Deep brain stimulation in movement disorders

PhD thesis

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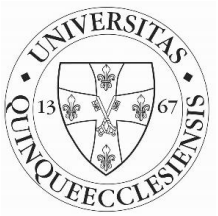

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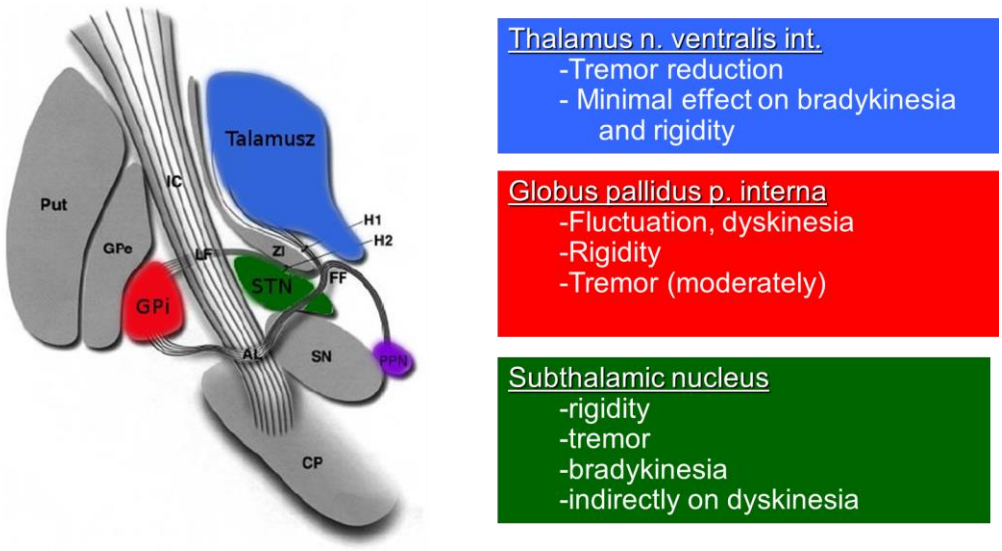
Abbreviations

BDI	Beck Depression Inventory
BFMDRS	Burke-Fahn-Marsden Dystonia Rating Scale
CGI	Clinical Global Improvement
DBS	Deep brain stimulation or deep brain stimulator
ET	Essential tremor
EQ-5D	EuroQol instrument for detecting health outcome
ESS	Epworth Sleepiness Scale
GPi	Globus pallidus pars internus
HRQoL	Health Related Quality of Life
HYS	Hoehn-Yahr Scale or Stage
MADRS	Montgomery-Asberg Depression Rating Scale
MDRS	Mattis Depression Rating Scale
MOCA	Montreal Cognitive Assessment
MDS	Movement Disorders Society
MDS-UPDRS	Movement Disorders Society sponsored Unified Parkinson's Disease Rating Scale
NMS	Non-Motor Symptoms
NMSS	Non-Motor Symptoms Scale
PD	Parkinson's Disease
PDSS	Parkinson's Disease Sleep Scale
PDSS-2	Parkinson's Disease Sleep Scale 2nd version
STN	Subthalamic nucleus
SES	Schwab England Scale
UPDRS	Unified Parkinson's Disease Rating Scale

Introduction and aims

The 28 year-old deep brain stimulation (DBS) revolutionized the treatment of movement disorders including drug-resistant tremor, advanced Parkinson's disease (PD) and dystonia. Based on its high efficacy demonstrated by numerous multicenter, randomized and controlled trials and relatively small side-effect profile, more than 100,000 patients have been undergone DBS implantation worldwide. Approximately 80% of indications for DBS is the pharmacologically not efficiently treatable PD and considerably less patients receive DBS for other movement disorders. The most frequently applied surgical target for PD is the bilateral subthalamic DBS (STN DBS) capable of improving all cardinal symptoms. Besides the symptomatic improvement, STN DBS can also dramatically and permanently extend the ON time and the health-related quality of life (HRQoL). Based on its high efficacy and relatively good side-effect profile, the number of implantations and indications are continuously growing.

The effects of stimulation is highly depend on the stimulation parameters. The high frequency stimulation can temporarily and functionally inhibit, whereas, the low frequency stimulation can functionally aggravate the target area. Depending on the site of electrode implantation, different disorders and different symptoms may be treated. At moment routinely three different targets are established for the treatment of movement disorders. In case of subthalamic deep brain stimulation (STN DBS), the cardinal symptoms of Parkinson's disease (rigidity, tremor, bradykinesia) can be improved. The pallidal deep brain stimulation (internal part of globus pallidus stimulation) is an established treatment option for primary dystonia. In case of thalamic deep brain stimulation (ventral intermediate nucleus stimulation), tremor can be alleviated (e.g. in case of essential tremor).



Stimulation of different target has different symptomatic effect.

At Department of Neurosurgery, University of Pécs more than 350 patients received DBS therapy since 2001. The patient selection and postoperative care of these patients are performed at Department of Neurology, University of Pécs. The focus of my PhD thesis was the clinical examination of these patients treated by DBS.

4.

Bilateral subthalamic deep brain stimulation can improve sleep quality in Parkinson's disease

Recently the non-motor symptoms (NMS) of Parkinson's disease (PD) have been increasingly recognized as a major burden of quality of life. Among the NMS, sleep-related problems are among the most important and troublesome. Although sleep problems can be present in up to 90% of PD patients, only a few study focused on the outcome of different therapeutic options to improve sleep quality.

