AMNESIA IN MAN FOLLOWING TRANSECTION OF THE FORNIX

A REVIEW

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SUMMARY

Published accounts of the effects of fornix damage on memory in man are critically evaluated. Most weight is given to cases of surgical transection of the fornix, though other causes of fornix damage are briefly discussed. It is concluded that fornix transection causes amnesia.

INTRODUCTION

The role of the fornix in memory is of central importance in understanding the functional basis of amnesia. There is ample modern evidence that amnesia is often associated with damage to either the hippocampus (Cummings \textit{et al.}, 1984; Zola-Morgan \textit{et al.}, 1986) or the mamillary bodies (Mair \textit{et al.}, 1979; Dusoir \textit{et al.}, 1990). The fornix provides a powerful connection between these two structures, projecting from the subiculum of the hippocampus to the medial mamillary nuclei (Swanson and Cowan, 1975). Delay and Brion (1969) put forward the hypothesis that a single functional pathway subserving memory runs from the hippocampus through the fornix to the mamillary bodies, and that the same functional consequence, namely amnesia, results from interruption of this pathway at any of its stages. To assess the adequacy of this hypothesis, the effects of direct damage to the fornix must be established. Experimental studies in rhesus monkeys have shown that surgical transection of the fornix produces memory impairments analogous to those of human amnesic patients (Gaffan, 1991\textit{a,b}). In man, circumscribed lesions of the fornix are uncommon but the available reports on the effects of such lesions on memory clearly deserve careful study, even though the older of these reports are often lacking in detail. Since we know of no existing secondary source which adequately assesses this evidence, we present here a brief review of it.

Amnesia has often been attributed to fornix damage in patients with tumours (by Rudge and Warrington, 1991, for example), wounds (Grafman \textit{et al.}, 1985), vascular accidents (Brion \textit{et al.}, 1969) or other degenerative processes (Grünthal, 1964). Because of the widespread damage additional to fornix lesions in such cases, this evidence is not so conclusive as the evidence from discrete surgical transection of the fornix, which we review in detail below; nonetheless, it is clearly consistent with Delay and Brion's hypothesis. However, in a patient described by Woolsey and Nelson (1975), destruction

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of the fornix by a tumour was reported to have had no effect on memory. Woolsey and Nelson found at autopsy that a tumour had destroyed 80% of the fornix bilaterally in a patient who, according to his sister, had shown no memory impairment. This observation cannot be taken as conclusive, however, since the patient had rapidly growing tumours and was in a state of profound mental confusion, or worse, for the last 10–14 days of his life; much of the fornix damage observed at autopsy may therefore have been produced at a time when not even the most informal assessment of memory could have been made. Thus, the evidence from patients with widespread lesions involving the fornix is consistent with the hypothesis that fornix damage produces amnesia, but is not conclusive. We turn now to the evidence from patients with surgical transection of the fornix.

A number of patients with intractable temporal lobe epilepsy have been operated upon to transect the fornix unilaterally or bilaterally. The rationale for this surgery, first put forward by García Bengoechea et al. (1954), was to interrupt the spread of epileptic activity through the fornix from the hippocampus in patients thought to have a primary site of epileptic discharge in the hippocampus. This procedure appears to be no longer carried out, however, since the effects on epilepsy were on the whole disappointing (Sonnen et al., 1976; Marosséro et al., 1980). In assessing the reported effects on memory in this patient group the difference between unilateral and bilateral transection is crucial. Łuczywek and Mempel (1980) and Oxbury and Oxbury (1989) have shown that, in patients with a diseased epileptogenic hippocampus, unilateral ablation of the hippocampus itself does not impair memory by comparison with the patient’s own pre-operative ability and can, if it alleviates epilepsy, even improve it; furthermore, the pre-operative memory ability of such patients is poorer than normal. These effects are understandable functionally, since epileptogenic hippocampal tissue shows morphological abnormalities which suggest that its normal function is severely impaired while cells are still alive and capable of generating epileptic discharge (Scheibel et al., 1974). Unilateral transection of a fornical column which projects from a hippocampus in this diseased state should equally be expected not to produce a memory impairment. Bilateral transection of the fornix in such patients, on the other hand, should be expected to impair memory, according to Delay and Brion’s hypothesis, since this procedure will affect the output of the normal hippocampus in the other hemisphere. As is well known, a bilateral ablation including the hippocampus itself in a single epileptic patient produced such a severe memory disorder that the procedure was not repeated for the alleviation of epilepsy in spite of its success in this regard (Scoville and Milner, 1957).

