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Review Article

A systematic review of the impact of subthalamic nucleus stimulation on the quality of life of patients with Parkinson's disease

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ABSTRACT

The objective of this paper is to systematically and critically review the available literature on the effects of subthalamic nucleus (STN) stimulation on the quality of life (QoL) of patients with Parkinson's disease (PD). A systematic review of the literature published from 1993 to May 2013 was conducted using PubMed, Cochrane Library, MEDLINE, EBSCO host, CINAHL, and CEPS + CETD, in addition to hand searching selected periodicals and checking reference lists. The review included randomized and non-randomized controlled trials, published in English, comparing STN stimulation with the best medical therapy on the QoL of patients with PD. The time over which QoL was evaluated ranged from baseline to 24 months. Two reviewers independently assessed the study quality and the extracted data. Of the over 273 potential studies examined, we identified seven pertinent articles published between 2002 and 2013 involving 1193 participants. Six of the seven studies were randomized controlled trials (RCTs). Almost all reported statistically significant outcomes. All the studies using QoL outcome variables included the Parkinson's Disease Questionnaire-39 (PDQ-39) ($n = 7$) and two also used the Short Form-36 (SF-36) questionnaire ($n = 2$). There was significant improvement in QoL (PDQ-39) up to 6 months following STN-deep brain stimulation (DBS) in three RCTs and in one nonrandomized trial and up to 12, 18, and 24 months postoperatively in one RCT each, compared with no improvement in the medical therapy groups. There was a 22% improvement in the physical summary score on the SF-36 questionnaire versus no change in the drug-only group. The quality of the trials was limited by the potential for bias associated with inadequate concealment, no reported intention-to-treat analysis, and small sample size. Moreover, there were problems in some studies with confounding factors. The main points to emerge from this review of studies on STN-DBS in patients with PD demonstrate an overall positive effect on QoL. Based on these studies, the benefits may last for 2 years. The review clearly highlights the need for well-designed, methodologically standardized outcome measurement research into the effectiveness of STN stimulation in PD.

1. Introduction

Parkinson's disease (PD) is a common progressive bradykinetic disorder that can be accurately diagnosed. It is characterized by severe pars compacta nigral cell loss and accumulation of aggregated alpha-synuclein in specific brain stem, spinal cord, and cortical regions [1]. The crude prevalence rate of PD has been reported to range from 15 to 12,500 per 100,000, and the incidence of PD from 15 to 328 per 100,000, with the disease being less common in Asian countries [2]. There is currently no cure for the disease, but symptoms related to PD can be treated by both medicine and surgery. Since the late 1960s, levodopa and other dopaminergic-based therapies have been the basis of medical treatment for PD. Despite effective control of symptoms, especially in the early stages of the disease, the use of levodopa and other dopaminergic therapies eventually results in motor fluctuations and dyskinesia, side effects that may be equal to or worse in severity than the motor impairment of the disease itself [3]. Given these limitations, surgical therapy has emerged as an additional option for PD treatment and has provided PD patients with improved clinical control of symptoms and/or reduced adverse events.

Conflicts of interest: none.

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Deep brain stimulation (DBS) evolved from experience with thalamotomies for PD in the 1950s and 1960s. Early in surgical therapy, many DBS groups implanted the ventral intermediate (Vim) nucleus of the thalamus target in PD patients. However, this approach gradually fell out of favor with realization that stimulation of the Vim was most effective for upper extremity tremors, with much less measured efficacy for the other cardinal motor features of PD (e.g., bradykinesia and rigidity) [4]. The globus pallidus interna (GPi) emerged in the early 1990s as a potential target for DBS therapy. However, the GPi target was quickly overtaken by the subthalamic nucleus (STN) [5,6], following studies showing that STN lesions were very effective in reducing major motor disturbances in parkinsonian primates [7] and that drastic reduction in medication could be realized in some human cases [8]. At present, STN-DBS is the most common surgical procedure for PD [3].

Because levodopa-responsive parkinsonian symptoms are improved by high-frequency stimulation of the STN [3,9], neurostimulation has become an established treatment for advanced PD with medically intractable fluctuations and dyskinesia. It is typically used after the disease has been present for 11–13 years [10–12] when quality of life (QoL), social adjustment (psychosocial competence) [13], and professional activity are already severely impaired [14].

