

BILATERAL THALAMIC LESIONS AFFECT RECOLLECTION- AND FAMILIARITY-BASED RECOGNITION MEMORY JUDGMENTS

Mark M. Kishiyama¹, Andrew P. Yonelinas^{2,3}, Neal E.A. Kroll^{2,3}, Michele M. Lazzara⁴, Eric C. Nolan², Edward G. Jones³ and William J. Jagust¹

(¹Helen Wills Neuroscience Institute, University of California, Berkeley, CA, USA; ²Department of Psychology, University of California, Davis, CA, USA; ³Center for Neuroscience, University of California, Davis, CA, USA; ⁴SAM Technology, Inc., San Francisco, CA, USA)

ABSTRACT

The contribution of the thalamus to different forms of explicit memory is poorly understood. In the current study, explicit memory performance was examined in a 40-year-old male (RG) with bilateral anterior and medial thalamic lesions. Standardized tests indicated that the patient exhibited more severe recall than recognition deficits and his performance was generally worse for verbal compared to nonverbal memory. Recognition memory tests using the remember-know (R/K) procedure and the confidence-based receiver operating characteristic (ROC) procedure were used to examine recollection- and familiarity-based recognition. These tests revealed that RG had deficits in recollection and smaller, but consistent deficits in familiarity. The results are in agreement with models indicating that the anteromedial thalamus is important for both recollection- and familiarity-based recognition memory.

Key words: thalamus, amnesia, memory, recollection, familiarity

INTRODUCTION

The medial temporal lobes (MTL) play a critical role in supporting explicit memory for past events. For example, patients with extensive damage to the MTL exhibit severe impairments on tests that require the recall or recognition of previously studied items (Scoville and Milner, 1957; Corkin, 1984; Shimamura and Squire, 1987; Haist et al., 1992; MacAndrew et al., 1994; Kopelman and Stanhope, 1998). Moreover, different MTL structures support distinct types of explicit memory (Eichenbaum et al., 1994; Aggleton and Brown, 1999; Yonelinas 2002; Yonelinas et al., 2002; Kishiyama et al., 2004; but also see Squire, 1994; Squire and Zola, 1998). For example, the hippocampus is necessary for the process of recollection whereby qualitative or associative information about prior events is retrieved, while surrounding temporal lobe regions, including the perirhinal cortex, support the process of familiarity assessment which allows the detection of recently presented items. Patients with damage restricted to the hippocampus exhibit severe deficits on tests that require recollection such as free recall, and recognition tests that require the retrieval of associative information such as the location or source in which the item was studied, but their performance is relatively preserved on single item recognition tests that can be based on familiarity assessment (e.g., Aggleton and Shaw, 1996; Yonelinas, 2002). In contrast, patients with more extensive temporal lobe damage exhibit severe deficits in recall, associative recognition, and item

recognition tests (e.g., Squire and Zola-Morgan, 1991; Aggleton and Saunders, 1997; Aggleton and Brown, 1999; Yonelinas, 2002). In addition, several procedures designed to estimate the contribution of recollection and familiarity within recognition tasks – described in more detail below – have indicated that patients with damage to the hippocampus and surrounding temporal cortex have impairments in both processes whereas patients with more selective hippocampal damage have selective deficits in recollection (e.g., Yonelinas et al., 1998, 2002; Kishiyama et al., 2004; but see Manns et al., 2003).

Prior investigations of the neuroanatomical substrates of recollection and familiarity have focused on the MTL. However, because these regions do not operate in isolation, recent studies have begun to focus on other regions of the brain, such as the thalamus. Lesions to the thalamus, particularly to the anterior and medial dorsal regions, result in deficits in explicit memory tests (von Cramon et al., 1985; Gentilini et al., 1987; Graff-Radford et al., 1990; Calabrese et al., 1993; Van der Werf et al., 2000, 2003). However, the extent to which the thalamus supports recollection and familiarity is not yet known.

There are two competing hypotheses regarding the contribution of the thalamus to recollection and familiarity. First, because of the major projections from the hippocampus via the fornix to the anterior nuclei (AN) of the thalamus (e.g., Aggleton et al., 1986; Aggleton and Saunders, 1997), one may expect thalamic lesions, like hippocampal lesions, to lead to selective deficits in recollection. Alternatively, the thalamus may play a critical role

in both recollection and familiarity. For example, Aggleton and Brown (1999) have developed a model based primarily on results from studies of rats and nonhuman primates in which recollection is subserved by a circuit linking the hippocampus and the AN of the thalamus, whereas familiarity is subserved by a circuit linking the perirhinal cortex to the mediodorsal nucleus (MD) of the thalamus. Thus, damage to the thalamus should lead to deficits in recollection and familiarity, as long as the lesion includes both the anterior and medial dorsal regions.

The existing evidence suggests that thalamic lesions can disrupt recollection, but it is not yet clear whether they disrupt familiarity-based recognition. On one hand, some thalamic patients exhibit more pronounced deficits on memory tests that require recollection, like free recall (Hanley et al., 1994) and temporal order recognition (Shuren et al., 1997) than on simple item recognition that can be supported by recollection and familiarity. Note, however, that the patient studied by Hanley et al. (1994) was subsequently tested on a remember/know recognition task, and this patient was found to report both "remember" and "familiarity-based" recognition responses at rates that were comparable to controls, indicating that neither process was affected (Hanley et al., 2001). The well-preserved recognition memory performance in that patient may reflect the fact that the thalamic lesion was small and limited to the left AN. In contrast, a patient with left MD damage was found to be less likely to report that recognized items were accompanied by "remember" responses than were controls (Edelstyn et al., 2002), suggesting that recollection was more disrupted than familiarity. However, other thalamic patients have been found to exhibit pronounced deficits in both recall and recognition (e.g., Winocur et al., 1984; Clarke et al., 1994; Isaac et al., 1998), suggesting that familiarity may also be disrupted. Unfortunately, because direct measures of familiarity were not obtained in these latter studies, it is not known if familiarity was preserved or disrupted in these patients.

