List length effects in item method directed forgetting in adults with and without Alzheimer's disease

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LIST LENGTH EFFECTS IN ITEM METHOD DIRECTED FORGETTING IN ADULTS WITH AND WITHOUT ALZHEIMER’S DISEASE

by

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ABSTRACT

This study seeks to explore changes in cognitive control due to normal aging as well as due to Alzheimer’s disease (AD) through the item-method directed forgetting (DF) paradigm. The earliest significant manifestations of AD are deficits in patients’ episodic memory as well as deficits in cognitive control – the ability to keep goal relevant information in mind despite interference. Cognitive control is thought to be paramount to an array of higher cognitive functions involved in planning and organization, as well as behavioral regulation. The DF paradigm looks specifically at intentional forgetting, whereby individuals are instructed to remember certain words and to forget others, and are then tested on both the remember items and the forget items. The DF effect refers to an increased accuracy for remember items compared to forget items, and the mechanisms of DF is thought to be closely tied to cognitive control. Greater understanding of the process of intentional forgetting may lead to discovery of strategies that can improve patient memory and potentially improve their quality of life. The DF paradigm employed in this study utilizes item-method cueing, where words to be studied are each immediately followed by the cue to remember or forget, and testing is done through a yes-no recognition task. The effect of list length – the total number of items to be studied is also examined (low, medium, high), along with an examination of source memory
accuracy to words that are recognized, i.e. whether the word was a remember word or a forget word. Results comparing younger adult controls (YCs) and older adult controls (OCs) shows overall higher hit rates (percentage of correctly recognized items) across the three list lengths for YCs. Hit rate for the low condition is significantly higher compared to the medium and high list lengths. A DF effect is shown for both YCs and OCs for the low and medium conditions only, but no significant difference between the groups is present. This is contrary to the present literature, where OCs show limited to no DF effect. Source memory data shows greater accuracy for remember items compared to forget items, while performance on the task was significantly greater for YCs compared to OCs, demonstrating an age-related breakdown in source memory accuracy. A single participant with mild cognitive impairment due to AD has been tested, and the performance is shown to mirror that of OCs. Data collected thus far is still limited and more needs to be collected before further conclusions may be drawn. Greater understanding of the process of intentional forgetting may lead to discovery of strategies that can improve patient memory and potentially improve their quality of life.
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INTRODUCTION

The US population is growing older. It was estimated in 2012 that over 41 million people are over 65 years old with a steep upward trend (US Department of Health and Human Services). With an aging population comes a burgeoning list of social and healthcare issues that the nation must address in the coming decades. Alzheimer’s disease (AD) among them is rapidly becoming a paramount issue affecting between 7.5 – 15% of those over the age of 65 equating to 3 – 6 million individuals (Alzheimer’s Association, 2014). According a practical guide for clinicians, AD is the cause for approximately 65% of all dementias and is concurrent with another 10% of other dementias (Budson & Solomon, 2011). According to trajectory figures by the Alzheimer’s Association in 2010, the cumulative cost of AD is likely to exceed $20 trillion by 2050. The burden of the disease on individuals and society is only bound to grow in the coming decades. The devastation wrought by AD on the patients and all those who surround them makes it ever more vital to discover means to improve memory in AD patients and help reduce the burden.

AD is a neurodegenerative disease characterized by accumulation in the brain of senile plaques composed of beta-amyloid protein (Aβ) and neurofibrillary tangles composed of the tau protein. This accumulation, possibly caused by defects in protein cleavage or clearance, can cause a cascading list of issues including inflammation, oxidative injury, and altered kinase/phosphatase activities (Budson & Solomon, 2011).
AD affects an array of neurological function by disrupting particular brain regions including the hippocampus, amygdala, the parietal, temporal, and frontal lobes. Subcortical regions including the basal forebrain cholinergic nuclei, the locus ceruleus, the raphe nuclei, and parts of the thalamus are also affected (Kowall & Budson, 2011). Clinical symptoms include episodic memory loss, word-finding and visuospatial difficulties, and frontal/executive dysfunction causing issues with reasoning and judgment.

Mild cognitive impairment (MCI) is a condition commonly referring to a prodromal stage of Alzheimer’s disease or another dementia. Such patients are not functionally impaired enough to meet criteria for dementia but show deficits in cognition that manifest in neuropsychological testing. There are two variants of MCI: “amnestic” and “non-amnestic”. In amnestic MCI, patients typically develop AD, while those with non-amnestic MCI go on to develop non-Alzheimer’s dementia (Budson & Solomon, 2011). In one study involving a cohort of 88 amnestic MCI patients, 44% were found to have gone on to develop Alzheimer’s disease (Schmidtke & Hermeneit, 2007). Patients suffering from MCI due to AD manifest similar memory deficit symptoms as in AD, though to a lesser extent, but memory deteriorates progressively over time. Patients with the amnestic variant MCI typically exhibit difficulties in episodic memory, but no other problems in other domains, whereas non-amnestic MCI patients exhibit symptoms in other domains outside of episodic memory. Imaging studies have revealed that amnestic and non-amnestic MCI patients both exhibit a similar pattern of hypometabolism in the posterior cingulate gyrus as compared to controls, but there is also reduced metabolism in
the medial temporal lobe only in patients with the amnestic variant, which is closely related to episodic memory (Clerici et al., 2009).

