Recovery of Anterograde Amnesia in a Case of Craniopharyngioma

Ron C. Kupers, PhD; Audrey Fortin, PhD; Jens Astrup, MD; Albert Gjedde, MD; Maurice Ptito, PhD, DM

**Background:** Studies of the amnesic syndrome have indicated that telencephalic and diencephalic structures are critical components of the memory system. The exact role of the mammillary bodies (MBs) in human memory remains elusive, since few cases of selective MB damage have been reported.

**Objective:** To study a case of severe anterograde amnesia due to a third-ventricle craniopharyngioma with severe MB compression.

**Design:** Case report.

**Setting:** Neurosurgery clinic of an academic hospital.

**Patient:** A 53-year-old woman who developed severe anterograde amnesia due to a third-ventricle craniopharyngioma strongly compressing the MBs and, to a lesser extent, the right hippocampus.

**Interventions:** Surgical excision of the tumor and neuropsychological testing and positron emission tomography during an associative memory test before and 2 months after tumor removal. A postsurgical magnetic resonance image did not show evidence of damage to the hypothalamus, thalamus, hippocampus, or MBs.

**Main Outcome Measures:** Changes in brain imaging data and results of neuropsychological testing.

**Results:** After tumor removal, the patient showed a complete recovery of memory functions. Performance on the associative memory test was at chance level before surgery and dramatically improved postoperatively. Results of the preoperative positron emission tomographic study showed no activity in memory-related structures. In contrast, a significant blood flow increase occurred in the anterior thalamic nuclei postoperatively.

**Conclusions:** These behavioral and brain imaging data stress the importance of the MBs in this patient’s amnesia. Our data further suggest that the clinical prognosis of decompressing the mammillothalamic tract is excellent, even in cases of massive compression.


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IT IS GENERALLY ACCEPTED THAT the critical components of the memory system are not only the medial temporal lobe (MTL) but also diencephalic structures such as the dorsomedial and anterior thalamic nuclei, fornix, septal nuclei, and the mammillary bodies (MBs), as well as the frontal lobes. Memory loss associated with thalamic lesions and related structures is described as “diencephalic amnesia” and to a certain extent resembles amnesia in cases of MTL lesions or Korsakoff syndrome. There is controversy regarding which of these structures, the dorsomedial thalamus or the MBs (or a combination of both), are involved in the amnesic syndrome. In humans, damage restricted to the MBs or the mammillothalamic tract produces severe and permanent memory impairments.

We studied a patient who developed severe anterograde amnesia due to tumor compression of the right hippocampus and the MBs. Tumor removal abolished the functional lesion and led to a complete recovery of memory functions.

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**REPORT OF A CASE**

A 53-year-old, right-handed woman with no neurologic antecedents developed acute onset of memory problems in July 1999 that turned rapidly into a full anterograde amnesic syndrome. The episode that prompted her husband to take her to the hospital, besides her continuous forgetting of his requests, was preparation for their holidays. When the husband arrived home from work, the patient had completely forgotten that they were leaving the next day and nothing had been prepared.

The patient arrived at the neurologic ward of the hospital in September 1999. She was alert, oriented for place, person, and time, and did not show signs of d-
mentia or speech impairment. A T1-weighted magnetic resonance image of the brain showed a suprasellar craniopharyngioma with a diameter of 3.5 cm extending into the third ventricle to the level of the foramina Monroi, and elevating and compressing the MBs by 2.5 cm, as well as the cerebral peduncles. The tumor did not reach the

Figure 1. Preoperative and postoperative magnetic resonance images (MRIs) and \(^{18}\)F-fluorodeoxyglucose positron emission tomography (FDG-PET), showing (from left to right) horizontal, sagittal, and coronal sections. A, Preoperative views of the craniopharyngioma from MRIs (upper row) and FDG-PET (lower row). Note the compression of the right hippocampus and mammillary bodies. B, Postoperative MRIs (upper row) and FDG-PET (lower row) showing complete removal of the tumor and normal perfusion of the brain. The left part of the brain is shown to the left. The PET data acquisition (45 minutes) started 1 hour after an intravenous bolus injection of 365 MBq (9.9 mCi) of FDG.
left hippocampus but was impinging on the mesial surface of the right hippocampus by 4 mm. The tumor was predominantly cystic but had a small solid part in relation to the pituitary stalk in the suprasellar cistern. The temporal horns of the lateral ventricles were in their normal place on both sides, and no structural abnormalities were seen in temporal and frontal lobes, amygdalae, thalamus, or fornix (Figure 1A, upper row). This was confirmed by the 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) results (Figure 1A, lower row) showing normal FDG uptake in these regions.

