Detection and Explanation of Sentence Ambiguity Are Unaffected by Hippocampal Lesions but Are Impaired by Larger Temporal Lobe Lesions

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ABSTRACT: We address the recent suggestion that the "hippocampal system" is important for understanding ambiguities in language (MacKay et al., J Cogn Neurosci 1998;10:377–394). Seven amnesic patients and 11 controls first decided whether a sentence was ambiguous and then tried to explain the ambiguity. Three amnesic patients with damage limited to the hippocampal formation and one amnesic patient with primarily diencephalic damage performed like the controls in all respects. Thus, the ability to comprehend ambiguity is independent of the hippocampal formation. By contrast, three patients with larger temporal lobe lesions, which extended beyond the medial temporal lobe, were impaired to about the same degree as the noted amnesic patient H.M. (as reported by Lackner, Neuropsychologia 1974;12:199–207; MacKay et al., J Cogn Neurosci 1998;10:377–394). Patient H.M., like our 3 impaired patients, has some damage outside the medial temporal lobe. However, patient H.M. also had additional difficulties on these and other language tests that the patients with larger temporal lobe lesions did not exhibit. Accordingly, it is possible that H.M.'s impairment has a different basis. *Hippocampus 2000;10:759–770.*

KEY WORDS: amnesia; hippocampus; memory; medial temporal lobe

INTRODUCTION

Since the first description of patient H.M. in 1954 (Scoville, 1954), evidence has accumulated that damage to the hippocampus and adjacent medial temporal lobe structures leads to severe and lasting memory impairment. The prevalent view has been that H.M. and other amnesic patients suffer from a pure memory deficit with sparing of language abilities, reasoning, and other intellectual functions. The hallmark of the deficit is impaired acquisition of new declarative knowledge (anterograde amnesia) (Milner, 1972; Iversen, 1977; Squire, 1992; Mayes, 1988; Parkin, 1986).

Among the perceptual and intellectual functions other than memory that have been studied in amnesic patients, language functions have been a focus of recent interest. Subsequent to a report that H.M.'s conversational speech was slow (Corkin, 1968), Lackner (1974) examined H.M.'s language processing capabilities using ambiguous sentences, and concluded that "H.M.'s ability to detect various kinds of linguistic ambiguity appears essentially normal." Lackner (1974) noted that H.M.'s ability to detect sentence ambiguity was below the level that would be predicted from his IQ, but wrote that "it is uncertain how unusual H.M.'s performance should be considered."

The issue of H.M.'s language abilities was subsequently taken up by MacKay et al. (1998a,b; see also MacKay and James, 2000), who reevaluated H.M.'s performance on the ambiguity detection task of Lackner (1974) as well as on a task of ambiguity explanation (Corkin, unpublished recording, 1973). Both tasks were given to 3 individuals who were matched to H.M. with respect to age, education, and verbal IQ. Compared to these individuals, H.M. was distinctly impaired both at detecting and explaining sentence ambiguity. MacKay et al. (1998b) concluded that an intact "hippocampal system" is a prerequisite for normal speech processing, and that

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"memory storage and retrieval involving verbal materials are inherent aspects of normal language production."

To date, the issue of how hippocampal damage, and memory impairment, might relate to language function has been explored only in patient H.M. Unfortunately, H.M. is not an ideal patient for addressing questions about the role of the hippocampus itself in language function. First, his lesion includes not only the hippocampus, but also adjacent medial temporal lobe structures as well as some more lateral damage at the temporal pole (Corkin et al., 1997). In addition, H.M. had petit mal seizures beginning at age 10 and grand mal seizures beginning at age 16, which raises the question as to whether his language development was fully normal.

The present study explored the ability to understand linguistic ambiguity in patients with adult-onset amnesia. We asked whether patients with memory impairment can detect and explain linguistic ambiguity. We also asked whether lesions limited to the hippocampal formation or diencephalon impair the ability to understand linguistic ambiguity and what the effect might be of large temporal lobe lesions that extend beyond the medial temporal lobe.

Four of our patients had isolated memory impairment and damage restricted to the hippocampal formation or primarily the diencephalon. Three other patients had profound amnesia and lesions that included the hippocampal formation but which also extended beyond the medial temporal lobe. We used the identical materials that Lackner (1974) had used to test ambiguity detection and ambiguity explanation, and compared the performance of our patients to H.M.'s performance, as previously reported.

METHODS

Amnesic Patients

We studied 7 amnesic patients, 6 men (A.B., P.H., G.T., E.P., G.P., and N.A.) and one woman (L.J.). Three of the patients (A.B., L.J., and P.H.) have damage limited to the hippocampal formation. Patient A.B. became amnesic after a cardiac arrest in 1976. He is unable to participate in magnetic resonance (MR) studies but is presumed to have hippocampal formation damage on the basis of etiology and a normal neurologic examination. Patient L.J. became amnesic with no known precipitating event during a 6-month period beginning in late 1988. Her memory impairment has remained stable since that time. MR imaging identified that the hippocampal formation was reduced in area 34% bilaterally (Reed and Squire, 1998). Patient P.H. had a 6-year premorbid history of 1–2-min attacks (presumably of epileptic origin) in association with gastric symptoms and transient memory impairment. In 1989, he suffered a series of small attacks that resulted in marked and persisting memory impairment. MR imaging shows a 22% reduction in size of the hippocampal region bilaterally (Polich and Squire, 1993).

Patient N.A. has been amnesic since 1960, when at age 22 he sustained a penetrating brain injury with a miniature fencing foil. The amnesia primarily affects verbal material. MR imaging shows three major areas of damage: a left thalamic lesion 3–4 mm wide, which approximates the position and orientation of the internal medullary lamina and extends for 20 mm anterioposteriorly; a marked disruption of the posterior hypothalamus with missing mammillary nuclei bilaterally; and damage to the right anterior temporal lobe for a distance of about 3.5 cm from the pole to midway through the amygdaloid complex. The latter damage is thought to have occurred during exploratory neurosurgery done at the time of his injury. The hippocampal formation appears intact on both sides (Squire et al., 1989).

Three other patients developed profound amnesia after herpes simplex encephalitis (E.P. in 1992, G.P. in 1987, and G.T. in 1990). All three have large, radiologically confirmed bilateral lesions of the temporal lobe that include the hippocampal region, the amygdala, and the adjacent perirhinal, entorhinal, and parahippocampal cortices. Variable damage is also present lateral to these structures (see Figs. 1–3). E.P.'s damage is primarily medial temporal but also involves the anterior portion of the fusiform gyrus. Moreover, the lateral temporal cortex and the insula are reduced in volume bilaterally (Fig. 1). Like E.P., G.P.'s damage is primarily medial temporal, but his damage extends further laterally. Anteriorly, the damage includes the fusiform gyrus as well as the inferior, medial, and superior temporal gyri. More caudally, the damage is limited to the fusiform gyrus and the inferior temporal gyrus (Fig. 2). G.T. has the most severe damage, which extends laterally to involve most of the temporal lobes bilaterally (Fig. 3).

