JGG 2024;72:76-82
doi: 10.36150/2499-6564-N711

Effect of Lee Silverman Voice Treatment® BIG on the major motor symptoms in patients with moderate Parkinson's disease: an observational study

Masanobu Iwai[1,2], Soichiro Koyama[3,4], Kazuya Takeda[3,4], Yuichi Hirakawa[1,4], Ikuo Motoya[1,4], Hiroaki Sakurai[3,4], Yoshikiyo Kanada[3,4], Yohei Okada[2,5], Nobutoshi Kawamura[6], Mami Kawamura[6], Shigeo Tanabe[3,4]

[1] Department of Rehabilitation, Kawamura Hospital, Gifu, Japan; [2] Graduate School of Health Sciences, Kio University, Nara, Japan; [3] Faculty of Rehabilitation, School of Health Sciences, Fujita Health University, Toyoake, Aichi, Japan; [4] Graduate School of Health Sciences, Fujita Health University, Toyoake, Aichi, Japan; [5] Neurorehabilitation Research Center, Kio University, Nara, Japan; [6] Department of Neurology, Kawamura Hospital, Gifu, Japan

Background and aims. This study investigated the effect of Lee Silverman Voice Treatment® BIG (LSVT® BIG) on four major motor symptoms (tremor, rigidity, bradykinesia, and postural instability/gait disorder) in patients with Parkinson's disease classified as Hoehn and Yahr (HY) stages II-III.

Methods. This retrospective, observational, single-center study included 17 patients with Parkinson's disease classified as HY stages II-III. To examine the effect of the LSVT® BIG, the total scores of the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III and each score of the major motor symptoms (tremor, rigidity, bradykinesia, and postural instability/gait disorder) extracted from the MDS-UPDRS Part III were assessed pre- and post-LSVT® BIG. The Wilcoxon signed-rank test was used for statistical analysis.

Results. The total scores of MDS-UPDRS Part III, bradykinesia, and postural instability/gait disorder improved when comparing pre- and post-LSVT® BIG (median [interquartile range]: 24 [16-36] to 18 [13-22], 8 [6-11] to 6 [5-8], and 5 [3-8] to 3 [1-5], respectively). The tremor and rigidity scores showed a trend toward improvement but did not achieve statistical significance (median [interquartile range]: 4 [0-6] to 3 [0-5], and 4 [2-10] to 4 [2-6], respectively).

Conclusions. These results suggest that LSVT® BIG for patients with Parkinson's disease classified as HY stages II-III is effective for improving bradykinesia and postural instability/gait disorder. The findings have important clinical implications for preliminarily estimating the effect of LSVT® BIG on each major motor symptom.

Key words: Parkinson's disease, Lee Silverman Voice Treatment® BIG, motor symptom

Received: December 20, 2023
Accepted: May 3, 2024
Published online: May 30, 2024

Correspondence
Shigeo Tanabe
E-mail: tanabes@fujita-hu.ac.jp

How to cite this article: Iwai M, Koyama S, Takeda K, et al. Effect of Lee Silverman Voice Treatment® BIG on the major motor symptoms in patients with moderate Parkinson's disease: an observational study. Journal of Gerontology and Geriatrics 2024;72:76-82. https://doi.org/10.36150/2499-6564-N711

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder affecting the motor system. The four major motor symptoms of PD include tremors, rigidity, bradykinesia, and postural instability/gait disorder (PIGD) [1-4]. Tremors, rigidity, and bradykinesia appear in the early stages of PD; although troublesome, they are often mild and rarely debilitating [5,6]. PIGD appears in the advanced stage of the disease, and includes postural changes with camptocormia and/or Pisa syndrome, postural instability, and gait disorder with freezing gait and/or festinating gait. These are major problems that increase the frequency of falls. PD motor symptoms gradually worsen over time, thus resulting in a decline in functional and daily living activities [7,8].

It is imperative to treat moderate motor symptoms in patients undergoing exercise therapy. Previous studies reported that the average duration between the onset of motor symptoms and the diagnosis of PD is approximately 2 to 3 years, and most patients exhibit symptoms at HY stages II-III at the time of diagnosis [9,10]. Patients or their caregivers often overlook the initial signs of PD because these symptoms are often associated with normal physiological aging [11]. In some cases, when patients experience motor symptoms, they consult traditional practitioners before consulting a neurologist [9].

