Retrograde Amnesia: Possible Role of Mesencephalic Reticular Activation in Long-Term Memory

Abstract. A patient with cerebral trauma recovered considerably from the resulting anterograde but not retrograde amnesia. The persistence of retrograde amnesia is attributed to a lesion in the ventral tegmental region, which suggests a role for mesencephalic reticular activation in long-term retrieval.

Two types of memory deficits are commonly identified: anterograde amnesia (AA), an inability to learn and retain new information after the onset of pathology; and retrograde amnesia (RA), an inability to retrieve information acquired prior to the onset of pathology, usually involving loss of remote memory (1). Parallel recovery from AA and RA is a common clinical finding (2), as is RA recovering first with AA recovering later or not at all (3).

Double dissociation between the two types of amnesia and the presence of RA without AA have been described (1, 4), but cases are rare and sparsely documented. We now report a case of considerable recovery from AA but not RA, which may offer insights into mechanisms of long-term retrieval.

A 36-year-old, right-handed, college-educated male had an open skull fracture in the right parieto-occipital and temporal areas and herniation of the right hemisphere with compression of the left mesencephalon at the tentorial notch. In surgery, a small portion of macerated brain was removed, the dural laceration was sewn over, and the bone-plate replaced. Six weeks later, a ventriculostomal shunt was performed. There was hemiparesis with spasticity of the distal upper right extremity, a right Babinski’s sign, and a left superior quadrantanopsia. The patient was disoriented, his speech anemic and agrammatic. There was profound AA: his recall of seeing a person did not exceed 2 to 3 minutes, and his ability to retain names was still shorter. There was also profound RA. The patient maintained that he was 16 to 18 years old and mentioned his parents’ address as his residence. He revealed no knowledge of his subsequent life history, his marriage, children, or past employment. His command of general information was equally impaired.

During the 2-year course of recovery the patient became fully oriented; linguistic and motor deficits virtually disappeared, but the quadrantanopsia remained. Recent memory was improving. A continuity of experience became possible; he could keep track of weekly and monthly events and retain information from newspapers and television. There was no parallel recovery from the 20-year deep RA. The patient’s past history was reconstructed for him, but lacked a sense of authenticity. Command of general information did not improve beyond what he had been taught during this time; he could not answer questions like, “Who wrote Hamlet?” or “What is the capital of France?”

Table 1 summarizes the patient’s performance on tests of memory over a 1.5-year period. Tasks of recent memory—the Wechsler Memory Scale (5), and the Buschke Selective Reminding Test (6)—showed significant improvement, while tests of remote memory—the Boston Retrograde Amnesia Battery (7), and the general knowledge battery (8)—did not (except the “recall” part of BRA, where the scores were lowest). The Wechsler memory quotient changed from 86 to 106, and the Wechsler Adult Intelligence Scale IQ from 86 to 105 (verbal, 90 to 112; performance, 82 to 95). Both memory and IQ are now within the normal range and mutually consistent (9). Performance on the other tests remains deficient.

The patient’s performance on verbal recognition subsections of the general knowledge battery was inversely related to the degree of categorical proximity between correct and alternate choices. Pairwise comparisons of adjacent steps were significant (10) (Closest, 43 percent correct; intermediate, 58 percent; distant, 77 percent; z = 1.70, P < .05. Intermediate, 58 percent; distant, 77 percent; z = 2.47, P < .01). Such dissociation has been interpreted as related to retrieval rather than to storage (11).

A series of computerized tomographic (CT) examinations was performed during the early course of recovery (in 1977 and 1978), through the use of sections 8 mm thick and supplemental coronal and overlapping sections. Findings included moderate ventricular enlargement, a region of rarefaction in the right middle and posterior temporal areas, and a small region of rarefaction along the left midtemporal convexity. The ventricular shunt tip was in place within the lateral ventricle. The findings were consistent with atrophic changes within the temporal lobes, as a result of both trauma and surgery.

Ventricular dilation (thus probable increased intracranial pressure, periventricular atrophy, or both) and bilateral temporal damage (both convexal and mesial) have been implicated in memory deficits, but not with RA as the predominant and relatively isolated component (12). It was concluded that the CT findings could not fully account for our patient’s condition.

Since relative recovery from AA in the presence of persistent severe RA has not been interpreted neuroanatomically, some speculation was necessary. Reverbation in cortico-thalamic-limbic loops may constitute a crucial stage in consolidation (13). It is possible that long-term retrieval involves similar stages, but in a reverse order. It could be hypothesized further that, whereas in the process of consolidation the reverberation can be initiated by external stimulation, for retrieval some intrinsic reticular activation is necessary. These considerations led to

