Neuron 49, 459–466, February 2, 2006 ©2006 Elsevier Inc. DOI 10.1016/j.neuron.2005.12.020

The Hippocampus Supports both the Recollection and the Familiarity Components of Recognition Memory

Peter E. Wais,[1] John T. Wixted,[1,*] Ramona O. Hopkins,[5,6] and Larry R. Squire[1,2,3,4]
[1]Department of Psychology
[2]Department of Psychiatry
[3]Department of Neurosciences
University of California, San Diego
La Jolla, California 92093
[4]Veterans Affairs Medical Center
San Diego, California 92161
[5]Psychology Department and Neuroscience Center
Brigham Young University
Provo, Utah 84602
[6]Department of Medicine
Pulmonary and Critical Care Division
LDS Hospital
Salt Lake City, Utah 84143

Summary

The receiver operating characteristic (ROC) has been used to investigate the component processes of recognition memory. Some studies with this technique have been taken to indicate that the hippocampus selectively supports the process of recollection, whereas adjacent cortex in the parahippocampal gyrus supports the process of familiarity. We analyzed ROC data from young adults, memory-impaired patients with limited hippocampal lesions, and age-matched controls. The shape of the ROC changed in similar ways from asymmetric to symmetric, as a function of the strength of memory (strong to weak) in both the young adults and the patients. Moreover, once overall memory strength was similar, the shape of the patient ROC was asymmetric and matched the control ROC. These results suggest that the component processes that determine the shape of the ROC are operative in the absence of the hippocampus, and they argue against the idea that the hippocampus selectively supports the recollection process.

Introduction

One of the most widely studied examples of declarative memory is recognition memory, the capacity to judge an item as having been encountered previously. Recognition memory is commonly thought to consist of two component processes, recollection and familiarity (Mandler, 1980). Recollection involves remembering specific details about the episode in which an item was encountered, and familiarity involves simply knowing that an item was presented, even when no information can be retrieved about the episode itself. A fundamental but controversial issue concerns the anatomical basis of this distinction: how are recollection and familiarity supported by the brain structures important for declarative memory? Some studies suggest that the hippocampus is critical for recollection, whereas familiarity is supported by the adjacent cortex in the parahippocampal gyrus (Brown and Aggleton, 2001; Fortin et al., 2004; Yonelinas et al., 2002). Other studies suggest that the hippocampus is important for both recollection and familiarity (Manns et al., 2003; Wixted and Squire, 2004).

Signal detection techniques have recently been used to address these anatomical questions about the component processes of recognition memory (Fortin et al., 2004; Yonelinas et al., 1998, 2002). The receiver operating characteristic (ROC) is a plot of the hit rate versus the false alarm rate across different decision criteria. For example, multiple pairs of hit and false alarm rates can be obtained by asking subjects to provide confidence ratings for their yes/no recognition decisions. A pair of hit and false alarm rates is then computed for each level of confidence, and the paired values are plotted across the confidence levels to construct an ROC.

The approach has been to compare the shape of the normal ROC to the ROC produced by memory-impaired patients (Yonelinas et al., 1998, 2002) or rats with hippocampal lesions (Fortin et al., 2004). These ROCs were typically curvilinear, but they differed in that the curve produced by controls was asymmetrical (as is usually the case), and the curve produced by the patients (and by the rats with lesions) was symmetrical (Figure 1). These data have been interpreted in the light of a dual-process/detection model (Yonelinas et al., 1998), which holds that the degree of asymmetry in an ROC directly reflects the degree to which the recollection process is involved in recognition decisions. Accordingly, a symmetrical ROC indicates that recognition decisions were based solely on familiarity, but an asymmetrical ROC indicates that recollection occurred for some of the items as well (Yonelinas et al., 1998). By this view, the finding that memory-impaired patients (and hippocampal rats) yield a symmetrical ROC, instead of the more typical asymmetrical ROC, suggests that the recollection process is selectively impaired.

Although the two ROC curves just described are qualitatively different with respect to symmetry, they are also quantitatively different because memory-impaired patients (and rats with lesions) have weaker memories than controls. Indeed, the standard signal detection model of recognition memory (Macmillan and Creelman, 2005), in contrast to the dual process/detection model, explains the transition from asymmetrical to symmetrical ROCs as a simple loss of memory strength (Glanzer et al., 1999). If symmetry of the ROC is related to memory strength, then the difference in symmetry between impaired and unimpaired subjects may simply reflect the difference between weaker and stronger memories (not qualitative differences in the integrity of underlying recognition memory processes).

We first analyzed the shape of the ROC over a wide range of memory strength conditions by testing young adults after one of five retention intervals (1 hr, 1 day, 1 week, 2 weeks, and 8 weeks). These conditions were included to determine how the ROC changes as memory

