

Progress in deep brain stimulation of the pedunculopontine nucleus and other structures: implications for motor and non-motor disorders

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Deep brain stimulation (DBS) was introduced in the late 1980s for the treatment of Parkinson's disease (PD). Since the 1990s, other pathologies and anatomical targets have been considered. Increasing impetus to expand the potential role of DBS in the treatment of atypical parkinsonism, essential tremors, dystonia, and Tourette syndrome was provided by advances in the knowledge of neuronal circuits and basal ganglia function, which provided the rationale for justifying DBS in motor disorders. It is undeniable that a great deal of the scientific contributions came from basic anatomical and neurophysiological studies. Undoubtedly, DBS is now considered an accepted neurosurgical therapy for patients failing to respond to medications, but interest has now moved beyond motor disorders to include psychiatric and neurological disorders such as obsessive–

compulsive disorders, depression, epilepsy, schizophrenia, pain and Alzheimer's disease. In addition, in recent years impairment of consciousness has been considered for DBS therapy, especially since an intriguing role in the maintenance of waking of the pedunculopontine nucleus, which is the most recent brainstem nucleus introduced for DBS in the treatment of motor disorders, has been demonstrated.

As the experience with DBS progressed, it appeared that, in addition to the choice of the target according to clinical signs, critical issues for DBS were patient selection, preoperative and postoperative assessment, stimulation setup, and target localization. The latter issue is rather enigmatic, since if on the one hand intraoperative recordings may help in the correct localization of subthalamic or pallidal sites, on the other hand, when trying to localize brainstem structures for targeting, such as the pedunculopontine nucleus, neurons may have degenerated and do not provide a clear mapping of the region reached by the recording electrode. Hence, when implanting brainstem structures for DBS, new neurophysiological approaches are required to identify the targeted region. Finally, some key questions arise: are the effects of DBS the consequence of a focal action on the targeted region, are they the result of modulation of neuronal pathways triggered by stimulation of a favorable distant site, or of a site in which multiple neuronal tracts run close to another?

The collection of papers included in this Special Issue is intended to provide an overview of the application of DBS according to the above-mentioned disorders and the problems that arise. It also includes a number of selected contributions presented by world's leading experts in DBS, as well as the basic physiological issues relevant to this practice. Thus, the issue describes the main results of the International Conference:

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The contributions were subjected to standard peer-review procedures by the Editor of *The Journal of Neural Transmission*. A peculiar characteristic of this issue is that the clinical papers are introduced by specific contributions giving an up-to-date comprehensive view of the anatomofunctional properties of the basal ganglia that underlie the application of DBS in neurological and psychiatric disorders. Thus, we are confident that the collection of papers presented in this Special Issue will provide a timely overview of the use of DBS for motor and non-motor disorders and developing areas of the basic science behind DBS.

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