Episodic memory is the explicit and declarative memory system responsible for remembering particular episodes in life, such as a particular birthday party or dinner with a friend. Episodic memory impairment is often the most apparent symptom in AD patients. The earliest affected regions in AD are the hippocampus and temporal lobe, manifesting in degradations in episodic memory, leading to anterograde amnesia and a rapid rate of forgetting, ultimately resulting in difficulties remembering (Budson & Solomon, 2011). Anterograde amnesia refers to difficulty learning new information. AD patients also show retrograde amnesia, or difficulty retrieving previously learned information. The hippocampus and other medial temporal lobe structures are analogous to the “file cabinet” component of episodic memory, where information is stored for later retrieval. Deficits in memory manifest in various ways in AD, but all tend to converge on the idea of rapid forgetting of information. Patients with AD may repeatedly ask a question they’ve asked several times prior, repeat the same stories, forgetting the task at hand or something more threatening like forgetting to turn off the stove.

Research has also shown that both healthy older adults and patients with MCI due to AD have greater difficulties in maintaining cognitive control, the ability to keep goal relevant information in mind despite interferences (Paxton. Barch, Racine, & Braver, 2008). Cognitive control is thought to be a label for a larger set of higher order cognitive functions. There are a number of mechanisms identified as having involvement in exerting cognitive control including: attentional control, inhibition, set shifting, and
working memory updating (Miyake, Emerson, Witzki, Howarter, & Wager, 2000). Attentional control is used in the coordination of information between cognitive processing systems. Inhibition involves the ability to keep irrelevant stimuli from affecting the performance of a present task, such in Stroop tasks (i.e. being asked to read the word “red” that is presented in the color green). Set shifting involves keeping multiple sets of information in mind while maneuvering between both concurrently, which can be gauged using tasks such as Trail Making Test Part B (Adjutant General’s Office, 1944). Working memory updating is the act of replacing outdated information with new and more relevant information, such as in forward and backward digit span tests in the Montreal Cognitive Assessment (Nasreddine, 2005). Cognitive control is a concept closely tied to executive function, which refers to higher order cognition involved in planning and organization, as well as behavioral regulation (i.e. inhibiting inappropriate behavior).

It has been suggested that cognitive control is important in maintaining information in working memory for longer periods of time and thus better allowing the information to be committed to longer term memory stores (Unsworth, & Brewer, 2007). Cognitive control is important in excluding irrelevant information that may have entered working memory from being incorporated into episodic memory. Ultimately cognitive control is utilized in the encoding and retrieval of episodic memories. In examining the influence of cognitive control on working/episodic memory, it was found that those with higher measures of cognitive control performed better on recognition and recall tests after studying a list of items (Rosen, & Engle, 1997; Unsworth, & Brewer, 2010). In such yes
– no recognition tests, participants are shown different items and asked whether that item was a studied item or a completely new item. In recall tests, participants are asked to produce studied items on their own, which is thought to be more cognitively effortful compared to yes-no recognition memory tests.

Studies have shown that amnestic MCI patients exhibit frontal lobe atrophy, which can result in executive dysfunction in these patients. Three fronto-subcortical circuits originating in the prefrontal cortex (PFC) are responsible for executive control functions: working memory (dorsolateral PFC), inhibition (lateral orbital cortex), and response conflict (anterior cingulate cortex) (Reinvang, Grambaite, & Espeseth, 2012). In patients with AD and MCI due to AD, there is a rapid rate of forgetting, as there are disruptions in the encoding of information into memory. However, these patients also exhibit impairments to executive functioning / cognitive control, and can often experience difficulties in inhibiting irrelevant information.

Counter-intuitively, patients may have a difficult time intentionally forgetting irrelevant information and blocking it from entering their memory. In our daily living, we are often confronted with information that is not desirable of committing to memory. Irrelevant information and misinformation require the ability to intentionally forget in order to maintain the integrity of memories. Take for example a classroom example where a professor makes a mistake during lecture and later corrects it; the misinformation is then directed to be forgotten. Intentional forgetting thus helps prevent interference by the misinformation in the encoding and retrieval of relevant information. Common scenarios for patients may involve remembering wrong appointment days, incorrect
medications, or misinformation regarding their condition, all of which would exacerbate the difficulties already faced by those coping with the condition. An inability to forget in AD patients may help explain the increased incidence of false memories already observed in AD patients (Budson, Daffner, Desikan, & Schacter, 2000; Waring, Wolk, & Budson, 2008).

One way of examining and further exploring intentional forgetting and the influence of cognitive control on memory in patients with MCI due to AD is through the Directed Forgetting (DF) paradigm (MacLeod, 1998). In the DF paradigm, participants are shown one stimulus at a time (i.e. a word or picture), which is then followed by a cue to either remember or to forget the item. Participants are asked to remember the items they are cued to remember as best as they can, and to “forget” or inhibit items they are cued to forget. In the testing phase, a recognition test is administered and participants are shown items and asked whether that item is an old item or a completely new item. Critically, participants are tested on their memory for both “Remember” and “Forget” items. The DF paradigm examines the ability to exert cognitive control by presenting participants with task-relevant items that are cued to be remembered (TBR) and task-irrelevant items cued to be forgotten (TBF). The DF effect refers to a better memory on the recognition test for TBR items than the TBF items. The DF effect is scored and measured by taking the difference between the number of TBR and TBF items identified correctly: TBR accuracy – TBF accuracy (Titz & Verhaeghen, 2010). A greater DF effect indicates a better ability to intentionally forgetting.
The DF effect has previously been examined from various different perspectives and several mechanistic explanations have been worked out that are both inhibitory and non-inhibitory depending on the experimental cueing method. In the list method, two lists are presented with a cue between the lists to continue remembering the first list or to forget the first list while a second list is presented for study (Block, 1971; Bjork, Bjork, & Anderson, 1998). Retrieval-inhibition is thought to be at work for the list method since encoding already occurred when the cue is given (Geiselman, Bjork, & Fishman, 1983; Basden, Basden, Gargano, 1993). It is proposed that an inhibitory mechanism blocks access to List 1 items (the list to be forgotten), which would reduce the proactive interference on List 2 items (Bjork, 1989).

