dissimilar rather than phonologically similar (for a review see Huntley & Howard, 2010; Baddeley, 2000). The ARM refers to internalized repetition of verbal information required for maintenance and is characterized by subvocal refreshing. Evidence for subvocal rehearsal has been demonstrated by the word length effect (WLE), characterized by a greater word span for shorter words compared to longer words (Baddeley, 2000). However, the ARM may be repressed by attentionally demanding synchronous articulation, known as articulatory suppression (AS), that interferes with subvocal rehearsal, such as mouthing an irrelevant word

simultaneously during the encoding of new information (for a review see Huntley & Howard, 2010). The PSE, WLE, and AS have been used in prior studies to assess deficits of the phonological loop among patients with AD.

Collette et al. (1999) also assessed phonological loop impairments among AD patients, examining PSE and WLE performance. PSE was assessed by comparing span level for phonologically similar and dissimilar words. This study used a constant-length span procedure to assess PSE, adapted from Belleville, Peretz, & Malenfant (1996). The two subcomponents of the phonological loop were further assessed with a non-word repetition task (utilized to assess the PSS and the WLE), while articulation rate assessed the ARM component of the phonological loop. When disease severity was accounted for, only AD patients with low span performance exhibited phonological loop deficits, while AD patients with a higher span typically did not demonstrate phonological loop impairments. Peters et al. (2007) also assessed phonological loop functioning in AD patients utilizing the PSE and WLE. AD patients exhibited similar PSE and WLE to that of control participants, however, AD patients recalled fewer words overall in comparison to young and elderly control participants. Therefore, studies suggest verbal WM deficits vary among AD patient types.

Discrepancies in impairments observed within the literature suggest phonological loop deficits may not occur within early stages of the disease as some AD patients exhibited similar PSE and WLE as control participants (Peters et al., 2007). This provides greater clinical distinction between patient populations diagnosed with AD, as evidence suggests deficiencies in the phonological loop are observed in more severe cases.

4 THE VISUOSPATIAL SKETCHPAD

The visuospatial sketchpad component of the Baddeley and Hitch WM model is devoted to visual imagery and spatial processing (for a review see Huntley & Howard, 2010). It serves as a temporary mental workspace for incoming visual and spatial information, which can then be maintained and manipulated within working memory. Tasks typically used to assess visuospatial functioning include a visual patterns task (Della Sala et al., 1999; MacPherson et al., 2007) and the Corsi block tapping task (Fischer, 2001; Guariglia, 2007). Nonetheless, inconsistencies exist in the literature regarding whether the visuospatial sketchpad itself is impaired in AD, or if the deficits exhibited reflect impairments of the central executive.

Alescio-Lautier et al. (2007) compared performance on visual and visuospatial tasks in individuals with AD, amnesic-form MCI, and healthy elderly controls. Participants studied one memory image that was comprised of several different images for both the visual and visuospatial task. The goal of the visual task was for participants to recognize the individual images later at test. For the visuospatial memory task, participants needed to recognize the spatial location of the individual images at test. Results demonstrated deficits in visual and visuospatial memory for both AD and MCI patients. However, AD patients consistently exhibited the greatest impairment in all conditions. Consistent with prior research, deficits observed on various tasks used to assess visuospatial memory have been shown to also be influenced by attentional resources (for a review see Huntley & Howard, 2010). This interaction has been observed in studies using the Corsi block-tapping task (Fischer, 2001). Yet,

attentional issues did not seem to influence performance on this visuospatial task (Alessio-Lautier et al., 2007).

The Corsi block-tapping task serves as a nonverbal measure of spatial memory in which the examinee is expected to replicate the prior block-tapping sequence demonstrated by the examiner (Guariglia, 2007). The length of to-be-remembered sequences increases as the task continues, requiring participants to efficiently recruit both visual and spatial components of working memory. Guariglia (2007) assessed AD patients on this task and further subdivided them into mild or moderate dementia groups that corresponded with their Mini-Mental State Examination scores. Results indicated overall poorer performance on the Corsi block-tapping task for AD participants, however, mild AD patients exhibited the greatest deficits in visuospatial memory compared to healthy controls (Guariglia, 2007). Deficits in performance on this task have been found among mild and moderate AD patients when compared to young and elderly control participants in various other studies as well (for a review see Huntley & Howard, 2010). However, discrepancies in the literature exist regarding whether visuospatial deficits begin in the initial stages of AD or develop with disease progression (for a review see Huntley & Howard, 2010; Guariglia, 2007). In addition, prior research suggests that executive functions, such as temporal sequencing, are required for this task, leading researchers to believe the impairments observed are not only a result of deficits in the visuospatial sketchpad component of working memory, but the central executive as well (Carlesimo et al., 1994).

5 THE EPISODIC BUFFER

The episodic buffer component is a newer addition to the Baddeley and Hitch model and addresses the binding problem associated with multimodal information and the influence of long-term memory within working memory (Baddeley, 2000). This system serves as an interface between the two slave systems, the phonological loop and visuospatial sketchpad, and is important in the acquisition of new information (Germano et al., 2008). Deficits in this system pose great impairments in learning for AD patients and can be characterized by the inability to strategically organize incoming information through means of chunking or clustering information based on long-term memory knowledge (Germano et al., 2008). Tasks utilized to assess functioning of the episodic buffer include those that evaluate the ability to maintain visual, verbal, and spatial information, either separately or simultaneously, requiring participants to use organizational techniques when encoding this multimodal information (for a review see Huntley & Howard, 2010).

