

# Contributions of the Left Intralaminar and Medial Thalamic Nuclei to Memory

## Comparisons and Report of a Case

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• A patient complained of memory disturbance after a small left thalamic infarction. Neuropsychological testing revealed her memory to be normal provided that she was allowed to rehearse or use semantic encoding strategies. When these strategies were prevented, her performance was impaired. Mapping of the lesion demonstrated involvement of the caudal intralaminar nuclei (centre médian and parafascicular nuclei), and portions of the medial nuclei (medioventral [reuniens], centromedial, and the most inferior aspect of the mediodorsal nucleus). The majority of mediodorsal nucleus, the mammillary bodies, the mammillothalamic tract, and the anterior thalamic nuclei, were spared. A comparison among our patient's performances and those of alcoholic Korsakoff patients, patient NA, and amnesic patients with circumscribed diencephalic lesions suggests that there are two distinct behavioral and anatomic types of memory impairment associated with diencephalic lesions. The severe amnesia associated with damage to the mammillary bodies, midline nuclei, mammillothalamic tract, and/or dorsomedial nucleus of the thalamus (eg, Korsakoff and NA) is characterized by encoding deficits that never approximate normal performance. The memory disturbance associated with damage to the intralaminar and medial nuclei of the thalamus is milder and is characterized by severe distractibility.

(*Arch Neurol.* 1992;49:1050-1058)

Discrete lesions of the thalamus can cause severe and lasting amnesia. Although it remains uncertain which thalamic structures are critical for memory, evidence from human and animal research suggests that one or more of the following structures are important: the anterior nuclei,<sup>1</sup> the midline nuclei,<sup>2,3</sup> the mammillothalamic and amygdalofugal tracts,<sup>3,5</sup> and the mediodorsal nucleus.<sup>6,7</sup> It has also been suggested on anatomic grounds that the contribution of smaller nuclei (medioventral [reuniens], paracentral, and paraventricular) cannot be excluded.<sup>8</sup> It has been difficult to ascribe specific importance to any single thalamic structure because thalamic lesions, both in animals and in humans, almost invariably affect more than one thalamic structure and because the neu-

ropsychological evaluation of patients in the literature varies considerably from case to case. In fact, the patients whose behavioral deficits have been studied most extensively, alcoholic Korsakoff's and patient NA (who became amnesic after a fencing foil penetrated his brain), have all had extrathalamic damage as well as damage to several areas within the thalamus. When we encountered a patient with a discrete thalamic lesion who complained of memory dysfunction, therefore, we studied her extensively to characterize the nature of her deficits. We found that her deficits differed in important respects from those of the usual "diencephalic" amnesic, and that the locus of her lesion also differed from that of most patients reported with thalamic amnesia. We suggest that the localization of her lesion to the caudal intralaminar thalamic nuclei probably accounts for the nature of her deficits.

### REPORT OF A CASE

#### History and Neurological Examination

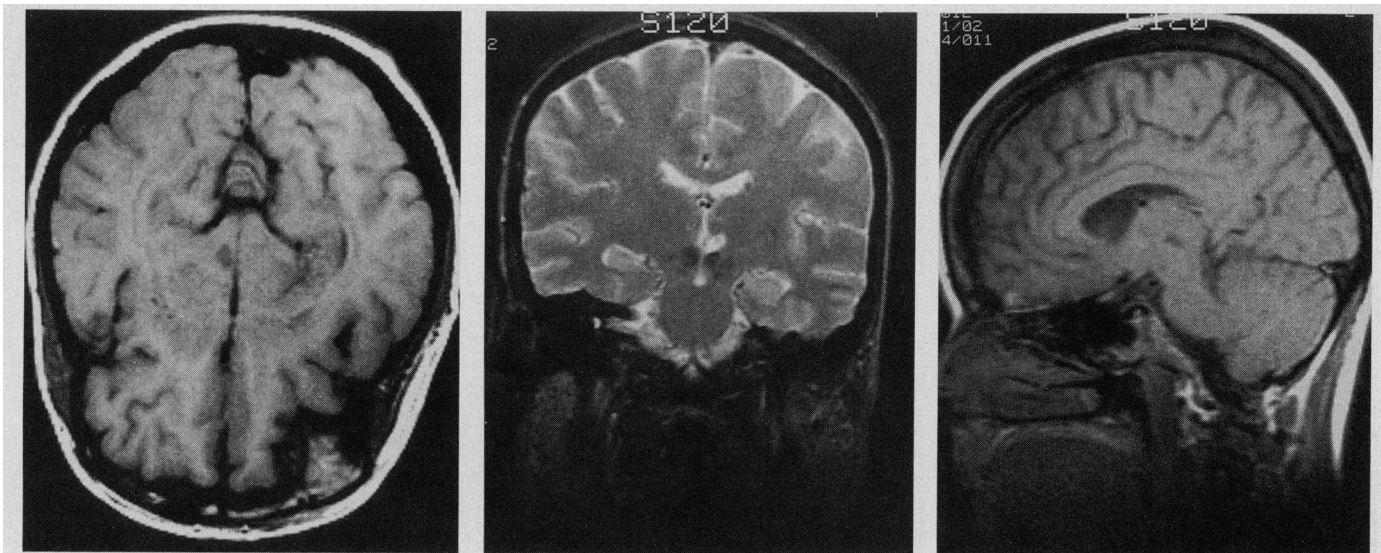
A 44-year-old, left-handed woman with 12 years of education and a consistently good work history, including managerial positions at retail stores, presented to us. There was no history of focal neurologic symptoms and there was no history of diabetes, hypertension, or migraine. She was taking no medication. On May 21, 1988, she was admitted to the hospital with lightheadedness, dizziness, and transient loss of consciousness. On awakening, she was alert and oriented but had right arm weakness, slurred speech, and diplopia. On examination there was right superior rectus muscle weakness, reduced fine motor control in the right hand, and decreased pain sensation in the right hand. Magnetic resonance imaging (T<sub>1</sub>- and T<sub>2</sub>-weighted images) 8 days after the stroke showed a nonhemorrhagic, 1-cm lesion in the medial thalamus. An electroencephalogram performed 2 days after admission was slightly slow on the left side. Over the next 3 months her symptoms largely resolved. A second electroencephalogram was read as normal. On August 23, 1988, she was readmitted to the hospital with slurred speech, occipital headache, and abnormal sensations on the right side, all of which subsided in less than 24 hours. Since then she has been followed up regularly and has had no new neurologic symptoms. Laboratory studies included a complete blood cell count, erythrocyte sedimentation rate, antinuclear antibodies, rheumatoid factor, VDRL, hemagglutination treponemal test for syphilis, lipid profile, antiphospholipid antibodies, and cerebrospinal fluid cell count, protein, glucose, IgG, myelin basic protein, and oligoclonal bands—all showing normal results.