![Fig. 1. Computerized tomographic scan images of the mesencephalic lesion. Transverse sections, each 5 mm thick, demonstrating the lesion extending from (a) the ventral tegmental portion of the upper mesencephalon to (b) the ventral portion of the pontomesencephalic junction. The patient’s left is to the reader’s left.](image-url)
<table>
<thead>
<tr>
<th>Task</th>
<th>T₁</th>
<th>T₂</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wechsler Memory</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>53.2</td>
<td>69.4</td>
<td>2.18*</td>
</tr>
<tr>
<td><strong>Buschke Selective Reminding</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total recall</td>
<td>53.1</td>
<td>91.5</td>
<td>4.67†</td>
</tr>
<tr>
<td>Long-term storage</td>
<td>36.1</td>
<td>80.0</td>
<td>5.55†</td>
</tr>
<tr>
<td>Long-term retrieval</td>
<td>20.0</td>
<td>74.6</td>
<td>7.31†</td>
</tr>
<tr>
<td>Consistent retrieval</td>
<td>0.0</td>
<td>56.2</td>
<td>9.25†</td>
</tr>
<tr>
<td><strong>Boston Retrgrade Amnesia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recognition</td>
<td>36.7</td>
<td>43.3</td>
<td>0.75</td>
</tr>
<tr>
<td>Recall</td>
<td>11.7</td>
<td>30.0</td>
<td>2.47*</td>
</tr>
<tr>
<td>Famous faces</td>
<td>27.4</td>
<td>39.7</td>
<td>1.58</td>
</tr>
<tr>
<td><strong>General knowledge battery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal recall</td>
<td>58.3</td>
<td>66.7</td>
<td>0.84</td>
</tr>
<tr>
<td>Verbal recognition</td>
<td>64.8</td>
<td>59.3</td>
<td>-0.69</td>
</tr>
<tr>
<td>Visual recognition</td>
<td>30.8</td>
<td>28.5</td>
<td>-0.18</td>
</tr>
</tbody>
</table>

*P < .02, †P < .001.

the decision to repeat CT studies (in May 1979) with particular attention to the mesencephal ganglion, and with sections 5 mm thick.

In addition to confirming the earlier findings, these studies revealed a narrow band of hypodensity in the median and left paramedian zones, extending from the ventral tegmental portion of the upper mesencephalon (where the midline was reached and crossed) caudally to the ventral portion of the ponto-mesencephalic junction (Fig. 1). This was confirmed by coronal reconstruction.

Further analysis revealed changes in average density within the region where the ventral tegmental nucleus is found and a component of the medial forebrain bundle originates. In its caudal extension, the hypodense region probably overlapped with the trajectory of locus coeruleus projections into the medial forebrain bundle. There were no abnormalities in dorsomedial or anterior thalamic nuclei, mammillary bodies, or the temporal stem.

The ventral tegmental area is identified with the ventral tegmental pathway—a subdivision of the cholinergic reticular formation projecting into limbic structures (14). It constitutes a major source of the ascending portion of the medial forebrain bundle, which in turn projects into the hippocampi via the medial septum (14) and into the mammillary bodies via the mammillary peduncle (15). The locus coeruleus projections into the medial forebrain bundle are the major sources of noradrenergic influences on the septum, hippocampi, and other limbic structures (16).

In our patient, ascending reticular projections into limbic structures most often implicated in memory (hippocampi and mammillary bodies) seem to have been severed, while those into the thalamus and neocortex were spared. That this was the apparent cause of profound RA in the absence of comparably severe AA or a general arousal deficit may indicate that 'selective mesencephalic reticular activation of limbic structures constitutes a fundamental component of long-term retrieval. The importance of such activation has been demonstrated in animals (17). The rarity of this pattern of memory deficits can be attributed to the fact that only a small lesion of precise location can affect the above described regional area without affecting surrounding mesencephalic structures. If the mesencephalic structures are affected, the resulting impairment to the patient's overall arousal level (18) will override a selective memory deficit.

EIKHONEN GOLDBERG
Department of Psychiatry, Downstate Medical Center, State University of New York, Brooklyn 11203

SANFORD P. ANTIN
Harbor CAT Scan, Neurology Center, Brooklyn 11209

ROBERT M.UILDER, JR.
LOUIS J. GERSTMAN
Department of Psychology, City College, City University of New York, New York 10031

JAMES E. O. HUGHES
Department of Neurosurgery, St. Luke's-Roosevelt Medical Center, New York 10025

STEVEN MATTIS
Department of Neurology, Montefiore Hospital, Bronx, New York 10467

References and Notes
7. M. S. Albert, N. Butters, J. Levin, Arch. Neurol. 36, 211 (1979). Only items corresponding to the 1950's, 1960's, and 1970's were used.
8. The authors designed a chronology-free test of remote memory for general knowledge. It consists of visual recognition, verbal recall, and verbal recognition sections. The test includes three subsections, each with a different degree of categorical proximity between correct and alternative choices. The battery was validated on 20 normal, college-educated males, with a mean age of 36 and a range of 10 years. Each subject performed all sections of the test with above 95% percent accuracy.
10. One-tailed test of the difference between two proportions with standard correction for chance.
15. M. B. Carpenter, Core Test of Neuroanatomy (Williams & Wilkins, Baltimore, ed. 4, 1978).
19. We thank R. Hamilton, J. Hirschy, and G. Abbott for conducting some of the CT studies, and Y. F. Huang for his helpful discussion of the results of those studies.
20 February 1981; revised 22 May 1981