Title

Understanding perirhinal contributions to perception and memory: Evidence through the lens of selective perirhinal damage

Authors

Inhoff, Marika C
Heusser, Andrew C
Tambini, Arielle
et al.

Publication Date

2019-02-01

DOI

10.1016/j.neuropsychologia.2018.12.020

Peer reviewed

HHS Public Access

Author manuscript

Neuropsychologia. Author manuscript; available in PMC 2020 February 18.

Published in final edited form as:

Neuropsychologia. 2019 February 18; 124: 9–18. doi:10.1016/j.neuropsychologia.2018.12.020.

Understanding perirhinal contributions to perception and memory: Evidence through the lens of selective perirhinal damage

Marika C. Inhoff[1], **Andrew C. Heusser**[2], **Arielle Tambini**[3], **Chris B. Martin**[4], **Edward B. O'Neil**[5], **Stefan Köhler**[6], **Michael R. Meager**[7,13], **Karen Blackmon**[7,10], **Blanca Vazquez**[7], **Orrin Devinsky**[7,8,9], and **Lila Davachi**[11,12]

[1] Department of Psychology, University of California, Davis, C.A. USA

[2] Department of Psychology, Dartmouth University, Hanover N.H. USA

[3] Department of Psychology and Helen Wills Neuroscience Institute, University of California, Berkeley, C.A. USA

[4] Department of Psychology, University of Toronto, Ontario, Canada

[5] Department of Psychology, University of Toronto Scarborough, Ontario, Canada

[6] Brain and Mind Institute and Department of Psychology, Western University, London, Ontario, Canada

[7] Department of Neurology, New York University School of Medicine, Langone Medical Center, New York, N.Y., USA

[8] Department of Neurosurgery, New York University School of Medicine, New York N.Y., USA

[9] Department of Psychiatry, New York University School of Medicine, New York N.Y., USA

[10] Department of Physiology, Neuroscience and Behavioral Sciences, St. George's University School of Medicine, St. George, Granada, West Indies

[11] Department of Psychology, Columbia University, New York N.Y. USA

[12] Nathan Kline Institute, Orangeburg N.Y. USA

[13] Department of Psychology, New York University, New York N.Y. USA

Abstract

Although a memory systems view of the medial temporal lobe (MTL) has been widely influential in understanding how memory processes are implemented, a large body of work across humans and animals has converged on the idea that the MTL can support various other decisions, beyond

Contact information for corresponding author: Lila Davachi, Ph.D., Columbia University, 1190 Amsterdam Ave, New York, NY 10027, ld24@columbia.edu.

those involving memory. Specifically, recent work suggests that perception of and memory for visual representations may interact in order to support ongoing cognition. However, given considerations involving lesion profiles in neuropsychological investigations and the correlational nature of fMRI, the precise nature of representations supported by the MTL are not well understood in humans. In the present investigation, three patients with highly specific lesions to MTL were administered a task that taxed perceptual and mnemonic judgments with highly similar face stimuli. A striking double dissociation was observed such that I.R., a patient with a cyst localized to right posterior PRc, displayed a significant impairment in perceptual discriminations, whereas patient A.N., an individual with a lesion in right posterior parahippocampal cortex and the tail of the right hippocampus, and S.D., an individual with bilateral hippocampal damage, did not display impaired performance on the perceptual task. A.N. and S.D. did, however, show impairments in memory performance, whereas patient I.R. did not. These results causally implicate right PRc in successful perceptual oddity judgments, however they suggest that representations supported by PRc are not necessary for correct mnemonic judgments, even in situations of high featural overlap.

Keywords

Perirhinal cortex; memory; perception; hippocampus; medial temporal lobe

1. INTRODUCTION

Beginning with work with H.M., neuropsychological, neuroimaging, and animal work have converged on the medial temporal lobe (MTL) as an area that is critical for memory (Scoville and Milner, 1957). As such, investigations of MTL function have largely focused on elucidating how the hippocampus, perirhinal cortex (PRc) and parahippocampal cortex (PHc) contribute to memory. Recent models propose that MTL subregions differentially contribute to distinct aspects of memory, with the hippocampus supporting memory through its well characterized connectivity and interactions with MTL cortical regions (Brown and Aggleton, 2001; Davachi, 2006; Diana et al., 2007; Lavenex and Amaral, 2000; Libby et al., 2012). Indeed, much empirical work has supported the idea that the hippocampus, PRc, and PHc support processes related to subsequent relational and item memory (Davachi et al., 2003; Dougal et al., 2007; Kirwan and Stark, 2004; Ranganath et al., 2004; Sperling et al., 2003; Staresina and Davachi, 2008, 2009; Vilberg and Davachi, 2013) as well as differentially supporting associative versus item representations (LaRocque et al., 2013; Liang et al., 2012; Staresina et al., 2012).

Although these models have greatly advanced our understanding of the brain areas involved in supporting different aspects of memory, they do not address whether or how MTL regions might support processes beyond memory. Another body of work, however, has provided evidence that PRc may be critically involved in representing certain types of perceptual information. Investigations in non-human primates have demonstrated that ablations to the PRc produce deficits in visual discrimination performance under conditions of high feature ambiguity, where the use of feature conjunctions are required for discrimination (Bussey, Saksida, & Murray, 2002; 2003; Bartko, Winters, Cowell, Saksida, & Bussey, 2007;

Buckley, Booth, Rolls, & Gaffan, 2001; Bussey et al., 2002; 2003). Similarly, patients with MTL damage that includes PRc demonstrate behavioral deficits in visual discrimination tasks with high levels of featural overlap whereas patients with selective hippocampal damage that spares PRc do not (Barense et al., 2005; Lee et al., 2005). Consistent with these results, fMRI studies have demonstrated that PRc is recruited during oddity discrimination judgments that place demands on feature integration (Barense et al., 2009, 2011; Lee et al., 2008; O'Neil et al., 2009), but not during color and shape discriminations (Devlin and Price, 2007), providing convergent evidence that PRc is involved in adjudicating between similar and/or complex visual stimuli.

Models seeking to incorporate these results have suggested PRc contains representations that can be used to support both perceptual and mnemonic processing (Bussey & Saksida, 2007; Cowell, Bussey, & Saksida, 2006; Graham, Barense, & Lee, 2010; Murray & Bussey, 1999), and that mnemonic processes may rely on the integrity of perceptual representations supported by PRc (Graham et al., 2010). Although neuropsychological work has provided evidence in support of this idea, these investigations have largely sought to delineate PRc contributions to perception and memory by comparing performance of individuals with damage circumscribed to the hippocampus to patients that have both hippocampal and broader MTL damage including PRc. The rare occurrence of patients with selective damage to PRc has made it difficult to assess the PRc's unique contributions to memory judgments involving high levels of featural overlap, as any deficits observed could be due to hippocampal damage alone or combined damage to both regions.

Here, we provide a causal test of the role of PRc supporting perceptual and mnemonic judgments in patient I.R., an individual with a congenital lesion restricted to right posterior PRc. This type of lesion profile is exceedingly rare, and to our knowledge it is only the second instance of an investigation in a patient with damage that disproportionately involved PRc (see Bowles et al., 2007, 2010; Martin et al., 2011). Thus, such a patient is highly informative in our understanding of the functional contributions of PRc to aspects of behavior. I.R. participated in a task that involved both perceptual and mnemonic judgments on simultaneously presented face stimuli with overlapping features, allowing for an assessment of whether unilateral damage to PRc impacts perceptual and mnemonic abilities. In order to bridge patient and neuroimaging investigations, this task has been previously shown to activate right PRc during both perceptual and mnemonic judgments (O'Neil, Cate, & Kohler, 2009). To assess the specificity of PRc involvement in perceptual and mnemonic judgments, we also assessed performance of patient A.N., an individual with a lesion extending from right PHc to the right hippocampal tail, and patient S.D., an individual with bilateral hippocampal damage, in this same task. By comparing performance across patients with these distinct lesion profiles, the current investigation extends our understanding of how MTL regions differentially support perceptual and mnemonic judgments.

2. MATERIALS AND METHODS

2.1 Patients.

Three (3) patients were recruited from New York University's Patient Registry for the Study of Perception, Emotion, and Cognition (NYU-PROSPEC) to participate in the experiment.

