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Temporal Discrimination Deficits as a Function of Lag Interference in Older Adults

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Abstract

A vital component of episodic memory is the ability to determine the temporal order of remembered events. Although it has been demonstrated that the hippocampus plays a crucial role in this ability, the details of its contributions are not yet fully understood. One proposed contribution of the hippocampus is the reduction of mnemonic interference through pattern separation. Prior studies have used behavioral paradigms designed to assess this function in the temporal domain by evaluating the ability to determine the order of remembered events as a function of proximity in time. Results from these paradigms in older adults (OA) have been mixed, possibly due to limitations in controlling elapsed time and narrow range of temporal lags. Here, we introduce a novel behavioral paradigm designed to overcome these limitations. We report that OAs are impaired relative to younger adults at moderate and high temporal lags but not at low lags (where performance approached floor). We evaluated OAs' ability to benefit from primacy (enhanced order judgment on the first few items of any given sequence) and found two distinct subgroups: one group was on par with young adults [aged-unimpaired (AU)] and the other group was two standard deviations below the mean of young adults [aged-impaired (AI)]. Temporal discrimination performance in AU adults was consistent with a pattern separation deficit, while performance in AI adults was consistent with a generalized temporal processing deficit. We propose that the task introduced is a sensitive marker for episodic memory deficits with age, and may have diagnostic value for early detection of age-related pathology.

Keywords

hippocampus; pattern separation; interference; temporal discrimination; neurocognitive aging

INTRODUCTION

The ability to determine the temporal order of remembered events is paramount to adaptive fitness. All inferences of cause and effect or action and consequence are predicated upon the knowledge that one event happened before another in time. This ability has been examined across species including humans (Perlmutter et al., 1981; Tolentino et al., 2012),

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rodents (Fortin, Agster, and Eichenbaum, 2002; Kesner, Gilbert, and Barua, 2002), and birds (Clayton and Dickinson, 1998). Prior work has repeatedly demonstrated that the hippocampus plays an important role in memory for temporal order (i.e., sequence memory; Fortin et al., 2002; Kesner et al., 2002; Hopkins, Waldram, and Kesner, 2004; Devito and Eichenbaum, 2011; Tubridy and Davachi, 2011). One proposal for how the hippocampus supports temporal memory is that it performs a pattern separation computation for temporal information in memory (Hunsaker and Kesner, 2013; Jacobs et al., 2013). Pattern separation is a computation by which overlapping neural representations ("patterns" of neural activity) are made more distinct (separated), allowing them to be stored as separate representations. It is thought to be accomplished at a neural level within hippocampal circuitry (Yassa and Stark, 2011).

Although evidence for temporal pattern separation can only be directly observed by recording neural input/output transformations, developing behavioral tasks that may be sensitive to changes in this computation is crucial to determining its functional significance. In humans, aging is associated with changes in hippocampal circuitry (particularly the dentate gyrus and CA3 regions) that lead to impaired pattern separation, which is associated with deficits in discrimination abilities in mnemonic interference tasks (Yassa et al., 2011b). While older adults (OA) do reliably demonstrate failures to discriminate among mnemonic experiences that are perceptually similar (e.g., similar objects, scenes, locations, words, etc.; Toner et al., 2009; Yassa et al., 2011a,b; Holden et al., 2012; Ly et al., 2013; Reagh et al., 2013; Stark et al., 2013), much less is known about their ability to discriminate among experiences that occurred in close proximity in time (i.e., temporal interference).

Perlmutter et al. (1981) investigated temporal order memory in OAs by showing them a sequence of drawings on paper. After viewing the sequence in its entirety, they were shown pairs of objects from the sequence and asked to determine which of the objects appeared earlier in the original sequence. The study found no differences between young adults (YA) and OAs with respect to the number of correct responses, however the authors noted that OAs took more time with the task.

In a more recent investigation by Tolentino et al. (2012), which was modeled after temporal pattern separation tasks in rodents (Gilbert et al., 2001), participants were shown a digital representation of an overhead view of an eight-arm radial maze. A dot appeared at the end of each of the arms for 2 s followed by a 2 s intertrial-interval, thus comprising a sequence of eight events. The order of arms was randomized from trial to trial. In the test phase, two dots simultaneously appeared at the ends of two arms, and the participants were asked to indicate in which arm the dot appeared earlier in the original sequence. In contrast to Perlmutter et al. (1981), the authors found that OAs were impaired relative to younger adults in this task, which they suggested might be attributed to a deficit in pattern separation of temporal information in OAs.

