



## OLGU SUNUMU / CASE REPORT

### Early-term results of deep brain stimulation in Parkinson's disease: a case report

Parkinson hastalığında derin beyin stimülasyonunun erken dönem sonuçları: olgu sunumu

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#### Abstract

Subthalamic nucleus deep brain stimulation (STN-DBS) is an alternative treatment in Parkinson's disease. The aim of this case report is to present a case with a positive effect of STN-DBS on early-term results in Parkinson's disease. A 45-year-old man who underwent STN-DBS surgery as a treatment method for Parkinson's Disease was presented. He was assessed in preoperative and postoperative period. STN-DBS surgery reduced the clinical severity of Parkinson's disease, the patient walked a certain distance in a shorter period, increased number of motion repetitions at a certain time interval, and decreased anxiety and depression level. In conclusion STN-DBS surgery has a positive effect on physical functions in Parkinson's disease and it may be useful to perform follow-up study in order to evaluate changes in cognitive functions.

**Keywords:** Parkinson's disease, subthalamic nucleus, physical function, cognitive function, emotional status

#### Öz

Subtalamik çekirdek derin beyin stimülasyonu (STN-DBS) Parkinson hastalığında alternatif bir tedavi yöntemidir. Bu çalışmanın amacı Parkinson hastalığında STN-DBS'nin erken dönem sonuçları üzerine etkisini bir olgu bağlamında incelemektir. Parkinson hastalığında bir tedavi yöntemi olarak STN-DBS cerrahisi geçiren 45 yaşında erkek hasta sunuldu. Olgu ameliyat öncesi ve sonrası olmak üzere iki kez değerlendirildi. STN-DBS cerrahisinin Parkinson hastasında Parkinson Hastalığının klinik şiddetini azalttığı, hastanın belirli mesafe arasını daha kısa sürede yürüdüğü, belirli zaman aralığında hareket tekrar sayısının arttığı, anksiyete ve depresyon düzeyinin azaldığı belirlendi. Sonuç olarak STN-DBS'in Parkinson hastalığında fiziksel fonksiyonlar üzerine olumlu etkisi belirlenmiş olup, kognitif fonksiyonlardaki değişikliklerin değerlendirilebilmesi için işlem sonrası izlem çalışmasının yapılması yararlı olabilir.

**Anahtar kelimeler:** Parkinson hastalığı, subtalamik çekirdek, fiziksel fonksiyon, duygusal durum, bilişsel fonksiyonlar

## INTRODUCTION

Parkinson's disease (PD) is the second most common chronic neurodegenerative disease after Alzheimer's disease<sup>1</sup>. As the main cause of PD is the loss of nigrostriatal dopaminergic neurons, disruption of dopamine and acetylcholine balance in the basal ganglia is also effective in the development of the disease<sup>2,4</sup>. The main and early symptoms of

PD include bradykinesia /akinesia, rigidity, rest tremor; later findings are postural instability and walking and balance disorders and it is a progressive movement disorder<sup>1,3-5</sup>. In addition to the general symptoms; there may be symptoms such as cognitive and behavioral disorders, communication problems, urinary problems, sexual dysfunction, falls, some problems with daily living activities (DLA), walking and balance problems, weight loss, excessive sweating, and sleep disorders<sup>5-7</sup>.

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In PD, motor symptoms are well known. Treatments (pharmacological / physiotherapy / surgical) are mostly focused on this area<sup>3</sup>. Pharmacological treatment (the most effective drug used is Levodopa) is symptomatic and individual to eliminate the signs and symptoms of the disease<sup>1,6</sup>. Physiotherapy is used in conjunction with pharmacological treatment to eliminate rigidity in the muscles and joints, to correct postural deformities, to remove walking difficulty, to acquire fine skills of hand, to maintain normal function and independence in order to relieve breathing difficulty. The aim of surgical treatment is to burn the structures of the brain areas such as subthalamic nucleus, globus pallidus internus and ventralis intermediate nucleus of the thalamus with high frequency sound waves (decrease activity of abnormally increased cells) or through deep electrodes placed in these regions to prevent signs and symptoms clinically by providing electrical stimulation (increase dopamine activity)<sup>2,4,6,8-11</sup>.