At the time of behavioral testing, I.R. was a 19-year-old, right-handed, English speaking male with 12 years of education who suffered from medically refractory epilepsy. MRI results revealed a congenital, well-circumscribed nonenhancing cystic region in right posterior PRc (Figure 1, left panel, see Supplementary Figure 1 for detailed view of lesion profile). S.D. was a 34-year-old bilingual (English and Bengali), right-handed male with 16 years of education also suffering from intractable epilepsy. MRI scan results indicated the presence of bilateral hippocampal damage (Figure 1, right panel, see Supplementary Figure 2 for detailed view of lesion profile). A.N. was a 15-year-old, right-handed, English speaking, female with 9 years of education who suffered from medically refractory epilepsy. Evaluation of A.N.'s MRI image revealed a large lesion in right posterior PHc cortex, which extended through the tail of the right hippocampus (Figure 1, center panel; see Supplementary Figure 3 for detailed view of lesion profile). MNI normalized masks of each patient's lesion site are also available on NeuroVault (https://neurovault.org/collections/RCUBJXUH/). All patients were candidates for surgical resection of affected MTL regions, but did not receive such treatment prior to study participation.

2.2 Controls

A total of 34 control participants with normal or corrected-to-normal vision were recruited from the New York University and New York City communities. All procedures were approved by the human subjects Institutional Review Board of New York University. We performed a binomial test on performance associated with perceptual and mnemonic judgments (collapsing across all levels of difficulty) in each control participant. This procedure resulted in the removal of 7 control participants on the basis of chance memory performance, indicating that these participants did not pay attention during the task. Chance memory performance was also observed in these 7 participants when assessing performance on easy and hard memory trials separately.

Of the remaining 27 control participants, 6 were age and education matched +/− 4 years to S.D. (M age = 33.83, SD age = 0.41; M edu = 16.33, SD edu = 1.366), and 21 were age and education matched +/− 4 years to I.R. (M age = 19.33, SD age = 1.98; M edu = 14.05, SD edu = 1.88). Of the 21 age and education matched controls for I.R., 8 were also age and education matched (+/− 4 years) to A.N. (M age = 17.5, SD age = 1.60; M edu = 12.13, SD edu = 1.45). In order to provide a full picture of patient deficits relative to controls, we report each patient's score relative to his or her specific age and education matched controls in addition to relative to all controls.

2.3 Materials

The materials and procedure were taken from an fMRI investigation of PRc involvement in perception and memory conducted in healthy participants (see O'Neil et al., 2009). Stimuli presented during memory and perception test trials were comprised of face triplets that were generated by morphing two distinct Caucasian faces. Facial morphs were used due to the high degree of featural overlap in facial stimuli and prior work indicating that patients with broad MTL lesions are significantly impaired at discriminating perceptually similar face stimuli (Lee et al., 2005a). All faces displayed a neutral expression, and distinctive non-facial features, such as hair or clothing, were cut from the images. To generate triplets in the

memory test trials, two individual faces were identified as end points on a morphing continuum, with the third face in the triplet falling an equal distance from the other two faces. On perception test trials, the position of the third face on the morphing continuum was systematically manipulated to create three levels of difficulty. Specifically, the distance between the oddball face and one of the end point faces was varied to make the oddball face more or less distinctive relative to the two endpoint faces. Importantly, faces used in perception test trials were trial-unique.

2.4 Experimental procedures

As outlined in O'Neil et al., each run began with an initial study phase during which participants were presented with 12 unique target faces for 3000 ms each (1000 ms inter-stimulus interval) and asked to memorize them (Figure 2, left panel) (2009). In order to manipulate difficulty, half of the faces were presented a single time during this study period (hard memory trials), while the remaining faces were presented three times (easy memory trials). Participants were instructed to encode the entire face and not to focus on specific features, like the nose or mouth. Following the study period, participants were entered into a test phase where memory and perceptual abilities were assessed (Figure 2, right panel). Each run included six trials from each difficulty level of the memory and perception tasks. Participants were presented with a 1 second cue (M to indicate memory, O to indicate oddity) prior to each trial to provide information about the upcoming trial type. During memory trials, participants were presented with a face triplet, and asked to select the face that had been viewed during the initial study phase. Perception trials required participants to also view a face triplet, but to select the face that was the most distinctive, or the "odd one out" in the triplet. Participants had 5 seconds to make a response, and each trial was followed by a fixation cross. All patients and control participants were read detailed task instructions and asked to verbally describe the different trial types prior to beginning the experiment. Additionally, all patients and control participants completed a practice session before beginning the first experimental run, ensuring full understanding of the task. I.R., the first patient to be run in the current investigation, completed six runs of task. A.N. and S.D., who participated after I.R., were only able to complete four runs due to time constraints. All control participants completed six task runs.

2.5 Neuropsychological evaluation

Neuropsychological evaluations of I.R., S.D., and A.N.[1] were conducted by trained and licensed neuropsychologists affiliated with NYU PROSPEC.

Neuropsychological testing of I.R. revealed an average FSIQ on the Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV). His Verbal Comprehension Index (VCI=103) and Perceptual Reasoning Index (PRI=100) scores were in the average range. His Working Memory Index (WMI=95) was also average. His performance on the Processing Speed Index (PSI=86) was a weakness, and about 1 SD below his VCI and PRI performances, see

[1]Patient A.N. underwent neuropsychological evaluation at the age of 15, and could not be administered the same battery of tests as adult patients S.D. and I.R. The majority of the standardized measures used to evaluate A.N.'s neuropsychological functioning pre-surgically were developed and normed for use with adolescents, and these tests are counterparts or have similar procedures and interpretations as the adult tests administered to S.D. and I.R.

Table 1. I.R. displayed intact attention, working memory, language abilities, and visuospatial skills, and there was no evidence of a decline in general cognitive functioning relative to premorbid estimates. He displayed some difficulty with executive functions, specifically in the areas of novel problem solving and nonverbal fluency. Copy performance for a complex figure (RCF) was average. His ability to recall the figure after a delay was low average (RCF Delay), see Tables 2 and 3. His ability to learn simple to fairly detailed geometric figures ranged from average (WMS-IV VP-I) to high average (BVMT-R), see Table 2. His ability to recall these figures following a delay was low average (WMS-IV VPII) to high average (BVMT-R Delay). His recognition performances for these measures were average, see Table 3. In terms of verbal learning, I.R.'s immediate and delayed performance on a list-learning test (RAVLT Learning) was average. Following a delay, his recall was low average (RAVLT Delay), while he showed a high average performance on a recognition paradigm (RAVLT Recognition), see Table 4. His learning and delayed recall performances on a prose test (WMS-IV LM-I) were average. He correctly answered 22 of 30 questions on a yes/no recognition trial, see Table 5. At the time of participation, I.R. was taking two anti-epileptic medications (Keppra and Trileptal, dosage uncertain).

Pre-surgical WADA test results revealed (11/12) 91.7% left hemisphere memory (right injection) and (5/12) 41.7% right hemisphere memory (left injection), suggesting impaired right hemisphere memory functioning.

S.D.'s performance on the Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV) indicated an FSIQ in the average range. His Verbal Comprehension Index (VCI=114) was high-average, and his Perceptual Reasoning Index (PRI=100) score was average. He had an average Working Memory Index (WMI=108) and his Processing Speed Index was low average (PSI=86). This lower performance on PSI on the WAIS-IV was notable, as it is one to two standard deviations below the other WAIS-IV index scores, see Table 1 for comparison. S.D.'s performances on other cognitive measures, such as confrontation naming, phonemic fluency, visual tracking, mental flexibility, concept formation and problem solving, and set-shifting we all average or better. He also demonstrated difficulty with semantic fluency (borderline range) compared to phonemic fluency (average range). His ability to copy a complex figure (RCF) was impaired, and almost 2.5 SD below the normative mean for his age. His performance when recalling the figure after a delay, was significantly impaired and void of most details, see Tables 2 and 3. His ability to learn simple to fairly detailed geometric figures ranged from low average (BVMT-R) to high average (WMS-IV VP-I), see Table 2. His ability to recall these figures following a delay was low average (WMS-IV VP-II) to average (BVMT-R Delay). His recognition performances for these measures were average, see Table 3. In terms of verbal learning and memory, S.D. showed an average ability to learn words across learning trials (CVLT-II Learning). His delayed recall of the word-list was impaired according to age corrected norms (CVLT-II Delay). His performance on a forced-choice recognition paradigm, showed improvement compared to free recall, but was still below expectation (CVLT-II Recognition), see Table 4. His performance for learning on a prose test (WMS-IV LM-I) was average. His delayed recall was also average (WMS-IV LM-II) and he correctly answered 27 of 30 questions on a yes/no recognition trial (WMS-IV LM-Rec.), see Table 5.

At the time of testing, S.D. was taking Felbatol (600 mg) 3x daily, Frisium (5 mg) daily, and Sabril (500 mg tab twice daily) to control seizure events.

S.D. has yet to undergo a WADA procedure. He underwent implantation of a neurostimulator in 3/2016, which was three years after participating in this study, at that time a WADA was not clinically indicated.

