Early Cognitive Decline in Older Adults Better Predicts Object than Scene Recognition Performance

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ABSTRACT: There is an ongoing debate regarding the nature of memory deficits that occur in the early stages of mild cognitive impairment (MCI). MCI has been associated with atrophy to regions that process objects, namely perirhinal and lateral entorhinal cortices. However, it is currently unclear whether older adults with early MCI will show memory deficits that are specific to objects, or whether they will also show memory deficits for other stimulus classes, such as scenes. We tested 75 older adults using an object and scene recognition task with stimulus-specific interference (i.e., exposure to irrelevant object or scene stimuli). We found an interaction ($P = 0.05$) whereby scores on the Montreal Cognitive Assessment, a neuropsychological test with high sensitivity to MCI, shared a stronger relationship with object recognition than with scene recognition performance. Interestingly, this relationship was not modulated by the stimulus category of interfering items. To further explore these findings, we also tested an amnesic patient (DA) with known medial temporal lobe damage. Like older adults with early signs of MCI, DA showed poorer object recognition than scene recognition performance. Additionally, his performance was not modulated by the stimulus category of interfering material. By demonstrating that object memory is more predictive of cognitive decline than scene memory, these findings support the notion of perirhinal and lateral entorhinal cortex dysfunction in the early stages of MCI. © 2016 Wiley Periodicals, Inc.

KEY WORDS: aging; object recognition; scene recognition; mild cognitive impairment

INTRODUCTION

Many prominent models attempt to explain how different components of the medial temporal lobes (MTL) support declarative memory (e.g., recollection and familiarity, Yonelinas, 2002; complementary learning systems, Norman and O'Reilly, 2003; pattern separation and completion, Bakker et al., 2008; and relational accounts, Cohen and Eichenbaum, 1993). More recently, several theories have focused on the distinct stimulus classes supported by different MTL subregions (Litman et al., 2009; Graham et al., 2010; Ranganath and Ritchey, 2012; Liang et al., 2013). Under these accounts, the perirhinal cortex (Buckley and Gaffan, 1998; Brown and Aggleton, 2001; Murray and Richmond, 2001; Barense et al., 2005; Lee et al., 2005a,2005b, 2006; Barense et al., 2007; Burke et al., 2012) and lateral entorhinal cortex (Deshmukh and Knierim, 2011; Reagh and Yassa, 2014) have been implicated in supporting visual object representations. In contrast, the parahippocampal cortex (Epstein and Kanwisher, 1998; Soojin and Chun, 2009), medial entorhinal cortex (Eichenbaum and Lipton, 2008) and the hippocampus support representations of spatial scenes (Lee et al., 2005a,2005b, 2008 Zeidman et al., 2014). Notably, although numerous studies propose stimulus-specificity across MTL regions, it is unclear how degeneration of these areas, for instance in association with age-related cognitive decline, affects corresponding object and scene representations.

One of the most consistent and robust memory deficits associated with healthy aging is relatively poorer spatial or context memory in comparison to item memory (Lipman and Caplan, 1992; Newman and Kaszniak, 2000; Bastin and Van der Linden, 2006; for meta-analyses see Spencer and Raz, 1995; Old and Naveh-Benjamin, 2008). Converging evidence indicates that age-related declines in hippocampal function (Monti et al., 2005; Antonova et al., 2009; Wimmer et al., 2012), resting blood flow (Heo et al., 2009), and connectivity (Schiavetto et al., 2002) are at least in part responsible for such spatial memory deficits. However, whether this relative advantage for single object memory persists during pathological aging, such as mild cognitive impairment (MCI) remains an important open question. Individuals with the amnestic variant of MCI demonstrate memory decline with minimal impairments in daily living, and preserved general cognitive function (Winblad et al., 2004). The majority of these individuals (80% over 6 years; Petersen, 2004) go on to develop Alzheimer's disease (AD). As such, amnestic MCI is often considered to be an early transitional phase between healthy aging and AD. In early disease stages, the perirhinal and lateral entorhinal cortices are disproportionately impacted, compared to other MTL structures (Braak and Braak, 1991; Kordower et al.,

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2001; Khan et al., 2014). Given the role of these regions in object processing, one result of early-stage pathology may be the loss of the object memory advantage that typically occurs in healthy older adults, relative to scene or spatial memory. Although many recent behavioral tasks intended to distinguish MCI from healthy aging have utilized both object (Barbeau et al., 2004; Newsome et al., 2012; Stark et al., 2013; Yeung et al., 2013; Monti et al., 2014) and spatial (Cheng and Pai, 2010; Lithfous et al., 2013; Reagh et al., 2014) memory measures, clarification as to whether object or scene recognition memory is impacted to a disproportionate degree in early MCI is critical. If both perirhinal and lateral entorhinal cortex atrophy is more pronounced in early MCI, then object-based tasks should be more sensitive to cognitive decline than scene-based tasks. However, this prediction has never been directly tested by examining object and scene memory simultaneously.

Perirhinal cortex dysfunction affects not only object recognition, but also the ability to resolve object-based interference (Bartko et al., 2010; McTighe et al., 2010; Barense et al., 2012). These findings have been accounted for by a recent representational hierarchical model (Cowell et al., 2010; Graham et al., 2010). According to this view, the perirhinal cortex sits at the apex of the ventral visual stream, supporting complex, conjunctive representations of objects. The perirhinal cortex is required only when a task necessitates conjunctive representations at the object-level, but not when simple features represented earlier in the ventral visual stream are sufficient for task completion. The representational hierarchical model makes an important prediction: if complex, object-level representations within the perirhinal cortex are damaged, interference from incidental, irrelevant features becomes overwhelming. A stream of visual input creates interference at the feature-level, simply because different objects tend to share lower-level features (e.g., shapes and colors). However, the higher-level conjunctive representations normally maintained in the perirhinal cortex are unique to individual objects even when objects share features, thus shielding against feature-level interference.

If the perirhinal cortex is affected in the earliest stages of cognitive decline, it follows that individuals with MCI will be impaired on tasks that involve exposure to visual interference. Two recent experiments investigated this question in cases with diagnosed MCI and those deemed at-risk for MCI based on a failing score (<26) on the Montreal Cognitive Assessment (MoCA), a brief standardized neuropsychological measure that is sensitive in distinguishing controls from MCI patients (Nasreddine et al., 2005; Damian et al., 2011). For both visual discrimination (Newsome et al., 2012) and spontaneous object recognition assessed by eye movements (Yeung et al., 2013), cases with MCI and cases deemed to be at-risk for MCI demonstrated increased vulnerability to visual object-based interference. Previous research has corroborated the finding that older adults with MCI are particularly vulnerable to mnemonic interference (Cowan et al., 2003; Ebert and Anderson, 2009; Dewar et al., 2012). Notably, however, these studies employed tasks that primarily used word stimuli and verbal narratives. To our knowledge, no studies to date have directly investigated the effects of stimulus-specific interference in MCI—in particular, whether the nature of the interfering stimuli between encoding and retrieval (i.e., objects and scenes) lead to stimulus-specific deficits.