*Correspondence: jwixted@ucsd.edu

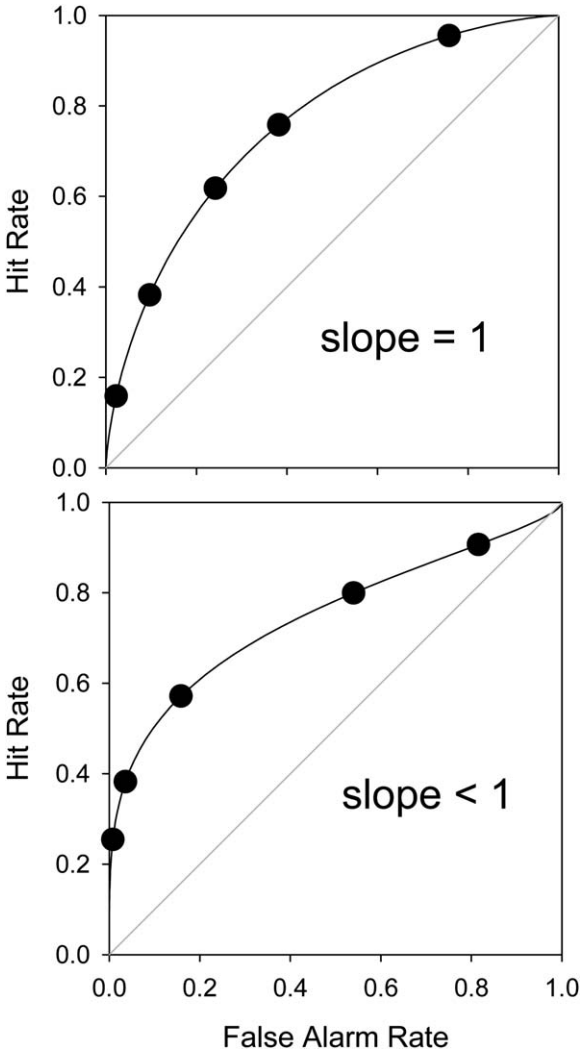

Figure 1. Hypothetical ROC Data Illustrating Symmetrical and Asymmetrical ROC Plots

The degree of asymmetry evident in an ROC is typically quantified by a "slope" parameter obtained by fitting the standard signal detection model (Macmillan and Creelman, 2005) to the data. A slope of 1.0 denotes a symmetrical ROC, whereas a slope less than 1.0 denotes an asymmetrical ROC. The dual process/detection model would yield a recollection parameter estimate of 0 for the symmetrical ROC at the top and an estimate greater than 0 for the asymmetrical ROC at the bottom.

strength weakens. We next tested six memory-impaired patients with bilateral damage thought to be limited to the hippocampal region (CA fields, dentate gyrus, and subiculum), as well as a matched control group. If the hippocampus selectively subserves recollection, and if the asymmetry of an ROC is indicative of recollection, then these patients would be expected to yield a symmetric ROC regardless of memory strength. Alternatively, if the hippocampus does not selectively support recollection (because recollection depends on adjacent medial temporal lobe structures as well), then hippocampal patients should produce asymmetrical ROCs like the matched controls, once differences in memory strength are accounted for.

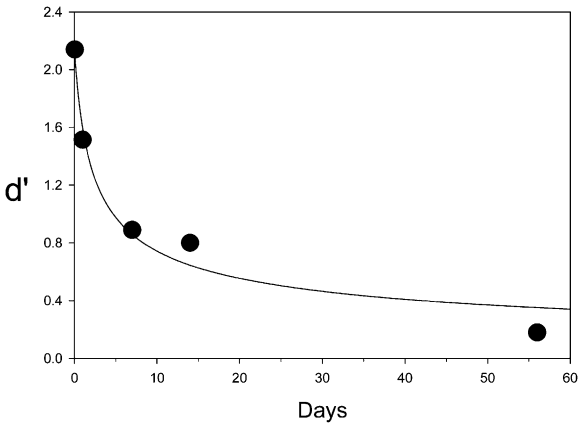

Figure 2. Recognition Memory Performance of Young Adults Tested with 50-Item Lists at Retention Intervals of 1 hr, 1 day, 1 week, 2 weeks, and 8 weeks

Performance for 19–24 subjects/group was quantified by the standard, bias-free measure of recognition memory (d′), as derived from signal-detection theory, in which d′ = z (Hit Rate) minus z (False Alarm Rate). The solid curve represents the least squares fit of a three-parameter power function that typically provides a good fit of forgetting data (Wixted, 2004).

Results

The recognition performance of the young adults decayed as expected over time (Figure 2). Performance in the 8 week condition, although low, was above chance levels ($t_{(18)} = 2.43$, $p < 0.05$). The ROCs were curvilinear at every retention interval and, as is generally the case, were accurately described by the standard signal-detection model (Figure 3). In addition, the ROC was, as expected, asymmetric at the short (1 hr) retention interval (slope = 0.63) and became ever more symmetric as performance decreased. Still, the slopes remained less than 1.0 (ps < 0.05) up to the longest retention interval, which yielded a slope of 1.03 (indicating a symmetric ROC). These data establish that as memory strength weakens, the slope of the ROC increases toward 1.0 and that the shape of the ROC remains curvilinear even when memory strength is very weak.

One can fit the dual-process/detection model (Yonelinas et al., 1998) to these ROC data to derive estimates of recollection and familiarity, something that is commonly done (e.g., Aggleton et al., 2005; Fortin et al., 2004; Yonelinas et al., 2002), and the results are shown in Table 1. The increasing symmetry of the ROC as a function of retention interval is reflected in the fact that the recollection estimate decreases over time to a value close to zero (i.e., a symmetric ROC yields a recollection estimate of zero). The familiarity parameter from this model also decreases over time but is still greater than zero even at the 8 week retention interval. Thus, according to this model, our results imply that recollection faded faster than familiarity.