A.N.'s neuropsychological assessment revealed a high average FSIQ, her Verbal Comprehension Index (VCI=112) was in the high average range and her Perceptual Reasoning Index (PRI=108) was in the average range, as measured by the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV). Her Working Memory Index was average (WMI=102) and her Processing Speed Index was very superior (PSI=136), see Table 1. All academic achievement skills were at or above age and grade expectations. Language skills (viz., naming, verbal fluency), basic attention, and visuomotor skills were intact. Complex visual tracking and set-shifting (viz., Trailmaking B) was a relative weakness (borderline range). Learning and memory performance showed a clear material specific deficit, with her verbal memory (WRAML-2, Verbal Memory Index = 105) being superior to her visual memory (Visual Memory Index = 88). In regards to specific subtest performances, she had a borderline performance when learning designs, following a delay her recognition was Average (WRAML-2 Design Memory). Her copy of the Rey Complex Figure (RCF) was in the average range. Although, following a delay, her recall of the figure was just short of two standard deviations below the mean, see Tables 2 and 3. On a test of verbal list-learning, her immediate, delayed, and recognition performances all fell in the average range (WRAML-2 Learning). Her performance on a measure of prose memory was high average for immediate and delayed recall (WRAML-2 Story Recall) and average for recognition (WRAML-2 Story Rec.), as she correctly answered 32 of 40 questions on a yes/no recognition trial, see Tables 4 and 5. A.N.'s subjective report (BASC-2) revealed distresses from anxiety, excessive somatic concerns, and difficulties with interpersonal relationships (with both her parents and teachers). At the time of testing, A.N. was not taking any medications to control seizure events.

Pre-surgical WADA test results from 8/2013 revealed (12/12) 100% left hemisphere memory (right injection) and (3/12) 25% right hemisphere memory (left injection), suggesting impaired right hemisphere memory functioning.

2.6 Analysis

In order to compare individual patient performance relative to groups of control participants, we employed a modified independent samples t-test (Crawford and Howell, 1998). This modified statistical test was derived specifically for situations where individual scores are compared against normative samples with less than 50 participants. Because of a large literature implicating PRc, hippocampus, and PHc in tasks probing perception and memory, significance was assessed at the level of .05. To assess whether individual participants' and patients' scores differed significantly from performance that would be expected by chance, a binomial test was used with a chance value of 33%. In order to provide a full picture of patient scores, individual patients were compared to age and education matched controls, all control participants, and chance levels of performance. Analyses were conducted on all

available data. Since patient A.N. and S.D. completed 4/6 runs, we also ran a control analysis subsampling the first 4 runs for all controls and patients to ensure that power differences between subjects did not drive the observed effects. Conclusions were not altered when only N = 4 runs were included for analysis.

3. RESULTS

3.1 Perceptual oddity judgments

In order to assess performance on perceptual oddity judgments, the scores of I.R., A.N., and S.D. were compared to the performance of age and education matched controls, all controls, and to chance levels of performance. When collapsing across difficulty, neither A.N. nor S.D. displayed oddity judgment performance that was significantly different from each patient's age and education matched controls [A.N.: $t = .1.09$, p = .1557, 1-tailed; S.D.: $t = -1.7439$, p = .07, 1-tailed], whereas I.R.'s performance was significantly lower than age and education matched control performance ($t = -2.83$, p = .005, 1-tailed). The same pattern of results was observed when each patient was compared relative to all control participants [A.N.: $t = .7626$, p = .226, 1-tailed; S.D.: $t = -.964$, p = .172 1-tailed; I.R.: $t = -3.07$, p = 0.0025, 1-tailed]. Additionally, patients A.N. and S.D. performed significantly above chance levels of performance (33%) [A.N.: p < .000001; S.D.: p < .0001, binomial test], whereas PRc patient I.R. did not display performance that was significantly different from chance (p = .08, binomial test) (Figure 3, right panel).

To assess the specificity of I.R.'s impairment and to rule out any deficits in MTL patients A.N. and S.D., perceptual judgments were also assessed by difficulty (Figure 4). I.R. was significantly impaired relative to age and education matched controls across all levels of difficulty [*easy*: $t = -2.6637$, p = .008, 1tailed; *medium*: $t = -1.862$, p = .0387, 1-tailed; *hard*: $t = -1.99$, p = .03, 1-tailed]. This deficit persisted when comparing I.R. to all control participants [*easy*: $t = 2.787$, p = .0049, 1-tailed; *medium*: $t = -2.074$, p = .0241, 1-tailed; *hard*: $t = -2.22$, p = .01, 1-tailed] and his performance was also not significantly different from chance at any level of difficulty [*easy*: p = .11; *medium*: p = .11; *hard*: p = .86, binomial test]. Unlike I.R., however, neither A.N. nor S.D. were significantly impaired relative to age and education matched controls at easy or medium difficulty levels [A.N. *easy*: $t = -0.105$, p = 0.46, 1-tailed; A.N. *medium*: $t = .333$, p = .374, 1-tailed; S.D. *easy*: $t = -1.386$, p = .112, 1-tailed; S.D. *medium*: $t = 0$, p = .5, 1-tailed]. A.N.'s performance on hard perceptual judgments was not significantly different from controls [t = 0.942, p = 0.189, 1-tailed], however S.D.'s performance displayed a trend toward significance [t = −1.989, p = 0.0516, 1-tailed]. Similar results were observed when comparing A.N. and S.D. to all control participants [A.N. *easy*: $t = 0.0419$, p = .482, 1-tailed; A.N. *medium*: $t = .4713$, p = .321, 1-tailed; A.N. *hard*: $t = 1.181$, p = .1241, 1-tailed; S.D. *easy*: $t = -1.231$, p = .115, 1-tailed; S.D. *medium*: $t = .417$, p = .321, 1-tailed; S.D. *hard*: $t = -1.172$, p = .126, 1-tailed]. In contrast to I.R., A.N. and S.D. displayed performance that was significantly different from chance performance on both *easy* and *medium* difficulty judgments [A.N. *easy*: p < .0001, A.N. *medium*: p < .001; S.D. *easy*: p = .004, S.D. *medium*: p < .001; binomial test]. Although A.N. displayed performance that was significantly different from chance on *hard* perceptual judgments (p < .001, binomial test), S.D. did not (p = .3921, binomial test).

3.2 Memory judgments

In order to evaluate memory abilities in our patients, performance on memory judgments was also assessed. When collapsing across levels of difficulty, A.N. performed significantly lower than age and education matched controls [$t = -2.15$, p = 0.03, 1-tailed] whereas S.D.'s scores trended toward significance [$t = -1.9$, p = .057, 1-tailed]. When compared against all controls, both patients displayed significant deficits [A.N.: $t = -1.989$, p = 0.0287, 1-tailed; S.D.: $t = -2.197$, p = 0.0186, 1-tailed], (Figure 3, left panel). I.R., on the other hand, did not display performance that was significantly different from age and education matched control participants ($t = -.347$, p = 0.366, 1-tailed) or all control participants ($t = -.2566$, p = .4, 1-tailed). In line with these results, neither A.N. nor S.D. displayed memory performance that was significantly different from chance [A.N.: p = .13, binomial test; S.D.: p = .22, binomial test], whereas I.R.'s judgments were significantly better than chance performance (p < .00001, binomial test).

Memory performance was also assessed as a function of difficulty, with results revealing that A.N. displayed a significant or trending impairment relative to age and education matched controls on hard and easy memory judgments, respectively [*easy*: $t = -1.41$, p = .10, 1-tailed; *hard*: $t = -2.69$, p = .0155, 1-tailed]. S.D.'s performance relative to age and education matched controls trended toward significance at both levels of difficulty [*easy:* $t = -1.578$, p = 0.08, 1-tailed; *hard*: $t = -1.91$ p = 0.0565, 1-tailed] (Figure 5). Compared to all controls, A.N. displayed a significant impairment in making *hard* memory judgments [$t = 1.77$, p = 0.044, 1-tailed] whereas her impairment trended toward significance for *easy* memory judgments [$t = -1.767$, p = 0.05, 1-tailed]. S.D. was significantly impaired across both difficulties when compared to all controls [*easy*: $t = -1.96$, p = 0.03, 1-tailed; *hard*: $t = -1.767$ p = 0.04, 1-tailed]. Consistent with the idea that A.N. and S.D. were impaired at memory judgments across difficulties, neither A.N. nor S.D. displayed responses that were significantly different from chance for either difficulty [A.N. *easy*: p = .1994, binomial test; A.N. *hard*: p = .3921, binomial test; S.D. *easy*: p = .39, binomial test; S.D. *hard*: p = .39, binomial test]. In contrast to A.N. and S.D., I.R.'s performance on *easy* and *hard* memory judgments was not significantly different from either age and education matched control participants [*easy*: $t = -.2507$, p = .40, 1-tailed; *hard*: $t = -.349$, p = .36, 1-tailed] or all control participants [*easy*: $t = -.1827$, p = .428, 1-tailed; *hard*: $t = .3594$, p = .362, 1-tailed]. Additionally, I.R.'s performance was significantly greater than chance across both difficulties [*easy*: p < .0001, binomial test; *hard*: p = .0072, binomial test].