To resolve the discrepancy between these two studies, it is necessary to examine their differences more closely. Perlmutter et al. (1981) used a free-response paradigm (i.e., subject-terminated response window). It is possible that the older participants in this study did have a deficit in temporal memory ability, but were able to overcome it through greater encoding times or by spending more time mentally reconstructing the sequence during the test phase. Participants only had a 5 s response window in Tolentino et al. (2012), thus potentially capturing a deficit that may have been obscured in Perlmutter et al. (1981). Conversely, all trials in Tolentino et al. (2012) were perceptually very similar. It is possible that the deficits in the OA group were a result of the inability to distinguish between the perceptual representations rather than being a deficit of temporal memory *per se*.

Additionally, although Perlmutter et al. (1981) varied temporal lag between test pairs, the authors did not analyze performance as a function of temporal distance. Tolentino et al. (2012) did parametrically vary the temporal distance between test pairs, but the maximal distance between test pairs was only six events, which limited the paradigm's ability to manipulate temporal interference to a short duration.

To resolve these discrepancies and limitations, we developed a novel temporal discrimination task that uses visually distinct object stimuli, controls exposure and response times, and has a greater range of temporal distances between test pairs.

We hypothesized that the ability of participants to determine the temporal order of remembered events would be enhanced as the temporal distance between the events increased (i.e., when temporal interference is reduced). Furthermore, because aging is thought to disrupt pattern separation within the hippocampus, we hypothesized that OAs would be impaired relative to controls at closer time-spans, but would recover as the temporal distance increased.

MATERIALS AND METHODS

Participants were divided into two groups based upon age. The YA group consisted of adults between the ages of 18 and 35 years of age (n = 27, 19 female, mean age = 22 ± 4). The OA group consisted of nondemented adults between the ages of 59 and 83 (n = 44, 33 Female, mean = 70 ± 7). We enrolled twice as many OA's in the study as YA's as we expected to see quite a bit of individual variability in the OA group given our prior work (Reagh et al., 2013; Stark et al., 2013). Exclusion criteria included current or past history of major physical and mental illnesses, substance abuse, alcoholism, and traumatic brain injury. Participants were recruited from the Johns Hopkins community and greater Baltimore County using email announcements, fliers on campus and at local retirement communities, and advertisements in local newspapers. All participants were compensated for participation. Participants provided signed informed consent and all procedures were approved by the local Institutional Review Board.

All participants completed a battery of neuropsychological tests, which included the Mini-Mental State Examination (Folstein, Folstein, and McHugh, 1975), the Rey Auditory Verbal Learning Test (RAVLT; Rey, 1941) and Digit Span Backwards and Forwards (Lezak et al., 2004). One participant from each group was excluded due to technical problems with data collection.

The Mnemonic Discrimination–Temporal Task was written in Python using the PsychoPy module (Peirce, 2007, 2008). Stimuli were images of common objects presented against a white background. All images were scaled such that their largest dimension was equal to one-filth of the height of the screen. The images used were a subset of the images provided by Brady et al. (2008). Images were manually selected such that all objects were unique, and such that the ambiguity of the size of each depicted object was minimal (e.g., no pictures of miniature cars were used).

Each participant completed 12 testing blocks. Each block consisted of a study phase and a test phase. Two types of blocks were used. Variable lag (VL) blocks were used to investigate the effect of temporal lag on discrimination performance. Serial position (SP) blocks were used to investigate the effect of primacy and recency while holding temporal lag constant. Each participant received six VL and six SP blocks, with the order randomized.

VL Blocks

The study phase consisted of 30 trials (Figure 1). During each trial, the participant was shown a single object in the center of the screen. The object was shown for 3.5 s and a blank white screen was shown for 500 ms between each trial. For each trial after the first, participants were instructed to press the “V” key if they believed the object currently depicted to be smaller than the object previously depicted, or the “N” key if they believed the object currently depicted to be larger than the object previously depicted. The objects used in each sequence were pseudorandomly determined for each participant such that each object was only used in one block per subject.

Immediately after the conclusion of each study phase, the test phase consisting of 15 trials began. During each trial two objects from the previous study phase were simultaneously presented at the center of the screen. Participants were asked to press the “V” button if they believed that the object on the left side of the screen appeared earlier in the previous study sequence, or the “N” button if the object on the right side of the screen appeared earlier in the previous study sequence. The images were shown to the participants for 3.5 s with a 500 ms interstimulus-interval between trials. Each object appeared only once during the test sequence and only objects from the previous study sequence were used. The side of the screen corresponding to the object appearing earlier in the sequence was counterbalanced. Five levels of temporal lag (quantified according to number of intervening trials during study) were included in the test trials (three trials of each lag type): 0-lag, 5-lag, 10-lag, 15-lag, and 28-lag. Each of these lag categories varied by ±1 lag to allow for a greater degree of randomization with the only exception being the 0-lag which was constant. The first three trials of each test sequence consisted of 28-lag trials. This condition was designed to combine possible effects of primacy and recency with effects of temporal distance to make 28-lag trials easily separable. One hundred sequences fitting these criteria were created using a randomization algorithm, and six of the created sequences were randomly chosen for each participant.

