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Preserved frontal memorial processing for pictures in patients with mild cognitive impairment

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ABSTRACT

Amnestic mild cognitive impairment (aMCI) has been conceptualized as a transitional stage between healthy aging and Alzheimer's disease (AD). Therefore, understanding which aspects of memory are impaired and which remain relatively intact in these patients can be useful in determining who will ultimately go on to develop AD, and subsequently designing interventions to help patients live more engaged and independent lives. The dual-process model posits that recognition memory decisions can rely on either familiarity or recollection. Whereas research is fairly consistent in showing impaired recollection in patients with aMCI, the results have been mixed regarding familiarity. A noted difference between these studies investigating familiarity has been stimulus type. The goal of the current investigation was to use high-density event-related potentials (ERPs) to help elucidate the neural correlates of recognition decisions in patients with aMCI for words and pictures. We also hoped to help answer the question of whether patients can rely on familiarity to support successful recognition. Patients and controls participated in separate recognition memory tests of words and pictures while ERPs were recorded during retrieval. Results showed that ERP components typically associated with familiarity and retrieval monitoring were similar between groups for pictures. However, these components were diminished in the patient group for words. Based on recent work, the authors discuss the possibility that implicit conceptual priming could have contributed to the enhanced ERP correlate of familiarity. Further, the authors address the possibility that enhanced retrieval monitoring may be needed to modulate increased familiarity engendered by pictures.

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1. Introduction

Researchers and clinicians conceptualize mild cognitive impairment (MCI) as a transitional state between healthy aging and dementia (Petersen, 2004). Petersen and colleagues have divided MCI into distinct subtypes based on whether these patients demonstrate memory impairment (amnestic subtype) or impairment in some other cognitive domain (nonamnestic subtype). The amnestic subtype (aMCI) has received a great deal of attention, as it has been associated with a estimated tenfold increase in yearly conversion rate to Alzheimer's disease (AD) compared to age-matched controls with no cognitive impairment (Petersen). Characterization of the exact nature of the memory impairment associated with the amnestic subtype has only recently taken shape. Using experimental psychology and cognitive neuroscience to characterize aspects of memory early in the disease course can be useful in not only helping to determine who will go on to ultimately develop AD, but also in designing interventions to help patients live more engaged and independent lives by relying on aspects of memory that remain relatively intact.

In understanding how memorial decisions are made, researchers have proposed a dual-process model of recognition memory (Jacoby & Dallas, 1981; Yonelinas, 1994). Although there is much debate as to whether these two processes are completely independent, the dual-process model posits that recognition decisions can rely on the processes of *recollection* or *familiarity* (Yonelinas, 1994). Recollection refers to the retrieval of specific context-bound information about an item or event, whereas familiarity is defined as a more general, acontextual sense that an item or event has been previously encountered. These two constructs are often commonly experienced in daily life. For example, the unexpected sight of a particular man on a crowded city street may elicit an immediate feeling of knowing him without being able to produce any specific details about who he is or how he is known. After some deliberation, details may come to mind regarding the man's identity—perhaps the waiter at a restaurant you had visited one week earlier. Familiarity describes the initial feeling of knowing the man without

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being able to place him, while recollection captures the subsequent remembering of the specific details of his identity.

Recollection has been well studied in both healthy and diseased memory. Research suggests that the hippocampus (Cansino, Maquet, Dolan, & Rugg, 2002; Dobbins, Rice, Wagner, & Schacter, 2003; Eldridge, Knowlton, Furmanski, Bookheimer, & Engel, 2000; Yonelinas, Otten, Shaw, & Rugg, 2005), prefrontal regions (Burgess & Shallice, 1996; Dobbins, Foley, Schacter, & Wagner, 2002; Simons, Owen, Fletcher, & Burgess, 2005), and parietal regions (Ally, Simons, McKeever, Peers, & Budson, 2008; Skinner & Fernandes, 2007; Wagner, Shannon, Kahn, & Buckner, 2005) are activated during recollection. Event-related potential (ERP) studies of recognition memory associate recollection with a medial parietal old/new effect where studied items elicit more positive scalp activity than unstudied items (see Rugg & Curran, 2007; Friedman & Johnson, 2000 for reviews). This parietal effect increases with study–test repetitions (Johnson, Hashtroudi, & Lindsay, 1993), when items are rated as consciously recollected (Smith, 1993; Smith & Guster, 1993), and when source information is retrieved along with the studied item (Trott, Friedman, Ritter, Fabiani, & Snodgrass, 1999; Wilding, Doyle, & Rugg, 1995; Wilding & Rugg, 1996). However, recent work with parietal lesion patients has shown that parietal cortex is not critical to successful memory retrieval (Ally, Waring, McKeever, Milberg, & Budson, 2008; Simons et al., 2008), and in fact, an ERP study has shown that parietal regions are activated to a similar degree for falsely remembered items as they are for correctly remembered items (Goldmann et al., 2003). Although the exact role of parietal cortex in episodic retrieval remains unclear at present, recent hypotheses have suggested perhaps the parietal old/new effect indexes the amount of information retrieved (Fjell, Walhovd, & Reinvang, 2005; Vilberg, Moosavi, & Rugg, 2006), subjective aspects of recollection (Ally, Simons, et al., 2008; Davidson et al., 2008), or attention to memorial representations (Cabeza, Ciaramelli, Olson, & Moscovitch, 2008; Ciaramelli, Grady, & Moscovitch, 2008).

A number of behavioral, neuropsychological, and ERP studies have suggested that recollection becomes degraded during the normal aging process (Daselaar, Fleck, Dobbins, Madden, & Cabeza, 2006; Fjell et al., 2005; Joyce, Paller, McIsaac, & Kutas, 1998; Howard, Bessette-Symons, Zhang, & Hoyer, 2006; Jacoby, 1999; Jennings & Jacoby, 1993, 1997; Morcom & Rugg, 2004; Nielsen-Bohlman & Knight, 1995; Rugg, Mark, Gilchrist, & Roberts, 1997; Rybash & Hoyer, 1996; Senkfor & Van Petten, 1998; Swick & Knight, 1997; Spencer & Raz, 1995; Titov & Knight, 1997; Yonelinas, 2001). It has been hypothesized that a decline in the attentional resources allocated at encoding and/or retrieval, perhaps due to frontal lobe changes associated with normal aging, may be responsible for a decrease in recollection in this group (Anderson, Craik, & Naveh-Benjamin, 1998; Park, Smith, Dudley, & Lafronza, 1989; Salthouse, 1994; Whiting & Smith, 1997). In addition to the changes that accompany normal aging, patients with aMCI and AD undergo pathological changes in brain regions critical to recollection. By the time memory loss is clinically evident, warranting a diagnosis of aMCI, significant AD neurofibrillary pathology is seen in limbic regions, including transentorhinal regions, perirhinal cortex, amygdala, nucleus basalis (Arriagada, Growdon, Hedley-Whyte, & Hyman, 1992; Braak & Braak, 1991; Mesulam, 2000; Van Hoesen, Hyman, & Damasio, 1991), and most prominently in hippocampus and entorhinal cortex (Gomez-Isla et al., 1996). These regions continue to be affected as AD progresses (Mesulam, 1999), with pathology spreading further to neocortical areas such as temporal, parietal, occipital association, and frontal cortex in clinical AD (Braak & Braak, 1991; Delacourte et al., 1999; Grady et al., 1988; Ibanez et al., 1998; McKee et al., 2006).