The next question of interest is how the shape of the ROC changes as a function of memory strength for the patients with hippocampal lesions and how the performance of the patients compares with the performance of their matched controls. The recognition performance of the hippocampal group in the 50-item condition (H-50,

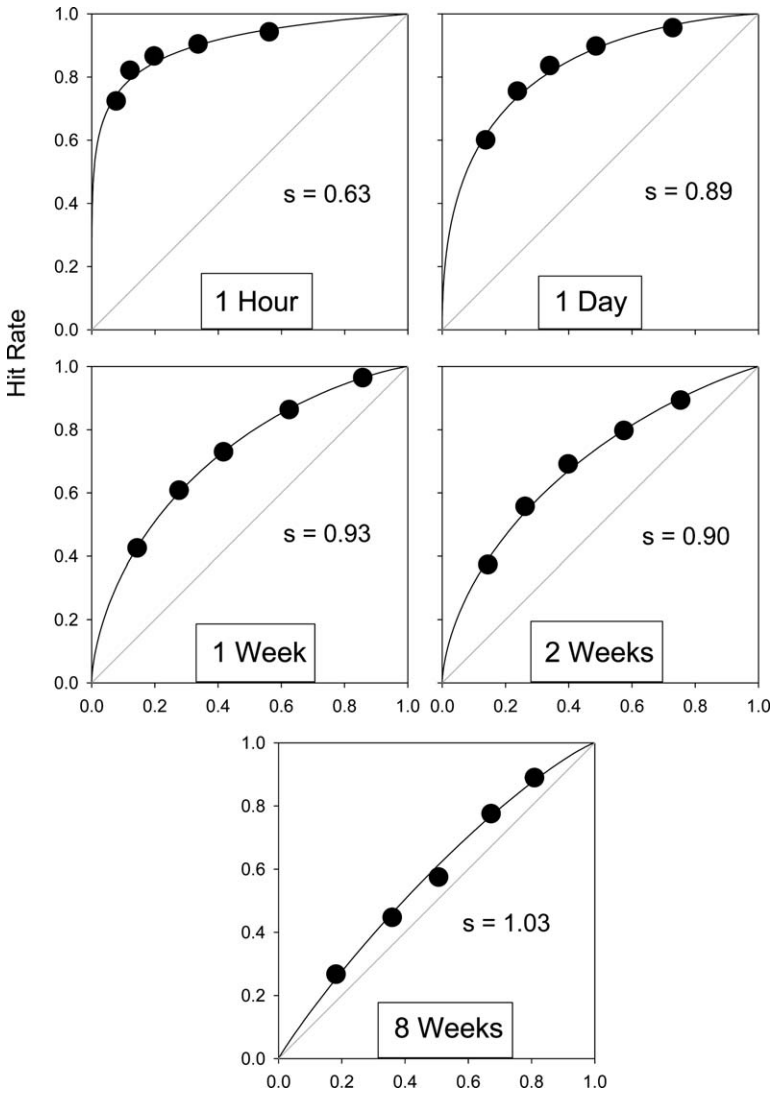

Figure 3. ROC Data Produced by the Young Adults at Each Retention Interval

Following convention, the smooth curves represent the best fits from the standard signal-detection model (Macmillan and Creelman, 2005), and the slope (denoted by s) values represent one of the parameters that is estimated when performing those fits. The chi-square test comparing each slope value to 1.0 was significant for the 1 hr, 1 day, and the 2 week conditions ($\chi^2[1] \geq 6.21$, $p < 0.05$) and was marginal for the 1 week condition, $\chi^2(1) = 2.70$, $p = 0.10$. For the 8 week condition, the slope of 1.03 did not differ significantly from 1.0. Previous work with rats suggested that the ROC might be linear after a long retention interval (Fortin et al., 2004). The degree of linearity in the ROC from the 8 week condition was assessed by comparing the fit of a one-parameter curvilinear signal-detection model with the slope fixed at 1.0 (to match the data that we obtained at the 8 week retention interval) and the fit of a one-parameter pure-recollection version of the dual-process/detection model with the familiarity parameter fixed at 0 (to match the linear plot reported for rats in Fortin et al., 2004). The chi-square goodness-of-fit statistic associated with the former (10.94) was much lower than the latter (22.03), indicating that the curvilinear function offered a better description of the data than the linear function even at the longest retention interval.

Figure 4) was poorer than control performance (C-50) ($p < 0.05$). When only ten items were studied instead of 50, patient performance (H-10) substantially improved ($p < 0.05$) to a level closer to that of the controls ($p > 0.25$). The ROCs produced by the patients and controls were all curvilinear (Figure 5). The slope of the ROC from the H-50 condition (1.14) was greater than the slope of the ROC from the H-10 condition (0.83, $p < .05$) and also greater than the slope of the ROC from the C-50 condition (0.83, $p < .05$). Thus, as was true of the young adults, the hippocampal ROC was more symmetric when memory was weak compared to when memory was relatively strong (H-50 versus H-10, respectively). Further, when the overall strength of memory was similar for patients and controls, as it was in the H-10 and C-50 conditions, the degree of asymmetry in the ROC was similar as well. These findings accord with earlier work (Glanzer et al., 1999), showing that whatever method is used to alter memory strength (e.g., study time, repetition, word frequency, or list length) the results are the same: the symmetry of the ROC (and the slope) increases as memory strength decreases.

Table 1. Model-Based Estimates for Recollection and Familiarity

Condition	Recollection	Familiarity
1 hour	0.52	1.26
1 day	0.13	1.21
1 week	0.09	0.74
2 weeks	0.07	0.62
8 weeks	0.02	0.25
H-50	0.00	0.83
H-10	0.22	1.21
C-50	0.23	1.64

Parameter estimates obtained by fitting the dual-process/detection model (Yonelinas et al., 1998) to the ROCs produced by the young adults across the five retention-interval conditions, the hippocampal patients across the two list-length conditions (H-50 and H-10), and controls for the patients (C-50). The recollection estimate is a probability (representing the probability of all-or-none recollection), and the familiarity estimate is a d′ value (representing the standardized distance between the means of the target and lure distributions).