Germano et al. (2008) examined the ability to strategically organize semantically-similar words in order to improve recall in patients with mild AD and very mild AD. Compared to healthy elderly control participants, patients with mild AD were not able to cluster semantically similar words at encoding, leading to poorer performance. In spite of that, those with very mild AD were able to use organizational skills to improve their performance as well as elderly controls. Chunking and clustering newly-learned information improves memory for that information. These strategic encoding skills allow for the creation of a more meaningful episode, which can be more easily retrieved. Deficits seen among mild AD patients reflect greater impairment of the episodic buffer as the

disease progresses (Germano et al., 2008). Other studies examined similar impairments among AD patients in their inability to organize information by concept and or create associations between words presented (Grober et al., 1985; Carlesimo et al., 1998).

Similar to Germano et al. (2008), Huntley et al. (2011) assessed the use of chunking strategies in those with very mild AD to mild AD. The experiment implemented a digit span task and a spatial span task, each with a structured trial in which the information presented at encoding was organized to promote chunking efforts, and an unstructured trial in which the to-be-encoded information did not follow a pattern or order. When external organization was provided for the verbal digit span task, all three groups demonstrated adequate use of chunking abilities to improve working memory. The control and very mild AD groups performed well on structured trials of the spatial span task too, but those with mild AD did not exhibit improvements in working memory when given external structure for the spatial trials. Therefore, providing patients with encoding strategies to improve working memory is beneficial only to those within the early stages of AD (Huntley et al., 2011).

Although the ability to chunk information is regulated by the episodic buffer, higher cognitive processes are also necessary to adopt such an encoding strategy to improve memory (Huntley et al., 2011). Considering that various executive functions are required for the strategic organization of information and that frontal brain activity is often observed during encoding, researchers have speculated that the central executive contributes during tasks that require episodic binding (Huntley et al., 2011; Baddeley, Allen, & Hitch, 2011). However, studies have suggested greater involvement of long-term memory during the binding process rather than dependence on the central executive (Baddeley, Allen, & Hitch, 2011). This distinction has been difficult to determine as attentional resources are required at initial encoding yet the binding process relies on associations of an experienced event held within long-term memory (Baddeley, Allen, & Hitch, 2011).

6 DIRECTIONS FOR FUTURE RESEARCH

One limitation present within the existing literature is the lack of tasks that can separately assess the individual components of working memory. Many tasks designed to assess the subsidiary systems of working memory, by necessity, require the central executive as well. Therefore, it is difficult to determine whether deficits observed are impairments of one specific component of working memory or an interaction among systems, potentially leading to discrepancies among the literature. Although challenging, future studies need to establish tasks that better control for attentional processes and that specifically measure aspects of the phonological loop and visuospatial sketchpad separately.

Future studies should also establish a standardized measure to assess functioning of the episodic buffer. Prior studies have modified pre-existing tasks that incorporate the processing of multimodal information; however, an established task may lead to more accurate and informative results.

Future studies should also include AD patients of differing disease severities to better differentiate between impairments exhibited at each stage of the disorder. This would help clinicians gain a better understanding of the progression of WM impairments in AD as well as provide clinical markers that may further

distinguish between earlier and later stages of AD. Recognizing specific WM component deficits associated with AD also may assist clinicians in providing more detailed diagnostic criteria that can distinguish AD from other memory disorders. As such, additional studies that compare performance in AD patients and individuals with other memory disorders would be beneficial for further understanding the differences between the conditions, which has implications for treatment plans and coping strategies for patients.

7 CONCLUSION

Alzheimer's disease is a neurodegenerative disorder that impairs various aspects of cognitive functioning. Working memory impairments have been observed in the earliest stages of AD and often further degrade as the disease progresses. This review identified the deficits that are observed most consistently at various stages of the disease, as well as recognized the components of working memory that require additional research. Attentional and executive function deficits associated with the central executive component of the Baddeley and Hitch model have been the most documented early impairments seen among AD patients (Stopford et al., 2012). Deficits in the phonological loop have also been heavily reported in AD. Impairments in the verbal short-term store and articulatory rehearsal mechanism components progress with disease severity (for a review see Huntley & Howard, 2010; Collette et al., 1999) yet the phonological loop seems to remain intact in earlier stages of the disorder. Deficits in the maintenance and manipulation of visuospatial information have been observed among patients with AD, although more research is needed to further specify the visuospatial impairments (for a review see Huntley & Howard, 2010). The inability to strategically organize incoming information as well as greater difficulty integrating multimodal information are characteristic of impairments exhibited by AD patients relating to the episodic buffer component of working memory (Germano et al., 2008). Thus, the fact that specific working memory impairments can be observed in different stages of AD indicate that WM measures may be able to assist in providing clinical markers for disease severity differentiation. Defining common WM deficits associated with specific stages of AD can also provide valuable clinical distinctions between AD and other memory-related disorders.

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