In the current study, we examined a patient with bilateral thalamic lesions that included the AN and the MD, using two different procedures designed to measure the contribution of recollection and familiarity to recognition memory. First, the remember-know (R/K) procedure (Tulving, 1985) was used in which the patient and control subjects were required to indicate for each recognized item whether they could remember any qualitative information about the study event in which the item was earlier encountered, or whether the item was familiar in the absence of recollection. The proportion of remember and familiar responses was used to estimate the proportion of items that was accepted on the basis of recollection and familiarity. Second, the receiver operating characteristic (ROC) procedure (Yonelinas, 1994) was used in which the

patient and control subjects were required to rate the confidence of their recognition responses. These responses were used to plot ROCs, and a nonlinear regression method was then used to quantify the ROCs to derive parameter estimates of recollection and familiarity. Although these two measurement procedures have been found to yield similar estimates of recollection and familiarity in previous studies (e.g., Yonelinas, 2001), they were both included in the current study in order to verify that the results are not limited to a single measurement method. The R/K procedure was used in Experiments 1 and 2 to examine recognition memory for words and pictorial materials, respectively. The ROC procedure was used in Experiments 3 and 4 to examine memory for words and faces, respectively.

CASE HISTORY

The patient (RG) was a 40-year-old right-handed male who presented acutely to the emergency department with a complaint of headache for 24 hours. His wife had noticed odd behavior since the onset of the headache, and described him as lethargic, irritable, confused, and forgetful. His past medical history was unremarkable except for a history of cigarette smoking, substance abuse, and a family history of myocardial infarction. On neurological examination, he was alert and fully oriented, but with poor attention and short term memory (he recalled 0 out of 3 words at 5 minutes). Language was normal. Cranial nerves, motor, sensory, reflexes, and cerebellar function were normal.

Laboratory examinations included a lumbar puncture that initially showed mildly elevated protein (56) and white cells (6) and normal glucose. Magnetic resonance imaging (MRI) scans revealed acute infarcts in the left cerebellar hemisphere, left pons, and bilaterally in the thalamus. The minor lesions outside the thalamus were not expected to be related to the patient's cognitive impairments because they fell in regions that are not directly linked to these cognitive functions. Echocardiogram, carotid ultrasound, evaluation for hypercoagulability, and a cerebral angiogram performed one week after admission were all normal. Over the course of an 8-day hospitalization, his condition gradually improved. At the time of discharge he remained amnesic for new learning but was otherwise well. The presumptive diagnosis was stroke secondary to cerebral emboli.

Since the time of his stroke, patient RG has resumed running a small business, but continues to complain of memory problems, and has subsequently hired an assistant. The patient's wife corroborates RG's memory problems, and reports that he is more anxious since the stroke. RG initially displayed a lack of insight into his cognitive deficits. However,

an evaluation conducted approximately 15 months after his stroke revealed that this condition had improved.

NEURORADIOLOGICAL FINDINGS

High-resolution MRI scans were performed ten months after the stroke as part of a functional magnetic resonance imaging study (not reported here), using a 1.5 Tesla GE CV/I MRI System (GE Medical Systems, Waukesha, WI). The scans included a sagittal T-1 weighted localizer scan, a high-resolution proton density and T2-weighted oblique coronal fast spin echo scan, and an IR-prepped 3-D T1 weighted oblique coronal SPGR scan. Scans were acquired parallel to the long axis of the hippocampus. For illustration purposes and to aid in lesion quantification, the subject's scans were resliced and presented in standard axial and coronal orientations.

The high-resolution scans revealed that the left thalamic lesion was anterior and lateral, undercutting the anterior thalamic radiation and encroaching on the mammillothalamic tract (MTT), AN, and internal medullary lamina (IML). Although the lesion did not appear to encroach on the MD, the IML damage likely disconnected the MD (e.g., Jones, 1985; von Cramon et al., 1985). The right thalamic lesion was anterior and medial including all of the AN, the MTT, and the anterior pole of the MD. The MRI scan illustrating patient RG's thalamic lesions is presented in Figure 1.

NEUROPSYCHOLOGICAL ASSESSMENT

Neuropsychological testing began seven months after the patient's stroke. The patient's test scores are presented as z-scores, based on the published age-matched norms. Note that z-scores between -1 and -1.63 are indicative of below normal or moderate impairment and that z-scores lower than -1.64 ($p < .05$, one-tailed), are indicative of significant impairment. RG performed at the normal to low-normal range on tests of intelligence and language comprehension. On the Wechsler Adult Intelligence Scale-Revised (WAIS-R); (Wechsler, 1981) he performed slightly below normal on the Vocabulary scale ($z = -1.00$), within the normal range of the Performance scale ($z = -.47$), and was normal on the forward ($z = 0.00$) and backward ($z = .08$) Digit Span subtests. In addition, he performed within the normal range on the National Adult Reading Test ($z = -.60$; Nelson, 1982) and the Tokens Test of language comprehension ($z = -.07$) (Benton and Hamsher, 1989).