Table 1 summarizes the neuropsychological findings for all 7 amnesic patients. All have moderately severe to very severe amnesia. None is capable of independent living.

Control Subjects

Eleven healthy control subjects were recruited from volunteers and employees at the San Diego Veterans Affairs Medical Center and the University of California at San Diego (UCSD) retirement community. They were matched to the amnesic patients with respect to age (control mean = 66.8; range, 52–74; patient mean = 64.1) and education (control mean = 13.5; range, 12–16; patient mean = 14.9 years). The mean raw score for the control group on the WAIS-R vocabulary subtest was 51.5 (range, 36–69), and the score on the WAIS-R information subtest was 20.1 (range, 14–26). It was not possible to match all the patients and controls with respect to verbal IQ scores, because the three postencephalitic patients have abnormally low scores on some subtests (Table 1). However, 5 of the control subjects were closely matched to the 3 patients with damage limited to the hippocampal formation with respect to age (control mean = 67.2; range, 59–74; patient mean = 65.7 years), the WAIS-R information subtest (control mean = 22.2; range, 15–26; patient mean = 21.7), and the WAIS-R vocabulary subtest (control mean = 54.2; range, 36–69; patient mean = 58) subscores.

Materials and Procedure

Sixty-five ambiguous sentences taken from Lackner (1974) were administered together with 25 unambiguous sentences, which were matched to the ambiguous sentences with respect to length

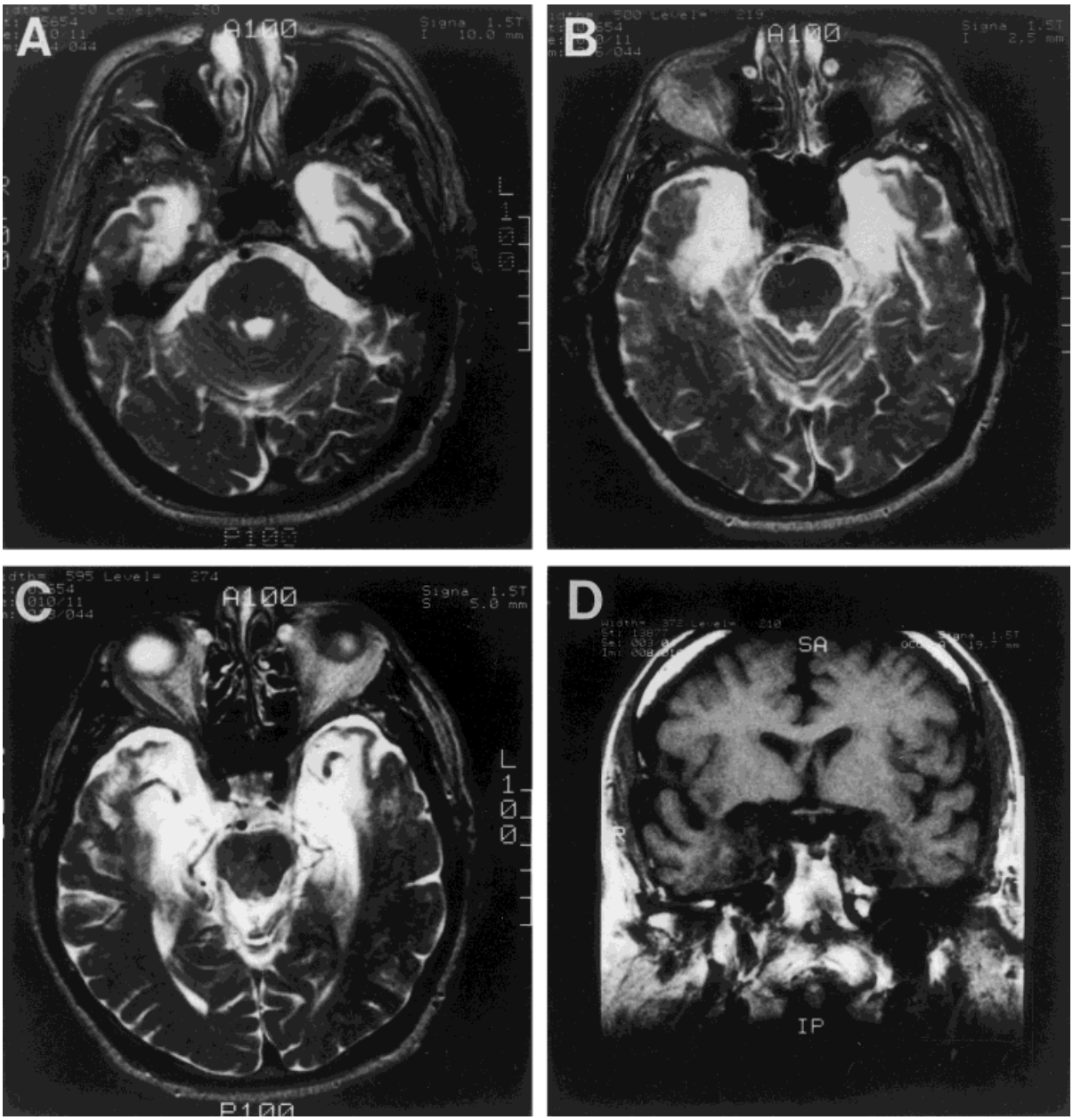

FIGURE 1. Magnetic resonance images showing the extent of bilateral temporal lobe damage in patient E.P. A–C: T2-weighted axial images through the temporal lobe. The images are continuous 5-mm sections (with 2.5-mm gaps) and are arranged from ventral (A) to dorsal (C). Damaged tissue is indicated by bright signals. The damage extends 7 cm caudally from the temporal pole, bilaterally, and includes the amygdala, hippocampal region (dentate gyrus, cell fields of the hippocampus proper, and subicular complex), entorhinal cortex, perirhinal cortex, and rostral parahippocampal cortex (about 20% on the left and 60% on the right). The lesion also extends laterally to include the rostral portion of the fusiform gyrus. D: Coronal T1-weighted image through the amygdala. Damaged tissue is indicated by dark signals. The lateral temporal cortex (inferior, middle, and superior temporal gyri) is reduced in volume bilaterally, particularly on the right side. The insula is also reduced in volume bilaterally, with more substantial loss on the left side than on the right side (also see Fig. 2 of Buffalo et al., 1998). Scale bars = 5 cm; images are oriented according to radiological convention (the right side of the brain is on the left side of the image).

and topic (total = 90 sentences). There were five types of ambiguity: deep structure (DS, 15 items), surface structure (SS, 15 items), particle-preposition (PP, 15 items), lexical (L, 15 items), and phonetic (P, 5 items). Participants read each sentence aloud from index cards, except for the phonetically ambiguous items which were read aloud by the experimenter. Table 2 gives an example of each type of ambiguity.

