Recollection- and Familiarity-Based Memory in Healthy Aging and Amnestic Mild Cognitive Impairment

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Little is known about the cognitive mechanisms of the memory impairment associated with amnestic mild cognitive impairment (aMCI). We explored recollection and familiarity in 27 healthy young adults, 45 healthy older adults, and 17 individuals with aMCI. Relative to the younger adults, recollection was reduced in the older adults, especially among those with aMCI. Familiarity did not differ among groups. In the healthy younger and older adults, better performance on a set of clinical memory measures that are sensitive to medial temporal lobe functioning was associated with greater recollection. In addition, among the healthy older adults better executive functioning was also associated with greater recollection. These results are consistent with the notion that recollection is a product of strategic processes mediated by the prefrontal cortex that support the retrieval of context-dependent memories from the hippocampus. Hippocampal atrophy associated with aMCI may disrupt this brain network, and thereby interfere with recollection.

Keywords: amnestic mild cognitive impairment, aging, memory, recollection, familiarity

Considerable research focuses on factors that predict who will progress from aMCI to dementia, including apolipoprotein E4 allele carrier status (Devanand et al., 2005), cerebrospinal fluid tau (Schönknecht, Pantel, Kaiser, Thomann, & Schröder, 2007), measures from structural and functional imaging (e.g., Devanand et al., 2007; Hirao et al., 2005; Rossini et al., 2006; Tapiola et al., 2008), and standardized neuropsychological testing (Griffith et al., 2006; Perri, Serra, Carlesimo, & Caltagirone, 2007; Tabert et al., 2006; Tierney, Yao, Kiss, & McDowell, 2005). Moreover, cognitive rehabilitation methods to improve functioning in hopes of delaying progression to dementia are beginning to appear in the literature (Belleville et al., 2006; Rapp, Brenes, & Marsh, 2002; Rozzini et al., 2007; Troyer, Murphy, Anderson, Moscovitch, & Craik, 2008). However, relatively little research has investigated the cognitive mechanisms of memory deficits in aMCI. Gaining a better understanding of how memory is affected in aMCI will not only improve researchers’ understanding of preclinical dementia, but also will help target processes for rehabilitation.

In the current study, we focused on the role of automatic and controlled memory mechanisms, because evidence from neuropsychological and neuroimaging studies suggests that controlled mechanisms would be particularly affected in aMCI. Controlled memory mechanisms are conscious, effortful processes whereas automatic memory processes operate outside conscious control. Amieva, Rouche-Leroyer, Fabrigoule, and Dartigues (2000) compared memory for unrelated word pairs with memory for related word pairs, under the presumption that the former requires more controlled memory processes. Only memory for the unrelated word pairs discriminated older individuals who became demented two years later from those who did not. Perri, Carlesimo, Serra,
and Caltagirone (2005) argued that aMCI participants’ deficits in controlled memory processes contributed to their failure to benefit from categorizable over unrelated word lists, and to their engagement in less semantic clustering than healthy controls. Finally, it has been argued that performance on yes-no recognition tests relies more on controlled memory processes, whereas performance on forced-choice recognition tests can be mediated by automatic memory processes (Bastin & Van der Linden, 2003; Norman & O’Reilly, 2003). Westerberg et al. (2006) and Bennett, Golob, Parker, and Starr (2006) both found that a yes-no recognition test discriminated individuals with aMCI from healthy controls better than did a forced-choice recognition test.

The conclusion from these studies that controlled, but not automatic, memory processes are affected by aMCI is intriguing, but strictly inferential. No study to date has provided direct estimates of controlled and automatic processes in aMCI. According to dual-process models of memory (e.g., Jacoby, 1991; Mandler, 1991), controlled and automatic processes (hereafter referred to as recollection and familiarity, respectively, following Jacoby, 1991) independently mediate memory performance. Recollection refers to conscious retrieval of items bound to their context (e.g., spatial location, temporal position, or source modality), whereas familiarity refers to the automatic feeling, devoid of contextual detail, that an item has been recently experienced. There are various means to estimate the separate influences of recollection and familiarity: (1) the process dissociation procedure, that pits recollection and familiarity against each other (Jacoby, 1991); (2) signal detection analyses to generate receiver operating characteristic curves (Yonelinas, 1994, 2002); and, (3) the remember-know paradigm (Tulving, 1985). Considerable research using these methods has revealed that healthy aging is associated with reductions in recollection (Hay & Jacoby, 1996, 1999; Howard, Bessette-Symons, Zhang, & Hoyer, 2006; Jacoby, 1999; Jennings & Jacoby, 1993, 1997; Prull, Crandell Dawes, McLeish Martin III, Rosenberg, & Light, 2006; Rybash & Hoyer, 1996; Rybash, Santoro, & Hoyer, 1998; Saltzhouse, Toth, Hancock, & Woodard, 1997; Titov & Knight, 1997). By contrast, familiarity is reported as either spared in old age (Hay & Jacoby, 1996, 1999; Howard et al., 2006; Jacoby, 1999; Jennings & Jacoby, 1993, 1997; Salthouse et al., 1997; Titov & Knight, 1997), or reduced, but such reductions are typically of a smaller magnitude than the declines in recollection (Duarte, Ranganath, Trujillo, & Knight, 2006; Rybash & Hoyer, 1996; Schmitter-Edgecombe, 1999; Toth & Parks, 2006). However, no research with these techniques has been carried out examining individuals with aMCI.