The Lee Silverman Voice Treatment® BIG (LSVT® BIG) is a popular exercise therapy employed in clinical practice for patients with PD classified as HY stages II-III. Conceptually, the LSVT® BIG focuses on improving self-perception and movement patterns by proprioceptive recalibration via a therapist's imitation and tactile or visual cues [12,13]. Particularly, LSVT® BIG was developed to improve bradykinesia [14]. Previous studies showed that LSVT® BIG improved the scores of the Unified Parkinson's Disease Rating Scale (UPDRS) Part III, which includes an evaluation of four major motor symptoms (tremor, rigidity, bradykinesia, and PIGD) in patients with PD, including those with HY stages II-III [11,15,16]. For example, Ebersbach et al. reported that LSVT® BIG significantly improved the UPDRS Part III scores in patients with PD compared with Nordic walking or unsupervised home-based training programs [15].

However, to our best knowledge, there have been no reports regarding the effects of LSVT® BIG on tremor, rigidity, bradykinesia, and PIGD. Thus, the present study aimed to investigate the effect of LSVT® BIG on each of the four major motor symptoms in patients with PD classified as HY stages II-III.

METHODS

Study design and participants

This retrospective, observational, single-centre study was conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology statement [17].

Convenience sampling of inpatients and outpatients between July 2018 and August 2022 at Kawamura Hospital was used to recruit the patients. The inclusion criteria were as follows: (1) PD diagnosis by a neurologist according to the UK Parkinson's Disease Association Brain Bank Clinical Diagnostic Criteria [18], (2) PD classified as HY stages II-III, (3) underwent the LSVT® BIG as a prescribed therapy based on clinical decision and not for research purposes, and (4) ability to understand verbal instructions. The following patients were excluded: a history of neuromuscular disease (except for PD) and with missing data. The levodopa (L-dopa) equivalent daily dosage was calculated using a previously published formula [19]. All patients remained on regular L-dopa medications during the LSVT® BIG period.

LSVT® BIG

LSVT® BIG was prescribed for patients with PD who were able to understand verbal commands; were on stable levodopa medication; and who had recently experienced increasing motor symptoms, difficulty with functional movements, and impaired activities of daily living (ADLs) according to self- or family reports. The study involved all patients receiving 16 face-to-face exercise sessions with physical therapists certified in LSVT® BIG. Each session lasted an hour long, 4 times a week for 4 weeks. Additionally, a daily home exercise program was implemented. The exercise sessions comprised four parts in order of increasing difficulty: (1) standardised whole-body movements, (2) functional tasks, (3) hierarchy tasks, and (4) BIG walking.

Standardised whole-body movements consisted of seven daily exercises performed with maximal amplitude and effort. The functional tasks consisted of multiple repetitions of five functional component tasks tailored to each individual. These exercises were functionally goal-directed ADLs based on participants' self-identified movement problems, with sessions being conducted during the first half of each session (30 min or more).

Hierarchy tasks consisted of one complex multistep task tailored to achieve participants' goals and interests. BIG walking involves ambulating with high-amplitude (large) and high-effort movements for distance and time. These exercise sessions were conducted in the second half

of each session (30 min or less). These exercises were multidirectional, sustained, and repetitive whole-body movement patterns: two in a sitting position and five in a standing position. The patients were instructed to encourage their performance within the range of 7-8/10 on a modified Borg scale of their perceived maximum effort [11,20]. In addition, the patients were instructed to perform larger movements during routine activities to provide continuous exercise in everyday movements.

Assessment

The assessments were conducted by a physical therapist who did not provide the LSVT® BIG. They were performed the week before the LSVT® BIG was started and 4 weeks after the LSVT® BIG was completed. All assessments were made during the "on" medication state (i.e., 1 hour after medication) to eliminate the difference in the medication cycle (e.g., on/off state). The Mini-Mental State Examination was used in the cognitive assessment. This examination is the most commonly used scale in cognitive function evaluation, with an established reliability (Pearson's correlation coefficient [rho; ρ] $\geq$ 0.82) and concurrent validity (Pearson's correlation coefficient [rho; ρ] $\geq$ 0.66) [21].