Consistent with these areas of pathological involvement, behavioral studies suggest that recollection is impaired in patients with aMCI (Ally, Gold, & Budson, 2009a; Westerberg et al., 2006; Wolk, Signoff, & DeKosky, 2008) and patients with mild AD (Ally et al., 2009a; Balota, Burgess, Cortese, & Adams, 2002; Budson, Daffner, Desikan, & Schacter, 2000; Gallo, Sullivan, Daffner, Schacter, & Budson, 2004; Koivisto, Portin, Seinela, & Rinne, 1998; Knight, 1998; Smith & Knight, 2002). It has been proposed that in the face of impaired recollection, patients with mild AD become *over* reliant on familiarity (Budson et al., 2000; Budson, Desikan, Daffner, & Schacter, 2001; Budson et al., 2002; Gallo et al.; Pierce, Sullivan, Schacter, & Budson, 2005; Smith & Knight). Though the evidence is fairly clear that familiarity is aberrant in patients with AD (Ally et al., 2009a; Budson et al., 2000; Budson et al., 2002; Gallo et al.; Pierce et al.; Westerberg et al.), it remains unclear as to whether this process is impaired or disrupted in patients with aMCI.

ERP research has typically associated familiarity with an early midfrontal old/new effect, or FN400, where familiar unstudied items elicit more positive scalp activity between 300 and 500 ms than unfamiliar unstudied items (Ally & Budson, 2007; Curran, 2000; Goldmann et al., 2003; Rugg & Curran, 2007; Rugg et al., 1998). Woodruff, Hayama, and Rugg (2006) showed that the magnitude of the early frontal old/new effect varied directly with familiarity strength based on confidence ratings. Studies of healthy older adults show that familiarity remains intact (Ally, Waring, et al., 2008; Howard et al., 2006; Yonelinas, 2001), whereas the evidence for intact familiarity in patients with aMCI remains mixed. Westerberg et al. (2006) administered two separate picture recognition memory tests to groups of healthy older adults, patients with aMCI, and patients with mild AD. The first test required subjects to make standard old/new recognition memory decisions, while the second test required subjects to make forced-choice recognition decisions in which the target was grouped with highly related foils. Based on earlier evidence (Bastin & Van der Linden, 2003; Gardiner, Java, & Richardson-Klavehn, 1998), it has been suggested that standard recognition memory tests rely more on the process of recollection, whereas forced-choice tests rely more on familiarity. Results of Westerberg et al. showed that patients with aMCI and mild AD performed significantly worse on the standard old/new test compared to the healthy older adults, but performance on the forced-choice test was indistinguishable for the aMCI group and the healthy older adults. The authors concluded that while recollection is impaired in patients with aMCI, familiarity remains intact, and that it could be successfully used even in difficult tasks requiring subjects to identify a target from highly similar foils.

In contrast, two recent studies using words found impaired estimates of familiarity in patients with aMCI. In a multi-experiment study, Wolk et al. (2008) used process-dissociation and task-dissociation techniques to show that patients with aMCI demonstrated both impaired recollection *and* familiarity. Similarly, Ally et al. (2009a) examined recollection and familiarity in patients with aMCI and mild AD using confidence-based receiver operating characteristic (ROC) curves and a depth of processing manipulation. Patients with aMCI showed decreased estimates of recollection and familiarity in both shallow and deep encoding conditions compared to the healthy older adults. However, estimates of familiarity for the aMCI group were not as impaired as the mild AD group. It should be noted that in both the Wolk et al. and Ally et al. studies, when the two processes were directly compared, familiarity was estimated to be at least as impaired as recollection in patients with aMCI. Because previous research has shown that recollection tends to be impaired in healthy older adults, but familiarity remains relatively spared, Wolk et al. proposed that impairment in familiarity may reflect early tangle pathology in the perirhinal and entorhinal regions, thereby being a possible marker for early pathological changes indicative of future AD.

Ally et al. (2009a) discussed stimulus type as a possible reason for the conflicting results regarding familiarity in patients with

aMCI. Westerberg et al. (2006) used pictures, whereas Wolk et al. and Ally et al. used words. It is entirely plausible that pictures and words differentially affect familiarity in patients with aMCI. This hypothesis has some support from the study by Ally, Waring, et al. (2008), which showed that pictures differentially affected recollection in healthy older adults. The goal of the current investigation is to use ERPs to help elucidate the neural correlates of recognition for pictures versus words in patients with aMCI, and to provide neurophysiologic evidence as to whether familiarity might remain intact in these patients. On the basis of the findings of Westerberg et al., we predicted that for pictures, early frontal ERP activity would be similar for patients with aMCI and healthy older adults, suggesting intact familiarity. In contrast, on the basis of the Wolk et al. (2008) and Ally et al. (2009a) studies, we predicted that for words, early frontal ERP activity would be degraded in patients with aMCI compared to healthy older adults, suggesting impaired familiarity. In addition to examining the early frontal effect, we also examined the parietal and late frontal effects. As stated earlier, the parietal effect is thought to reflect recollection, and typically occurs between 500 and 800 ms post-stimulus. We predicted that the parietal effect would be significantly diminished in patients with aMCI for both pictures and words, suggesting impaired recollection. The late frontal effect, which is thought to reflect executive retrieval monitoring, typically occurs at right anterior frontal regions between 1000 and 1800 ms post-stimulus (Allan, Wilding, & Rugg, 1998; Ranganath, Heller, & Wilding, 2007; Wilding & Rugg, 1996). Executive abilities remain intact in a number of patients with aMCI, suggesting that that there are qualitative differences between aMCI and AD (Bisiacchi, Borella, Bergamaschi, Carretti, & Mondini, 2008; Voss & Bullock, 2004). In fact, Bisiacchi et al. (2008) proposed that executive dysfunction may be the separating feature signifying a pathological change in the brain leading to dementia. Therefore, we predicted that the late frontal effect would remain intact, or even be enhanced as a compensatory mechanism, in patients with aMCI for pictures and words, suggesting intact executive retrieval monitoring.

2. Materials and methods

2.1. Design overview

Each subject completed two separate study-test sessions consisting of words and pictures. Each session consisted of 50 stimuli at study and 100 stimuli at test (50 old, 50 new). Order of study-test condition was counterbalanced across subjects, with a 10-min break between sessions. High-density ERPs were recorded at test.

2.2. Subjects

Eighteen healthy older adults (nine female) with a mean education of 15.2 years, and an age range of 69–83 (mean 74.6) participated in the experiment. Eighteen patients with a diagnosis of probable aMCI (Petersen, 2004) (eight female) with a mean education of 17.3 years, and an age range of 62–86 (mean 71.8) participated in the experiment. Patients with aMCI (either single or multiple domain) in the current study reported a subjective memory compliant, showed abnormal memory performance for their age as evidenced by performing greater than 1.5 standard deviations below the healthy adult group on either the recall or the recognition portion of the word list memory test of the CERAD, and did not display functional impairment according to caregiver report. Subjects were excluded if they had a history of cerebrovascular disease, another neurodegenerative disorder, another brain disorder or injury, or if they were currently being treating for a psychiatric disorder such as major depression. Healthy older adults were also excluded if they had a first-degree relative with a history of a memory disorder or Alzheimer's disease. Written informed consent was obtained from all participants and from their caregivers where appropriate. Participants were paid $25/h for their participation.

All subjects were right-handed, English was their native language, and subjects were required to have corrected 20/30 or better color vision. The human subjects committees of the Bedford VA Hospital and Boston University School of Medicine approved the study. All subjects completed a brief neuropsychological battery to evaluate their cognitive functioning, administered in a separate 45-min session. Subjects were first administered the Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975), for which a score of 27 or better was required for the healthy older adults. Subjects were then administered the CERAD word list memory test (Morris et al., 1989), Trail Making Test Part B (Adjutant General's Office, 1944), Verbal Fluency (Monsch et al., 1992), and the 15-item Boston Naming Test (Mack, Freed, William, & Henderson, 1992). Demographic and neuropsychological test data can be seen in Table 1.

Table 1
Demographic and standard neuropsychological test data by group.