In the item method of cueing, each item is immediately followed by a TBR or TBF cue. The mechanism at work for the item method has been proposed to operate during the encoding phase through differential encoding between TBR and TBF items, selective rehearsal of TBR items, attentional inhibition and/or separation of TBR and TBF items into distinctive sets, all of which allow greater availability of TBR items during the memory test (Basden et al., 1993; Basden & Basden, 1998; Bjork, Bjork, & Anderson, 1998; MacLeod, 1999; Sahakyan & Foster, 2009). Selective rehearsal refers to increased efforts to encode TBR items compared to TBF items. Attentional inhibition is the purposeful blocking of TBF items from being maintained in working memory. Separation of TBR and TBF items into sets establishes a clearer distinction between the items, and thus greater clarity of memory during the testing phase. The item method
explores the within-individual effect of directed forgetting whereby both TBR and TBF items are presented to each individual.

A meta-analysis of DF research shows that the DF effect is present in both younger and older adults, but the effect is smaller in older adults. Studies exploring age-related DF differences have largely employed the item method, as the demonstrated differences have been more consistent across studies (Titz & Verhaeghen, 2010). This is thought to be because in the list method, encoding of TBF list items would have already been complete when the cue to forget is shown, while in the item method the cue and the item are less separated in time. Studies have shown that age-related effects in DF may be attributed to age differences in how TBR items are processed and recalled (Salthouse, Siedlecki, Krueger, 2006). In the study conducted by Salthouse et al. multiple measures of memory control were employed in studying age-related differences in memory control, a concept similar to cognitive control. Many measures of memory control were employed, including directed forgetting, multiple trial word recall, tasks involving proactive interference, and retrieval inhibition of episodic and semantic memory. The researchers found few statistically independent cognitive variables underlying age-related differences in cognitive ability, but the experimental variables with the greatest influence were related only to episodic memory ability.

It has been shown that older adults have greater difficulties in inhibiting the processing of goal-irrelevant information (Zacks, Radvansky, & Hasher, 1996; Hasher & Zacks, 1988; Hasher, Zacks, & May, 1999). This inability to inhibit would likely translate to poorer memory performance on recognition and recall of TBR, as TBF items would
also be incorporated into memory along with TBR items. As previously mentioned, the mechanisms of item method DF all operate on encoding, thus emphasizing differences in encoding and intentional recollection of TBR items as an explanation for age-related differences (Titz & Verhaeghen, 2010).

By utilizing the DF paradigm, cognitive control and episodic memory may be examined in healthy adults (young and old), and patients with MCI due to AD. Thus far, only one study has directly examined DF in AD patients while no studies have examined MCI due to AD. Studies have found an absence of directed forgetting effects with AD patients (El Haj, Postal, Le Gall, & Allain, 2011). This may be plausibly explained by inhibition decline identified in AD patients (Amieva, Phillips, Sala, & Henry, 2004) as well as by deficits in cognitive control as afore mentioned. In Stroop tasks involving conflicting stimuli requiring selective attention, AD patients exhibit poorer performance as a result of slower speed of processing (Ben-David, Tewari, Shakuf, & Van Lieshout, 2014). Set shifting, another task requiring cognitive control has also proven to be more difficult for AD patients who have more impaired cognitive processing (Perri, Monaco, Fadda, Caltagirone, & Carlesimo, 2014).

Few studies have examined the relationship between episodic memory, cognitive control, and the influence of MCI due to AD on these constructs. In one study, patients with very mild AD were shown to have poorer performance on executive function tasks as compared with healthy older adults (Baudic et al., 2006). It has been suggested that the disruption of dopaminergic systems in the prefrontal cortices may help explain the age-related declines in cognitive control (Braver, Satpute, Rush, Racine, & Barch, 2001), and
also possibly in AD patients. The AD pathophysiology leads to impairment of multiple regions of the frontal lobes responsible for executive function, response inhibition, and attentional control, including dorsolateral, ventromedial, and anterior cingulate cortex (Collette, Schmidt, Scherrer, Adams, & Salmon, 2009). As a result, it has been shown that patients with MCI due to AD show deficits on tasks involving cognitive control. There is decline in cognitive control with natural aging, which is relatively gradual as compared to AD whereby it deteriorates precipitously as demonstrated through tasks involving executive functions, working memory, and inhibition (Pereiro, Juncos-Rabandan, & Facal, 2014; Sylvain-Roy, Bherer, & Belleville, 2014).

Due to the deficits in cognitive control in AD patients and the importance of such control in a multitude of memory tasks that utilize mechanisms required for activities of daily living, support of cognitive control may prove to be a window into improving the memory for patients suffering from AD and MCI due to AD. Improving memory can lead to strategies that may be implemented to improve their quality of life. Through the DF paradigm, it is the hope that strategies may be developed in healthy older adults and patients with MCI to help improve their episodic memory. The DF effect hypothesized to be a measure of how cognitive control influences memory. When cognitive control mechanisms are not impaired and are operating efficiently, a greater DF effect should be observed. That is, better memory for TBR items and worse memory for TBF items, is expected when there is greater cognitive control. This paradigm allows an exploration into strategies that could maximize the effect, and thus allowing greater cognitive control for patients with MCI due to AD.
The present study seeks to explore the influence of cognitive control on memory, using the item method DF paradigm. Participants undergo three conditions (low, medium, high) that vary in list length, the total number of items shown, and tested using a yes – no recognition test. Participants respond “yes” to items they think they had been shown, and respond “no” to new words they think were not shown. Observation of changes in list length may shed light on how the active remembering and forgetting of information is influenced by how much information is needed to be remembered. In one study of item-method directed forgetting, when cognitive processing conditions were more difficult (low vs. high cognitive load), DF effects were diminished in the high load condition (Lee, 2012). This suggested that the amount of information that an individual is presented with during a directed forgetting task may influence their overall performance in the paradigm itself. However, this study used a recall test and not a recognition test, which intrinsically is more challenging and further study using a recognition test may provide more detail on the mechanisms at work.