To begin, participants were told how sentences could be ambiguous and were given 11 practice items, all ambiguous, to illustrate the possible types of ambiguity they would encounter. Except for

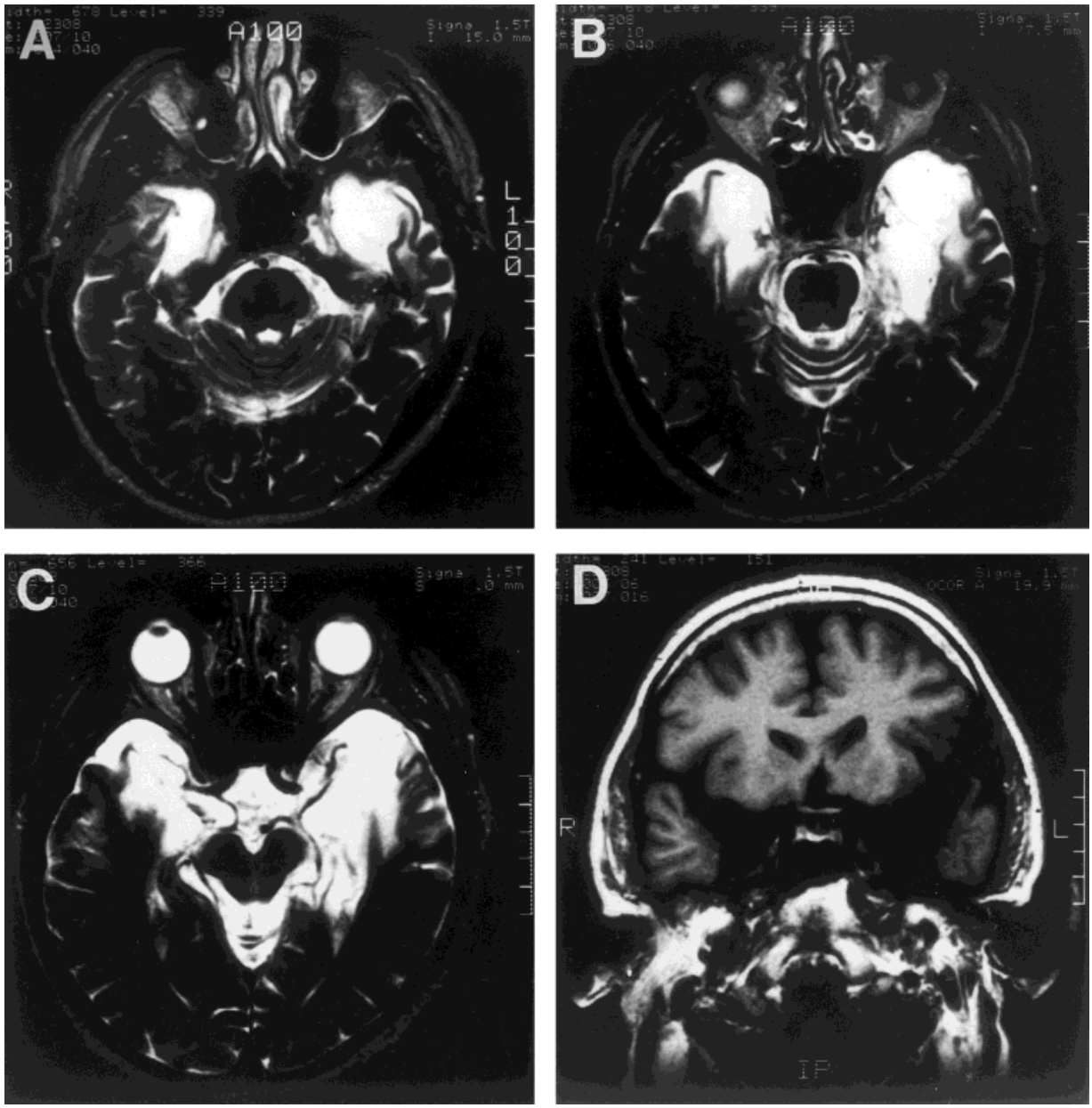

FIGURE 2. Magnetic resonance images showing the extent of bilateral temporal lobe damage in patient G.P. A–D are arranged as in Figure 1. The damage extends through the anterior 7 cm of the left temporal lobe and the anterior 6 cm of the right temporal lobe. The damage bilaterally includes the amygdala, the hippocampal region, and the entorhinal, perirhinal, and parahippocampal cortices. Lateral damage is most severe in the anterior 1 cm of the temporal lobe, where it includes the fusiform gyrus as well as the inferior, middle, and superior temporal gyri. From 1 cm to 4.5 cm caudally, the lateral damage is restricted to the fusiform gyrus and the inferior temporal gyrus. The insular cortex is also damaged, with the lesion extending further caudally on the left side (3 cm) than on the right side (2.5 cm). Scale bars = 5 cm.

the seven phonetic (P) sentences (five of them ambiguous), which were presented first, the test items were intermixed with respect to type of ambiguity. Participants first decided whether the presented sentence was ambiguous or not (Ambiguity Detection). A card asking, "Does this sentence have one meaning or two meanings?" was always in view. Next, regardless of how participants responded in the case of the ambiguous sentences, they were told that the sentence was ambiguous and then asked to explain the ambiguity by stating both meanings in their own words (Ambiguity Explanation). A 15-min break was given after half of the sentences had been presented.

For the amnesic patients, particular effort was made to reduce the memory load associated with the task: First, after each group of 10 sentences, the instructions were repeated briefly and six of the practice items were presented. After the break, the instructions were given again, together with 10 of the original practice items. Second, if patients gave one meaning of a sentence that had been identified as ambiguous but did not provide a second meaning