RG exhibited some evidence of a mild executive function deficit. His scores on the FAS ($z = .28$) and Animal ($z = .08$) tests of Word Fluency (Rosen, 1980) were in the normal range.

However, his scores on the Wisconsin Card Sorting Test (WCST) (Grant and Berg, 1948) indicated a moderate impairment. In particular, he scored below normal on both the categories ($z = -1.28$) and conceptual level responses ($z = -1.08$) of the WCST and was below normal in terms of his total number of errors ($z = -1.60$). However, he obtained a normal ($z = .39$) Cognitive Estimate score on the Trail Making Test (TMT) (Reitan, 1958) and obtained perfect scores with both the four and five disk problems on the Tower of Hanoi Test (Glosser and Goodglass, 1990).

RG's long-term explicit memory was impaired, particularly for recall tests of verbal materials. His score on the Wechsler Memory Scale-Revised (WMS-R) (Wechsler, 1987) Delayed Logical ($z = -1.15$) recall test was below normal, and he was significantly impaired on the Delayed Paired Associate Learning (PAL) ($z = -5.14$) subtest. However, on the Delayed Visual Reproduction subtest he scored within the normal range ($z = -.07$). His scores on the Rey-Osterrieth Complex Figure Test (Osterrieth, 1944) were also in the normal range (Copy: $z = .46$; 3-min Delay: $z = -.31$; 30-min Delay: $z = -.09$), as were his scores on the Warrington Recognition Memory Test (WRMT; Warrington, 1984) (Words: $z = .00$; Faces: $z = -.30$).

Retrograde amnesia was not formally tested, but RG spontaneously reported fairly detailed stories about events immediately prior to his stroke and more distant stories from his youth. In addition, RG's wife reported that changes in his behavior since the stroke primarily involved difficulty forming new memories, whereas his remote memory appeared to be intact.

In sum, RG exhibited memory impairments and mild executive function deficits that are consistent with previous studies of patients with anterior and medial dorsal thalamic lesions (Van der Werf et al., 2000). His memory impairments were particularly pronounced for delayed verbal recall.

EXPERIMENT 1: WORD RECOGNITION (R/K)

In Experiment 1, recognition memory for words was investigated using the R/K procedure. Control subjects and the patient studied a list of words then were given a recognition test in which they indicated whether each test word was remembered, familiar, or new.

Methods

Subjects and Materials

The subjects included RG and six age-matched control subjects (three women and three men) recruited from the local community (age $M = 44.3$ years, $SD = 2.3$ years). Five of the controls were college educated and reported no history of