Four months following her stroke, the patient was referred for evaluation with continuing complaints of memory and concentration problems. Specifically, she described difficulty remembering dates, conversations, and material she had read. She noticed an inability to perform simultaneous activities that she was previously able to accomplish. For example, she volunteered to cook for a community organization but found that she could not talk with other

Accepted for publication June 10, 1992.

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**Fig 1.**—Left, Axial (TR: 2000, TE: 80 2/2); center, coronal (TR: 2400, TE: 80 2/2); and right sagittal (TR: 600, TE: 20 1/1) sections showing our patient's lesion.

volunteers and work at the same time. She started bringing work home to save herself embarrassment. In daily activities, she was devastated by her stroke. She was no longer able to work as she could not keep up with the cognitive demands and fatigued quickly. Her social activities changed. She stated that she now socialized with retired persons partly due to living circumstances and partly due to the pace of conversations and activities. This represented a marked change in functioning from premorbid levels. Last, the patient had complaints of word-finding problems.

On examination, she was normotensive with normal pulses and no carotid or cranial bruits. Other than a 2/6 systolic ejection murmur, her general physical examination was normal. On neurologic examination, she was alert and oriented. Her digit span was 7 numbers forward, and she recalled two of three words after distraction. She was able to name nine words that started with the letter *s* in 1 minute. When speaking, she sometimes hesitated as if to find a word. However, her repetition, comprehension, and naming were normal. There was no right-left confusion or finger agnosia, but she had difficulty with serial 7s. She could copy a cube, and there was no evidence of neglect. Except for a slight subjective decrease of touch and pain sensation on the right side the remainder of the neurological examination was normal.

Results of routine laboratory studies were normal, as were sedimentation rate, antinuclear antibody, lupus anticoagulant, antiphospholipid and anticardiolipin antibodies, and a three-dimensional echocardiogram.

### Lesion Localization

A magnetic resonance imaging scan was performed on a 1.5-Tesla scanner approximately 9 months after her stroke. Axial, coronal, and sagittal sections through the lesion are shown in Fig 1. The anterior and posterior commissures were identified on the midsagittal section (not shown), and the ratio of the anterior-posterior commissure distance on the scan to that of the atlas of Schaltenbrand and Bailey<sup>9</sup> was used to map the anteroposterior extent of the lesion on the midsagittal section of the atlas. Coronal sections from the atlas that traversed the lesion were used for mapping (Fig 2). The lateral extent of the lesion was estimated, again comparing landmarks (including the midline of the third ventricle, the lateral margin of the putamen, and the insular cortical surface) on the axial and coronal magnetic resonance imaging sections with similar measurements in the atlas. Because of differences in the plane of the section, it was more difficult to map the vertical extent of the lesion directly from magnetic resonance imaging to the atlas, but estimates were made based on measurements in the other two planes and adjusting for differences in the plane of the section. We judged that errors caused

by tilt of the sections (ie, right up, left down on axial sections, or right forward, left back on coronal sections) would be small since the lesion was close to the midline.

The lesion was confined to the left thalamus and mesencephalic gray matter. It was oval, about 1 cm in its longest anteroposterior dimension, 0.8 cm at its widest, and 0.8 cm high. It involved almost the entirety of the parafascicular nucleus, a large portion of the centre médian, and portions of the reunions or medioventral and centromedial nuclei. The rostral border of the lesion was in the inferior portion of the mediodorsal nucleus, and the caudal border was just superior to the red nucleus, in the central mesencephalic gray matter. The mammillary bodies, mammillothalamic tract, anterior thalamic nuclei, and the vast majority of mediodorsal nuclei appeared normal. No other lesions were apparent on the magnetic resonance imaging scan.

### Neuropsychological Assessment

During testing the examiners noted a disinclination to use the right hand, although no other signs of neglect were detected. Our patient demonstrated a full range of emotions with normal intensity. Her conversational speech was within normal limits, as tone, quality, and speed were unaltered. She underwent neuropsychological testing at approximately 4 and 11 months after her stroke. She was taking no medication other than aspirin at the time of these assessments. No appreciable change occurred on any of the repeated measures; therefore, only the most recent test scores are discussed. Table 1 summarizes these test results.

Intellectual functions were well within the average range (verbal IQ, 102; performance IQ, 107; and full-scale IQ, 104), with subtest scores ranging from 9 to 13. Digit symbol (a scaled score of 6) was the only abnormal subtest score, owing largely to slow performance. Tests of executive and motor functions provided mixed results. The patient's pointing span on the Wechsler Memory Scale-Revised<sup>10</sup> was below expectations. The Wisconsin Card Sorting Test<sup>11</sup> was within normal limits but Trails B of the Trail Making Test<sup>12</sup> was slow (116 seconds) with one error (normative data from Heaton<sup>13</sup>). Finger tapping was slow bilaterally (second percentile from Trahan et al<sup>14</sup>) but more pronounced on her nondominant right hand. Speech and language testing was largely within normal limits but exceptions were noted in the Controlled Oral Word Association Test (33rd percentile from Benton and Hamsher<sup>15</sup>) and reading comprehension, indicating problems with seventh-grade material.<sup>16</sup> No errors in comprehension, repetition, or naming (ie, Western Aphasia Battery<sup>17</sup> and Boston Naming Test<sup>18</sup>) were evident. A sensory perceptual examination (from the Halstead-Reitan Battery<sup>19</sup>) indicated three of four auditory extinctions on the right side with no