Deep brain stimulation (DBS) performed in 1987 by Benabid et al.<sup>12</sup> is a safe and effective alternative to treatment of some movement disorders such as PD<sup>8,13</sup>. DBS does not cure the disease, but alleviates the symptoms, improves the quality of life of the patient and reduces or terminates the amount of drug used and provides independence in daily living activities<sup>6,10</sup>. In this case report, we aimed to evaluate the effect of subthalamic nucleus deep brain stimulation on early-term results in Parkinson's disease.

## CASE

A 45-year-old man who was 62 kg in weight and 163 cm in height was implanted with DBS in May 2018 in Department of Neurosurgery of a university hospital in Turkey. He had a history of PD for 6 years and used Levodopa in his preoperative evaluation. No pathological finding was found in physical examination and other system examinations. Hemogram and biochemistry values were within normal limits in laboratory tests. Until the day of surgery, the patient who was using antiparkinsonian drugs was operated according to clinical procedures and after surgery, he was followed-up according to clinical procedures.

Demographic and disease characteristics of the patient were examined after written and verbal consent was obtained in the preoperative period. In

order to compare motor skills, emotional state, cognitive functions and daily living activities which may be related with disease and surgical intervention, pre-test in the preoperative period and post-test in the post-operative period were used. Post-tests were used 2 months after the activation of the programmable pulse generator which was implanted. This generator activated 3 months later after the implantation. So, post-tests were used in the sixth month after the surgery. The study was performed in accordance with the Declaration of Helsinki.

## Measures

The Unified Parkinson's Disease Rating Scale (UPDRS) was used to determine the clinical severity of PD and the Hoehn & Yahr Parkinson's Disease Level Scale was used to determine the stage of PD. UPDRS was developed in 1987 by Fahn et al<sup>14</sup> and the Turkish validity and reliability study was performed by Akbostancı et al. in 2000<sup>15</sup>. To assess the severity of the disease, the change of symptoms over time, and treatment efficacy in the clinical evaluation of patients with PD. The lowest total score is 0 and the highest score is 199. 199 represents the worst disability level and 0 represents there is no disability. UPDRS was found to be 21 points in the preoperative period and 8 in the postoperative period of the patient. The Hoehn & Yahr Parkinson's Disease Level Scale was developed by Hoehn and Yahr in 1967 to determine the clinical stage and severity of PD<sup>16</sup>. The Turkish validity and reliability was not performed of the scale, but it was adapted to Turkish language by Turkish official of Movement Disorders Society<sup>17</sup>. The scale evaluates the severity of the disease together with activity independence and divides it into 5 stages. Stage 1 shows the lowest disease severity, while stage 5 shows the highest disease severity. In the preoperative period, the stage of PD was in stage 1, and the disease was maintained at stage 1 in the postoperative period.

## Hand functions, mobility, and balance ability

In order to evaluate mobility and balance, Timed up and Go Test, 12 Meters Walking Test, Chair Stand Test were used. Hand Writing Test was used to evaluate hand functions. In the Timed Up and Go Test, after measuring the distance of 3 meters, the distance determined by the start command was

measured in how many seconds the patient walked without help. The patient who walked 3 meters before the operation in 4 seconds, walked in 2 seconds after the operation. In the 12 Meters Walking Test, after measuring the distance of 12 meters, by the start command was measured in how many seconds the patient walked without help. The patient who walked 12 meters before the operation in 13 seconds, walked in 9 seconds after the operation. In the Chair Stand Test, the patient was placed on the middle part of a chair with a height of 43.18 cm (12 inches), with the back of the chair perpendicular to the center and the legs pressed on the ground and the arms crossed on the chest. In this position, he was asked to stand up and sit down as long as he could in 30 seconds with the start command, and the number of lifts he made was recorded exactly. In the preoperative period, the patient who had to stand 13 times was counted as 18 after the operation. In the Hand Writing Test, the patient wrote a sentence (I love to do sports outside the home-in Turkish) to evaluate the hand functions. How long the patient wrote the desired sentence was recorded in seconds with the help of a stopwatch. The writing time was 20 seconds in the preoperative period and the patient wrote the same text in 19 seconds in the postoperative period. Since the affected side of the patient was the right side of the patient and the patient's dominant side was the left side, the difference between the preoperative and postoperative period was not clear.

