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Research Paper

Subthalamic Nucleus Deep Brain Stimulation in Early-onset Parkinson's Disease: Clinical Outcomes in LRRK2 Mutation Carriers Compared to Non-Carriers

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ABSTRACT

Introduction: Subthalamic nucleus deep brain stimulation (STN-DBS) is an established treatment for early-onset Parkinson's disease (EOPD). While the effect of STN-DBS on patients with *LRRK2 G2019S* mutation has been largely investigated, data specific to EOPD patients with this mutation remain scarce. This study examines the impact of the *LRRK2 G2019S* mutation on STN-DBS outcomes in EOPD patients in Morocco, a developing country where such treatment is challenging to provide.

Methods: A prospective cohort study was conducted at the University Hospital of Ibn Rochd in Casablanca. Genomic DNA was analyzed for the *LRRK2 G2019S* mutation, and clinical data were collected before and after surgery. Motor outcomes, including dyskinesia, motor fluctuations, and reduction in levodopa equivalent daily dose (LEDD), were assessed one year post-DBS.

Results: Seventeen EOPD patients who underwent STN-DBS were included, with 10(58.8%) being carriers of the *LRRK2 G2019S* mutation. The mean age of participants was 57.2±8.4 years, with a mean age at onset of 37.9±6.2 years. Motor fluctuations were present in 88.2% of patients, and 94.1% experienced dyskinesia. Following DBS, both mutation carriers and non-carriers demonstrated significant improvements in motor symptoms, with a mean improvement of 61.3% in the unified PD rating scale (UPDRS) III. Dyskinesia and motor fluctuations, as measured by specific UPDRS IV items, improved by 77.1% and 83.8%, respectively, with a mean LEDD reduction of 60.6%. Improvements were comparable between *LRRK2 G2019S* carriers and non-carriers. All patients were satisfied with the treatment, though one patient had a hardware-related infection.

Conclusion: STN-DBS is effective in managing motor symptoms and reducing medication needs in EOPD patients, regardless of *LRRK2 G2019S* mutation status.

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Highlights

- STN-DBS is effective in managing motor symptoms in EOPD.
- *LRRK2* mutations do not significantly affect clinical outcomes post-DBS.
- Dyskinesia and motor fluctuations were reduced in both carriers and non-carriers.
- EOPD patients showed a 61.3% improvement in motor function after one year of DBS.
- LEDD was reduced by 60.6% after DBS.

Plain Language Summary

Parkinson's disease (PD) that starts before the age of 50, called early-onset PD (EOPD), can be difficult to manage. In Morocco, doctors studied a treatment called deep brain stimulation (DBS), where electrodes are placed in the brain to help control movement problems. They also examined whether a genetic mutation, *LRRK2 G2019S*, influenced the effectiveness of the treatment. The study followed 17 EOPD patients at Ibn Rochd University Hospital in Casablanca who underwent DBS. Genomic testing identified 10(58.8%) as *LRRK2 G2019S* carriers. Before surgery, most patients (88.2%) experienced motor fluctuations and dyskinesia (94.1%), which are uncontrolled movements caused by the disease or medication. One year after surgery, patients showed significant improvements, including better movement control, fewer side effects, and lower medication needs. Results were similar regardless of whether patients had the genetic change. This study shows that DBS can be very effective for people with EOPD, even in places with limited medical resources. It also suggests that having the *LRRK2 G2019S* mutation does not affect the effectiveness of DBS, which could help inform future treatment decisions.

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder that predominantly affects individuals in their 60s, with prevalence increasing with age, impacting 1% to 2% of those over 65 (Ascherio & Schwarzschild, 2016; Van Den Eeden et al., 2003). Early-onset PD (EOPD) has been variably defined, with the maximal age ranging from 40 to 60 years, until expert consensus in 2022 set the threshold at motor symptom onset before 50 (Mehanna et al., 2022), which accounts for approximately 3% to 7% of PD cases (Mehanna & Jankovic, 2019). Genetic factors are strongly associated with EOPD, with the likelihood of detecting genetic mutations increasing as the age of onset decreases (Blauwendraat et al., 2020). In North Africa, specific mutations, such as the *LRRK2 G2019S* mutation, are prevalent among PD patients (El Otmani et al., 2023), although their precise relationship with EOPD has not been thoroughly investigated.