Although the mean age of the two groups did not differ significantly, the controls were, on average, 4.5 years older than the patients. Accordingly, we performed an additional ROC analysis after excluding the three oldest controls. The mean age of the remaining five controls

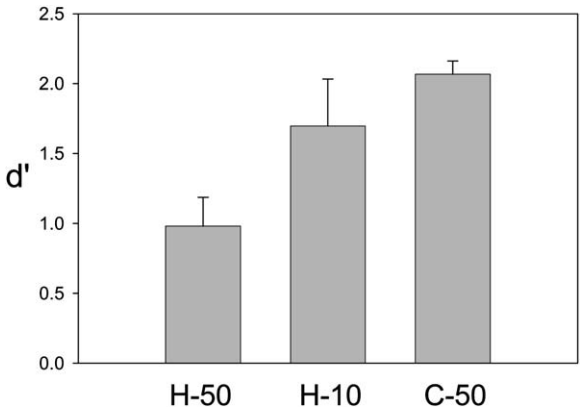

Figure 4. Recognition Memory Performance of the Hippocampal Patients and Controls

Patients were tested with 50-item lists in the H-50 condition and 10-item lists in the H-10 condition. Controls were tested with 50-item lists in the C-50 condition. A retention interval of 3 min was used in all cases. The mean score of the controls (C-50) was greater than that of the patients in the H-50 condition, $t_{(12)} = 5.23$ ($p < .01$), but similar to the d′ score obtained by the patients in the H-10 condition ($p > 0.25$). The d′ score in the H-10 condition was also greater than in the H-50 condition ($t_{[5]} = 4.63$, $p < 0.01$). The error bars represent standard errors.

was the same as that of the patients (56 years). The slope of the ROC for these five controls was now 0.80, instead of 0.83, and was still similar to and not significantly different from the slope of 0.83 produced by the patients.

As with the ROC data produced by the young adults in our study, the ROC data produced by the patients and their controls can be fit by the dual-process/detection model (Yonelinas et al., 1998) to derive theoretical estimates of recollection and familiarity. As shown in Table 1, the recollection parameter estimate was equal to zero in the H-50 condition (its lowest possible value) and was greater than zero (0.23) for the controls (C-50). Similarly, the familiarity estimate was lower in the H-50 condition than for the controls (0.83 versus 1.64). In contrast, the estimated probability of recollection in the H-10 condition was virtually identical to that of the controls (0.22 and 0.23, respectively). Thus, according to this model, the recollection process is present in both patients and controls, and the nearly identical recollection estimates offer no evidence of a selective deficit in that process after hippocampal lesions. Finally, the familiarity estimates for the two groups were similar as well (1.21 and 1.64, $p = 0.11$).

The traditional signal detection model and the dual-process/detection model are both commonly fit to ROC data, as we have done here, but the signal detection model usually provides the better fit. This was true of our ROC data as well. Specifically, the chi-square goodness-of-fit statistic associated with the fits of the signal detection model was lower (indicating a better fit) than that of the dual-process/detection model for all five of the ROCs in Figure 3 and for all three of the ROCs in Figure 5. Summed across the eight ROCs, the chi-square value for the signal-detection fits was 72.2, whereas the corresponding value for the dual-process/detection fits was 107.2. This result agrees with the findings of a recent study (Heathcote, 2003) that manipulated a number of variables in four experiments and found that the signal detection model provided a better fit in every condition of every experiment. Thus, the dual-process/detection model does not adequately account for ROC data, as others have noted (Glanzer et al., 1999; Heathcote, 2003), and studies of familiarity and recollection are likely to be misled to the extent that they depend on this model.

One of the six hippocampal patients, AB, was ineligible for MRI because he wears a pacemaker, though his history, neurological exam, and computer-assisted tomography (CAT scan) are consistent with a limited hippocampal lesion (Schmolck et al., 2002). The findings were similar when AB's data were excluded. Thus, the slopes of the patient ROCs were now 1.15 and 0.85, respectively, for the H-50 and H-10 conditions (compare Figure 5), and the difference between these values was marginally significant ($p = 0.059$).

Discussion

The performance of memory-impaired patients with selective hippocampal lesions differed quantitatively, but not qualitatively, from that of controls. The ROC from the patients exhibited the same relationship between symmetry and memory strength as the ROC from the young adults. Moreover, the patient ROC was identical to that of age-matched controls when the overall strength of memory was similar (H-10 versus C-50). Accordingly, the component processes of recognition memory that determine the shape of the ROC appear to be operative in patients with hippocampal lesions, and these processes are not differentially impaired.

The specific implications of our findings differ somewhat depending on which of two prominent models is used to interpret the data. According to the traditional signal-detection model (Macmillan & Creelman, 2005), an asymmetrical ROC reflects greater variance in the memory strengths of the targets relative to the lures. The exact manner in which recollection and familiarity combine to determine the variance of the targets is not constrained by this model. One possibility is that items supported by recollection, or by both recollection and familiarity, tend to have greater and more variable memory strength than items supported mainly by familiarity (Wixted & Stretch, 2004). In any case, the fact that the ROCs produced by patients and controls exhibited the same characteristics as a function of memory strength suggests that the component processes of recognition, however they might combine to produce memory strength, do so in the same way for patients and controls.

The dual-process/detection model (Yonelinas et al., 1998) explicitly connects the degree of asymmetry in the ROC to the probability of recollection: the more asymmetric the ROC, the greater the contribution of recollection. Yet, if the hippocampus selectively supports recollection, then the absence of that process in the hippocampal patients should have been evident as a more symmetrical ROC, even when overall memory strength was similar for patients and controls. Contrary to that prediction, Table 1 indicates that recollection was normal in the hippocampal group under those conditions (H-10 versus C-50).