SP Blocks

Because it is impossible to dissociate the effects of SP (i.e., primacy and recency) from the effects of temporal distance within the longest lag condition in the VL blocks, we added an equal number of SP blocks. In these blocks, the study phase was identical. During test, all pairs had a temporal distance of 10 ± 1 images, but varied based upon the serial order of the images in the study sequence. Three conditions were used: primacy, recency, and middle. Trials in the recency condition consisted of the last three objects of the study sequences paired with objects occurring 10 ± 1 images before them. These trials were always presented first in the test phase. Trials in the primacy condition consisted of the first three objects in the study sequence paired with objects occurring 10 ± 1 images after them. Trials in the middle condition consisted of three objects from the middle of the sequence that occurred 10 ± 1 images apart. The order of primacy and middle trials was randomly determined for each participant.

We quantified performance in the VL blocks using mean discrimination accuracy (probability of making a correct order judgment) within each temporal lag bin for each participant. We analyzed the results of the SP blocks in the same way but using the SP bins instead of temporal lag bins.

Statistical Analyses

All analysis of variance (ANOVA) of behavioral data were performed using SPSS v. 20.0 (IBM, released 2011, Armonk, NY) and all post hoc comparisons were performed using custom Excel for Mac v.14.3.6 (Microsoft, released 2011, Redmond, WA) spreadsheets. Post hoc comparisons were all performed using contrasts. Contrasts weigh the means of conditions to generate a sum of squares for the compared condition. This sum of squares is then divided by the appropriate error term, which provides an F-statistic for evaluating statistical significance of the comparison. Contrasts are more appropriate than post hoc *t*-tests because they operate within the same variance space as the omnibus ANOVA. All contrasts were corrected for Type I error inflation due to multiple comparisons using Scheffe's method. This method adjusts the critical F-statistic for contrasts on the basis of the number of conditions modeled in the ANOVA (Scheffe's $F = F^{*} n$ [conditions] −1), and is a conservative correction but is less susceptible to Type II error than Bonferroni correction.

RESULTS

Older Adults Exhibit a General Temporal Order Discrimination Deficit

To investigate the differences between the groups, we performed a 2 × 5 factorial ANOVA with temporal lag as the within-subjects factor and age as the between-subjects factor. Because the difference in the groups' sizes was not due to participant drop-out, we used unweighted calculations. The ANOVA resulted in a significant main effect of age [$F(1,68) = 36.72$, $P < 0.001$], a significant main effect of temporal distance [$F(4,272) = 84.46$, Greenhouse-Geisser corrected $P < 0.001$], and a significant interactions between age and temporal distance [$F(4,272) = 5.48$, Greenhouse-Geisser corrected $P = 0.001$].

To parse the main effect of temporal distance, we used trend analysis. The majority of the variance (94.6%) was accounted for by a linear trend [$F(1,68) = 246.47$, $P<0.001$]. This demonstrates that performance on the task linearly increased as the temporal distance between test objects increased (Figure 2).

To more closely investigate the interaction between age and group, we used post hoc contrast–contrast interactions. We calculated a Scheffe's critical F (9.62) value for the contrast–contrast interactions to correct for family-wise error caused by multiple comparisons. All contrast–contrast interactions were corrected for nonsphericity. Using our conservative critical F, the only significant contrast–contrast interaction between the groups was 5-lag versus 15-lag [$F(1,68) = 16.12$], suggesting that OA's are less able to benefit from this moderate increase in temporal distance than YA's, but can do so at larger temporal distances. Although the contrast–contrast interaction between the 15-lag and 28-lag conditions was not significant [$F(1,68) = 0.92$] it is important to note that YA performance in the 28-lag condition was near ceiling (mean = 94.79%).

Because we used a blocked design, there was a possibility that the build-up of proactive interference over the course of the task may influence behavior in later blocks. To test this possibility, we conducted a 6 × 5 × 2 ANOVA with Block and Lag as within-subjects factors, and Group as a between-subjects factor. Neither the main effect of Block nor the interactions between Block and the other variables were significant (all P's > 0.05).

SP Effects are Diminished in Older Adults

To examine the effect of SP on discrimination in YA and OAs, we used a 2 × 3 factorial ANOVA with SP (three levels: primacy, recency, and middle) as the within subjects factor and age as the between subjects factor. The ANOVA revealed a significant main effect of SP [$F(2,136) = 19.96$, $P < 0.001$], a significant main effect of age [$F(1,68) = 36.62$, $P < 0.001$], and a significant interaction between age and SP [$F(2,136) = 4.28$, Greenhouse-Geisser corrected $P = 0.018$].