Subthalamic nucleus deep brain stimulation (STN-DBS) is a well-established treatment for managing motor and non-motor complications, as well as reducing the need for dopaminergic medication in advanced stages of PD (Deuschl et al., 2006). Emerging evidence supports its efficacy in EOPD (Krause et al., 2022) compared to late-onset PD patients (Knipe et al., 2011; Kumar et al., 2005). While STN-DBS appears particularly effective in patients carrying the *LRRK2 G2019S* mutation (Leaver et al., 2022) including motor ratings and levodopa-equivalent daily dose (LEDD), data specifically focusing on EOPD patients with these mutations remain limited, with no previous studies investigating this relationship.

This study aims to fill this gap by exploring the impact of the *LRRK2 G2019S* mutation on the clinical outcomes of EOPD patients undergoing STN-DBS, in a Moroccan cohort.

Materials and Methods

Study design and population

This prospective study was conducted at the University Hospital of Ibn Rochd in Casablanca, Morocco. The study included patients diagnosed with EOPD, defined in our cohort as disease onset at age 45 or younger—a threshold established before the 2022 consensus, which

later set the cutoff at motor symptom onset before age 50—who underwent STN-DBS between June 2007 and June 2023. Participants were selected according to the UK PD Society Brain Bank diagnostic criteria (Hughes et al., 1992). Eligibility for DBS was determined based on the CAPSIT-PD criteria (Defer et al., 1999), which included an acute levodopa challenge test demonstrating improvement greater than 50% in motor symptoms measured by the unified PD rating scale (UPDRS) III, a neuropsychological assessment with a Moroccan version of the Mattis scale exceeding a score of 140, a favorable psychiatric status evaluated preoperatively by a psychiatrist to rule out contraindication (with depression assessed using the Montgomery–Åsberg depression rating scale [MADRS] scale), and preoperative MRI findings showing no substantial atrophy, signal abnormalities, or structural lesions. All patients provided informed consent before their inclusion in the study, and the local ethics committee approved the research.

Genomic DNA was extracted from saliva samples using the Oragene-DNA kit. Genotyping for *LRRK2* mutations was performed using TaqMan SNP genotyping assays, with polymerase chain reaction (PCR) and real-time detection. Based on genetic results, patients were divided into two groups: Those who tested positive for the *LRRK2 G2019S* mutation (carriers) and those who did not (non-carriers). The non-carriers did not have any known monogenic mutations, including *PARKIN*, *PINK1*, *DJ-1*, or *GBA*.

Surgical procedure

A stereotactic neurosurgical implantation of leads into the STN was performed under local anesthesia. Precise coordinates for targeting the dorsolateral part of the STN were calculated using a 1.5-T brain MRI. During the procedure, three recording microelectrodes were inserted, and neuronal activity was recorded starting from 10 mm above the target. After placing the DBS leads, we assessed the effect of the stimulation current while the patient was awake, monitoring for motor improvements and side effects. Postoperative CT scans were conducted to identify complications. Pulse generators were implanted on the same day or shortly thereafter, and programming of the DBS device began 2 to 4 weeks post-surgery, with adjustments made during follow-up visits.

Data collection and statistical analysis

We collected demographic and clinical data for all patients. Motor symptoms were evaluated before surgery and reassessed one year after surgery. A genetic study was conducted in conjunction with the surgical procedure, with some analyses completed up to 18 months before the procedure. To ensure a standardized evaluation of post-surgical outcomes, we established a one-year follow-up period. The primary outcome measures included improvements in motor function, evaluated using the UPDRS Part III during OFF periods, as well as a reduction in dyskinesia and motor fluctuations based on specific UPDRS IV items.

Additionally, a decrease in the levodopa equivalent daily dose (LEDD) was calculated using the conversion formulae proposed by Tomlinson et al. (2010). Improvements were quantified by calculating the percentage change between pre- and post-surgery scores. This was achieved by subtracting the initial value from the final value, dividing the result by the initial value, and then multiplying by 100. Any complications related to DBS surgery or device implantation were also recorded.