Because sleep-related problems are certainly multicausal, instruments capable of measuring most domains of sleep-disturbances are needed in the clinical practice. The original Parkinson's Disease Sleep Scale (PDSS) was published in 2002, and it had 15 visual analogue scale-based items. Although PDSS was utilized in many studies, some of its weaknesses were recently identified including the inability to specifically identify and measure the presence and severity of sleep apnea, rapid eye movements sleep behavioral sleep disorder and restless legs syndrome. To overcome these disadvantages, a new scale, the Parkinson's Disease Sleep Scale 2nd version (PDSS-2), was developed and published in 2011.

The PDSS-2 scale is composed of 15 items evaluating three domains. Each domain consists of clusters of five questions evaluating motor symptoms at night, PD symptoms at night and disturbed sleep [9]. The sum of the 15 responses gives the total score of PDSS-2 with the maximum value of 60 points and higher scores meaning more nocturnal disturbance. The reliability, precision and test-retest validity of PDSS-2 is good, making it suitable for measuring changes over a longer period of time. Despite its advantages over PDSS, the assessment of sleep quality before and after bilateral STN DBS with the PDSS-2 has not been reported in the literature; thus, the responsiveness of the PDSS-2 to DBS treatment is unknown. The objective of the present study was to analyze how bilateral subthalamic deep brain stimulation therapy can change sleep disturbances as assessed by the newly developed PDSS-2, Non-Motor Symptoms Scale and the non-motor section of the Movement Disorders Society-sponsored Unified Parkinson's Disease Rating Scale (MDS-UPDRS).

Methods

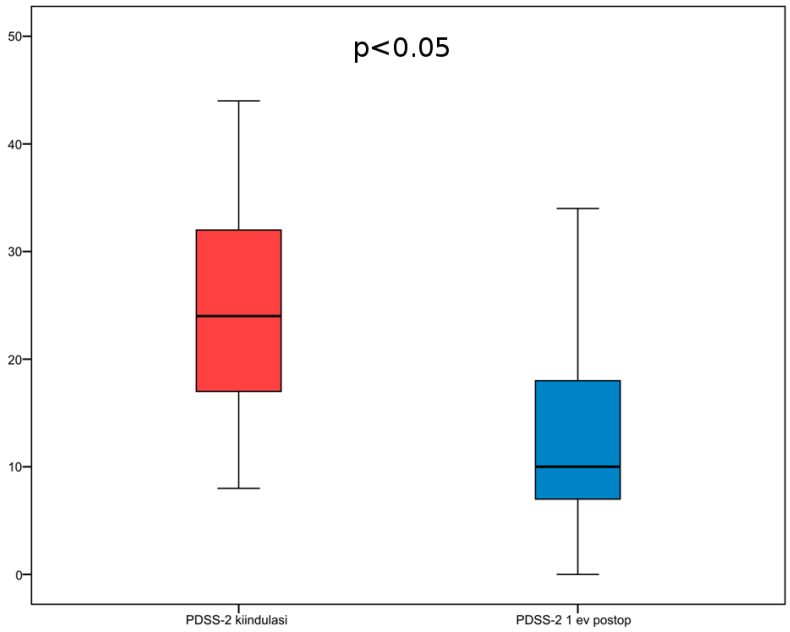
In this prospective study, 25 consecutive patients undergoing bilateral subthalamic deep brain stimulation at the University of Pécs were enrolled (18 males, age: 59.9 ± 8.7 years, disease duration: 11.0 ± 4.8 years). Patients were examined twice: 1 week prior to the DBS implantation (baseline) and 12 months postoperatively. Severity of PD symptoms was globally assessed by the Hungarian validated version of the MDS-UPDRS. The recently published MDS-UPDRS is a validated scale to assess non-motor aspects and motor aspects of experiences of daily living, motor examination and motor complications. Included in the non-motor part, MDS-UPDRS has two items evaluating the presence and severity of nighttime sleep problems and daytime sleepiness. Besides, we also applied the Clinical Global Impression – Severity scale (CGI-S) to evaluate the overall illness severity. To assess non-motor symptoms globally, the Non-Motor Symptoms Scale (NMSS) was also included. Presence and severity of sleep disturbances were specifically measured by PDSS-2. The threshold indicating sleep problems is

11 points for the Hungarian version of PDSS-2. Meantime, daytime sleepiness was assessed by the Epworth Sleepiness Scale with the cutoff value of 8 points. As part of the neuropsychological domain, depression (Beck and Montgomery Depression Scales) and cognitive performance (Montreal Cognitive Assessment, Mattis Dementia Rating Scale and Addenbrook Cognitive Examination) were also examined. Health-related quality of life was measured by the Hungarian validated version of PDQ-39.

Results

While the antiparkinsonian medication was significantly reduced from 814 mg (median, IQR: 564-914 mg) to 420 mg (IQR: 250-594 mg, p=0.001), the total score of MDS-UPDRS improved from 81 (median, IQR: 63-103 points) to 55 points (median, IQR: 46-75 points, p<0.001). Besides, all domains of MDS-UPDRS also improved 12 months after DBS implantation. Health-related quality of life also improved from 29 (IQR: 18-40) to 15 (IQR: 9-28) points (p=0.002) measured by the PDQ-39 Summary Index. With the exception of hallucinatory symptoms and sexual dysfunction, all domains of NMSS improved after DBS treatment.