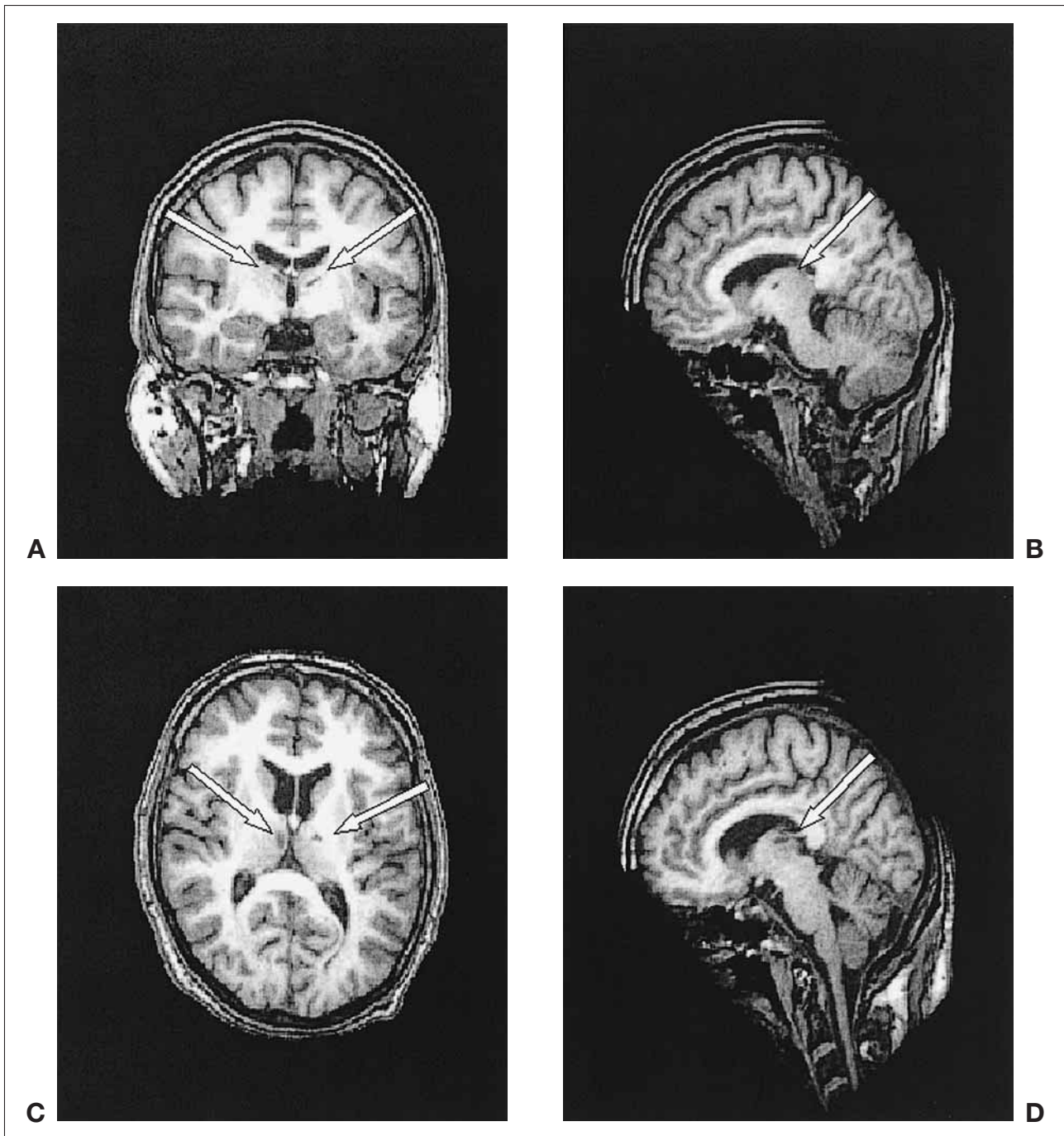


Fig. 1 – MRI scan including (a) coronal, (b) left sagittal, (c) axial, and (d) right sagittal slices illustrating the patient's bilateral thalamic lesions. The right side of the brain appears on the left and the left side appears on the right.

substance abuse. Because RG was not college-educated and reported a history of substance abuse, an additional control subject was included who reported a similar history of substance abuse and also had no college education. However, this control subject performed at similar levels to the other control subjects on all experiments. All of the control subjects scored within the normal range on the Digit Span (forward and backward) and the delayed Logical Memory, PAL, and Visual Reproduction subtests of the WMS-R. All subjects gave their written consent prior to testing and were paid \$10/hour for their participation.

One hundred and fifty words with word frequency ratings ranging from 1-53 (Kucera and Francis, 1967) served as test items. One hundred words were randomly chosen from the test list to be presented as study items, and the remaining fifty served as test lure items.

Design and Procedure

During the study phase, control subjects and the patient were read a list of 100 words and were required to make a verbal response to each item. For the first 25 and last 25 items in the list,

subjects were required to indicate how many syllables were in each word. For the middle 50 items, subjects were required to rate the pleasantness of each item. At time of test subjects were read a list containing a mixture of all the studied items plus 50 new words and were required to respond "remember", "familiar", or "new" to each item. They were told to respond 'remember' if they could recollect any qualitative information about the item from the study episode (e.g., whether they had previously made a syllable or pleasantness judgment about the word). They were told to respond "familiar" if they were sure the item was presented during the study phase, but they could not recollect any qualitative information about the prior presentation of the item. Note that we used the term "familiar" rather than "know" because some subjects found the latter term confusing. Nonetheless, to be consistent with previous studies we will refer to these as "know" responses for the remainder of the paper. Subjects were told to respond, "new" if they thought the item had not been presented during the study phase. To ensure that the subjects understood the test instructions they were asked to explain why they made each response for the first 20 items in the test list.

Given that control subjects performed at ceiling levels of recognition for the items that had been studied under the pleasantness rating conditions, only performance on the items studied under the syllable counting conditions will be reported.

Results and Discussion

The proportion of remember and know responses for RG and the controls are presented in Table I. Estimates of recollection and familiarity were derived using the "remember" and "know" responses (Yonelinas and Jacoby, 1995) and are presented in Figure 2. Because all subjects were instructed to respond "remember" when an item was recollected, the probability of a "remember" response was used as an estimate of recollection (i.e., $R = \text{'remember'}$). Because all subjects were instructed to respond "know" when an item was familiar in the absence of recollection [i.e., $\text{'know'} = F(1 - R)$], familiarity was estimated as the probability of a "know" response given the item was not recollected [i.e., $F =$

TABLE I
Proportion of remember and know responses
for Experiments 1 and 2

Experiment 1				
Responses:	"R"	"K"	"R"	"K"
Item type:	Old	Old	New	New
RG	.02	.14	0	.06
Controls	.50	.27	.03	.17
Experiment 2				
Responses:	"R"	"K"	"R"	"K"
Item type:	Old	Old	New	New
RG	.38	.13	.10	.08
Controls	.59	.18	.07	.18

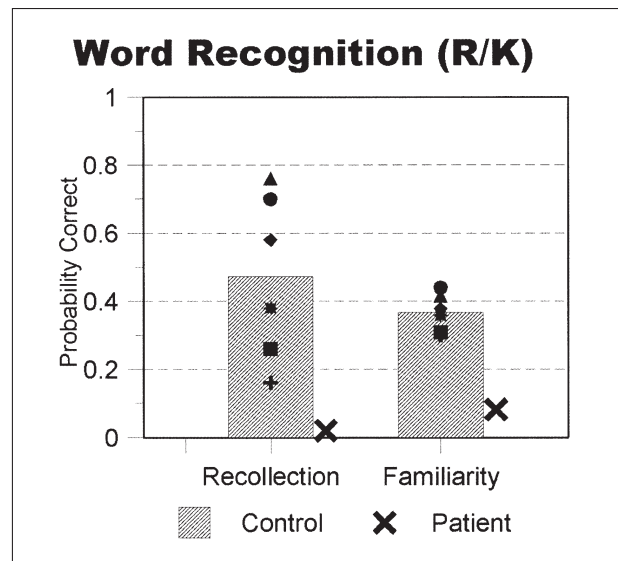


Fig. 2 – Recollection and familiarity accuracy for patient RG and the age-matched control subjects in the Word Recognition (R/K) test. The bars represent the mean accuracy of all control subjects. The individual scores of the control subjects are represented by various shapes (e.g., a triangle, a circle, a square). The scores of patient RG (the X symbol) are to the right of the control subjects' scores.