3.4 Control performance

As a manipulation check and replication of the behavioral results reported by O'Neil et al. (2009), control scores across each level of difficulty in the perception and memory judgment tasks were assessed. In line with the results reported by O'Neil and colleagues, a one-way repeated measures ANOVA revealed a significant main effect of difficulty across both the memory ($F_{(1,26)} = 20.6$, p < .0001) and perception ($F_{(2,52)} = 53.4$, p < .0001) tasks. Planned paired t-tests were computed to verify the difficulty manipulation across tasks, revealing significant differences in the expected direction between difficulty levels for perceptual judgments [*easy* vs. *medium*: t(26) = 7.99, p < .000001, 2-tailed; *easy* vs. *hard*: t(26) = 8.42,

$p < .000001$, 2-tailed; *hard* vs. *medium*: $t(26) = 8.4171$, $p < .000001$, 2-tailed] and memory judgments [*easy* vs. *hard*: $t(26) = 4.54$, $p < .001$, 2-tailed].

4. DISCUSSION

The role of MTL regions in aspects of cognition beyond memory is a topic of debate, and an emerging view is that PRc contains representations that are important for perceptual and mnemonic judgments that occur under conditions of high feature ambiguity (Bartko et al., 2007; Bussey and Saksida, 2007; Graham et al., 2010). Here, we provide a critical test of this idea by assessing the performance of three patients with lesions to highly specific MTL regions in a task where perceptual and mnemonic judgments require the ability to discriminate between visual stimuli with highly overlapping features. Results revealed a double dissociation such that I.R., an individual with a congenital cyst in right posterior PRc, demonstrated significant impairments in making perceptual oddity judgments across all levels of difficulty, whereas A.N., a patient with damage to right posterior hippocampal and right PHc did not. S.D., an individual who sustained bilateral hippocampal damage, displayed a pattern of results that were similar to patient A.N., with impaired perceptual performance at easy and medium difficulty levels. In contrast, I.R.'s memory performance was not significantly different from controls, whereas S.D. and A.N. displayed significant mnemonic impairments across both easy and hard levels of difficulty. These results were consistent with neuropsychological evaluations, which indicated that both A.N. and S.D. were strongly impaired on memory judgments, as measured by the RCFT delayed recall performance, whereas I.R.'s performance fell within average levels. Together, these results suggest that the right posterior PRc, the location of the I.R.'s cyst, is important for perceptual decisions requiring comparisons between visually presented, novel stimuli that are similar. Importantly, stimuli included in the perceptual oddity judgments were trial unique, precluding the use of familiarity or novelty in making correct responses.

The present results are consistent with a large body of work that has implicated the PRc in representing perceptual information (Baxter, 2009; Buckley & Gaffan, 2006; Buckley et al., 2001; Bussey et al., 2002, 2002; Eacott, Gaffan, & Murray, 1994; Murray & Bussey, 1999), however they are not necessarily consistent with patient and fMRI work that have attributed mnemonic judgments in situations of high featural overlap to PRc (Barense et al., 2005; Barense et al., 2011; Devlin & Price, 2007; O'Neil et al., 2009). There are many reasons why this might be the case. PRc contributions to perception and memory in humans have largely been elucidated by comparing performance of patients with localized hippocampal damage and patients with damage to both the hippocampus and the broader MTL (Barense et al., 2005; Barense, Rogers, Bussey, Saksida, & Graham, 2010; Behrmann, Lee, Geskin, Graham, & Barense, 2016; Buffalo, Reber, Squire, et al., 1998; Holdstock, Gutnikov, Gaffan, & Mayes, 2000; Lee, Buckley, et al., 2005; Lee, Bussey, et al., 2005; Levy, Shrager, & Squire, 2005; Shrager, Gold, Hopkins, & Squire, 2006; Stark & Squire, 2000). Although patients with broad MTL damage included in these investigations have a common site of lesion overlap in the PRc, damage also often extends into amygdala, temporal cortex, collateral sulcus, and the anterior and posterior hippocampus. As such, the lack of specificity in these investigations makes clarifying the precise contributions of representations supported by PRc difficult.

FMRI has also been used to query the role of PRc in perception and memory, however evidence has been mixed. O'Neil and colleagues scanned participants as they completed the task used in the present investigation, and found that activity in right anterior PRc was associated with both retrieval of previously encoded faces and perceptual oddity judgments with novel face stimuli (O'Neil et al., 2009). Critical to the argument that PRc is involved in supporting memory and perception judgments, activity in right anterior PRc was able to differentiate between correct and incorrect judgments in both tasks. An additional investigation by O'Neil and colleagues found similar patterns of activation in right PRc and ventral visual regions across recognition memory and perceptual oddity judgments, suggesting that representations in these areas may be similar (O'Neil et al., 2013). Other work, however, suggests that PRc may not be involved in supporting memory judgments. An investigation by Lee and colleagues assessed neural activity in a task where participants were required to make perceptual oddity judgments on a series of faces (Lee et al., 2008). Interestingly, they did not find significant activation changes in PRc with repeated presentation of stimuli across trials, as might be expected if PRc was representing mnemonic information about the stimuli. Although these studies suggest that right PRc plays a role in perceptual judgments, proponents of a memory systems view of PRc have suggested that PRc activation in these tasks can be explained by incidental encoding of stimuli in perceptual oddity judgment tasks. The results of the present investigation make this explanation unlikely, and they highlight that fMRI BOLD activation should not be used as evidence that an area is necessary to support aspects of cognition.

The present investigation adds to our understanding of hippocampal contributions to mnemonic judgments. In particular, evidence for hippocampal involvement in memory for face stimuli has been mixed, with some investigations finding impaired memory for faces presented from a fixed viewpoint in individuals with hippocampal damage (Milner, 1968a; Warrington and Taylor, 1973), and others finding intact performance (Bird et al., 2007, 2008; Olsen et al., 2015; Reed and Squire, 1997). This lack of consistency can be ascribed to a number of factors, including differences in the encoding and retrieval demands of the tasks employed. Notably, the memory task in the current experiment required participants to choose the studied face from an array that included highly similar morphed lure faces. In order to facilitate accurate memory judgments at test, patients and control participants were explicitly instructed to encode the entire face and to refrain from focusing on any particular facial feature while learning faces in the Study blocks. In light of prior work demonstrating that hippocampal damage is associated with fewer eye movement transitions across facial features (Olsen et al., 2015), it is possible that A.N. and S.D. may not have successfully encoded the gestalt-like representations of face stimuli required to perform memory judgments. Additionally, A.N. and S.D. may have been impaired on memory judgments because of the nature of the memory test. It is possible that the use of morphed lure faces may have required a highly detailed, hippocampally-dependent representation of the previously viewed face. This view is broadly consistent with prior work demonstrating that patient H.C., an individual with bilateral hippocampal damage, was impaired at making recognition judgments with face stimuli at short delays when lure faces were composed of visually similar morphs (Ezzyat and Olson, 2008; Rose et al., 2012). Finally, the current investigation suggests that the right hippocampus may be particularly important for face

memory; although A.N. displayed intact left hemisphere memory performance on a WADA evaluation, A.N.'s impairment in identifying target faces suggests that the right hippocampus plays a critical role in supporting face memory judgments with highly similar lure faces.

It is also interesting to consider the current results in light of investigations indicating that the hippocampus may also play a role in perceptual judgments (Lee et al., 2012; Yonelinas, 2013). In particular, S.D.'s performance on hard oddity trials was numerically closer to I.R. than to A.N., and was trending toward impairment relative to all age- and education-matched controls. These results raise the possibility that sufficiently difficult perceptual judgments may be supported by the hippocampus or recruit hippocampal representations. Consistent with this idea, work in fMRI has found that hippocampal activity tracks confidence in identifying differences in global featural relationships across two simultaneously presented visual images (Aly et al., 2013). This idea is also consistent with A.N.'s intact performance when making hard perceptual judgments, and suggests that A.N.'s intact hippocampus may have supported these judgments.