The main effect of age suggests that YAs performed better in this task than did OAs. To parse the main effect of SP (collapsing across age), we conducted pairwise comparisons using Tukey's procedure. All comparisons were significant ($P < 0.01$) meaning that, holding temporal lag constant, temporal order was easiest to judge when one of the images in the test pair occurred at the beginning of the study sequence (primacy), somewhat harder to judge when one of the images in the test pair appeared at the end of the sequence (recency), and hardest to judge when both images appeared in the middle of the sequence. We calculated simple main effects of age at each SP, and all were significant as well [primacy: $F(2,204) = 29.5$, $P < 0.0001$; recency: $F(2,204) = 31.71$, $P < 0.0001$; middle: $F(2,204) = 5.91$; $P < 0.05$], suggesting that the YA group outperformed the OA group in every condition (Fig. 2).

We then considered the interaction between SP and age. We found that the contrast–contrast interaction between primacy + recency versus middle and old versus young was significant and accounted for the majority of the interaction [$F(2,134) = 9.13$; Scheffe's $F(6.13)$; $P < 0.001$; proportion of interaction = 0.99], suggesting that the effect of SP changes with age. Since we observed an effect of age even on the middle lag condition in the SP blocks, which suggests a more general impairment in temporal processing, we attempted to control for such a deficit by calculating the benefit of primacy and recency for each participant. These scores were calculated by subtracting the participant's mean performance on the middle condition from their mean performance in the primacy or recency conditions. The benefit of primacy was greater for the YA group (mean = 0.18, std = 0.14) than for the OA group (mean = 0.08, std = 0.20; $t = 2.33$, $P < .03$, two-tailed). Similarly, we found that the benefit of recency was diminished in the OA group (mean = 0.01, std = 0.14) compared to the YA group (mean = 0.11, std = 0.13; $t = 3.01$, $P < 0.004$, two-tailed). Taken together, these results suggest that, in addition to general task deficits, the OA group experienced attenuated enhancement of performance for items occurring at the beginning or ending of the list compared to the enhancement enjoyed by the YA group.

Individual Differences in Task Performance in Older Adults

A key goal of aging research is to identify behavioral and biological markers that serve as early indicators of pathological aging. Examining individual differences in OAs offers a powerful means by which to investigate subclinical neuropsychological impairments that may predict later cognitive decline. Past behavioral studies of aging have dichotomized aged subjects into impaired and unimpaired groups based on memory performance. For example, studies in rodents used performance on the Morris Water Maze (Gallagher, Burwell and Burchinal, 1993; Gallagher et al., 2003, 2006) whereas studies in humans have used neuropsychological measures (Stark et al., 2010; Holden et al., 2013). In both cases comparing aged-impaired (AI) versus aged-unimpaired (AU) individuals has allowed for detailed analyses of behavior and neural systems.

When determining how best to separate the groups, we considered a recent study by Bruno et al. (2013), which reported that a diminution of the effect of primacy in free recall of words was an early indicator of later cognitive decline. Upon examination of participant accuracy on the primacy condition in our SP blocks, we noticed that the distribution was somewhat bimodal with one high-accuracy group (~90%, on par with YA performance) and one low-accuracy group (~70%, more than two standard deviations lower than the YA mean). Using the cutoff criterion of two standard deviations from the mean of YA performance, we split the OA group into AI ($n = 22$) and AU groups ($n = 21$).

We performed a 3 × 5 ANOVA using group (YA vs. AI vs. AU) as the between subjects factor and temporal lag as the within subjects factor. There was a significant main effect of group [$F(2,67) = 31.23$ $P < 0.001$], a significant main effect of temporal lag [$F(4,268) = 81.66$, Greenhouse-Geisser corrected $P < 0.001$], and a significant interaction between group and temporal lag [$F(8,268) = 4.58$, Greenhouse-Geisser corrected $P < 0.001$]. To parse the interaction between group and interference, we used contrast–contrast interactions, which were corrected for nonsphericity. To correct for family-wise error inflation by multiple comparisons, we calculated a Scheffe's critical $F(9.62)$. The contrast of 5-lag versus 15-lag and AI versus the other two groups was significant [$F(1,67) = 18.57$].

To further investigate the group differences, we calculated simple main effects of group for each temporal lag condition. There was a significant simple main effect of group at the 28-lag condition [$F(2,335) = 22.24$, $P < 0.001$], at the 15-lag condition [$F(2,335) = 21.88$, $P < 0.001$], and at the 10-lag lag condition [$F(2,335) = 18.61$, $P < 0.001$]. Pairwise group differences were investigated using simple effects contrasts, corrected for multiple comparisons using Scheffe's procedure. Significant contrasts all had F's higher than Scheffe's critical F(6.05) and are indicated in Figure 3a.