**Table 1.—Summary of Neuropsychological Testing: 1-Year Follow-up\***

Intellectual Functions (VIQ=102, PIQ=107, and FSIQ=104)			
Verbal Scale		Performance Scale	
Information	11	Picture completion	10
Digit span	9	Picture arrangement	9
Vocabulary	9	Block design	10
Arithmetic	9	Object assembly	12
Comprehension	10	Digit symbol	6
Similarities	13		
Memory Functions (WMS-R MI=100)			
Verbal Memory		Nonverbal Memory	
Digit span, 8 forward, 6 back		Pointing span, 4 forward, 4 back	
WMS stories		WMS visual retention	
Immediate, 9.5		Immediate, 9	
Delay, 8		Delay, 9	
Retention, 84%		Retention, 100%	
California Verbal Learning Test		Continuous Visual Memory Test	
Monday list, 5, 10, 13, 8, 13		Hits, 38	
Tuesday list, 5		False alarms, 18	
Monday immediate, 11		d-Prime, 2.32	
Delay, 12		Correct, 84	
Recognition, 16		Rey-Osterrieth Complex Figure	
Selective Reminding Test		Copy, 34	
Recall, 5, 7, 7, 9, 8, 9, 10, 10, 11, 10, 12		Immediate, 23	
LTS, 84		Delay, 22	
LTR, 81		Retention, 96%	
CLTR, 56		Milner Facial Recognition	
STR, 20		9/12	
Levels of processing, No. (%)		Rates of forgetting nonverbal, No. (%)	
Semantic, 11/12 (92 correct)		5 min, 28/30 (93)	
Phonemic, 8/12 (67 correct)		1 h, 27/30 (90)	
Orthographic, 4/12 (33 correct)†		24 h, 24/30 (80)	
Rates of forgetting verbal, No. (%)		48h, 24/30 (80)	
30 min, 10/12 (83 retention)			
8 h, 10/12 (83 retention)			
24 h, 10/12 (83 retention)			
Release from proactive interference, No. (%)			
12/15 (80), 10/15 (66), 10/15 (66)			
5/15 (33), shift, 10/15 (66)			
Other Findings			
Verbal fluency, 27 (30%-33%ile)		Trails A, 30 s	
Boston Naming, 63/64		Trails B, 116 s†	
Spache Reading, 5/8 at 7th-grade level†		Wisconsin Card Sorting, 6/6 categories in 128 sorts	
Praxis WAB, no errors		Finger tapping	
Sequential commands WAB, no errors		RH=33†	
Repetition WAB, no errors		LH=40	
Naming WAB, no errors		Sensory perceptual examination	
		3/4 Right ear extinction†	

\*VIQ indicates verbal IQ; PIQ, performance IQ; FSIQ, full-scale IQ; WMS-R, Wechsler Memory Scale-Revised; MI, memory index, WMS, Wechsler Memory Scale; LTS, long-term storage; LTR, long-term retrieval; CLTR, consistent long-term retrieval; STR, short-term retrieval; WAB, Western Aphasia Battery; RH, right hand; and LH, left hand.

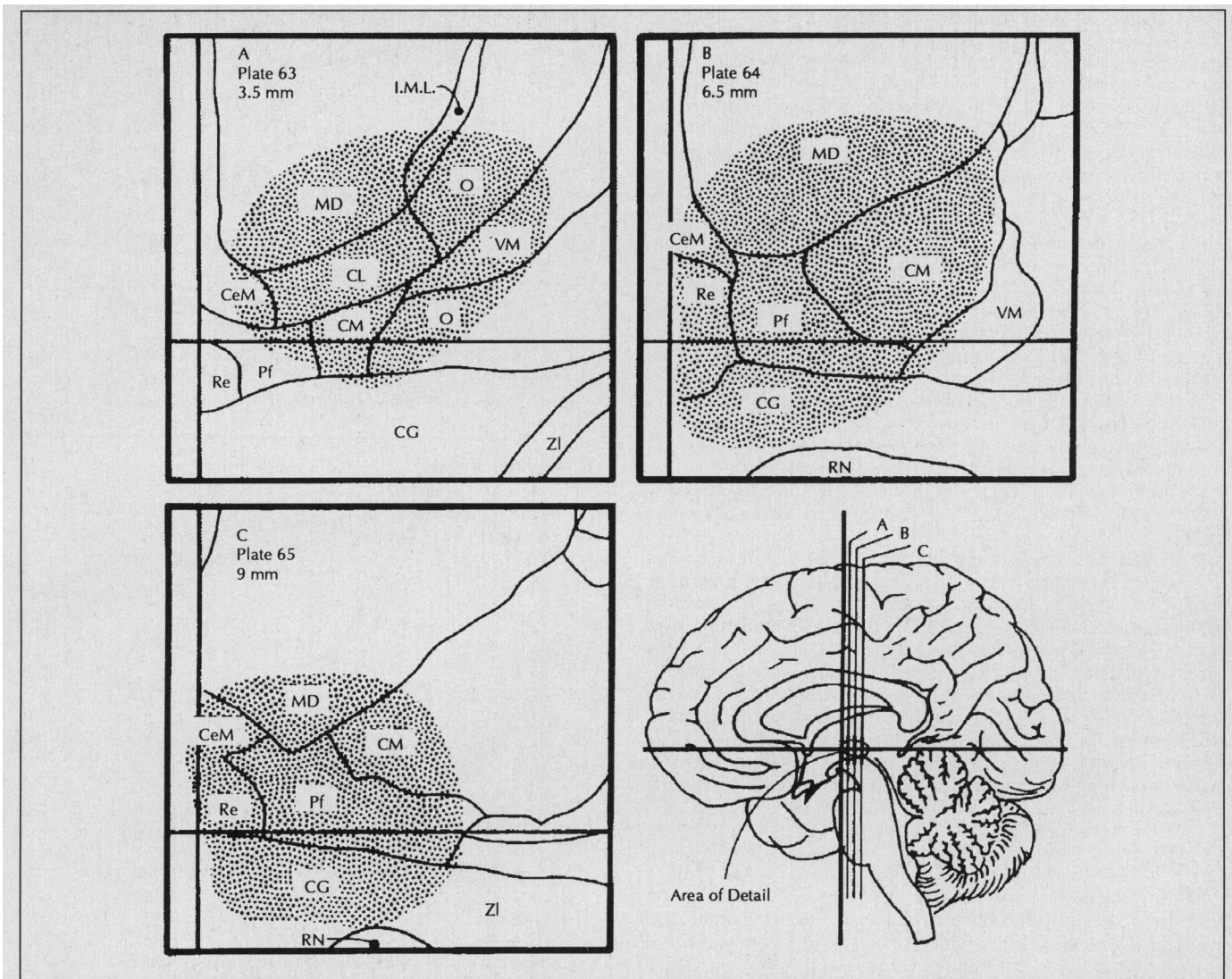
†Outside the range of normal.

