Parkinsonism and Related Disorders xxx (2017) 1–8

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Parkinsonian gait improves with bilateral subthalamic nucleus deep brain stimulation during cognitive multi-tasking

Gaurav Chenji, MS [a, c, 1], Melissa L. Wright, MPT [a, e, 1], Kelvin L. Chou, MD [a, b, c], Rachael D. Seidler, PhD [d, e], Parag G. Patil, MD PhD [a, b, c, *]

[a] Surgical Therapies Improving Movement Program, University of Michigan, Ann Arbor, MI, USA
[b] Department of Neurology, University of Michigan, Ann Arbor, MI, USA
[c] Department of Neurosurgery, University of Michigan, Ann Arbor, MI, USA
[d] Deparment of Psychology, University of Michigan, Ann Arbor, MI, USA
[e] School of Kinesiology, University of Michigan, Ann Arbor, MI, USA

A R T I C L E I N F O

Article history:
Received 4 November 2016
Received in revised form
12 February 2017
Accepted 21 February 2017

Keywords:
Parkinson's disease
Deep brain stimulation
Dual-task
Gait
Cognitive impairment

A B S T R A C T

Background: Gait impairment in Parkinson's disease reduces mobility and increases fall risk, particularly during cognitive multi-tasking. Studies suggest that bilateral subthalamic deep brain stimulation, a common surgical therapy, degrades motor performance under cognitive dual-task conditions, compared to unilateral stimulation.
Objective: To measure the impact of bilateral versus unilateral subthalamic deep brain stimulation on walking kinematics with and without cognitive dual-tasking.
Methods: Gait kinematics of seventeen patients with advanced Parkinson's disease who had undergone bilateral subthalamic deep brain stimulation were examined off medication under three stimulation states (bilateral, unilateral left, unilateral right) with and without a cognitive challenge, using an instrumented walkway system.
Results: Consistent with earlier studies, gait performance declined for all six measured parameters under cognitive dual-task conditions, independent of stimulation state. However, bilateral stimulation produced greater improvements in step length and double-limb support time than unilateral stimulation, and achieved similar performance for other gait parameters.
Conclusions: Contrary to expectations from earlier studies of dual-task motor performance, bilateral subthalamic deep brain stimulation may assist in maintaining temporal and spatial gait performance under cognitive dual-task conditions.

1. Introduction

In Parkinson's disease, gait impairments reduce mobility and increase fall risk, leading to patient injury and loss of independence [1,2]. Kinematic alterations in parkinsonian gait include reduced velocity, stride length, increased double-limb support (DLS) time, and stride-to-stride variability [3,4]. Gait impairments worsen under real-world conditions when ambulation is paired with simultaneous cognitive challenges, such as when navigating a complex environment [2,5,6]. Under such “dual-task” conditions, patients experience further degradation in gait than when examined without a cognitive challenge [2].

When patients with Parkinson's disease are treated with subthalamic deep brain stimulation (STN DBS), both unilateral and bilateral DBS alleviate changes in gait velocity, stride length, and gait asymmetry under single-task conditions [3,7–10]. Compared with unilateral STN DBS, bilateral STN DBS produces additional gait improvement [10–12]. However, recent studies suggest that the superiority of bilateral DBS may not be maintained under dual-tasking. A study of upper-extremity function found that bilateral STN stimulation worsens motor performance under cognitive dual-task conditions [13]. However, these effects were not observed for gait under dual-task conditions [14]. Although degraded performance may be expected, the relative impact of bilateral to unilateral STN DBS on gait performance under cognitive dual-task

* Corresponding author. 1500 E, Medical Center Drive, SPC 5338, Ann Arbor, MI 48109-5338, USA.
E-mail address: pgpatil@med.umich.edu (P.G. Patil).
[1] G. Chenji and M. L. Wright contributed equally to this work.

http://dx.doi.org/10.1016/j.parkreldis.2017.02.028
1353-8020/© 2017 Published by Elsevier Ltd.

conditions remains unknown.

Based on prior studies, we hypothesize that compared to unilateral stimulation, bilateral stimulation results in a decline in gait performance under dual-task conditions. We examined walking kinematics under single- and dual-task conditions in patients with Parkinson's disease treated with bilateral STN DBS. Bilateral, unilateral left-sided and right-sided stimulation states were examined off medications under single- and dual-task walking. Contrary to expectations, we find that bilateral STN DBS exceeds unilateral STN DBS gait performance, under cognitive dual-task conditions.

2. Materials and methods

2.1. Patients

Seventeen patients with advanced Parkinson's disease who had undergone bilateral STN DBS surgery at the University of Michigan were enrolled in this study. Eligibility criteria for DBS at our center include an established diagnosis of Parkinson's disease, 30% improvement in MDS-UPDRS Part III motor scores with levodopa, the presence of motor fluctuations or severe rest tremor not adequately managed by medications, and an absence of significant dementia or depression on formal neuropsychological testing [15]. Inclusion criteria for the study included DBS surgery within 5 years, stable optimized stimulation settings for 3 months, ability to ambulate independently for 25 feet in the on stimulation/off medication state, and stable cognitive ability as evaluated by the Mini-Mental State Examination [16]. Non-native English speakers were excluded from the study. Written informed consent was obtained from all patients. The Medical School Institutional Review Board of the University of Michigan approved this study.