Surgical transection of the fornix has also sometimes been necessary in the course of removing a colloid cyst from the third ventricle. These patients must be considered separately from the epileptic patients. Colloid cysts always originate in the taenia choroidea at the interventricular foramen, rather than in nervous tissue (Nitta and Symon, 1985), and there is therefore no reason to suspect neural pathology in the hippocampus in these patients. Thus, there are no grounds for expecting unilateral fornix damage to be without effect on memory in these patients (unlike the epileptic patients), although on general grounds one might expect the effect of a unilateral transection to be less severe than that of a bilateral transection.

Thus the functional effects relevant to the Delay-Brion hypothesis concern memory disorder following bilateral fornix transection in patients with temporal lobe epilepsy,
and memory disorder following either unilateral or bilateral fornix transection in colloid cyst patients. These are reviewed in turn below. We begin with the colloid cyst patients, since they present the clearer picture.

**Fornix Damage in the Removal of Colloid Cysts**

Colloid cysts need to be removed from the third ventricle immediately inferior to the fornix, and this removal is accomplished surgically by an approach into the lateral ventricle either through the corpus callosum or through the frontal lobe. In order to remove the cyst the surgeon may then sometimes have to sacrifice the fornix either unilaterally or bilaterally. Two descriptions of single cases (Sweet *et al.*, 1959; Christiansen, 1971) have reported that the surgeon intentionally transected the fornix bilaterally in order to gain access to the cyst. Both of the patients had severe memory disorder as a result of this procedure. Cameron and Archibald (1981) reported severe memory impairment following intentional transection of the left fornix in removal of a colloid cyst, also in a single case. Carmel (1985) described 2 patients in whom the surgeon intentionally transected the right fornix. Again, a severe memory impairment was observed in these patients. Equally important evidence indicates that removal of a colloid cyst does not of itself entail memory disorder, if the fornix is not damaged. Carmel (1985) observed no memory impairment in a large series of patients in whom fornix section had not been necessary in removing the cyst. Nitta and Symon (1985) reported that in 36 cases they had never found it necessary to transect either of the columns of the fornix, and that the surgical procedure did not produce memory disorder in any of these patients.

This evidence was recently further strengthened in a study by Gaffan *et al.* (1991). They used magnetic resonance imaging to demonstrate that 2 patients who had become amnesic as a result of an operation to remove a colloid cyst did indeed, as suspected, have fornix damage. The scans further confirmed that no other damage was visible except for the incision in the corpus callosum. Furthermore, the memory impairments of these 2 patients were documented by formal psychological tests (Gaffan *et al.*, 1991; Hodges and Carpenter, 1991).

Memory deficit following colloid cyst removal was also attributed to fornix damage by Jeeves *et al.* (1979). The only negative instance comes from a paper by Cairns and Mosberg (1951), one of the most influential of early reports on colloid cyst removal. The patients in this report are described as having no serious memory impairment as a result of surgery. The surgical descriptions make it clear that the fornix was transected in one of the patients in the course of the operation to remove the cyst; it is not clear whether the transection was unilateral or bilateral. No formal memory tests were conducted. Cairns and Mosberg were among the first to establish that a colloid cyst (which is itself an immediately life-threatening condition in the patients from whom it is removed) could be safely removed without life-threatening consequences, and it may have been that a memory impairment seemed unimportant in this context. Furthermore, before the impact of Scoville and Milner's report on hippocampal damage and amnesia in 1957, surgeons will not have been alert to the possibility that fornix transection could cause memory disorder; it is possible that an isolated case of memory disorder was attributed to some other cause.
A report by Dott (1938) has also been cited (by Garcia-Bengochea and Friedman, 1987) as showing that fornix transection in the course of colloid cyst removal does not necessarily result in memory impairment. However, each of the 2 patients described in Dott’s report had a large hypophyseal tumour invading the third ventricle, not a colloid cyst. It appears from the detailed description of the operations on these 2 patients that the tumours had destroyed the mamillary nuclei bilaterally, in which case no further memory impairment would be expected from transecting the fornix, according to Delay and Brion’s hypothesis. It is not clear whether these 2 patients had memory disorder before surgery, since Dott’s account is primarily concerned with their vegetative disorders.