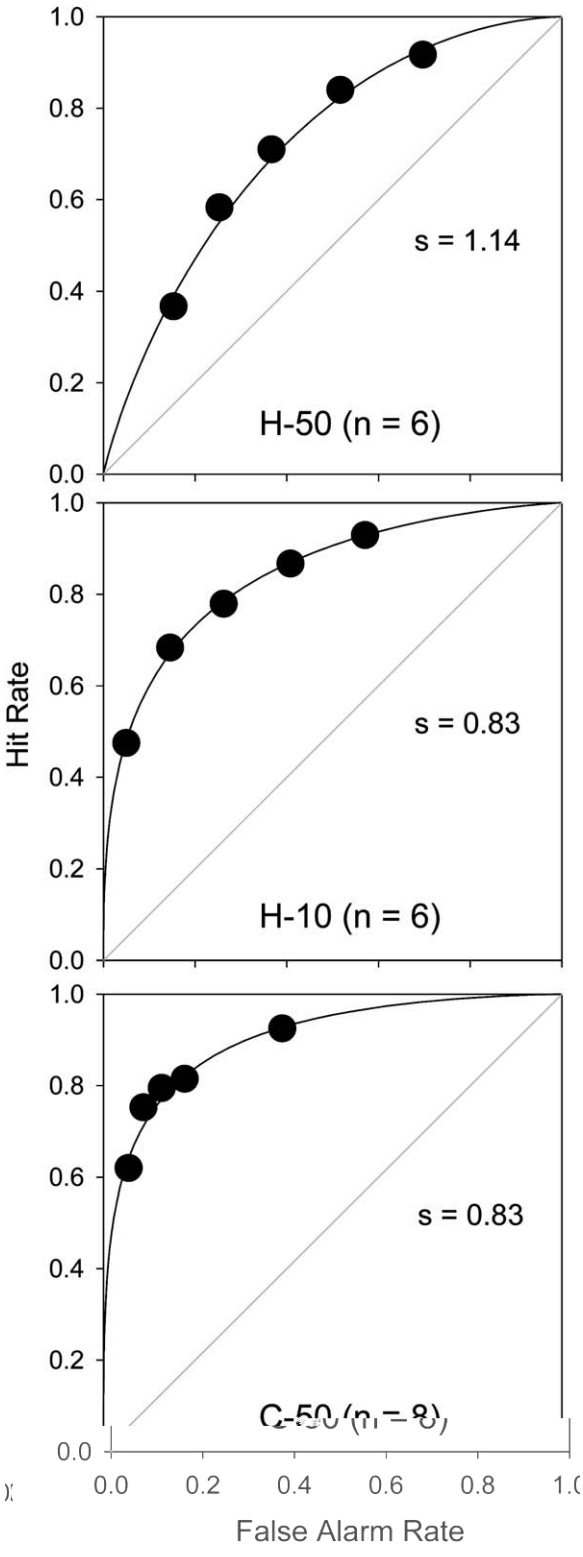

Figure 5. ROC Data Produced by the Hippocampal Patients and Controls

Top shows the data for the hippocampal patients in the 50-item condition, middle shows the data for the hippocampal patients in the 10-item condition, and bottom shows the data for the controls in the 50-item condition. The slope of 1.14 for the H-50 ROC was not different from 1.0 ($p < 0.10$), indicating that the ROC was symmetric. The slope of 0.83 for the H-10 ROC and the slope of 0.83 for the C-50 ROC were both less than the slope of 1.14 for the H-50 ROC ($\chi^2[1] \geq 4.70$, $p < 0.05$) and were significantly less than 1.0 by a one-tailed test ($\chi^2[1] \geq 2.70$, $p \leq 0.05$).

Fortin et al. (2004) studied odor recognition memory in rats and analyzed the shape of the ROC under conditions very similar to the conditions of our study. ROCs in their experiment were generated by varying the reward magnitude and the effort needed to acquire the reward (i.e., a reinforcement biasing manipulation). Control rats produced a typical asymmetrical, curvilinear ROC when recognition was tested after a short (30 min) retention interval. By contrast, rats with hippocampal lesions tested under the same conditions exhibited weaker memory and produced a symmetrical curvilinear ROC. Both these results match what we found with humans. Control rats were also tested after a longer (75 min) retention interval, which yielded a level of recognition memory performance similar to that of the hippocampal rats. Even so, the ROC associated with this long retention-interval condition was not symmetrical (as in the hippocampal rats) but was essentially linear. Fortin et al. (2004) interpreted their data in terms of the dual-process/detection model (Yonelinas et al., 1998) and argued that responding in the long-delay condition was based purely on recollection (presumably because familiarity faded rapidly to zero as the retention interval increased). This finding contrasts sharply with the increasingly symmetric and always curvilinear ROCs that we found in young adults as the retention interval increased. Even at the longest retention interval, where the ROC necessarily becomes more linear as it approaches the diagonal, our data were symmetric and curvilinear rather than linear. Further, according to the parameter estimates of the dual-process/detection model (Yonelinas et al., 1998) that were applied to our data from young adults (Table 1), recollection faded more rapidly than familiarity as retention interval increased, not the other way around.

A linear ROC in an Old/New recognition procedure—which is what the control rats exhibited after a long retention interval—is an unprecedented finding despite more than 40 years of ROC data. The only published linear ROCs known to us were obtained by distinctly different recognition memory procedures—namely, source memory and associative recognition procedures (Yonelinas, 1997, 1999)—and a substantial body of subsequent research has shown that even those ROCs are virtually always curvilinear, not linear (e.g., Hilford et al., 2002; Qin et al., 2001; Slotnick and Dodson, 2005). For the more commonly used Old/New recognition memory procedure, we are unaware of a single linear ROC in the human literature.

