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Neuropsychological functioning following bilateral subthalamic nucleus stimulation in Parkinson's disease☆

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Abstract

The cognitive effects of subthalamic nucleus (STN) stimulation in Parkinson's disease (PD) have been examined. However, there are no reported studies that evaluate, by incorporating a disease control group, whether neuropsychological performance in surgical patients changes beyond the variability of the assessment measures. To examine this issue, 17 PD patients were tested before and after bilateral STN stimulator implantation, both on and off stimulation. Eleven matched PD controls were administered the same repeatable neuropsychological test battery twice. Relative to changes seen in the controls, the surgery for electrode placement mildly adversely affected attention and language functions. STN stimulation, per se, had little effect on cognition. The STN DBS procedure as a whole resulted in a mild decline in delayed verbal recall and language functions. There were no surgery, stimulation, or procedure effects on depression scale scores. In contrast to these group findings, one DBS patient demonstrated significant cognitive decline following surgery.

Keywords: Parkinson's disease; Neuropsychological assessment; Cognition; Deep brain stimulation (DBS)

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Over the last decade, deep brain stimulation (DBS) has gradually come to be regarded as a safe and effective treatment for medically refractory Parkinson's disease (PD) (Gross & Lozano, 2000). Stimulation of the subthalamic nucleus (STN), in particular, has become very useful as it reduces the spectrum of PD motor symptoms (e.g., tremor, bradykinesia, rigidity, and levodopa-induced dyskinesia), often allows for a reduction in the dosage of antiparkinson medication (Moro, Scerrati, Romito, Tonali, & Albanese, 1999), and has been hypothesized to possibly slow disease progression (Rodriguez, Obeso, & Olanow, 1998). Although there is a rapidly growing literature regarding the motor benefits of STN DBS, the neuropsychological ramifications of this procedure are relatively understudied and the findings available in the literature have been mixed.

Looking at the short-term (3–6 months post surgery) cognitive effects of STN DBS, Ardouin et al. (1999b) reported on a series of PD patients who had undergone either bilateral STN ($n = 49$) or internal pallidum (GPi; $n = 14$) electrode placement. By comparing the presurgical baseline to the postsurgical stimulation-on condition in their combined sample, these investigators found a decline in verbal fluency and improvements on the Trail Making Test (TMT) parts A and B. Post hoc comparisons revealed that on both parts of the TMT, the subset of STN subjects improved whereas the GPi subjects remained the same across conditions. The investigators did not, however, include a measure that might separate the individual effects of the purely motor versus the cognitive components of this task. Depression scores also significantly improved in their STN group. After a similar postsurgical interval, Saint-Cyr and co-workers found that STN DBS adversely affected working memory, speed of processing, nonverbal learning, verbal and nonverbal memory, verbal fluency, and set-shifting, with older patients at particular risk for developing these cognitive impairments (Saint-Cyr, Trepanier, Kumar, Lozano, & Lang, 2000; Trepanier, Kumar, Lozano, Lang, & Saint-Cyr, 2000). Hariz et al. (2000) reported the case of a 53-year-old man with a 10-year history of PD and baseline moderate memory deficits who demonstrated cognitive deterioration postoperatively. This patient's new impairments were such that his ability to execute his activities of daily living was reduced, despite the marked motor improvement he experienced as a result of his bilateral STN DBS. Finally, in a small sample of PD patients who underwent unilateral STN DBS ($n = 3$), two of the three subjects demonstrated minimal cognitive change whereas the third subject declined in verbal fluency, verbal learning and memory, and executive functioning (Morrison et al., 2000b).

Assessment of cognitive functioning at longer follow-up intervals (9–12 months post surgery) has revealed more mixed findings. Some authors report no significant cognitive decline (Burchiel, Anderson, Favre, & Hammerstad, 1999; Limousin et al., 1998; Moro et al., 1999) or only isolated reductions in verbal fluency (Pillon et al., 2000) following bilateral STN DBS. Limousin et al., however, commented that although in most subjects, there was minimal postoperative cognitive change, one of their subjects who demonstrated baseline frontal lobe dysfunction, became even more impaired in this area following surgery. In contrast, the deficits described by Saint-Cyr et al. (2000) in their short-term follow-up evaluation largely persisted at the 12-month follow-up. Although learning ability recovered somewhat, performance on frontal lobe tasks either did not improve or continued to decline. It could be argued that the persistent deficits observed at long-term follow-up were related to Parkinson's disease progression, rather than to the DBS, per se. However, if this were the case, all studies with