The current study looks for differences in cognition across young controls (YCs), older controls (OCs), and patients with MCI due to AD. Based on the literature on aging and cognitive control, it is expected that YCs, with the greatest abundance of cognitive resources, should perform the best across the three list length conditions, as measured by the highest hit rate (HR) and the lowest false alarm (FA) rate on the recognition test. Hit rate is the percentage of correctly identified old items, while false alarm rate is the percentage of new items falsely identified as old items. It is also expected OCs should perform better than MCI. Based on the literature on DF aging studies, it is expected that
the overall DF effect should be greatest for YCs, as shown in the meta-analysis conducted by Titz and Verhaeghen (2010), while for those with MCI due to AD the overall DF effect is expected to be the lowest. The magnitude of the DF effect is measured in terms of the difference in HR for TBR items minus the HR for TBF items.

Based on the preliminary data so far, it is expected in the low condition, that there would be no effect for YCs, as their abundance of cognitive resources would be able to encode all TBR and TBF items with ease. In the medium condition, YCs should show a DF effect as the greater number of items would make it more difficult to encode both TBR and TBF items equally. For OCs on the other hand, the DF effect is expected to be present in the low condition, but the effect should be greater for the medium condition. In the high condition, YCs and OCs should have similar performance and the DF effect is expected to be small or not present. In those with MCI due to AD, it is expected performance across the conditions should be similar to that of OCs, but with a lower level in each of the conditions due to an impairment in cognition.

In addition, the current study is also interested in exploring source memory of YCs, OCs, and MCI due to AD through the DF paradigm. Source memory is defined as a form of contextual memory and the remembrance of where or when information was incorporated into memory (Kreutzer, Caplan, & DeLuca, 2011). Remembering where an acquaintance was first encountered or when a party took place are both examples of source memories. Source memory encoding and recall is an effortful process requiring cognitive resources for both the relevant information consisting the memory itself and the contextual information along with it.. Source memory has been shown to be impaired in
patients with frontal lobe lesions, such as in the case of AD patients. Source memory, also called source monitoring, is an effortful process that is very closely related to recollection.

In this study, source memory ability is gauged by asking participants to determine whether the words they identify as old items are TBR or TBF items, and the source memory accuracy for both Remember and Forget items is measured by the percent correct. It is expected that TBR source memory should be better, as the mechanisms that are responsible for the DF effect ought to lead to encoding of richer detail for those items. There should be a stepwise decline across the conditions, as there is an increase in the quantity of information to be encoded. Overall, YCs is expected to perform the best due to their more efficient cognitive mechanisms for recall, while MCI should show deficits in source memory as compared to OCs. In the low condition, it stands to reason that OCs and YCs will perform similarly – being able to identify the source items as TBR or TBF, as OCs cognitive resources should typically not be exhausted. In the medium condition however, OCs should have lower source memory accuracy. In the high condition, YCs and OCs source memory performance is again expected to be similar since the difficulty of the task should diminish the cognitive advantages held by YCs.

The source accuracy for TBR items is expected to be higher than for TBF items with the same reasoning that HR for TBR items is expected to be higher than that for TBF items. The same mechanisms believed to be responsible for the DF effect: differential encoding between TBR and TBF items, selective rehearsal of TBR items, attentional inhibition and/or separation of TBR and TBF items into distinctive sets ought
to have the same effect on source memory accuracy. Ultimately, these mechanisms would also contribute to greater source memory for TBR items.
Method

Participants

Twenty total of participants were recruited for this study. Healthy young adults were recruited through online and community postings. Healthy older adults were spouses of patients that have previously completed studies in the laboratory, or were recruited via postings at community or senior centers. Patients were from the Memory Disorders Clinic at the VA Boston Healthcare System and the Boston University Alzheimer’s Disease Center in Boston, MA. There were 10 participants in the Younger Control group (YCs), 9 participants in the Older Control group (OCs), and 1 participant in the mild cognitive impairment due to Alzheimer’s disease (MCI).

Patients with MCI due to AD also met criteria set by the NIA-AA (Albert et al., 2011). These include (1) a cognitive concern about a change, in comparison to the individual’s previous level, expressed by the patient, an informant, or a clinician, (2) impairment in one or more cognitive domains, (3) preservation of independence in functional abilities, and (4) the patient is not demented and the cognitive changes are sufficiently mild that there is no drastic impairment in social or occupational functioning. The evidence of lower performance in one or more cognitive domains should be greater than would be expected for the patient’s age and educational background.

Patients were assessed and diagnosed by a Neurologist or a Neuropsychologist, and were otherwise healthy. Participants were also screened for a history of depression, substance abuse, stroke, traumatic brain injury, or other neurologic disorders. All
participants were native English speakers and had normal or corrected to normal vision. Written informed consents were obtained from all participants and obtained from their caregivers when appropriate.

