



## Therapeutic Significance of Frequency of Deep Brain Stimulation in Intractable Epilepsy

Harinder Jaseja<sup>1\*</sup> and Alok Gupta<sup>2</sup>

<sup>1</sup>Consultant, Vellore EEG Center, Gwalior, India

<sup>2</sup>Consultant Neurosurgeon, Artemis Health Institute, Gurgaon, India

\*Corresponding author: Harinder Jaseja, Consultant, Vellore EEG Center, 8, C-Block, Harishanker-puram, Lashkar, Gwalior-474002, MP, India, Tel: 91-751-2631147, E-mail: [dr\\_jaseja@yahoo.com](mailto:dr_jaseja@yahoo.com)

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Deep brain stimulation (DBS) is emerging as a viable alternative therapy in intractable epilepsy (IE), and although the exact mechanism and electrophysiology of its action remain elusive, some neuroscientists even believe that DBS may in near future become a first line treatment for the patients with IE who are not suitable candidates for epilepsy brain surgery.

In addition to the exact placement of electrodes in the target site, the successful outcome of DBS depends largely upon correct choice of its stimulation parameters (especially voltage, frequency, pulse-width and mode of stimulation) and optimal stimulation parameters (SPs) are those that reduce seizures optimally with minimum side effects and minimum consumption of the device-battery. The DBS in the patients with IE is commonly delivered at initial SP settings of 5-6 voltage in the frequency range of 130-180 Hz and pulse width varying from 60-90 microseconds by a monopolar intermittent mode of stimulation (1-min ON and 5-min OFF). The frequency of stimulation (FOS) selected is invariably in the high range for reasons outlined below.

In the authors' opinion, the FOS is of utmost importance in the determination of success and efficacy of the DBS as changes in FOS can potentially exercise maximum impact on the seizure profile (frequency, duration, severity of seizures and interictal epileptiform discharge rates) of the patients. It is generally agreed that analogous to vagal nerve stimulation (VNS), DBS is also effective at high-frequency stimulation (HFS) in reducing seizures [1-3], whereas low-frequency stimulation (LFS) is generally ineffective and can even exacerbate existing seizures [2].

The main objectives of selection of SPs for a successful DBS that have been postulated earlier also [4] are induction of EEG-desynchronization with reduction (or even possibly abolishment) of interictal epileptiform discharges (IEDs). This is in keeping with the generally accepted electrophysiological concept that EEG-desynchronization is associated with seizure resistance and reduction

in the occurrence of IEDs and seizures. It has been suggested that LFS induces EEG synchronization, whereas HFS is associated with desynchronization, which might have a therapeutic effect in epilepsy as it has been found to be effective in both animal models and patients with epilepsy [5,6]; LFS is assumed to have anti-epileptic properties but the efficacy is highly debated [5,6] and from their study [5], the researchers have concluded that HFS at 130Hz is more effective than LFS (5Hz) in affecting excitability in epileptic rats. In 2007, a study by Boex et al. [3] also identified that HFS, but not LFS, was associated with a reduction of the interictal discharges and seizures. In Parkinson's disease also, another neurological disorder characterized by abnormal neuronal synchrony, the usual FOS of the subthalamic nucleus is in the range of 130-180 Hz [7] and in one study [8], FOS at 90 Hz or more yielded the best results, whereas, FOS at 10 Hz or even 50 Hz failed to yield the required clinical effect. From a previous study also [9], the researchers have suggested that the effects of hippocampal DBS depend upon the frequency and topography of stimulation and a patterned stimulation with LFS and HFS resulted in desynchronization and exhibited anti-kindling effects in animal models of epilepsy.

Thus, in view of the above electrophysiological findings, we suggest that the FOS in DBS plays a crucial role in determining the clinical outcome of DBS therapy in IE and the selection of optimal FOS may be based on its ability to induce EEG-desynchronization that can be assessed with a simultaneous EEG monitoring. This is especially in view of the observations that the optimal FOS may vary from patient to patient and therefore require individual settings. Admittedly, larger well-designed prospective studies are recommended that may in the course of time validate the therapeutic significance of the FOS and the utility of EEG monitoring in determining the optimal FOS.

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