At baseline, 13 patients reported sleep problems, but 1 year after the DBS implantation only 3 did (p=0.012, McNemar test). Simultaneously, the total score of PDSS-2 decreased from 24 (IQR: 17-32) to 10 (IQR: 7-18) points (P<0.001). Although all domains of the PDSS-2 improved, only 6 items showed a significant decrease after DBS implantation. “Bed sleep quality”, “Restlessness of legs and arms at night”, “Urge to move legs and arms at night”, “Uncomfortable and immobility at night”, “Muscle cramps in arms and legs” and “Tremor on waking” items had significant improvement. Before DBS implantation, 15 patients reported daytime sleepiness, which decreased to 9 patients 1 year after the operation (p=0.032, McNemar test). Meanwhile, the total score of ESS improved from 9 (IQR: 6-13) to 5 (IQR: 4-11) points (P=0.003. Both depression-measuring tools (BDI and MADRS) demonstrated a significant improvement in depressive symptoms; whereas, the neurocognitive performance on neuropsychological tests (MDRS, ACE and MOCA) did not change.



Severity of sleep problems (measured by PDSS-2 total score) had a significant improvement 1 year after deep brain stimulator implantation.

6.

Discussion

The aim of the present study was to identify the beneficiary effects of bilateral subthalamic deep brain stimulation on sleep quality by the utilization of the recently developed PDSS-2. As far as the authors are aware, this is the first prospective study utilizing the PDSS-2 and MDS-UPDRS scales to assess the longitudinal changes in sleep disturbances. Since the PDSS-2 has distinctive items on different aspects of sleep disturbances specific for PD, we were able to analyze what components of sleep responded to DBS therapy. According to our data, RLS-related problems, some nocturnal OFF symptoms, tremor on waking and general sleep quality improved significantly after STN DBS therapy. In the total score of PDSS-2 a median of 58.3% improvement could be detected 12 months after the DBS implantation.

Subthalamic deep brain stimulation not only can decrease the number of patients reporting clinically relevant sleep problems but also improve the general sleep quality. This improvement can be consistently demonstrated by the PDSS-2, NMSS and the MDS-UPDRS. Besides sleep, most domains of non-motor symptoms and the health-related quality of life can be improved by DBS therapy.

Bilateral deep brain stimulation can preserve working status in Parkinson's disease

According to the current guidelines, STN DBS is only indicated in the cases of drug-resistant tremor or severe motor fluctuations unmanageable by pharmacological treatment. The average disease-duration at the time of surgery is around 15 years by when the health-related quality of life (HRQoL) and sociocultural functioning is usually impaired. In general, the longer disease-duration is associated with the more likely appearance of levodopa-resistant and therefore DBS-resistant symptoms and higher impact on the working capability. One of the most important part of patient selection; therefore, is the appropriate timing of surgery. If the DBS implantation is preformed 'too late', the presence and severity of DBS-resistant symptoms (e.g. postural instability, neurocognitive impairment or speech problems) might interfere with or worsen the outcome. On the contrary, if the surgery is performed 'too early', we might operate those patients who could have been otherwise well treated pharmacologically and needlessly expose them with the potential surgical risks. Moreover, with 'too early' operations we might also include some non-idiopathic cases because the atypical features might be hidden in the early stages of the disease course.

Based on the hypothesis that the STN DBS treatment applied at earlier stages of the disease may be superior to the best medication, a multicenter study, called EarlyStim, was initiated. In this prospective study, patients receiving STN DBS had significantly larger improvement in HRQoL (-7.8 improvement on PDQ-38) than patients on best medical treatment (+0.2 point worsening, p=0.002).

Inspired by the results of EarlyStim study, our research group tried to evaluate if STN DBS might have an impact on the working status of PD patients. Our a priori hypothesis was that STN DBS could preserve working capability of patients having an active job at the time of DBS implantation.

Methods

In the present study those patients were included who underwent bilateral STN DBS implantation at University of Pécs and participated in our prospective DBS registry. Patients were eligible for STN DBS surgery if they had the clinical diagnosis of PD in accordance with the UK Brain Bank criteria and at least 5 years of documented disease duration; were under the age of 75 years of age; had parkinsonian motor symptoms or dyskinesia that limited their ability to perform the activities of daily living despite of optimal oral pharmacological treatment.

Out of the group of patients having at least 2 years postoperative follow-up, first we identified those patients who had an active job at the time of their STN DBS surgery and whose age was comparable with the inclusion criteria of EarlyStim study (18-60 years). Having an active job was assessed by direct inquiry. Only regular (>1 day/week), either part-time or full-time work was defined as active job. Altogether 20 PD patients were identified meeting the above mentioned criteria whom we classified into the group of 'Active job'. To perform pairwise comparison, we chose another 24 patients out of our registry who did not have an active job at the time of their surgery ('No job' group) by the utilization of a custom-made program. The automatic selection process was made in a way that for each participant in