The linear ROC reported for rats by Fortin et al. (2004) was obtained with a procedure that was necessarily quite different from the confidence-based method so widely used with humans. In their procedure, rats were required to sniff a cup filled with scented sand on each recognition test trial. If the test odor did not match a scent that had been presented on an earlier list (i.e., if the odor was new), then digging in the sand would yield a food reward. If instead the odor did match a prior scent (i.e., if the odor was old), then a reward could be obtained by approaching a cup located elsewhere in

the chamber. The magnitude of reward for correct Old and New responses, and the difficulty of obtaining reward, were varied across conditions to change bias. An ideal ROC procedure would manipulate bias without affecting memory strength. Yet providing differential reward outcomes with experimental animals sometimes does affect memory strength as well as bias (e.g., Savage et al., 1999), and it would be important to determine if the novel procedure used by Fortin et al. (2004) succeeded in holding memory strength constant across the varying biasing conditions. If memory strength were affected by the biasing manipulations, then the shape of the ROC would be affected. In any case, the phenomenon observed by Fortin et al. (2004)—that is, a linear ROC after a long retention interval—is not observed with humans.

Another study by Yonelinas et al. (1998) involved ROC data from three memory-impaired patients and found slopes of 0.90 and 1.06 for a strong and weak memory condition, respectively, similar to what we found with our hippocampal patients (H-10 versus H-50). Like Fortin et al. (2004), these authors also tested healthy controls in a weak memory condition, so that the ROC slopes produced by patients and controls could be compared when the overall strength of memory was comparable. Even then, the slope of the ROC was substantially more asymmetric (slope = 0.55) than that of the patients, leading to the suggestion that patients lacked the recollection component that was revealed in the controls. However, the patients in that study were, on average, greater than 70 years of age, whereas the control subjects tested in the weak memory condition were undergraduates. Our own findings show as well that older subjects have a more symmetric ROC than undergraduates when memory strength is equated. For example, the mean d′ scores of the older controls at a 3 min retention interval was similar to that of the young adults at the 1 hr retention interval (2.07 and 2.14, respectively, see Figures 2 and 4), yet the slopes of their corresponding ROCs differed markedly (0.83 versus 0.63, respectively, $p < 0.05$). When we eliminated the confound of age by comparing patients and age-matched controls (H-10 versus C-50), the slope difference was eliminated and the ROCs exhibited a similar degree of asymmetry.

Our conclusion that recollection and familiarity are similarly impaired after hippocampal damage is consistent with work reporting that recall and recognition are impaired to a similar degree in patients with hippocampal lesions (Manns et al., 2003). Recall is thought to depend only on recollection, whereas recognition is thought to depend on both recollection and familiarity. Yonelinas et al. (2002) compared recall and recognition performance in a large group of cardiac arrest patients who were assumed to have hippocampal damage. Although it was reported that recall (and therefore recollection) was differentially impaired in these patients, Wixted and Squire (2004) pointed out that this conclusion rested entirely on the obviously aberrant recognition performance of one of 55 control subjects. When that single outlier was removed from the analysis, recall and recognition were impaired to a similar degree.

Several recent single-case studies have also addressed questions about recollection and familiarity in patients with hippocampal damage, but the findings are mixed and do not yield a consistent view. Two patients had similarly impaired recall and recognition for verbal material but relatively good performance on one or more tests of visual recognition (Barbeau et al., 2005; Cipolotti et al., 2006). Two other patients were reported to have impaired recall but performed relatively well on both verbal and visual recognition tests (Mayes et al., 2002; Bastin et al., 2004). Finally, Aggleton et al. (2005) described a patient whose ROC was more symmetric than that of controls, even when memory strength was equated. This result was interpreted to mean that recollection was impaired and familiarity spared, but it is not clear that the difference between the patient and the controls was reliable. One of the seven controls yielded a recollection estimate even lower than that of the patient. Further, the patient's performance after shallow or deep encoding conditions suggests a different conclusion. The benefits to memory of deep encoding conditions are thought to depend especially on recollection. Yet, the patient's recognition performance was equally impaired in both conditions. Specifically, the patient's d′ scores were 64% and 58% of the control d′ scores in the deep and shallow conditions, respectively.

One possible reason for the discrepancy among these case studies is that the patients differ in how much damage has occurred to structures beyond the hippocampus as well as in how much damage has occurred on the left and right sides. These factors complicate attempts to interpret individual patient data. We suggest that questions about the relative importance of the hippocampus for recollection and familiarity are best addressed by group studies of patients with thoroughly documented lesions limited to the hippocampus.

In the five patients we studied with MRI (all but AB), the hippocampus was reduced in volume bilaterally by a mean of 44%. Two patients with similar volume loss in the hippocampus, as measured by MRI, were found in postmortem neurohistology to have a nearly complete loss of hippocampal neurons (Rempel-Clower et al., 1996). Thus, it is reasonable to suppose that there was little or no preserved hippocampal function in our patients. If so, and if the slope of the ROC is an indicator of recollection, then the idea that the hippocampus selectively subserves a recollection process is discounted by our findings.

Recollection and familiarity remain useful constructs that help to explain a number of findings. For example, fast recognition responses (putatively based on familiarity) are not affected by the degree to which a list of items is semantically organized by the subject, whereas slower recognition responses (putatively based on recollection) are affected by semantic organization (Mandler and Boeck, 1974). However, the simple idea that these processes can be dichotomized and assigned to separate brain structures is challenged by our results. Both processes appear to be supported by the hippocampus and by the structures in the adjacent parahippocampal gyrus. The recollection process may be additionally reinforced by strategic, effortful search directed by the frontal lobes (Buckner and Wheeler, 2001; Wheeler et al., 1995). We suggest that the processes of recollection and familiarity are better viewed as

related to memory strength and as contributing jointly to recognition memory performance (Wixted and Stretch, 2004). Within the medial temporal lobe, the hippocampus and the adjacent cortex do not exclusively support one process or the other.