"know"/(1 - R)]. To account for false alarm rates, accuracy was measured using a hits-minus-false-alarm-rate index. For example, recollection was measured as the probability of a remember response to an old item minus the probability of a remember response to a new item.

As can be seen in Figure 2, patient RG's recollection and familiarity scores were well below the mean estimates for the age-matched control group. In fact, his recollection and familiarity scores were lower than those of every one of the subjects in the control group. Moreover, his recollection score was approximately zero, indicating that recollection was profoundly disrupted.

To contrast his performance to that of the controls, his overall recognition, recollection, and familiarity scores were standardized based on the means and standard deviations of the controls. Overall recognition accuracy was measured using d' (see MacMillan and Creelman, 1991) such that a hit was defined as the proportion of old items receiving a remember or know response, and the false alarm rate was defined as the proportion of new items receiving a remember or know response. The estimates of recollection and familiarity were measured using probability correct (see above). Note that z-scores between -1 and -1.63 are indicative of below normal or moderate impairment and that z-scores lower than -1.64 ($p < .05$, one-tailed), are indicative of significant impairment. Our predictions were one-tailed because we expected that thalamic damage would lead to impaired memory performance.

The analysis indicated that RG was significantly impaired in overall recognition accuracy ($z = -1.87$). He also showed evidence of moderate

impairment in recollection ($z = -1.12$), and he was significantly impaired in familiarity ($z = -5.04$). Note that his z -score for recollection likely underestimates his true recollection deficit because his recollection score was at floor (approximately zero).

EXPERIMENT 2: PICTURE RECOGNITION (R/K)

In Experiment 2, recognition memory for pictorial stimuli was examined using the R/K procedure. Control subjects and the patient studied a list of clip-art object images and then were given a recognition memory test in which they indicated whether each test item was remembered, familiar, or new.

Methods

Subjects and Materials

The control subjects were the same as those who participated in Experiment 1. A total of 660 thumbnail object images (e.g., animals, tools, symbols, etc.) from MasterClips Premium Image Collection (MasterClips, 1998) served as study and test items. Six hundred were randomly selected for the study list and the remainder served as test lure items.

Design and Procedure

Control subjects and the patient were seated in front of a laptop computer. During the study phase subjects were presented with a total of 600 items at a rate of one object every 850 msec. Because these items were previously used in a study of stimulus novelty (Kishiyama et al., 2004), a small number of items (i.e., 30) were isolated from the majority on the basis of color (e.g., most of the items were presented in yellow and a small subset were presented in red). Subjects were told that color was not important and that they were to remember all objects. During the test phase, subjects were presented with a mixture of 60 old items (30 red and 30 yellow items) and 60 new items (30 red and 30 yellow items) and were required to make remember, know, and new responses as in Experiment 1. Because stimulus novelty was not of direct interest here responses for red and yellow items were collapsed.

Results and Discussion

The proportion of remember and know responses for RG and the controls are presented in Table I. Estimates of recollection and familiarity were derived in the same manner as in Experiment 1, and are presented in Figure 3. As in the previous experiment, the estimates of recollection and

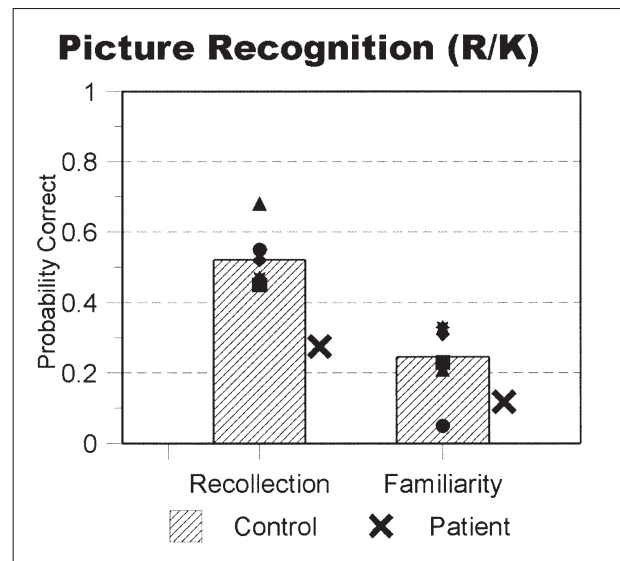


Fig. 3 – Recollection and familiarity accuracy for patient RG and the age-matched control subjects in the Picture Recognition (R/K) test. The symbol representations are the same as those in Fig. 2

familiarity for RG were well below the average estimates for the control group. RG's recollection score was lower than those of all the controls, and his familiarity score was lower than all but one control subject. Contrasts between RG's and the controls' overall recognition, recollection, and familiarity performance were conducted in the same way as in Experiment 1. The patient exhibited significant impairments in overall recognition ($z = -4.87$) and recollection ($z = -2.72$), and he showed a moderate impairment on familiarity ($z = -1.14$).

