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Can the Clinical Outcome of Deep Brain Stimulation Be Predicted?

Christian Saleh
Paris, France

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is widely considered to be an effective and safe treatment modality for advanced Parkinson disease (PD). STN DBS results in significant motor improvement and concomitant reduction in drug dose. However, over the last decade, neuropsychiatric complications following STN DBS for PD gained increasing attention. Multiple reasons were indicated for their occurrence. Behavioural and emotional alterations were related to the localization of the stimulating contacts, stimulation settings, potential current spread into neighbouring structures, natural disease course, postoperative L-dopa reduction and the patient's presurgical vulnerability to neuropsychiatric disorders. Schneider et al. [1] state in a recently published issue of *Stereotactic and Functional Neurosurgery* that 'affective side effects of DBS, which may have profound effects on post-surgical healing, suicidal tendencies and progression cannot be predicted'. To elucidate this aspect, the authors 'conducted a prospective longitudinal study to identify presurgical variables that predict postsurgical affective symptoms'. Schneider et al. [1] conclude that preexisting psychopathological and motor symptoms can predict postoperative affective side effects of DBS surgery. The authors [1] write that 'motor symptoms were able to predict changes in manic symptoms from pre- to postoperative assessments above and beyond possible changes due to medication, with higher levels of pre-operative motor symptoms leading to larger increases in manic symptoms' and 'higher performance in cognitive flexibility tasks prior to brain surgery was associated with depressive symptoms following the surgery'. Although the study by Schneider et al. [1] is a valuable attempt to better foresee the postsurgical course, it remains questionable in light of the complexity of the DBS procedure and the multitude of factors potentially involved in causing limbic adverse effects if a few presurgical factors are capable of predicting in such a differentiated way the postoperative outcome.

This hypothesis overlooks that postoperative limbic effects are not predictable in carefully selected patients [2], are not avoidable when physiological mapping is applied to increase targeting precision [3–5] and are rarely elicitable with intra-operative test stimulation [5, 6].

Malpositioning of the electrode [5], postoperative electrode migration [5], brain shift [7] and DBS lead movement caused by the magnetic field of the MR scanner [8], surprisingly scarcely

studied factors, have a far greater impact on the postoperative course than the presurgical state of the patient, as they alter the final lead location and the volume of tissue activated [9].

Motor improvement is almost always reported in parallel to neuropsychiatric alterations [10, 11]. This critical clinical observation not only underlines that the STN is modulating motor, cognitive and emotional functions [12, 13] but it also underscores that the currently applied electrode may be inappropriate for selective target stimulation [9, 14].

The difficulty predicting and comprehending DBS-associated neuropsychiatric complications has therefore several fundamental, interrelated main causes: the pathophysiologies of PD and of mood disorders are largely unknown [15, 16], the understanding of the functional anatomy of the basal ganglia involved in 'psychomotor behaviour' [13] remains fragmentary [13, 17], the mechanism of action of DBS continues to be elusive [18] and the applied DBS technology, from the currently applied electrode design [9] to imaging techniques to localize the implanted electrodes [19], remains inadequate.

A recent randomized trial [20] has shown that although DBS is considered a more effective treatment for PD with respect to medical therapy, it is also associated with far more serious adverse effects [21–23].

The considerable amount of conflicting clinical results for the same surgical variable reported in the last two decades therefore raises not only questions as to the predictability of the clinical outcome of DBS that Schneider et al. [1] attempted to address in their elegant study, but it may also raise the question if a treatment that on the one hand is scarcely predictable and on the other hand is associated with the utmost serious adverse effects can still be considered as implicitly safe [24].

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Dr. med. Christian Saleh
 25 bis, rue des Envierges
 FR-75020 Paris (France)
 Tel. +33 67 977 7656, E-Mail chs12us75010@yahoo.com