In sum, despite the development of a number of object and scene memory tasks designed to differentiate healthy aging from MCI, none have directly compared whether recognition of either stimulus category is more strongly associated with cognitive decline. The current study aimed to resolve this conflict by investigating whether older adults showing signs of MCI-related cognitive decline would demonstrate disproportionate object recognition compared to scene recognition deficits, and whether these individuals would be especially vulnerable to object interference. We classified older adults as at-risk for MCI on the basis of MoCA performance (which was corroborated by an extensive neuropsychological battery; Table 1), and tested them on a version of a recognition memory interference task used previously with functional magnetic resonance imaging in young participants (Watson and Lee, 2013; O'Neil et al., 2015). This task allowed us to compare object and scene memory directly, under conditions of object, scene, or baseline interference, and crucially, is known to recruit perirhinal cortex during object recognition following exposure to irrelevant objects. Additionally, we were interested in how known MTL damage would impact recognition for object and scenes under conditions of interference. To this end, we also tested amnesic patient DA who incurred extensive MTL damage as a result of viral encephalitis (Table 2) and was expected to show both object and scene recognition deficits, as well as increased vulnerability to interference. We predicted that: (1) MoCA scores will be positively associated with object recognition performance, (2) the association between MoCA scores and object recognition performance will be stronger than that of MoCA scores and scene recognition performance, and (3) object interference, relative to scene and baseline interference, will be particularly damaging to individuals at-risk for MCI as well as patient DA.

METHODS

Participants

Older adults

Eighty older adults were recruited through the Adult Volunteer Pool at the University of Toronto St. George Campus. Participants were screened for a history of psychological illness, traumatic brain injury, and current use of neuroleptic medications. Participants all had normal or corrected-to-normal vision. We excluded two participants due to visibly poor concentration for reasons of religious fasting and inadequate sleep. One participant was excluded for using a verbal strategy that included spoken descriptions of the studied stimuli. Lastly two participants were excluded due to improper administration of the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005). All exclusions were made immediately, before the data

TABLE 1.

Average Raw Scores for Neuropsycholgical Battery Given to At-Risk Older Adults and Raw Scores from Patient DA

Test	At-risk older adults	Patient DA
MoCA (/30)	23.7 (1.2) Impaired	–
WMS-IV LM immediate recall (/50)[a]	24.0 (7.8) Range: 9–40 (16%ile)	7, 1%ile
WMS-IV LM delayed recall (/50)[a]	15.4 (6.2) Range: 2–25 (17–25%ile)	1, 1%ile
WMS-IV LM recognition (/30)[a]	21.7 (3.2) Range: 16–27 (>75%ile)	–
Rey copy (/36) [a]	30.8 (3.35) Range: 23–36 (29–40%ile)	0, <1%ile
Rey immediate recall (/36) [a]	13.4 (4.9) Range: 5–24 (41–59%ile)	–
Rey delayed recall (/36) [a]	10.3 (4.2) Range: 4–20 (19–28%ile)	0, <1%ile
WASI verbal IQ	114.0 (13.9) Range: 87–138 (75%ile)	–
WASI performance IQ	116.2 (23.5) Range: 75–170 (79%ile)	–
WASI full-scale IQ	113.0 (16.9) Range: 81–146 (77%ile)	117, 87%ile
VOSP shape detection (/20)	19.3 (0.8) Range: 7–20 (Pass)	–
VOSP incomplete letters (/20)	16.9 (4.4) Range: 9–20 (Pass)	–
VOSP silhouettes (/30)	18.7 (1.9) Range: 14–27 (Pass)	–
VOSP object decision (/20)	15.9 (4.2) Range: 11–20 (Pass)	–
VOSP dot counting (/10)	9.8 (0.4) Range: 9–10 (Pass)	–
VOSP progressive silhouettes (/20)	11.2 (3.6) Range: 6–20 (Pass)	–
VOSP position discrimination (/20)	19.71 (0.5) Range: 19–20 (Pass)	–
VOSP number location (/10)	9.0 (1.2) Range: 6–10 (Pass)	–
VOSP cube analysis (/10)	8.2 (1.9) Range: 4–10 (Pass)	–
Trails A	41.4 s (14.5 s) Range: 18.58 s–88.00 s (26-49%ile)	–
Trails B	101.3 s (35.5 s) Range: 57.25 s–202.00 s (26-49%ile)	–
Digit span forward (/9)[a]	6.0 (1.2) Range: 4–8 (Normal Range)	–
Digit span backward (/8)[a]	4.6 (1.2) Range: 0–8 (Normal Range)	–

For each test, the average raw score is given, with standard deviation immediately to the right in parentheses. The range of raw scores is also given, as well as percentile (%ile) scores for the group average relative to established norms, where available. For comparison, we depict test results for DA which overlap with tests from our at-risk group. DA's full neuropsychological profile was originally published in Rosenbaum et al. (2008), MoCA = Montreal Cognitive Assessment; WMS-IV LM = Wechsler Memory Scale, 4th ed., Logical Memory subtest; Rey = Rey–Osterreith Complex Figure Test; WASI = Weschler Abbreviated Scale of Intelligence; VOSP = Visual Object and Spatial Perception battery. Missing two at-risk participants from all tests. [a]Missing one additional participant.

were analyzed. Our final sample included 75 older adults. Immediately after the experiment, all participants were given the MoCA as per scripted instructions. The MoCA was always administered after the experimental task to prevent potential bias from the experimenter during administration. Our sample was divided into 42 healthy adults ($M_{age} = 69.81$, SD = 5.63,

TABLE 2.

Z-scores of Medial Temporal lobe Volumes for Patient DA

	Left PRC	Left EC	Left PHC	Left HC	Right PRC	Right EC	Right PHC	Right HC
DA	−9.75	−6.65	−4	−4.14	−7.12	−6.02	−3.13	−5.19

Detailed examination of MTL structures in DA was accomplished using manual tracing on the normalized and coregistered T1-weighted images according to Insausti et al. (1998) for the hippocampus (HC), entorhinal cortex (EC), and perirhinal cortex (PRC) and according to Callen et al. (2001) for the parahippocampal cortex (PHC). *Z* scores were calculated using mean volumes corrected for head size for four controls demographically matched to DA (for further details, see Rosenbaum et al., 2005, 2008; Ryan et al., 2013).