Predictions about the relationship between aMCI and these processes can be formulated based on results from human neuroimaging and animal lesion research. Prefrontal and medial temporal lobe regions have been implicated in recollection and familiarity. In prefrontal cortex, dorsolateral regions of the right hemisphere, and bilateral anterior and superior medial regions have been linked to both processes (see Skinner & Fernandes, 2007, for a review). However, activation in these same regions has also been associated with processes that would support recollection and/or familiarity. For example, right prefrontal regions have been linked to postretrieval monitoring (e.g., Cabeza, Anderson, & Locantore, 2003; Henson, Rugg, Shallice, & Dolan, 2000), anterior regions to source retrieval (e.g., Cansino, Maquet, Dolan, & Rugg, 2002; Kahn, Davachi, & Wagner, 2004), and superior medial regions to attentional control (MacDonald, Cohen, Stenger, & Carter, 2000). It is thus unclear to what extent these activations reflect recollection or familiarity, or the underlying mechanisms that support these processes.

In the medial temporal lobes, the hippocampus appears to be involved in contextual recollection, whereas neighboring perirhinal and parahippocampal cortex are associated more with familiarity (for a review, see Aggleton & Brown, 2006; but see Squire, Stark, & Clark, 2004), with extensive medial-temporal damage affecting both processes (Yonelinas, 2002). In a functional MRI study by Daselaar, Fleck, Dobbins, Madden, and Cabeza (2006), age-related reductions in recollection co-occurred with reductions in hippocampal activity, and age-related sparing of familiarity co-occurred with intact rhinal activation. The earliest volumetric loss in individuals with aMCI occurs in the hippocampus and entorhinal cortex, with volumes in these regions typically intermediate to those associated with healthy aging and AD (Jack Jr. et al., 2000; Killiany et al., 2000, 2002). Given these findings, our primary hypothesis was that aMCI would be associated with decrements in recollection that are greater than those associated with normal aging, but that familiarity would be more comparable across groups.

To this end, we developed an experimental process-dissociation task involving a long series of words, half presented visually on a computer screen, and half presented auditorily via computer speakers. Each word was repeated after a lag of 0, 3, or 12 intervening words, in either the Same modality (e.g., visual the first time, visual the second time) or a Different modality (e.g., visual the first time, auditory the second time). The task was conducted twice with different sets of words: once under Inclusion instructions, wherein participants were instructed to say “no” to new words and “yes” to repeated words regardless of the modality, and once under Exclusion instructions, wherein participants were instructed to say “no” to new items and to words repeated in a different modality, and “yes” to words repeated in the same modality.

The critical data were the probabilities of “yes” responses to Different modality repetitions under Inclusion versus Exclusion instructions. Under Inclusion instructions (say “yes” to any repeated word), recollection for the repeated word in its original modality [R] or familiarity [F] for the word in the absence of recollection for its original modality [F(1-R)] would lead to a correct “yes” response. By contrast, under Exclusion instructions (only say “yes” if the word has been repeated in its original modality), only familiarity for the word itself in the absence of recollection for its original source modality [F(1-R)] would lead to an erroneous “yes” response. Hence, an estimate of recollection was derived by subtracting the probability of “yes” responses to Different modality repetitions under Exclusion instructions from the probability of “yes” responses to Different modality repetitions.

The discrepancy regarding the age-related effects on familiarity may depend on how these estimates are derived (Healy, Light, & Chung, 2005), or on the level of recollection. Prull et al. (2006) found age equivalence in familiarity estimated from a process-dissociation procedure, but familiarity decrements in older adults when familiarity was estimated from a remember-know paradigm or from receiver-operating characteristic curves. Yonelinas (2002) argued that age-related decrements are evident in both recollection and familiarity when recollection is high, but are specific to recollection when recollection is low.
under Inclusion instructions. An estimate of Familiarity was then
derived by dividing the probability of “yes” responses to Different
modality repetitions under Exclusion instructions [that is, F(1-R)]
by 1-R.

Application of Inclusion and Exclusion conditions to estimate
recollection and familiarity has been criticized in the past because
some participants may be confused by the subtle differences in
task instructions, and because response bias is not always equated
between the two conditions (Curran & Hintzman, 1995; Graf &
Komatsu, 1994). To address these issues, we also derived esti-
mates of recollection and familiarity from the Exclusion task only.
Correct “yes” responses to Same modality repetitions could be
mediated by recollection, familiarity, or both [R + F(1-R)], while
erroneous “yes” responses to Different modality repetitions would
be mediated only by familiarity in the absence of recollection
[F(1-R)]. Therefore, the difference between these probabilities
provides an estimate of recollection. Correspondingly, the proba-
bility of “yes” responses to Different modality repetitions divided
by 1-R provides an estimate of familiarity. Demonstrating corre-
spondence between estimates of recollection and familiarity be-
tween the two methods would suggest that the results are not likely
due to confusion on the part of the participants or to differences in
response bias between tasks, and thus would support greater con-
fidence in the stability of the estimates.