Participants were administered neuropsychological battery testing prior to the experiment, consisting of the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh 1975), Consortium to Establish a Registry for Alzheimer’s Disease (CERAD) Word List Memory Test (Morris et al., 1989), Trail Making Test Parts A & B (Adjutant General’s Office, 1944), Verbal Fluency to letters and categories (FAS; Monsch et al., 1992), the short form Boston Naming Test (BNT-15; Mack, Freed, Williams, & Henderson, 1992), and the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005). This brief neuropsychological test battery took approximately 30-45 minutes to complete.

Experiments took place at the participants’ homes or at the Boston VA Hospital in Jamaica Plain, MA. Participants were paid $10/hour for their participation. This study was approved by the Institutional Review Board at the VA Boston Healthcare System in Jamaica Plain, MA.

Materials

Testing was done using a 17” Dell PC laptop computer with the E-Prime software (Schneider, Eschman, Zuccolotto, 2002). The stimuli consisted of 416 words total, 3 to 10 letters in length, from the MRC Psycholinguistic Database (Coltheart et al.,
1981), appearing with low to mid frequency. The words were moderately to highly imaginable and concrete with ratings of 350 – 700. All words were counterbalanced across each condition in the experiment.

**Procedure**

The experiment consisted of 3 separate sessions each set 1 week apart. In each session participants were administered one of three conditions. There were three Memory Load conditions in the experiment, each consisting of a study phase and a test phase. The test phase came immediately after the study phase. In the Low Memory Load condition, participants studied a set of 16 words and then were tested on 32 words, half old and half new. In the Medium Memory Load condition, participants studied a set of 64 words and then were tested on 128 words (half old, half new). In the High Memory Load condition, participants studied a set of 128 words and then were tested on 256 words (again, half old and half new). In all conditions, half of the study words were cued to be remembered (TBR) and the other half of the study were cued to be forgotten (TBF).

In the study phase, participants were told that they would see words appear on the screen one at a time, followed by a cue to either actively remember or forget the word. They were instructed to read each word to themselves. At the beginning of each study phase trial, participants saw a screen with a row of stars (*** that appeared for 500 milliseconds (ms), followed by a 250 ms blank screen. After the blank screen, a word appeared for 3000 ms in the center of the screen. A cue to remember or forget appeared after 250 ms following each target word on a separate screen. For remember cues,
participants saw the sentence “Remember this word!” after each target word. For forget cues, participants saw the sentence “Forget this word!” after each target word. Following the presentation of the memory cue, there was a 250 ms blank screen, followed by another screen with a row of stars for 500 ms. After this was completed the next study phase trial was initiated.

In the memory test, participants were told that they would see words appear again on the screen one at a time. For each word, participants are instructed to respond “Yes” if the word shown was an old word they studied before, regardless of the cue, and “No” if the word is completely new. It was emphasized that their performance was only judged on their performance on remembering the words they were supposed to remember and their memory of forget words was less important. If participants responded “Yes” to a memory test word, they were asked to determine if the word was a Remember or Forget word, and were instructed to take their best guess if they did not know the answer. If the participant responded “No” to a memory test word, they were asked to judge whether they “Liked” or “Disliked” the word.

At the beginning of each memory test trial, participants saw a row of stars (***)
presented for 500 ms. The memory test probe was then shown until the participant responded. If the participant responded “Yes”, a 250 ms blank screen appeared before the participant was asked if the word was a “Remember” or a “Forget” word. If the participant responded “No”, there is a 250 ms blank screen before asked to state whether they “Liked” or “Disliked” the word. In each case, responses were self-paced. After they gave a response, the next memory test trial would begin.
The study phase instructions, study phase stimuli, test phase instructions, and the testing phase are shown as they are presented during experimentation.
Figure 1. The sequence of how stimuli are presented to participants during the study phase is shown in the schematic. Each word is presented for 3000 ms and is followed by the Remember or Forget cue for 250 ms and a blank screen with “***” is shown for 500 ms before the next trial and the cycle repeats until the study phase is complete.
Results

Participants

The mean age of Older adults is 78.67 years old (SD = 5.87), with a mean education of 16.16 years (SD = 2.12). The mean age of Younger adults is 23.9 (SD = 0.92) years old, with a mean education of 17.45 (SD = 0.9) years.

Standard Neuropsychological tests

Table 1 shows the means and standard deviations of the standard neuropsychological tests of all older adults and MCI due to AD participants.

<table>
<thead>
<tr>
<th>Test</th>
<th>Patient with MCI due to AD</th>
<th>Older adults (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>30</td>
<td>29.22 (1.20)</td>
</tr>
<tr>
<td>MoCA</td>
<td>25</td>
<td>27.67 (1.93)</td>
</tr>
<tr>
<td>CERAD Immediate Recall</td>
<td>14</td>
<td>23.56 (4.50)</td>
</tr>
<tr>
<td>CERAD Delayed Recall</td>
<td>3</td>
<td>8.22 (1.48)</td>
</tr>
<tr>
<td>CERAD Recognition</td>
<td>9</td>
<td>9.89 (0.333)</td>
</tr>
<tr>
<td>Trails A Time</td>
<td>34</td>
<td>39.00 (13.49)</td>
</tr>
</tbody>
</table>
Table 1: Results of the Neuropsychological tests for the one patient with MCI due to AD and also for healthy older adult controls.