EXPERIMENT 3: WORD RECOGNITION (CONFIDENCE)

In Experiment 3, recognition memory for words was examined using the confidence ROC procedure. Control subjects and the patient studied a list of words then were given a recognition memory test in which they were required to rate the confidence of their recognition responses. Recognition performance was plotted as a function of response confidence and the function was quantified to derive parameter estimates of recollection and familiarity.

Methods

Subjects and Materials

The control subjects were the same as those who participated in Experiments 1 and 2. Four hundred and eighty words were selected to serve as study and test items, three hundred and sixty of which were randomly selected to serve as study items and the remainder served as test lure items.

Design and Procedure

Control subjects and the patient were tested in two similar sessions conducted at least one week apart. In the first session, subjects heard 160 words and were required to make a verbal response to each item. For the first 80 items they were required to indicate whether the word was abstract or concrete, and for the remaining items they were required to indicate how many syllables were in each word. Subjects were then presented with a test list containing all the studied items plus 80 new items and were required to make recognition memory judgments using a 6-point confidence scale from *certain it was new* (1) to *certain it was old* (6). Subjects were instructed to spread their responses across the whole range from 1 through 6 and were reminded of this after they made their first few responses. The second session was similar to the first except that the order of encoding conditions was reversed. The pattern of performance in the two test sessions and in the two encoding conditions in each session was similar, so performance was collapsed across these factors.

Results and Discussion

The average ROC for the age-matched control group along with the ROC for RG is presented at the top of Figure 4. The proportion of old items accepted as new and the proportion of old items accepted as old are plotted on the x- and y-axes, respectively. The left most point on each function represent the proportion of items receiving the most confident old responses (i.e., a 6 response), and each consecutive point includes items receiving the next most confident old response (e.g., the second point includes items receiving 5 or 6 responses).

RG's ROC fell below that of the control average indicating that he exhibited a deficit in overall recognition performance. The ROCs for each subject were quantified by fitting a nonlinear equation to the observed ROCs using a sum of squares search algorithm (Yonelinas et al. 1998). The equation [i.e., $P(\text{"old"}|\text{old}) = P(\text{"old"}|\text{new}) + R + (1 - R) \Phi(d'/2 - c_i) - \Phi(-d'/2 - c_i)$] assumes that recognition reflects the contribution of recollection (R) and an independent familiarity process (d' reflects the distance between two equal-variance Gaussian strength distributions; c_i reflects the response criterion at point i ; and F reflects the cumulative response function). To facilitate comparison to recollection, which was measured as a probability, each d' value was converted to the probability of a hit given the false alarm rate (i.e., proportion of new items receiving a response of 4, 5, or 6). Familiarity accuracy was then measured by subtracting the false alarm rate from the calculated hit rate.

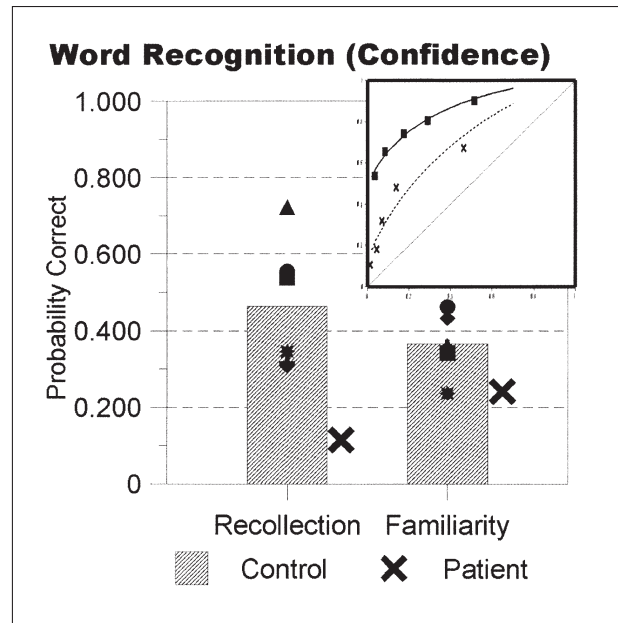


Fig. 4 – Recollection and familiarity accuracy for patient RG and the age-matched control subjects in the Word Recognition (Confidence) test. The symbol representations are the same as those in Fig. 2. The ROCs for patient RG (dotted line) and the control subjects (solid line) are presented in the upper right of the graph.

Parameter estimates for recollection and familiarity were derived for each subject and are presented in Figure 4. As can be seen in Figure 4, RG's recollection and familiarity scores were lower than the mean scores from the control group. Moreover, his recollection score was lower than those of all the control subjects, and his familiarity score was below all but one of the controls. Contrasts between RG's and the controls' overall recognition, recollection, and familiarity performance were conducted in the same way as in Experiment 1. However, d' scores for overall recognition accuracy were derived from the average proportions of hit and false alarm rates of confidence responses 4-6, and recollection and familiarity estimates were measured using probability correct (see above). The patient showed a moderate impairment in overall recognition ($z = -1.50$) and familiarity ($z = -1.55$), and he was significantly impaired in recollection ($z = -2.09$).

EXPERIMENT 4: FACE RECOGNITION (CONFIDENCE)

In Experiment 4, recognition memory for line drawings of faces was examined using the confidence ROC procedure. Control subjects and the patient studied a list of faces then were given a recognition test in which they rated the confidence of their recognition judgments. The ROC was quantified to derive estimates of recollection and familiarity.