We also wanted to explore the putative neural mechanisms of
recollection and/or familiarity decrements in aging and aMCI. Glisky,
Polster, and Routheauex (1995) have argued that performance on a set
of standardized memory measures reflects medial temporal lobe func-
tioning, as amnesic patients with brain damage involving the hip-
pocampus are impaired on these measures. All of the participants in
the current study were administered the memory measures constitut-
ing this medial temporal lobe composite. Given the association be-
tween recollection and the hippocampus, we predicted that higher
recollection estimates would be associated with higher medial tem-
poral lobe scores. However, frontal lobe scores were not related to familiarity. However,
Prull et al.’s (2006) process dissociation task produced the opposite pattern: an association of older adults’ frontal lobe scores with famil-

Method

Participants

Younger and older adults were recruited via a volunteer research
participant pool at Baycrest, a geriatric hospital and research facility
in Toronto, as well as by flyers and community talks targeting older
adults with concerns about their memory. Additional older partici-
pants were recruited via the volunteer research participant pool at the
University of Toronto, Mississauga. For inclusion in the study, par-
ticipants had to be native English speakers or to have learned English
before starting primary school, have at least a high school degree, and
be right-handed. Participants were included only if they had no
previous or current medical or psychiatric conditions (even if con-
trolled by medication) or current medications that are likely to affect
cognitive functioning, including stroke; epilepsy; neurodegenerative
disease; brain tumor; multiple sclerosis; heart disease; previous head
trauma followed by loss of consciousness exceeding five minutes,
persistent neurological deficits or known structural brain abnormali-
ties; diabetes mellitus; hypertension; hypercholesterolemia; hypo-
or hyperthyroidism; psychiatric disorder; neuroleptic use; anticonvulsant
use; benzodiazepine use; alcohol or substance abuse; or use of cog-
nitive enhancing agents. In addition, participants had to score within
normal limits on the Hospital Anxiety and Depression Scale (Zig-
mund & Snaith, 1983), and within normal limits in neuropsycholog-
tical testing, excepting the memory domain for participants with
mCI. Finally, for inclusion in the analyses, we wanted to be sure that
participants had understood the particular task instructions. We op-
erationalized this as making fewer than five errors out of 24 trials for
same and different repeats at Lag 0 on the experimental task [see
Procedure].

The data reported here are from 27 younger and 62 older adults.
Of the older adults, 45 were neuropsychologically normal, and 17
met neuropsychological criteria for aMCI (Winblad et al., 2004).
We operationalized these clinical criteria as follows: (1) perfor-
mance on one or more memory measure was 1.5 SD or more below
general cognitive functioning and intellectual ability (as assessed by the
DRS and Matrix Reasoning); (2) performance on all non-
memory measures was within the normal range; and, (3) partici-
pants reported no difficulties with activities of daily living.
The study was approved by the research ethics boards at Baycrest and
the University of Toronto. All participants provided informed
consent and were paid a small honorarium for their participation
($25 for younger adults and $40 for older adults).

Materials and Design

A pool of 576 two-syllable nouns was selected from the MRC
Psycholinguistic Database (http://www psy. uwa.edu.au/MRCDa taBase/ uwa_mrc.htm), and grouped into 48 sets of 12 words equated for word
length, Kučera and Francis (1967) word frequency, concreteness,
and imageability (all Fs (47, 528) < 1). The orders of the word
sets and words within the sets were independently randomized sepa-
ately for each participant, and then the first 12 sets (144 words) were
assigned to the Inclusion task, and the second 12 sets (144 words)
were assigned to the Exclusion task. The next six sets (72 words) were

2 Participants were not administered the Wisconsin Card Sorting Test,
WAIS–R Mental Arithmetic, or WMS-R Mental Control tasks that partly
contribute to the frontal lobe factor recommended by Glisky et al. (1995).
used for Inclusion practice trials, and the next six sets (72 words) were used for Exclusion practice trials.3

Words were repeated at one of three lags (0, 3, or 12 intervening words), and were presented in one of four modality conditions: auditory-auditory (AA), auditory-visual (AV), visual-auditory (VA), or visual-visual (VV), representing the presentation modality for the first and second time the word is presented. To balance lags and conditions across trials within each task, eight unique 24-trial sets were developed, each consisting of four repetitions at each lag. For each participant, the order of these eight trial sets was randomized separately for Inclusion and Exclusion. The eight trial sets were then assigned to the first 192 trials of each task, and the first four sets were reproduced to compose the remaining 96 trials. Within each trial set, the order of modality conditions (AA, AV, VA, VV) was separately randomized for each lag.

In summary, each task (Inclusion and Exclusion) contained 288 trials, with 144 words each presented twice. Within each task, each lag was tested four times in each of the 12 24-trial runs, with each of the four modality conditions tested once at each lag. In total for each lag within each task, there were 24 words repeated in the Same modality (AA and VV), and 24 words repeated in the Different (AV and VA) modality. The same procedures described above were used to create three 24-trial practice lists for each task. The order of task (Inclusion and Exclusion) was counterbalanced across participants.