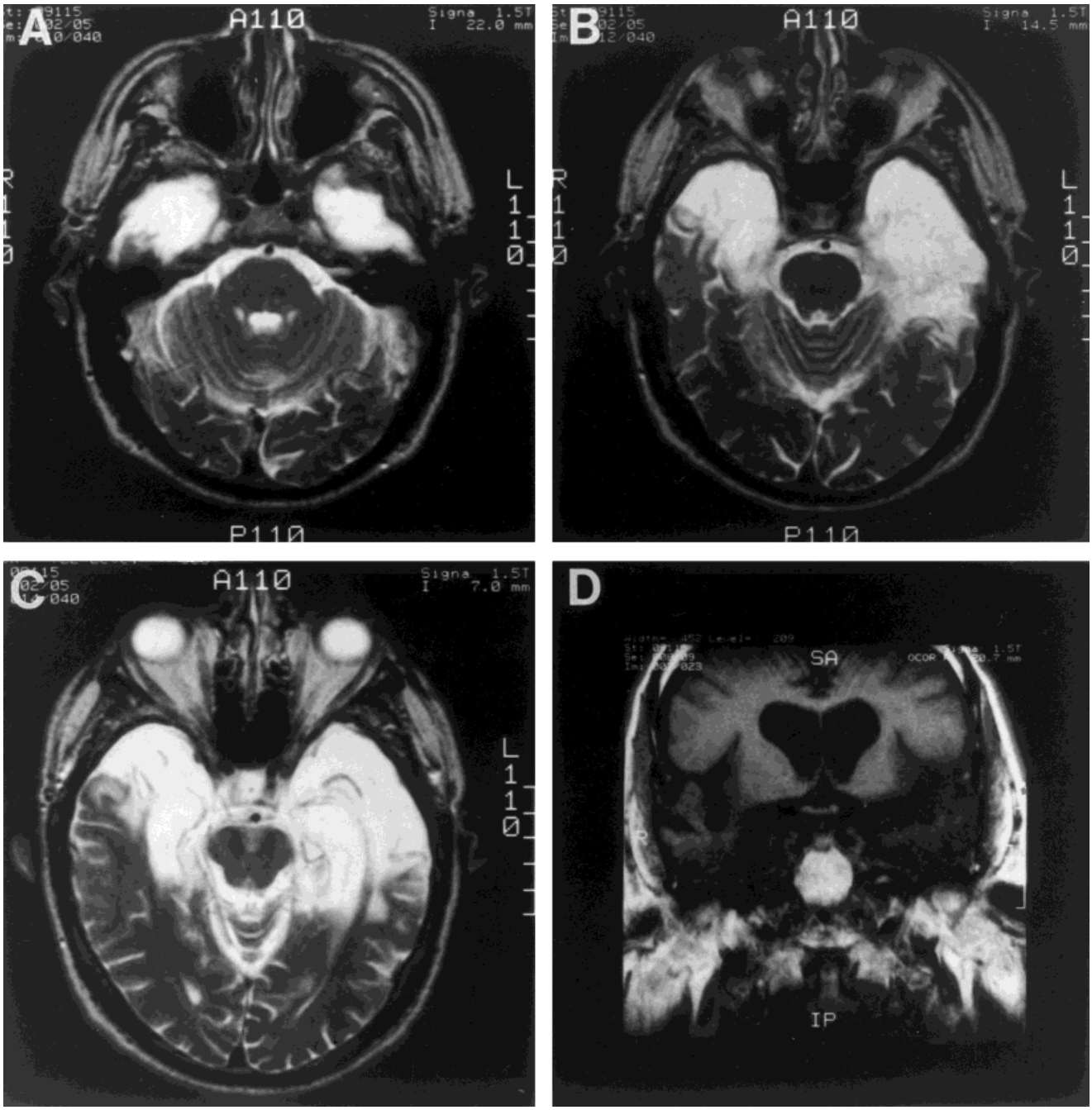

FIGURE 3. Magnetic resonance images showing the extent of bilateral temporal lobe damage in patient G.T. A–D are arranged as in Figure 1. The damage extends through the anterior 7 cm of the left temporal lobe and the anterior 5 cm of the right temporal lobe. The damage bilaterally includes the amygdala, the hippocampal region, and the entorhinal, perirhinal, and parahippocampal cortices. Lateral cortical regions (fusiform gyrus, and inferior, middle, and superior temporal gyri) are also damaged bilaterally at the level of the temporal pole. The damage to the fusiform gyrus continues caudally from the temporal pole for 6.0 cm on the left and for 4.5 cm on the right. The damage to the inferior, middle, and superior temporal gyri extends caudally from the temporal pole for 4.5 cm on the left and for 2.5 cm on the right. There is also bilateral insular damage, more extensive on the left than on the right (see also Fig. 3 of Buffalo et al., 1998). Scale bars = 5 cm.

spontaneously, their first meaning was then presented to them, repeatedly if needed: "You just said this sentence means [meaning A], but it could also mean something else." All sessions were tape-recorded for later scoring and for calculating the time needed by the participants to make their responses.

Scoring

Scoring was the same for all participants and was done after the test sessions on the basis of tape recordings from the sessions. The measure of performance in the task of Ambiguity Detection was

TABLE 1.

*Characteristics of Amnesic Patients**

Patient	Year of birth	Education	WAIS-R			Boston Naming Test	WMS-III indices	
			Full IQ	Information subscore	Vocabulary subscore		Working memory	General memory
A.B.	1937	20	104	27	65	57	81	47
P.H.	1922	19	118	21	59	58	121	72
L.J.	1937	12	98	17	50	55	96	66
N.A.	1938	13	109	23	59	59	99	62
E.P.	1922	12	101	17	33	42	99	54
G.T.	1936	12	92	4	28	18	108	49
G.P.	1946	16	98[a]	13[a]	36[a]	40	99	57

*L.J. is female; the other patients are male. Wechsler Adult Intelligence Scale-Revised (WAIS-R) and Wechsler Memory Scale-III (WMS-III) indices yield a mean score of 100 with an SD of 15 in the normal population. The maximum score for the Boston Naming Test (Kaplan et al., 1983) is 60. [a]G.P.'s scores are based on the Wechsler Adult Intelligence Scale 3 (WAIS-III).

the percentage of sentences correctly identified as ambiguous and nonambiguous (after Lackner, 1974). For the task of Ambiguity Explanation, responses were scored as described by MacKay et al. (1998b), and also according to a supplementary scoring method of our own (see below). The method of MacKay et al. (1998b) assigns each response to one of five categories. A response that explained both meanings correctly without any assistance from the experimenter was scored as "Both meanings, no help." If both meanings were explained correctly, but help was needed to produce one or both of them, the response was scored as "Both meanings, one with help" or "Both meanings, both with help," respectively. Finally, if only one meaning was explained correctly, either with or without help, responses were scored as "One meaning, no help" or "One meaning, with help," respectively.

This method has the disadvantage that the nature and amount of assistance that individuals receive during the test are neither well-controlled nor reflected in the score. Accordingly, we adopted a structured testing procedure that controlled the amount of assistance given, and we also developed a supplementary scoring system based on this procedure. Specifically, we identified five "help levels" and scored each response from 0–5. A response that explained both meanings spontaneously received the maximum score of 5. A score of 4 was assigned when an individual gave both meanings but took more than 1 min to explain the meanings or required some help by the examiner to structure their response (but not with respect to content). Individuals who did not produce both meanings spontaneously were given a prepared cue that hinted at the area of ambiguity (see Table 2). A score of 3 was given when the cue was successful in eliciting both meanings. If the cue proved unhelpful, the area of ambiguity was identified explicitly (score of 2). If a correct response was not provided at this point, the examiner explained the ambiguity. If the participant clearly demonstrated

TABLE 2.