On October 14, 1999, the cystic tumor was surgically removed de visu without injuring the surrounding pituitary gland or hypothalamus. A histologic examination confirmed the diagnosis of cystic craniopharyngioma. Two days after surgery, the patient developed polyuria because of diabetes insipidus, which was treated with desmopressin acetate. The patient’s memory problems disappeared completely, and she returned to her normal occupations.

A magnetic resonance image obtained 1 month after the surgery confirmed the total removal of the tumor (Figure 1B, upper row). An FDG-PET scan taken at the same time indicated normal brain metabolism in the MTL and upper brainstem (Figure 1B, lower row) showing normal FDG uptake in these regions.

Formal neuropsychological testing was performed before and 2 months after surgery (Table 2). To elucidate the mechanisms involved in memory loss and recovery, a PET study was performed preoperatively and postoperatively. The patient gave informed consent and the protocol was approved by the Ethics Committee of Aarhus County, Denmark. We used a nonspatial associative learning test (adapted from Henke et al11). One hour before the start of the PET study, the subject was presented a picture series of 10 faces, each associated with a particular house, and she had to learn the specific face-house pairings. After 4 presentations of the series, pairs of stimuli were presented in which only 50% were correctly paired, and she had to indicate whether the pairings were correct. Twelve sequential measurements (2 conditions repeated 6 times each) of regional cerebral blood flow (rCBF) were acquired. Visual stimuli were displayed on a large monitor placed in front of the subject at a rate of 1 pair every 3 seconds. In the baseline condition, pairs of either 2 houses or 2 faces were presented, and the subject had to indicate whether the images of each pair were the same (50% of the pairs) or different. In the test condition, pairs of previously learned face-house stimuli (50% of the pairs) were intermixed with new face-house combinations, and

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**Table 1. ROI Analysis of FDG Scans**

<table>
<thead>
<tr>
<th>Region of Interest</th>
<th>Preoperative</th>
<th>Postoperative</th>
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</thead>
<tbody>
<tr>
<td>Hippocampus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>83.2 ± 12.9</td>
<td>78.5 ± 7.9</td>
</tr>
<tr>
<td>Left</td>
<td>83.5 ± 11.9</td>
<td>81.8 ± 10.6</td>
</tr>
<tr>
<td>Asymmetry index</td>
<td>0.004</td>
<td>0.041</td>
</tr>
</tbody>
</table>

Abbreviations: FDG, 18F-fluorodeoxyglucose; rCMRGLc, regional cerebral metabolic rate of glucose.

*The asymmetry index was calculated for quantitative FDG–positron emission tomography (PET) metabolism, according to the following formula: [(Left−right region of interest [ROI] activity)/(left+right ROI activity)]/2. The ROIs for left and right hippocampus were drawn on coronal preoperative and postoperative magnetic resonance images, following the guidelines by Watson and colleagues.10 The FDG-PET scans were coregistered to the magnetic resonance images by means of Automated Image Registration (AIR 3.0) software (Roger Woods, Department of Neurology, University of California, Los Angeles, UCLA School of Medicine).

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**Table 2. Preoperative and Postoperative Neuropsychological Test Results**

<table>
<thead>
<tr>
<th>Test</th>
<th>Preoperative</th>
<th>Postoperative</th>
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<tbody>
<tr>
<td>WAIS–Revised, mean score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal (similarities)</td>
<td>16 (10 ± 5†)</td>
<td>ND</td>
</tr>
<tr>
<td>Performance IQ (block design)</td>
<td>15 (10 ± 5†)</td>
<td>15</td>
</tr>
<tr>
<td>Memory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test</td>
<td>Preoperative</td>
<td>Postoperative</td>
</tr>
</tbody>
</table>
| First immediate recall (AIR 3.0) software (Roger Woods, Department of Neurology, University of California, Los Angeles, UCLA School of Medicine).
the patient responded verbally as to whether the pairs were correct. Baseline and test conditions were performed in a random order. A PET camera (ECAT HR 47+; Siemens/CTI, Knoxville, Tenn) was used to measure changes in rCBF after intravenous injection of 500 MBq (13.5 mCi) of water labeled with oxygen 15. Presentation of the visual stimuli started 10 seconds before the injection and continued throughout the 60-second scanning window. The PET images were coregistered to the subject's magnetic resonance images and transformed into Talairach space. After a voxel-by-voxel subtraction of the baseline condition from the test condition, a statistical parametric map of the rCBF changes was created by means of a t statistic. Regions significantly activated were those that exceeded a t threshold of 3.6 (P<.05 corrected for multiple comparisons).