Procedure

The study involved two sessions. The first session consisted of a 2.5-hr neuropsychological assessment for the older adults, and an abbreviated 1-hr assessment for the younger adults. For both age groups, the assessment consisted of Digit Symbol from the Wechsler Adult Intelligence Scale, 3rd Edition (WAIS-III, Wechsler, 1997) and the Mill Hill vocabulary test (Raven, 1965) to confirm the standard findings in cognitive aging research of age-related psychomotor slowing and preserved semantic memory, as well as the four tests needed to create the medial temporal lobe score identified by Gliksy et al. (1995): the California Verbal Learning Test (Delis, Kramer, Kaplan, & Ober, 1987), Logical Memory, Visual Paired Associates, and Verbal Paired Associates from the Wechsler Memory Scale—Revised (WMS-R, Wechsler, 1987). The older adults also received: 1) tests on which performance is sensitive to frontal lobe functioning: phonemic (FAS) fluency, the Trail Making Test, and Digit Span from the WAIS-III; 2) tests to rule out dementia: the Mini-Mental State Examination (MMSE, Folstein, Folstein, & McHugh, 1975), the Dementia Rating Scale (DRS, Mattis, 1988), and Lawton and Brody’s (1969) Activities of Daily Living scale; 3) tests to rule out impairments in nonmemory domains: Matrix Reasoning and Block Design from the Wechsler Abbreviated Scale of Intelligence (WASI, Wechsler, 1999), semantic (Animal) fluency; and, 4) the Hospital Anxiety and Depression Scale (HADS, Zigmund & Snaith, 1983) to rule out mood disturbances.

The second session lasted 1.5 to 2 hours, and began with the Inclusion and Exclusion tasks reported here. These tasks were followed by additional experimental tasks that are not relevant to the current study. E-Prime software (version 1.1, Service Pack 3; Psychological Software Tools, Inc.) was used to control stimuli presentation and response collection for the Inclusion and Exclusion tasks. The Inclusion and Exclusion tasks each contained 288 trials, presented in two blocks of 144 trials each, with a break in between blocks. On each trial, a word was presented auditorily via computer speakers playing prerecorded audio files or visually in the center of the computer screen in black, 40-point Arial lowercase font against a white screen for 850 ms (the longest duration of the auditory files). Participants were instructed to take as much time as they needed to respond verbally “yes” or “no” to each word with responses entered by the examiner. Following each response, a cross-hair was displayed for a 1000 ms interstimulus interval.

As described above, for the Inclusion task, participants were instructed to say “no” to words the first time they were presented, and “yes” to repeated words, regardless of their modality (same or different). For the Exclusion task, participants were instructed to say “no” to words the first time they were presented and “yes” to words that were repeated in the other modality (i.e., AV and VA words), and to say “yes” to words that were repeated in the same modality (i.e., AA and VV words).

Both tasks began with a 24-trial practice block. If participants responded correctly to all four 0-Lag repetitions in the current practice block, then they proceeded to the experimental task. Otherwise, the instructions were repeated and participants attempted another practice block. After up to three practice blocks, regardless of whether the participant passed the third practice block, the program proceeded to the instructions for the experimental blocks. All participants passed the practice blocks for the Inclusion task, with younger adults, healthy older adults, and aMCI participants requiring an average of 1.19, 1.13, and 1.18 blocks of practice, respectively, F(2, 86) < 1. Three aMCI participants did not pass the third practice block for the Exclusion task, but nevertheless passed our inclusion criteria for the task itself (see below) and thus their data were included in the analyses. Young and healthy older participants required significantly fewer practice blocks for the Exclusion task than did the participants with aMCI (Ms = 1.04, 1.24, and 1.65, respectively), F(2, 86) = 7.24, p = .001, ηp² = .14. Ensuring that participants understood the specific task before starting the experimental trials was thought to be more important than equating exposure to the task prior to the experimental trials. Greater exposure to the task in the aMCI group would be expected to lessen their performance deficit on the actual task; yet as will be seen below, these deficits were significant nonetheless.

For the experimental trials, data were retained for participants whose accuracy was > .82 (i.e., no more than 4 errors out of 24) in the same (AA and VV) and different (AV and VA) repetition conditions at Lag 0 in each task, as worse performance indicated that they had not understood the task instructions (e.g., applied Inclusion rules during Exclusion, or vice versa). The data from one healthy older participant and two participants with aMCI were excluded from the analyses for failing to meet this criterion.

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3 Pilot versions of these tasks consisted of larger word sets requiring a total of 576 words. In the data reported here, each participant was presented with a random subset of 432 of these words representing 36 sets of 12 words equated for length, frequency, concreteness, and imageability.
Results

Demographics and Neuropsychological Results

Demographic and neuropsychological test data are presented in Table 1. The healthy older and aMCI groups did not differ in age, \( t(60) < 1 \), and all three groups had comparable levels of education, \( F(2, 86) < 1 \). Group differences in performance on the neuropsychological tests were explored using independent sample \( t \) tests using a Bonferroni-adjusted \( p < .001 \) to correct for multiple comparisons. Comparisons between the younger and older groups were made to explore age-related effects. Diagnosis of aMCI was a clinical judgment based on performance on the entire battery of neuropsychological tests. Therefore, the pattern of significant and nonsignificant differences between the healthy older adult and aMCI groups is reported to confirm that diagnosis of aMCI was consistent with published criteria (Winblad et al., 2004).