Examples of Types of Ambiguities and Cue Questions

Type of ambiguity	Example	Cue question
Deep structure (DS)	The man took his stick and hit him three or four times.	Whose stick was it?
Surface structure (SS)	Jack left with a dog he found last Saturday.	What happened last Saturday?
Particle-preposition (PP)	He looked over the old stone wall.	What exactly did he do concerning the old stone wall?
Lexical (L)	He insists upon wearing light clothes in the summer.	What kind of clothes did he like to wear in the summer?
Phonetic (P)	I am not surprised that he found the wait (weight) annoying.	What did he find annoying?
Nonambiguous	The teacher looked at the boy who was laughing.	

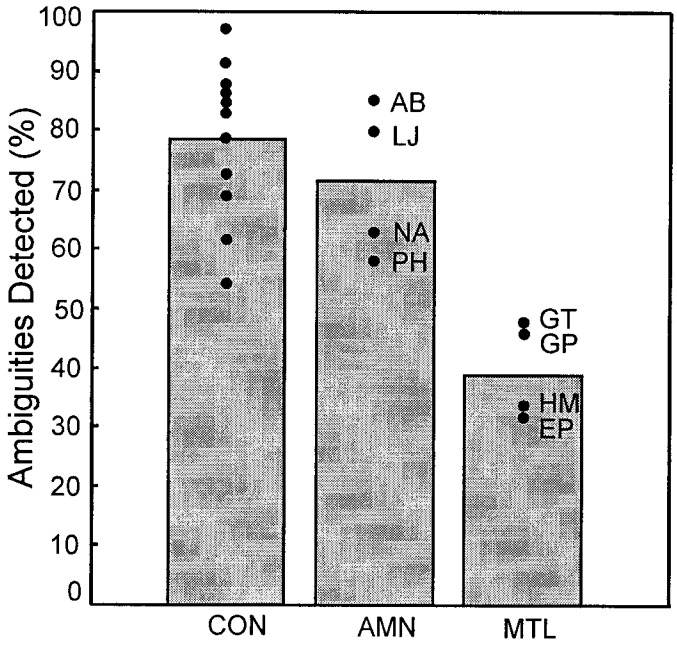

FIGURE 4. Percentage of 65 ambiguous sentences correctly identified as ambiguous. CON, 11 controls; AMN, 4 amnesic patients; MTL, 4 patients with large medial temporal lobe lesions. Circles show the scores for individual participants. The data for patient H.M. are from Lackner (1974), using the same materials and procedure as were used here.

understanding (e.g., an "aha-reaction"), a score of 1 was given, and if understanding was doubtful, a score of 0 was given.

In summary, following Lackner (1974), we determined the percent of ambiguous sentences that participants detected correctly as ambiguous (Ambiguity Detection). We also assessed the ability of participants to explain each ambiguous sentence (Ambiguity Explanation), using both the five response categories described by MacKay et al. (1998b) and our own 0–5 scale. Finally, we determined how long it was after each ambiguous sentence was presented that participants began stating the correct second meaning, as well as the time needed to complete the task (excluding the time taken to repeat the instructions to the amnesic patients).

RESULTS

Ambiguity Detection

The 4 amnesic patients with hippocampal formation damage or diencephalic damage (AMN) were as able as controls to detect ambiguity in sentences (Fig. 4; controls, mean 78.6%, range 54.0–96.9%; AMN, mean 71.6%, range 58.6–84.6%; $t[13] = 0.93$, $P > 0.10$). The 5 controls who were matched to the 3 patients with hippocampal formation damage scored 84% correct (84% vs. 75.1% for the 3 patients, $t[6] = 1.3$, $P > 0.10$). By contrast, the 3 patients with large medial temporal lobe lesions (E.P., G.T., and G.P.) obtained a mean score of 41.6%, similar to the 33.8% score obtained by H.M., as reported by Lackner (1974). It should be pointed out that H.M. had the test sentences read to him and, in contrast to our procedure, did not see them in writing. Together, our 3 patients performed more poorly than either the control group ($t[12] = 4.5$, $P < 0.001$) or the amnesic patients with more restricted lesions ($t[5] = 3.4$, $P < 0.02$). Indeed, there was no overlap between the scores of the control group and the scores of the patients with large medial temporal lobe lesions.

Table 3 shows how often each group of participants detected each type of ambiguous sentence as well as how often they identified the nonambiguous sentences as nonambiguous. The controls (CON) and the 4 amnesic patients (AMN) performed similarly across all the categories ($t[13] < 1.5$, $P > 0.10$). In contrast to patient H.M., who identified only 58% of nonambiguous sentences as nonambiguous (MacKay and James, 2000), the 3 patients

TABLE 3.

Detection of Ambiguous and Nonambiguous Sentences*

	Detection of nonambiguous sentences (n = 25)	Deep structure (n = 15)	Surface structure (n = 15)	Particle-preposition (n = 15)	Lexical (n = 15)	Phonetic (n = 5)
CON	90.9	75.8	73.9	80.0	84.8	80.0
AMN	89.0	75.0	68.3	65.0	80.0	65.0
MTL	93.3	42.2	33.3	44.5	35.6	66.7
H.M.	58.0[a]	46.7	40.0	33.3	20.0[b]	

*Percent of unambiguous sentences correctly identified as unambiguous and percent of each type of ambiguous sentence correctly identified as ambiguous. n = number of items of each type. CON, 11 controls; AMN, 4 amnesic patients; MTL, 3 patients with extensive medial temporal lobe damage; H.M., amnesic patient H.M. H.M.'s data for ambiguity detection (five rightmost columns) are from Lackner (1974). Sentences were read to H.M. and he did not see them in writing.

[a]H.M. was tested with different nonambiguous sentences than were the other participants (MacKay and James, 2000).

[b]H.M.'s combined score for lexical and phonetic ambiguity.

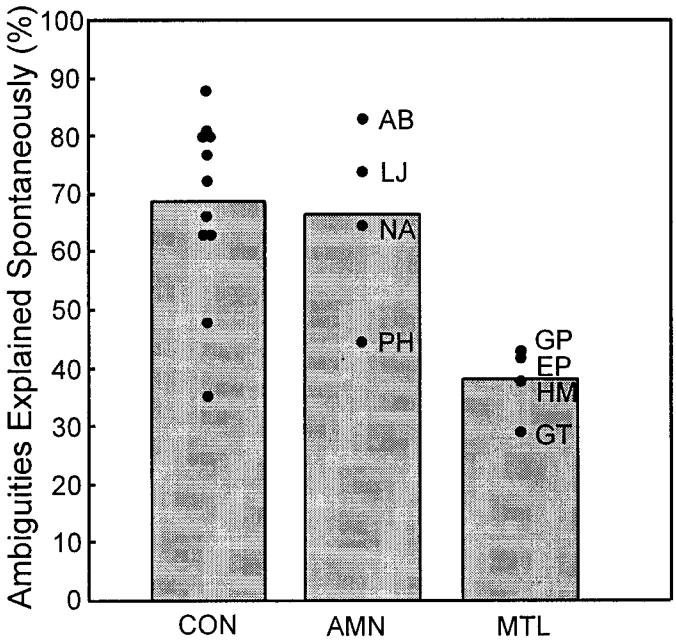

FIGURE 5. Percentage of 65 ambiguous sentences which participants could explain spontaneously. This designation corresponds to the category "Both meanings, no help" (MacKay et al., 1998b; see Table 4) or to a score of 5 on a 0–5 scale (our scoring method; see Table 5). Circles show scores for individual participants. CON, 11 controls; AMN, 4 amnesic patients; MTL, 4 patients with large medial temporal lobe lesions. The data for amnesic patient H.M. are from MacKay et al. (1998b); the materials they used to test H.M. were similar but not identical to the materials we used (see text).

with large medial temporal lobe lesions were as capable as controls at this task (93.3% correct). However, with one exception (the five items that were phonetically ambiguous), the 3 patients were significantly impaired at detecting each type of ambiguity ($t[12] > 3.3$, $P < 0.01$).