other apparent deficits. No problems in visuoanalytic or visuospatial constructional abilities were evident on the Rey-Osterrieth Complex Figure<sup>20</sup>—copy, immediate, or delayed recall (normative data from Lezak<sup>21</sup>).

### Memory Tests

Mild problems were evident on tests of verbal memory and list learning. Although she showed eventual learning and good retention on the logical stories of the Wechsler Memory Scale-Revised<sup>10</sup>

and the California Verbal Learning Test (CVLT),<sup>22</sup> the rate at which the patient acquired verbal information was slow (ie, two standard scores below normal on the first trial of the CVLT). She also tended to recall only the first and last parts of the Wechsler stories. She did demonstrate semantic clustering on the CVLT, however, and was able to recall and recognize items after delays. She was also able to retain information over extended delays as she demonstrated normal rates of forgetting for both verbal and nonverbal<sup>23,24</sup> material after delays of 5 minutes and 1, 24, and 48 hours.



**Fig 2.**—Lesion plotted on corresponding sections of a stereotaxic atlas (details of sections in the coronal plane). Dark lines in plates A through C correspond to Y (horizontal) and Z axes (vertical grid). Dark lines in brain illustration represent X (horizontal) and Z (vertical) axes. Speckled area represents lesion. CG indicates central gray; CL, central lateral nucleus; CM, centre médian nucleus; CeM, central medial nucleus; MD, mediodorsal nucleus; O, oralis (principal ventral medial nucleus); Pf, parafascicular nucleus; Re, reuniens (medioventral nucleus); RN, red nucleus; VM, ventral medial; and ZI, zona incerta. Plates redrawn and modified from Schaltenbrand and Bailey.<sup>9</sup> Measurements in millimeters under plate numbers indicate distance of the plane of section posterior to the point midway between the anterior and posterior commissures.

The patient's neuropsychological evaluation suggested specific verbal memory and cognitive problems. She could retain information once acquired but had difficulty incorporating new items into long-term memory. She also appeared compromised in her ability to attend to and process multiple bits of information simultaneously. Given several tasks to coordinate at once, her cognitive problems became more pronounced. She appeared to be suffering from specific deficits that were severely impairing her daily functioning.

To define the factors underlying her memory problem, several tests were selected and administered to the patient and a sample of age- and education-matched control subjects. These tests examined her ability to encode information in short-term memory, hold information over time without rehearsal, and to enter, consolidate, and retrieve information from long-term memory.

#### Control Subjects

Four healthy female (mean age, 43 years; SD, 4 years) volunteers provided direct matches on age and geographic region. All were employees of the Department of Veterans Affairs Medical Center, Gainesville, Fla, engaged in either retail sales, secretarial, or clerical

positions. Their mean education level was equivalent to the patient's (mean, 13.5 years). All control subjects were right-handed and none had a history of neurologic disease or insult. Published normative data were also used for comparisons.

#### MATERIALS AND PROCEDURES

Four tests of memory formed the basis for this comparison. All subjects received the tests in a random order. The first task involved the Level of Processing Paradigm of Craik and Tulving.<sup>23</sup> Subjects were shown 36 words printed separately on index cards. After examining each word for 5 seconds, subjects answered whether the: (1) word was printed in upper (or lower) case letters, (2) word rhymed with a given word, or (3) word was a member of a given semantic category. Items were balanced for the number of positive (yes) and negative (no) responses. Recall was tested in a recognition format after a 20-minute delay with intervening motor tasks (ie, trials of finger tapping). The subject was shown four words printed on an index card and asked to select the previously seen word from among three words not previously seen. Percentage correct recognition was calculated for each of the three conditions (ie, orthographic, phonologic, and semantic) by dividing the number of cor-

rect responses obtained by the total possible for that condition.

The second test involved the Release From Proactive Inhibition technique.<sup>26</sup> On each trial, a subject's memory for three words from the same semantic category was tested. Following presentation of the three words, the subject was required to engage in a 15-second distractor task (eg, counting backward from a target number by three). The distractor was given immediately after the words to prevent rehearsal in short-term memory. Subjects were then required to recall the three words. Subjects were tested in six blocks of five trials. In half of the blocks, the first four trials of words were members of the same semantic category (eg, items of furniture), but on the fifth trial the category shifted (eg, body parts). The category does not shift on the fifth trial for the remaining blocks; rather, words in the fifth trial of these blocks belong to the same category as the previous four trials (no shift condition). Percentage correct recall across trials for both shift blocks was calculated by dividing the total words obtained by the total words possible.

The distraction technique of Brown<sup>27</sup> and Peterson and Peterson<sup>28</sup> constituted the third task. Subjects were required to recall three consonant trigrams after either 3, 9, or 18 seconds of interference (ie, counting backward by three from a given number). There were five trials counterbalanced for each of the delay conditions. Percentage correct recall for consonants across the 3-, 9- or 18-second delay conditions was obtained by the total possible.