Methods

Subjects and Materials

The control subjects were the same as those in Experiments 1-3. One hundred and sixty-five colored line drawings of faces of men and women who were unlikely to be identified (e.g., non-famous business leaders and authors) were selected from Corel-Draw's collection of drawings of faces. The faces were approximately 10-15.5 cm wide and 12.5-18 cm high when presented on a 38 cm computer monitor. 85 were randomly selected for the study phase and the remainder served as test lures.

Design and Procedure

The experiment was divided into two similar sessions that were conducted at least one week apart. In the study phase, control subjects and the patient were presented with 85 faces sequentially. The first 5 faces were treated as practice items and were therefore not included in the test phase. Subjects were required to judge the age of each face and to try to remember them for a later memory test. Each face remained on the screen for 3 seconds, and the next face was not presented until after the subject estimated the age of the face on the computer keyboard (e.g., 2 = 20 sec, 3 = 30 sec, etc.). In the test phase, subjects were presented with a mixture of 80 old and 80 new faces, and were required to make recognition confidence judgments. The test instructions were the same as those used in Experiment 3.

Results and Discussion

The average ROC for the age-matched control group along with the ROC for RG is presented at the top of Figure 5. The ROCs were plotted and analyzed in the same way as in Experiment 3. RG's ROC was slightly lower than that of the controls, suggesting that his overall recognition memory was poorer than the controls. Estimates of recollection and familiarity are presented in Figure 5. Estimates of recollection for RG were lower than the control average, but two of the 6 controls, performed more poorly than RG. The estimate of familiarity for RG was also lower than the control average, and it was lower than all but one of the controls. Contrasts between RG's and the controls' overall recognition, recollection, and familiarity performance were conducted in the same way as in Experiment 1, and measures of overall recognition, recollection, and familiarity were derived in the same manner as in Experiment 3. The patient was significantly impaired in overall recognition ($z = -1.64$), and he showed a moderate impairment in familiarity ($z = -1.11$), but his recollection score was in the low-normal range ($z = -.79$).

Thus, the results of this experiment are similar in

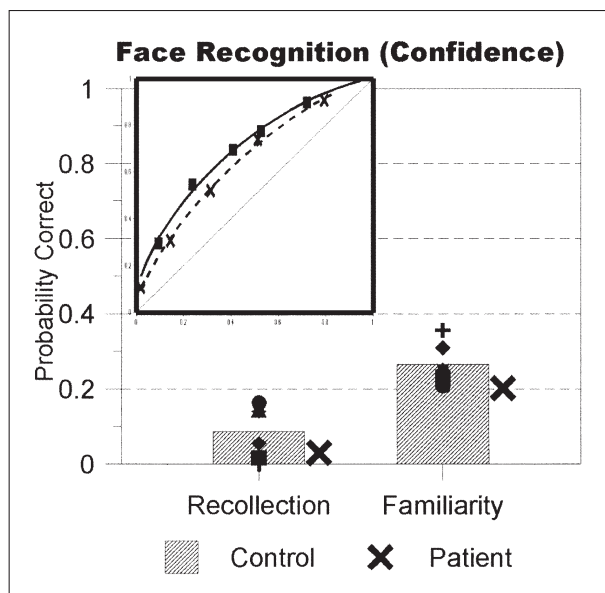


Fig. 5 – Recollection and familiarity accuracy for patient RG and the age-matched control subjects in the Face Recognition (Confidence) test. The symbol representations are the same as those in Fig. 2. The ROCs for patient RG (dotted line) and the control subjects (solid line) are presented in the upper left of the graph.

pattern to those of the previous experiments in that RG exhibited low performance in recognition, recollection, and familiarity, but the deficits were somewhat less pronounced than those seen in the earlier experiments. Unlike the previous experiments, overall performance was very low for all subjects (see Figure 5), and thus floor effects likely obscured the magnitude of the patient's deficits.

GENERAL DISCUSSION

Memory performance was examined in a 40-year-old male with bilateral thalamic lesions. Consistent with several previous reports of patients with anterior and medial thalamic lesions, standard neuropsychological tests indicated that the patient exhibited memory impairments on tests of explicit memory (Graff-Radford et al., 1990; Pepin and Auray-Pepin, 1993; Daum and Ackerman, 1994; Isaac et al., 1998; Van der Werf et al., 2000, 2003). Most importantly on tests of recognition designed to measure recollection and familiarity, the patient exhibited deficits in both memory processes. Overall recognition memory was significantly or moderately impaired for words, pictures, and faces. Recollection was significantly impaired for pictures (Experiment 2), moderately or significantly impaired for words (Experiments 1 and 3, respectively), and in the low-normal range for faces (Experiment 4). Familiarity was found to be significantly or moderately reduced for words (Experiments 1 and 3, respectively), and moderately reduced for pictures (Experiment 2) and faces (Experiment 4). Thus, the results indicate that the

thalamus plays a critical role in both recollection and familiarity.

Two competing hypotheses regarding the contribution of the thalamus to recollection and familiarity-based recognition were contrasted in the current study. The first hypothesis was that the thalamus plays a selective role in recollection. The second hypothesis was that the thalamus plays a critical role in both processes. The current results show that thalamic damage can disrupt both recollection and familiarity, and thus the results are most consistent with the second hypothesis. This hypothesis was based on the model of Aggleton and Brown (1999) in which recollection is assumed to be supported by a circuit linking the hippocampus and the AN of the thalamus, whereas familiarity is supported by a circuit linking the perirhinal cortex and the MD of the thalamus. As would be expected by that model, RG's lesions included the AN in both hemispheres. Moreover, the MD was directly involved on the right side, whereas the left hemisphere lesion included the IML and thus likely disrupted the MD on the left.