Data were analyzed using SPSS software, version 21 (Armonk, NY: IBM Corp). Descriptive statistics were used to summarize demographic and clinical characteristics of the study population. Continuous variables were expressed as Mean±SD, while categorical variables were presented as frequencies and percentages. The normality of continuous variables was assessed using the Shapiro-Wilk test. Depending on the distribution, comparisons between *LRRK2* mutation carriers and non-carriers were performed using t-tests for normally distributed data and the Mann-Whitney U test for non-normally distributed data. For categorical variables, the chi-square test was used, or the Fisher exact test when expected counts were low. A $P<0.05$ was considered statistically significant.

Results

Sociodemographic and clinical characteristics

Seventeen EOPD patients who underwent STN-DBS were included, selected from a cohort of 62 PD patients who underwent surgery at our center. Of these, 10 (58.8%) carried the *LRRK2 G2019S* mutation. The mean age at disease onset was 37.9 years, and the majority of the sample were females (64.7%). The mean age at surgery was 49.6 years, with an average disease duration of 11.7 years. In terms of clinical presentation, motor fluctuations were present in 88.2% of the patients, and dyskinesia affected 94.1%. The akinetic-rigid PD subtype was the most common (47.1%), followed by mixed type (41.2%) and tremor-dominant type (11.8%). The mean daily dosage of levodopa was 894 mg. All patients were on dopa therapy, 16 out of 17 were on dopamine

agonists, 5 were on trihexyphenidyl, and 12 used amantadine. Nearly one-quarter of the patients (23.5%) were on antidepressants. Table 1 presents the demographic and clinical characteristics of the sample.

When comparing carriers and non-carriers, *LRRK2 G2019S* patients were more likely to present with the mixed PD subtype. In contrast, non-carriers were predominantly affected by the akinetic-rigid or tremor-dominant subtypes (P=0.011). No other significant differences were found in the demographic or clinical characteristics between the two groups, as shown in Table 1.

Stimulation settings

We used three stereotactic trajectories (central, internal, and posterior) for all patients to measure electrophysiological activity. The central trajectory was selected for 7 of 10 mutation carriers and 5 of 7 non-carriers, as it provided the longest neuronal recording and the most significant improvement. Regarding DBS settings, in the *LRRK2 G2019S* group, 15 leads were used in monopolar stimulation and 5 in bipolar stimulation, with an average voltage of 2.3V (range: 1.7–2.9) at one year. Among the non-carriers, 11 leads were used in monopolar stimulation and 3 in bipolar stimulation, with an average voltage of 2.4V (range: 1.4–3.2) at one year.

Clinical outcomes one year after DBS

After one year of STN-DBS, both *LRRK2 G2019S* mutation carriers and non-carriers demonstrated significant improvements in motor symptoms, with no significant difference between *LRRK2* carriers and non-carriers. The mean improvement in UPDRS III score was 61.3% for the overall cohort. Improvements in dyskinesia and motor fluctuations were also comparable between the two groups, with an overall improvement of 77.1% and 83.8%, respectively. The reduction in LEDD was also notable. The overall cohort achieved a mean decrease of 60.6%. Table 2 provides an overview of these improvements observed in both patient groups.

Table 1. Demographic and clinical characteristics of participants stratified by *LRRK2* carrier status

Demographic and Clinical Variables		Mean±SD/No. (%)			P*
		Overall	LRRK2	Non-LRRK2	
Demographics	Age (y)	57.2±8.4	58.2±8.4	55.9±8.7	0.807
	Sex, male	6(35.3)	2(20)	4(57.1)	0.115
Family history	Familial	9(52.9)	7(70)	2(28.6)	0.059
	Sporadic	8(47.1)	3(30)	5(71.4)	
Clinical characteristics	Age at onset (y)	37.9±6.2	37.2±4.8	38.9±8.1	0.520
	Age at DBS (y)	49.6±6.6	48.8±5.5	50.7±8.1	0.624
	Disease duration (y)	11.7±1.2	11.6±1.3	11.9±1.2	0.800
PD subtype	Akinetic-rigid type	8(47.1)	3(30)	5(71.4)	0.010
	Mixed type	7(41.2)	7(70)	0(0)	
	Tremor-dominant type	2(11.8)	0(0)	2(28.6)	
	Daily dosage of levodopa (mg)	894±422	896±380	891±507	0.601
	Motor fluctuations	15(88.2)	9(90)	6(85.7)	0.585
	Dyskinesia	16(94.1)	10(100)	6(85.7)	0.218

Abbreviations: DBS: Deep brain stimulation; LRRK2: Leucine-rich repeat kinase 2; PD: Parkinson's disease. NEUROSCIENCE

*The Mann-Whitney U test, the chi-square or Fisher exact test, as appropriate. Variables are expressed as Mean±SD for continuous data and as number (percentage) for categorical data. Statistical comparisons between *LRRK2* carriers and non-carriers were conducted using the Mann-Whitney U, chi-square, or Fisher exact tests, as appropriate.