30 females) with an average score of 27.04 on the MoCA (SD = 1.23, Range: 26–30) and 33 older adults considered at-risk for MCI (M_{age} = 69.33, SD = 6.33, 19 females), with an average score of 23.70 on the MoCA (SD = 1.20, Range: 21–25). A classification of "at-risk" was based on a MoCA score of less than 26/30, as this score yields an optimal balance of sensitivity and specificity (Nasreddine et al., 2005; Smith et al., 2007; Damian et al., 2011). There were no significant differences in age ($t(73) = 0.34$, $P = 0.73$) or education ($t(73) = 0.46$, $P = 0.65$) between the two groups. All participants were provided informed consent and were compensated for their time. Participants were tested in the Barense laboratory at the University of Toronto. This study was approved by the University of Toronto Ethics Review Board.

Neuropsychological battery

In a follow-up session we administered a neuropsychological test battery to participants with MoCA scores of less than 26 in order to better characterize the cognitive status of this group (Table 1), with the exception of two older adults who were unable to return for testing. The battery consisted of the Logical Memory subtest from the Wechsler Memory Scale (4th ed.; Wechsler, 2009), Trails A and B (Reitan and Wolfson, 1985), the Digit Span subtest from the Wechsler Adult Intelligence Scale (4th ed.; Wechsler, 2008), the Rey–Osterrieth Complex Figure Test (Osterrieth, 1944), the Weschler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999), and the Visual Object and Space Perception battery (VOSP; Warrington and James, 1991).

Patient DA

DA was 62-yr-old at the time of testing. He is a right handed man with 17 yr of education. He contracted herpes simplex encephalitis in 1993 and suffered severe MTL lesions as a result. As outlined in Rosenbaum et al. (2008) and Ryan et al. (2013), his left hemisphere has less than one third of hippocampus and entorhinal cortex remaining, with near complete perirhinal cortex and parahippocampal cortex loss. His right hemisphere is most severely damaged including hippocampal, perirhinal, entorhinal, and parahippocampal cortex along the entire extent, as well as anterior temporal lobe. His damage on the right extends to other areas as well; ventral frontal cortex, anterior cingulate cortex, anterior and posterior temporal cortex, and occipital cortex. Furthermore, there are additional small lesions in right posterior thalamus and left middle temporal gyrus. Table 2 demonstrates severe bilateral MTL volume loss which extends to the anterior temporal lobe in the right hemisphere.

DA presents with graded retrograde amnesia, ranging 30 years prior to his diagnosis, as well as severe anterograde amnesia. His general cognitive functioning is intact (Rosenbaum et al., 2008). DA has retained semantic memory and is able to learn some new semantic information (Westmacott and Moscovitch, 2002). He has high working memory performance and is able to visually imagine both objects and scenes and mentally reconstruct novel combinations of them (Ryan et al., 2013). His complete cognitive and neuropsychological profile can be found in Rosenbaum et al. (2008) and Ryan et al. (2013).

DA's performance was compared against eight controls, who were matched for age (M_{age} = 65.0), education ($M_{education}$ = 16.6 years) and gender. No differences were found between DA and controls in age ($t(7) = -1.00$, $P = 0.18$) or education ($t(7) = 0.12$, $P = 0.45$) using Crawford's *t* tests optimized for single case studies (Crawford and Howell, 1998).

Interference Match-to-Sample Task

Experimental procedure

Participants performed an interference match-to-sample task adapted from Watson and Lee (2013) that followed similar procedures (Fig. 1). The task was administered on a laptop using Presentation version 17.1 (www.neurobs.com). Participants were seated ∼20 in. from the screen.

Study phase. Every trial contained a study phase, an interference phase, and a test phase. At study, stimuli were comprised of real-world objects overlaid on virtual scene images. The study image was presented on screen for 2,800 ms and participants were instructed to remember both the object and scene across a delay period.

Interference phase. Following the study phase, an instruction screen informed participants which type of interference would ensue: object, scene, or number interference (control condition). If the number condition ensued, participants were informed to watch either the top or bottom number. Instructions stayed onscreen for 1,000 ms, after which the interference phase began. During interference, participants were shown a

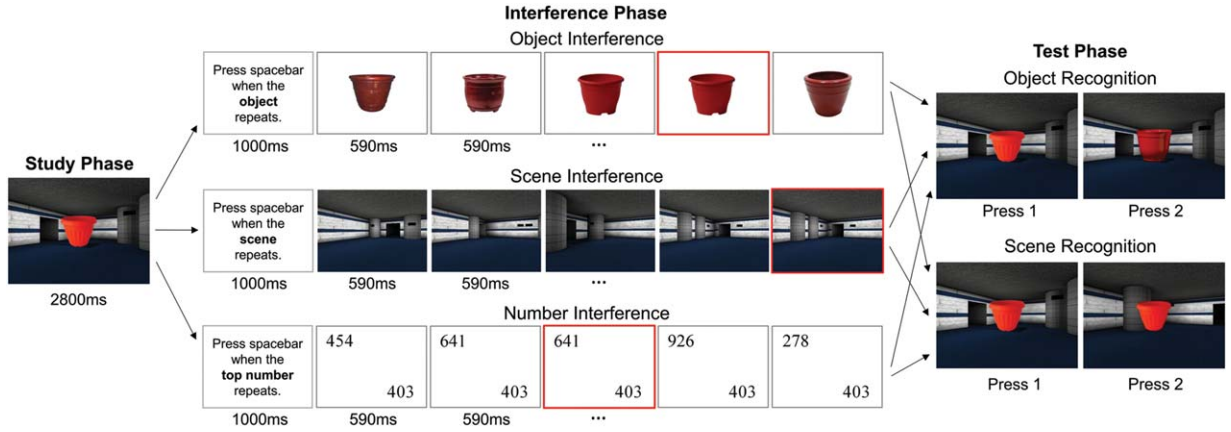

FIGURE 1. Task schematic demonstrating all possible combinations of interference type crossed with recognition type. Each trial was composed of a study, interference, and test phase. During the study phase, participants viewed an image of an object overlaid on a scene. The interference phase was composed of a series of five novel objects, scenes, or numbers, during which participants were instructed to detect a repeating item (target images outlined in red). During the test phase, participants identified the studied stimulus from a similar foil. The foil differed from the studied item either by the object (object recognition trials) or by the scene (scene recognition trials). The foil also differed from the interfering items. The order of trial types was intermixed and counterbalanced. Study images were trial unique. [Color figure can be viewed at wileyonlinelibrary.com]

stream of five images, presented sequentially for 590 ms each with 250 ms ISI. Participants completed a 1-back task in which they were instructed to press the spacebar when two successive stimuli were identical. The presentation of the 1-back target within the interference sequence was pseudo-random (i.e., third–fifth position, which never repeated more than three trials in a row) and fully counterbalanced. Responses that occurred between 200 and 1,230 ms after the repeated stimulus appeared on screen were taken as correct. This meant that participants could respond during the presentation of the repeated stimulus, or during the proceeding ISI, or during the presentation of the next stimulus (or during presentation of the test items, if the last stimulus in the sequence repeated). If multiple responses were made, the first response was taken as the final response, and other responses were disregarded.