Consistent with much previous research, the healthy older adults outperformed the younger adults in vocabulary, but had significantly slower psychomotor speed (Digit Symbol). The young adults also performed better than the healthy older adults on each of the CVLT measures reported in Table 1, Verbal Paired Associates I, and Visual Paired Associates I. However, there were no age-related effects on Logical Memory I, Visual Paired Associates II, or Verbal Paired Associates II (the latter two owing to ceiling performance in both groups).

Participants with aMCI demonstrated significant long-term episodic memory deficits relative to their healthy counterparts on every episodic memory measure. With one exception, there were no differences between these two groups on any of the nonmemory measures, including MMSE, DRS, ADLs, Digit Symbol, Matrix Reasoning, Block Design, Trail Making, and phonemic and semantic fluency. The exception was the superior performance of the healthy older adults on the Mill Hill vocabulary test, on which the aMCI participants performed similarly to the young adults. Perhaps the difficult nature of the vocabulary test revealed early semantic deficits. It should be noted that participants with fluency impairments were excluded from this study for having deficits in multiple cognitive domains.

Following Glisky et al. (1995), performance on the CVLT Delayed Cued Recall, WMS-R Logical Memory I, WMS-R Verbal Paired Associates I, and WMS-R Visual Paired Associates II was standardized, and then these \( z \)-scores were averaged to obtain a

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<tr>
<th>Table 1 Mean Demographic Data and Neuropsychological Performance in Younger, Older, and aMCI Participants (SD in Parentheses)</th>
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<td>Demographics</td>
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<td>Age (years)</td>
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<td>Education (years)</td>
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<td>General abilities</td>
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<td>MMSE</td>
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<td>Long-term episodic memory</td>
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<td>WMS-R Logical Memory</td>
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<td>WMS-R Visual PA II</td>
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<td>WAIS-III Digit Symbol</td>
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<td>WAIS II Block Design</td>
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<td>Digit Span Forward Longest List</td>
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<td>Hospital Anxiety and Depression Scale</td>
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Note. CVLT = California Verbal Learning Test; WMS-R = Wechsler Memory Scale-Revised; WAIS-III = Wechsler Adult Intelligence Scale-III; WASI = Wechsler Abbreviated Scale of Intelligence. Means are total scores unless otherwise noted.

\( ^a \) Age effect (Young \( \neq \) Old, \( p < .001 \)).  
\( ^m \) MCI effect (Old \( \neq \) MCI, \( p < .001 \)).
composite medial temporal lobe score. Compared to the healthy older adults’ composite medial temporal lobe score ($M = 0.05, SD = .42$), the corresponding scores for the younger adults were reliably higher$^4$ ($M = 0.67, SD = .28$), $t(69) = 7.57, p < .001$, whereas those for older adults with aMCI were reliably lower ($M = -1.18, SD = .55$), $t(23) = 8.32, p < .001$.5

FAS, Trails B, and longest list on Backward Digit Span scores were standardized across the two older adult groups and then averaged to obtain a composite frontal lobe score. These measures were not administered to younger adults. Compared to healthy older adults’ composite frontal lobe scores ($M = 0.09, SD = .76$), the corresponding scores for the older adults with aMCI were marginally lower ($M = -0.27, SD = .60$), $t(37) = 1.97, p = .06$. 

Experimental Task Performance

The proportions of “yes” responses on the Inclusion and Exclusion tasks were analyzed separately for new words (i.e., false alarms), and repeated words. Partial $\eta^2$ effect sizes are reported for all significant effects. Significant interactions were further explored with Tukey’s HSD post hoc comparisons.

New Words. “Yes” responses to new words were analyzed in a $3 \times 2$ mixed ANOVA as a function of Group (Young, Old, aMCI) and Task (Inclusion, Exclusion). False alarms were higher in the Inclusion ($M = .03$) than Exclusion ($M = .02$) task, $F(1, 86) = 27.84, p < .001, \eta^2 = .25$, and higher in the aMCI group ($M = .03$) than the younger group ($M = .01$), with the older group falling in between ($M = .02$) but not significantly different from the other two groups, $F(2, 86) = 6.51, p = .002, \eta^2 = .13$. The interaction was not significant. To adjust for these task and group differences in false alarm rates, the probabilities of “yes” responses to new items were subtracted from the probabilities of “yes” responses to repeated items.

Repeated Words. “Yes” responses to repeated words were analyzed separately for the Inclusion and Exclusion tasks in $3 \times 3 \times 2$ mixed ANOVAs as a function of Group (Young, Old, aMCI), Lag (0, 3, 12), and Repetition Modality collapsed into Same (AA and VV) versus Different (AV and VA). The proportions of “yes” responses to repeated words in the Inclusion task are shown in Figure 1 (top panel). These proportions were higher in the younger group ($M = .92$) and healthy older group ($M = .88$) than in the aMCI group ($M = .83$), $F(2, 86) = 11.88, p < .001, \eta^2 = .22$. The ability to recognize a word as repeated declined as the Lag increased, $F(2, 172) = 120.19, p < .001, \eta^2 = .58$, more so for participants with aMCI than the other two groups, $F(4, 172) = 5.85, p < .001, \eta^2 = .12$. Recognition of repetitions was higher for Same than Different Modality repetitions, $F(1, 86) = 12.64, p = .001, \eta^2 = .13$, an advantage that increased as the Lag increased, $F(2, 172) = 5.94, p = .003, \eta^2 = .07$. However, the better recognition of Same than Different Modality repetitions was comparable among groups, $F(2, 172) = 1.91, p = .16$, and the three-way interaction was not significant, $F(4, 172) = 1.22, p = .30$.