The HY stage was evaluated to determine disease severity. The Movement Disorder Society-sponsored revision of UPDRS (MDS-UPDRS) Part III was used for specific assessment. Briefly, the MDS-UPDRS is a modified version of the UPDRS that provides a more detailed evaluation of PD symptoms [22]. It is a 33-item scale, and the maximum score is 132 points, with higher scores indicating more severe motor symptoms. The MDS-UPDRS Part III has high internal consistency (Cronbach's alpha = 0.93) and concurrent validity in patients with PD [23].

In this study, the MDS-UPDRS Part III was used to quantify the overall motor symptoms, including tremor, rigidity, bradykinesia, and PIGD. Furthermore, based on the definition used by Duncan and Earhart [24], the scores for each of the four major motor symptoms were calculated by summing the items corresponding to each symptom: tremor (3.15-3.18), rigidity (3.3a-3.3e), bradykinesia (3.4-3.8 and 3.14), and PIGD (3.9-3.13).

Statistical analysis

The total MDS-UPDRS Part III scores were calculated for each patient, and individual scores of the four major motor symptoms, that is, tremor, rigidity, bradykinesia, and PIGD, were extracted. Concerning the individual scores, all data were first subjected to the Shapiro-Wilk test for normality. Subsequently, normally distributed data were analysed using a paired *t*-test, whereas non-normally distributed data were analysed using the Wilcoxon signed-rank test. All statistical analyses were performed using R software (version 4.1.0; R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at $p < 0.05$.

RESULTS

All 17 patients recruited were eligible and included in the study (Fig. 1). The patient characteristics are presented in Table I. The assessment results before and after the 4-week LSVT® BIG are illustrated in Figure 2 and 3. The total scores of the MDS-UPDRS Part III significantly improved when compared pre- and post-LSVT® BIG (median [interquartile range]: 24 [16-36] to 18 [13-22]; $p < 0.01$). The bradykinesia and PIGD scores were also significantly improved (median [interquartile range]: 8 [6-11] to 6 [5-8], $p < 0.01$; 5 [3-8] to 3 [1-5], $p < 0.01$). Although the tremor and rigidity scores showed some improvement following LSVT® BIG, the results did not achieve significance (median [interquartile range]: 4 [0-6] to 3 [0-5], $p = 0.31$; 4 [2-10] to 4 [2-6], $p = 0.05$).

DISCUSSION

The effects of LSVT® BIG on tremor, rigidity, bradykinesia, and PIGD in PD remain unclear to date. The current study results indicate that LSVT® BIG significantly improves the total, bradykinesia, and PIGD scores. Meanwhile, although the tremor and rigidity scores show a trend toward improvement, they did not achieve

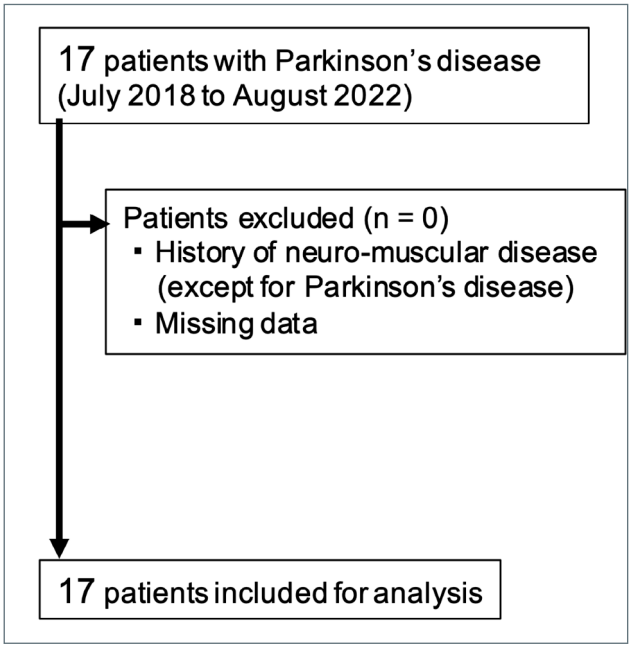

Figure 1. Flowchart of patient enrolment.