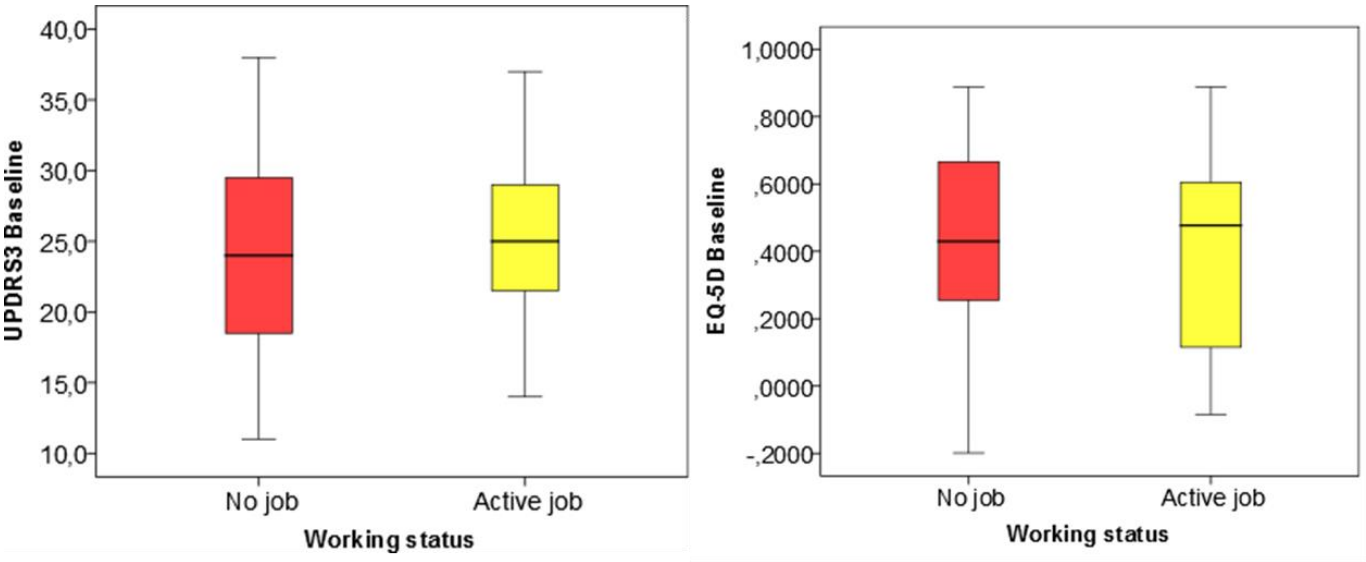
the ‘active job’ group we picked a ‘partner’ who had similar age, disease-duration and fluctuation-duration, and the same disease type. Theses matched patients were considered as the ‘No job’ group. We utilized this automatic pairwise selection process to create a ‘no job’ group with balanced and comparable baseline characteristics to the ‘Active job’ group.

Changes in the working capability and the health-related quality of life were considered as co-primary endpoints. Our primary aim was to identify what portion of young patients having active job at the time of DBS surgery maintained their active job 2 years postoperatively. On the contrary, we also investigated how many young patients not having an active job at DBS initiation returned to work. For evaluating HRQoL, the EuroQol Instrument (EQ-5D) was assessed.

Changes in major motor and non-motor symptoms were considered as secondary endpoints of the study. Severity of Parkinson’s disease was rated by both Hoehn-Yahr Scale (HYS) and Unified Parkinson’s Disease Rating Scale. The most important secondary outcome of our study was the change in UPDRS part III. The secondary outcome measures also included changes in activities in daily living measured by the UPDRS part II and Schwab and England Scale (SES). Each scale was assessed by three times (baseline: 1 week preoperatively, and follow-ups: 12 and 24 months postoperatively).

Results

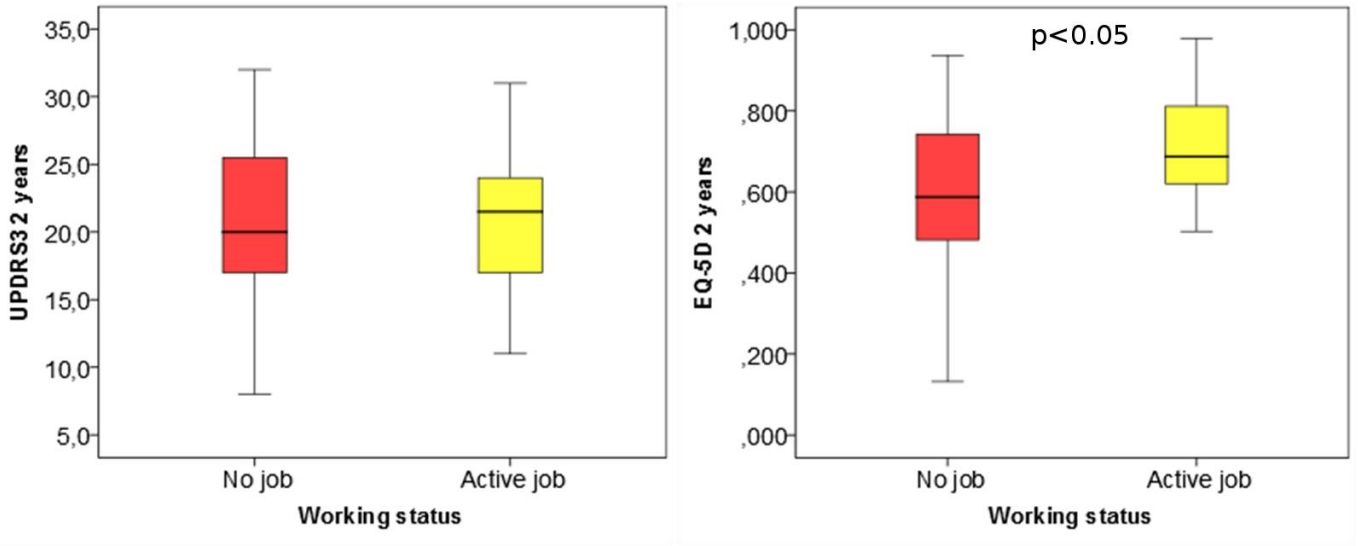
For the final analyses, the data of only 20 pairs were included. Due to the pairwise group selection, the most important baseline PD characteristics were comparable (e.g. age, sex, disease duration, disease type and HYS). The dosage of antiparkinson medication, severity of motor symptoms (UPDRS-III), major neuropsychiatric symptoms and HRQoL were also similar at baseline. At baseline 18 patients had a full-time and two patients had a part-time job in the ‘Active group’.