The results presented here suggest that I.R. displays deficits in identifying differences between similar faces on perception trials, yet I.R. is also able to correctly identify old faces presented among similar lure faces. How is I.R. able to accomplish this? One possibility is that representations supported by I.R.'s intact hippocampus may have provided a memory signal that allowed for the identification of old faces. In particular, rather than making a memory judgment based on perceptual comparisons across visually similar target and lure faces, I.R. may have relied on memory of whether each *individual* face was old or new. Although the current task was not designed to assess the possible contributions of recollection and familiarity, it is also possible that the memory task used here may have necessitated reliance on hippocampally-mediated recollective processes; subtle differences between the target and lure faces required participants and controls to use highly detailed information to correctly identify the target. If this were the case, the current results fit in well with a large prior literature linking hippocampal processes to recollection (Yonelinas, 2002).

It is also possible that different subregions of PRc differentially support representations that are important for mnemonic and perceptual judgments. This idea is consistent with a evidence in humans (Wang et al., 2016) and animals (Burwell, 2001; Burwell and Amaral, 1998; Lavenex et al., 2004; Suzuki and Amaral, 1994) indicating that the anterior PRc is a distinct subregion, displaying a unique pattern of structural and functional connectivity relative to posterior PRc. Given that lesions to only a specific subregion of PRc are exceedingly rare, this idea has not been well investigated, however the results presented here suggest that anterior PRc, spared in patient I.R., may be more involved in memory judgments whereas posterior PRc may support information important for perceptual judgments.

There may also be interhemispheric differences in the type of information represented by PRc. In particular, it may be that right PRc, damaged in I.R., is important for perceptual judgments, whereas I.R.'s intact left PRc supports mnemonic judgments. This idea is supported by I.R.'s neuropsychological WADA evaluation, which indicated intact left hemisphere memory performance coupled with impaired right hemisphere memory

performance. Additional evidence supporting the idea of interhemispheric differences comes from work in patient N.B., an individual with damage that includes left PRc but spares the hippocampus, and work with patients that have broader unilateral temporal lobe damage. These investigations have indicated that lateralized damage to the right temporal lobe is associated with deficits in memory for non-verbalizable information (Glosser et al., 1998; Jones-Gotman, 1986; Martin et al., 2011; Milner, 1968b), suggesting that I.R.'s deficit in making perceptual oddity judgments may reflect a role for right PRc in representing the perceptual features of non-verbalizable stimuli like faces. Work in patient N.B. has also indicated that left PRc supports familiarity (Bowles et al., 2007, 2016), further underscoring the idea that I.R.'s unimpaired memory performance may also have been supported by the intact left PRc.

As is always the case in clinical work, it is unknown how medications that control seizure events may have affected patient task performance. Despite this unknown, participant S.D. displayed a similar pattern of task performance as A.N., who was not on anti-epileptic medications at the time of testing. Additionally, S.D. and I.R., who were both taking anti-epileptic medication at the time of testing, displayed opposite performance profiles, making it unlikely that medication played a significant role in the results reported here. It is also important to note that the patients studied in the current investigation vary in age and years of education, in addition to differences in lesion site. Interestingly, both A.N. and S.D. displayed similar task performance profiles, despite their large difference in ages, whereas I.R., whose age fell between A.N. and S.D., displayed an opposite pattern of task responses. Future work in patients with more comparable demographics can more precisely delineate whether and how maturational factors may affect the involvement of MTL regions in representing perceptual and mnemonic information. Finally, although high resolution MRI revealed highly specific structural damage in each patient, neurological disorders like epilepsy may cause broader biochemical or electrical abnormalities. As such, we cannot rule out the possibility that abnormalities not detected with MRI may have played a role in the results reported here.

Taken together, the current investigation provides an important lens through which prior investigations into perceptual and mnemonic functions in patients with broader lesion profiles can be viewed. In particular, the results presented here suggest that right PRc plays a causal role in successful perceptual discrimination of visual stimuli with highly overlapping features, but the site of damage in right posterior PRc is not critically involved in supporting memory decisions with highly overlapping visual stimuli.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This work was funded by DART Neuroscience and NIH ROI MH074692 to L.D. We thank two anonymous reviewers for their comments, A. Patil and B. Sherman for data collection assistance, and I.R., A.N. and S.D. for their dedicated involvement in this investigation.

REFERENCES

Aly M, Ranganath C, and Yonelinas AP (2013). Detecting Changes in Scenes: The Hippocampus Is Critical for Strength-Based Perception. Neuron 78, 1127–1137. [PubMed: 23791201]

Barense, Bussey TJ, Lee ACH, Rogers TT, Davies RR, Saksida LM, Murray EA, and Graham KS. (2005). Functional Specialization in the Human Medial Temporal Lobe. J. Neurosci 25, 10239–10246. [PubMed: 16267231]

Barense, Henson RNA, Lee ACH, and Graham KS. (2009). Medial temporal lobe activity during complex discrimination of faces, objects, and scenes: Effects of viewpoint. Hippocampus NA-NA.

Barense, Rogers TT, Bussey TJ, Saksida LM, and Graham KS. (2010). Influence of Conceptual Knowledge on Visual Object Discrimination: Insights from Semantic Dementia and MTL Amnesia. Cereb. Cortex 20, 2568–2582. [PubMed: 20150429]

Barense, Henson RN, and Graham KS. (2011). Perception and conception: temporal lobe activity during complex discriminations of familiar and novel faces and objects. J. Cogn. Neurosci 23, 3052–3067. [PubMed: 21391761]

Bartko SJ, Winters BD, Cowell RA, Saksida LM, and Bussey TJ (2007). Perirhinal cortex resolves feature ambiguity in configural object recognition and perceptual oddity tasks. Learn. Mem 14, 821–832. [PubMed: 18086825]

Baxter MG (2009). Involvement of Medial Temporal Lobe Structures in Memory and Perception. Neuron 61, 667–677. [PubMed: 19285463]

Behrmann M, Lee ACH, Geskin JZ, Graham KS, and Barense MD (2016). Temporal lobe contribution to perceptual function: A tale of three patient groups. Neuropsychologia 90, 33–45. [PubMed: 27150707]

Bird CM, Shallice T, and Cipolotti L (2007). Fractionation of memory in medial temporal lobe amnesia. Neuropsychologia 45, 1160–1171. [PubMed: 17129591]

Bird CM, Vargha-Khadem F, and Burgess N (2008). Impaired memory for scenes but not faces in developmental hippocampal amnesia: A case study. Neuropsychologia 46, 1050–1059. [PubMed: 18155255]

Bowles B, Crupi C, Mirsattari SM, Pigott SE, Parrent AG, Pruessner JC, Yonelinas AP, and Köhler S (2007). Impaired familiarity with preserved recollection after anterior temporal-lobe resection that spares the hippocampus. Proc. Natl. Acad. Sci. 104, 16382–16387. [PubMed: 17905870]

Bowles B, Crupi C, Pigott S, Parrent A, Wiebe S, Janzen L, and Köhler S (2010). Double dissociation of selective recollection and familiarity impairments following two different surgical treatments for temporal-lobe epilepsy. Neuropsychologia 48, 2640–2647. [PubMed: 20466009]

Bowles B, Duke D, Rosenbaum RS, McRae K, and Köhler S (2016). Impaired assessment of cumulative lifetime familiarity for object concepts after left anterior temporal-lobe resection that includes perirhinal cortex but spares the hippocampus. Neuropsychologia 90, 170–179. [PubMed: 27378441]

Brown MW, and Aggleton JP (2001). Recognition memory: what are the roles of the perirhinal cortex and hippocampus? Nat. Rev. Neurosci 2, 51–61. [PubMed: 11253359]

Buckley MJ, and Gaffan D (2006). Perirhinal cortical contributions to object perception. Trends Cogn. Sci 10, 100–107. [PubMed: 16469525]

Buckley MJ, Booth MC, Rolls ET, and Gaffan D. (2001). Selective perceptual impairments after perirhinal cortex ablation. J. Neurosci 21, 9824–9836. [PubMed: 11739590]

Buffalo EA, Reber PJ, Squire LR, and others (1998). The human perirhinal cortex and recognition memory. Hippocampus 8, 330–339. [PubMed: 9744420]

Burwell RD (2001). Borders and cytoarchitecture of the perirhinal and postrhinal cortices in the rat. J. Comp. Neurol 437, 17–41. [PubMed: 11477594]

Burwell RD, and Amaral DG (1998). Cortical afferents of the perirhinal, postrhinal, and entorhinal cortices of the rat. J. Comp. Neurol 398, 179–205. [PubMed: 9700566]

Bussey TJ, and Saksida LM (2007). Memory, perception, and the ventral visual-perirhinal-hippocampal stream: Thinking outside of the boxes. Hippocampus 17, 898–908. [PubMed: 17636546]

Bussey TJ, Saksida LM, and Murray EA (2002). Perirhinal cortex resolves feature ambiguity in complex visual discriminations. Eur. J. Neurosci 15, 365–374. [PubMed: 11849302]

Bussey TJ, Saksida LM, and Murray EA (2003). Impairments in visual discrimination after perirhinal cortex lesions: testing “declarative” vs. “perceptual-mnemonic” views of perirhinal cortex function. Eur. J. Neurosci 17, 649–660. [PubMed: 12581183]

Cowell RA, Bussey TJ, and Saksida LM (2006). Why Does Brain Damage Impair Memory? A Connectionist Model of Object Recognition Memory in Perirhinal Cortex. J. Neurosci 26, 12186–12197. [PubMed: 17122043]

Crawford JR, and Howell DC (1998). Comparing an Individual’s Test Score Against Norms Derived from Small Samples. Clin. Neuropsychol. Neuropsychol. Dev. Cogn. Sect. D 12, 482–486.