2.2. Experimental design

Prior to gait testing, baseline MDS-UPDRS Part III motor scores were collected while patients were *on* medication with bilateral STN stimulation. Patients were then subsequently examined at least 12 h after stopping dopaminergic medication under three stimulation states (bilateral DBS, unilateral left DBS, unilateral right DBS). The order of stimulation testing conditions was determined through a computer-generated random sequence and programmed by a third-party clinician. Investigators and patients were blinded to stimulation state. Each adjustment of DBS state was followed by 90–120 min of rest to minimize carryover effects between conditions. MDS-UPDRS Part III motor scores and gait were evaluated for each stimulation state. Patients were not evaluated under off-medication/off-stimulation states due to safety concerns related to freezing and falling.

For each stimulation state, gait was evaluated under single-task (walking alone) and dual-task (walking while simultaneously meeting a cognitive challenge) conditions. Cognitive tasks included forward counting in English by threes or alternate alphabet letter-naming. In order to minimize learning effects, cognitive tasks were counterbalanced for each patient and were different for each walking trial. Starting numbers ranged from zero to ten and letters from A to G; these were provided verbally to the patient just prior to each walking trial.

Quantitative gait analysis was performed using a validated, commercially available instrumented walkway system (GAITRite; CIR Systems, Inc., Franklin, NJ) [17]. It measures 16 feet (487 cm) in length and 2 feet (61 cm) in width, and records timing and location of foot strikes through implanted mechanical sensors at a sampling rate of 80 Hz. Patients performed walking trials wearing comfortable flat-soled shoes at a self-selected pace. Three walking trials were performed for each stimulation state and cognitive task condition. A rest period of 2–3 min separated each walking trial. Patients first attempted to perform walking trials without an assistive device. If the patient was unable to complete the trials without an assistive device, then the least restrictive device (cane or walker) was allowed throughout the study for safety. Mechanical artifacts due to assistive devices were removed prior to analysis of footfalls. Three walking trials were included in a gait test to calculate the gait variables for each testing condition.

2.3. Data analysis

Evaluated gait parameters included step length, step length variability, cadence, normalized velocity, double-limb support (DLS) time, and functional ambulation performance index. Step length (cm) is the measured distance from heel center of the foot to heel center of the opposite foot. Step length variability (cm) is defined as standard deviation of the step length. Cadence is the rate of stepping (steps/min). Velocity (cm/sec) is defined as the distance traveled divided by the time elapsed between first contact of the first and last footfalls. Normalized velocity (sec^{-1}) is obtained after dividing the velocity by the average leg length. Gait cycle time (sec) is the elapsed time between the first contacts of two consecutive footfalls of the same foot. DLS is the gait cycle time between heel contact of one footfall to the toe-off of the opposite footfall, in seconds. Hence, right DLS is the percentage of the gait cycle between right heel contact and left toe-off.

The functional ambulation performance index quantifies gait performance at a self-selected pace [18,19]. Parameters utilized to calculate the index include standard velocity normalized to leg length, step to leg length ratio, step time, left and right leg asymmetry of step length, and dynamic base of support. Values are deducted from an initial score of 100 points based on deviations in gait parameters. Calculation of the index was performed by software provided with the instrumented walkway system.

2.4. Statistical analysis

Statistical analysis was performed using SPSS Statistics for Macintosh, Version 21.0 (IBM Corp., Armonk, NY). Spatiotemporal parameters of gait and MDS-UPDRS motor scores were analyzed with repeated measures of ANOVA, with the three stimulation states and the three gait tasks as repeated measures. The Greenhouse-Geisser correction was used when the assumption of sphericity was violated. *Post hoc* contrasts with Bonferroni adjustment for multiple comparisons were used to evaluate differences between stimulation states, task complexity, and interactions between the two, if significance was achieved. A P-value less than 0.05 is considered significant.

3. Results

3.1. MDS-UPDRS motor score for unilateral and bilateral DBS

Seventeen DBS patients met inclusion/exclusion criteria and were enrolled in the study. Table 1 reports patient demographics, Mini-Mental State Examination scores, and MDS-UPDRS motor scores for patients under each stimulation state. Patient MDS-UPDRS motor scores with bilateral DBS stimulation, both on and off medication, were improved compared to unilateral stimulation to the right or left side ($P = 0.0005$ and $P < 0.0001$, respectively).

3.2. Functional ambulation performance

Fig. 1A shows the effects of stimulation state and task condition on functional ambulation performance index. There was a main

Please cite this article in press as: G. Chenji, et al., Parkinsonian gait improves with bilateral subthalamic nucleus deep brain stimulation during cognitive multi-tasking, Parkinsonism and Related Disorders (2017), http://dx.doi.org/10.1016/j.parkreldis.2017.02.028