Buschke's<sup>29</sup> Selective Reminding Memory Test was the fourth test of memory. The words used in this task correspond to the Hannay and Levin<sup>30</sup> Form 2. The task consisted of recalling 12 unrelated words on successive trials. On the first trial all 12 items were read aloud at a rate of two words per second. After the first trial, only those items that were not recalled were presented again before the next recall. Repetitions of the list proceeded in this fashion until the subject obtained all the words on the list two times or until 12 trials had been given. The test provides measures of short-term recall, long-term storage, long-term recall, consistent long-term retrieval, and random long-term retrieval (see references 29 and 30 for scoring procedures).

## RESULTS

Data obtained in experiment one were analyzed using measures of central tendency and percentage correct responses. Comparisons between our patient's performances and those of the control subjects were evaluated by establishing 95% confidence limits for the control subjects' scores using conservative estimates of the variance.<sup>31</sup> Limits corresponded to the 0.05 level of significance for one- and two-tailed tests.

The patient performed similarly to control subjects on only one test, the release from proactive interference test. The average percent correct recall for the control subjects on trials 1 through 5 in the shift condition indicated a build-up and release from proactive interference (86.25%, 80.25%, 48.25%, 60.55%, and 91.75%, respectively). The patient's scores (80%, 66%, 66%, 33%, and 66%) similarly indicate build-up and release from proactive interference.

She was significantly different from the control subjects on the levels of processing, Peterson-Peterson, and selective reminding tests. Results from the levels of processing task are given in Fig 3. Her ability to recognize words encoded at deeper levels, both semantic and phonologic, was within the range of the control subjects. However, she was markedly impaired when words were processed orthographically (confidence range for control subjects, 12-6.5; patient's score, 4).

The patient's deficits were pronounced on the Peterson-Peterson paradigm. Figure 4 includes results obtained from the patient, control subjects, and, for comparison, a group of Korsakoff patients.<sup>32</sup> Distraction significantly affected her recall at 9- and 18-second delays relative to normal subjects.

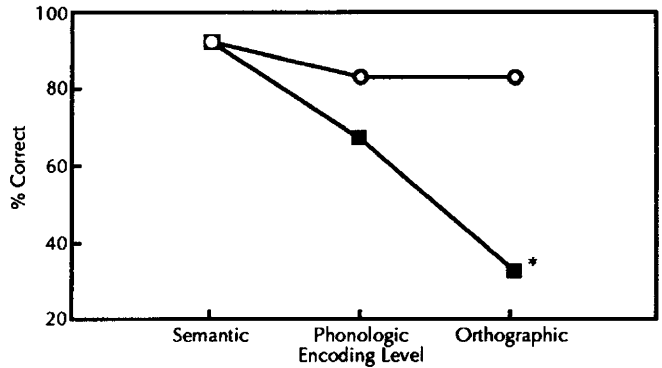


Fig 3.—Levels of processing task. Comparison of our patient with control subjects. Solid squares indicate our patient; open circles, control subjects. Asterisk indicates a score outside the range of normal.

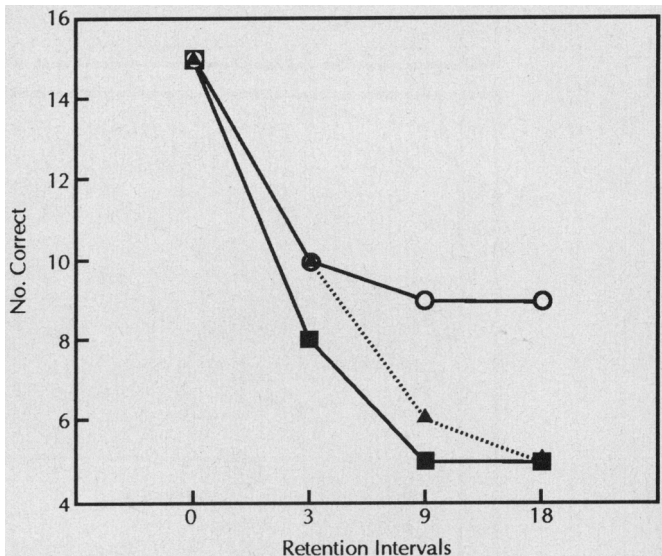


Fig 4.—Comparison of our patient with control subjects and alcoholic Korsakoff patients on the Peterson-Peterson task. Triangles indicate alcoholic Korsakoff patients; circles, control subjects; and squares, our patient. Data on alcoholic Korsakoff patients from Butters and Cermak.<sup>32</sup>

Her performance was also below the alcoholic Korsakoff patients at 9- and 18-second delay recall periods.

Scores from both control subjects and a comparison group of nonforgetful seniors<sup>33</sup> were used to evaluate our patient's performance on the selective reminding test. Table 2 lists these results. Her scores differed most from control subjects on measures of long-term retrieval, long-term store, and random long-term retrieval. She also showed an overreliance on short-term memory and a lack of consistency in retrieval from long-term memory. The scores of the comparison group fell in between those of the patient and the age-matched control subjects and were not significantly different from either. Even so, our patient's scores on the three indexes were below those obtained by subjects 20 years older. Thus, in spite of a relatively normal neurologic examination, her cognitive complaints were verified by detailed neuropsychological tests.

## COMMENT

### Comparative Neuropsychology of Memory Impairment

This patient was able to semantically encode information. Evidence for spared semantic encoding comes from her normal performance on the release from Proactive Interference



**Table 2.—Comparison of Our Patient With Control Subjects on the Selective Reminding Test\***

SRMT Indexes	Control Subjects, Mean (SD)	Nonforgetful Seniors† (n=78) Mean (SD)	Patient Mean (SD)
Recall	124 (15)	...	101 (2.3)
LTR	122 (14)	...	81 (2.9)‡
STR	7 (5.9)	...	20 (1.0)§
LTS	122 (16)	97.2 (19.6)	84 (3.1)
CLTR	112 (26)	68.3 (30)	56 (2.8)§
RLTR	7 (7.4)	21.3 (12.3)	36 (2.6)‡

\*LTR indicates long-term retrieval; STR, short-term retrieval; LTS, long-term storage; CLTR, consistent long-term retrieval; and RLTR, random long-term retrieval.