Interfering objects were novel objects, chosen to share features in common with the study object. Interfering scenes were novel scenes, designed to share features in common with the study scene. Interfering numbers were composed of randomly varying digit strings. All images were trial unique. Number interference was included as a control condition because numbers share few visual features with objects or scenes. On the basis of pilot experiments to match difficulty across the different interference types, we included two numbers during number interference, where one remained constant with each presentation (non-target number). Because the non-target number remained constant, it was not informative for the 1-back decision. The target number appeared in both positions (top and bottom) an equal number of times throughout the experiment. The end of the interference phase was marked by a fixed ISI of 1,000 ms.

Test Phase. At test, two object-and-scene images were presented side-by-side on screen. One image was identical to the study image (target), whereas the other image (foil) differed from the target by one visually similar element: either the object or the scene. This differing element allowed for assessment of either object or scene memory. That is, when the object differed but the scenes were identical, the recognition decision was based on the object (and vice versa for scenes). Foils for the recognition test were not viewed at interference. Novel images were always used. Using numbers 1 and 2 on the keyboard, participants indicated whether the left (1) or right (2) image was the target. The recognition memory target appeared on either the right of left side of the screen an equal number of times across the experiment, and was pseudo-randomized to never appear in the same position for more than three consecutive trials. The end of the test phase was marked by a fixed ITI of 1,500 ms.

The three interference conditions and two recognition types were combined in a fully factorial design to result in six different trial types: both object and scene recognition could be preceded by object, scene or number interference. There were 36 trials for each condition, resulting in a total of 216 trials. Trials were ordered such that all trial types preceded or followed each other an equal number of times (i.e., Latin square design). Additionally, the occurrence of each of the 216 study images as followed by object, scene, or number interference was counterbalanced across participants.

Prior to beginning the task, participants were given 12 practice trials, two for each of the six conditions, to ensure understanding of the instructions. These were comprised of 36 novel object and scene stimuli. The order of practice trials was randomized.

Stimuli

Images of objects were taken from the Hemera Photo Objects database (Volumes I and II) and virtual reality scenes were created using a commercially available game (Deus Ex,

TABLE 3.

Proportion of Hits for Interference 1-Back Task

	Object recognition			Scene recognition		
	Object interference	Scene interference	Number interference	Object interference	Scene interference	Number interference
Healthy Older Adults	0.92 (0.13)	0.89 (0.15)	0.96 (0.11)	0.92 (0.13)	0.88 (0.17)	0.95 (0.10)
At-Risk Older Adults	0.83 (0.22)	0.81 (0.23)	0.89 (0.14)	0.83 (0.23)	0.81 (0.23)	0.88 (0.15)
DA Controls	0.97 (0.03)	0.95 (0.03)	0.98 (0.03)	0.98 (0.04)	0.94 (0.02)	0.98 (0.02)
DA	0.44	0.31	0.78	0.47	0.5	0.75

Standard deviations are indicated in parentheses.

Ion Storm L.P) and a freeware software editor (Dues Ex Software Development Kit v.1112f).

A total of 1,188 objects and 1,188 scenes were collected. Of these, 216 object and scene pairs were used to create study items and targets at test, and an additional 108 pairs were used to create foils at test. To create interfering stimuli, 216 sets of 4 unique objects and scenes were required for each of the study objects and study scenes. That is, each study image had a corresponding set of 4 similar objects and 4 similar scenes. All object and scene interfering stimuli were designed to contain similar low-level features (shapes, colors, etc.) as the study images. Interfering objects were chosen from the same basic-level category (e.g., watering cans, mantle clocks) and shared overlapping visual features with the study object. Interfering scenes contained similar wall textures and geometric features (e.g., stairs, doors, and windows) as the study scene, which were reshaped and rearranged to create a different, but visually similar scene. During number interference, Presentation 17.1 randomly generated two sets of three digits, in black Times New Roman, 72 point font on a white background. One digit string was placed on the top left corner of the box and the other was placed on the bottom right.

Task difficulty in young adults

To test whether object and scene recognition were equated in difficulty, we tested a sample of 15 young adults on our task. We found that object recognition performance ($M = 0.84$, $SD = 0.10$) was significantly higher than scene recognition performance ($M = 0.79$, $SD = 0.12$; $t(14) = 2.44$, $P < 0.05$). Critically, because we hypothesized that at-risk older adults should perform more poorly on object recognition than scene recognition; this imbalance did not confound the interpretation of our results. That is, because object recognition was the easier condition, any observed group differences in object recognition could not be attributed to task difficulty.

Planned Analyses

Older adults

Interference 1-back task. To examine performance on the interference 1-back task, we calculated accuracy as the average proportion correct within each condition. These data were then subjected to a 2 (group) × 2 (recognition type) × 3 (interference type) repeated measures ANOVA with a between-subject factor of group (at-risk for MCI and healthy controls) and two within-subjects factors of recognition type (object and scene) and interference type (object, scene, and number). The 1-back task was included to ensure participants paid attention to interfering material. Pilot testing was done to ensure performance across all conditions was as matched as possible, thus we did not predict differences in 1-back accuracy between conditions.

Recognition task. To examine performance on the recognition task, we used an omnibus logistic linear mixed-effect regression model (Baayen et al., 2008) implemented using the glmer function from the lme4 statisics package in R 3.1.2 (Bates, 2007). Accuracy was modeled at the trial level, with every trial coded as either correct or incorrect. A mixed-effect model allowed us to treat MoCA score as a continuous variable in our within-subjects design. This powerful approach allows for the simultaneous analysis of within-subject and between-subject variation and accounts for nesting conditions within-participants (i.e. repeated measures) and for between-subject variation as estimated by continuous measures.

We included only trials in which participants correctly responded to the 1-back decision during the interference phase. Across all older adults, accuracy during the 1-back task was 88%, resulting in 12% of trials being excluded from analysis (Table 3).

Our dependent variable was recognition memory accuracy, coded as 1 for correct and 0 for incorrect on a per trial basis. Our independent variables were MoCA score, recognition type, and interference type, all of which were crossed in the model to test the three-way interaction (see Supporting Information for formulas and R code). MoCA scores were grand mean-centered and both categorical variables were effect coded, with recognition type coded as "−1" for object recognition and "1" for scene recognition. Interference type had three levels and thus required two effect codes. For the first effect code, object, scene, and number interference were coded as "1," "0," and "−1" respectively, and for the second, as "0," "1," and "−1," respectively.

A 2-level mixed model was used to predict recognition memory accuracy. We estimated a random intercept (i.e., participants were entered as a random effect). We modeled random slopes for recognition type and interference type, because they were measured at the trial level, while MoCA scores were measured at the participant level (Aguinis et al., 2013). The multilevel equations that describe the model are provided in the supplementary materials. We used an unstructured covariance matrix and the between-within method for estimating degrees of freedom.