	OC	aMCI
Age	74.6 (4.1)	71.8 (9.2)
Years education	15.2 (2.7)	17.3 (4.2)
MMSE	29.4 (0.8)	28.1 (1.3)
CERAD		
Immediate	22.3 (3.1)	14.1 (4.6)
Delayed	7.6 (1.4)	2.5 (1.8)
Recognition	9.9 (0.4)	7.8 (1.7)
Trails-B	83.5 (22.2)	117.7 (66.3)
FAS	48.6 (7.4)	40.7 (11.4)
CAT	50.4 (11.6)	35.4 (13.7)
BNT-15		
No cue	14.5 (1.0)	13.6 (1.5)
Semantic cue	0.1 (0.3)	0.1 (0.5)
Phonetic cue	0.4 (0.9)	0.9 (1.3)

Notes: OC = healthy older adults; MMSE = Mini Mental State Examination; CERAD = CERAD Word List Memory Test; Trails-B = Trail Making Test Part B; FAS and CAT = Verbal Fluency; BNT-15 = 15-item Boston Naming Test.

2.3. Experimental material and methods

The color pictures used in the current study were the same stimuli set used by Ally and Budson (2007). The original pool of experimental stimuli consisted of 480 high-resolution clip-art style color pictures of nameable objects (nouns) and 480 words corresponding to the names of the objects. From the total pool, 200 pictures were randomly selected and were piloted in a naming study involving five subjects. Pictures with poor naming reliability scores were replaced as needed. The final 200 items were counterbalanced across study-test lists for word length, concreteness, and imagibility ratings. In addition, condition order (pictures, words) and study status (old, new) were counterbalanced across subjects. Color pictures were presented in central vision on a white background, with an average height of 13 cm and an average width of 15 cm, and a visual angle subtended of 7°. Words were presented in central vision in black uppercase letters 4 cm in height, also on a white background, with a visual angle subtended of 5.6°. All stimuli were presented on a 21-in. flat screen computer monitor positioned 48 in. from the subject.

Each trial began with a 1000 ms fixation character ("+") prior to the presentation of the stimuli. Study stimuli were then presented for 2000 ms followed by the question, "Do you like this item?" Subjects were then prompted to button press to signify their like/dislike judgment and to remember the items for a subsequent memory test. Test stimuli were presented for 1500 ms, followed by the question, "Is this item old or new?" Subjects were then prompted to verbally signify their old/new judgment, and the experimenter entered the response on a button box. Subjects were asked to hold their responses until the question appeared immediately after stimuli presentation to minimize response-related ERP artifact during the commonly used 1800 ms epoch. We acknowledge that asking participants to keep their response "in mind" (or alternatively, inhibiting their natural inclination to respond before the prompt) may affect the electrophysiological data; particularly the late frontal effect. However, because subjects would be engaging in this activity in all trials, this activity should be removed when subtracting correct rejections from hits.

2.4. ERP procedure

Subjects were seated in a hardback chair and fitted with an Active Two electrode cap (Behavioral Brain Sciences Center, Birmingham, UK). A full array of 128 Ag–AgCl BioSemi (Amsterdam, the Netherlands) "active" electrodes were connected to the cap in a pre-configured montage which places each electrode in equidistant concentric circles from 10–20 position Cz (Web Appendix Figure A). Active electrodes are amplified through the electrode at the source and do not require abrading of the skin or measuring skin-electrode impedance levels. In addition to the 128 scalp electrodes, two mini-biopotential electrodes were placed on each mastoid process. Finally, vertical and horizontal EOG activity was recorded from bipolar electrodes placed below the left eye and on the outer canthus of the left and right eye. EEG and EOG activity was amplified with a bandwidth of 0.03–35 Hz (3 dB points) and digitized at a sampling rate of 256 Hz. Recordings were referenced to a vertex reference point, but were later re-referenced to a common average reference to minimize the effects of reference-site activity and accurately estimate the scalp topography of the measured electrical fields (Ally & Budson, 2007; Curran, DeBuse, Woroch, & Hirshman, 2006; Dien, 1998; Norman, Tepe, Nyhus, & Curran, 2008).

Table 2
Behavioral performance for healthy older adults and patients with aMCI using the discrimination index Pr (percent hits–percent false alarms).

	Percent hits	Percent FA	Pr
Older adults			
Picture	0.96	0.07	0.89
Word	0.88	0.08	0.80
aMCI			
Picture	0.91	0.15	0.76
Word	0.79	0.24	0.55

The sampling epoch for each test trial lasted for a total of 2000 ms, which included a 200 ms pre-stimulus baseline period. This pre-stimulus period was used to baseline correct averaged ERP epochs lasting 1800 ms. ERPs were averaged and corrected using the EMSE Software Suite (Source Signal Imaging, San Diego, CA, USA). Trials were corrected for excessive EOG activity using the EMSE Ocular Artifact Correction Tool. The tool first allows the investigator to manually distinguish artifact data from artifact-free data. Then, using a covariance technique that simultaneously models artifact and artifact-free EEG, a logarithmic ratio of artifact data to clean data is produced by EMSE. Finally, ocular artifact is subtracted from the recording where it is detected by the correction tool. Trials were discarded from the analyses if they contained baseline drift or movement greater than 90 μV. Individual bad channels were corrected with the EMSE spatial interpolation filter.

3. Results

3.1. Behavioral performance

Recognition accuracy was calculated using the discrimination index Pr (%Hits − %False Alarms; Snodgrass & Corwin, 1988) to compare the performance of the healthy older adults and the patients with aMCI. A repeated measures ANOVA with the factors of Group (older adults, aMCI) and Condition (word, picture) was performed. The results of the ANOVA revealed an effect of Group [$F(1,30) = 13.18$, $p = 0.001$], such that overall accuracy was better for the healthy older adults compared to the patients with aMCI, and an effect of Condition [$F(1,30) = 38.69$, $p < 0.001$], indicating that pictures were better remembered than words for both groups. There was also an interaction of Group and Condition [$F(1,30) = 5.66$, $p = 0.024$]. Follow-up analyses of this interaction shows that although both healthy older adults [$t(15) = 3.68$, $p = 0.002$] and patients with aMCI [$t(15) = 4.94$, $p < 0.001$] demonstrated greater memory for pictures than for words, this picture superiority effect was larger in the patients with aMCI [$t(15) = 2.34$, $p = 0.028$]. Further analyses of the aMCI data revealed more hits and fewer false alarms for the picture compared to the word condition [$t(15) = 2.52$, $p = 0.025$; $t(15) = 2.94$, $p = 0.011$]. Table 2 shows the behavioral data for both groups.

In addition to accuracy, response bias was analyzed using the measure C (Snodgrass & Corwin, 1988).[1] A repeated measures ANOVA with the factors of Group (older adults, aMCI) and Condition (word, picture) was performed. There were no main effects of Group [$F(1,30) < 1$] or Condition [$F(1,30) = 1.41$, $p = 0.245$), and there was no interaction of Group and Condition [$F(2,30) < 1$].

3.2. ERP results

Two separate sets of analyses were performed on the ERP data. The first set of analyses was guided by previous research and began with ANOVAs performed on selected time intervals (300–500, 500–800, 1000–1800 ms) previously associated with three components of the old/new ERP effect (early frontal effect, parietal effect, late frontal effect, respectively) as described above (Ally & Budson, 2007; Budson, Droller, et al., 2005; Curran et al., 2006; Curran, 2000, 2004). Mean amplitudes were calculated for these three time intervals, which were then averaged across groups of seven electrodes that formed eight separate regions of interest [left anterior inferior (LAI), right anterior inferior (RAI), left anterior superior (LAS), right anterior superior (RAS), left posterior superior (LPS), right posterior superior (RPS), left posterior inferior (LPI), and right posterior inferior (RPI), see Web Appendix Figure A]. Regions included in the ANOVA depended on the time interval of interest, such that the four anterior regions were used for the early and late frontal effects (LAI, RAI, LAS, and RAS) and the two parietal regions were used for the parietal effect (LPS and RPS). The older adult control waveforms and scalp topographies were formed from a mean (range) of 43 (39–50) hits and 46 (31–50) correct rejections for the word condition and 47 (43–50) hits and 47 (42–49) correct rejections for the picture condition. The MCI waveforms and scalp topographies were formed from a mean of 39 (21–48) hits and 38 (23–48) correct rejections for the word condition and 44 (35–50) hits and 42 (34–49) correct rejections for the picture condition. The older adult control group had an average of 3.9 trials rejected due to artifact or drift in the word condition and 2.9 trials rejected in the picture condition. In contrast, the MCI group had an average of 5.5 trials rejected in the word condition and 3.1 trials rejected in the picture condition. There were no statistical differences between groups in the number of trials rejected for words [$t(30) = 0.636$, $p = 0.53$] or pictures [$t(30) = 0.061$, $p = 0.95$]. Older adult and aMCI grand average hit and correct rejection ERP waveforms for our two study-test condition comparisons can be seen in Figs. 1 and 2.