†From Larrabee et al.<sup>33</sup>

‡ $P < .01$ .

§ $P < .05$  (two tailed).

|| $P < .02$ .

test and her improvement on the levels of processing paradigm. Normal subjects typically show a release effect on the release from the Proactive Interference paradigm. They regain proficiency at remembering the three words after a shift in semantic category.<sup>26</sup> Build-up of proactive interference is interpreted as an ability to differentiate words in short-term memory according to semantic features. Since the patient also demonstrates this phenomenon, she apparently has the ability to make semantic distinctions in short-term memory.

She showed good recognition of words that were initially processed according to semantic rather than physical features. Craik and Lockhart<sup>34</sup> and later Craik and Tulving<sup>25</sup> proposed that the strength of a memory trace was related to the level at which it was initially processed. A semantic analysis of words is assumed to involve deeper levels of processing than phonemic or physical (orthographic) analysis. Alternative explanations of the levels of processing effect have been proposed<sup>35</sup> but regardless of disagreement the levels effect is unquestionably robust, occurring in amnesic patients<sup>36</sup> as well as in normal subjects.<sup>37</sup> We view this patient's performance on the Levels of Processing test as a preserved ability to retain words processed semantically but a subnormal ability to identify words when forced to encode them by less robust means.

Both the release from Proactive Interference and Levels of Processing tests manipulate encoding externally. They do not provide an indication of her spontaneous strategy for encoding information. To evaluate this ability we examined how well she clustered items according to semantic category on the CVLT. Her performance on this test indicated a good spontaneous use of semantic clusters. She averaged six clusters per learning trial (ranging from 1 to 9) and used clustering effectively during both immediate (seven clusters) and delayed (nine clusters) recall, which is above the average clustering score for normal females of similar age.<sup>22</sup> Thus, she spontaneously adopted a semantic clustering strategy that led to normal rates of encoding and recall. Since this strategy was not overtly encouraged, it appears that her preferred mode of processing is semantic, a strategy shown to produce the best rate of recall on list learning tasks in normal subjects.<sup>38</sup> This finding is consistent with our interpretation of our patient's normal ability to encode material semantically.

Buschke<sup>29</sup> designed the Selective Reminding Test to examine how memory items move from short- to long-term stores.

He distinguished between items placed in long- and short-term storage by controlling the times at which they were repeated to the subject during learning trials. This test was particularly useful for examining our patient because it demonstrated the difficulty she had consolidating information into long-term storage. Her problems reflect consolidation deficits more than retrieval problems because her delayed recall was excellent.

Our patient performed much worse on the Selective Reminding Test than on the CVLT. The Selective Reminding Test appears different from the CVLT in at least two ways. First, the semantic associations between items are not obvious on the Selective Reminding Test. Ruff et al<sup>38</sup> found that only 40% of normal subjects used clusters efficiently in the Selective Reminding Test. Second, list items are only repeated on the Selective Reminding Test if the subject cannot recall them from a previous trial. Thus, maintenance rehearsal through repetition is not an inherent strategy of the Selective Reminding Test. Her relatively poorer performance on the Selective Reminding Test may reflect an inability to process memory items without the use of direct encoding strategies. Consistent with this interpretation, she did not cluster items on recall trials of the Selective Reminding Test.

The patient shows a dramatic susceptibility to the effects of interfering tasks on the Peterson-Peterson paradigm. When rehearsal was prevented by use of a distractor task, she demonstrated a significant loss of information at 9- and 18-second delay intervals. She even performed below the level reported for Korsakoff patients on this task.<sup>32</sup> Although the psychometric qualities of the Peterson-Peterson task have not been described,<sup>39</sup> forgetting is assumed to reflect either trace decay and/or susceptibility to interference.<sup>35</sup> The effects of trace decay are short lived, occurring within 5 seconds.<sup>40</sup> Her performance at 3-second delay intervals remained within the range of normal subjects, suggesting that trace decay was not a significant factor leading to poorer retention on longer delay periods. Rather, her errors on longer delay trials reflect an inability to distinguish new items from those presented on previous trials. Baddeley<sup>35</sup> has suggested that distinguishing old from new items in the Peterson-Peterson paradigm is the primary task component accounting for the performance of normal subjects. Thus, she appears extremely susceptible to the effects of a simultaneous task that competes for her processing resources.

To learn whether the caudal intralaminar nuclei have a unique contribution to memory processes, we compared our patient's test scores with those of other patients who demonstrated memory disturbances following diencephalic lesions. Specifically, we reviewed test performances of Korsakoff patients and patient NA<sup>41</sup> and other cases with lesions involving either the mammillary bodies and midline nuclei<sup>2</sup> or the dorsomedial nucleus of the thalamus.<sup>42</sup>

The pathology of the Korsakoff syndrome is certainly more widespread than that observed in our case. Whereas our patient's lesion is largely confined to a small region involving and immediately surrounding the left caudal intralaminar nuclei, the pathological changes in Korsakoff syndrome may include this area (up to 50% of cases) in addition to many other thalamic (mediodorsal nuclei, 88.4% and medial Pulvinar, 95%) and hypothalamic nuclei (medial mammillary, 100%), as well as structures outside the diencephalon (eg, cerebral cortex, 56.9%).<sup>7</sup> Korsakoff patients exhibit a profound anterograde amnesia with differences between their Wechsler Memory Scale memory quotient and verbal IQ of approximately -15 points.<sup>32</sup> Our patient clearly does

not demonstrate a profound amnesia (ie, memory quotient, 100; verbal IQ, 102; difference, -2); although her scores on specific verbal memory tests, including certain subtests of the Wechsler Memory Scale, do demonstrate memory impairment that is out of proportion to other neuropsychological findings such as intelligence. The first distinction, then, between our patient and Korsakoff patients is at the level of global memory impairment.

