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Rapid Eye Movement Sleep: A Predictive Marker of Success and Efficacy of Deep Brain Stimulation in Intractable Epilepsy

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Intractable epilepsy (IE) accounts for a significant proportion (nearly 35%) of epilepsy cases worldwide and still remains a challenge with regard to its management, socio-economic burden and quality of life (QOL).

Deep brain stimulation (DBS) is progressively establishing as an alternative therapy in various neurological disorders not amenable satisfactorily to medication. In IE also, DBS of anterior thalamic nucleus (ATNDBS) has been approved by FDA and several studies have reported its success and efficacy including the randomized SANTE trials [1]. As is common with any therapeutic strategy, ATNDBS also has its own limitations: therapeutic success and efficacy are limited to intractable complex partial seizures with reporting of side effects like depression and cognitive/memory impairment [1].

Sleep and epilepsy are known to be intimately and complexly related with each other [2-4]. Moreover, thalamus plays a functional role in the sleep-wake cycle; hence, ATNDBS is very likely to influence sleep. However, the effects of ATNDBS on sleep in patients with epilepsy (PWE) have remained largely unexplored. This brief paper is aimed at presenting a hypothetical approach to unravel the association of sleep and seizures after ATNDBS in the patients with IE, based upon which prediction of success of ATNDBS in IE can be marked.

Depending upon clinical effects of ATNDBS on seizure-profile (frequency, severity, duration of seizures), ATNDBS invariably requires several programming-sessions before optimal DBS parameters (DBSPs) are finalized that result in optimal seizure control with minimum side effects. An EEG-guided approach to selection of DBSPs has been earlier proposed by the author [5,6] to ameliorate the disadvantages of currently deployed selection-mode of DBSPs like involvement of several sessions, and efficacy limited to intractable complex partial seizures. The basis of the EEG-guided selection mode of DBSPs is the attainment of EEG-desynchronization state inducible by a correct combination of DBSPs. EEG-desynchronization is well documented to suppress interictal epileptiform discharges (IEDs) and epileptic attacks. It has been suggested that the degree of desynchronization is inversely proportional to the likelihood of spatial and temporal summations of aberrant depolarizations [3]. The anti-epileptic influence of vagal nerve stimulation (VNS) is also largely attributed to its desynchronizing effect [7,8]. Similarly, rapid eye movement sleep (REMs), also considered by some researchers as the most potent anti-epileptic state in human sleep-wake cycle [9] owes its anti-epileptic property to the EEG-desynchronization present in REMs. Rapid eye movement sleep exerts its anti-epileptic action against focal interictal discharges, and both focal and generalized seizures [3]; indeed, REM sleep behavior disorder associated with dissociation of its desynchronizing property results in increase in IEDs and epileptic seizures [10,11].

The two most concerning features in an epilepsy patients, more so in patients with IE are the uncertainty and unpredictability of the seizure attacks. Even after treatment-initiation these features continue to prevail in the minds of PWE and adversely affect their QOL including their social interaction and independence.

It is, therefore, proposed that the REMs after ATNDBS, if detected in more than normal amounts (for the age of the patient), whether DBS induced or manipulatively enhanced, can serve as a marker of DBS success and efficacy and to at least some extent, assure the clinicians and patients of successful therapeutic outcome of the DBS that may in turn impact the patients' QOL favorably. For this, a simple polysomnography PSG) before and especially after DBS intervention will aid in the proper assessment of REMs. Even a history of increase in dreaming after ATNDBS can indirectly suggest enhanced REMs, which however, still requires a PSG for confirmation. An enhanced REMs (post ATNDBS) is therefore likely to significantly exercise wider therapeutic spectrum and enhanced control over most types of seizures; increased REMs also may improve memory consolidation and subsequently cognitive impairment reported with ATNDBS. Based on the strong anti- epileptic potential of REMs, pedunculopontine nucleus (PPN) has been recently proposed as a novel target for DBS in IE [12-14] (PPN stimulation enhances REMs); REMs has even been proposed as a biomarker of intractability [15].

Thus, in the author's opinion, the development of a marker of DBS success and efficacy in IE can be a milestone in the future of DBS technique; this would, however, require well designed retrospective and prospective studies.

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