Table 2. Clinical outcomes of patients with EOPD by study groups (*LRRK2* carriers vs non-carriers) one year after DBS

Clinical Parameters	Mean±SD							P*
	LRRK2 Carriers			Non-Carriers			Overall Improvement	
	Pre-DBS	Post-DBS	Improvement (%)	Pre-DBS	Post-DBS	Improvement (%)		
UPDRS III (OFF medication)	36.2±11.9	14.3±8.1	60.9±6.2	38.1±12	14±7.4	61.9±5.3	61.3±5.7	0.922
Dyskinesias (UPDRS IV)	6.1±5.9	1.5±3	75.5±9.3	6±5.9	1.3±2.5	79.3±8.4	77.1±8.9	0.454
Fluctuations (UPDRS IV)	4.6±2.2	0.85±1.5	81.5±8.8	4±2.3	0.7±1.4	87.1±4.9	83.8±7.8	0.158
LEDD	1152±814	474±407	58.5±8.2	1201±814	441±407	63.6±9.9	60.6±8.9	0.580

LEDD: Levodopa equivalent daily dose; UPDRS: Unified Parkinson's disease rating scale.

*The P compares the percentage changes in pre- and post-DBS variables between patients with and without the *LRRK2* mutation.

Note: Results are presented as Mean±SD, with comparisons conducted using the t-test or the Mann-Whitney U test as appropriate. A t-test or Mann-Whitney U test was used, as appropriate.

All patients reported improvements in their QoL and expressed satisfaction with the treatment outcomes. One patient experienced a hardware-related infection 18 months post-surgery, necessitating device replacement a year later. No other significant complications were reported in the cohort.

Discussion

This study demonstrates that STN-DBS is an effective intervention for managing motor symptoms and reducing medication needs in EOPD patients. However, our findings indicate that the *LRRK2 G2019S* mutation does not alter DBS outcomes, with no significant difference observed in motor function (P=0.922), dyskinesias (P=0.454), fluctuations (P=0.158), or LEDD reduction (P=0.580) when comparing carriers to non-carriers at one year after DBS. Our series is the first to examine the effect of DBS specifically on EOPD linked to the *LRRK2 G2019S* mutation. While previous studies (Leaver et al., 2022; Perju-Dumbrava et al., 2012; Sayad et al., 2016) have compared DBS outcomes in patients carrying the *LRRK2 G2019S* mutation, they focused on all PD patients and did not specifically target EOPD. Moreover, performing such advanced procedures in Morocco, a developing country with healthcare challenges, including workforce shortages and limited access to DBS specialists (Daghi et al., 2025), is a significant accomplishment.

Both *LRRK2* mutation carriers and non-carriers demonstrated significant improvements in motor function, consistent with previous reports on the efficacy of DBS in EOPD (Krause et al., 2022). A review of 12 studies comparing DBS responses across various forms of PD, including carriers of *LRRK2*, *PRKN*, and *GBA* mutations, found that DBS effectively controls motor symptoms regardless of the patient's genetic status or age at onset (Rizzone et al., 2019). While these studies confirmed the overall effectiveness of DBS, they also noted some differences in the response to DBS based on genetic factors. However, the very long-term effects of DBS remain uncertain among EOPD patients carrying the mutations.

While *LRRK2* mutations are the most common genetic cause of familial and sporadic PD in our region (El Otmani et al., 2023), it is still unclear whether this translates into differential DBS eligibility. In one study, patients with EOPD carrying *LRRK2*, *GBA*, or *PRKN* mutations were more frequently found in the DBS group compared to the non-DBS group (26.5% vs 16.8%; P=0.02) (Pal et al., 2016), suggesting a potential link between these mutations and eligibility for DBS. Our results align with this, as the prevalence of *LRRK2* mutations in our group was approximately 58%, which is notably higher than the 41% previously reported among PD patients in our country or any other reported prevalence globally (Bouhouche et al., 2017; El Otmani et al., 2023). As well, the higher prevalence of *LRRK2* mutations in our DBS group (58%) compared to the 5.1% reported in a previous study (Pal et al., 2016) confirms regional genetic differences, possibly driven by a founder effect in this area (El Otmani et al., 2023).