For significant effects in our omnibus model, we used the method of Aiken and West (1991) to probe the directionality of these effects (i.e., to probe simple effects). This method required effect codes to be re-coded as dummy codes, and for our continuous predictor of MoCA to be recoded using ±1 SD such that it reflected "high" scorers and "low" scorers, as is standard convention (Cohen and Cohen, 1983; West et al., 1996). We then ran a series of hierarchical logistic regression models with the newly coded variables. These results informed the directionality of the omnibus effects.

Patient DA. We calculated recognition memory accuracy as proportion correct for each condition. Analysis of DA's 1-back accuracy demonstrated that he was only able to identify 54% of the repeated stimuli. Thus, restricting the analysis to trials on which DA correctly responded during the 1-back task was deemed inappropriate, as it resulted in a loss of 46% of trials from the experiment, with most the notable trial loss coming from the experimental conditions (Table 3). Because of the diminished power inherent in single case-studies, we opted to analyze all trials for both DA and his age and education-matched controls. Importantly, DA was significantly above 25% chance-level accuracy on the 1-back task ($P < 0.001$), assuming a binomial distribution of performance, indicating that he did indeed pay attention to interfering stimuli. Given that the first image in the sequence never repeated, we also considered that chance level may have been 33%, which case DA's performance remains above chance ($P < 0.001$). We compared DA's recognition scores to matched controls (see Participants).

RESULTS

Older Adults

Neuropsychological battery

The results of the neuropsychological battery indicated that our at-risk group demonstrated episodic memory impairments consistent with those of MCI and the early stages of Alzheimer's disease (Hodges, 2000; Petersen et al., 1999). Performance was in the mild deficit to low average range relative to established norms on immediate and delayed recall of the Logical Memory test and delayed recall of the Rey Complex Figure Test (Table 1). In comparison, the at-risk group showed intact performance on non-mnemonic tests. Performance on both Rey figure copy and the VOSP were unimpaired, suggesting intact visual perception as assessed by these standard measures. The at-risk group was within the normal range for tests of semantic memory (Verbal IQ as assessed by the WASI) and executive function relative to established norms. In sum, the at-risk group showed cognitive declines that were specific to episodic memory, but normal performance in other cognitive domains.

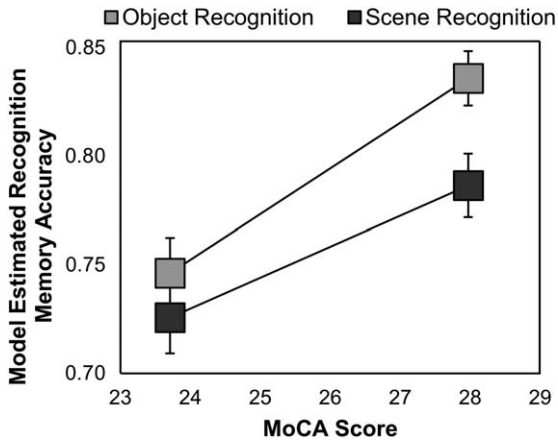

FIGURE 2. Model estimated recognition memory accuracy plotted as a function of MoCA score. Slopes for object recognition (light gray) and scene recognition (dark gray) are plotted separately. Squares represent model-estimated means of recognition memory of individuals falling ±1 standard deviation from the mean MoCA score. Both object and scene recognition memory slopes were significant. However, the interaction between recognition type and MoCA score indicated that MoCA score shared a stronger association with object recognition than with scene recognition. Error bars denote ±1 standard error.

Interference 1-back task

Data from the interference 1-back task are shown in Table 3. Our 2 × 2 × 3 repeated measures ANOVA examining proportion correct for the 1-back task revealed a main effect of group ($F(1,73) = 6.01$, $P < 0.05$), whereby the healthy group outperformed the at-risk group across conditions. Additionally, we found a main effect of interference ($F(2,147) = 7.05$, $P = 0.001$) whereby number interference was associated with the highest performance of the three interference conditions. Number interference 1-back performance was marginally higher than object interference 1-back performance ($t(74) = 1.94$, $P = 0.06$) and significantly higher than scene interference 1-back performance ($t(74) = 3.12$, $P < 0.01$). Performance on the 1-back task during object interference was also higher than during scene interference ($t(74) = 2.71$, $P < 0.01$). That participants performed well above chance on the 1-back task is important because inaccurate responses were the basis for trial exclusion from recognition memory analyses. It is worth noting that despite main effects of group and interference, even the conditions with the lowest performance (namely at-risk performance on both object and scene 1-back) were well above chance (chance level = 25%, $P < 0.001$, and chance level = 33%, $P < 0.001$, both assuming a binomial

distribution of performance). Thus, at most, six of 36 trials (associated with 81% accuracy) were excluded from recognition memory analyses.

Recognition task

Recognition memory accuracy was modeled at the trial level as a binomial distribution. Our predictors were recognition type, interference type, and MoCA score, with a random intercept and random slopes for recognition type and interference type. Because our model contained six random effects (the intercept, recognition type, two interference type effect codes, and two interaction terms for each interference type effect code crossed with recognition type) we optimized the estimation of model parameters when calculating the model's log likelihood by setting the "nAGQ" argument of the glmer function to 0. We report two reductions in prediction errors for both level 1 and level 2 predictors (i.e., Pseudo-R^2, akin to estimates of explained variance). With respect to individual outcomes, Pseudo-$R^2_1 = 0.01$, which is considered a small reduction in prediction error. With respect to predicting group means, Pseudo-$R^2_2 = 0.18$, which is considered a medium reduction in prediction error.

The omnibus model revealed a main effect of MoCA score ($b = 0.10$, $SE = 0.02$, $t(13854) = 4.05$, $P < 0.001$), whereby older adults with higher MoCA scores tended to have higher recognition memory accuracy generally across conditions (Fig. 2). There was also a main effect of recognition type ($b = -0.11$, $SE = 0.03$, $t(13854) = -3.81$, $P < 0.001$), whereby older adults generally exhibited higher recognition memory accuracy during object recognition than during scene recognition. Lastly there was a main effect of interference, tested using the log-likelihood ratio test ($F(2,\ 13554) = 6.35$, $P < 0.01$). This main effect was driven by significantly lower recognition memory accuracy across recognition types following object interference compared to both scene interference ($b = 0.19$, $SE = 0.05$, $t(13854) = 3.58$, $P < 0.001$) and number interference ($b = 0.11$, $SE = 0.05$, $t(13854) = 2.11$, $P < 0.05$), whereas recognition memory accuracy following scene and number interference did not significantly differ ($b = -0.08$, $SE = 0.06$, $t(13854) = -1.42$, $P > 0.05$; Fig. 3A).