The probability of responding “yes” to repeated words in the Exclusion task is shown in Figure 1 (bottom panel). Consistent with the task instructions, participants were much more likely to respond “yes” to Same than Different Modality repetitions, $F(1, 86) = 2599.48, p < .001, \eta^2 = .97$. The probability of “yes” responses was affected by the lag intervening between presenta-

\[ F(2, 172) = 9.66, p < .001, \eta^2 = .10, \] but decreased with increasing lag for Same Modality repetitions and increased with increasing lag for Different Modality repetitions, $F(2, 172) = 223.13, p < .001, \eta^2 = .72$. The difference between probabilities of “yes” responses to Same and Different repetitions decreased significantly from the younger group ($M$ difference = .87) to the older group ($M$ difference = .71) to the aMCI group ($M$ difference = .55), $F(2, 86) = 37.48, p < .001, \eta^2 = .47$. Finally, the three-way interaction among Group, Lag, and Repetition Modality was reliable, $F(4, 172) = 21.28, p < .001, \eta^2 = .33$. In short, relative to the younger adults, increases in Lag decreased “yes” responses to Same Modality repetitions and increased “yes” responses to Different Modality repetitions more for the healthy older participants, and even more for participants with aMCI.

A difference in response bias across the two tasks would be evident in the probabilities of “yes” responses to Same modality

4 $t$ tests were corrected for unequal variances.
5 When the scores of participants with aMCI were standardized to the mean and $SD$ of the healthy older adults, their composite memory scores were 1.73 standard deviations below their healthy counterparts, consistent with general guidelines for identifying aMCI (Petersen et al., 2001).
repetitions across the two tasks. As can be seen in Figure 1, participants applied more stringent criteria for the Exclusion than Inclusion task, particularly at the longer lags. These impressions were supported by a 3 (Group) x 2 (Task) x 3 (Lag) mixed ANOVA on the probability of “yes” responses to Same modality repetitions across the two tasks. As can be seen in Figure 1, participants applied more stringent criteria for the Exclusion than Inclusion task. Recollection estimates decreased as lags increased, \( F(2, 172) = 179.78, p < .001, \eta^2 = .68, \) more for the healthy older group than the younger group, and even more for the aMCI group, \( F(4, 172) = 14.37, p < .001, \eta^2 = .25. \) The analyses of Familiarity estimates included only Lags 3 and 12, as at Lag 0, Recollection estimates were equal to 1.00 for most participants and thus Familiarity was undefined. Even so, data from two young adults had to be excluded from the analysis of Familiarity because they had Recollection estimates of 1.00 at Lag 3 and/or Lag 12. Familiarity estimates did not differ as a function of Group, \( F(2, 84) = 2.16, p = .12, \) Lag, \( F(1, 84) = 2.24, p = .14, \) or their interaction, \( F(2, 84) = 1.78, p = .18. \)

Recollection and Familiarity estimates derived from the Exclusion task only are shown in Figure 2 (bottom panel). The pattern of Exclusion Recollection estimates was identical to those derived from both tasks, but the effects of Group, \( F(2, 86) = 38.19, \eta^2 = .47, \) Lag, \( F(2, 172) = 222.88, \eta^2 = .72, \) and their interaction, \( F(4, 172) = 20.91, \eta^2 = .33 (all p < .001) \) were numerically greater on Recollection estimates derived from the Exclusion task alone. Familiarity estimates from the Exclusion task at Lags 3 and 12 were definable (i.e., Recollection < 1) for all but one young participant. Again, the pattern obtained was similar to that derived from both tasks, with nonsignificant effects of Group, \( F(2, 85) < 1, \) Lag, \( F(1, 85) = 2.72, p = .10, \) or their interaction, \( F(2, 85) < 1. \) Hence, the two different estimation methods converged on the finding that, compared to young adults, healthy older adults and individuals with aMCI were impaired in recollection but not in familiarity, and the recollection deficit was more pronounced in older adults with aMCI than their healthy counterparts. It is also important to note that these critical findings were also obtained when the original data, uncorrected for false alarm rates, were analyzed.

**Correlation of Medial Temporal Lobe Scores and Frontal Lobe Scores With Recollection and Familiarity**

Table 2 shows the results of Pearson product–moment correlations of medial temporal lobe scores and frontal lobe scores with Recollection and Familiarity estimates at Lags 3 and 12 from the Exclusion task (similar results were obtained for correlations with estimates derived from both tasks). Note that the younger adults were not administered the tasks constituting frontal lobe scores. For the young and healthy older adults, but not participants with