The second set of analyses consisted of nonparametric permutation tests performed on the old/new scalp topographies for the older adult and aMCI groups seen in Fig. 3. Typically used in imaging studies to compare voxels between two different conditions, nonparametric permutation tests can be useful in analyzing high-density ERP data (Galan, Biscay, Rodriguez, Perez-Abalo, & Rodriguez, 1997; Greenblatt & Pflieger, 2004; Karniski, Blair, & Snider, 1994). Using this type of analysis allows researchers to use the entire data set rather than averaging over hundreds of millisecond and groups of electrodes, thereby avoiding losing valuable temporal and spatial data. The permutation test calculates the statistical probability of differences between groups or conditions in p-value form at every electrode site for every millisecond of recorded data. We chose to present the data in 50 ms time intervals. Note that these topographic maps represent an average of 50 ms going forward from the labeled time, such that 0 ms is the average from 0 to 49 ms, etc. Nonparametric permutation tests were used to examine differences in these topographic maps, and can be seen in Web Appendix Figures B and C. Only significant statistics will be discussed.

The initial ANOVA focused on the 300–500 ms time interval and used the factors of Group (older adults, aMCI), Condition (word, picture), Item Type (hit, correct rejection), and ROI (LAI, RAI, LAS, RAS). These results found a main effect of Group [$F(1,30) = 6.29$, $p = 0.018$], such that waveforms were more positive overall for older adults than for patients with aMCI. A main effect of Condition [$F(1,30) = 57.72$, $p < 0.001$] revealed that words were more positive overall than pictures, and an effect of ROI [$F(3,87) = 10.05$, $p < 0.001$] showed that left frontal regions were more positive than right frontal regions. There were also significant interactions of Item Type and Condition [$F(1,30) = 13.18$, $p = 0.001$], and Item Type and Group [$F(1,30) = 7.78$, $p = 0.009$]. Follow-up ANOVAs showed an overall effect of Item Type for the healthy older adults [$F(1,15) = 17.68$, $p = 0.001$], but not for the patients with aMCI [$F(1,15) = 2.16$, $p = 0.162$]. However, the aMCI group showed a significant interaction of Item Type and Condition [$F(1,15) = 11.67$, $p = 0.004$]. The post-hoc ANOVAs for the aMCI group revealed an effect of Item Type for pictures [$F(1,15) = 9.274$, $p = 0.010$], but not for

[1] Response Bias was calculated using the formula-$C = z_{FA} - d'/2 = 0.5(z_{FA} + z_H)$ provided by Snodgrass and Corwin (1988).

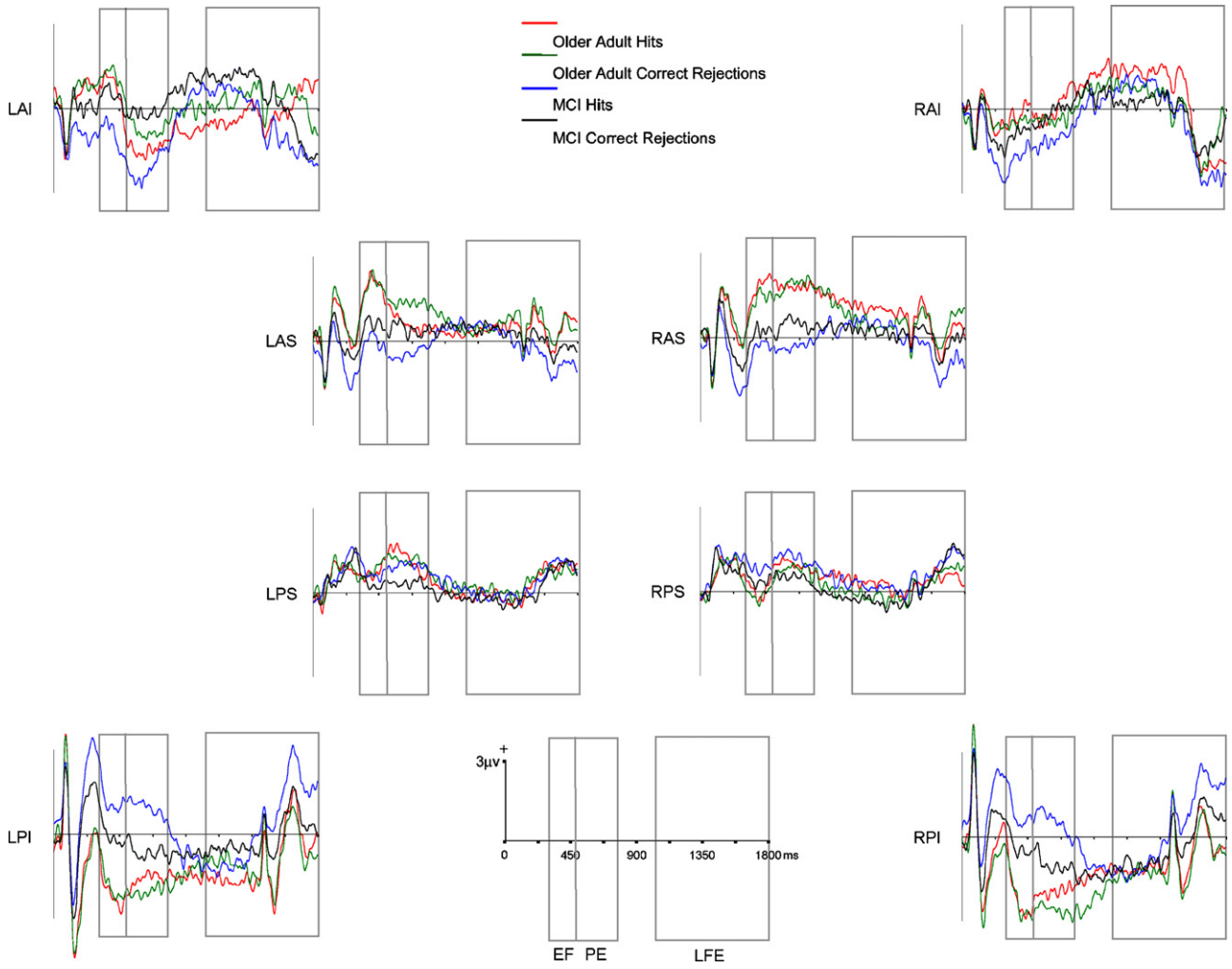

Fig. 1. Older adult and aMCI grand average hit and correct rejection ERP waveforms for the word condition. Each waveform represents the composite average of the seven electrodes subsuming each ROI. Components of interest are highlighted in gray: EF = early frontal effect (300–500 ms), PE = parietal effect (500–800 ms), LFE = late frontal effect (1000–1800 ms). ROIs are listed to the left of each waveform: left anterior inferior (LAI), right anterior inferior (RAI), left anterior superior (LAS), right anterior superior (RAS), left posterior superior (LPS), right posterior superior (RPS), left posterior inferior (LPI), and right posterior inferior (RPI).

words [$F(1,15) < 1$]. Follow-up between-subjects t-tests for the word condition revealed that the magnitude of the early frontal old/new effect was greater for the older adults than for the aMCI patients at three of the four frontal regions for words [LAI, $t(29) = 2.27$, $p = 0.031$; LAS, $t(29) = 2.47$, $p = 0.019$; RAS, $t(29) = 2.16$, $p = 0.039$] and a trend towards significance at the fourth [RAI, $t(29) = 1.95$, $p = 0.061$]. There were no between-group differences for pictures. These results show that the early frontal effect was present for both words and pictures in the older adults, but only for pictures in the aMCI group.

