Deep brain stimulation of the fornix

In 2008, Hamani et al reported an unexpected effect of hypothalamic stimulation in a 50-year-old man undergoing treatment for refractory obesity. When stimulation was initiated intraoperatively at the most ventral contact, the patient reported experiencing a sudden sense of déjà vu, recalling a scene from 20 years earlier that became increasingly vivid as stimulation intensity increased. When electrode coordinates were plotted into stereotactic space, the ventral-most contacts were found to be in close association with the fornix [1].

This unintended memory enhancement generated interest in targeting the fornix for the treatment of disorders of memory and cognition. [2] [3] [4] [5] [6].

Support for such a tentative approach may be derived from a single animal study [7] which ascribed improved memory performance to fornix DBS (measured by means of the object location task) in rats, which had received an injection of scopolamine, a muscarinic ACh receptor antagonist, allegedly causing a blockade of ACh receptors in the hippocampus and thus mimicking some aspects of AD. Fornix DBS was reported to reverse the scopolamine action.

Several studies in individuals with Alzheimer disease and in amnesic rats have demonstrated that DBS targeted to the fimbria-fornix, the region that appears to regulate hippocampal activity, can mitigate defects in hippocampus-dependent memory.

Judging from an extremely small number of cases, the fornix is currently the target most frequently chosen for treating dementia (one phase-I study and one feasibility study). Generally, chronic stimulation was well tolerated, except for sensations of warmth, flushing, and sweating as well as increases in heart rate and blood pressure at higher stimulus voltages (>7 V) in two studies [8] [9].

The neuropsychological results were highly variable both in validity and content, but might be interpreted with considerable reserve as indicating a stabilization of the disease progression after surgery, although there are no hard facts supporting this as yet. The stimulation parameters in both studies are similar with respect to voltage (2.5–3.5 V) and frequency (130 Hz). Pulse width varied between 60 and 90 µs. Although, taken at face value, these results may be seen as encouraging, they are still rather ambiguous. As a consequence, these observations may be spurious and should therefore be contemplated with all due caution. This is particularly true, when the episodic nature of the findings and the extremely small number of cases, defying proper statistical treatment, are factored in (N = 6 and N = 1). This is aggravated by the fact that only open-label designs were used and by the lack of a control groups. Supporting the idea of the fornix being an acceptable target structure, we gave an account of a study investigating the acute effects of DBS of the fornix on specific cognitive performances in patients with intractable epilepsy. This report alleged improved neuropsychological scores assessed with the MMSE during stimulation [10].

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