### Emotional status

Hospital Anxiety and Depression Scale (HAD) and the State and Trait Anxiety Inventory (STAI) were used to evaluate the emotional status. The Hospital Anxiety and Depression Scale was developed by Zigmond and Snaith in 1983 and the Turkish validity and reliability study was performed by Aydemir et al. in 1997<sup>18</sup>. Some items of the scale, which consists of 14 questions, measure anxiety while some items measure depression. It was found that the patient's anxiety score was 11 points and depression score was 13 points in the preoperative period, and the anxiety and depression scores were 7 in the postoperative period. Situation and Continuity Anxiety Scale (STAI) was developed in 1970 by Spielberger in order to measure anxiety and continuity anxiety level. In 1977, his validity and reliability were tested by Öner in Turkish<sup>19</sup>. While state anxiety scale determines how the individual feels himself/herself in a certain time and under

certain conditions, with the continuity anxiety scale, it is generally determined how the individual feels himself regardless of his/her condition and conditions. Total score obtained from both scales ranged from 20 to 80; a high score indicates high anxiety level and small score indicates low anxiety level. Preoperative state anxiety level was 34 and continuity anxiety level was measured as 44, and state anxiety level was 34 and continuity anxiety level was found to be 43 at the postoperative period.

### Cognitive functions

Cognitive functions were evaluated with Hodkinson Abbreviated Mental Test<sup>20</sup>. It was adapted to Turkish language in 2006 by Dirik et al.<sup>21</sup> The test consists of a total of 10 questions measuring the time and time orientation, memory and arithmetic abilities. Scoring is between 0 and 10. 0-2 wrong answer indicates that there is no cognitive dysfunction, 3-4 wrong answer is mild cognitive dysfunction, and 5 and above the wrong answer shows that there is an advanced cognitive dysfunction. The Hodkinson Abbreviated Mental Test score was determined as 9 true answers before and after the operation.

### Daily living activities

Schwab and England Daily Living Activities Rating Scale were used to evaluating the daily activities of the patient in PD. The scale allows the individual to determine the level of independence while performing daily activities<sup>22</sup>. The scale consists of a total of 10 items. The reliability and validity in Turkish of the scale has not been analyzed but it has been used in several studies<sup>6,23,24</sup>. The scale is rated 0-100% of the patient's dependence level. While 100% shows complete independence, 0% shows being completely dependent. The GIA scale, which was determined as 90% in the preoperative period, was found to be 100% in the postoperative period and the patient was found to be fully independent in the preoperative and postoperative period.

## DISCUSSION

PD is a neurodegenerative disease with a high incidence and is seen in 1-3% of all people over 65 years of age<sup>1,4</sup>. Men are affected 1.5 times more frequently than women<sup>1</sup>. In spite of the positive effects of drugs on the symptoms of the disease, because of the increase in undesirable side effects

and in the absence of drug efficacy, surgical treatment is preferred<sup>4,10,25</sup>. With DBS surgical procedure, all major symptoms such as tremor, rigidity, and bradykinesia have been improved and the drug treatment of the patient has been reduced<sup>4,6,10,26</sup>. Savaş et al.<sup>27</sup> reported a decrease in the average daily dose of a drug used by patients after STN DBS surgery. In the studies performed with STN DBS, it was reported that all parkinsonism parameters and UPDRS scores (tremor, rigidity, bradykinesia etc.) improved after surgery<sup>28-32</sup>. In our case, there were no differences in the clinical stage of PD and it was found that UPDRS scores improved after surgery.