Ambiguity Explanation

Figure 5 shows the percentage of ambiguous sentences for which participants could give both meanings without assistance. This response category corresponds to the designation "Both meanings, no help" (MacKay et al., 1998b). The 4 amnesic patients (AMN) performed as well as controls (66.2% vs. 68.5%), and the 3 patients with hippocampal formation damage performed similarly to their 5 matched controls (75.1% vs. 67.2% for the controls and patients, respectively; $t[6] = 0.75$; $P > 0.10$). The 3 patients with large medial temporal lobe lesions (E.P. , G.T., and G.P.) performed similarly to H.M (37.9% vs. 37.5% for the 3 patients and H.M, respectively). Together, our 3 patients explained significantly fewer ambiguous sentences spontaneously than either the control group ($t [12] = 3.2$, $P < 0.01$) or the 4 amnesic patients with more restricted lesions ($t[5] = 2.8$, $P < 0.05$).

Table 4 shows the frequency with which the responses of each group were assigned to the categories introduced by MacKay et al. (1998b). The amnesic patients performed similarly to the controls. By contrast, the 3 patients with large medial temporal lobe lesions performed similarly to patient H.M. Note, however, that with respect to the latter comparison, the materials used by MacKay et al. (1998b) to test H.M. were not identical to ours (which were taken from Lackner, 1974). In addition, for the scoring categories that involved assistance from the experimenter, it is difficult to compare the effects of the structured assistance that we provided in our study to the effects of the more informal assistance that H.M. received.

TABLE 4.

*Ambiguity Explanation**

	Both meanings, no help	Both meanings, one with help[a]	One meaning, no help[b]
CON	68.6	22.0	9.2
AMN	66.5	25.0	8.5
MTL	37.8	34.4	27.7
H.M.	37.5	34.4	28.1

*Percent of each response type following the method of McKay et al. (1998b). Data for H.M. are also from McKay et al. (1998b). The materials used to test H.M. were similar but not identical to the materials we used (see text). CON, 11 controls; AMN, 4 amnesic patients; MTL, 3 patients with extensive medial temporal lobe damage; H.M., amnesic patient H.M.

[a]This category also includes the category "Both meanings, both with help" (one instance in our data set, 9.4% of H.M.'s responses).

[b]This category also includes the category "One meaning, with help" (two instances in our data set, 12.5% of H.M.'s responses).

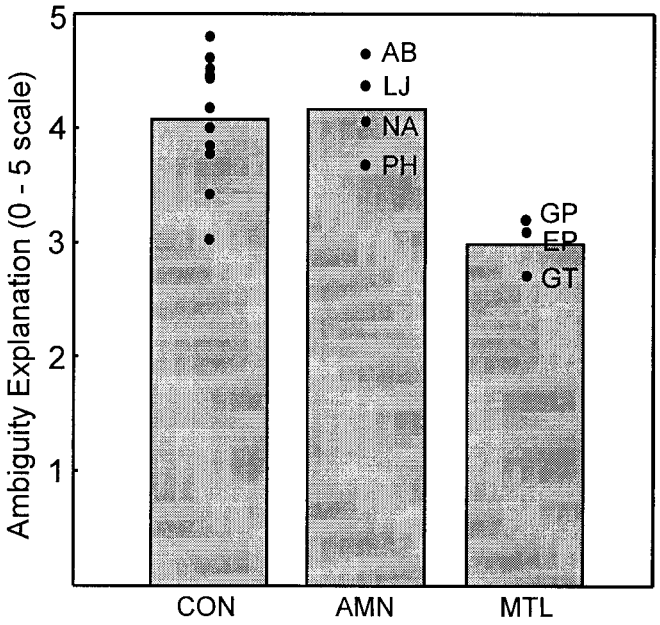

FIGURE 6. Responses to 65 ambiguous sentences were scored on a 0–5 scale (see text). Circles show scores for individual participants. CON, 11 controls; AMN, 4 amnesic patients; MTL, 3 patients with large medial temporal lobe lesions.

TABLE 5.

*Ambiguity Explanation (0–5 Scale)**

	5	4	3	2	1	0
CON	68.6	5.7	6.7	9.7	7.1	2.0
AMN	66.5	9.2	7.7	8.1	7.7	0.8
MTL	38.0	5.1	9.2	20.0	19.5	8.2

*Percent of responses receiving each score (0–5). 5, explained both meanings spontaneously; 4, took more than 1 min to explain both meanings spontaneously; 3, the cue was successful in eliciting both meanings; 2, explained both meanings after the area of ambiguity was identified explicitly; 1, clearly understood the ambiguity when it was explained; 0, did not understand the ambiguity when it was explained. CON, 11 controls; AMN, 4 amnesic patients; MTL, 3 patients with extensive medial temporal lobe damage.

Figure 6 shows the mean score for ambiguity explanation that participants received on our 0–5 scale. Controls averaged 4.1, and the 4 amnesic patients averaged 4.2. The 3 patients with hippocampal formation damage scored 4.2, and their 5 matched controls scored 4.4 ($t[6] = 0.59$, $P > 0.10$). The average score of 3.0 obtained by patients E.P., G.T., and G.P. was significantly below both the control score ($t[12] = 3.3$, $P < 0.01$) and the score of the 4 amnesic patients ($t[5] = 4.3$, $P < 0.01$). A score based on the 0–5 scale is not available for patient H.M.

The percent of items receiving each score (0–5) is shown in Table 5 for each group of participants. Table 5 illustrates how closely the performance of the 4 amnesic patients matched the performance of controls. Table 5 also shows that patients E.P., G.T., and G.P. had difficulty explaining the ambiguity in the sentences until the area of ambiguity was explicitly pointed out (score of 2). Even after the ambiguity was explained, these 3 patients failed to understand the ambiguity 8.2% of the time (4 sentences out of 65 for E.P. and G.P., and 9 sentences out of 65 for G.T.). By contrast, the controls and the 4 amnesic patients failed to understand only one of the ambiguous sentences, on average, after the ambiguity was explained.