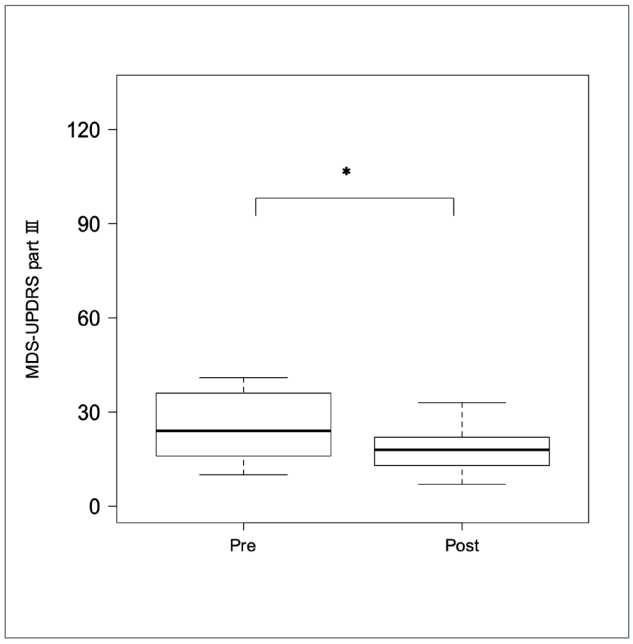

Figure 2. Differences in the scores of the total MDS-UPDRS Part III at pre- and post- LSVT® BIG.
The central thick lines of the boxplot represent medians; the box limits comprise the interquartile range from 25 and 75%. The boxplot whiskers extend to 1.5 times the interquartile range from the first and third quartiles.
*$p < 0.05$; LSVT®: Lee Silverman Voice Treatment; MDS-UPDRS Part III: Movement Disorders Society-Unified Parkinson Disease Rating Scale Part III.

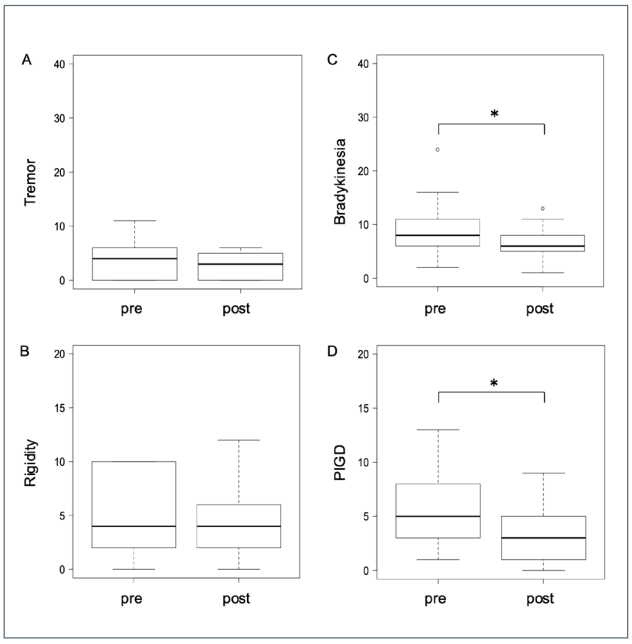

Figure 3. Differences in the scores of the four major motor symptoms A) tremor, B) rigidity, C) bradykinesia, and D) PIGD at pre- and post- LSVT® BIG.
The central thick lines of the boxplot represent medians; the box limits comprise the interquartile range from 25 and 75%. The boxplot whiskers extend to 1.5 times the interquartile range from the first and third quartiles. Circles represent outliers.
*$p < 0.05$; LSVT®: Lee Silverman Voice Treatment; PIGD: postural instability/gait disorder.

statistical significance. Our study findings on the impact of LSVT® BIG on the four major motor symptoms can lead to more effective therapeutic approaches.

Regarding the improvement in the total MDS-UPDRS Part III score, the result of this study was similar to that of the previous studies [15,16,25]. Ueno et al. examined the effect of LSVT® BIG in eight patients with PD classified as HY stages II-III [16]. The scores of the UPDRS Part III significantly improved (median [interquartile range]: 12.5 [8.8-12.5] to 8.5 [6.5-11.5]) after the LSVT® BIG. The results of this study support the effectiveness of LSVT® BIG. Thus, comparing the scores for the four major motor symptoms was deemed appropriate.