Approximately two-thirds of our DBS patients were female (64.7%), with a higher prevalence reported among the *LRRK2* group (80%). A previous meta-analysis in-

vestigating gender differences in patients carrying the *LRRK2* mutation confirms these findings (Chen et al., 2020). This may be due to earlier onset and faster progression in *LRRK2*-PD females, with evidence showing a 5-year earlier onset in this subgroup (Trinh et al., 2014). However, other studies have found no significant gender differences in *LRRK2* mutation prevalence (Gan-Or et al., 2015).

Multiple studies have shown that patients with a younger age at disease onset tend to exhibit better long-term outcomes, particularly in motor and axial symptoms (Shalash et al., 2014). In our study, STN-DBS resulted in significant improvements, with a 77.1% reduction in dyskinesia and an 83.8% reduction in motor fluctuations. These results surpass the 66.7% and 50% reductions reported in a previous local study and exceed outcomes from other STN-DBS studies across the African region (Daghi et al., 2024). Additionally, the reduction in LEDD in our cohort was 60.6%, slightly higher than the 51.72% reduction reported in a previous study from Rabat (Rahmani et al., 2018). All our patients reported satisfaction with the treatment, with only one patient experiencing an infection. These favorable outcomes are likely linked to the younger age at surgery (mean 49.6 years), as younger patients generally respond better to DBS, compared to older ages reported in Rabat and other studies (Daghi et al., 2024; Rahmani et al., 2018).

This study has several limitations. The sample size was relatively small, and the cohort was monocentric, which restricts the generalizability of our findings. Additionally, since the last surgical interventions and genetic studies were conducted up to 18 months ago, the follow-up period was limited to one year post-surgery. As a result, this timeframe may not adequately capture the long-term durability of DBS effects in EOPD patients. Future studies with larger, multicenter cohorts and longer follow-up periods are needed to confirm these results and to assess the long-term durability of DBS in this patient population. Moreover, while we did not evaluate other variants associated with EOPD, such as *PARKIN* or *GBA*, their potential influence on DBS outcomes warrants further exploration.

Conclusion

In conclusion, STN-DBS effectively manages motor complications and reduces medication needs in EOPD, irrespective of whether patients carry the *LRRK2 G2019S* mutation. At one year post-surgery, our patients experienced a 61.3% improvement in motor function, with reductions of 77.1% in dyskinesia and 83.8% in motor fluctuations, respectively, and a 60.6% decrease in daily medication doses.

Ethical Considerations

Compliance with ethical guidelines

The patients were fully informed about this research and gave consent to its publication.

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Authors' contributions

Conceptualization: Hicham EL Otmani, Bouchra EL Moutawaki, Mohammed Abdoh Rafai, Nadia Tahiri Jouti, and Abdelhakim Lakhda; Methodology: Hicham EL Otmani, Mohamed Daghi, and Suzanne Lesage; Investigation: Mohamed Daghi, Maha Abdallaoui and Suzanne Lesage; Validation: Bouchra EL Moutawaki, Mohammed Abdoh Rafai, Nadia Tahiri Jouti, Suzanne Lesage, and Abdelhakim Lakhda; Formal analysis: Mohamed Daghi; Data curation: Hicham EL Otmani, Mohamed Daghi, and Maha Abdallaoui; Project administration, Hicham EL Otmani, and Suzanne Lesage. Writing the original draft: Hicham EL Otmani and Mohamed Daghi; Review and editing: Hicham EL Otmani, Nadia Tahiri Jouti, and Suzanne Lesage, Abdelhakim Lakhda; Supervision: Hicham EL Otmani, Suzanne Lesage, and Abdelhakim Lakhdar;

Conflict of interest

The authors declared no conflict of interest.