<table>
<thead>
<tr>
<th>Trails B Time</th>
<th>84</th>
<th>85.56 (36.64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAS</td>
<td>33</td>
<td>52 (15.93)</td>
</tr>
<tr>
<td>CAT</td>
<td>43</td>
<td>44.89 (8.59)</td>
</tr>
<tr>
<td>BNT Hit</td>
<td>15</td>
<td>15 (0)</td>
</tr>
</tbody>
</table>

**Remember and Forget Hit Rates**

Comparison between groups across the three conditions using a mixed factor analysis of variance (ANOVA) with group (healthy younger adults vs healthy older adults) as a between subjects factor, and condition (low, medium, high) as a within subject factor, and cue type (TBR vs TBF) as a within subjects factor showed significant main effects of group ($F(1, 17) = 6.59, p = 0.020, \eta^2 = 0.279$), list length ($F(2, 34) = 9.77, p < 0.001, \eta^2 = 0.365$), and cue type ($F(1,17) = 15.14, p = 0.001, \eta^2 = 0.471$).

Young adult controls had a higher overall hit rate compared to older adult controls. Hit rates for the low condition were significantly higher than hit rates for the medium condition ($t(18) = 3.09, p = 0.006$), and was also significantly higher than for the high condition ($t(18) = 4.72, p < 0.001$). There was no significant difference between
hit rates for the medium and high conditions ($t(18) = 1.23, p = 0.234$). Hit rates for the remember cues were significantly higher compared to hit rate for forget cues.

There was an interaction present between list length X cue type ($F(2,34) = 9.69, p < 0.001, \eta^2 = 0.363$). Hit rates for remember cues were higher in low and medium conditions ($t(18) = 3.15, p = 0.005$ and $t(18) = 6.21, p < 0.001$ respectively)

No other significant effects were observed for hit rates (all $F$’s < 1, $p$’s > 0.1).

**False Alarms**

Comparison between groups and list length using a mixed factor ANOVA on false alarm rates to new items showed a significant main effect of list length ($F(2, 34) = 5.81, p = 0.007, \eta^2 = 0.255$). False alarm rates were marginally lower in the low versus medium condition ($t(18) = -2.33, p = 0.031$), significantly lower in the low versus high condition ($t(18) = -3.43, p = 0.003$). No difference was observed between the medium and high conditions ($t(18) = -1.60, p = 0.126$).

No significant effect of group was observed ($F < 1, p > 0.1$).

**Source Identification**

A mixed factor ANOVA conducted between group, list length, and cue type found a significant main effect of group ($F(1, 17) = 5.00, p = 0.39, \eta^2 = 0.227$). Healthy
young adult controls had higher correct source identification compared to healthy older adults.

There was an interaction present between list length X cue type ($F(2, 34) = 4.23, p = 0.023, \eta^2 = 0.199$). Correct source identification was higher for Remember cues versus Forget cues in the medium list length condition ($t(18) = 4.04, p = 0.001$), but was not in the low or high list length conditions ($t's < 1, p's > 0.1$).

A significant interaction was identified between group X list length ($F(2, 34) = 3.29, p = 0.049, \eta^2 = 0.163$). Younger adult controls had higher correct source identification in the low and medium list length conditions ($t(18) = 2.81, p = 0.012$ and $t(18) = 2.98, p = 0.008$ respectively), but not in the high list length condition ($t < 1, p > 0.1$).

No other significant effects were observed (all $F's < 1, p's > 0.1$).
Figure 2. Hit rates and false alarm rates for younger adult controls (YCs) and older adult controls (OCs) across all conditions for both to be remembered items and to be forgotten items. The Y-axis shows the proportion of Hit rates or false alarms with 1.0 being 100 %. YCs are shown in the blue bars, while OCs are shown in orange bars.
Figure 3. The proportion of correct source identification rates (on the y-axis) for younger and older adult controls across the low, medium, and high conditions to remember and forget items. Younger controls (YCs) are shown in blue bars, while older controls (OCs) are shown in orange bars.
Figure 4. The proportion on the y-axis for the hit rate for remember/forget items and false alarm rate for new items for the participant with Mild Cognitive Impairment due to AD across the low, medium, and high conditions.
Figure 5. The magnitude of the directed forgetting (DF) effect as measured by subtracting hit rates for forget items from hit rates for remember items. The Y-axis shows the magnitude of the difference in hit rates. Younger adult controls (YC) are shown in blue bars, and older adult controls (OC) are shown in orange bars.
Figure 6. The overall source memory accuracy that combines both the source memory accuracy for remember items and the source memory accuracy for forget items. The Y-axis shows the source memory accuracy as a proportion with 1.0 being 100% correct. Younger adult controls (YC) are shown in blue, and older adult controls (OC) are shown in orange.
Discussion

In the current study three groups of participants (YCs, OCs, and MCI) underwent an item-method directed forgetting paradigm utilizing a yes – no recognition memory test that included a source memory component. Three list lengths (low, medium, and high), varying in the number of items, were given to each participant over three separate sessions. We had predicted YCs to perform the best across the three list length conditions, as measured by the highest hit rate and the lowest false alarm rate on the recognition test. Hit rate is the percentage of correctly identified old items, while false alarm rate is the percentage of new items falsely identified as old items. We had also predicted OCs to perform better than MCI participants.

The results from the present study suggest that with normal aging, there is a pattern of change in performance between younger and older healthy adults (mean age 78.67 years, SD = 2.12). The pattern of change manifests itself in higher hit rates for YCs across all conditions, and for both to be remembered (TBR) and to be forgotten (TBF) items. This is as expected due to decline in cognitive control with healthy aging (Paxton et al., 2008), which decreases OCs ability to actively maintain goal-relevant information in mind, thus greater difficulty in encoding that information. This difference may also simply be due to declines in general episodic memory ability due to healthy aging.