**BILATERAL FORNIX TRANSECTION IN PATIENTS WITH TEMPORAL LOBE EPILEPSY**

The fullest review of this evidence was presented by Garcia-Bengochea and Friedman (1987). As far as we know, no new reports on this patient population have been published since Garcia-Bengochea and Friedman’s review appeared. As explained above, the distinction between unilateral and bilateral fornix transection is crucial for the interpretation of effects on memory in this patient population, since unilateral fornix transection in a hemisphere with a diseased hippocampus should be expected to have no effect on memory; Garcia-Bengochea and Friedman tabulated separately reports of bilateral and unilateral fornix transection. According to their account there were 142 published cases of bilateral fornix transection in epileptic patients, of whom none had shown persistent memory loss. We shall show that this conclusion, the most authoritative yet available, is not so strong as it appears. For each of these patients we need to ask what is the evidence that the fornix was transected bilaterally, and what is the evidence as to the effects on memory. This procedure is not as lengthy as it sounds, however, since many of these 142 patients can be immediately discounted from further consideration in the manner described in the following paragraph.

The 142 patients in question are listed in Table 1 of Garcia-Bengochea and Friedman’s review (1987), and come from a total of 9 sources. In alphabetical order, the sources are as follows. (1) Barcia-Salorio and Broseta are said to have described 42 such patients; in fact, these all had unilateral forniciotomies, ipsilateral to the presumed epileptogenic hippocampus (Barcia-Salorio and Broseta, 1976, p. 176). (2) Bouchard is said to have described 50 such patients; in fact, these all had unilateral forniciotomies, and the report contains a full discussion of the criteria for deciding which fornix to section (Bouchard, 1971, p. 61). (3) García-Bengochea et al. (1954, 1956) are said to have described 18 such cases; this is true. (4) Guixot is said to have described 2 such patients, but no reference is given. (5) Hassler and Riechert are said to have described one such patient. Hassler and Riechert’s report (1957) describes the severe amnesia produced by bilateral fornix section in this patient, which can be described as not persistent only in the sense that the patient subsequently died. (6) Marossero et al. are said to have described 4 such patients. This report makes no comment on the mental state of these patients or the effects of the surgery, beyond the statement that ‘the results have been disappointing’ (Marossero et al., 1980, p. 148). (7) Mundinger et al. are said to have described 3 such patients; in fact, 2 of these are described as having developed Korsakoff-like memory...
deficits (Mundinger et al., 1976, p. 178). (8) Sonnen et al. are said to have described 3 such patients; in fact these had ‘bilateral amygdalectomy and ipsilateral fornicomotomy’, i.e. ipsilateral to the presumed epileptogenic lesion (Sonnen et al., 1976, p. 216). (9) Sugita et al. are said to have described 20 such patients; these were indeed described as not showing memory problems, and the surgical intention had been to produce a bilateral lesion of the fornix (Sugita et al., 1971).

Thus, only two reports (those of García Bengochea et al. and of Sugita et al.) described patients with intended bilateral fornix lesions as having no memory impairment. The surgical methods in these two reports were very different from one another. Sugita et al. made stereotaxically guided heat lesions of the fornix. They describe the difficulty of achieving complete fornix transection by this means. Furthermore, one of their patients came to autopsy and the result (illustrated in Sugita et al., 1971, p. 46) clearly shows that more than half of the fornix was spared. Thus the likelihood is that many or all of Sugita et al.’s patients will have had substantial sparing of the fornix. García Bengochea et al., on the other hand, made bilateral fornix transections by open surgery, and the presumption must be therefore that the fornix was indeed transected bilaterally in all of their patients. Thus, García Bengochea et al.’s observations are much more critical than those of Sugita et al.