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References

Ascherio, A., & Schwarzschild, M. A. (2016). The epidemiology of Parkinson's disease: Risk factors and prevention. *The Lancet. Neurology, 15*(12), 1257-1272. [DOI:10.1016/S1474-4422(16)30230-7] [PMID]

Blauwendraat, C., Nalls, M. A., & Singleton, A. B. (2020). The genetic architecture of Parkinson's disease. *The Lancet. Neurology, 19*(2), 170-178. [DOI:10.1016/S1474-4422(19)30287-X] [PMID]

Bouhouche, A., Tibar, H., Ben El Haj, R., El Bayad, K., Razine, R., & Tazrout, S., et al. (2017). LRRK2 G2019S Mutation: Prevalence and clinical features in Moroccans with Parkinson's Disease. *Parkinson's Disease, 2017,* 2412486. [DOI:10.1155/2017/2412486] [PMID]

Chen, W., Yan, X., Lv, H., Liu, Y., He, Z., & Luo, X. (2020). Gender differences in prevalence of LRRK2-associated Parkinson disease: A meta-analysis of observational studies. *Neuroscience Letters, 715,* 134609. [DOI:10.1016/j.neulet.2019.134609] [PMID]

Daghi, M., Lakhdar, A., & El Otmani, H. (2025). Barriers to Accessing Deep Brain Stimulation for Parkinson's Disease Patients in Morocco. *Journal of Movement Disorders, 18*(1), 106-107. [DOI:10.14802/jmd.24225] [PMID]

Daghi, M., Lakhdar, A., & El Otmani, H. (2024). Deep brain stimulation for movement disorders treatment in Africa: The current status, outcomes, and challenges. *Clinical Neurology and Neurosurgery, 236,* 108113. [DOI:10.1016/j.clineuro.2023.108113] [PMID]

Defer, G. L., Widner, H., Marié, R. M., Rémy, P., & Levivier, M. (1999). Core assessment program for surgical interventional therapies in Parkinson's disease (CAPSIT-PD). *Movement Disorders: Official Journal of the Movement Disorder Society, 14*(4), 572-584. [DOI:10.1002/1531-8257(199907)14:43.0.co;2-c] [PMID]

Deuschl, G., Schade-Brittinger, C., Krack, P., Volkmann, J., Schäfer, H., & Bötzel, K., et al. (2006). A randomized trial of deep-brain stimulation for Parkinson's disease. *The New England Journal of Medicine, 355*(9), 896-908. [DOI:10.1056/NEJMoa060281] [PMID]

El Otmani, H., Daghi, M., Tahiri Jouti, N., & Lesage, S. (2023). An overview of the worldwide distribution of LRRK2 mutations in Parkinson's disease. *Neurodegenerative Disease Management, 13*(6), 335-350. [DOI:10.2217/nmt-2023-0025] [PMID]

Gan-Or, Z., Leblond, C. S., Mallett, V., Orr-Urtreger, A., Dion, P. A., & Rouleau, G. A. (2015). LRRK2 mutations in Parkinson disease; a sex effect or lack thereof? A meta-analysis. *Parkinsonism & Related Disorders, 21*(7), 778–782. [DOI:10.1016/j.parkreldis.2015.05.002] [PMID]

Hughes, A. J., Daniel, S. E., Kilford, L., & Lees, A. J. (1992). Accuracy of clinical diagnosis of idiopathic Parkinson's disease: A clinico-pathological study of 100 cases. *Journal of Neurology, Neurosurgery, and Psychiatry, 55*(3), 181-184. [DOI:10.1136/jnnp.55.3.181] [PMID]

Knipe, M. D., Wickremaratchi, M. M., Wyatt-Haines, E., Morris, H. R., & Ben-Shlomo, Y. (2011). Quality of life in young-compared with late-onset Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society, 26*(11), 2011–2018. [DOI:10.1002/mds.23763] [PMID]

Krause, P., Reimer, J., Kaplan, J., Borngräber, F., Schneider, G. H., & Faust, K., et al. (2022). Deep brain stimulation in Early Onset Parkinson's disease. *Frontiers in Neurology, 13,* 1041449. [DOI:10.3389/fneur.2022.1041449] [PMID]

Kumar, N., Van Gerpen, J. A., Bower, J. H., & Ahlskog, J. E. (2005). Levodopa-dyskinesia incidence by age of Parkinson's disease onset. *Movement Disorders: Official Journal of The Movement Disorder Society, 20*(3), 342–344. [DOI:10.1002/mds.20360] [PMID]