Walking disorders occur at every stage of PD. Studies reported increased mobility and balance test results after DBS surgery<sup>33-36</sup>. In our case, it was found that the mobility and balance ability improved according to the results of the scale we compared.

While mental functions are preserved in the early stages of PD, cognitive tests often show that attention, visual-spatial abilities, executive functions, and verbal fluency are affected. Various cognitive deficiencies associated with PD include difficulties with attention, problem-solving, inhibition, verbal fluency, mental flexibility, memory retrieval, word-finding, and visual-spatial abilities<sup>5,37</sup>. The thought flow and answering questions are slow, but the correct response can be delayed. In the course of PD, dementia develops in 20-30% of patients in the late period<sup>6,38</sup>. While some studies reported no change in cognitive functions<sup>37,39,40</sup>, others reported a significant difference between the pre-operative and post-operative values in the sub-parameter of attention from cognitive functions<sup>41-43</sup>. In our case, it was found that there was no change in cognitive functions in the preoperative and postoperative period.

Depression is the most common psychiatric disorder in PD. Major depression can be observed in about 30% of the patients<sup>5,44</sup>. Depression in PD is mild and self-blame, guilt, and failure are rare. However, loss of self-confidence, anxiety, and irritability are evident. It is thought that changes in brain chemistry along with physical disability play a role in the development of depression<sup>45</sup>.

Studies reported that there was a positive improvement in emotional states and neuropsychiatric changes<sup>40,46</sup> and patients' depression levels decreased after surgery<sup>42,47</sup>. In our

case, while decreased anxiety and depression scores were determined in the postoperative period, no change was observed in the state and continuity anxiety levels of the patient.

The most important symptom affecting the activities of daily living in patients with PD is slowing movements<sup>48</sup>. The patients are increasingly feeling their mild difficulties in performing their simple daily work, and this limitation progresses to the full limitation as the disease progresses. The decrease in motor functions such as tremor, hypokinesia, rigidity, which are the main symptoms of the disease negatively affect the activities of daily living and the quality of life of patients decreases<sup>6,49</sup>. Studies have shown a significant improvement in patients' quality of life scores, mobility and DLA levels after surgery<sup>5,6,32,46,50,51</sup>. Powell et al.<sup>52</sup> emphasized that the surgical treatment is controlled by adaptation of the neuromuscular system in Parkinson's patients and that with this improved compatibility, the risk of falling, mortality, and morbidity decreases, thus increasing the independence and quality of life. In our case, the DLA scale, which was determined as 90% in the preoperative period was determined as 100% in the postoperative period.

The results showed that STN DBS surgery had a curative effect on early-stage physical function, emotional status and DLA in Parkinson's patients, but had no effect on cognitive functions. The first 3-month period following DBS implantation is important to obtain an optimal outcome for patients, relatives and healthcare workers. Most patients require a bio-psycho-social adjustment to their new experience with an implanted electronic device. They also need to be informed about the possibilities and limitations of their treatment, as well as their baseless fears. Health professionals provide support for patients and caregivers in the pre- and postoperative period by providing training and exchange of experience and provide safe use of accessory devices by patients. Patients undergoing DBS surgery are also at risk of developing perioperative motor and non-motor side effects. Health professionals train patients and caregivers in addition to providing care for patients with significant motor or cognitive deficits.