Turning now to the evidence that these patients had unimpaired memory, this was based simply on a clinical impression. The full extent of García Bengochea et al.’s account (1954, p. 177) of the side-effects of bilateral fornix transection through a transfrontal approach is: ‘So far, in none of the 12 surviving cases there has been any unfavorable neurological or psychiatric sequela.’ Sugita et al.’s is equally brief. These operations were of course performed in an attempt to alleviate the very serious effects of intractable severe epilepsy, and the cognitive effects of the surgery were not the prime concern. Thus, García-Bengochea and Friedman (1987, p. 362) acknowledge that their inferences from the epileptic patients could be open to certain objections, ‘especially those concerned with detection and quantification of memory deficits’.

Nonetheless, a lack of formal neuropsychological testing cannot by itself explain the belief of García Bengochea et al. that bilateral fornix transection did not lead to memory impairment in their patients. If these patients had been similar to the colloid cyst patients described above, then the patients’ memory disorder would have been obvious without formal testing. However, it is by no means necessary to conclude that the evident dissimilarity between these two groups of patients was in their degree of memory impairment. In assessing effects on memory we should not forget that García Bengochea et al. (1954) made no claim that these surgeries alleviated behavioural or mental disorders in their patients. As candidates for what Scoville and Milner (1957, p. 11) described as ‘frankly experimental’ surgery, these patients would have been very ill indeed, not only in terms of the frequency of seizures but also in terms of the neurological and behavioural consequences. Almost all of the papers in the collections by Gillingham et al. (1976) and Umbach (1971) allude to the profound emotional and intellectual disorders which longstanding, severe and intractable temporal lobe epilepsy led to in their era, often including psychotic symptoms, mental retardation and uncontrollable aggressiveness. It cannot have been easy to detect clinically a specific memory impairment against this background. Indeed, in García Bengochea et al.’s second report on their patients (which is in most other respects simply a republication in Spanish of their first
report) the difficulty is specifically acknowledged: ‘No se han observado cambios en la memoria, pero éstos eran difíciles de evaluar, ya que la mayor parte de los pacientes presentaban cuadros psicóticos más o menos avanzados’ (Changes in memory have not been observed, but these were difficult to evaluate, because the majority of the patients presented more or less advanced psychotic syndromes) (García Bengochea et al., 1956, p. 156). In the same way, the effects of bilateral hippocampal ablation on memory were not at first detected when the ablations were made in an unsuccessful attempt to alleviate schizophrenia; they became obvious only when the ablation produced a dramatic alleviation of epilepsy (Scoville and Milner, 1957). We presume that if bilateral fornix transection had had as beneficial an effect on temporal lobe epilepsy and its consequences as bilateral hippocampal ablation did, its effects on memory would have been obvious to García Bengochea et al.

Clearly, no strong conclusion can be confidently drawn from the available evidence on memory after bilateral fornix transection in epileptic patients. With little verification available of the extent of the lesions, and in the total absence of psychometric data, it is impossible in retrospect to weigh the negative judgement of García Bengochea et al. (1954) and Sugita et al. (1971) against the positive judgements of Hassler and Riechert (1957) and Mundinger et al. (1976). The best that can be said is that of all these reports on fornix transection in epileptic patients, Hassler and Riechert’s paper stands out in its detailed and thoughtful consideration of all relevant aspects of the case presented, including the only published verification of a complete bilateral fornix transection in an epileptic patient.

CONCLUSION

We have considered the evidence from surgical transection of the fornix in detail, and we have documented the reasons for giving little weight to the mutually contradictory reports on the effect of this procedure in epileptic patients. Much clearer evidence comes from surgical fornix damage in patients with colloid cyst removal, and this evidence gives strong support to Delay and Brion’s hypothesis (1969).

REFERENCES


Zola-Morgan S, Squire LR, Amaral DG (1986) Human amnesia and the medial temporal region: enduring memory impairment following a bilateral lesion limited to field CA1 of the hippocampus. Journal of Neuroscience, 6, 2950–2967.

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