Experimental Procedures

Participants

The young adults were 115 undergraduates (37 males) who received class credit for their participation. The memory-impaired patients were five males and one female (AB, KE, LJ, RS, GW, JRW; mean age = 56 years, range = 46–67; mean education = 13.5 years). Estimates of the extent of medial temporal lobe damage were based on quantitative analysis of magnetic resonance images (MRI) for five of the six patients (all but AB) and either 19 controls (for KE, RS, GW, and JRW) or 11 controls (for the female patient, LJ) (Gold and Squire, 2005). The hippocampus was reduced in volume bilaterally by a mean of 44% ± 2.9% (SEM), and all values were more than three SDs below the control mean. For nine coronal MR images from each of five patients and a control, and for a detailed description of each lesion, see Supplemental Data. The adjacent parahippocampal gyrus was intact (mean volume reduction + 5.6% ± 4.3%; all values were within two SDs of the control mean). On the basis of two patients (LM and WH) with similar bilateral volume loss in the hippocampus for whom detailed postmortem neurohistological information was obtained (Rempel-Clower et al., 1996), this degree of volume loss likely reflects nearly complete loss of hippocampal neurons (also see Gold and Squire, 2005). Additional measurements, based on four controls for each patient, were carried out for the fusiform gyrus, insular cortex, and the lateral temporal, frontal, parietal, and occipital lobes (Bayley et al., 2005). With one exception (parietal lobe for RS), all values were within 1.3 SDs of the control mean. Additional information about the etiology of the memory impairment, volumetric measurements, and neuropsychological test performance appears in previous reports (Smith and Squire, 2005; Bayley et al., 2005). The controls for the patients were eight adults (six male) averaging 60.5 ± 3.6 years of age and 13.9 ± 1.0 years of education.

Stimuli

100 common English nouns were divided into two similar lists of 50 words each. Words were presented on a computer screen at both study and test. The two lists were counterbalanced within each retention-interval group so that across participants words were equally likely to be encountered as targets at study and as lures at test.

Procedure

After a 250 ms fixation cross, each word was presented for 2.5 s and rated as pleasant or unpleasant on the keyboard. After studying 50 words, the young adults were assigned to one of five retention interval conditions (19–24 subjects at retention intervals of 1 hr, 1 day, 1 week, 2 weeks, and 8 weeks). They returned later for a surprise memory test. For the test, the 50 target words were intermixed with 50 lures, and participants decided whether they recognized each item as having been presented before with a confidence scale of 1 (definitely New) to 6 (definitely Old). Following standard procedure, five pairs of hit and false alarm rates were computed for purposes of ROC analysis by cumulating responses from different points on the confidence scale (Macmillan and Creelman, 2005). The first hit and false alarm rate pair consisted of the proportion of targets and the proportion of lures that received a confidence rating of 6; the second pair consisted of the proportion of targets and the proportion of lures that received a confidence rating of 5 or 6, and so on down to the fifth pair, which consisted of the proportion of targets and the proportion of lures that received a confidence rating of 2 or more (confidence ratings of 1 are not included in an ROC analysis because 100% of the targets and 100% of the lures received a confidence rating of 1 or more). Before both the study and test sessions, participants acquainted themselves with the procedure by completing a brief practice run with novel items.

The memory-impaired patients and their controls followed the same procedure, except that the study-test interval was 3 min. The patients were also tested with shorter (ten-item) study lists. Specifically, the patients studied four different lists of ten words each, and a recognition test was administered 3 min after each study list. The study lists included four untested filler items (two at the beginning and two at the end of the list) to reduce primacy and recency effects. The retention interval was filled with continuous conversation.

ROC Analysis

The group ROC data were analyzed by means of maximum likelihood estimation by standard methods (Ogilvie and Creelman, 1968) and fits to the data were calculated using Microsoft Excel's Solver routine. Fits of the standard unequal-variance detection model (Macmillan and Creelman, 2005) involved estimating two theoretically significant parameters (the distance between the target and lure distributions—a parameter analogous to d'—and the ratio of the standard deviation of the lure distribution to the target distribution—which is the slope parameter) and five additional parameters, one for each confidence criterion (n criteria allow for n + 1 levels of confidence). We also fit the data with the dual-process/detection model, which has been used to interpret ROC data (Yonelinas et al., 1998; 2002). Fits of this model also involved estimating two theoretically significant parameters (probability of recollection and distance between the familiarity distributions) and five additional parameters, one for each confidence criteria. Goodness of fit for both models was assessed by the chi-square statistic.

Supplemental Data

The Supplemental Data for this article can be found online at http://www.neuron.org/cgi/content/full/49/3/459/DC1/.

Acknowledgments

This work was supported by National Institute of Mental Health Grant 24600 and the Medical Research Service of the Department of Veterans Affairs. We thank Rayshawn Tabaldo, Julie Tran, Jennifer Frascino, Yael Shrager, and Jeffrey Gold for assistance.

Received: August 23, 2005
Revised: October 18, 2005
Accepted: December 15, 2005
Published: February 1, 2006

References

Aggleton, J.P., Vann, S.D., Denby, C., Dix, S., Mayes, A.R., Roberts, N., and Yonelinas, A.P. (2005). Sparing of the familiarity component of recognition memory in a patient with hippocampal pathology. Neuropsychologia *43*, 1810–1823.

Barbeau, E., Felician, O., Joubert, S., Sontheimer, A., Ceccaldi, M., and Poncet, M. (2005). Preserved visual recognition memory without the hippocampus: evidence from a case study. Hippocampus *15*, 587–596.

Bastin, Ch., Van der Linden, M., Charnallet, A., Denby, Ch., Montaldi, D., Roberts, N., and Mayes, A. (2004). Dissociation between recall and recognition memory performance in an amnesic patient with hippocampal damage following carbon monoxide poisoning. Neurocase *10*, 330–344.