Leaver, K., Viser, A., Kopell, B. H., Ortega, R. A., Miravite, J., & Okun, M. S., et al. (2022). Clinical profiles and outcomes of deep brain stimulation in G2019S LRRK2 Parkinson disease. *Journal of Neurosurgery, 137*(1), 184-191. [DOI:10.3171/2021.7.JNS21190] [PMID]

Mehanna, R., & Jankovic, J. (2019). Young-onset Parkinson's disease: Its unique features and their impact on quality of life. *Parkinsonism & Related Disorders, 65,* 39-48. [DOI:10.1016/j.parkreldis.2019.06.001] [PMID]

Mehanna, R., Smilowska, K., Fleisher, J., Post, B., Hatano, T., & Pimentel Piemonte, M. E., et al. (2022). Age Cutoff for Early-Onset Parkinson's Disease: Recommendations from the International Parkinson and Movement Disorder Society Task Force on Early Onset Parkinson's Disease. *Movement Disorders Clinical Practice, 9*(7), 869-878. [DOI:10.1002/mdc3.13523] [PMID]

Pal, G. D., Hall, D., Ouyang, B., Phelps, J., Alcalay, R., & Pauciulo, M. W., et al. (2016). Genetic and clinical predictors of deep brain stimulation in young-onset Parkinson's Disease. *Movement Disorders Clinical Practice, 3*(5), 465-471. [DOI:10.1002/mdc3.12309] [PMID]

Perju-Dumbrava, L. D., McDonald, M., Kneebone, A. C., Long, R., & Thyagarajan, D. (2012). Sustained response to deep brain stimulation in LRRK2 parkinsonism with the Y1699C mutation. *Journal of Parkinson's Disease, 2*(4), 269-271. [DOI:10.3233/JPD-012121] [PMID]

Rahmani, M., Benabdeljlil, M., Bellakhdar, F., Faris, M. E. A., Jiddane, M., & Bayad, K. E., et al. (2018). Deep Brain Stimulation in Moroccan Patients With Parkinson's Disease: The Experience of Neurology Department of Rabat. *Frontiers in Neurology, 9,* 532. [DOI:10.3389/fneur.2018.00532] [PMID]

Rizzone, M. G., Martone, T., Balestrino, R., & Lopiano, L. (2019). Genetic background and outcome of Deep Brain Stimulation in Parkinson's disease. *Parkinsonism & Related Disorders, 64,* 8-19. [DOI:10.1016/j.parkreldis.2018.08.006] [PMID]

Sayad, M., Zouambia, M., Chaouch, M., Ferrat, F., Nebbal, M., & Bendini, M., et al. (2016). Greater improvement in LRRK2 G2019S patients undergoing Subthalamic Nucleus Deep Brain Stimulation compared to non-mutation carriers. *BMC Neuroscience, 17,* 6. [DOI:10.1186/s12868-016-0240-4] [PMID]

Shalash, A., Alexoudi, A., Knudsen, K., Volkmann, J., Mehdorn, M., & Deuschl, G. (2014). The impact of age and disease duration on the long term outcome of neurostimulation of the subthalamic nucleus. *Parkinsonism & Related Disorders, 20*(1), 47-52. [DOI:10.1016/j.parkreldis.2013.09.014] [PMID]

Tomlinson, C. L., Stowe, R., Patel, S., Rick, C., Gray, R., & Clarke, C. E. (2010). Systematic review of levodopa dose equivalency reporting in Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society, 25*(15), 2649-2653. [DOI:10.1002/mds.23429] [PMID]

Trinh, J., Amouri, R., Duda, J. E., Morley, J. F., & Read, M., Donald, A., et al. (2014). Comparative study of Parkinson's disease and leucine-rich repeat kinase 2 p.G2019S parkinsonism. *Neurobiology of Aging, 35*(5), 1125-1131. [DOI:10.1016/j.neurobiolaging.2013.11.015] [PMID]

Van Den Eeden, S. K., Tanner, C. M., Bernstein, A. L., Fross, R. D., Leimpeter, A., & Bloch, D. A., et al. (2003). Incidence of Parkinson's disease: Variation by age, gender, and race/ethnicity. *American Journal of Epidemiology, 157*(11), 1015-1022. [DOI:10.1093/aje/kwg068] [PMID]