Our primary predictions were that MoCA scores would be strongly associated with object recognition performance and that this association would be stronger than that of MoCA score and scene recognition performance. In line with this prediction, we found a **marginal** interaction between MoCA score and recognition type ($b = -0.02$, $SE = 0.01$,

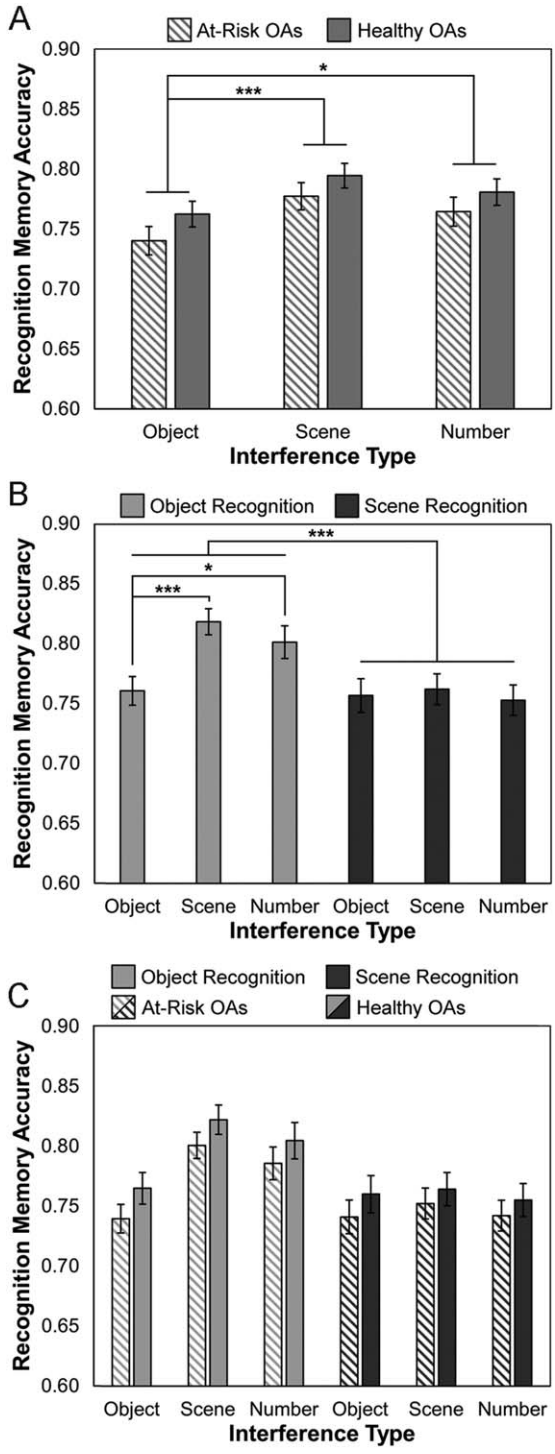

FIGURE 3. (A) Recognition memory accuracy for older adults at-risk for MCI (MoCA <26) and healthy older adults for each interference type, collapsed across recognition type. There were no significant differences in recognition memory accuracy (collapsed across recognition type) between older adult (OA) groups in any of interference types. There was a main effect of interference type, whereby object interference resulted in the lowest overall recognition memory performance. (B) Recognition memory accuracy plotted separately for each condition collapsed across participants. The recognition type by interference type interaction was driven by significantly lower accuracy during object recognition following object interference. Additionally, we found a main effect of recognition type whereby object recognition was significantly higher than scene recognition. (C) Full breakdown of group (at-risk and healthy) by recognition type (object and scene) by interference type (object, scene, and number). The three-way interaction between MoCA score, recognition type, and interference type was not significant. *$P < 0.05$, ***$P < 0.001$. Error bars denote ±1 standard error.

$t(13854) = -1.92$, $P = 0.05$; Fig. 2). Examination of simple effects revealed a significant slope of MoCA score within object recognition ($b = 0.13$, $SE = 0.02$, $t(13854) = 4.40$, $P < 0.001$) indicating that object recognition accuracy was highly associated with MoCA scores. Notably, there was also a significant slope of MoCA score with scene recognition ($b = 0.08$, $SE = 0.03$, $t(13854) = 2.75$, $P < 0.01$) indicating that scene recognition accuracy was also associated with MoCA scores. Thus, we interpret this interaction to reflect that scene recognition is reliably predicted by MoCA score, however, the predictive relationship between object recognition and MoCA score is stronger, which supports our primary hypotheses.

To further probe the MoCA score by recognition type interaction, we examined differences in accuracy between object and scene recognition among the highest and lowest performers on the MoCA, defined by the average scores of individuals falling ±1 standard deviation from the mean (Cohen and Cohen, 1983; West et al., 1996). The average accuracy of these high and low scoring individuals is estimated from the linear model (Fig. 2). Among individuals who obtained high MoCA scores, a large difference in recognition memory accuracy emerged between object and scene recognition ($b = -0.16$, $SE = 0.04$, $t(13854) = -3.89$, $P < 0.001$) such that object recognition accuracy was significantly higher than scene recognition. Among individuals who obtained low MoCA scores, there was no difference between object and scene recognition accuracy ($b = -0.05$, $SE = 0.04$, $t(13854) = -1.38$, $P > 0.05$). These results suggest that healthy older adults exhibit better object recognition compared to scene recognition, a finding in line with previous research (Spencer and Raz, 1994; Chalfonte and Johnson, 1996). However, lower MoCA scores appear to be associated with the loss of the object recognition advantage, consistent with evidence of perirhinal and lateral entorhinal cortex dysfunction.

Our third prediction was that interfering object stimuli would disproportionately impair object recognition memory among the at-risk group relative to their healthy counterparts. Interestingly, we did not find a significant interaction between interference type by MoCA score ($F(2, 13554) = 0.56$, $P > 0.05$), suggesting that recognition memory across both stimulus types in the at-risk group was not differentially impacted by the category of interfering stimuli (Fig. 3A). Additionally, we examined whether an interaction between MoCA score and interference type emerged within scene recognition and within object recognition separately, however neither of these interactions were significant (P's > 0.05; Fig. 3C). Thus, we did not find that older adults with low MoCA scores were differentially impacted by stimulus-specific interference.