At baseline (before operation) both the motor symptoms and the HRQoL were similar in the No job and Active job groups.

Two years postoperatively 16 patients from the ‘Active job’ group (80%) still had an active job (full-time job: 8 patients, part-time job: 8 patients). Despite of the comparable baseline characteristics and similar improvements in the motor symptoms and activities of daily living, only a single person (5%) from the ‘No job’ group returned to the world of active work (McNemar test; $p<0.01$). After bilateral STN DBS

implantation, the EQ-5D index significantly improved in both groups. However, 2 years after the operation the ‘Active job’ group members had significantly better HRQoL than the ‘No job’ patients did (0.687 vs. 0.587, medians, Mann-Whitney test, p<0.001). As far as the motor symptoms were concerned (UPDRS-III), both groups had similar baseline characteristics and experienced similar improvement after DBS implantation. Two years after the surgery, the motor severity was still comparable in both groups.



Even though the postoperative severity of motor symptoms (UPDRS-III) are comparable in both groups, those patients who had an active job at the time of the surgery had better health-related quality of life (EQ-5D, p<0.05).

Moreover, the changes in activities of daily living (SES, UPDRS-II) and antiparkinson medication were also similar in both groups.

Discussion

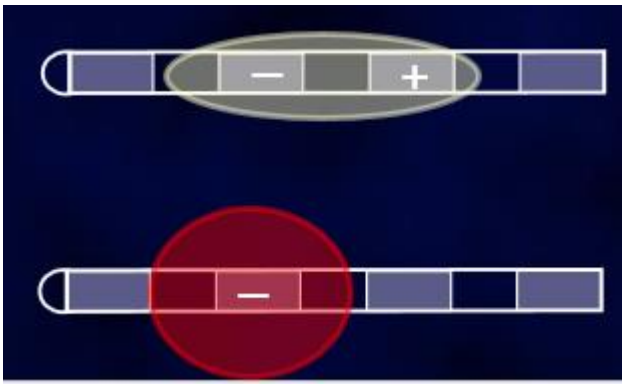
Our primary aim was to evaluate the hypothesized effect of STN DBS on preserving the working capability of PD patients. One of the most important findings of our study was that 80% of patients having an active job at the time of surgery still had an active job 2 years after the DBS implantation. Nevertheless, only a single patient returned to the world of work in the ‘No job’ group after the successful STN DBS therapy. Therefore, we can conclude that DBS might help preserve the working capability if it is performed in patients with active job. On the contrary, if DBS implantation is scheduled after losing the working capability, it might be insufficient to help patients return to work. Patients in the ‘Active job’ group experienced higher improvement in HRQoL than ‘No job’ patients did despite of the similar changes in motor and major non-motor symptoms. This finding might suggest that having an active job at the time DBS surgery might have a beneficial effect on the long-term outcome by being a positive predictive factor. However, further controlled and large multicenter studies are required to support this hypothesis.

10.

Comparison of the efficacy of unipolar and bipolar electrode configuration in Parkinson's disease

The efficacy of bilateral deep brain stimulation (DBS) of subthalamic nuclei (STN) in the treatment of drug-refractory advanced idiopathic Parkinson's disease is demonstrated by several randomized, controlled trials.

Based on the clinical situation and elicited side-effects, two types of stimulation modes might be applied for achieving optimal therapeutic improvement: unipolar and bipolar stimulation. In case of unipolar stimulation, one or more of the contacts are programmed to cathode (negative pole) against the case of implantable pulse generator, which results in spherical current distribution. In bipolar settings at least two contacts on the electrode are activated, one as cathode and another as anode (positive pole) resulting in a more focused current diffusion.



Schematic representation of bipolar (upper row) and unipolar (bottom row) stimulation modes.

In clinical routine, the unipolar stimulation is applied most frequently due to its energy saving properties and bipolar stimulation mode is usually reserved for cases where the unipolar stimulation elicit side-effects. From the clinical practice it is generally considered that bipolar stimulation is usually requires higher stimulation intensity (voltage or current intensity) than unipolar stimulation to achieve approximately the same clinical benefit. However, there is no information on how we should change amplitude of stimulation after switching from stimulation mode to the another. The aim of this study was to quantify the difference between the uni- and bipolar stimulation and provide a clinically applicable approach how to change between these modes.