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## REFERENCES

- De Rosa A, Tessitore A, Bilo L, Pelusu S, De Michele G. Infusion treatments and deep brain stimulation in Parkinson's Disease: The role of nursing. *Geriatr Nurs*. 2016;37:434-9.
- Luoma J, Pekkonen E, Airaksinen K, Helle L, Nurminen J, Taulu S, et al. Spontaneous sensorimotor cortical activity is suppressed by deep brain stimulation in patients with advanced Parkinson's disease. *Neurosci Lett*. 2018;683:48-53.
- Ulusoy EK, Ayar E, Bayındırlı D. Facial emotion recognition and discrimination deficit in idiopathic Parkinson patients. *Turk J Neurol*. 2015;21:16-21.
- Koçyiğit M, Akpek E, Güllü AÜ, Şenay Ş, Alhan C. Anesthesia experiences and coronary artery bypass surgery in a patient with deep brain stimulation. *Acıbadem Üniversitesi Sağlık Bilimleri Dergisi*. 2015;6:43-5.
- Combs HL, Garcia-Willingham NE, Berry DTR, van Horne CG, Segerstrom S. Psychological functioning in Parkinson's disease post-deep brain stimulation: Self-regulation and executive functioning. *J Psychosom Res*. 2018;111:42-9.
- Altuğ F, Acar F, Acar G, Cavlak U. The influence of subthalamic nucleus deep brain stimulation on physical, emotional, cognitive functions and daily living activities in patients with Parkinson's disease. *Turk Neurosurg*. 2011;21:140-6.
- Diez-Cirarda M, Ibarretxe-Bilbao N, Peria J, Ojeda N. Efficacy of cognitive rehabilitation in Parkinson's disease. *Neural Regen Res*. 2018;13:226-7.
- Giorgio Rizzone M, Martone T, Balestrino R, Lopiano L. Genetic background and outcome of deep brain stimulation in Parkinson's disease. *Parkinsonism Relat Disord*. 2019;64:8-19.
- Brahimaj B, Kochanski RB, Sani S. Microelectrode accuracy in deep brain stimulation surgery. *J Clin Neurosci*. 2018;50:58-61.
- Halpern C, Hurtig H, Jaggi J, Grossman M, Won M, Baltuch G. Deep brain stimulation in neurologic disorders. *Parkinsonism Relat Disord*. 2007;13:1-16.
- Savaş A, Akbostancı C. Surgical technique and management of Parkinson's Disease. *Türkiye Klinikleri J Neurol-Special Topics*. 2008;1(4):103-8.
- Benabid AL, Pollak P, Louveau A, Henry S, de Rougemont J. Combined (thalamotomy and stimulation) stereotactic surgery of the VIM thalamic nucleus for bilateral Parkinson disease. *Appl Neurophysiol*. 1987;50:344-6.
- Timmermann L, Jain R, Chen L, Maarouf M, Barbe MT, Allert N et al. Multiple-source current steering in subthalamic nucleus deep brain stimulation for Parkinson's disease (the VANTAGE study): A non-randomised, prospective, multicentre, open-label study. *Lancet Neurol*. 2015;14:693-701.
- Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P et al. Movement disorder society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *J Mov Disord*. 2008;23:2129-70.
- Akbostancı MC, Balaban H, Atbaşoğlu C. Birleşik Parkinson Hastalığı Değerleme Ölçeği Motor Muayene Bölümü ve Anormal İstemsiz Hareketler Ölçeği'nin değerlendiriciler arası güvenilirlik çalışması. *Parkinson Hastalığı ve Hareket Bozuklukları Dergisi*. 2000;3:7-13.
- Hoehn MM, Yahr MD. Parkinsonizm: Onset, progression and mortality. *Neurology*. 1967;17:427-42.
- Official MDS Translation 2016 International Parkinson and Movement Disorder Society (MDS). [https://www.movementdisorders.org/MDS-Files1/Education/Rating-Scales/MDS-UPDRS\\_Turkish\\_OfficialTranslation\\_FINAL.pdf](https://www.movementdisorders.org/MDS-Files1/Education/Rating-Scales/MDS-UPDRS_Turkish_OfficialTranslation_FINAL.pdf).
- Aydemir Ö, Güvenir T, Küey L, Kültür S. Validity and reliability of Turkish Version of Hospital Anxiety and Depression Scale. *Turk Psikiyatri Derg*. 1997;8:280-7.
- Öner N, Le Compte A. Durumluluk-Süreklilik Kaygı Envanteri El Kitabı. 2. Baskı, İstanbul: Boğaziçi Yayınevi, 1998.
- Hodkinson HM. Evaluation of a mental test scores for assessment of mental impairment in the elderly. *Age Ageing*. 1972;1:233-8.
- Dirik A, Cavlak U, Akdag B. Identifying the relationship among mental status, functional independence and mobility level in Turkish institutionalized elderly: Gender differences. *Arch Gerontol Geriatr*. 2006;42:339-50.
- Schwab RS, England AC. Projection technique for evaluating surgery in parkinson's disease. Third Symposium on Parkinson's Disease. Edinburgh, Livingstone, 1969.
- Balcı BD, Kara B, Colakoğlu BD, Çakmur R. Parkinson hastalarında ev programı egzersizlerinin