The goal of LSVT® BIG is to restore the ability of individuals with PD to sense when they are moving abnormally and to self-correct by increasing the amplitude of their movements with resultant improvements in the speed of movements to counteract bradykinesia (slow movement or low-amplitude movement) [12,14,25]. Bradykinesia is defined as slowness of movement, smaller movement than desired, and prolonged time required to initiate a movement [4,26]. Flood et al. reported that the LSVT® BIG significantly improved the 10-m walk, timed up-and-go (TUG), sit-to-stand times, and stride length during walking in patients with PD at HY stages I-III [27]. PIGD is defined as deficits in balance and gait and postural reflex impairment [28,29]. Although PD is historically considered to be a disorder of nigrostriatal dopaminergic denervation, improvement in PIGD symptoms is limited by dopaminergic treatment alone. Fleming Walsh et al. reported that LSVT® BIG significantly improved the 10-m walk, TUG, functional gait assessment, and Berg balance scale in patients with PD classified as HY stages II-IV [30].

Scores for tremor and rigidity showed a trend toward improvement but did not achieve statistical significance. These results suggest that improvement in these symptoms might require combination treatment with LSVT® BIG and other modalities, such as deep brain stimulation (DBS) therapy and dopaminergic treatments. In previous studies, DBS therapy or dopaminergic treatment reduced tremor and rigidity symptoms in patients with PD [31-33]. Wong et al. reported that DBS significantly improved tremors and rigidity in patients with PD [33]. Hacker et al. reported that DBS plus dopaminergic treatment better reduced tremor progression compared with dopaminergic treatment alone [31]. The findings have

Table I. Patient characteristics (n = 17).

Patient No.	Age (years)	Sex (M/F)	Type of medical care	MMSE score	Time since diagnosis (years)	LEDD (mg/day)	HY (baseline)
1	60	F	Outpatient	28	2	300	2
2	63	F	Outpatient	30	2	225	2
3	81	F	Outpatient	25	2	1049	2
4	76	F	Outpatient	24	3	650	2
5	64	M	Outpatient	30	4	225	2
6	77	F	Outpatient	30	6	340	2
7	57	F	Outpatient	27	7	600	2
8	64	M	Outpatient	28	7	829	2
9	65	F	Outpatient	22	10	1113	2
10	78	F	Outpatient	28	11	650	2
11	64	F	Outpatient	20	2	2423	3
12	68	F	Outpatient	30	2	863	3
13	78	F	Outpatient	30	4	2983	3
14	69	F	Outpatient	26	5	375	3
15	79	M	Inpatients	30	7	600	3
16	67	F	Outpatient	23	7	1548	3
17	77	F	Outpatient	25	7	550	3
Mean	69.8			26.8	5.2	901.4	2.4
(SD)	7.6			3.2	2.9	768.1	0.5

F: female; HY: Hoehn and Yahr; LEDD: levodopa equivalent daily dosage; M: male; MMSE: Mini-Mental State Examination; SD: standard deviation

important clinical implications for estimating the effect of the LSVT® BIG on the four major motor symptoms of PD.

This study has some limitations owing to its design. As this was a non-controlled study, direct comparison with other exercise therapies for patients with PD was not possible. Although significant differences were observed before and after the LSVT® BIG, it was not possible to definitively attribute the observed difference to the unique effects of the LSVT® BIG. Further studies with control groups are needed to clarify the conditions under which LSVT® BIG may be more effective and to select patients who may better benefit from this therapy.

CONCLUSIONS

LSVT® BIG significantly improves total MDS-UPDRS Part III, bradykinesia, and PIGD scores in patients with PD classified as HY stages II-III. Our findings have important clinical implications for estimating the effect of the LSVT® BIG on each major motor symptom in PD. In addition, the findings may also help determine treatment modalities. Specifically, LSVT® BIG can be used to improve overall PD symptoms and two individual scores: bradykinesia and PIGD, but it may need to be combined with other modalities when the target symptom is tremor or rigidity.

Acknowledgements

We thank the staff of the Department of Rehabilitation at Kawamura Hospital for their helpful technical assistance and Editage (www.editage.com) for English language editing.