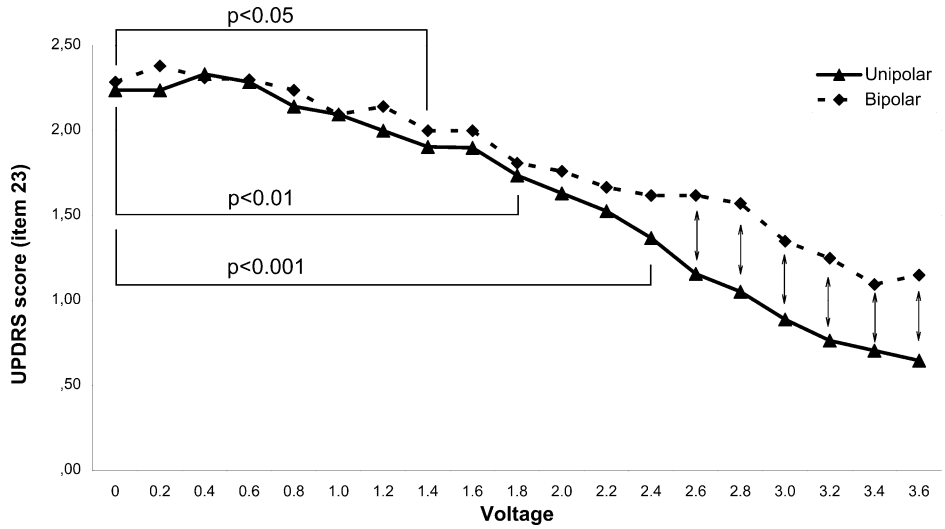
Methods

Twenty-one patients with PD (12 male, age 61.8 ± 7.1 years, disease duration 8.9 ± 2.1 years) were enrolled. All of them fulfilled the UK Brain Bank criteria for PD and underwent bilateral subthalamic DBS implantation 3.3 ± 1.5 years before the examination. In all cases STN DBS produced a stable and prominent improvement with unchanged stimulation parameters >1 year and a postoperative brain MRI verified the appropriate electrode position. The clinical efficacy of DBS was evaluated in a practically off period, after an overnight (>12 hours) drug withdrawal[10]. Severity of rest tremor, rigidity and bradykinesia was measured on the upper extremities based on the appropriate UPDRS items (20, 22

and 23). We started the examination with a randomly assigned order of bipolar or unipolar stimulation of the electrode contralateral to the side with the more prominent parkinsonian symptoms. The amplitude of stimulation was changed between 0 and 3.6 Volts by 0.2V increments while frequency and pulse-width remained constant (130 Hz and 60μs) while the severity of tremor, rigidity and bradykinesia was recorded. After finishing the evaluation of one stimulation mode, the patient had a 30 minutes long break before changing to the other mode.

Results

Fulfilling our expectation, unipolar stimulation was able to improve rest tremor, rigidity and bradykinesia to a larger extent than bipolar stimulation could. In the clinically most frequently applied amplitude range, usually 0.3-0.5V higher amplitudes were required in bipolar stimulation mode to achieve the same efficacy of the unipolar stimulation mode. Within the examined stimulation settings, unipolar stimulation produced persistent stimulation-related side-effects more often than bipolar stimulation did (19% vs. 0%, p<0.01).



The relationship between the amplitude of unipolar (solid line) and bipolar stimulation (dotted line) in Volts and severity of bradykinesia measured by the UPDRS item 23 is demonstrated (median). Significant improvements compared to the baseline were marked by the appropriate significance levels. Significant differences between the efficacy of uni- and bipolar stimulation are presented by vertical arrows (p<0.05).

Discussion

Although several studies evaluated the effects of unipolar STN DBS on various Parkinsonian symptoms and demonstrated that stimulation parameters have a great impact on clinical outcome, this is the first systematic comparison between the efficacy of unipolar and bipolar stimulation modes. For chronic stimulation in nearly 80-90% of the cases unipolar stimulation is applied because it requires lower stimulation intensity and therefore allow longer battery life compared to bipolar stimulation. In cases where higher Voltage levels are used, after changing to bipolar mode 0.3-0.5V higher amplitude may be needed to achieve similar symptomatic control without stimulation-induced side-effects. This difference represents approximately a 10-20% increment in the amplitude of unipolar stimulation.

12.

Deep brain stimulation in dystonia: review of 40 cases

Among the movement disorders, dystonia is one of the most devastating group. Dystonia is not a well-defined entity, but a syndrome characterized by the combination of involuntary patterned twitching movements and sustained muscle contractions. Depending on the etiology, tremor, myoclonus, bradykinesia or spasticity may accompany the dystonic symptoms. The disability and pain due to dystonia may have a high impact on the activities of daily living, in many cases with normal cognition. Despite of combined oral therapies, only a small number of cases responds to pharmacological therapy and experience substantial improvement in HRQoL. Therefore, the success of DBS treatment in dystonia represents a major breakthrough in the field of movement disorders.

The most experience in the treatment of drug-refractory dystonia is based on the bilateral pallidal DBS. Several multicenter and controlled studies and other prospective examinations proved its efficacy. Deep brain stimulation is available with full reimbursement at University of Pécs since 2001. Over the years more than 350 patients underwent DBS implantation. In the present study, our experiences with drug-refractory dystonia is summarized.