These between-subjects ANOVA and t-test results were supported by nonparametric permutation test findings. Scalp topographies for the word condition can be seen in Fig. 3a. Between 300 and 500 ms, the older adult group showed the classic old/new effect at right superior and inferior right frontal regions. In contrast, the aMCI group demonstrated a negative old/new effect at left frontal regions, with a positive old/new effect is seen at more posterior regions. These between-group differences are highlighted by the nonparametric analysis results. As can be seen in Web Appendix Figure B(1), p-value maps showed a greater old/new effect at frontal electrodes for the older adults compared to the patients with aMCI from approximately 250 to 750 ms in the word condition, because only the healthy older adults showed an early frontal old/new effect for words.

Scalp topographies for the picture condition can be seen in Fig. 3b. Similar to the word condition, healthy older adults showed the classic old/new effect for pictures at right superior and inferior frontal regions during the 300–500 ms time interval. In contrast to the brain activity elicited in the word condition, patients with aMCI showed a bilateral old/new effect at frontal regions during this time interval for the picture condition. These results are supported by the nonparametric analysis. As can be seen in Web Appendix Figure B(2), there were only very small differences at frontal regions from approximately 400 to 450 ms during this early time interval between the two groups for the picture condition, because both the healthy older adults and the aMCI group showed an early frontal effect for pictures.

The within-subjects ANOVA and t-tests findings for the aMCI group are also supported by nonparametric analyses. As can be seen in Web Appendix Figure C(2), the within-subject p-value maps for the aMCI group show that magnitude of the old/new effect is greater at frontal regions beginning around 250 ms and continuing throughout the majority of the recording epoch for the picture condition compared to the word condition; no such frontal differences were observed in the reverse contrast Web Appendix Figure C(1).

The parietal ERP effect was analyzed in the same way using parietal ROIs (LPS and RPS) for the 500–800 ms time interval. Results of

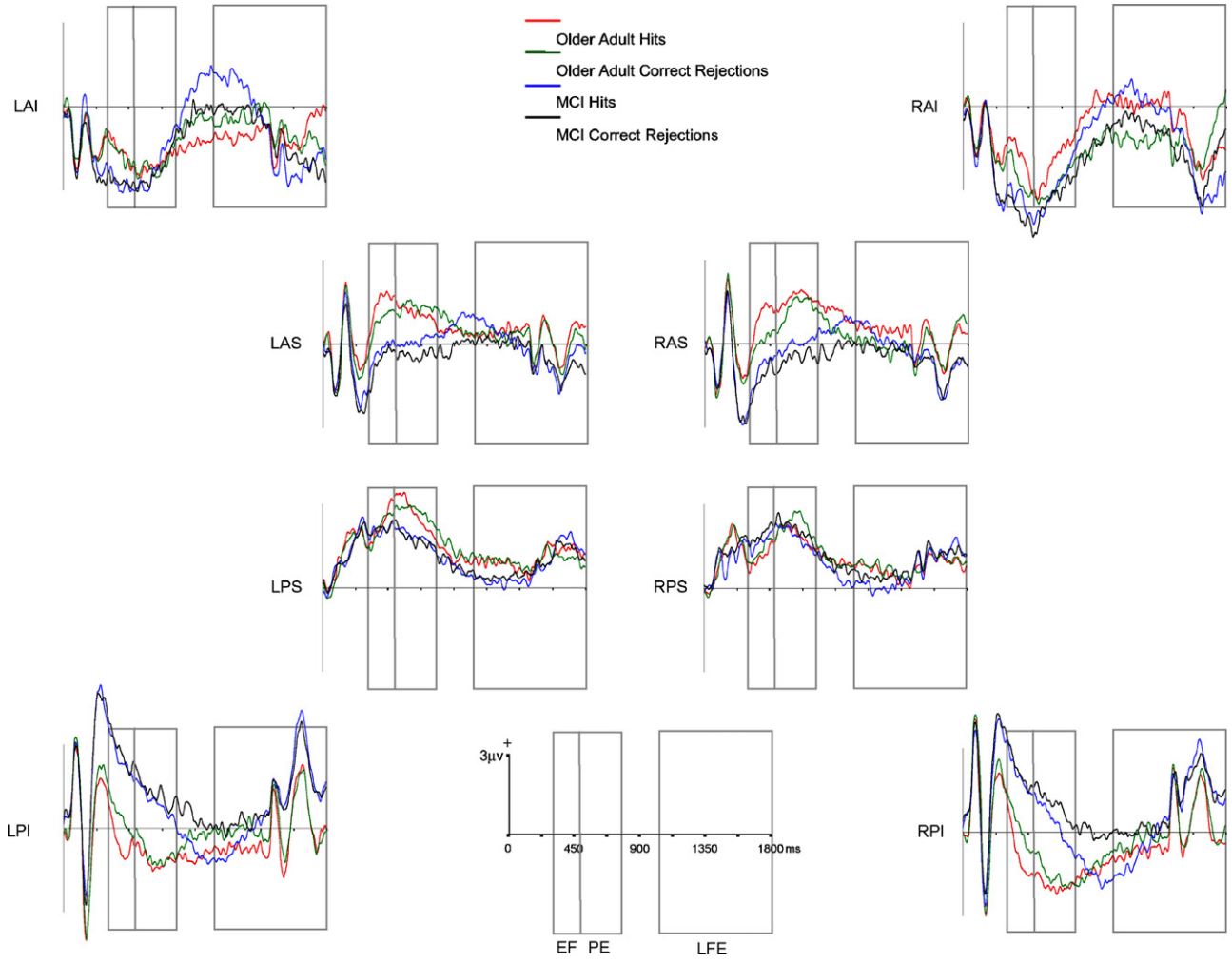

Fig. 2. Older adult and aMCI grand average hit and correct rejection ERP waveforms for the picture condition. Each waveform represents the composite average of the seven electrodes subsuming each ROI. Components of interest are highlighted in gray: EF = early frontal effect (300–500 ms), PE = parietal effect (500–800 ms), LFE = late frontal effect (1000–1800 ms). ROIs are listed to the left of each waveform: left anterior inferior (LAI), right anterior inferior (RAI), left anterior superior (LAS), right anterior superior (RAS), left posterior superior (LPS), right posterior superior (RPS), left posterior inferior (LPI), and right posterior inferior (RPI).

the ANOVA revealed a main effect of Condition [$F(1,30) = 122.49$, $p < 0.001$] such that the waveforms for pictures were more positive than the waveforms for words. A marginal effect of Group [$F(1,30) = 3.99$, $p = 0.055$] revealed that the waveforms trended towards being more positive for the healthy older adults compared to the patients with aMCI. The ANOVA also revealed an interaction of Condition and Item Type [$F(1,30) = 5.02$, $p = 0.033$], and a marginal interaction of Group, Condition, and Item Type [$F(1,30) = 3.69$, $p = 0.064$]. Follow-up analyses revealed no effect of Item Type for words [$F(1,15) = 1.19$, $p = 0.292$] or pictures [$F(1,15) = 1.95$, $p = 0.182$] for the patients with aMCI. There was also no effect of Item Type for words [$F(1,15) < 1$] for the healthy older adults. However, an interaction of Item Type and ROI [$F(1,15) = 4.55$, $p = 0.050$] revealed a significant old/new effect at region LPS [$t(15) = 2.88$, $p = 0.011$], but not at region RPS [$t(15) = 1.20$, $p = 0.248$] for pictures. These results demonstrate that whereas patients with aMCI did not show a parietal old/new effect for either words or pictures, healthy older adults showed a parietal effect for pictures but not words.