To summarize performance for each subject on the task we derived an overall measure of accuracy as a function of lag by calculating the area under the curve (AUC). A one-way ANOVA using group as the independent variable and AUC as the dependent variable was significant, and corroborated the main effect of group in the prior ANOVA [$F(2,67) = 30.45$, $P < 0.001$]. Pairwise comparisons using Tukey's honestly significant difference (HSD) revealed that there were significant pairwise differences across all pairs of groups (YA, AI, and AU; all $P < 0.005$).

Finally, to determine whether standard neuropsychological tasks may be sensitive to such a deficit in temporal memory and to evaluate the external validity of our procedure, we correlated the AUC in the variable temporal lag task and participants' score on the delayed recall component of the RAVLT. Across all participants, we found a significant positive correlation (Pearson $r = 0.54$, $P < 0.0001$, two-tailed). To determine whether the delayed recall component of the RAVLT alone could be used to arrive at the same AI versus AU distinctions in our study, we conducted two additional analyses: the first used RAVLT delayed recall as the dependent measure and compared the three groups (Young, AI, AU, based on primacy effects). Here, we found that the effect of group was significant [$F(2,67) = 18.11$, $P < 0.001$], but post hoc comparison of the AI versus AU groups using Tukey's HSD showed no significant difference ($P = 0.11$). In the second analysis, we used discrimination performance as the dependent measure and group status, along with lag as the independent measures. For group status, we redivided our OAs group into AI and AU based on their performance on the RAVLT delayed recall. We set our criterion for AU as performing below two standard deviations from the YA mean, which meant that those scoring eight or higher were considered AU ($n = 23$). A 3 × 5 ANOVA showed a significant effect of group [$F(2,67) = 21.88$, $P < 0.001$], but a post hoc contrast revealed that the difference between AI and AU did not survive our correction for multiple comparisons [$F(2,67) = 3.74$; Scheffe's critical $F = 6.13$]. Taken together, these data suggest that the RAVLT delayed recall is somewhat but not completely overlapping with our temporal discrimination task performance and that perhaps these tests are sensitive to different neural impairments.

DISCUSSION

In this study, we introduced a novel behavioral paradigm designed to assess temporal order memory. Specifically, we designed a paradigm that controlled exposure and response times, used visually distinct stimuli, and measured performance over a larger range of temporal distances than have previous studies. We designed the paradigm in an attempt to resolve conflicting results of previous behavioral studies examining the effect of aging on temporal order memory.

In general, we found that OAs were impaired relative to younger adults in determining the temporal order of previously experienced events. However, the extent of this impairment was subject to much individual variability in OAs. Using a variant on the task that selectively tested SP effects (i.e., primacy and recency), we found that about half of the OAs tested had impaired primacy judgments, whereas the other half were unimpaired. Using this task to classify older subjects into "AI" and "AU," we re-examined performance on the temporal order discrimination task and found that while both groups were impaired compared to the young, the impairment was much more dramatic in the AI group.

The AI group seems to have a general impairment in temporal memory (across all lags), whereas the AU group was impaired relative to younger adults only in the moderate lag conditions. The behavior in the AU group is consistent with a decreased efficacy of a pattern separation computation. When mnemonic interference is high or low, the groups perform equally, however with moderate interference, AU adults demonstrate deficits in performance, indicating that their ability to resolve mnemonic overlap has been diminished. Although this behavior is consistent with a deficit in a pattern separation process (Reagh et al., 2013), an investigation of neural activity during this task will be required to confirm that. The AI group, conversely, may have behavioral deficits that stem from a combination of pattern separation impairments and other general mnemonic impairment that may be subserved by other systems (e.g., prefrontal cortex). This is not unexpected, given that the same subjects also present with deficits in primacy judgments. Although the neural mechanisms underlying the primacy effect have not yet been fully elucidated, evidence suggests that the effect is dependent upon both the hippocampus (Kesner and Novak, 1982; Strange et al., 2002) and the dorsolateral prefrontal cortex (Innocenti et al., 2013). We have suggested in the past that such a general impairment (i.e., failure to show rescue of behavior in the most discriminable conditions) may be a hallmark of pathological aging (Reagh et al., 2013). This is also consistent with other reports that deficits in primacy may predict cognitive decline (Bruno et al., 2013).