The hit rate data also shows that as the number of items increased across the conditions, there is a decrease in hit rate, which is likely due to the fact of more information needing to be encoded. This trend shows the effect of list length being in
effect for both YCs and OCs, whose hit rates decreased with increasing list length. This is also true for false alarm rates to new items, which showed a trend of increasing as the list length increased from low to high. For false alarm rates, however, there was no significant difference between YCs and OCs, demonstrating a similar ability to correctly identify new items as new. This is interesting to note because one would expect that age-related declines in cognitive control would also lead to greater rates of false alarms. The data may be plausibly explained by the fact that false alarm rates are more closely related to familiarity, while cognitive control more directly affects recollection and recall of specific pieces of information.

The source memory data shows that OCs performed significantly worse on identifying the source of where information came from, compared to YCs as shown in Figures 3 and 6. Figure 3 separates source memory accuracy for TBR and TBF items, while Figure 6 combines the source memory accuracy for both TBR and TBF items. It was previously expected that OCs and YCs performances would be similar in the low condition, but the data shows otherwise, suggesting there is a source memory breakdown as a result of aging even in the low condition. This aging effect may follow a similar explanation as the data for hit rates data. Source memory, very closely tied to recollection, is a demanding task that requires much attentional resources in order to encode contextual cues along with the information itself. This task involving source memory becomes increasingly difficult with more information needing to be encoded. This is demonstrated by the fact that the difference for source memory performance is true for the low and medium conditions, but not for the high condition, where YCs
performs similarly to OCs. This could be a result of saturation of YCs cognitive capacity by the high quantity of information being encoded.

For the low and medium conditions, there was a higher hit rate for the remember items as compared to forget items, demonstrating the presence of a directed forgetting (DF) effect. The DF forgetting effect is not observed, however, in the high condition. In fact, the hit rates are numerically higher for TBF items in the high condition, as can be seen in Figure 2. The difference is not significant, but suggests that the cognitive load of the high condition exceeds the cognitive capacity of YCs and OCs, and it is increasingly more difficult to exert the cognitive control necessary to actively forget.

What is inconsistent with the literature is the fact that there is no age-related differences between YCs and OCs as was expected previously. As Titz & Verhaeghen (2010) had shown in a meta-analysis of directed forgetting studies, older healthy adults had a significantly lower DF effect as compared to younger healthy adults. The reasoning for the age-related impairment is told in terms of inhibitory deficits whereby older adults have greater difficulties in inhibiting material cued to be forgotten. The meta-analysis also revealed that the item cueing method resulted in the greatest DF effects. The item-method directed forgetting paradigm used in the present study should have produced an age-related difference according to literature.

There are a number of possible explanations for why an age-relate difference in DF is not observed. Although some significant findings were produced, the sample size of OCs and YCs thus far is still small, and the simple explanation is that there may be a
difference but it is simply not observable yet. Other explanations may be methodological. Practice effects may be causing a matching performance between groups, as a result of the experiment being separated into three separate sessions. Repeated exposure to the experimental methods could have allowed OCs to have more opportunity to improve over time, which is not the case for other studies with a single experimental session. Other studies often included recall tests as well, while this study only utilized a recognition test. Recall tests require participants to self-generate the items they were cued during the study phase. Recall tests are much more difficult and demanding, resulting in lower numbers of responses and thus more prone to variance, but would eliminate any guessing or chance. Incorporation of recall testing data would lead to more concrete findings that may lead to consistency with the present literature. The high level of education for the OCs in this study (mean education 16.16 years) may also be an explanation for the similar level of performance compared to YCs. Collecting data from a greater range of education for OCs and YCs could show greater differences between the age groups. Another possible explanation of the results may be that the task of intentional forgetting is equally difficult for both YCs and OCs. In the high condition, neither group showed a DF effect, but according to Figure 5, the difference between TBR and TBF items was greater in value, demonstrating that in this case, the OCs are marginally better to intentionally forget.

Thus far data has been collected from only one amnestic MCI participant, which is shown in Figure 4. It is not possible to draw any conclusions, but performance is interesting to note because the data approximates performance by healthy older controls.
MCI by definition is very variable, since most are still very functional and capable of independently carrying out activities of daily living. There is also degeneration of the medial temporal lobe, which is thought to negatively impact memory and thus leading to lower DF effect and lower source memory performance (Budson, & Kowall, 2011). As the study continues and more MCI data is collected, comparisons may be drawn more conclusively.

Amnestic MCI patients have been shown to exhibit some frontal lobe atrophy, which can result in execute function deficits for these patients. The three fronto-subcortical circuits, originating in the prefrontal cortex (PFC) are thought to be responsible for executive control functions: working memory (dorsolateral PFC), inhibition (lateral orbital cortex), and response conflict (anterior cingulate cortex) (Reinvang, Grambaite, & Espeseth, 2012). Working memory and inhibition have been previously discussed as being pivotal in cognitive control and intentional forgetting; response conflict refers to simultaneous activation of incompatible response tendencies (Braver, Barch, Gray, Molfese, & Snyder, 2001). It can be expected that these executive function deficits seen in these patients would lead to difficulties in intentional forgetting and the DF paradigm. As more data is collected from patients with MCI due to AD, it is expected that there would be no DF effect for these patients across all the conditions except possibly the low condition.