Korsakoff patients cannot use semantic information to facilitate memory in the same manner as our patient. Korsakoff patients show a normal decline in recall due to a build-up of proactive interference when learning successive groups of words from the same semantic category.<sup>43</sup> However, these patients fail to improve when semantic categories are shifted (ie, release from proactive interference). She demonstrates a normal build-up and subsequent release from proactive interference. Additionally, it is questionable whether Korsakoff patients benefit from procedures designed to control the level at which verbal memory items are processed. Originally, Cermak and Reale<sup>44</sup> and later Wetzel and Squire<sup>45</sup> found that Korsakoff patients did not improve on the Levels of Processing paradigm. Mayes and Meudell,<sup>36</sup> however, showed that if subjects are equated on the strength of their memory for items, Korsakoff patients improve as much as normal subjects on similar paradigms, although their performances always remain below the level of normal subjects. Our patient clearly shows successive improvement in recognition when words are encoded according to orthographic, phonologic, or semantic features during the initial presentation phase. Her recognition rates were excellent for semantic (92%), low for phonologic (67%), and significantly impaired for orthographically encoded words (33%) relative to normal control subjects. These data suggest fundamental differences in the abilities of Korsakoff patients and our patient to use semantic information. Whereas our patient uses these strategies to retain information at normal levels, Korsakoff patients may improve with them but are not able to reach the level of normal subjects.

Our patient does demonstrate some similarities to Korsakoff patients. Korsakoff patients and our patient alike show normal rates of forgetting.<sup>23,24,46</sup> They are different, however, in the rate at which they can acquire information. A comparison of our patient's performance with Korsakoff patients on similar tasks used to assess nonverbal rates of forgetting<sup>23,24</sup> indicated normal retention abilities for both over extended delays. However, Korsakoff patients required longer exposure periods (ie, four to eight times longer) to acquire the information than our patient. Thus, their rate of initial acquisition, at least for nonverbal information, appears much slower. This could be due in part to the laterality of our patient's lesion. We have no information on Korsakoff patients' rates of forgetting for verbal material that would be directly comparable with that obtained on this patient.

Our patient performed nearly identically to Korsakoff patients on the trigram test of Brown<sup>27</sup> and Peterson and Peterson.<sup>28</sup> Her performance fell rapidly (from 100% correct to 50%) after only 3 seconds of interference and, like Korsakoff patients, continued to become worse (33%) after 9 and 18 seconds. Neither our patient nor Korsakoff patients appear able to retain information if they are distracted by an interfering task.

Since our patient clearly can use semantic encoding strategies to retain information at normal levels, the difference between her and Korsakoff patients is in their poor ability to encode material by use of any strategy. This view is consis-

tent with data suggesting that Korsakoff patients require more repetitions to place items into memory.<sup>23,24,46</sup> Also, since both our patient and Korsakoff patients show normal rates of forgetting for material once learned,<sup>47</sup> it is again apparent that their primary difficulties are in encoding information rather than retention. The pervasiveness of encoding deficits in Korsakoff syndrome<sup>37</sup> may be grounded in the fact that multiple structures are involved. The memory problems demonstrated by our patient clearly show that damage to the intralaminar nuclei, which may occur in up to 50% of Korsakoff patients, can contribute to their amnesia, but is not sufficient to produce it.

Patient NA<sup>41</sup> is a purer example of diencephalic amnesia than Korsakoff patients because his lesion was largely confined to the thalamus and hypothalamus.<sup>48</sup> His lesion was more extensive than our patient's lesion, involving white matter tracts and the mammillary bodies bilaterally<sup>41</sup>; however, both patients had lesions involving the left centre médian-parafascicular complex and possibly the ventral mediodorsal nucleus and the reuniens nucleus. The largest difference between NA<sup>41</sup> and our patient in terms of neuropsychological performance is the severity of memory impairment. NA<sup>41</sup> memory quotient was 27 points below his full-scale IQ.<sup>48</sup> Both NA<sup>41</sup> and ours performed worse on verbal than nonverbal memory tests but NA's performance on verbal tests was markedly worse than that of our patient.<sup>48</sup> Another difference between NA and ours is that although NA showed semantic encoding abilities on the release from Proactive Interference and Levels of Processing paradigms, his performances on these tasks never reached the level of normal subjects. Thus, while our patient and NA both demonstrate similar levels of impairment for words that are not processed semantically, our patient could use semantic encoding to achieve the performance levels of normal subjects, something NA and other amnesic patients are unable to do.<sup>37</sup>

NA also performed poorly after only 3 seconds of interference on the Peterson-Peterson paradigm.<sup>49</sup> That Korsakoff patients, NA, and our patient share a common site of pathology, left intralaminar and medial thalamic nuclei, and a common processing deficit on the Peterson-Peterson test raises an interesting possibility that these anatomic areas are important in preventing information loss due to distraction. However, to support this theory it must be shown that isolated damage to other structures damaged in Korsakoff syndrome or in patient NA, such as the mediodorsal nucleus, mammillary bodies, or midline nuclei does not result in similar deficits on the Peterson-Peterson paradigm.

### Comparative Neuroanatomy of Memory Impairment

Several recent case reports of left thalamic infarcts,<sup>6,50</sup> hematoma,<sup>42</sup> and tumor<sup>51</sup> with radiologic confirmation of the lesion and detailed neuropsychological testing are available. Of these, Speedie and Heilman<sup>6</sup> and Brown et al<sup>42</sup> reported results for the Peterson-Peterson task. Both cases had damage to the left thalamus (ie, region of the mediodorsal nucleus<sup>6</sup>; the mediodorsal nucleus, anterior nucleus Pulvinar, and most probably white matter tracts<sup>42</sup>) and both patients displayed low memory quotients relative to their verbal IQs and deficits on list-learning tasks. However, only Speedie and Heilman's<sup>6</sup> patient showed deficits on the Peterson-Peterson paradigm. It is not possible to determine whether their patient also suffered damage to nuclei ventral to the mediodorsal nucleus. The patient of Brown et al,<sup>42</sup> however, performed better than control subjects on the interference task

**Table 3.—Comparison of Patients With Diencephalic Lesions\***

Source, y	Patient	Lesion Site	Full Scale IQ	MI†	Peterson-Peterson		
					3''	9''	18''
Brown et al, <sup>42</sup> 1989	1	Left, dorsomedial anterior and pulvinar	95	<b>86</b>	87	87	83
Mair et al, <sup>2</sup> 1979	2	Bilateral, mammillary bodies and midline nuclei	106	<b>60</b>	90	93	95
	3	Bilateral, mammillary bodies and midline nuclei	106	<b>60</b>	80	90	70
Present case	4	Left, intralaminar	104	100	<b>53</b>	<b>33</b>	<b>33</b>

\*Boldfaced scores indicate impairment.

