



## Deep Brain Stimulation in Patients with Traumatic Brain Injury; Facts and Figures

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Deep brain stimulation (DBS) is a functional neurosurgery procedure being performed by inserting two specific pace-making probes into specific deep brain nuclei and sending electrical stimulations in order to suppress or stimulate different nerve groups in the nuclei [1]. Currently DBS has been approved by Food and Drug Administration (FDA) for treatment of essential tremor, Parkinson's disease, dystonia and obsessive-compulsive disorder (OCD) [2]. DBS has also been used in research studies to treat chronic pain and has been used to treat various affective disorders, including major depression; neither of these applications of DBS have yet been FDA-approved [1]. While DBS has proven helpful for some patients, there is potential for serious complications and side effects.

Patients suffering from severe traumatic brain injuries (TBI) have several complications attributable to involvement of deep brain nuclei such as tremor, dystonia, behavioral changes, cognitive impairments and somatic symptoms [3]. According to previous successful results of treatment of such impairments using DBS in other population groups (Primary dystonia, Parkinson disease, Alzheimer disease, Multiple Sclerosis) [1], this idea came into existence

that DBS can also be effective in patients with severe traumatic brain injuries to treat tremor, dystonia and emotional and cognitive impairments. In this regards, some limited studies have been performed with controversial results. In 1990, Tsubokawa and co-workers [4] in Japan reported results of chronic DBS (stimulation target: the mesencephalic reticular formation and/or non-specific thalamic nucleus) in 8 patients with persistent vegetative state (PVS) after severe TBI. They found that chronic DBS was effective in alleviation of EEG patterns and behavioral arousal responses. After months of treatment, 4 (50.0%) patients emerged successfully from PVS and were able to communicate and express their demands by voice [4]. These researchers followed their study and in 2002 they reported their results in 20 patients [mesencephalic reticular formation in 2 cases and centre median nucleus/parafascicular (CM/PF) complex in 18 cases]. Seven of the patients emerged from the PVS, and became able to obey verbal commands. However, they remained in a bedridden state. These 7 cases revealed a desynchronization or slight desynchronization pattern on continuous EEG frequency analysis [5].

In 2007, a group in USA led by Schiff *et*

al. performed the first double-blind alternating crossover study on the subject, the results of which was published in Nature [6]. They demonstrated that bilateral DBS of central thalamus modulates behavioral responsiveness in a patient who remained in minimally conscious state (MCS) for 6 years following traumatic brain injury. They also found that the frequency of specific cognitively mediated behaviors and functional limb control and oral feeding were increased during periods in which DBS was on as compared with periods in which it was off [6]. The interesting point of this study was that they reported favorable results after DBS in patients who has had TBI several years ago [6] while the other studies have performed DBS in those who had recently had TBI [4,5].

Recently Lee *et al.*, [7], has shown that lateral fluid percussion TBI results in the attenuation of hippocampal theta oscillations in the first 6 days after injury, which correlate with deficits in the Barnes maze spatial working memory task. Theta band stimulation of the medial septal nucleus (MSN) results in a transient increase in hippocampal theta activity, and when delivered 1 min prior to training in the Barnes maze, it significantly improves spatial working memory. These results suggest that MSN

theta stimulation may be an effective neuromodulatory technique for treatment of persistent learning and memory deficits after TBI [7]. In the same way, Isaar and colleagues [8] showed that unilateral or bilateral DBS of the ventral intermediate nucleus and bilateral DBS of the globus pallidus internus may be effective and safe treatment modalities for intractable post-traumatic tremor.

Taking all these together, it seems that DBS may be effective in treatment of severe TBI complication and also level of consciousness, although evidence is scarce. Currently there is no large clinical trial on this issue to provide appropriate evidence for clinical practice. In 2011, Ali Rezai started a large clinical trial in the Ohio State University in order to determine the effects of DBS on brain functioning improvement in functional independence, community participation and subjective well-being [9]. The study has not been finished yet and the results have not been published. The cost-benefit of the modality is also important as DBS is an expensive choice of treatment which is not available everywhere [2]. Thus it seems that we should wait until the evidence support the use of DBS in severe TBI.

**Conflict of Interest:** None declared.

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