<table>
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<tr>
<th>Table 2</th>
<th>Correlations of Recollection (Rec) and Familiarity (Fam) Estimates at Lags 3 and 12, Derived From the Exclusion Task With Medial Temporal Lobe Scores and Frontal Lobe Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rec-Lag 3</td>
<td>Rec-Lag 12</td>
</tr>
<tr>
<td>Medial temporal lobe scores</td>
<td></td>
</tr>
<tr>
<td>Young</td>
<td>.50**</td>
</tr>
<tr>
<td>Healthy old</td>
<td>.45**</td>
</tr>
<tr>
<td>aMCI</td>
<td>.23</td>
</tr>
<tr>
<td>Frontal lobe scores</td>
<td></td>
</tr>
<tr>
<td>Healthy old</td>
<td>.15</td>
</tr>
<tr>
<td>aMCI</td>
<td>−.24</td>
</tr>
</tbody>
</table>

*\( p < .05 \) (one-tailed). **\( p < .01 \) (one-tailed).
aMCI, medial temporal lobe scores were significantly correlated with Recollection at both lags. Frontal lobe scores were significantly correlated with Recollection at Lag 12 for the healthy older adults, but not for participants with aMCI. None of the correlations with the Familiarity estimates were significant.

Discussion

Our primary goal was to explore recollection and familiarity as a function of healthy aging and amnestic Mild Cognitive Impairment (aMCI). To this end, healthy younger adults, healthy older adults, and older individuals with aMCI performed a continuous word recognition task in which each word was repeated at a variable lag of intervening words, in either the same or a different modality than its original presentation. Inclusion instructions required participants to say “yes” to any repeated word, whereas Exclusion instructions required participants to say “yes” only to words that were repeated in their original modality. Based on the results from previous research, we predicted that aging, and particularly aMCI, would be associated with decrements in controlled recollection, but not in automatic familiarity.

In the Inclusion task, recognition of previously presented words declined with increasing lag, more so for the healthy older than younger adults, and even more precipitously for participants with aMCI. This pattern reflects a general memory decrement, but from these data alone it is not possible to determine the relative contributions of controlled recollection or automatic familiarity to these deficits. By contrast, in the Exclusion task, some of the words that were repeated in a different modality would have felt familiar, a familiarity that would have to be opposed by recollection in order to correctly respond “no”. Thus, erroneous “yes” responses to these words represent familiarity in the absence of recollection. Healthy older adults, and especially participants with aMCI, proved more prone than younger adults to such instances.

When estimates of recollection and familiarity were computed, age-related reductions in recollection were found that were even greater among older adults with aMCI. By contrast, familiarity did not differ among the groups. These data replicate many previous reports of a selective effect of healthy aging on recollection (for review, see Yonelinas, 2002). They also provide the first direct assessment of the mechanisms underlying the memory deficit in aMCI: Individuals with aMCI have intact familiarity, but a marked difficulty recollecting prior items in their context. One would therefore expect people with aMCI to have frequent everyday memory failures, such as recognizing someone but failing to recollect the person’s name or where they know the person from (see Estévez-González et al., 2003), or repeating a story to someone because of a failure to recollect to whom the story has been told. It is normal to make these sorts of memory slips from time to time; however, given the extreme recollection decrements in aMCI, one would expect them to occur more frequently in individuals with aMCI than their healthy counterparts.

These effects of normal aging and aMCI held across two means of estimating recollection and familiarity, one that combined data across tasks, and another using within-task data. Thus, it is highly unlikely that participant confusion regarding the task instructions contributed to these results. Moreover, although the Inclusion task led to a more liberal response bias than the Exclusion task, the fact that the same pattern of results held when these estimates were derived from the Exclusion task data alone suggests the results cannot be attributed to task-related differences in response bias. Similarly, although participants with aMCI had a higher false alarm rate than the healthy younger and older participants, the same pattern of recollection deficits in aMCI across lags was obtained whether or not data were corrected for false alarm rates. Finally, it should be highlighted that the participants in this study were extremely healthy (see exclusion criteria), hence it is highly unlikely that the recollection deficits revealed in the two older groups relative to the younger group could be attributed to factors other than normal aging or aMCI. Indeed, recollection deficits would likely have been even greater had participants with some common conditions, such as controlled hypertension or hypercholesterolemia, been included. Nevertheless, participants’ health status was determined by self-report. Our ongoing studies include a physician’s assessment, laboratory tests, and structural brain imaging to make certain that recollection deficits cannot be explained by some other medical condition of which the participants are unaware.

For the healthy younger and older adults, recollection was correlated with performance on a set of clinical memory measures that are sensitive to medial temporal lobe functioning. Performance on these same measures bore no relation to familiarity. Similar relationships between medial temporal lobe scores and recollection in healthy older adults have been reported by Prull et al. (2006) and Davidson and Glisky (2002). The group differences in recollection may reflect age-related and aMCI-related effects on contextual recollection mediated by the hippocampus. Studies of humans and animals with brain lesions have shown that damage to the hippocampus impairs recollection-based, but not familiarity-based memory (e.g., Aggleton & Brown, 1999; Fortin, Wright, & Eichenbaum, 2004). Moreover, functional neuroimaging studies have reported activation in the hippocampus associated with contextual recollection (Cansino et al., 2002; Daselaar, Fleck, & Cabeza, 2006; Davachi, Mitchell, & Wagner, 2003; Eldridge, Knowlton, Furmanski, Bookheimer, & Engel, 2000; Ranganath et al., 2004; Yonelinas, Otten, Shaw, & Rugg, 2005), whereas activation in perirhinal and parahippocampal cortices have been implicated in familiarity-based item retrieval (Daselaar, Fleck, & Cabeza, 2006; Davachi et al., 2003; Ranganath et al., 2004). The hippocampal atrophy associated with prodromal AD (Jack Jr. et al., 2000; Killiany et al., 2000, 2002) likely contributed to the severely compromised recollection and medial temporal lobe scores in participants with aMCI in this study, causing a range restriction that limited the ability to detect a significant relationship. It is also intriguing that for participants with aMCI, there was a moderate correlation between familiarity at Lag 12 and medial temporal lobe scores \((r = .28)\) that would be statistically reliable if the same relationship were to hold in a larger sample. When considered along with the functional neuroimaging literature, it is possible that due to hippocampal atrophy, participants with aMCI rely more than their healthy counterparts on perirhinal/parahippocampal-based familiarity. This is certainly a hypothesis worth pursuing in functional neuroimaging studies.

