Amnesia after a discrete basal forebrain lesion

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Abstract
Destructive lesions of the basal forebrain are often associated with memory impairment and this structure is thought to contribute to memory function by providing a cholinergic input to critical structures associated with memory such as the hippocampus and amygdala. In previously reported cases of amnesia associated with damage in the basal forebrain, multiple neuroanatomical regions were damaged, and the critical lesion responsible for amnesia has not been identified clearly. We report a patient who developed primarily anteriorgrade amnesia after clipping of an unruptured anterior communicating artery aneurysm. Postoperative magnetic resonance imaging showed a discrete lesion, centring in the right diagonal band of Broca and including the anterior hypothalamus, septal nucleus, lamina terminalis, and paraterminal gyrus, and an indiscrete patchy lesion in the corresponding area on the opposite side. The nucleus basalis of Meynert was minimally affected and the diencephalon was not damaged. Single photon emission computed tomography showed marked hypoperfusion in the midline frontobasal region corresponding to the MRI lesion and hypoperfusion in the hippocampus bilaterally. It is concluded that disconnection of the pathway between the diagonal band of Broca and the hippocampus contributed to memory impairment.

Keywords: diagonal band of Broca; amnesia; time tagging

The amnesic syndrome has been found in patients with relatively discrete lesions in several cerebral sites including (a) the medial temporal lobes including the hippocampus, (b) median thalamic nuclei, (c) anterior thalamic nuclei, (d) basal forebrain, (e) fornix, (f) mammillary bodies, and (g) retrosplenial cortex. The basal forebrain has been considered to contribute to memory function by way of the pathways between nuclei of the diagonal band or the septal nucleus and the hippocampal region, thus providing a cholinergic input to the hippocampus. In most previously reported cases of amnesia associated with basal forebrain lesions, multiple neuroanatomically identified areas were damaged, and it has been difficult to identify the minimal lesion necessary to produce an amnesic syndrome except for patients in whom basal forebrain lesions were relatively well circumscribed.

We describe a patient who developed anteriorgrade amnesia as the result of a discrete lesion in the basal forebrain after clipping of an unruptured anterior communicating artery aneurysm.

Case report
A 61 year old right handed high school teacher, who had taught science for more than 35 years and had had good memory function, experienced a sudden onset of weakness in the right upper and lower limbs in July 1993, but recovered the next day. He was admitted to a hospital elsewhere and underwent MRI, which showed a small haemorrhage in the left external capsule. He underwent cerebral angiography, which showed an aneurysm 5 mm in diameter in the anterior communicating artery. He underwent surgical clipping of the aneurysm one month later. Immediately after the surgery, he developed disorientation and agitation. Although he became alert and oriented to person and place one month after the operation, he remained disoriented to date. He apparently had memory impairment at that time, but the details are not known to us. He had no motor or sensory deficits.

He visited the neurology outpatient service of the Osaka University Hospital four months after the operation. He was alert and did not have any focal neurological deficits. He did not seem to appreciate the graveness of his memory impairment. His language comprehension and expression were intact. He could repeat seven digits and perform serial subtraction without difficulty. He could learn five objects but could recall only one of them after five minutes. During the interview, his recall was aided by cuing. Recall of his remote personal history was relatively preserved but the dates were mixed up, and he mistook recent personal episodes as remote ones. He did not have confabulation and remained silent when he could not answer a question. An EEG showed no abnormality.

NEUROPSYCHOLOGICAL ASSESSMENT
Formal neuropsychological testing was performed several times over 36 months, and two series are presented here, the one at the initial...
evaluation in February 1994 and another 24 months later (tables 1 and 2).

First assessment
At the time of the first evaluation in February 1994, he was alert, cooperative, and oriented to person and place. His verbal IQ and non-verbal IQ fell within the normal range. The results of the Wisconsin card sorting test, trail making test, word fluency, and go/no go task to measure the frontal lobe function were normal. Performance on all other neuropsychological measures fell within the normal range.

He obtained a verbal memory quotient of 69, whereas the non-verbal memory quotient was 104 on the Wechsler memory scale-revised (WMS-R). He clearly showed mismatch between verbal and non-verbal memory function. He was able to repeat seven digits forward and five digits backwards, indicating an intact attention span. Although he could learn four out of 10 easy paired associates, he could not learn any of the difficult word pairs. He was impaired on a word list learning task, recalling no more than nine out of 15 words. Although his recall of the word list dropped to zero after performing an interfering word list, he had recognition of 40 out of 50 words presented in a
yes/no recognition paradigm. His recent non-verbal memory was relatively preserved. On the visual reproduction portion of the WMS-R, he obtained a non-verbal memory quotient of 104, which fell within the normal range. Immediate and delayed recall of the Benton visual retention test were moderately impaired. Memory for past public events was examined using the method described by Fukatsu et al and was within the normal range for the 1950s to the 1980s. He showed a limited period of retrograde amnesia for events before his operation. With the help of his family, a list for personal autobiographical memory was constructed with questions about significant personal events (for example, marriage, death, children’s accomplishments). Although he could recall almost all events, he could not tag these events in sequence.