The nonparametric analyses lend some support to these findings (Fig. 3a). Neither group showed a robust parietal old/new effect for words. The word scalp topographies for the healthy older adults showed a prominent old/new effect in bilateral occipital regions beginning around 650 ms, and extending into right lateral parietal regions beginning around 750 ms. This effect became more robust at right hemisphere occipital and lateral parietal regions around 800 ms and remaining until approximately 1150 ms. During this time interval, the aMCI group showed a bilateral occipital old/new effect. The nonparametric analysis revealed no parietal differences between groups for the word condition. However, the analysis revealed greater occipital activity for the aMCI group during this time interval.

The scalp topographies for the older adults in the picture condition showed a left hemisphere dominant parietal old/new effect beginning at around 500 ms and continuing more on the left side until approximately 650 ms (Fig. 3b). In contrast, patients with aMCI showed a diffuse centroparietal old/new effect for pictures from approximately 500 to 850 ms. The nonparametric analysis revealed no significant areas of difference between the two groups for pictures during the 500–800 ms time interval. However, within-subject analysis revealed that there were several areas where parietal activity was greater for pictures than words in the healthy older adults during the 500–800 ms interval. For the aMCI group, activity was greater at frontal regions for pictures during the recollection time interval.

Finally, the late frontal ERP effect was analyzed in a similar way using the anterior ROIs (LAI, RAI, LAS, and RAS) for the 1000–1800 ms time interval. The ANOVA revealed an effect of Condition [$F(1,30) = 7.34$, $p = 0.011$] such that pictures were more

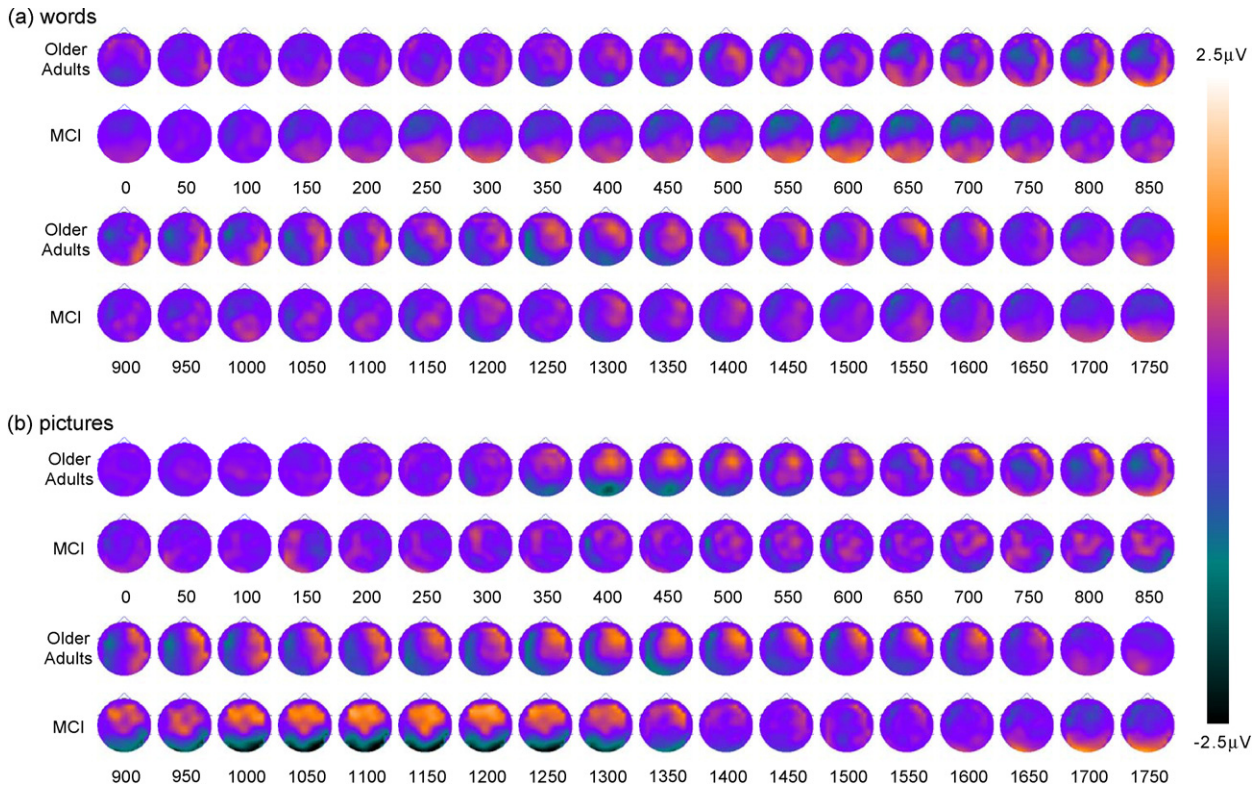

Fig. 3. Older adult and aMCI old/new scalp topography maps for the (a) word and (b) picture conditions. Topographies are presented in 50 ms averages going forward.

positive than words, and a weak trend towards an effect of Item Type [$F(1,30) = 3.31$, $p = 0.079$] because hits were somewhat more positive than correct rejections. There was also a marginal interaction of Condition, Item Type, and Group [$F(1,30) = 3.82$, $p = 0.060$], as well as significant interactions of Item Type, ROI, and Group [$F(3,87) = 3.02$, $p = 0.034$] and Condition, Item Type, ROI, and Group [$F(3,87) = 3.70$, $p = 0.032$]. Post-hoc ANOVAs revealed an overall effect of Item Type for the healthy older adults [$F(1,15) = 4.65$, $p = 0.048$], but not for the aMCI group [$F(1,15) = 1.73$, $p = 0.208$]. However, the aMCI group showed a significant interaction of Item Type and Condition [$F(1,15) = 6.39$, $p = 0.023$]. This interaction was due to a trend towards hits being more positive than correct rejections in the picture condition [$F(1,15) = 3.99$, $p = 0.062$], but not in the word condition [$F(1,15) < 1$]. Following-up on the four-way interaction of Condition, Item Type, ROI, and Group, paired-sample t-tests revealed a significant effect of Item Type for older adults at right frontal regions RAI [$t(15) = 4.55$, $p < 0.001$] and RAS [$t(15) = 2.52$, $p = 0.024$] for the picture condition and at region RAS [$t(15) = 2.42$, $p = 0.029$] for the word condition. The paired-sample t-tests revealed a significant effect of Item Type for the aMCI group at regions LAI [$t(15) = 2.93$, $p = 0.011$], RAI [$t(15) = 3.33$, $p = 0.005$], and RAS [$t(15) = 2.50$, $p = 0.025$] for the picture condition, and no effect of Item Type at any of the four regions for the word condition. Follow-up between-subjects t-tests revealed that the magnitude of the late frontal old/new effect for pictures was actually greater at the left inferior frontal region LAI [$t(29) = 2.47$, $p = 0.019$] for the aMCI group compared to the healthy older adults. These results demonstrate that healthy older adults showed a late frontal old/new for both words and pictures, whereas patients with aMCI showed a late frontal effect only for pictures.

Turning to the nonparametric analyses, the word scalp topographies for healthy older adults showed the classic right frontal old/new effect beginning at around 1050 ms and continuing throughout the majority of the remainder of the recording epoch (Fig. 3a). In comparison, the aMCI group demonstrated what appears to be a centroparietal old/new effect early in the interval with a right frontal old/new effect appearing later from approximately 1200 to 1650 ms. Consistent with our ANOVA findings that the old/new effect differed between groups at the right superior frontal region, Web Appendix Figure B(1) shows small superior frontal differences between groups (OC > MCI) from approximately 1050 to 1250 ms in the word condition.