The results of the current study are consistent with the Aggleton and Brown model in that anteromedial thalamic lesions lead to deficits in recollection and familiarity. However, because RG's lesions included both the AN and the MD we cannot conclude that damage restricted to either region alone would necessarily lead to a selective deficit in recollection or familiarity, respectively, as the model would suggest. In fact, evidence from several recent investigations indicate that lesions to the MD that do not include the AN do not appear to lead to recognition memory deficits, as the model predicts (Edelstyn et al., 2002; Van der Werf et al., 2003). In addition, Zoppelt et al. (2003) used the ROC procedure to estimate recollection and familiarity in patients with unilateral thalamic lesions and found that patients with damage to the medial MD had deficits in both recollection and familiarity whereas patients with damage to the lateral MD had deficits only in recollection. Thus, although the results of the current study indicate that the thalamus plays a critical role in the two different forms of explicit memory, future investigations are needed to better determine the functional characteristics of memory-related thalamic subregions.

Although RG did exhibit deficits in recollection and familiarity, it appears as though his recollection deficit was more pronounced than his familiarity deficit. First, his neuropsychological assessment indicated that he was more impaired on tests that required recollection, such as recall, than on tests of item recognition that could be supported by recollection and familiarity. For example, he exhibited deficits on the WMS-R Delayed Logical and PAL recall subtests, yet he performed in the normal range on the Words and Faces recognition tests of the WMRT. Second, in the current experiments, RG appeared to have more pronounced

deficits in recollection than familiarity. For example, in Experiments 1-3, RG had recollection estimates that were well below all of the controls, whereas his familiarity estimates were closer to, and in some cases overlapped with, those of the control group. Low levels of performance for all subjects in Experiment 4 made it difficult to assess this issue in that experiment. Standardizing the patient's recollection and familiarity estimates relative to the controls further illustrated the degree of the patient's deficits. In Experiments 1 and 4, the patient's recollection scores were approximately zero, so the z-scores of his recollection estimates are not directly interpretable. However, in Experiments 2 and 3 where estimates were above floor, his recollection deficits were moderately greater than his familiarity deficits. Thus, although RG exhibited deficits in both recollection and familiarity, his deficits in recollection were both more consistent and more pronounced than his deficits in familiarity.

As with several previous studies of thalamic patients (Speedie and Heilman, 1982; Kritchevsky et al., 1987; Graff-Radford et al., 1990; Isaac et al., 1998; Van der Werf et al., 2000), RG exhibited some evidence of a mild executive function deficit. He performed normally on verbal fluency tests, but was slightly below normal on card sorting, and displayed an initial lack of insight into his cognitive deficits – a condition that has previously been associated with executive dysfunction (e.g., Michon et al., 1992).

It is possible that the patient's executive function deficits contributed to his memory impairments, particularly the observed recollection deficits. That is, patients with executive function problems due to frontal lobe damage are impaired on recall and recognition tests that require recollection (Jetter et al., 1986; Gershberg and Shimamura, 1995; Kopelman et al., 1997), and these deficits are thought to reflect disrupted elaboration and monitoring processes that facilitate encoding and retrieval of explicit memory (Hirst and Volpe, 1988; Gershberg and Shimamura, 1995; Parkin et al., 1999). However, given the extent of his memory impairments, it seems unlikely that they could be due solely to his relatively mild executive dysfunction.

Given that RG performed normally on the Warrington recognition memory tests, it is surprising that he exhibited pronounced deficits on the four recognition experiments in the current study. However, other patient groups that perform normally on the Warrington tests (Aggleton and Shaw, 1996) do exhibit severe deficits when tested on other recognition tests (Reed and Squire, 1997). Thus, the Warrington tests may not provide a particularly sensitive measure of recognition memory impairment.

RG's scores on the standardized tests suggest that his impairment was greater for verbal than nonverbal materials. For example, he performed in

the normal range on recall tests of nonverbal memory (i.e., the Rey-Osterrieth Complex Figure Test and Visual Reproduction subtest of the WMS-R), yet he exhibited severe impairments on recall tests of verbal memory. These results alone suggest that the thalamic lesions may have disproportionately disrupted his verbal hemisphere. If he is normally lateralized, then these results would suggest that the damage to the left thalamus was more profound than the damage to the right. However, in the current recognition tests, he exhibited deficits in tests for words, pictures, and faces, indicating that his deficits were not limited to verbal materials. Whether these deficits arose because of the verbalizable nature of the faces and pictures used in the current study is not clear.

In summary, explicit memory performance was examined in a patient with bilateral thalamic lesions. Consistent with prior reports of patients with thalamic damage, the patient exhibited deficits on explicit long-term memory. On recognition memory tests using the R/K and ROC procedures, the patient exhibited deficits in recollection and familiarity-based recognition. The findings are consistent with those from the animal literature indicating that the thalamus is a crucial component in both medial temporal lobe networks supporting explicit memory.

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Mark Kishiyama, Helen Wills Neuroscience Institute, 210C Barker Hall, NC #3190, University of California, Berkeley, CA, 94728-3190, USA.
e-mail: mmkishiyama@berkeley.edu

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