Follow up assessment
He was assessed in February 1996, 30 months after surgery. He showed mild improvement in memory performance, predominantly in non-verbal memory (tables 1 and 2). Immediate and delayed recall of the Benton visual retention test fell within the normal range. Although his verbal memory quotient on the WMS-R increased from 69 to 82, it remained impaired compared with his non-verbal memory quotient of 108. He achieved normal maximal learning of a word list learning task, but he continued to show severely impaired delayed recall. On memory for past public events and personal autobiography, he could recall each event fairly well. However, he could not arrange these events in sequence and mistook the latest event for one having occurred years before.

NEUROIMAGING EXAMINATION
Brain MRI with a 1.5 Tesla superconducting system (General Electric), disclosed a small discrete lesion in the basal forebrain slightly to the right of the midline in February 1996 (fig 1). Mapping of the lesion by superimposing on two schematic coronal sections from the Haines neuroanatomical atlas indicated that the lesion was in the basal forebrain including...
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by the clinical finding and the result of the amnesiawith preserved cuing may be due to both anterograde and retrograde memories, his markedly improved recall and recognition of timetagging of this information. Because cuing patient showed different ability to learn information correctly, our relation between multiple components, and episode, computation, and recoding of the availability of contextual memory is thought to This may be due to the difference in the temporal tagging of information. The clinical presentation was similar to the previously reported cases of amnesia after damage to the basal forebrain and adjacent structures. As reviewed previously, those cases were mostly associated with a ruptured anterior communicating artery aneurysm. However, previously reported cases did not have such a discrete lesion in the basal forebrain as our patient, whose anterior communicating artery aneurysm was unruptured.

Our patient could learn test items in the memory evaluation batteries, but he had difficulty in recall and could not develop a proper time sequence for this information even when he could recall. This was striking and was different from memory impairment described in patients HM and DRB, whose failures were in learning both types of information. The availability of contextual memory is thought to depend on the recording of separate information that is composed of a perceived episode, computation, and recording of the relation between multiple components, and time tagging of this information. Despite his ability to learn information correctly, our patient showed difficulty in his daily living. This may be due to the difficulty in forming time tagging of this information. Because cuing markedly improved recall and recognition of both anterograde and retrograde memories, his amnesia with preserved cuing may be due to a deficit in retrieval. This notion was supported by the clinical finding and the result of the Rey’s auditory verbal learning test.

It is difficult to ascertain the minimal lesion necessary to cause the amnesic syndrome associated with a basal forebrain lesion, because of the extent and variability of the previously reported lesions. There are only two patients in the literature who had a relatively well-circumscribed lesion. Damasio et al described a patient (case 1) who had haematomas in the left gyrus rectus and midline septal nuclei, who subsequently underwent surgical clipping of the ruptured left anterior cerebral artery aneurysm. The extent of the lesion was delineated by CT. Another patient described by Morris et al had a low grade glioma near the posterior extent of the right gyrus rectus involving the lamina terminalis and developed severe amnesia postoperatively. Postoperative MRI showed a discrete lesion involving the right diagonal band of Broca, preoptic area, anterior hypothalamus, lamina terminalis, and paraterminal gyrus. There are some similarities and dissimilarities among these two cases and ours. Damasio et al found a mismatch between auditory-verbal and non-verbal memories as we did. On the other hand, the patient described by Morris et al had a lesion predominantly on the right side, but did not have such a mismatch. Our patient also had a lesion mostly to the right of the midline on MRI, but possessed an area of profound hypoperfusion in the midline frontobasal region expanding to both sides corresponding to the lesion on the MR image (fig 3). In addition, the isotope uptake in the hippocampus was below 50% of the maximal isotope uptake in the cerebellum bilaterally, but slightly more reduced on the left side (fig 3).

Discussion

In summary, our patient showed (a) anterograde amnesia, (b) mild retrograde amnesia for both semantic and personal episodic information, (c) benefit from cuing, and (d) defects in the temporal tagging of information. The clinical presentation was similar to the previously reported cases of amnesia after damage to the basal forebrain and adjacent structures. As reviewed previously, those cases were mostly associated with a ruptured anterior communicating artery aneurysm. However, previously reported cases did not have such a discrete lesion in the basal forebrain as our patient, whose anterior communicating artery aneurysm was unruptured.

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the diagonal band and the hippocampus. This idea is supported by the result of SPECT showing a lesion in the basal forebrain and reduction of blood perfusion in the hippocampus bilaterally. It is also possible that amnesia caused by a lesion in the basal forebrain with interference of the medial temporal function may develop impairment in the time tagging of information.

We obtained written informed consent to report on this patient.