- denge ve fonksiyonel kapasite üzerine etkisi. *Noro Psikiyatırs Ars.* 2010;47:53-7.
24. Oğuz S, Tekeoğlu A, Mutluay F, İşsever H, Kızıltan G, Özekmekçi S et al. Parkinson hastalarında üst ekstremiteler performansının değerlendirilmesi: Dokuz Delikli Peg Testi ile Birleştirilmiş Parkinson Hastalığı Değerlendirme Ölçeği'nin karşılaştırılması. *Turk J Physiother Rehabil.* 2009;20:49-55.
  25. Kalenka A, Schwarz A. Anaesthesia and Parkinson's disease: how to manage with new therapies? *Curr Opin Anaesthesiol.* 2009;22:419-24.
  26. Holzl JAH, Neef N, Beudel M, Drost G, Oterdoom DLM, Kremer NI et al. Deep brain stimulation for essential tremor: A comparison of Targets. *World Neurosurg.* 2018;110:580-4.
  27. Savaş A, Akbostancı C, Kanpolat Y. Surgical Treatment of Parkinson's Disease. *Türkiye Klinikleri J Neurosurg-Special Topics.* 2008;1:5-12.
  28. Tabbal SD, Ushe M, Mink CW, Revilla F, Wernle AR, Hong M et al. Unilateral subthalamic nucleus stimulation has a measurable ipsilateral effect on rigidity and bradykinesia in Parkinson Disease. *Exp Neurol.* 2008;211:234-42.
  29. Slowinski JL, Putzke JD, Uitti RJ, Lucas JA, Turk MF, Kall BA, et al. Unilateral deep brain stimulation of the subthalamic nucleus for Parkinson Disease. *J Neurosurg.* 2007;106:626-32.
  30. Llumiguano C, Kosztolany P, Kovacs N, Doczi T, Balas I. Bilateral STN DBS improves manual performance time in Parkinson's Disease. *J Mov Disord.* 2008;23:114-14.
  31. Moro E, Lozano AM, Pollak P, Agid Y, Rehnrcrona S, Volkmann J et al. Long-term results of a multicenter study on subthalamic and pallidal stimulation in Parkinson's Disease. *J Mov Disord.* 2010;25:578-86.
  32. Zhang JG, Zhang K, Ma Y, Hu H, Yang AC, Chu JS, et al. Follow-up of bilateral subthalamic deep brain stimulation for Parkinson's Disease. *Acta Neurochir Supp.* 2006;99:43-7.
  33. Nilsson MH, Fransson PA, Jarnlo GB, Magnusson M, Rehnrcrona S. Research the effects of high frequency subthalamic stimulation on balance performance and fear of falling in patients with Parkinson's Disease. *J Neuroeng Rehabil.* 2009;6:1-10.
  34. Lubik S, Fogel W, Tronnier V, Krause M, König J, Jost WH. Gait analysis in patients with advanced Parkinson Disease: Different or additive effects on gait induced by levodopa and chronic STN stimulation. *J Neural Transm.* 2006;113:163-73.
  35. Follett KA, Weaver FM, Stern M, Hur K, Harris CL, Luo P, et al. Pallidal versus subthalamic deep-brain stimulation for Parkinson's disease. *N Engl J Med.* 2010;362:2077-91.
  36. Kelly VE, Israel SM, Samii A, Slimp JC, Goodkin R, Shumway-Cook A. Assessing the effects of subthalamic nucleus stimulation on gait and mobility in people with Parkinson Disease. *Disabil Rehabil.* 2010;32:929-36.
  37. Yılmaz R, Akbostancı MC, Mercan FN, Sorgun MH, Savaş A. No effect of different stimulation conditions on verbal fluency and visuospatial orientation in patients with subthalamic nucleus deep brain stimulation. *Stereotac Funct Neurosurg.* 2015;93:326-32.
  38. Apaydın H, Emre M. Parkinson hastalığında demans ve tedavisi. *Türkiye Klinikleri J Neur.* 2003;1:206-12.