Scores on the 0–5 scale for each type of ambiguity and for each group of participants are shown in Table 6. These results again emphasize how closely the performance of the 4 amnesic patients (AMN) matched the performance of the controls. In contrast, E.P., G.T., and G.P. were marginally impaired relative to controls at explaining surface structure and phonetic ambiguities ($t[12] > 2.1$, $P < 0.10$), and significantly impaired for each of the other types of ambiguity ($t[12] > 2.8$, $P < 0.05$).

Response Time

Another way to compare performance among participants is to calculate how much time they required to explain the ambiguity in each sentence. In those cases when both meanings of the sentence were explained spontaneously (score of 5), the controls and the 4 amnesic patients required 10.6 and 10.1 s, respectively, to begin stating the correct second meaning. Patients E.P., G.T., and G. P. required 19.4 s ($t[12] = 3.4$, $P < 0.01$ compared to controls). Overall, the controls and the 4 amnesic patients took nearly the identical amount of time to complete testing on all 90 sentences (controls = 68.8 min, amnesics = 67.8 min). Patients E.P., G.T., and G.P. were much slower (mean = 109.5 min), consistent with their difficulty explaining ambiguity ($t[12] = 3.1$, $P < 0.01$, compared to controls).

Correlations

Verbal IQ (specifically, WAIS-R subtests for information and vocabulary) strongly correlated with both the ability to detect ambiguity in sentences and the ability to explain the ambiguity (Table 7). The finding of a significant correlation within the control group itself suggests that verbal intelligence was an important predictor of the ability to detect and explain sentence ambiguity. Indeed, information and vocabulary subscores in the control group correlated significantly with the ability to explain each of the different ambiguity types (except phonetic and lexical ambiguities), as well as with the mean time to begin stating the correct second meaning and the time needed to complete testing ($r > 0.65$, $P < 0.05$). In the patient group, the vocabulary subscore correlated significantly with the ability to detect and explain ambiguity. Finally, for the patients, the Immediate Auditory Memory Index from the WMS-III also correlated with ambiguity detection and explanation (note: the Immediate Auditory Memory Index is derived from the Logi-

TABLE 6.

*Ambiguity Explanation by Type of Ambiguity**

	Deep structure ($n = 15$)	Surface structure ($n = 15$)	Particle-preposition ($n = 15$)	Lexical ($n = 15$)	Phonetic ($n = 5$)
CON	4.2	3.6	4.2	4.5	4.3
AMN	4.3	3.9	4.3	4.3	3.6
MTL	3.2	2.5	3.1	2.9	3.3

*Mean score obtained for each ambiguity type (0–5 scale). n = number of items of each type. CON, 11 controls; AMN, 4 amnesic patients; MTL, 3 patients with extensive medial temporal lobe damage.

TABLE 7.

Correlations Between Ambiguity Detection and Explanation Scores and Test Scores From WAIS-R and WMS-III[†]

	Controls (n = 11)				Patients (n = 7)			
	Information	Vocabulary	Immediate auditory memory	Immediate visual memory	Information	Vocabulary	Immediate auditory memory	Immediate visual memory
Ambiguity detection	0.73*	0.62*	0.61*	−0.18	0.54	0.78*	0.76*	0.09
Score (0–5)	0.72*	0.63*	0.50	−0.22	0.75 P = 0.051	0.89**	0.89**	0.05

[†]Ambiguity detection = percent correct score, Fig. 1; score (0–5) = ambiguity explanation score, Fig. 3; Information, WAIS-R information subscore; Vocabulary, WAIS-R vocabulary subscore; Immediate Auditory Memory (subtests Logical Memory I and Verbal Paired Associates I) and Immediate Visual Memory (subtests Faces I and Family Pictures I) are indices from the WMS-III.
*$P < 0.05$.
**$P < 0.01$.

cal Memory I test and the Verbal Paired Associates I test. It does not measure immediate memory but rather assesses prose recall and paired-associate learning, and is sensitive to amnesia; mean patient score, 65; range, 56–74). Of all six WMS-III indices, only this score was significantly related to performance on the tests of ambiguity (see Table 7 for the absence of correlations with the Immediate Visual Memory Index, which involves nonverbal materials; mean patient score, 60; range, 49–68). The control group obtained normal scores on the Immediate Auditory Memory Index (mean, 108.7; range, 92–134) and the Immediate Visual Memory Index (mean, 101; range, 84–124). Nevertheless, in the control group, the Immediate Auditory Memory Index also correlated with ambiguity detection. The correlation with ambiguity explanation (r = .50) did not reach significance (P = 0.12).

DISCUSSION

Participants first decided whether a given sentence was ambiguous or not and then tried to explain the ambiguity. Three amnesic patients with damage limited to the hippocampal formation and one amnesic patient with primarily diencephalic damage performed similarly to the control group in all respects. By contrast, 3 patients with more extensive medial temporal lobe damage were impaired. These 3 patients performed similarly to the noted amnesic patient H.M. (as reported by Lackner, 1974; MacKay et al., 1998b). Measures of verbal IQ reliably predicted performance in both the control group and the patient group. Further, in both groups, performance on the Immediate Auditory Memory Index (WMS-III) also correlated with the ability to detect ambiguity.

It is unlikely that the different performance in the two patient groups can be explained by incomplete hippocampal formation damage in the patients with limited hippocampal formation lesions. We previously described patients who resemble the patients in the current study with respect to quantitative MR imaging findings and memory impairment (Squire et al., 1990). These patients proved on later neurohistological examination to have essentially complete cell loss in the CA1 and CA3 cells of the hippocampus and substantial cell loss in the CA2 region and in the dentate gyrus (Rempel-Clower et al., 1996).

Three of our patients, as well as patient H.M., have extensive damage to the medial temporal lobe. In addition, each of these 4 patients has additional damage. E.P. has bilateral damage to the anterior fusiform gyrus, and the lateral temporal cortex and insular cortex are reduced in volume bilaterally. G.T. has extensive bilateral damage to the temporal lobe neocortex as well as the insular cortex. G.P. has bilateral damage to anterolateral temporal cortex, fusiform gyrus, and insular cortex. Recent MR imaging analysis of H.M (Corkin et al., 1997) indicates that he also has temporal lobe damage beyond the medial temporal structures ordinarily associated with memory impairment. Specifically, at the temporal poles, H.M.'s lesion extends laterally, to involve the rostralmost aspects of the middle and superior temporal gyri (Figs. 2K, 4C, and 4D in Corkin et al., 1997; compare with Figs. 44–46 and 159–163 in Duvernoy, 1991). In addition, "the subcortical white matter associated with the anterior portions of the superior, middle and inferior temporal gyri may also have been compromised by the resection" (Corkin et al., 1997).

