EDITORIAL COMMENTARY

What basal forebrain lesions cause amnesia?

The evidence that amnesia in humans is caused by lesions of the medial temporal lobes is very strong, but there is considerably less evidence that basal forebrain lesions can also cause amnesia. Although there is a large body of animal data indicating that basal forebrain structures play a part in memory, the human evidence is limited to a few case studies. One feature of the patients reported on is that although they have fairly specific brain damage, there is invariably damage to more than one structure so that strong inferences about the effects of very focal damage on memory are difficult or impossible. Most attention has been focused on the corticopetal, mainly cholinergic system, which comprises the septum, the diagonal band of Broca, and the basal nucleus of Meynert (see Phillips *et al.*¹). Damage to this system might plausibly be related to amnesia because it will reduce the cholinergic modulation of medial temporal lobe and neocortical structures implicated in the storage of those types of information for which explicit memory is poor in amnesic patients. There are, however, two other parts of the basal forebrain: the extended amygdalae and the ventral striatopallidal system. The paper by Goldenberg *et al.* in this issue (pp 163–8)² is of particular interest because it reports a case study of a patient with a specific amnesia for verbal material after a vascular incident that destroyed a large part of the left nucleus accumbens as well as causing partial damage to several other structures within the left hemisphere. Importantly, the septum, the diagonal band of Broca, and the nucleus basalis seemed to be undamaged, as did the medial temporal lobes and midline diencephalon. The authors argue that the accumbens lesion was critical in producing the memory deficit and that it acts as a junction between the extended amygdalae and ventral striatopallidal components of the basal forebrain as well as providing corticopetal outputs. It may be of interest that the patient described by Phillips *et al.*¹ had accumbens as well as diagonal band damage.

Several comments should be made about this report. Firstly, SPECT disclosed reduced blood flow to the left medial temporal lobe region, which suggests that this

region was no longer being optimally modulated so that its memory processing functions would be impaired. Chatterjee *et al.*³ provided evidence that reduced blood flow to the right medial temporal lobes could be returned to normal in a patient with damage to the diagonal band by cholinergic augmentation (physostigmine and lecithin treatment) at doses found to improve recall when the dose level was optimised in a procedure that did not use a double blind control. Secondly, however, the modulation in patients with basal forebrain lesions may not be mediated by cholinergic inputs into the medial temporal lobe region or at least not solely by these as there are animal studies which indicate that modulation is mediated not only by cholinergic neurons, but also by noradrenergic and probably other transmitters (see Abe *et al.*⁴). This matter needs careful investigation in patients with memory problems after accumbens lesions where modulation may be dopaminergic (see Podgoraia *et al.*⁵). Finally, as with all other case studies of basal forebrain lesions that produce amnesia, the damage in the patient of Goldenberg *et al.* is not completely focal, which reduces the certainty of their interpretation. Confidence will only increase as the number of similar patients reported on increases. It is vital that such future patients are given a very careful neuropsychological as well as MRI examination so that the specific features of their memory deficit can be accurately characterised.

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- 2 Goldenberg G, Schuri U, Gromminger O, *et al.* Basal forebrain amnesia: does the nucleus accumbens contribute to human memory? *J Neurol Neurosurg Psychiatry* 1999;67:163–8.
- 3 Chatterjee A, Morris MK, Bowers D, *et al.* *J Neurology Neurosurg Psychiatry* 1993;56:1282–9.
- 4 Abe K, Horikuchi M, Yoshimura K. Potentiation by DSP-4 of EEG slowing and memory impairment in basal forebrain-lesioned rats. *Eur J Pharmacol* 1997;321:149–55.
- 5 Podgoraia EK, Galkina OV, Il'iuchenok R, *et al.* The molecular basis of dopamine synapse activity in the mechanisms of learning and amnesia. *Zh Vyssh Nerv Deiat Im I P Pavlova* 1996;46:122–8.