  39. Fraix V, Houeto JL, Lagrange C, Le Pen C, Krystkowiak P, Guehl D et al. Clinical and economic results of bilateral subthalamic nucleus stimulation in Parkinson's disease. *J Neurol Neurosurg Psychiatry.* 2006;77:443-9.
  40. Witt K, Daniels C, Reiff J, Krack P, Volkmann J, Pinski MO et al. Neuropsychological and psychiatric changes after deep brain stimulation for Parkinson's disease: A randomized, multicentre study. *Lancet Neurol.* 2008;7:605-14.
  41. Zangaglia R, Pacchetti C, Pasotti C, Mancini F, Servello D, Sinforiani E et al. Deep brain stimulation and cognitive functions in Parkinson's disease: A three-year controlled study. *J Mov Disord.* 2009;24:1621-8.
  42. Funkiewiez A, Ardouin C, Caputo E, Krack P, Fraix V, Klinger H et al. Long term effects of bilateral subthalamic nucleus stimulation on cognitive function, mood, and behaviour in Parkinson's Disease. *J Neurol Neurosurg Psychiatry.* 2004;75:834-9.
  43. Appleby B, Duggan P, Regenber A, Rabins PV. Psychiatric and neuropsychiatric adverse events associated with deep brain stimulation: A meta-analysis of ten years experience. *J Mov Disord.* 2007;22:1722-8.
  44. Reijnders JS, Ehrt U, Weber WE, Aarsland D, Leentjens AF. A systematic review of prevalence studies of depression in Parkinson's disease. *J Mov Disord.* 2008;23:183-9.
  45. Bhattacharjee S, Vadieli N, Goldstone L, Alrabiah Z, Sherman SJ. Patterns and predictors of depression treatment among older adults with Parkinson's Disease and depression in ambulatory care settings in the United States. *Parkinsons Dis.* 2018;2018:3402983.
  46. Martínez-Martín P, Valdeoriola F, Tolosa E, Pilleri M, Molinuevo JL, Rumia J et al. Bilateral subthalamic nucleus stimulation and quality of life in advanced Parkinson's Disease. *J Mov Disord.* 2002;17:372-7.
  47. Wang X, Chang C, Geng N, Li N, Wang J, Ma J et al. Long-term effects of bilateral deep brain stimulation of the subthalamic nucleus on depression in patients with Parkinson's disease. *Parkinsonism Relat Disord.* 2009;15:587-91.
  48. Nomm S, Toomela A, Vaske M, Uvarov D, Taba P. An alternative approach to distinguish movements of

- Parkinson disease patients. IFAC-PapersOnLine. 2016;49:272-6.
49. Onur E, Yemez B, Cengizçetin N, Mertol S, Yaka E, Gürzylçın N et al. Factors affecting on depression and quality of life patients with Parkinson's disease. *Noro Psikiyatı Ars.* 2007;44:49-53.
  50. Brozova H, Barnaure I, Alterman RL, Tagliati M. STN-DBS frequency effects on freezing of gait in advanced Parkinson Disease. *Neurology.* 2009;72:770-1.
  51. Yamada K, Hamasaki T, Kuratsu JI. Subthalamic nucleus stimulation applied in the earlier vs. advanced stage of Parkinson's Disease-retrospective evaluation of postoperative independence in pursuing daily activities. *Parkinsonism Relat Disord.* 2009;15:746-51.
  52. Powell DW, Blackmore SE, Puppa M, Lester D, Murray NG, Reed-Jones RJ et al. Deep brain stimulation enhances movement complexity during gait in individuals with Parkinson's disease. *Neurosci Lett.* 2018; doi:10.1016/j.neulet.2018.05.010.