Although we did not find that interference type interacted with MoCA score, we did find a significant interference type by recognition type interaction, suggesting that interfering material differentially impacted accuracy for each recognition type across all participants ($F(2, 13554) = 6.35$, $P < 0.01$; Fig. 3B). Within object recognition, object interference was associated with lower recognition memory accuracy than scene interference ($b = 0.34$, $SE = 0.08$, $t(13854) = 4.65$, $p < 0.001$) and

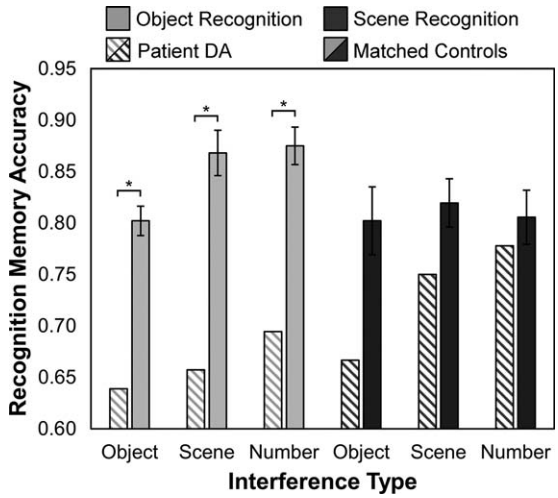

FIGURE 4. Recognition memory accuracy for patient DA and matched controls. Patient DA performed significantly worse than controls on all three object recognition conditions relative to controls. However, his performance was not significantly different from controls during scene recognition conditions. *$P < 0.05$. Error bars denote ±1 standard error.

number interference ($b = 0.24$, $SE = 0.08$, $t(13854) = 3.11$, $P < 0.01$) whereas scene and number interference did not differentially impact object recognition accuracy ($b = -0.11$, $SE = 0.08$, $t(13854) = -1.33$, $P > 0.05$). Within scene recognition, accuracy was not differentially impacted by any of the three interference types (all P's > 0.05). These results suggest that, although accuracy was higher during object recognition on average, it was also associated with higher vulnerability to object interference across older adults, such that accuracy dropped to the level of scene recognition for that condition. In support of this claim, an analysis of simple effects revealed higher accuracy in object recognition than scene recognition under scene interference ($b = -0.34$, $SE = 0.08$, $t(13854) = -4.52$, $P < 0.001$) and number interference ($b = -0.28$, $SE = 0.09$, $t(13854) = -3.10$, $P < 0.01$), but not under object interference ($b = 0.02$, $SE = 0.08$, $t(13854) = 0.25$, $P > 0.05$). In sum, these results suggest that object recognition was more susceptible to stimulus-specific interference than scene recognition across our older adults.

Patient DA

Next, we examined recognition memory accuracy in MTL patient DA and his eight matched controls using two-tailed Crawford's t tests (Crawford & Howell, 1998). All significant effects survived family-wise Bonferroni correction (adjusted P values shown). The analyses revealed that DA was significantly impaired on object recognition following all three interference conditions: object interference ($t(7) = -3.80$, $P_{adj} < 0.05$), scene interference ($t(7) = -3.45$, $P_{adj} < 0.05$), and number interference ($t(7) = -3.32$, $P_{adj} < 0.05$). This indicated that, like older adults with low MoCA scores, DA had a general deficit in his ability to recognize objects compared to healthy matched controls (Fig. 4). In contrast, although numerically

lower, there were no significant differences in DA's ability to recognize scenes after any of the three interference types: object interference ($t(7) = -1.37$, $P_{adj} = 0.63$), scene interference ($t(7) = -0.99$, $P_{adj} = 0.99$), and number interference ($t(7) = -0.35$, $P_{adj} = 0.99$). Thus, contrary to our hypotheses, DA's recognition memory for scenes appeared to be somewhat intact. Additionally, DA's recognition performance was not differentially impacted by interference type, relative to controls. This finding is in line with our above result that at-risk older adults were not differentially impacted by interference type compared to healthy older adults.

DISCUSSION

The current study provides novel evidence that stimulus-specific recognition deficits are associated with cognitive decline. In particular, the results suggest that cognitive decline is associated with object recognition performance to a stronger degree than with scene recognition performance. This relationship revealed that older adults who obtained low scores on the MoCA were impaired to a greater extent on object than on scene recognition, relative to their healthy peers. Consequently, these older adults appeared to have lost the object (relative to scene) recognition advantage that is characteristic of healthy aging (Lipman and Caplan, 1992; Spencer and Raz, 1995; Newman and Kaszniak, 2000; Bastin and Van der Linden, 2006; Old and Naveh-Benjamin, 2008). These results are consistent with established findings that the perirhinal and lateral entorhinal cortices are the origin sites of pathology in early stages of cognitive decline.

In line with our predictions, we found an interaction between MoCA score and recognition type which indicated that cognitive decline, as indexed by MoCA score, was more strongly associated with object recognition than scene recognition performance (Fig. 2). However, it is worth noting that scene recognition performance was also significantly associated with MoCA score. This finding is consistent with past research. Numerous studies suggest that the transition from MCI to Alzheimer's disease is accompanied by a spread in pathology from origin sites perirhinal and lateral entorhinal cortices to other MTL regions that are known to process scenes and spatial relationships, such as the hippocampus (Braak and Braak, 1991; Raz et al., 2004), parahippocampal (Hyman et al., 1984), and medial entorhinal cortex (Mitchell et al., 2002). As such, it is likely that the lateral entorhinal and perirhinal cortices are not the only regions affected in the early stages of cognitive decline. In support of this, many studies have found deficits in spatial processing tasks among individuals with amnestic MCI, as well as various memory impaired older adult groups (Cheng and Pai, 2010; Lithfous et al., 2013; Reagh et al., 2014), findings which are consistent with the results presented here. In addition, some studies have found that the ability to discriminate object targets from highly similar foils is impaired even in healthy aging (Burke et al., 2011; Ryan et al., 2012; Reagh et al., 2016;). In one such study, Reagh et al. (2016) directly compared object and spatial discrimination in older adults. In contrast to the current study, healthy aging was associated with poorer object than spatial discrimination. These dissimilarities may be due to qualitatively different spatial tasks, namely, recognition of object location as compared to recognition of scene images used here, or alternatively, to the different demands of two-alternative forced choice recognition as compared to old-new discrimination when lures are highly similar. Thus, although cognitive decline associated with both healthy and pathological aging can adversely impact the MTL broadly, the interaction presented here between stimulus-recognition domain and a sensitive measure of MCI-related cognitive decline (i.e., the MoCA) suggests that object recognition is most severely impacted in MCI-related decline. This is consistent with evidence that perirhinal and lateral entorhinal cortices are among the most vulnerable structures to AD-related pathological aging.

Previous studies found strong evidence that older adults at-risk for MCI were more susceptible to interference from visually similar objects than their healthy counterparts (Newsome et al., 2012; Yeung et al., 2013). Additionally, others demonstrated that perirhinal cortex lesions resulted in increased susceptibility to interference (Bartko et al., 2010; McTighe et al., 2010; Barense et al., 2012). We did not, however, find that exposure to interfering objects differentially impaired object recognition performance in the at-risk group or patient DA relative to healthy controls, as was predicted (Figs. 3A and 4). Viewed in this context, the present results suggest constraints on when and how interference will adversely impact object recognition in individuals with perirhinal cortex dysfunction. For example, it has been suggested that patients with MCI are more susceptible to proactive rather than retroactive interference (Ebert and Anderson, 2009), and previous studies reporting that at-risk individuals were vulnerable to interference had used proactive interference designs (Newsome et al., 2012; Yeung et al., 2013). In these studies, representations of visually similar features built up across the experimental session. Consequently, more interfering material was presented and more time was allowed for representations of interfering features to accumulate. This combination of circumstances allowed by proactive designs may be more detrimental to individuals with perirhinal cortex dysfunction, as this region is thought to support complex, conjunctive representations of objects that are essential for tasks that cannot be solved on the basis of object single features (Cowell et al., 2010; Graham et al., 2010).