A significant correlation was also found between performance on clinical measures that are sensitive to frontal lobe functioning and recollection at Lag 12 in the healthy older adults. This relationship has been reported previously (Davidson & Glisky, 2002), and is consistent with neuroimaging findings showing activation of
the prefrontal cortex during recollection-based retrieval (see Skinner & Fernandes, 2008). It has been suggested that the prefrontal cortex mediates strategic processes such as attentional control, monitoring, and source retrieval that support the actual retrieval (i.e., ephorphy) of context-dependent memories via the hippocampus. Such an account of prefrontal and hippocampal involvement of recollection-based retrieval would explain the association of recollection with both medial temporal and frontal lobe scores.

Participants with aMCI did not show a relationship between frontal lobe scores and recollection as did their healthy counterparts. Various factors could account for this. First, due to our aim to restrict this study to participants with multiple-domain aMCI, we may have been too rigorous in excluding participants with mild executive problems and thus truncated the relationship between frontal lobe scores and recollection. Brooks, Weaver, and Scialfa (2006) reported that among older adults with MCI or probable mild dementia, performance on clinical memory measures was worse for individuals with impairments on at least one measure of executive functioning. However, there was a trend in our data toward lower frontal lobe scores in participants with aMCI than their healthy counterparts, which has also been reported by others (e.g., Kramer et al., 2006). Second, some canonical tests of executive functioning that were not included in the present study (e.g., card sorting) provide measures that may be more sensitive to aMCI and be more highly correlated with recollection. Third, the aMCI sample size in this study was also relatively small, and it will be important to explore these relationships further in larger samples. Fourth, an intriguing possibility is that hippocampal atrophy associated with aMCI may disrupt hippocampal-fronital brain networks that support recollection. In summary, on the basis of the current study, we cannot rule out the possibility that frontal lobe dysfunction contributes to aMCI-related deficits in recollection. Ongoing studies in our laboratory explore the contribution of executive functioning to recollection in healthy aging and aMCI more comprehensively.

Although well supported by theory and prior research findings, medial temporal lobe scores and frontal lobe scores are indirect indices of hippocampal and prefrontal functioning. These scores are affected by the clinical measures selected to comprise them, and the processes that support performance on the selected tests are undoubtedly multifactorial and mediated by multiple brain regions. Moreover, recollection and familiarity are not fixed properties of individuals’ memory system, but rather are quite sensitive to particular task demands. Both of these factors could account for some inconsistencies between the current results and those of other studies, such as the findings of significant correlations between healthy older adults’ familiarity estimates and frontal lobe scores (Prull et al., 2006), and between medial temporal lobe scores and familiarity (Davidson & Glisky, 2002) that were not obtained in the present study.

In conclusion, we report the first direct assessment of the cognitive mechanisms underlying memory impairment in aMCI. Familiarity for prior items is intact in aMCI, but recollection for items in their context is markedly disrupted. This selective effect of aMCI on recollection likely reflects disrupted hippocampal functioning, but future studies should also explore the contributions of executive functioning to recollection deficits in aMCI, and seek to confirm the relationships of hippocampal and frontal functioning with recollection in healthy older adult and aMCI populations, using functional neuroimaging techniques. It would also be interesting to explore these relationships in participants with multiple-domain amnestic MCI. Patients with concomitant executive dysfunction, in particular, may have even greater difficulties with recollection given the reported role of the frontal lobes in this controlled memory process. Finally, a longitudinal study would allow one to map the progression of aMCI and its effects on recollection, familiarity, and their neural underpinnings.

The results from this study have clinical implications as well. Rehabilitation aimed at improving memory functioning in healthy older adults should focus on enhancing contextual recollection. Strategies could be taught that facilitate binding of information to its context, such as elaboration and association. Alternatively, recollection could be trained directly, as has proven to be successful and to generalize to other memory tasks in healthy older adults (Jennings & Jacoby, 2003; Jennings, Webster, Kleykamp, & Dagenbach, 2005). Whether or not similar efforts would be successful in improving memory performance among individuals with aMCI is an empirical question, given that the plasticity of hippocampally mediated functions may be restricted by atrophy. However, as training recollection may help to delay progression from aMCI to dementia, this is a goal worth pursuing.

References


Received July 2, 2007
Revision received August 24, 2007
Accepted September 10, 2007