Davachi L (2006). Item, context and relational episodic encoding in humans. Curr. Opin. Neurobiol 16, 693–700. [PubMed: 17097284]

Davachi L, Mitchell JP, and Wagner AD (2003). Multiple routes to memory: Distinct medial temporal lobe processes build item and source memories. Proc. Natl. Acad. Sci 100, 2157. [PubMed: 12578977]

Devlin JT, and Price CJ (2007). Perirhinal Contributions to Human Visual Perception. Curr. Biol 17, 1484–1488. [PubMed: 17764947]

Diana RA, Yonelinas AP, and Ranganath C (2007). Imaging recollection and familiarity in the medial temporal lobe: a three-component model. Trends Cogn. Sci 11, 379–386. [PubMed: 17707683]

Dougal S, Phelps EA, and Davachi L (2007). The role of medial temporal lobe in item recognition and source recollection of emotional stimuli. Cogn. Affect. Behav. Neurosci 7, 233–242. [PubMed: 17993209]

Eacott MJ, Gaffan D, and Murray EA (1994). Preserved recognition memory for small sets, and impaired stimulus identification for large sets, following rhinal cortex ablations in monkeys. Eur. J. Neurosci 6, 1466–1478. [PubMed: 8000570]

Ezzyat Y, and Olson IR (2008). The medial temporal lobe and visual working memory: Comparisons across tasks, delays, and visual similarity. Cogn. Affect. Behav. Neurosci 8, 32–40. [PubMed: 18405044]

Glosser G, Deutsch G, Cole L, Corwin J, and Saykin A (1998). Differential lateralization of memory discrimination and response bias in temporal lobe epilepsy patients. J Int Neuropsychol Soc 4, 502–511. [PubMed: 9745239]

Graham KS, Barense MD, and Lee ACH (2010). Going beyond LTM in the MTL: A synthesis of neuropsychological and neuroimaging findings on the role of the medial temporal lobe in memory and perception. Neuropsychologia 48, 831–853. [PubMed: 20074580]

Holdstock JS, Gutnikov SA, Gaffan D, and Mayes AR (2000). Perceptual and mnemonic matching-to-sample in humans: Contributions of the hippocampus, perirhinal and other medial temporal lobe cortices. Cortex 36, 301–322. [PubMed: 10921661]

Jones-Gotman M (1986). Right hippocampal excision impairs learning and recall of a list of abstract designs. Neuropsychologia 24, 659–670. [PubMed: 3785653]

Kirwan CB, and Stark CEL (2004). Medial temporal lobe activation during encoding and retrieval of novel face-name pairs. Hippocampus 14, 919–930. [PubMed: 15382260]

LaRocque KF, Smith ME, Carr VA, Witthoft N, Grill-Spector K, and Wagner AD (2013). Global Similarity and Pattern Separation in the Human Medial Temporal Lobe Predict Subsequent Memory. J. Neurosci 33, 5466–5474. [PubMed: 23536062]

Lavenex P, and Amaral DG (2000). Hippocampal-neocortical interaction: A hierarchy of associativity. Hippocampus 10, 420–430. [PubMed: 10985281]

Lavenex P, Suzuki WA, and Amaral DG (2004). Perirhinal and parahippocampal cortices of the macaque monkey: Intrinsic projections and interconnections. J. Comp. Neurol 472, 371–394. [PubMed: 15065131]

Lee, Yeung L-K, and Barense MD. (2012). The hippocampus and visual perception. Front. Hum. Neurosci 6.

Lee ACH, Bussey TJ, Murray EA, Saksida LM, Epstein RA, Kapur N, Hodges JR, and Graham KS (2005a). Perceptual deficits in amnesia: challenging the medial temporal lobe ‘mnemonic’ view. Neuropsychologia 43, 1–11. [PubMed: 15488899]

Lee ACH, Buckley MJ, Pegman SJ, Spiers H, Scahill VL, Gaffan D, Bussey TJ, Davies RR, Kapur N, Hodges JR, et al. (2005b). Specialization in the medial temporal lobe for processing of objects and scenes. Hippocampus 15, 782–797. [PubMed: 16010661]

Lee ACH, Scahill VL, and Graham KS (2008). Activating the Medial Temporal Lobe during Oddity Judgment for Faces and Scenes. Cereb. Cortex 18, 683–696. [PubMed: 17615247]

Levy DA, Shrager Y, and Squire LR (2005). Intact visual discrimination of complex and feature-ambiguous stimuli in the absence of perirhinal cortex. Learn. Mem. 12, 61–66. [PubMed: 15647593]

Liang JC, Wagner AD, and Preston AR (2012). Content Representation in the Human Medial Temporal Lobe. Cereb. Cortex 23, 80–96. [PubMed: 22275474]

Libby LA, Ekstrom AD, Ragland JD, and Ranganath C (2012). Differential Connectivity of Perirhinal and Parahippocampal Cortices within Human Hippocampal Subregions Revealed by High-Resolution Functional Imaging. J. Neurosci 32, 6550–6560. [PubMed: 22573677]

Martin CB, Bowles B, Mirsattari SM, and Köhler S (2011). Selective familiarity deficits after left anterior temporal-lobe removal with hippocampal sparing are material specific. Neuropsychologia.

Milner B (1968a). Visual recognition and recall after right temporal-lobe excision in man. Neuropsychologia 6, 191–209.

Milner B (1968b). Material-specific and generalized memory loss. Neuropsychologia 6, 175–179.

Murray EA, and Bussey TJ (1999). Perceptual–mnemonic functions of the perirhinal cortex. Trends Cogn. Sci 3, 142–151. [PubMed: 10322468]

Olsen RK, Lee Y, Kube J, Rosenbaum RS, Grady CL, Moscovitch M, and Ryan JD (2015). The Role of Relational Binding in Item Memory: Evidence from Face Recognition in a Case of Developmental Amnesia. J. Neurosci 35, 5342–5350. [PubMed: 25834058]

O'Neil EB, Cate AD, and Kohler S (2009a). Perirhinal Cortex Contributes to Accuracy in Recognition Memory and Perceptual Discriminations. J. Neurosci 29, 8329–8334. [PubMed: 19571124]

O'Neil EB, Cate AD, and Kohler S (2009b). Perirhinal Cortex Contributes to Accuracy in Recognition Memory and Perceptual Discriminations. J. Neurosci 29, 8329–8334. [PubMed: 19571124]

O'Neil EB, Barkley VA, and Köhler S (2013). Representational demands modulate involvement of perirhinal cortex in face processing: Representational Demands Modulate Perirhinal Cortex. Hippocampus 23, 592–605. [PubMed: 23460411]

Ranganath C, Yonelinas AP, Cohen MX, Dy CJ, Tom SM, and D'Esposito M (2004). Dissociable correlates of recollection and familiarity within the medial temporal lobes. Neuropsychologia 42, 2–13. [PubMed: 14615072]

Reed JM, and Squire LR (1997). Impaired recognition memory in patients with lesions limited to the hippocampal formation. Behav. Neurosci 111, 667. [PubMed: 9267644]

Rose NS, Olsen RK, Craik FIM, and Rosenbaum RS (2012). Working memory and amnesia: The role of stimulus novelty. Neuropsychologia 50, 11–18. [PubMed: 22044651]

Scoville WB, and Milner B (1957). Loss of recent memory after bilateral hippocampal lesions. J Neurol Neurosurg Psychiat 20, 11–21. [PubMed: 13406589]

Shrager Y, Gold JJ, Hopkins RO, and Squire LR (2006). Intact Visual Perception in Memory-Impaired Patients with Medial Temporal Lobe Lesions. J. Neurosci 26, 2235–2240. [PubMed: 16495450]

Sperling R, Chua E, Cocchiarella A, Rand-Giovannetti E, Poldrack R, Schacter DL, and Albert M (2003). Putting names to faces: NeuroImage 20, 1400–1410. [PubMed: 14568509]

Staresina BP, and Davachi L (2008). Selective and shared contributions of the hippocampus and perirhinal cortex to episodic item and associative encoding. J. Cogn. Neurosci 20, 1478–1489. [PubMed: 18303974]

Staresina BP, and Davachi L (2009). Mind the Gap: Binding Experiences across Space and Time in the Human Hippocampus. Neuron 63, 267–276. [PubMed: 19640484]

Staresina BP, Henson RNA, Kriegeskorte N, and Alink A (2012). Episodic Reinstatement in the Medial Temporal Lobe. J. Neurosci 32, 18150–18156. [PubMed: 23238729]

Stark CE, and Squire LR (2000). Intact visual perceptual discrimination in humans in the absence of perirhinal cortex. Learn. Mem 7, 273–278. [PubMed: 11040258]

Suzuki WA, and Amaral DG (1994). Perirhinal and Parahippocampal Cortices of the Macaque Monkey: Cortical Afferents. J. Comp. Neurol 497–533.