At this point more data needs to be collected. It may be important to reconcile the present data with the literature and ensure that there is an age-related change in DF before proceeding forward. Lack of age-related directed forgetting effects in the current data
may occur for several reasons. Our older adult sample may be more highly educated than those in other studies, which may account for why their performance approximates that of young controls. Our study is also methodologically different in some ways compared to other investigations. Participants perform the directed forgetting task repeated across three sessions, and lack of age-related differences may be due to a practice effect. However, if this were the case, directed forgetting effects would be more diminished across all conditions. In order to draw clearer conclusions, our sample size needs to be doubled to attain adequate statistical power. The ultimate goal of this study is to identify strategies that may maximize the ability of AD patients and MCI due to AD patients to intentionally forget. These strategies may improve patient memory and thus eventually translate to a better quality of life. Future directions may include further manipulations using list lengths in order to alter the level of cognitive control that individuals are shown to exert.
References


Hasher, L., Zacks, R. T., & May, C. P. (1999). Inhibitory control, circadian arousal, and age. Inhibitory control, circadian arousal, D. Gopher, & A. Koriat (Eds.), Attention and


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Education

Boston University, Graduate Medical Sciences – Class of 2015

Cornell University, College of Arts and Sciences – Undergraduate Class of 2013

Boston Latin School – High school Class of 2009

Research and Work Experiences

Regeneron Pharmaceuticals as a Summer Intern for two consecutive summers (2011 and 2012) in Tarrytown, NY

- Drug research to find effective treatments for common allergens such as Fel d1 from cats, Peanut, and house dust mite

  - Sensitization of humanized mice with particular allergen, followed by treatment with candidate antibodies, and then extraction of mice blood, sera, lungs, kidneys, lymph nodes, and broncho-alveolar lavage fluid.

  - Testing of sera and blood using enzyme-linked immunosorbent assays (ELIZA’s) for various immune response related antibodies (IgE, IgG1, IgG2a..)

  - Flow cytometry (FACS) staining carried out with broncho-alveolar lavage fluid for immune response related cells including eosinophils, basophils, neutrophils, etc.

  - Cross-section of lungs are mounted to slides in order to analyze the level of respiratory, particularly bronchiolar inflammation. Lungs also used to extract and quantify treatment antibody levels.

  - Use of scientific analytical software including ImageJ and Prism to graph and visualize collected data.
Boyce Thompson Institute for Plant Research at Cornell University as an Undergraduate research assistant for 4 consecutive semesters (2010 – 2012) in Ithaca, NY

- Use of *Arabidopsis thaliana* plant to study root development, particularly the role of proteins in the AT-hook family and their role in the control of cell-to-cell signaling as mobile transcription factors during the root developmental process.

- Generating AHL-1 and AHL-13 gene constructs containing over-expression promoters and the green fluorescent protein, using the Gateway Technology from Invitrogen.

- DNA sequencing, restriction digestion, gel electrophoreses to verify the gene constructs.

- Transformation of *E. coli* using heat shock, and extraction of DNA from *E. coli* culture. Transformation of *Agrobacterium* using electro-shock, and infecting flowering plants with the *Agrobacterium* culture to generate transgenic plants.

- Observe expression of GFP in vascular root of transgenic plants using a laser scanning confocal microscope

- Testing possible interaction of AHL-1 and AHL-13 proteins with the AHL-4 protein, which has been identified as a mobile transcription factor, and forms a complex with the AHL-3 protein

  - Using the Yeast Two-hybrid system from Invitrogen as well, which uses MaV203 competent Yeast cells with reporter genes (HIS3, URA3, and lacZ) integrated in its gene.

  - AHL-1 and AHL-13 genes were inserted into the pDEST 22 prey vector, while the AHL-4 gene was inserted into the pDEST 32 bait vector, and both vectors were transformed into the same competent yeast cells, which were subsequently grown on selective plates, where growth indicated interactions.

Joslin Diabetes Center as a summer Intern for one summer (2010) in Boston, MA

- Immunostaining of pancreatic tissue fluorescent antibodies to identify islet of Langerhans in pancreatic tissue

  - Fluorescent microscopy used to photograph stained tissue, which is subsequently used to generate beta and alpha cell counts.

  - ImageJ used to measure pancreatic area
Performing PCR, gel electrophoresis and Western Blotting

**Cornell Entomology Department** as an Undergraduate research lab assistant for one semester (2009) in Ithaca, NY

- Research of lab involving the study of mosquito as a vector for infectious diseases
- Mosquito wing dissection and measurement
- Data entry, general maintenance, solution making, and autoclaving
- Capturing wild mosquitoes in wooded areas
- Various tasks involving organizing, sorting, and breeding mosquitoes for research purposes.

**Teaching and Tutoring Experiences**

**Cornell University** as an Undergraduate Teaching Assistant for 3 Semesters (2012-2013) in Ithaca, NY

- General Biology TA for Introductory Biology Individualized Instruction
  - Write and administer oral exams to students
  - Teaching lab sections and grading of lab reports
  - Completing unit objectives for ten units throughout the semester
  - Work in study center to answer student questions and assist them in course
- Learning Strategy Center Study Group Leader for Evolutionary Biology and Biodiversity
  - Assume leadership of 6-10 students
  - Facilitate active learning through group discussions and group activities, while reinforcing and expanding course knowledge for students

**Volunteering and Charity Experiences**

**Acting on Aids Cornell Chapter** as the charity Vice president (2011-12) and Treasurer (2010) in Ithaca, NY

- Apply for funding from the Student Assembly Financial Commission
- Organize and schedule general and executive board meetings
-Collaborating with on-campus organizations and professors to host AIDS awareness events

-Raise money to fund and support children through World Vision in areas heavily affected by HIV/AIDS

Brigham and Women’s Hospital as a Transplant Research Lab Volunteer for one summer (2008) in Boston, MA

- Observation of standard surgical procedures done on mice including heart and liver transplants, as well as skin grafts.

Children’s Hospital Boston as a clinical volunteer for one summer (2007) in Boston, MA

- Supervision of outpatients, ages 4-14, and assisting with general patient needs

- Visiting and accompanying impatient with extended illness.