†Memory index (MI) (X, 100; SD, 15).

and clearly demonstrated thalamic damage anterior and superior to that of our patient (Table 3). This case suggests that damage to the mediodorsal nucleus and anterior nucleus is not sufficient to produce deficits on the Peterson-Peterson paradigm.

Regarding damage to the mammillary bodies and midline nuclei, Mair et al<sup>2</sup> examined two Korsakoff patients using the Peterson-Peterson interference procedure. Pathological study confirmed that both patients had extensive cell loss in the mammillary bodies and a thin band of gliosis lying medial to, but not involving, the mediodorsal nuclei. In spite of their severe amnesias, both patients' performances on the interference task either equaled or exceeded the levels obtained by their control subjects (Table 3). These cases suggest that bilateral damage of the mammillary bodies or midline nuclei is not sufficient to produce a deficit performance on the Peterson-Peterson task.

Deficits on the Peterson-Peterson interference task are thus not an integral part of the amnesic syndrome resulting from diencephalic lesions, but are one part of a double dissociation (Table 4): the patient of Brown et al<sup>42</sup> and those of Mair et al<sup>2</sup> summarized above demonstrate severe amnesia without abnormalities on the interference task, and had lesions that spared the region involved in the present case. In our case, only a mild memory problem is evident but severe impairment is noted on the Peterson-Peterson task. Involvement of the intralaminar nuclei may account for the differences in performance between these patients. Involvement of the ventral mediodorsal nucleus, in our case, should be considered. However, it seems unlikely that this lesion could account for our findings since larger lesions of the mediodorsal nucleus have not been shown to produce deficits on the Peterson-Peterson task.<sup>28</sup> Additionally, while it is likely that our patient's behavioral problems are related to the involvement of the mesencephalic gray matter and caudal intralaminar nuclei, consideration must be given to the contribution of the medioventral (reuniens) and centromedial nuclei that were also involved by the lesion. The connections of midline nuclei to the hippocampus have suggested that they may have a role in memory.<sup>8,52-54</sup> We do not know how these lesions may have influenced our findings.

#### Diencephalic Memory Disturbances

Based on the differences we have discussed, we propose that there are at least two types of memory disturbance associated with diencephalic lesions. One is the amnesic syndrome previously described by Lhermitte and Signoret,<sup>55</sup> Squire,<sup>37,46</sup> and Squire et al,<sup>48</sup> which is characterized by weak encoding, regardless of the strategy used, but normal rates of forgetting for acquired information. The second type is a memory defect associated with lesions involving the intralaminar and medial nuclei of the left thalamus. The latter is characterized by a normal ability to semantically encode

**Table 4.—Matrix of Memory Function by Distractibility**

	Normal Performance on the Peterson-Peterson Task	Abnormal Performance on the Peterson-Peterson Task
Normal memory index	Normal subjects	Our patient
Amnesic	Patients 1, 2, and 3	Some Korsakoff patients

material and good retention of acquired information; however, when active semantic processing or rehearsal strategies are interrupted, severe encoding deficits become apparent.

It has long been believed that the caudal intralaminar nuclei may be important for normal arousal and/or attention. Stimulation in this region of the thalamus produces the recruiting response of the cortical electroencephalogram.<sup>56,57</sup> There are extensive connections to the centre médian-parafascicular nucleus from the brain-stem reticular formation,<sup>58</sup> including cholinergic innervation from the pedunculo-pontine and lateral dorsal tegmental nuclei and serotonergic innervation from the dorsal raphé nuclei. Anatomically, the parafascicular nucleus is adjacent to the central mesencephalic gray matter, which was also involved by the lesion. Efferent connections of the intralaminar nuclei include the striatum and neocortex.<sup>58,59</sup> The projections of the caudal intralaminar nuclei are heaviest to the putamen. These connections presumably play a role in preparing an organism to move.<sup>60</sup> Cortical efferents of the intralaminar nuclei, however, are light and project diffusely to most cortical areas. These diffuse thalamocortical projections appear to be involved in regulating cortical rhythms<sup>56</sup> and maintaining cortical tone (reviewed by Jones<sup>58</sup>). In Luria's conceptualization, the intralaminar nuclei would also be part of a functional system subserving cortical tone. Interestingly, as Christensen<sup>61</sup> points out, memory disturbances resulting from damage to this system are characterized by susceptibility to distraction.

Our observations on neuropsychological tests of memory span, attentional switching, and speeded performance indicate that our patient has deficits in attention and concentration. These appear most pronounced on tasks involving simultaneous cognitive operations and are suggestive of increased distractibility. Heightened distractibility, an attentional deficit, may not only explain her poor memory performance on neuropsychological tests but also the problems she encounters in environmental settings where distracting stimuli cannot be controlled. The double dissociation between our patient and amnesic patients with circumscribed diencephalic lesions suggests that the intralaminar nuclei are



not memory structures per se. Rather, they appear part of a functional system important in regulating attention for simultaneous activities, possibly through maintaining adequate cortical tone. Lesions in this area may give rise to memory disturbances through changing levels of distractibility. Given the anatomy of the intralaminar nuclei, this case may also speak to the reticular formation's contribution to memory processes.

This study was supported by the Research Service, Department of Veterans Affairs, Gainesville, Fla.

We thank Russell Bauer, PhD, for use of his nonverbal rates of forgetting paradigm and Jimmy Franco for illustrations.

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