Vilberg KL, and Davachi L (2013). Perirhinal-Hippocampal Connectivity during Reactivation Is a Marker for Object-Based Memory Consolidation. Neuron 79, 1–11. [PubMed: 23849191]

Wang Ritchey Libby, and Ranganath (2016). Functional connectivity based parcellation of the human medial temporal lobe. Neurobiol. Learn. Mem

Warrington EK, and Taylor AM (1973). Immediate memory for faces: Long- or short-term memory? Q. J. Exp. Psychol 25, 316–322. [PubMed: 4807292]

Yonelinas AP (2002). The Nature of Recollection and Familiarity: A Review of 30 Years of Research. J. Mem. Lang 46, 441–517.

Yonelinas AP (2013). The hippocampus supports high-resolution binding in the service of perception, working memory and long-term memory. Behav. Brain Res 254, 34–44. [PubMed: 23721964]

Highlights

- To understand the nature of perceptual and mnemonic representations supported by the medial temporal lobe, perception and memory abilities were tested in three patients with localized MTL damage
- A patient with focal damage to right posterior perirhinal cortex displayed impaired perceptual abilities, but was not impaired at a memory task
- Two patients with damage to the hippocampus and parahippocampal cortex displayed impaired performance on the memory task, but were largely not impaired in a task taxing perceptual judgments

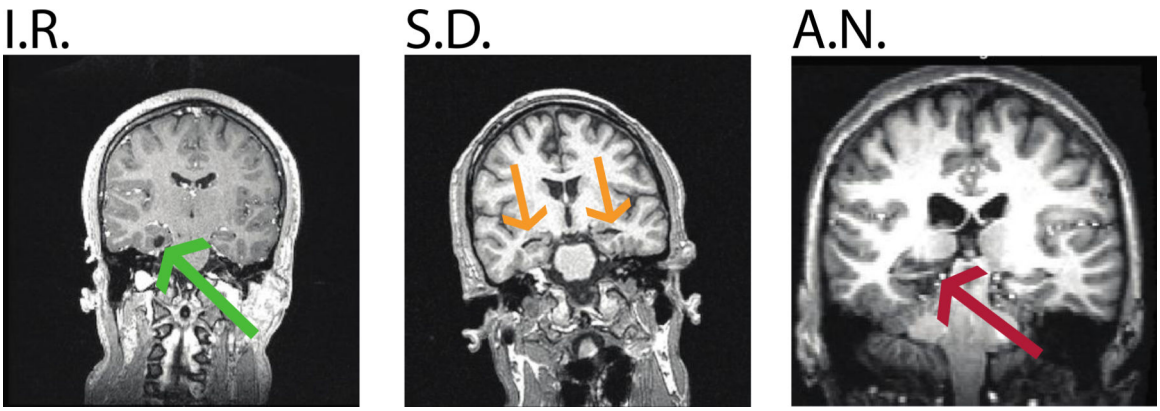

Figure 1.
Structural images of lesion profiles.

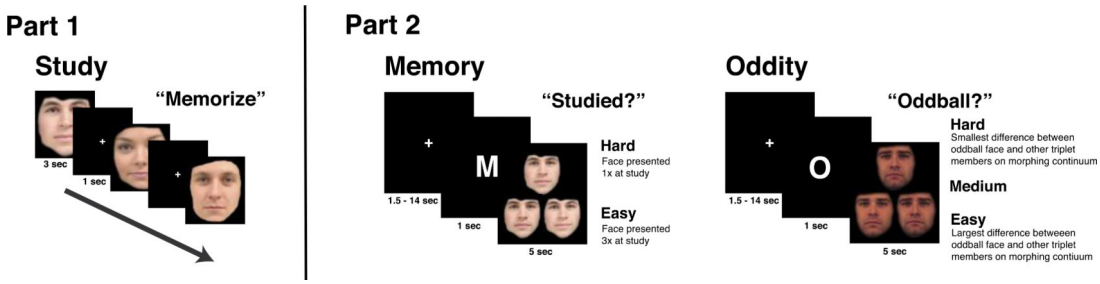

Figure 2.

Experimental design - Each of the six behavioral task runs included an initial Study phase. Participants were presented with a single face on the screen, and asked to memorize it. Following the study phase, participants were entered into a test phase with memory and perceptual oddity trials. In this phase of the experiment, participants were asked to indicate which of three similar faces appeared during the study phase (memory), or which of three novel, morphed faces was most dissimilar from the other two (Perceptual Oddity).

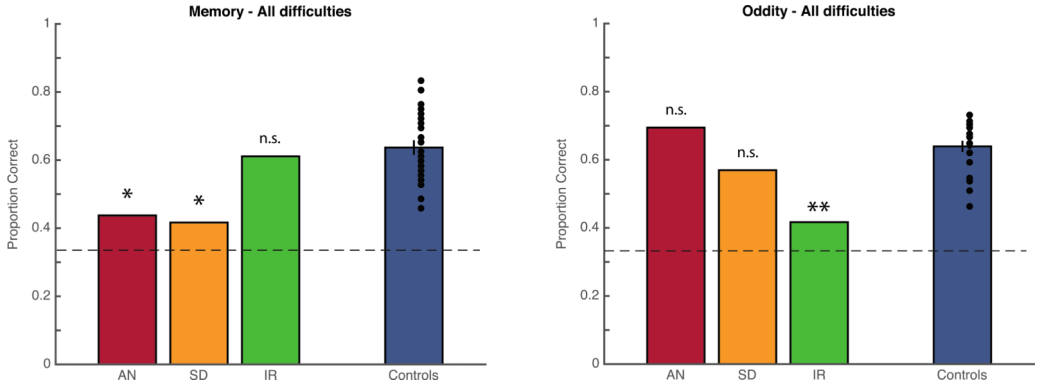

Figure 3.

Memory and oddity performance collapsed across difficulty (Left) Proportion correct responses for memory test trials, collapsing across *easy* and *hard* trial types. (Right) Proportion correct responses collapsing across *easy*, *medium*, and *hard* trial types. Dashed line denotes chance performance (33%). * denotes significance at $p < .05$, 1-tailed relative to all controls, ** denotes significance at $p < .01$, 1-tailed relative to all controls.

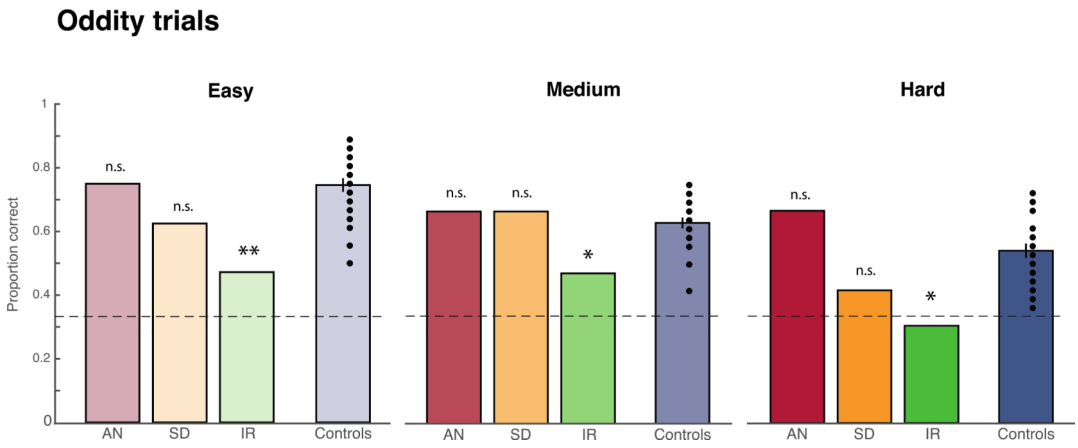

Figure 4.