Bayley, P.J., Gold, J.J., Hopkins, R.O., and Squire, L.R. (2005). The neuroanatomy of remote memory. Neuron *46*, 799–810.

Brown, M.W., and Aggleton, J.P. (2001). Recognition memory: what are the roles of the perirhinal cortex and hippocampus? Nat. Rev. Neurosci. *2*, 51–61.

Buckner, R.L., and Wheeler, M.E. (2001). The cognitive neuroscience of remembering. Nat. Rev. Neurosci. *2*, 624–634.

Cipolotti, L., Bird, C., Good, T., Macmanuse, D., Rudge, P., and Shallice, T. (2006). Recollection and familiarity in dense hippocampal amnesia: a case study. Neuropsychologia *44*, 489–506.

Fortin, N., Wright, S., and Eichenbaum, H. (2004). Recollection-like memory retrieval in rats is dependent on the hippocampus. Nature *431*, 188–191.

Glanzer, M., Kim, K., Hilford, A., and Adams, J.K. (1999). Slope of the receiver-operating characteristic in recognition memory. J. Exp. Psychol. Learn. Mem. Cogn. *25*, 500–513.

Gold, J.J., and Squire, L.R. (2005). Quantifying medial temporal lobe damage in memory-impaired patients. Hippocampus *15*, 79–85.

Heathcote, A. (2003). Item recognition memory and the receiver operating characteristic. J. Exp. Psychol. Learn. Mem. Cogn. *29*, 1210–1230.

Hilford, A., Glanzer, M., Kim, K., and DeCarlo, L.T. (2002). Regularities of source recognition: ROC analysis. J. Exp. Psychol. Gen. *131*, 494–510.

Macmillan, N.A., and Creelman, C.D. (2005). Detection Theory: A User's Guide, Second Edition (Mahwah, NJ: Lawrence Erlbaum Associates, Inc.).

Mandler, G. (1980). Recognizing: the judgment of previous occurrence. Psychol. Rev. *87*, 252–271.

Mandler, G., and Boeck, W.J. (1974). Retrieval processes in recognition memory. Mem. Cognit. *2*, 613–615.

Manns, J.R., Hopkins, R.O., Reed, J.R., Kitchener, E.G., and Squire, L.R. (2003). Recognition memory and the human hippocampus. Neuron *38*, 127–133.

Mayes, A.R., Holdstock, J.S., Isaac, C.L., Hunkin, N.M., and Roberts, N. (2002). Relative sparing of item recognition memory in a patient with adult-onset damage limited to the hippocampus. Hippocampus *12*, 325–340.

Ogilvie, J.C., and Creelman, C.D. (1968). Maximum-likelihood estimation of receiver operating characteristic curve parameters. J. Math. Psychol. *5*, 377–391.

Qin, J., Raye, C.L., Johnson, M.K., and Mitchell, K.J. (2001). Source ROCs are (typically) curvilinear: comment on Yonelinas (1999). J. Exp. Psychol. Learn. Mem. Cogn. *27*, 1110–1115.

Rempel-Clower, N., Zola, S.M., Squire, L.R., and Amaral, D.G. (1996). Three cases of enduring memory impairment following bilateral damage limited to the hippocampal formation. J. Neurosci. *16*, 5233–5255.

Savage, L., Pitkin, S., and Careri, J. (1999). Memory enhancement in aged rats: the differential outcomes effect. Dev. Psychobiol. *35*, 318–327.

Schmolck, H., Kensinger, E.A., Corkin, S., and Squire, L.R. (2002). Semantic knowledge in patient H.M., and other patients with medial and lateral temporal lobe lesions. Hippocampus *12*, 520–533.

Slotnick, S.D., and Dodson, C.S. (2005). Support for a continuous (single-process) model of recognition memory and source memory. Mem. Cognit. *33*, 151–170.

Smith, C., and Squire, L.R. (2005). Declarative memory, awareness, and transitive inference. J. Neurosci. *25*, 10138–10146.

Wheeler, M.A., Stuss, D.T., and Tulving, E. (1995). Frontal lobe damage produces episodic memory impairment. J. Int. Neuropsychol. Soc. *1*, 525–536.

Wixted, J.T. (2004). On common ground: Jost's (1897) law of forgetting and Ribot's (1881) law of retrograde amnesia. Psychol. Rev. *111*, 864–879.

Wixted, J.T., and Squire, L.R. (2004). Recall and recognition are equally impaired in patients with selective hippocampal damage. Cogn. Affect. Behav. Neurosci. *4*, 58–66.

Wixted, J.T., and Stretch, V. (2004). In defense of the signal detection interpretation of remember/know judgments. Psychon. Bull. Rev. *11*, 616–641.

Yonelinas, A.P. (1997). Recognition memory ROCs for item and associative information: the contribution of recollection and familiarity. Mem. Cognit. *25*, 747–763.

Yonelinas, A.P. (1999). The contribution of recollection and familiarity to recognition and source memory: an analysis of receiver operating characteristics and a formal model. J. Exp. Psychol. Learn. Mem. Cogn. *25*, 1415–1434.

Yonelinas, A., Kroll, N.E.A., Dobbins, I., Lazzara, M., and Knight, R.T. (1998). Recollection and familiarity deficits in amnesia: convergence of remember/know, process dissociation and receiver operating characteristic data. Neuropsychology *12*, 323–339.

Yonelinas, A., Kroll, N.E., Quamme, J.R., Lazzara, M.M., Sauve, M.J., Widaman, K.F., and Knight, R.T. (2002). Effects of extensive temporal lobe damage or mild hypoxia on recollection and familiarity. Nat. Neurosci. *5*, 1236–1241.