One pertinent question is whether or not standard neuropsychological testing that is commonly used to assess medial temporal lobe and prefrontal cortical function is sensitive to the age-related deficits reported herein. We examined scores on the RAVLT delayed recall (Rey, 1941) a word list learning test that is sensitive to medial temporal lobe (MTL) dysfunction (Lezak, Howieson, and Loring, 2004). Although prior studies in humans have used scores on the RAVLT delayed recall as a criterion for dividing aged subjects into AI and AU groups, these studies examined memory for objects independent of temporal information. While the RAVLT assesses word list learning, it does not assess the temporal sequence in which those words were presented. Thus, we reasoned that it may not be sensitive to impairments affecting temporal memory specifically, and as such may not be the best criterion for discerning gross temporal memory impairment from more subtle impairment. We found that although there is an age-related decline in RAVLT delayed recall, consistent with prior work (Stark et al., 2013), there was no difference between the AI and AU groups. This suggests that our temporal memory task may be sensitive to more subtle impairments in memory function than standard neuropsychological testing and may offer potential avenues for diagnosis and prediction of cognitive decline.

The results of our study are consistent with Tolentino et al. (2012). We extend these results here using a greater range of temporal distances and using a SP task as an additional means by which to examine individual differences with age. Our techniques allowed us to investigate the nuances of the age-related deficit in detail. Because the present study used a paradigm that was very similar to that of Perlmutter et al. (1981) with regard to the nature of the stimuli presented, it is likely that the inconsistency of the results between Perlmutter et al. (1981) and both the present study and Tolentino et al. (2012) stems from the use of a free response paradigm in Perlmutter et al. (1981). Both Tolentino et al. (2012) and the present study controlled presentation time and response time windows. This suggests that there may be deficits that are masked in behavioral paradigms that do not explicitly control elapsed time.

Together, these studies highlight the importance of using converging experimental design to bridge the gap between animal and human research. While our approach (varying temporal lag interference) is conserved across species, our particular task design was optimized for human participants. An alternative approach is to design behavioral tasks that are analogous across species. One previously discussed example is Tolentino et al. (2012), who modeled their temporal order memory task after prior work in rodents by Gilbert, Kesner and Lee, (2001). Another example is Allen et al. (in press) who created a sequence recognition task that was designed with cross-species applications in mind. The authors found that behavior (accuracy, frequency, and types of errors) were highly conserved across species suggesting that the task is reliant on similar mechanisms in rodents and humans. Together, these analogous studies provide strong evidence for shared cognitive processes underlying temporal memory across species.

The present study extends a growing body of literature suggesting that OAs do not perform as well as YAs on mnemonic discrimination tasks that putatively assess pattern separation. Although the nature of the discriminations made in these studies vary widely–including object identity (Toner et al., 2009; Yassa et al., 2011a; Stark et al., 2013), spatial location (Stark et al., 2010; Holden et al., 2012; Reagh et al., 2013), and words (Ly et al., 2013) —the nature of the deficits is often very similar, that is, OAs are impaired relative to younger adults when the discrimination involves moderate similarity, but often “catch up” to younger adults when there is sufficient dissimilarity (i.e., the conditions with the least interference). With this in mind, we propose that it is a distinct possibility that these behavioral tasks, although the information domains are varied, assay a shared domain-general neural computation, that is, hippocampal pattern separation (Azab, Stark, and Stark, 2013) that declines in normal aging.

One potential limitation of this study is that the sample size was not large enough to allow us to investigate individual differences in detail. Our analysis of group differences based on dichotomized primacy performance is nevertheless informative. Future studies with larger samples are necessary to examine the full range of individual differences in temporal discrimination and other potential predictor variables.

Although the neural basis of temporal memory in YA and OA has not been examined in detail, the tasks presented herein offer a potential paradigm for future imaging studies addressing these questions. The MTL and the prefrontal cortex are especially vulnerable to the effect of aging (Burke and Barnes, 2006), thus cognitive tasks that target these systems are likely to be the most sensitive to age-related changes in cognition. The neural correlates of performance on this task as well as age-related changes in performance have yet to be elucidated. This neurobiological validation is going to be necessary before these assays are used in a diagnostic or predictive fashion.