Oddity performance by trial difficulty

Patients are compared relative to all control participants. Dashed line denotes chance performance (33%); ** denotes significance at $p < .01$, 1-tailed relative to all controls; * denotes significance at $p < .05$, 1-tailed relative to all controls.

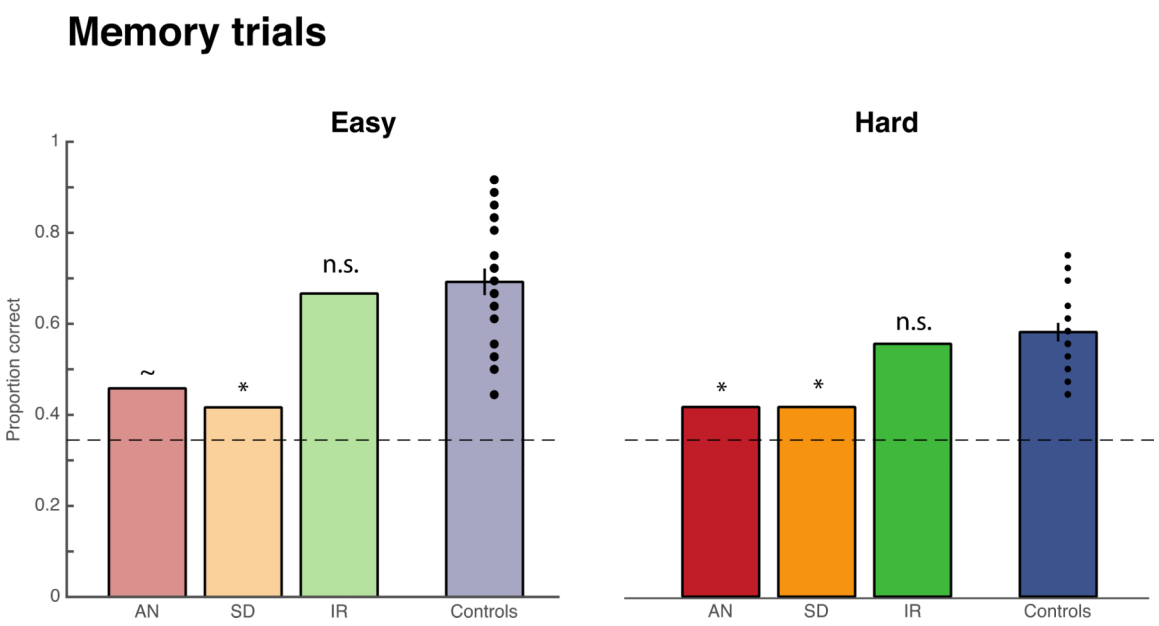

Figure 5.

Memory performance by trial difficulty. Dashed line denotes chance performance (33%); * denotes significance at $p < .05$, 1-tailed relative to all controls; ~ denotes trending significance at $p < .1$, 1-tailed relative to all controls.

Table 1:

Patient Score Comparisons on Tests of Intelligence

	Full Scale Intelligence	Verbal Intelligence	Non-verbal Intelligence	Attention Concentration	Mental Processing Speed
Patient	**FSIQ**	**VCI**	**PRI**	**WMI**	**PSI**
IR	96	103	100	95	86
SD	104	114	100	108	86
AN*	119	112	108	102	136

Normative Scores: Standard Scores (SS) have a mean of 100 and a SD of 15.

Intelligence performances were derived using the WAIS-IV, unless noted (WISC-IV*).

Table 2:

Patient Score Comparisons on Tests of Visual-Spatial Construction and Immediate Visual Memory for Geometric Shapes & Figures.

	Visual-Spatial Construction	Immediate Visual Memory		
Patient	**RCFT-Copy**	**BVMT-R Immediate**	**WMS-IV VP-I**	**WRAML-2 Design Immediate**
IR	−0.1	1.0	−0.67	--
SD	−2.3	−0.8	1.0	--
AN	−0.17	--	--	−1.67

Normative Scores: Z-scores have a mean of 0.0 and a SD of 1.0.

RCFT: Rey Complex Figure Test; **RCFT-Copy**: Copy Trial Score.

BVMT-R: Brief Visuospatial Memory Test-Revised; **BVMT-R Immediate**: Immediate Recall Memory Total Score.

WRAML-2: Wide Range Assessment of Memory and Learning-Second Edition; **WRAML-2 Design Immediate**: Design Subtest Immediate Memory Score.

Table 3:

Patient Score Comparisons on Tests of Visual Delayed & Recognition Memory for Geometric Shapes & Figures.

	Delayed Visual Memory			Recognition Visual Memory		
Patient	**RCFT Delay**	**BVMT-R Delay**	**WMS-IV VP-II**	**BVMT-R Recognition**	**WMS-IV VP-Rec.**	**WRAML-2 Design Rec.**
IR	−1.1	0.9	−1.0	0.0	6/7 (85.7%)	--
SD	−19.3	0.0	−1.0	0.0	7/7 (100%)	--
AN	−1.93	--	--	--	--	28/46 (60%); z=−0.67

Normative Scores: Z-scores have a mean of 0.0 and a SD of 1.0.

Only raw scores are available for WMS-IV VP-Recognition; raw scores and normative z-scores are presented for WRAML-2 Design Recognition.

RCFT: Rey Complex Figure Test; **RCFT-Delay**: Delayed Recall Memory Score.

BVMT-R: Brief Visuospatial Memory Test-Revised; **BVMT-R Delay**: Delayed Recall Memory Score; **BVMT-R Recognition:** Recognition Memory Score.

Table 4:

Patient Score Comparisons on Tests of Verbal Word List-Learning/Memory.

	Verbal Immediate Memory			Verbal Delayed Memory			Verbal R	
Patient	**CVLT-II Learning**	**RAVLT Learning**	**WRAML-2 Learning**	**CVLT-II Delay**	**RAVLT Delay**	**WRAML-2 Delay**	**CVLT-II Recognition**	**RAVL**
IR	--	0.16	--	--	−0.77	--	--	
SD	−0.5	--	--	−1.5	--	--	−1.5	
AN	--	--	0.0	--	--	−0.67	--	

Normative Scores: Z-scores have a mean of 0.0 and a SD of 1.0.

CVLT-II: California Verbal Learning Test-Second Edition; **CVLT-II Learning**: Total Immediate Recall Memory Score; **CVLT-II Delay**: Delayed Recall Memory Score; **CVLT-II Recognition:**

Recognition memory scores for verbal list-learning.

RAVLT: Rey Auditory Verbal Learning Test; **RAVLT Learning**: Total Immediate Recall Memory Score; **RAVLT Delay**: Delayed Recall Memory Score; **RAVLT Recognition:** Recognition memory scores for verbal list-learning.

WRAML-2: Wide Range Assessment of Memory and Learning-Second Edition; **WRAML-2 Verbal Learning**: List-Learning Subtest Total Immediate Memory Score; **WRAML-2 Verbal Learning Delayed**: List-Learning Subtest Delayed Memory Score; **WRAML-2 Recognition:** Recognition memory scores for verbal list-learning

Table 5:

Patient Score Comparisons on Tests of Verbal Prose Learning/Memory.

	Verbal Immediate Memory		Verbal Delayed Memory		Verbal Recognition Memory	
Patient	**WMS-IV LM-I**	**WRAML-2 Story Memory**	**WMS-IV LM-II**	**WRAML-2 Story Memory Recall**	**WMS-IV LM-Rec.**	**WRAML-2 Story Memory Rec.**
IR	0.0	--	0.0	--	22/30 (73%)	--
SD	0.33	--	−0.33	--	27/30 (90%)	--
AN	--	0.67	--	0.67	--	32/40 (80%); z=−0.33

Normative Scores: Z-scores have a mean of 0.0 and a SD of 1.0.

WMS-IV: Wechsler Memory Scale-Fourth Edition; **WMS-IV Logical Memory I (LM-I)**: Total Immediate Recall Memory Score; **WMS-IV Logical Memory II (LM-II)** Delayed Recall Memory Score; **WMS-IV Logical Memory Recognition:** Recognition memory scores for story.

WRAML-2: Wide Range Assessment of Memory and Learning-Second Edition; **WRAML-2 Story Memory**: Total Immediate Memory Score; **WRAML-2 Story Memory Delayed**: Delayed Memory Recall Score; **WRAML-2 Story Memory Recognition:** Recognition memory scores for story.