Our 3 patients differed in three important ways from patient H.M. First, our patients acquired their lesion well into adulthood, and each had an unremarkable premorbid history. By contrast, H.M. began to have seizures at a young age (10 years) and had surgery at age 27. Second, H.M. scored only 58% correct in deciding whether nonambiguous sentences were ambiguous or not (MacKay and James, 2000; our Table 3). Yet, our 3 patients with extensive medial temporal lobe damage had no difficulty with this task. Third, patient H.M. often had difficulty explaining even one meaning of the ambiguous sentences that he was given. Specifically, fully 21.9% of the ambiguous sentences given to H.M. were scored either as "both meanings, both with help" or "one meaning with help" (MacKay et al., 1998b; our Table 4). Yet, for our 3

patients with extensive medial temporal lobe damage, this designation was rare (E.P., 0%; G.P., 1.5 %; G.T., 0 %). The finding that our patients did not have difficulty explaining the first meaning of ambiguous sentences indicates that this difficulty is unlikely to derive from medial temporal lobe damage.

A similar observation was made (Zaidel et al., 1995) in a group of young adults who had sustained left or right unilateral temporal lobe surgery to relieve long-standing, severe epilepsy (mean age at seizure onset, 10.5 years; mean age at surgery, 22.7 years). On a 13-item task of ambiguity explanation similar to the one used in the present study, the patients were deficient at finding even one meaning (for 27% of the sentences in the case of the patients with left unilateral removals, and for 13% of the sentences in the case of the patients with right unilateral removals). Both groups of patients also explained fewer second meanings than individuals in a normative sample. These observations raise the possibility that a history of long-standing epilepsy beginning in childhood or adolescence can have a negative effect on the development of language skills and, specifically, that patient H.M. may not have fully developed his language skills prior to surgery.

There appear to be at least three ways to understand impaired performance in our patients with postencephalitic amnesia. First, poor performance could occur because of the severe memory impairment itself. In asking for the second meaning of the sentences, we did observe difficulties that seemed related to severe amnesia. For example, for 12 sentences out of 65, patient G.T. repeated the first meaning that he had already given, apparently having forgotten that he had just provided that same meaning a few seconds earlier. In addition, among all 7 memory-impaired patients, the ability to detect and explain ambiguity correlated with scores on the Immediate Auditory Memory Index of the Wechsler Memory Scale (WMS-III). Finally, the 3 patients with the most severe amnesia (E.P., G.T., and G.P.) were also the three who performed the poorest in the ambiguous sentence task. However, it is also true that these 3 patients were the only ones with anomia (Table 1), the only ones with impaired scores on the Information and Vocabulary subtests of the WAIS-R (Table 1), and the only ones with lesions that extended outside the medial temporal lobe. Thus, while severe amnesia could have contributed to the impairment, it seems unlikely to provide a satisfactory explanation for it.

Second, damage to the medial temporal cortex, not the hippocampus itself, could have produced the impairment in our 3 postencephalitic patients. All three have damage to the perirhinal cortex, which in monkeys has been reported to impair visual processing (Eacott et al., 1994; Buckley and Gaffan, 1997, 1998; but see Buffalo et al., 1998,1999). The effects of perirhinal cortex lesions need to be explored further. In any case, it is unclear how supposed defects in visual perceptual processing might relate to difficulty in detecting ambiguity in sentences. Unfortunately, it has not been possible to test patients with extensive damage to the medial temporal lobe whose lesions do not extend lateral to this region.

A third possibility is that cortical regions outside the medial temporal lobe, for example the fusiform gyrus or more lateral regions of the temporal lobe, might be important for language, and for detecting and explaining ambiguity in particular. The damage in each of our 3 postencephalitic patients extends laterally to include at least some damage to the fusiform gyrus and more lateral neocortex as well. Lesions of the anterior lateral inferotemporal cortex in humans produce semantic deficits (Hodges et al., 1992; Garrard et al., 1997; Tranel et al., 1998). For example, patients with extensive cortical damage in this region are impaired at naming pictures, naming in response to verbal descriptions, sorting pictures into conceptual categories, and demonstrating knowledge about semantic attributes. Yet, they have intact perceptual abilities as indicated by their ability to copy complex objects and figures (Srinivas et al., 1997).

These considerations give support to the idea that damage lateral to the medial temporal lobe could impair the ability to detect and explain ambiguity as part of a broader impairment in semantic processing. It is of interest that the controls and the 4 amnesic patients with more restricted lesions (A.B., P.H., L.J., and N.A.) were best at detecting lexical ambiguity (Table 3), which would seem to require semantic knowledge. However, detecting lexical ambiguity was very difficult for patients E.P., G.T., and G.P. In addition, these 3 patients have anomia and also obtained low scores on the information and vocabulary subtests of the WAIS-R (Table 1). Thus, it seems plausible that they have an impairment in semantic knowledge, including some difficulty with word meanings, which could be expected to disadvantage them in tests of sentence ambiguity.

If the deficit in ambiguity detection and explanation in our patients is due to damage outside the medial temporal lobe, then such damage may also be able to account for H.M.'s performance on tests of sentence ambiguity. As noted above, H.M. does have some damage outside the medial temporal lobe, albeit less extensive damage than any of our 3 postencephalitic patients. Alternatively, it is possible that his difficulty on the sentence tasks has a different basis. Specifically, H.M. often had difficulty explaining even one meaning of the sentences he was given, and none of our 3 patients had this difficulty. In another test, H.M. also made many grammatical and linguistic errors, whereas other patients with more extensive medial and lateral temporal lobe damage performed like controls (Schmolck et al., 2000). Accordingly, perhaps it is the case, as suggested above, that H.M.'s language skills were not developed fully prior to his surgery.

In summary, the present findings make two points about the medial temporal lobe and the ability to appreciate ambiguity in sentences. First, the ability to comprehend ambiguity is independent of the hippocampal region. Damage to the hippocampal region impairs memory but does not affect the ability to detect or explain ambiguity. Second, amnesic patients who have larger lesions that include the perirhinal, entorhinal, and parahippocampal cortices within the medial temporal lobe, and who also have damage to the fusiform gyrus and more lateral temporal neocortex, are impaired at detecting and explaining ambiguity. This impairment could be a consequence of severe memory impairment, it could be caused by damage to the medial temporal cortical structures adjacent to the hippocampus, or it could be caused by damage to cortical structures outside the medial temporal lobe. The last alternative seems most plausible. Performance on tests of ambiguity correlated with measures of verbal IQ in controls and patients alike, and all 3 of our postencephalitic patients have impaired verbal IQ subtest scores and anomia. In addition, deficits in

language and semantic knowledge have been described following anterolateral inferotemporal cortex damage. There may be a common basis for impairments in verbal IQ, naming, and the comprehension of ambiguity. In addition, the ability to form new memories is independent of the ability to detect and explain ambiguity in sentences.

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