Caregiving in Parkinson's Disease and Deep Brain Stimulation

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In Parkinson's disease (PD) patients, the progressive nature of the disease and the variability of disabling motor and non-motor symptoms contribute to the growing caregiver burden (CB) of PD partners and conflicts in their relationships. In advanced stages of the disease, Deep Brain Stimulation (DBS) improves PD symptoms and patients quality of life but the effect of DBS on CB of PD partners seems to be heterogeneous. The CB in the context of DBS framing both pre-, peri- and postoperative aspects aims to be illuminated, and further recognition of caregiver burden in partners of PD patients with DBS will be stimulated.

caregiver burdenParkinson's diseasedeep brain stimulationneuropsychiatric symptomsburden of normalitycaregiver coping capabilitymarital conflicts

1. Introduction

Caregiver burden (CB) has been defined as "the extent to which caregivers perceive that caregiving has an adverse effect on their emotional, social, financial, physical and spiritual functioning" ^[1] and occurs in the context of providing informal care for relatives with chronic diseases. Parkinson's disease (PD) is a complex disorder with increasing disabling motor and non-motor symptoms over time, which results in an increased risk of CB in partners of PD. In advanced stages of the disease, higher symptom severity of PD patients is associated with higher CB of their partners ^[2]. Non-motor symptoms seem to impact CB even more than motor impairment ^[3]. CB can have detrimental effects on the quality of caregiving, as well as the mental health of the caregiver. Therefore, it is pivotal to engage further family members to uncover and reduce CB and prevent premature institutionalization ^{[4][5]}.

In advanced disease stages, device-aided therapies as Deep Brain stimulation (DBS) provide substantial improvement of PD symptoms and quality of life (QOL) [6][7]. It is of interest, whether caregiver also profit from DBS in terms of CB reduction, since DBS might be associated with side effects or postoperative changes of the marital relationship due to the sudden motor symptom improvement in the sense of burden of normality. This review aims to provide a concise overview of factors contributing to CB in PD in the context of DBS.

2. Preoperative Caregiver Burden—DBS Yes or No?

2.1. Caregiver Burden Due to Insufficient PD Symptom Control in Advanced Stages

Optimal control of both motor and non-motor symptoms becomes difficult as the therapeutic window narrows in advanced stages of the disease. Motor symptoms worsen with occurrence of unpredictable motor fluctuations such as peak-dose dyskinesia and wearing-off, as well as gait dysfunction, freezing of gait, postural instability and higher risk of falls. Caregiver burden of PD partners is positively correlated with PD patients motor symptoms, overall disability, and impaired activities of daily living ^{[3][8]}. Beside these motor symptoms ^[9], non-motor aspects as neuropsychiatric PD symptoms with depression, psychosis or impulse control disorders contribute to the caregiver burden of PD partners ^{[3][10][11][12]}. Thus, the burden of the progressive disease increases for both, patient and caregiver, and raises attention to DBS as an effective, interventional therapy.

2.2. Caregiver Expectations of DBS

Subthalamic nucleus deep brain stimulation (STN-DBS) is a well-established therapy for PD and considered even earlier in the course of the disease when the first clinical signs of motor fluctuations and medically refractory symptoms such as tremor appear ^{[7][13]}. DBS treatment is associated with substantial symptomatic relief and maintenance of activities of daily living even in the long-term of about 10 years ^[14]. The lower the preoperative quality of life (QOL), the higher the improvement in QOL after 24 months ^[15]. Therefore, DBS is often considered a "game changer" for both PD patients and their caregivers and raises high expectations of DBS effects on QOL.

As to the great involvement of partners in caregiving, the decision to undergo DBS surgery should take into account the caregivers and patients expectations and fears. DBS represents an invasive operation of the brain with potential intraoperative complications such as intracranial bleeding, infection and the need for electrode revision ^[16], which might elicit fears and concerns in terms of intraoperative adverse events in patients and caregivers. Complication rates are low, but must be disclosed to the caregiver and care recipient. PD patients as well as caregiver fear the idea of "becoming another person" by DBS, so the concept of an individual identity and possible, mostly transient disease- and medication-related mood changes should be discussed prior to surgery ^[17]. ^[18]. One of the most important factors represent unrealistic expectations of beneficial DBS effects, since patient and caregiver might overestimate DBS effects on particular non-responsive symptom complexes as the lack of DBS effects on dopa-resistant features as freezing of gait or speech. The anticipated beneficail effects as well as potential lack of DBS effects must be disclosed to patient and caregiver, since unrealistic, unmet expectations contribute to the postoperative patient and caregiver dissatisfaction and increased CB ^[17].

3. Postoperative Aspects of Caregiver Burden

3.1. Caregiver Burden Outcome after STN-DBS Implantation of PD Dependants

There are unexpected, heterogeneous results of CB outcome after implantation of STN-DBS in PD. Despite improvement in motor function and higher social functioning of PD patients postoperatively, CB was variable and

did not change in all caregivers 6 months after STN-DBS.