During the neuropsychological examination, the patient was alert and behaved in a socially appropriate manner. She was aware of her memory problems and was apologetic about them. She was verbally fluent and used an elaborate vocabulary. The test results indicated a high level of intellectual functioning consistent with her education (bachelor’s degree) and professional activities (teacher). Verbal subtest scores showed excellent abstraction abilities. Nonverbal subtest scores indicated superior constructional abilities. Subjective observations gathered during the interviews did not give evidence of concrete thinking or perseveration tendencies. Preoperative and postoperative language test scores for naming familiar objects were in the normal range. However, implicit learning of the same objects was weak preoperatively but improved significantly after surgery. The patient also performed poorly in another implicit learning task, in which she had to recall 3 real objects in 3 hiding places in the testing room. After surgery, she easily recalled the objects and the hiding places. Preoperative tests of verbal memory functions showed deficits in the recall of a short text and in learning and recalling 10 unrelated words. Learning and immediate recall of a 3-word list was just adequate. However, 5 minutes later she could not remember any of the words. Visuospatial memory tested with abstract design was below the reference range in the first assessment. Postoperatively, learning, recalling, and recognition results were all in the reference range for verbal and visuospatial memory. Both preoperatively and postoperatively, the patient performed well on parts A and B of the Trail-Making Test, a test associated with sustained attention. Although there was a moderate improvement in performance, the difference between preoperative and postoperative results differed by less than 1 SD.

During the preoperative PET study, the patient performed at chance level on the nonspatial associative memory test (55% correct responses). Postoperatively, performance increased dramatically (98% correct responses) and was at the level of performance in age-matched controls. Preoperatively, significant rCBF increases occurred in the anterior cingulate and cerebellum during recall (Figure 2A). No rCBF increases were seen in hippocampus or thalamus. Postoperatively, significant loci of activation were observed in the cerebellum, the frontal lobe, and the anterior portion of the thalamus (Figure 2B).

This case showed full recovery of severe anterograde amnesia after removal of a craniopharyngioma strongly compressing the MBs and, to a lesser extent, the right hippocampus. Few cases of anterograde amnesia following selective damage of the MBs have been described. In some cases the memory loss was permanent, either because the MBs were irreversibly damaged or because of a combined lesion of the medial thalamus and MBs. In a patient with a tumor invading the MB, partial memory improvements were observed after tumor removal. Our patient represents, to our knowledge, the first reported case of full recovery from anterograde amnesia after surgical decompression of the MBs and right hippocampus.
Lesions of the MTL and medial diencephalic structures may induce anterograde amnesia. The spectrum of symptoms observed in disconnection syndromes depends on the extent of the afferent input to a specific brain region. Because the hippocampus has major projections to the limbic system and into the MBs via the fornix, the question arises as to whether the differential memory effects of one or the other structures. Transection or damage of the fornix produces selective anterograde amnesia. Anterograde amnesia has also been observed in patients with thalamic damage. This often seems to involve the MBs or the mammillothalamic tract. The thalamic recipient zones of the mammillary tract (anterior nuclei) project to the anterior cingulate, which in turn sends axons to the MT and prefrontal cortex. The latter structure has a role in executive functions that are affected by thalamic lesions. These data suggest that the thalamus is involved in memory and that the mammillothalamic tract thereby plays an important role. Several lines of evidence also point to the importance of the mammillothalamic tract in the anterograde amnesia in our patient. Magnetic resonance images indicated a strong compression of the MBs and a milder compression of the right hippocampus with no damage to the surrounding structures as evidenced by FDG-PET.

Since both the MBs and the right hippocampus were compressed, it is difficult to disentangle their respective roles in the production of the amnesic syndrome. We have a few arguments favoring a role for the MBs. First, the lack of asymmetry between verbal and nonverbal memory impairment argues against a functional role of the right hippocampus. Second, our region-of-interest analysis showed that FDG uptake in the right hippocampus before and after surgery was basically unchanged. However, these arguments do not completely rule out a potential role of the right hippocampus, since there is also evidence against the material-specific hypothesis and we obtained only 1 FDG scan preoperatively and postoperatively. Postsurgically, our patient regained full memory functions. At the same time, increased activation was observed in the anterior thalamic nuclei and the supplementary motor area and pre–supplementary motor area, consistent with results by others. Together, the data suggest that the amnesic syndrome was secondary to a massive mammillothalamic tract compression. Our case further suggests that the clinical prognosis of decompressing the mammillothalamic tract is excellent, even in cases of massive compression.

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REFERENCES