Conflict of interest statement

The authors declare no conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

MI: conceptualisation, data curation, formal analysis, investigation, methodology, software, writing - original draft; SK: conceptualisation, formal analysis, methodology, supervision; writing - review & editing; KT: conceptualisation, formal analysis, methodology, supervision; writing - review & editing; YH: conceptualisation, data curation, formal analysis, investigation; IM: conceptualisation, formal analysis, project administration; HS: conceptualisation, project administration, writing - review & editing; YK: conceptualisation, project administration, writing - review & editing. YO: conceptualisation, methodology, supervision, writing - review & editing; NK: conceptualisation, project administration; MK: conceptualisation, project administration; ST: conceptualisation,

formal analysis, methodology, project administration, software, supervision, writing - review & editing.

Ethical consideration

This study was approved by the Human Ethics Committee of Kawamura Hospital (approval number: 30-004). The study was conducted in accordance with the International Committee of Medical Journal Editors guidelines and the Declaration of Helsinki. Owing to the study's retrospective nature, opt-out consent was obtained from each patient, and the details were made available on our hospital's bulletin board.

References

1 de Lau LM, Breteler MM. Epidemiology of Parkinson's disease. Lancet Neurol 2006;5:525-535. https://doi.org/10.1016/S1474-4422(06)70471-9

2 Jankovic J, McDermott M, Carter J, et al. Variable expression of Parkinson's disease: a base-line analysis of the DATATOP cohort. The Parkinson Study Group Neurology 1990;40:1529-1534. https://doi.org/10.1212/wnl.40.10.1529

3 Politis M, Wu K, Molloy S, et al. Parkinson's disease symptoms: the patient's perspective. Mov Disord 2010;25:1646-1651. https://doi.org/10.1002/mds.23135

4 Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord 2015;30:1591-1601. https://doi.org/10.1002/mds.26424

5 Rowe S, Sue CM. Towards the optimal care of Parkinson's disease: a guide for GPs. Med Today 2023;24:19-25.

6 Castilla-Cortázar I, Aguirre GA, Femat-Roldán G, et al. Is insulin-like growth factor-1 involved in Parkinson's disease development? J Transl Med 2020;18:1-17. https://doi.org/10.1186/s12967-020-02223-0

7 Skorvanek M, Martinez-Martin P, Kovacs N, et al. Differences in MDS-UPDRS scores based on Hoehn and Yahr stage and disease duration. Mov Disord Clin Pract 2017;4:536-544. https://doi.org/10.1002/mdc3.12476

8 Sperens M, Georgiev D, Eriksson Domellöf M, et al. Activities of daily living in Parkinson's disease: time/gender perspective. Acta Neurol Scand 2020;141:168-176. https://doi.org/10.1111/ane.13189

9 Assadeck H, Daouda MT, Djibo FH, et al. Clinical profile of Parkinson's disease: experience of Niger. J Neurosci Rural Pract 2018;9:214-218. https://doi.org/10.4103/jnrp.jnrp_337_17

10 Femi OL, Ibrahim A, Aliyu S. Clinical profile of parkinsonian disorders in the tropics: experience at Kano, northwestern Nigeria. J Neurosci Rural Pract 2012;3:237-241. https://doi.org/10.4103/0976-3147.102589

11 Millage B, Vesey E, Finkelstein M, et al. Effect on gait speed, balance, motor symptom rating, and quality of life in those with stage I Parkinson's disease utilizing LSVT BIG®. Rehab Res Pract 2017;2017:9871070. https://doi.org/10.1155/2017/9871070

12 Farley BG, Koshland GF. Training BIG to move faster: the application of the speed-amplitude relation as a rehabilitation strategy for people with Parkinson's disease. Exp Brain Res 2005;167:462-467. https://doi.org/10.1007/s00221-005-0179-7

13 Peterka M, Odorfer T, Schwab M, et al. LSVT-BIG therapy in Parkinson's disease: physiological evidence for proprioceptive recalibration. BMC Neurology 2020;20:276. https://doi.org/10.1186/s12883-020-01858-2

14 Fox C, Ebersbach G, Ramig L, et al. LSVT LOUD and LSVT BIG: behavioral treatment programs for speech and body movement in Parkinson disease. Parkinsons Dis 2012;2012:391946. https://doi.org/10.1155/2012/391946