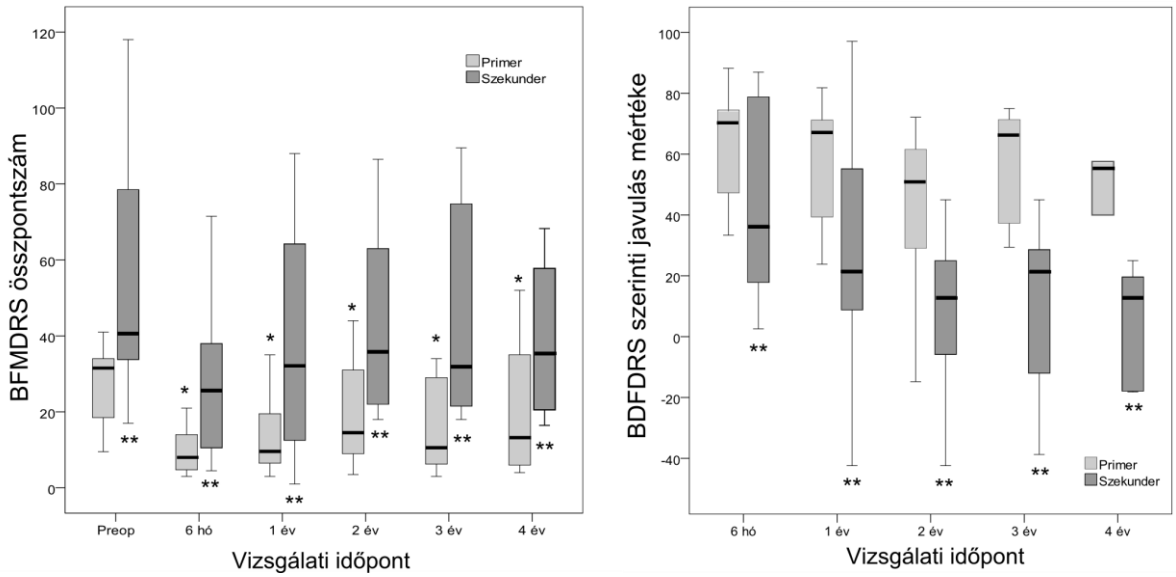
Methods

In this partly prospective and partly retrospective study those patients were enrolled who underwent DBS implantation at University of Pécs. All together the data of 40 consecutive patients' was analyzed (age: 43.7 ± 17.7 years; sex: 22 males and 18 females; disease-duration: 16.1 ± 9.3 years; etiology: 24 primary and 16 secondary dystonia; topographic distribution: 24 generalized, 12 segmental and 4 hemidystonia).

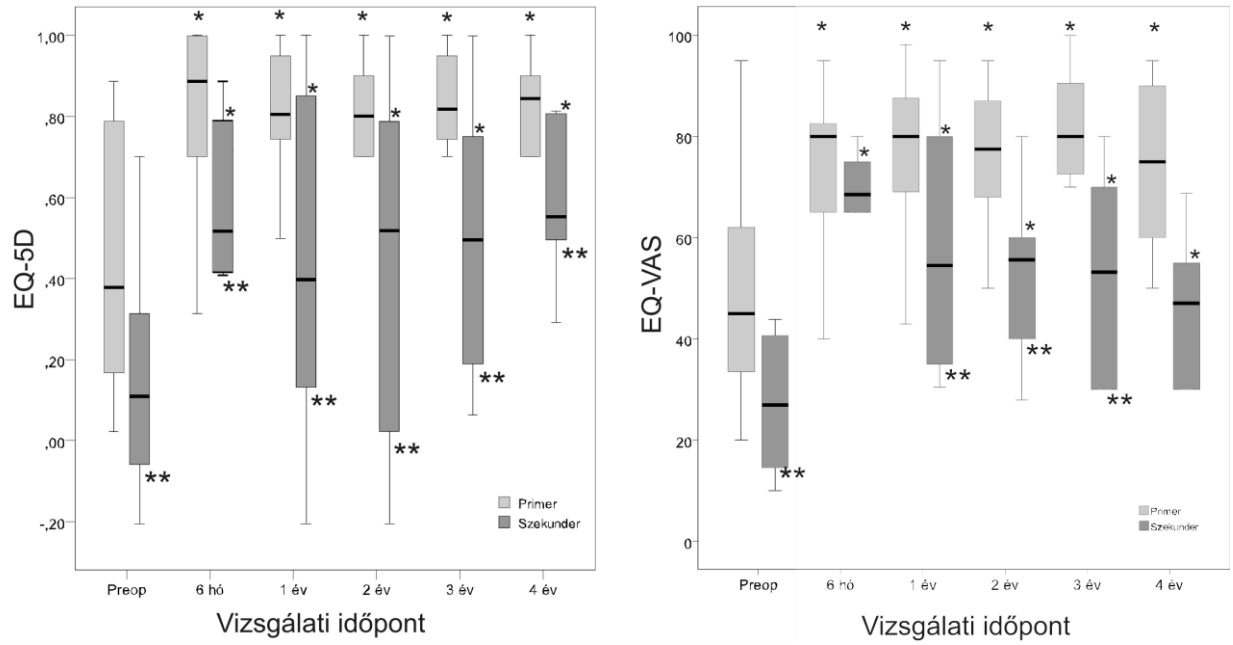
Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) was utilized to measure the severity of dystonia. BFMDRS was developed in a way that an external investigator could also obtain the scores based on a structured video-taped examination of 9 bodily parts. The score on BFMDRS ranges between 0-120, higher values representing more severe dystonia. In this study, the severity of dystonia was re-evaluated based on the video-taped examinations in a way that the rater did not know the type of examination (e.g. preoperative vs. postoperative). Following the international guidelines, DBS therapy was considered as successful if an improvement >25% was recorded. Health-related quality of life was measured by the Hungarian validated version of EQ-5D instrument.