There might be several factors contributing to this incongruent development of QOL of patients and caregivers postoperatively:

1. The preexisting neuropsychiatric and medical condition of the caregivers themselves might play a role in the development of postoperative CB ^[19]. Higher age of the caregiver is one important mediator of postoperative CB ^[20]. The caregiver grows older along with the PD patient and might as well suffer from illnesses. Besides, the preoperative Beck Depression Inventory (BDI) score is an important predictor of postoperative CB one year after DBS surgery ^[20]. Thus, the well-being of the caregiver should also be addressed in the context of their PD partners DBS surgery.

2. The postoperative extent of neuropsychiatric symptoms within PD patients significantly influences the CB of their relatives. Postoperatively, CB was shown to be associated with the patients degree of apathy and depression ^[19]. In PD patients and caregivers, postoperative caregiver burden was significantly related to PD patients BDI score (Beck depression inventory), caregiver-rated attentional impulsiveness of PD patients or patients hypersexuality ^[2].

3.Postoperative marital conflicts due to changes of the relationship affect CB. DBS surgery profoundly changes caregiver responsibilities and disease-related symptoms due to the sudden relief of disability. With STN-DBS, social maladjustment as a result of the dramatic improvement of the clinical status and identity challenge can occur as part of the "burden of normality" syndrom ^[21].

4. DBS is a symptomatic, but not disease-modifying therapy, thus in the long- term, disease progression with reemergence of motor symptoms, onset of cognitive impairment and loss of autonomy of PD patients might result in re-occurrence of increased CB ^[22]. This might contribute to the observation that CB increases in caregivers of some PD patients within the first 2 years after STN-DBS ^[23]. Still, long-term observations of CB are scarce and need to be obtained in larger cohorts of long-term caregivers (**Figure 1**).



Figure 1. Pre-and postoperative mediators of caregiver burden of partners of PD patients with DBS.

3.2. Caregiver Burden in Partners of PD Patients with Globus Pallidus Internus Stimulation

The globus pallidus internus (Gpi) is an alternative DBS target for PD patients beside STN implantation. The Gpi is supposed to have a lower risk of dysarthria, neuropsychiatric complications and impaired cognition ^[24]. The discussion of the favourable target in PD is still controversial. There is also scarce information on caregiver burden in Gpi patients ^[25]. In a cohort with 275 DBS patients, including PD patients implanted in both, STN and Gpi, caregiver burden measured by the Multidimensional Caregiver Strain Index (MCSI) was associated with PD patients age at surgery and interval since surgery ^[25]. Overall, QOL increased in these specific DBS patients, whereas CB of the relatives was not regularly improved in the longterm. CB of partners of PD patients with STN and Gpi was mostly reduced shortly after DBS implantation, but increased over time along with disease progression and reduced QOL. Further research in larger cohorts is needed on CB in caregivers of PD patients with Gpi stimulation.

4. Future Caregiving Challenges

DBS research is further advancing and new promising technologies are in the pipeline. Closed-loop systems with beta oscillations as internal biomarkers for independent, self-regulated adaption of stimulation are one example of current technological developments, which might improve PD patient outcome, reduce neuropsychiatric side effects and thus could potentially decrease CB ^[26]. Still, these new systems might lead to increased DBS programming burden, which might be associated with increased CB. Another promising field is telemedicine with remote access for DBS programming ^[27]. Optimization of DBS parameters is often performed only by movement disorders specialists at specific, distant university hospitals, resulting in difficult transport and care coordination ^[28]. Telemedicine has already proven to reduce CB due to more flexible patient treatment and reduction of transportation issues to outpatient clinics. Telehealth with teleprogramming of DBS has become particularly important during the COVID-19 pandemic with overall satisfactory patient experience ^[29].

5. Conclusions

Informal caregivers play an important role in the daily care of PD patients before and after DBS surgery. Caregiver burden does not improve in all caregivers after STN-DBS in contrast to dramatic improvement of motor and non-motor symptoms and quality of life in PD patients. Relevant factors for postoperative CB are caregiver coping capabilities, postoperative onset of neuropsychiatric symptoms of PD patients, marital conflicts and the awareness of the symptomatic nature of DBS therapy. But, there is still a lack of information on long-term caregiver burden and predictors after STN-DBS.

Potential tools to reduce postoperative CB represent "preparedness of the caregivers", which could be protective against postoperative caregivers distress ^[30]. Caregivers should be informed about the specific postoperative aspect of STN-DBS and the potential effect on their own QoL. They should be more intensively integrated into the pre- and postoperative processes. Another option to reduce CB of STN-DBS patients could be cognitive behavioral therapy for caregivers ^[31], which could substantially modify CB prior to and after STN-DBS surgery. Additionally, self-management programs to retain social participation can help the caregiver to maintain well-being during the course of the disease ^{[32][33]}.

In summary, there are heterogeneous results on CB changes in partners of PD patients after STN-DBS or GPI-DBS, but there are therapeutic options available to reduce CB.

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