Several randomized, controlled trials of DBS have confirmed its efficacy [10,11,15,16]. The end points of these trials included QoL, the severity of motor symptoms when the patient was not taking medication, and the number of hours per day spent in the "on" state without dyskinesia. QoL significantly improves in the majority of patients after STN-DBS, but not in all [17]. The reasons for this may be multidimensional, but their identification seems to be important for optimized treatment results [18]. When movement disorders cannot be adequately controlled with available treatments, there may be profoundly detrimental effects on patients' health-related QoL (HRQoL) [19]. Therefore, the focus has shifted to the measurement of patient-based outcomes to assess (1) the impact of the disease and (2) the efficacy of interventions. Moreover, the major patient-based outcome is QoL or HRQoL [20].

Despite a rapid increase in the number of studies on STN-DBS in people with PD, there is some disagreement on the impact of STN stimulation. The New England Journal of Medicine Quality of Life Study revealed improvements in Parkinson's Disease Questionnaire-39 (PDQ-39) scores, including subscales for mobility, activities of daily living (ADLs), emotional well being, stigma and bodily discomfort, after treatment with bilateral STN-DBS [10]. This review seeks to identify studies that provide information about outcomes of STN-DBS in patients with PD, and summarize and compare QoL and other results from these studies with the disease-specific PDQ-39 [21,22].There are two types of HRQoL instruments, namely, generic and disease specific [23]. Generic instruments are multidimensional questionnaires that cover a variety of areas. Therefore, this study used disease-specific and generic instruments as useful tools. They provide more information about the impact of STN stimulation on the QoL of patients with PD.

The aim of this study is to systematically and critically review the available literature on the impact of STN stimulation on QoL outcomes among patients with PD.

2. Materials and methods

2.1. Search methods

A search strategy was developed to identify published studies on the impact of STN stimulation on QoL or HRQoL in patients with PD. An expert panel was established to guide the systematic review process. The search for eligible studies was comprehensive and involved multiple strategies. Data were sought from published studies in English and Chinese language journals. Searches were limited to human-based studies. An initial limited literature search of PubMed was conducted to identify relevant keywords contained in title, abstract, and study descriptions. We used medical subjects headings to select search terms. STN-DBS was first applied for PD in 1993 [24]. Similar strategies were used in searching other bibliographic databases for relevant research articles published between 1993 and May 2013 (Table 1). In addition, we reviewed references from articles identified in the aforementioned searches to include any additional papers related to outcomes of DBS that may have been missed.

Table 1
Electronic databases searched.

Database		Data searched
PubMed	1993 to May 2013	March 2013 to May 2013
Cochrane Library	1993 to May 2013	March 2013 to May 2013
MEDLINE via Ovid online	1993 to May 2013	March 2013 to May 2013
EBSCO host	1993 to May 2013	March 2013 to May 2013
CINAHL	1993 to May 2013	March 2013 to May 2013
CEPS + CETD	1993 to May 2013	March 2013 to May 2013

We used the following terms as keywords: "deep brain stimulation", "subthalamic nucleus stimulation", "neurostimulation", "quality of life", "health-related quality of life", and "Parkinson's disease". The keywords used to search for publications that met the design criteria were "randomized controlled trial/s", "controlled trial/s", "random allocation", "clinical trials", and "random".

The reference lists of all relevant articles were checked. The literature search was carried out on May 31, 2013, and papers were included in the review if retrieved before July 1, 2013.

To identify potentially eligible articles, two reviewers (J.-L.J. and S.-T.T.) screened the titles and abstracts obtained from the electronic search strategy. Retrieved abstracts were further scrutinized to include only studies that had at least 6 months of follow-up time. In addition, authors scanned abstracts to ensure the presence of outcome data, including presurgical and postsurgical QoL or HRQoL scores. If a decision could not be made regarding the eligibility for inclusion, the full text of the article was examined. Full-length articles of all selected abstracts were retrieved and assessed by the same reviewers for the following inclusion criteria.

2.2. Inclusion criteria

2.2.1. Types of studies

The selection criteria were studies restricted to randomized or nonrandomized control trials on the effectiveness of STN-DBS for the treatment of idiopathic PD. Randomized controlled trials (RCTs) provide the best possible evidence on clinical outcomes. If filtering only identified a small number of RCTs, clinical controlled trials could also be included. The use of nonrandomized data required careful consideration of the comparability of the treatment and control groups in those studies. Retrieved abstracts were further scrutinized to include only those studies with at least 6 months of follow-up time.

Excluded from the review were investigations that primarily examined factors that predicted changes in QoL and other systematic reviews relevant to this topic [20,25]. Studies documenting only nonmotor outcomes (e.g., cognitive function) or surgical parameters (e.g., microelectrode recording) were not considered in our review. We also excluded publications if the electrode implantation site was not the STN. Only articles meeting the inclusion criteria were retained for analysis.