Results

In primary dystonia, the severity of dystonia improved from 31 points to 10 points (68% improvement, $p<0.01$) one year after DBS implantation; whereas, the size of improvement in the secondary dystonia group was not significant (from 40 to 31.5 points, 21.2% improvement, $p>0.05$). However, the HRQoL significantly improved in both groups (0.378 vs. 0.788 and 0.110 vs. 0.388, $p<0.01$). In one year timeframe, 83.3% of the primary and 37.5% of the secondary dystonia cases responded to DBS therapy.



Severity of dystonia (measured by BFMDRS) and the size of improvement compared to baseline (in percentage) in primary (marked by light green boxplots) and secondary dystonia (dark grey) are demonstrated. The level of 100% represents the baseline severity. In the boxplot diagrams, the median values are marked by thick black lines, whereas the 25th and 75th percentiles represent the bottom and the top of the boxes. Statistically significant changes between the postoperative and the baseline values are marked by * ($p<0.05$). Significant differences between the primary and the secondary group are marked by ** ($p<0.05$).



Helath-related quality of life (EQ-5D summary index values) and EQ-5D visual analogue scale (EQ-5D VAS) in primary (light gray) and secondary (dark gray) dystonia. Statistically significant changes between the postoperative and the baseline values are marked by * ($p<0.05$). Significant differences between the primary and the secondary group are marked by ** ($p<0.05$).

Discussion

In primary dystonia, the vast majority of patients experienced clinically meaningful and sustained improvement with DBS therapy. Although we noticed considerably less improvement in the severity of dystonia in the secondary dystonic cases, the relief in pain could still improve the HRQoL significantly.

Conclusions

In my PhD thesis, the following statements can be concluded:

1. There are a relatively few data available on the effects of STN DBS in sleep quality. Therefore, our aim was to identify the effects of bilateral subthalamic deep brain stimulation on sleep quality by the utilization of the recently developed PDSS-2 test battery. According to our data, RLS-related problems, some nocturnal OFF symptoms, tremor on waking and general sleep quality improved significantly after STN DBS therapy. Besides sleep, most domains of non-motor symptoms and the health-related quality of life also improved by DBS therapy.
2. Inspired by the results of EarlyStim study, our research group tried to evaluate if STN DBS might have an impact on the working status of PD patients. One of the most important findings of our study was that the vast majority of patients having an active job at the time of surgery still had an active job 2 years after the DBS implantation. Nevertheless, only a few portion of patients returned to the world after DBS if they did not have an active job at the time of surgery. Therefore, we can conclude that DBS might help preserve the working abilities if it is performed in patients with active working status. Similarly, patients with active job at surgery experienced higher improvement in HRQoL than those patients who did not have an active job. These findings might suggest that having an active job at the time DBS surgery might have a beneficial effect on the long-term outcome by being a positive predictive factor. However, further controlled and large multicenter studies are required to support this hypothesis.
3. Based on the clinical situation and elicited side-effects, two types of stimulation modes might be applied for achieving optimal therapeutic improvement in the treatment of Parkinson's disease: unipolar and bipolar stimulation. Our study was the first systematic comparison between the efficacy of unipolar and bipolar stimulation modes demonstrating the superiority of unipolar stimulation mode in the treatment of rigidity, tremor and bradykinesia. From clinical point of view we considered as an important finding that approximately 0.4-0.5V higher amplitude was required to achieve the same level of improvement during bipolar stimulation than in unipolar mode.
4. Based on the review of the data of patients underwent DBS implantation at University of Pécs, we demonstrated that pallidal DBS can improve health-related quality of life not only in primary dystonia, but also in secondary dystonia cases. Our article was commented by an Editorial in the journal of the 'Ideggyógyászati Szemle'.

List of publications

Publications related to the thesis

1. *Deli Gabriella, Aschermann Zsuzsanna, Ács Péter, Bosnyák Edit, Janszky József, Faludi Béla, Makkos Attila, Kovács Márton, Komoly Sámuel, Balás István, Dóczi Tamás, Kovács Norbert* ***(2015)*** Bilateral subthalamic stimulation can improve sleep quality in Parkinson's disease. *JOURNAL OF PARKINSONS DISEASE* 67(7-8):245-50
   IF:1,910
2. *Deli Gabriella, Balás István, Komoly Sámuel, Dóczi Tamás, Janszky József, Aschermann Zsuzsanna, Nagy Ferenc, Bosnyák Edit, Kovács Norbert* ***(2015)*** Korábban és hatékonyabban: A mély agyi stimuláció szerepe a munkaképesség megőrzésében. *IDEGGYÓGYÁSZATI SZEMLE / CLINICAL NEUROSCIENCE* 67 (megjelenés alatt)
   IF:0.386
3. *Deli Gabriella, Balás István, Komoly Sámuel, Dóczi Tamás, Janszky József, Illés Zsolt, Aschermann Zsuzsanna, Tasnádi Emese, Nagy Ferenc, Pfund Zoltán, Bóné Beáta, Bosnyák Edit, Kuliffay Zsolt, Szijjártó Gábor, Kovács Norbert* **(2012)** Dystonia kezelése mély agyi stimulációval: 40 eset tapasztalatainak összefoglalása. *IDEGGYÓGYÁSZATI SZEMLE / CLINICAL NEUROSCIENCE* 65:(7-8) 249-260.
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