ISB 2013 BRAZIL
XXIV CONGRESS OF THE INTERNATIONAL SOCIETY OF BIOMECHANICS
XV BRAZILIAN CONGRESS OF BIOMECHANICS

Deep brain stimulation can influence gait in individuals with essential tremor: Two case studies

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SUMMARY
This is the first pilot study of its kind to assess the effect of acute posterior subthalamic area (PSA) deep brain stimulation on gait, in patients with essential tremor (ET). Two participants with ET underwent 3D biomechanical gait analysis pre and post PSA deep brain stimulation. Peak ankle joint power exhibited increases with micro-lesioning and high-frequency stimulation in both participants. We postulate that the dorsal PSA may have a regulatory role in gait, with deep brain stimulation holding therapeutic potential for gait disorders.

INTRODUCTION
There is evidence to suggest that deep brain stimulation of the PSA may have a role in improving the gait of patients with ET. Animal studies have shown that the Zona Incerta (ZI), located in the PSA, is involved in locomotor control [1]. However, the hypothesis that the ZI, and thus the PSA surgical target, is involved in the control of gait has not been tested in humans. Therefore, the aim of this pilot study was to perform a 3D kinematic and kinetic gait analysis in two ET patients undergoing PSA deep brain stimulation.

METHODS
Two male clinical participants (ET1 and ET2), aged 60 and 63 (Fahn-Tolosa-Marin score of 67 and 85 respectively) underwent a non-randomised phase I/II clinical trial of PSA deep brain stimulation for ET. Surgeries were performed at the Sir Charles Gairdner Hospital using the MRI-directed implantable guide tube technique [2].

Both participants underwent gait analysis using standard 3D gait analysis techniques [3] on two occasions under their preferred walking speed; pre-operatively and post-operatively. Two days following the pre-operative baseline gait assessment, participant ET1 underwent a unilateral brain implant while ET2 underwent bilateral brain implants. The post-operative gait analysis protocol comprised of three stimulation settings: 1) micro-lesioning, 2) stimulation to the dorsal ZI (dZI), and 3) stimulation to the caudal ZI (cZI). The stimulation settings were standardized for both regions at a pulse width of 60 µs, frequency of 130 Hz, and amplitude of 3.0 V and were randomized and double blinded to both the assessors and participants to reduce biasness.

A synchronized 12-camera VICON MX 3D motion analysis system (100 Hz) and a Kistler force plate (2000 Hz) were used to collect raw 3D trajectories and ground reaction force data. Following a residual analysis [4] all marker trajectories and ground reaction force data were filtered using a fourth-order, 8 Hz zero-lag low-pass Butterworth filter. Lower limb joint angle kinematic and kinetic data were calculated using a customized model [3] in the VICON Nexus pipeline, while discrete values and waveform data were outputted using a custom MATLAB program. Data were time-normalised to 101 data points as a percentage of the gait cycle. Joint moment and power were normalized by bodyweight (N•m/kg and W/kg respectively). Spatiotemporal parameters and sagittal plane kinematic and kinetic variables were analyzed. Preliminary data (pre-operative analysis) did not produce a high effect size between groups and no statistical scores were obtained due to the limited sample and the research being treated as an initial pilot study.

RESULTS AND DISCUSSION
Participant ET1
Spatiotemporal parameters
Gait velocity did not differ between post-operative conditions, except in the case of dZI stimulation where velocity increased from 1.1 ± 0.05 m/s at baseline to 1.32 ± 0.05 m/s for dZI stimulation. This slight increase in velocity can be attributed to an increase in cadence from 103 ± 1 steps/min at baseline, to 117 ± 0 steps/min for dZI stimulation. Double support times in all three post-operative conditions were also seen to decrease by 9-15 %, when compared with the baseline level with dZI stimulation having the most change from 1.33 ± 0.01 s to 1.13 ± 0.03 s.

Kinematics

The most prominent kinematic changes were observed at the ankle joint. Ankle range of motion (ROM) showed a marked increase of 37 % from 29 ± 0.8° at baseline to 37 ± 2.0° as a result of micro-lesioning and stimulation. The increase in ankle ROM can be largely attributed to the increase in the peak ankle plantar-flexion angle achieved at toe-off.

Kinetics

Mean peak flexion-extension ankle power generation increased following micro-lesioning when compared with baseline levels, with even greater improvements observed with dZI stimulation (Figure 1). Baseline ankle power increased from 3.12 ± 0.08 W/kg to 4.44 ± 0.56 W/kg with micro-lesioning and subsequently, mean ankle power increased from the 87th percentile to well above the 95th percentile of normal population values [4] (Figure 1). Furthermore, mean ankle power further increased to 5.52 ± 0.16 W/kg with dZI stimulation.