Consistent with past research in younger adults (Watson and Lee, 2013; O'Neil et al., 2015), we found that across all participants, object interference had a detrimental impact on object recognition relative to scene recognition (Fig. 3B). Interestingly, and in contrast to these studies, the same finding was not observed for scenes. That is, we did not find that scene interference disproportionately impacted scene recognition. Indeed, a main effect of recognition type, whereby object recognition was generally higher than scene recognition across our

participants, is supported by evidence that poorer scene memory relative to single item memory generally occurs with aging (Lipman and Caplan, 1992; Spencer & Raz, 1995; Newman & Kaszniak, 2000; Bastin and Van der Linden, 2006; Old and Naveh-Benjamin, 2008). Stimulus-specific interference did not, however, exacerbate this effect. One possible interpretation of this result is that an inability to coherently represent scene images renders this stimulus category susceptible to any manner of interference in older adults, such as task-related interference (i.e., the 1-back task). The idea that exertion of mental effort during a retention interval is able to disrupt consolidation has been an important interpretation of classic studies of retroactive interference (Jenkins and Dallenbach, 1924; Skaggs, 1925). Additionally, the interference mechanisms associated with non-specific effects of mental effort are thought to differ from those associated with similarity of interfering material (Wixted, 2004). Thus it is conceivable that the interference 1-back task produced cognitive strain that masked additional effects of interference due to stimulus similarity, due to impoverished scene representations of older adults. An alternative account is that, in older adults, scene representations are not vulnerable to any manner of interference. We posit that scene representations are supported, in part, by the hippocampus (Lee et al., 2005a,2005b, 2008; Zeidman et al., 2014). Hippocampally dependent memories are thought to be more vulnerable to forgetting through decay than through interference (Sadeh et al., 2014, 2016). Thus, it is possible that in older adults, decay is the primary manner of forgetting for scene stimuli.

With regard to our interference 1-back task, there is considerable evidence that attentional processes may be deficient in individuals in the early stages of MCI (Hutchison et al., 2010; Gordon et al., 2015). Indeed, our finding that the at-risk group demonstrated poorer performance on the 1-back task relative to healthy controls is consistent with past work showing that individuals with mild AD have difficulty selecting relevant information and filtering out irrelevant information (Balota and Faust, 1991). These reports have emphasized the stimulus-general nature of attentional deficits, and various studies have shown that attentional selection is impaired along the MCI-AD continuum across a number of stimulus types (e.g., Levino et al., 2005; Tse et al. 2010; Monti et al., 2014). We do not believe, however, that attentional deficits in the at-risk group were confounds in our task for two reasons. First, both object and scene recognition were always preceded by a 1-back task, and thus, general attentional deficits could not have contributed to poorer object recognition alone. Second, the scene interference 1-back task appeared to be the most difficult of the three interference conditions (i.e., 1-back accuracy was lowest in this condition). We did not, however, find differences between high and low MoCA scorers in either of the scene interference conditions. Thus, the fact that scene interference did not produce the lowest object recognition performance suggests that it is stimulus-specific dysfunction, and not attentional deficits, that contributed to our primary results.

In line with our hypotheses, patient DA showed impaired object recognition relative to matched-controls. However, contrary to our predictions given his extensive hippocampal damage, DA's scene recognition performance was not impaired relative to matched controls (Fig. 4), a finding that seems to present a challenge to the representational account of MTL function. Previous reports on patient DA have suggested that he is able to use unique strategies to compensate for deficits classically thought to be present with hippocampal damage. For example, DA is able to spontaneously fuse together elements of stimuli in a way that benefits task performance, a unitization strategy that was not available to others with comparable hippocampal damage (Ryan et al. 2013). The nature of the scene recognition test employed by the current study was such that scene targets and foils shared low-level features and were unique only with respect to their conjunction of features (i.e., the locations of walls, stairs, columns, etc. relative to each other). In this way, scene recognition required recognizing associations between features. When considered with previous reports of DA's spontaneous ability to unitize disparate stimulus-elements (Ryan et al., 2013), and with the suggestion that a portion of DA's remaining left hippocampal tissue may be functional (Rosenbaum et al., 2008), it is plausible that DA was able to use an association-based strategy that disproportionately benefited scene recognition, but was not applicable to object recognition because objects contain fewer distinct elements. Nonetheless, DA's near-complete ablation of most MTL structures and impaired object recognition performance are consistent with evidence that object recognition deficits are MTL-dependent.

This task was adapted from previous studies (Watson and Lee, 2013; O'Neil et al., 2015b) and with these adaptations, we found that object and scene recognition were no longer equated in difficulty, and that object recognition resulted in higher performance than scene recognition in a group of young adults. That is, we found that condition most closely associated with cognitive status was actually easier. This pattern of results is inconsistent with a task difficulty explanation (i.e., those in the early stages of cognitive decline are most affected by difficult tasks). We show that, in spite of object recognition being easier than scene recognition, MoCA score was more predictive of object recognition accuracy.

These findings take advantage of an emerging body of evidence suggesting that the role of the MTL is not limited to long-term memory (Hannula et al., 2006; Hartley et al., 2007; Olsen et al., 2012). That the MTL is engaged in remembering an image across a short delay interval has been shown, specifically under conditions of visual interference, even with no mnemonic demands (Barense et al., 2012; Watson and Lee, 2013; O'Neil et al., 2015). We suggest that interference obviates the ability to use simple visual features to solve the task, regardless of the time delay. That is, under interference, the complex stimulus representations supported by MTL subregions are necessary to solve the task, and thus, the MTL supports performance under conditions of interference, regardless of the length of the delay.

The present results provide novel evidence that although cognitive decline can predict both object and scene memory performance, it shares a stronger relationship with object memory performance. Moreover, our data demonstrate that cognitive decline is associated with the loss of the object recognition advantage that is characteristic of healthy aging. This is consistent with evidence that individuals in a preclinical phase of MCI may have dysfunction in object-processing brain regions, such as perirhinal and lateral entorhinal cortices (Braak and Braak, 1991; Kordower et al., 2001; Khan et al., 2014). We show similar object recognition impairments in patient DA with known MTL damage. More generally, the results underscore the importance of using stimulus-specific memory effects to probe MTL integrity and its decline with pathology. Taking advantage of these neural properties will further our understanding of how the MTL supports memories of our visual world.

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