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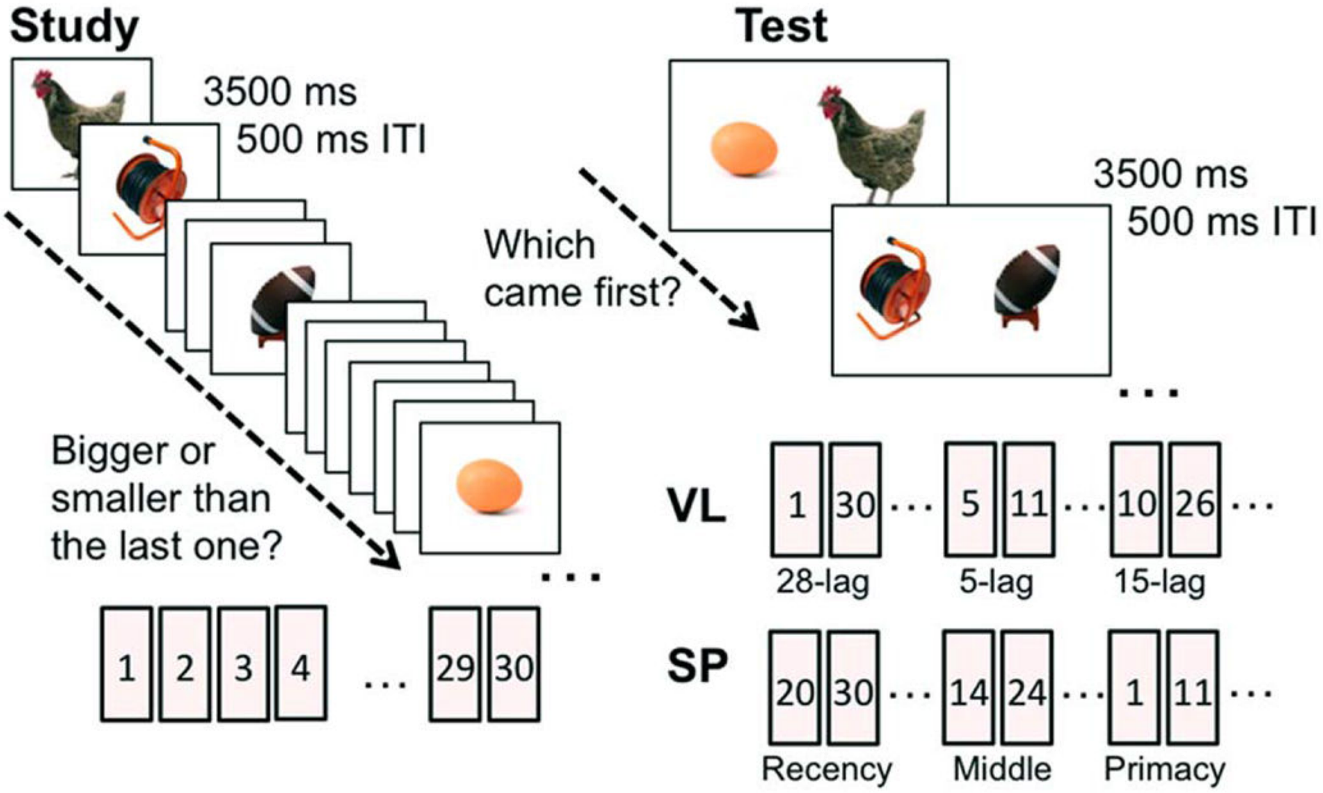

FIGURE 1.

Task Schematic. During the study phase, subjects viewed pictures one at a time and were asked to indicate for each picture if the item shown was bigger or smaller than the one before. Each block consisted of 30 trials. During the test phase, participants viewed pairs of images on the screen and were asked to indicate which came first. During the VL blocks, the two stimuli were chosen such that during the study phase they were presented at a specific lag (number of intervening items). Sample lags are shown (5, 15, 28). During the SP blocks, the two stimuli were chosen such that the lag was always 10 intervening items but the SP during study was either at the beginning (primacy), end (recency), or the middle of the sequence. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.].