15 Ebersbach G, Ebersbach A, Edler D, et al. Comparing exercise in Parkinson's disease – the Berlin LSVT®BIG study. Mov Disord 2010;25:1902-1908. https://doi.org/10.1002/mds.23212

16 Ueno T, Sasaki M, Nishijima H, et al. 2017 LSVT-BIG improves UPDRS III scores at 4 weeks in Parkinson's disease patients with wearing off: a prospective, open-label study. Parkinsons Dis 2017;2017:8130140. https://doi.org/10.1155/2017/8130140

17 von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg 2014;12:1495-1499. https://doi.org/10.1016/j.ijsu.2014.07.013

18 Hughes AJ, Daniel SE, Kilford L, et al. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinicopathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992;55:181-184. https://doi.org/10.1136/jnnp.55.3.181

19 Tomlinson CL, Stowe R, Patel S, et al. Systematic review of levodopa dose equivalency reporting in Parkinson's disease. Mov Disord 2010;25:2649-2653. https://doi.org/10.1002/mds.23429

20 Janssens J, Malfroid K, Nyffeler T, et al. Application of LSVT BIG intervention to address gait, balance, bed mobility, and dexterity in people with Parkinson disease: a case series. Phys Ther 2014;94:1014-1023. https://doi.org/10.2522/ptj.20130232

21 Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.

22 Goetz CG, Fahn S, Martinez-Martin P, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): process, format, and clinimetric testing plan. Mov Disord 2007;22:41-47. https://doi.org/10.1002/mds.21198

23 Goetz CG, Tilley BC, Shaftman SR, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results. Mov Disord 2008;23:2129-2170. https://doi.org/10.1002/mds.22340

[24] Duncan RP, Earhart GM. Randomized controlled trial of community-based dancing to modify disease progression in Parkinson disease. Neurorehabil Neural Repair 2012;26:132-143. https://doi.org/10.1177/1545968311421614

[25] Ebersbach G, Grust U, Ebersbach A, et al. Amplitude-oriented exercise in Parkinson's disease: a randomized study comparing LSVT-BIG and a short training protocol. J Neural Transm (Vienna) 2015;122:253-256. https://doi.org/10.1007/s00702-014-1245-8

[26] Berardelli A, Rothwell JC, Thompson PD, et al. Pathophysiology of bradykinesia in Parkinson's disease. Brain 2001;124:2131-2146. https://doi.org/10.1093/brain/124.11.2131

[27] Flood MW, O'Callaghan BPF, Diamond P, et al. Quantitative clinical assessment of motor function during and following LSVT-BIG® therapy. J Neuroeng Rehabil 2020;17:92. https://doi.org/10.1186/s12984-020-00729-8

[28] Herman T, Weiss A, Brozgol M, et al. Gait and balance in Parkinson's disease subtypes: objective measures and classification considerations. J Neurol 2014;261:2401-2410. https://doi.org/10.1007/s00415-014-7513-6

[29] Lo RY, Tanner CM, Albers KB, et al. Clinical features in early Parkinson disease and survival. Arch Neurol 2009;66:1353-1358. https://doi.org/10.1001/archneurol.2009.221

[30] Fleming Walsh S, Balster C, Chandler A, et al. LSVT BIG® and long-term retention of functional gains in individuals with Parkinson's disease. Physiother Theory Pract 2022;38:629-636. https://doi.org/10.1080/09593985.2020.1780655

[31] Hacker ML, DeLong MR, Turchan M, et al. Effects of deep brain stimulation on rest tremor progression in early stage Parkinson disease. Neurology 2018;91:E463-E471. https://doi.org/10.1212/WNL.0000000000005903

[32] Relja MA, Petravic D, Kolaj M. Quantifying rigidity with a new computerized elbow device. Clin Neuropharmacol 1996;19:148-156. https://doi.org/10.1097/00002826-199619020-00003

[33] Wong JK, Viswanathan VT, Nozile-Firth KS, et al. STN versus GPi deep brain stimulation for action and rest tremor in Parkinson's disease. Front Hum Neurosci 2020;14:578615. https://doi.org/10.3389/fnhum.2020.578615