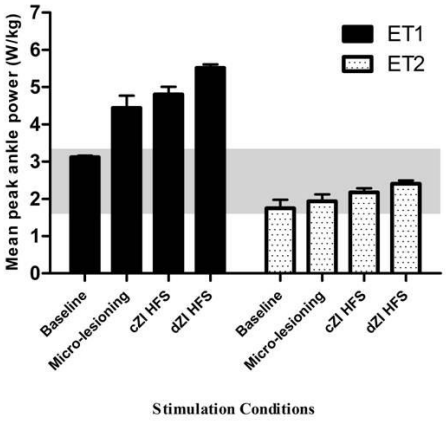

Figure 1: Mean peak ankle power generation of both participants across all stimulation conditions. Shaded area represents the normal range (two standard deviations) of values from a normal elderly population

Participant ET2

Spatiotemporal parameters

Gait velocity did not change with micro-lesioning. There was a small increase from 0.92 ± 0.07 m/s to 1.09 ± 0.05 m/s with cZI stimulation and 1.02 ± 0.05 m/s with dZI stimulation. The slight increase in velocity for dZI stimulation can be attributed to an increase in cadence from 110 steps/min to 126 steps/min. Also consistent with findings in ET1, there were decreases in double support time of 7 % (dZI) and 17 % (cZI).

Kinematics

As in ET1, the most prominent kinematic changes were seen at the ankle joint. Ankle ROM did not increase though peak ankle dorsi-flexion reduced from a baseline level of 19.0 ± 4.3° to 12.5 ± 3.6° with micro-lesioning.

Kinetics

The combination of micro-lesioning of the PSA and dZI stimulation resulted in a 38 % increase in mean peak flexion-extension ankle power production (Figure 1). All gait trials showed the same effect, with changes mirroring those seen in ET1 and provide further support the role of the dZI in the regulation of walking gait (Figure 1).

The increase in ankle power production and cadence, and decreased double support time for both ET1 and ET2 was not an expected finding following micro-lesioning or stimulation. This limited sample is the first evidence of increased ankle power production following deep brain stimulation in patients with ET. The unique finding of the increase in cadence is indicative of a change in the rhythmic aspect of gait. This resulted in a decrease in double support time, possibly reflecting the participants' increased confidence in the performance of the gait task. Due to a paucity of deep brain stimulation research investigating gait kinetics and kinematics across other brain sites, the specificity of these early results to the dZI zone is unknown, except to say that the effect on gait is more pronounced than stimulation to the cZI.

The neural control of gait is far from completely understood, and we present no evidence to either support or refute current theories of locomotor control or dysfunction in ET. What has been convincingly shown by others is that the mechanical work done at the ankle is fundamental to an efficient walking pattern [5]. We consider it important therefore, that the most notable gait alteration common to both participants was increased ankle power generation. Thus the PSA in general and the dZI voxel in particular may play a role in gait regulation, at least in an ET population.

CONCLUSIONS

A combination of micro-lesioning of the PSA and acute dZI stimulation resulted in an increase in peak ankle power in two ET participants. Interestingly, neither participant complained of problems with gait and nor exhibited gross abnormalities of gait on clinical examination, and both expressed a sense of improvement in gait during at least one stimulation experimental condition. The increase in ankle power generation was the most striking effect of micro-lesioning of the PSA and stimulation of dZI on the gait patterns of the two participants. The dZI region of the PSA may play a role in gait control. Electrical stimulation experiments of the PSA and other brain sites in ET and other movement disorders including Parkinson's disease will reveal more about the role of the PSA in gait control.

REFERENCES

1. Mitrofanis J. Some certainty for the "zone of uncertainty"? Exploring the function of the zona incerta. *Neuroscience* 2005;**130**:1–15.
2. Thani NB, Bala A, Lind CRP. Accuracy of magnetic resonance imaging-directed frame-based stereotaxis. *Neurosurgery* 2011;**70**:114-123.
3. Besier TF, Sturnieks DL, Alderson JA, Lloyd DG. Repeatability of gait data using a functional hip joint centre and a mean helical knee axis. *J Biomech* 2003;**36**:1159–1168.
4. Winter DA. *The biomechanics and motor control of human gait: Normal, elderly and pathological.* Waterloo, ON:University of Waterloo Press, 1991.
5. Novacheck TF. The biomechanics of running. *Gait Posture* 1998;**7**:77–95.