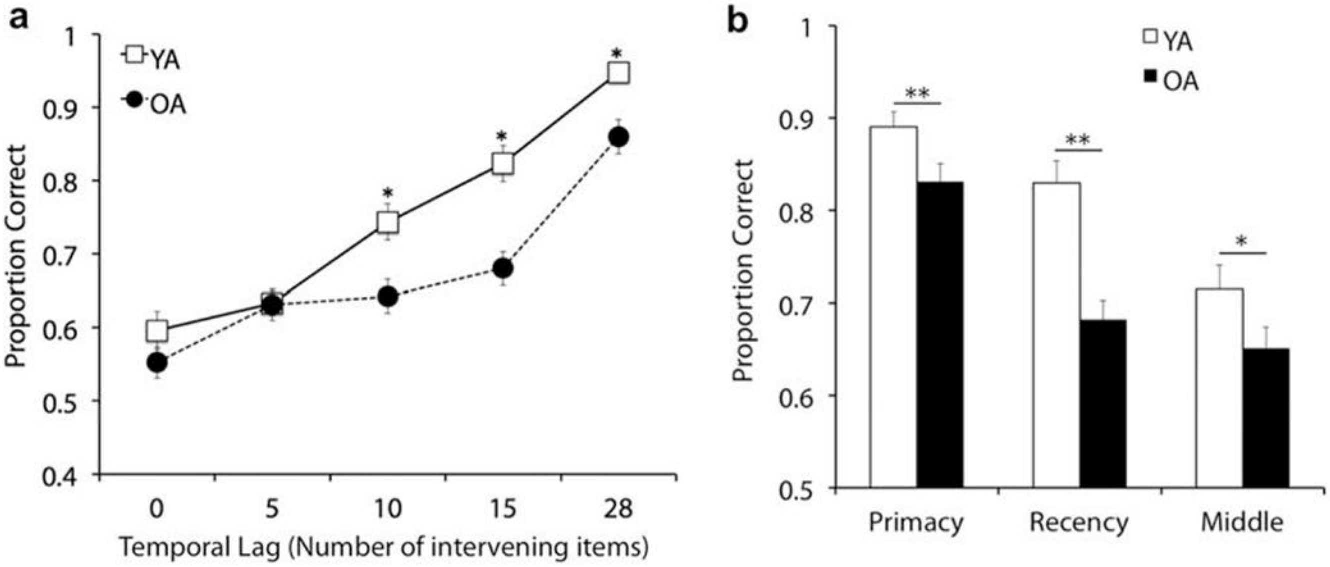

FIGURE 2.

Impaired temporal discrimination in OA. (a) Discrimination performance in YAs and OAs at all lag levels in the VL conditions. Performance in both groups linearly increased as a function of increasing temporal lag. OAs were selectively impaired at the higher lags (10, 15, and 28). (b) Discrimination performance in YA and OA in the SP conditions showing impaired performance in OA across all conditions. The interaction between condition and age was significant indicating that the magnitude of the difference between groups in the primacy/recency conditions was larger than in the middle condition.

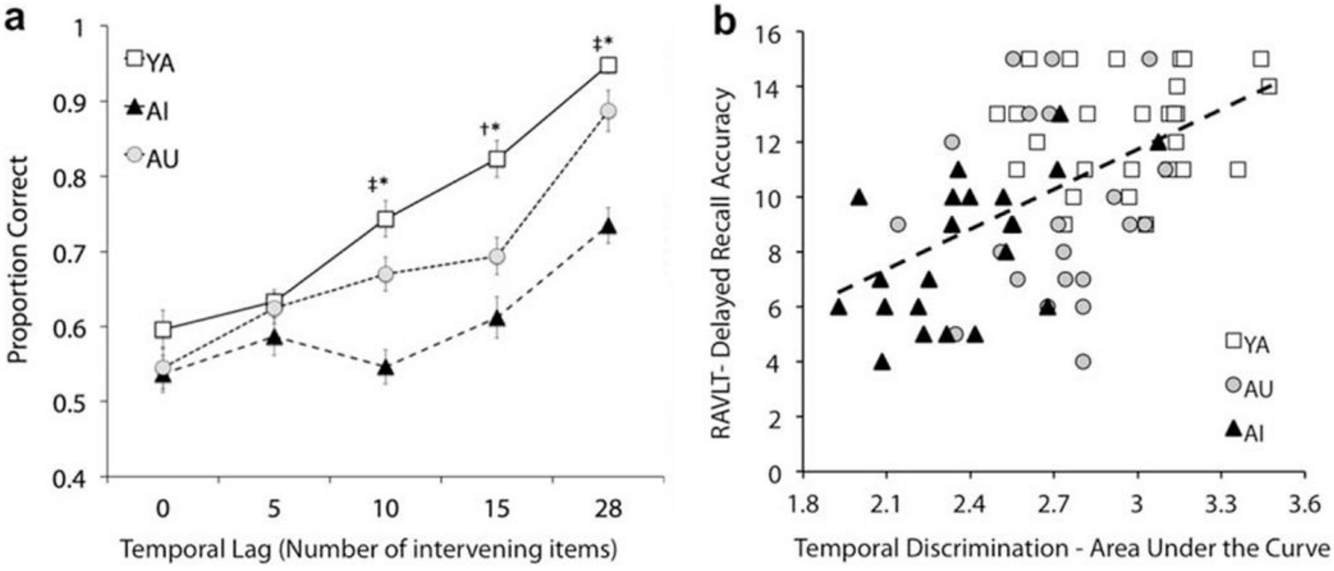

FIGURE 3.

Individual differences in temporal discrimination in OAs. (a) Discrimination performance in YAs, OAs who were impaired on primacy condition (AI), and OAs who were unimpaired on primacy condition (AU). Performance in all groups linearly increased as a function of increasing temporal lag. Performance in the AU group was lower than YA group only at lag 15. Performance in the AI group was lower than the YA group at lags 10, 15, and 28 and lower than the AU group at lags 10 and 28 († - AU < YA; ‡ - AI < AU; AI< YA).
(b) Correlation between temporal discrimination performance (quantified as area under the curve) and RAVLT—delayed recall component.