Similar to the word condition, the older adult scalp topographies for the picture condition show the classic right frontal old/new effect from approximately 750 ms throughout the remainder of the recording epoch in the picture condition (Fig. 3b). Although beginning slightly later, the patients with aMCI showed a similar bilateral frontal old/new effect to the healthy older adults during this time interval for the picture condition, beginning around 900 ms and ending more on the right at approximately 1600 ms. Web Appendix Figure B(2) shows no differences between groups (OC > MCI) in the picture condition. However, consistent with the ANOVAs and follow-up t-tests, Web Appendix Figure B(2) (MCI > OC) shows that the magnitude of the old/new effect is actually greater for patients with aMCI compared to healthy older adults at left inferior and superior frontal regions in the picture condition. The within-subjects permutation test was also consistent with the ANOVAs and t-tests. Web Appendix Figure C shows that patients with aMCI demonstrated a greater old/new effect at frontal regions late in the recording epoch for the picture > word condition [Web Appendix Figure C(2)] compared to the word > picture condition [Web Appendix Figure C(1)].

4. Discussion

The present study set out to use ERPs to understand the neural basis of the picture superiority effect in patients with aMCI and to help determine whether these patients can successfully use

familiarity to support recognition memory decisions for pictures. Our ERP data were generally consistent with our hypotheses. We predicted that the neural correlate of familiarity would be similar between the patients with aMCI and healthy older adults for pictures, but not for words. The data were consistent with this prediction. The early frontal old/new effect was similar between groups for pictures, but was diminished in patients with aMCI for words compared to healthy older adults. We also predicted that, due to impaired recollection, patients with aMCI would show diminished parietal activity for both pictures and words compared to healthy older adults. This hypothesis was also confirmed. Whereas healthy older adults showed a parietal effect for pictures, patients with aMCI showed no evidence of a parietal old/new effect for either words or pictures. Lastly, we predicted that patients with aMCI would show intact executive retrieval monitoring, as reflected by the late frontal effect. To our surprise, we found that the late frontal effect was similar between groups for pictures only. Late frontal activity was diminished in patients with aMCI for words compared to healthy older adults.

These ERP results help us to better understand how patients with aMCI make veridical memorial decisions for pictures and words. As part of this understanding, we hoped to address the question of whether patients with aMCI can successfully use familiarity to support these decisions. The behavioral evidence has been mixed. Two recent studies used process-estimation techniques to provide evidence that familiarity is impaired in patients with aMCI for words (Ally et al., 2009a; Wolk et al., 2008), while another study used multiple-choice versus single-item conditions to show that familiarity remained intact in these patients for pictures (Westerberg et al., 2006). Our ERP results were very consistent with these behavioral studies, showing a relative absence of the early frontal effect in patients with aMCI for words, but no difference in the early frontal effect compared to controls for pictures. The fact that stimulus type may differentially affect the components of recognition memory has been previously discussed (Ally & Budson, 2007; Ally, Waring, et al., 2008; Budson, Dodson, Daffner, Schacter, 2005; Budson, Droller, et al., 2005; Hornberger, Morcom, & Rugg, 2004; Schloerscheidt & Rugg, 2004). In fact, Ally, Waring, et al. showed that pictures allowed healthy older adults to rely on successful recollection, where as words did not. Those data showed that the parietal old/new effect was similar between older adults and young controls for pictures, but was diminished in the older adults for words. It is clear that pictures provide a distinct memorial advantage (see Mintzer & Snodgrass, 1999 for review) and increase recollection over words (Ally & Budson, 2007; Dewhurst & Conway, 1994; Rajaram, 1996), but it is less clear as to why pictures might differentially affect familiarity.

A recent debate in the literature regarding the relationship between memorial familiarity and implicit memory may help to answer this question. Voss and Paller (2006, 2007a,b, 2008) have recently challenged the notion that the early frontal ERP effect reflects explicit memorial familiarity. Voss and Paller (2006) showed that the magnitude of the early frontal old/new effect was correlated with the magnitude of behavioral estimates of conceptual priming, and not with ratings of explicit memory processes across subjects. On the basis of further evidence using novel visual stimuli, these authors argued that the early frontal effect might be the neural correlate of conceptual priming for visual objects rather than familiarity (Voss & Paller, 2007a,b, 2008). While this evidence is fairly convincing, recent studies involving face (Curran & Hancock, 2007) and name (Stenberg, Hellman, Johansson, & Rosen, 2009) recognition have shown that the early frontal effect reflects explicit familiarity rather than implicit processes such as conceptual priming. This debate is complicated by the possibility that conceptual priming may overlap with familiarity, or play some role in engendering memorial familiarity (Willems, Salmon, & Van der Linden, 2008). Indeed, evidence from behavioral and ERP studies suggest that the *phenomenological experience* of familiarity may result from implicit memory processes such as priming and fluency (Jacoby & Whitehouse, 1989; Whittlesea, 1993; Whittlesea & Williams, 1998, 2001; Wolk et al., 2004).

Related to the current study, Hamilton and Geraci (2006) showed that the distinctive information provided by pictures makes them more easily processed, and that conceptual processing of this distinctive information likely drives the picture superiority effect. Evidence has shown that conceptual priming for picture stimuli appears to remain intact even into the moderate stages of AD (Martins & Lloyd-Jones, 2006). This finding has been extended into explicit memory. Wolk et al. (2005) revealed that patients with mild AD were able to use conceptual fluency based on prior experience to support their recognition judgments. To compliment these behavioral results, Wolk et al. showed that the early frontal old/new effect was similar for patients and healthy older controls when conceptual fluency was used to support recognition judgments. Therefore, it is certainly possible that conceptual priming for pictures contributed to the intact early frontal effect for pictures in patients with aMCI in the current investigation and led to the pronounced picture superiority effect in this group. Future studies could include behavioral measures to examine the contribution of conceptual priming and memorial familiarity more directly.

The results of the parietal old/new effect data were also consistent with our hypotheses. On the basis of previous behavioral evidence of impaired recollection for both pictures (Westerberg et al., 2006) and words (Ally et al., 2009a), we predicted that the parietal effect would be diminished for both in patients with aMCI. The aMCI ERP data revealed essentially no old/new effect at parietal regions for pictures or words. Healthy older adults showed a parietal old/new effect at left parietal regions for pictures, but not for words, suggesting that pictures allow healthy older adults to successfully use recollection in recognition decisions (Ally, Waring, et al., 2008). The lack of parietal activation during memory retrieval in patients with aMCI is not surprising given the number of recent findings suggesting early pathology in parietal cortex, and decreased connectivity to this region from the hippocampus (McKee et al., 2006; Zhou et al., 2008). It is also consistent with previous fMRI research showing significantly diminished parietal activation during memory retrieval in patients with aMCI compared to healthy older adults (Ries et al., 2006).

Despite the lack of a parietal effect, the prominent occipital activity for the aMCI group in the word condition extending from approximately 250 to 750 ms is worth noting. To follow-up on this activity, we performed a between-subjects repeated measures ANOVA using the two occipital regions, LPI and RPI, which yielded an interaction of Item Type, Condition, and Group [$F(1,30) = 5.23$, $p = 0.030$]. Follow-up analyses revealed that the healthy older adult group showed no occipital old/new effect for either words ($p = 0.305$) or pictures ($p = 0.119$). Although patients with aMCI showed no occipital old/new effect for pictures ($p = 0.621$), there was a robust old/new effect for words ($p < 0.001$), supported by the nonparametric analyses shown in Web Appendix Figure C(1). Although exactly what this occipital activity reflects is unclear, it has been reported in previous studies involving subjects with mild AD (Golby et al., 2005; Koenig et al., 2008; Troller et al., 2006). Similar to our current results, Troller et al. (2006) found increased cerebral blood flow to occipital regions using PET during successful verbal recognition in patients with mild AD. It has been speculated that areas in the temporal–parietal–occipital region might organize together in the face of hippocampal pathology to provide compensatory function in patients with AD (Scarmeas et al., 2004). Given that the occipital activity in the current study was only present in the word condition, this may be a likely hypothesis. In the face of impaired familiarity and recollection, patients

with aMCI may attempt to use strategies such as attempting to remember perceptual aspects of the study item or visual mental imagery to compensate for poor memory. Previous imaging research has shown that primary visual areas are activated when subjects engage in mental imagery (Kosslyn, Thompson, Kim, & Alpert, 1995), and these regions are reactivated at retrieval (Johnson & Rugg, 2007). Yet another possibility, given that occipital activity is greater for successfully identified studied items compared to successfully identified unstudied items, is that patients are visually processing the studied items longer or to a greater extent than unstudied items.

In addition to examining the ERP correlates of familiarity and recollection, we also analyzed the putative correlate of retrieval monitoring and verification. Evidence from neuropsychological (Ranganath & Knight, 2003), neuroimaging (Fletcher & Henson, 2001), and ERP (Friedman & Johnson, 2000; Wilding & Herron, 2006) studies suggest that lateral regions of prefrontal cortex are involved in control or monitoring of retrieval processes. ERP researchers have classically suggested that late right frontal old/new activity reflects the ongoing evaluation of a retrieval attempt, particularly when specific details, features, or source information are needed (Allan et al., 1998; Rugg & Wilding, 2000; Wilding & Rugg, 1996). More recent ERP work has suggested that the late right frontal effect may be critical when memory retrieval is weak (Wolk et al., 2009) or when subsequent retrieval attempts are needed (Ally & Budson, 2007). Because recent work has highlighted the fact that patients with aMCI demonstrate performance similar to healthy older adults on tasks of executive functioning (Bisiacchi et al., 2008) and inhibition (Zhang, Han, Verhaeghen, & Nilsson, 2007), we hypothesized that the late right frontal effect would remain intact in patients with aMCI. In fact, we predicted that this late frontal activity may even be enhanced in these patients due to impaired recollection (Wolk et al.). Our results were consistent with this hypothesis for pictures, but not for words. The late frontal effect for pictures was similar for patients with aMCI and healthy older adults at right frontal regions, and it was enhanced at left frontal regions in patients compared to controls. In contrast, the late frontal effect for words was significantly diminished in patients compared to controls at all frontal regions. Overall, these data are consistent with previous behavioral work showing that patients with mild AD demonstrate enhanced retrieval monitoring for pictures over words (Gallo, Chen, Wiseman, Schacter, & Budson, 2007). Gallo et al. speculated that the distinctive perceptual information provided by pictures may impel patients to engage in retrieval monitoring.

While this hypothesis certainly has merit, it should also be noted that the late frontal effect was enhanced in the same condition that the early frontal effect was enhanced. Specifically, during the retrieval of pictures, patients with a MCI demonstrated enhanced correlates of familiarity and retrieval monitoring. Ally, Waring, et al. (2008) suggested that perhaps in the absence of recollection, the late frontal effect reflects prefrontal regions working to confirm or deny a response based on other processes such as familiarity. After a sense of familiarity is engendered, prefrontal regions may be involved in judging the degree of familiarity, or may continue attempting to recollect information about the stimulus (Montaldi, Spencer, Roberts, & Mayes, 2006). Indeed, the frontal lobes have been implicated in response inhibition (Shimamura, 1995) and distinguishing between identical versus highly similar and familiar items, and thus are important in avoiding false recognition (Budson et al., 2002; Schacter, Curran, Galluccio, Milberg, & Bates, 1996; Swick & Knight, 1999).

Overall, the current results have shown that pictures and words differentially affect how memorial decisions are made in patients with aMCI. Pictures have a clear memorial advantage over words, but the debate as to why is far from settled. One hypothesis suggests that pictures are better remember because they are more likely to be represented by both image and verbal codes (dual coding), increasing the probability that they will be recollected compared to words (Paivio, 1986, 1991). Given our ERP data, it is certainly possible that the dual coding engenders an enhanced sense of familiarly in patients with MCI and recollection in older adults. However, in the current study, words alone did not elicit the neural correlate of familiarity in patients or the neural correlate of recollection in healthy controls, suggesting that there is something specifically related to pictures that affects the neural correlates of recognition memory. In fact, a large literature base suggests that the distinctive information provided by pictures allows them to be easily encoded and retrieved (see Mintzer & Snodgrass, 1999 for review) and allows for easier or enhanced recollection in healthy younger and older adults (Ally & Budson, 2007; Ally, Waring, et al., 2008; Budson, Dodson, Daffner, Schacter, 2005; Budson, Droller, et al., 2005; Dewhurst & Conway, 1994; Hamilton & Geraci, 2006; Rajaram, 1996). Further, patients with amnestic MCI and mild AD continue to show the picture superiority effect (Ally et al., 2009b), despite having impaired recollection. In the present study, we argue that it is likely this distinctive information enhances familiarity in patients with aMCI, a group known to have impaired recollection. In support of this hypothesis, evidence suggests that perhaps conceptual priming drives the picture superiority effect (Hamilton & Geraci, 2006) and may play a role in engendering a sense of familiarity for visual stimuli (Voss & Paller, 2008). Indeed, previous work has shown that conceptual priming remains intact in patients with aMCI (LaVoie & Faulkner, 2008) and mild to moderate AD (Martins & Lloyd-Jones, 2006). Although the current data did not directly examine the contribution of conceptual priming to the recognition of pictures, it certainly seems plausible that the interaction between conceptual priming and memorial familiarity contributed to the intact early frontal effect and enhanced recognition of pictures for patients with aMCI.

An unanswered question is whether the differences in the ERP effects between pictures and words simply reflect the differences in performance between the two conditions. In other words, would the pattern of ERP results remain the same had our subjects engaged in two tasks involving words where behavioral performance followed a similar pattern as in the current study? A recent study finding improved performance with a depth of processing manipulation showed that with multiple study-test repetitions of words, the neural correlate of recollection—but not the early frontal correlate of familiarity—was enhanced (De Chastelaine, Friedman, Cycowicz, & Horton, 2009). Related to the current data, our results reveal similar performance levels in the picture condition for patients with MCI (Pr = 0.76) and the word condition for healthy older adults (Pr = 0.80) [$t(30) = 0.899$, $p = 0.376$], but very different scalp topographies. Therefore, we suggest that simply boosting performance is not responsible for the enhanced early frontal effect in patients with MCI. Alternatively, we propose that pictures are a special class of stimuli that enhance recollection in individuals with healthy memory and enhance familiarity in patients with impaired recollection.

In summary, we found that pictures allowed patients with aMCI to utilize frontally based memorial processes to support successful recognition. Frontal ERP activity was similar between the two groups only for pictures during the critical time intervals associated with memorial familiarity and retrieval monitoring. Recent work has highlighted the need to investigate the interaction between implicit and explicit memorial processes (Voss & Paller, 2008). With respect to the current data, we have discussed the possibility that implicit conceptual priming for visual stimuli contributed to the enhanced ERP correlate of explicit memorial familiarity. The possibility exists that the interaction of these two processes allow patients with aMCI to use familiarity to support successful

recognition of pictures, but not words. Future studies can further investigate how implicit memory processes, which tend to remain intact even in the moderate stages of AD, can contribute to successful explicit memory in these patients. Additionally, future interventions can be aimed at exploiting these intact processes in pictures to allow patients to retain function and remain in the home longer.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neuropsychologia.2009.03.015.

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