Effects of Deep Brain Stimulation and L-dopa in Walking Features of Parkinsonian Patients

Maurizio Ferrarin*, Mario Rizzone, Leonardo Lopiano, Mauro Recalcati, Antonio Pedotti

Bioengineering Unit, Don Gnocchi Foundation Milan, Italy
Bioengineering Department, Polytechnic University, Milan, Italy
Neuroscience Department, University of Turin, Italy

Introduction

Gait function is highly affected in patients with Parkinson's disease (PD) and this has a profound impact on the motor ability of those patients. Typically, PD gait is slow and shuffling, stride length is shortened and velocity reduced. A reduced range of motion (ROM) at the joint level is also present [1]. A severe incapability to start walking or sudden freezing are characteristics of the advanced phase of PD. All of these symptoms are due to the alteration of the basal ganglia function relative to the loss of dopaminergic neurons in the substantia nigra pars compacta. In the advanced phase of PD it is often impossible to obtain a good improvement of the motor symptoms despite the best pharmacological treatment; therefore, recently the surgical approach has shown an increasing interest. It has been shown that, in the advanced PD phase, high frequency electrical stimulation (HFS) of the subthalamic nucleus (STN) can represent a good therapeutical option leading to a significant improvement of all the motor disturbances including gait [2]. Recently, these improvements have been quantified by means of a kinematic and dynamic analysis of PD patients walking with and without STN stimulation [3]. Other studies have concentrated on the effect of DBS on postural sway [4]. However, it is still unclear whether the mechanisms involved in STN stimulation are different from those induced by L-dopa.

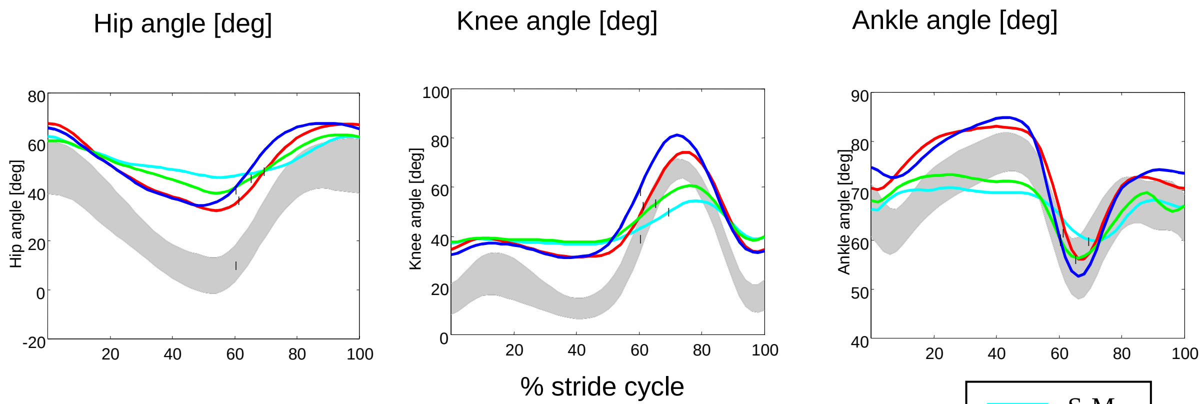
Goal of the present study is therefore to compare, in the same group of patients with PD, the effects on walking of STN stimulation and of L-dopa. Moreover, the presence of an additional effect of these two treatments is investigated.

Methods

Ten idiopathic PD patients implanted bilaterally with an STN stimulation system and ten age-matched controls were studied with a 3D gait analysis system (ELITE system, BTS, Italy e Kistler, Switzerland), adopting a full body acquisition protocol described in [3]. The patients have been analysed with (S+) and without (S-) STN stimulation and with (M+) and without (M-) a suprathreshold dose of pharmacological treatment (L-dopa); thus in the following four conditions: S-M-, S+M-, S-M+, S+M+. Mean values of stimulation parameters were: voltage=3.1±0.4V, rate=143.3±17.4Hz and pulse width between 60µs and 90µs. Post processing procedures of acquired data provided lower limb joint angular trajectories, joint moments and powers. Moreover, forward (pitch) and lateral (roll) rotation of the trunk and trunk lateral bending and torsion have been computed. A clinical evaluation, according to the UPDRS motor scores, has been performed too. Non parametric statistical analysis (ANOVA Friedman and Wilcoxon matched paired test) has been used to compare the four conditions.

Results

As regards the group analysis, the results showed that both the stimulation alone (S+M-) and the L-dopa alone (S-M+) significantly increased the stride length and the gait speed, with an additional effect when the treatments were applied simultaneously (S+M+). The cadence was more influenced by L-dopa. The significant increase of ROM (Range of Motion) of all lower limb joints during walking was similar in S+M- and in S-M+, while there was a slight additional effect of treatments (S+M+) only at knee and ankle. The increase of pelvic tilt was greater in S-M+ than in S+M-, and there was an additional effect of L-dopa on stimulation. Finally, the range of lateral bending and torsion of the trunk, which were reduced in the basal condition (S-M-) condition, increased similarly in S-M+ and in S+M-. The exaggerated forward inclination of the trunk found in S-M- reduced towards control values in all therapeutic conditions. Concerning the dynamic data, the peak of power production during the push off phase, increased similarly with stimulation and L-dopa alone, without achieving the control values and not showing any additional effect.



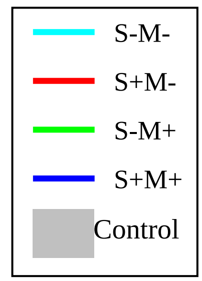


Fig. 1 – Example of Kinematric profiles of the lower limb joints in the sagittal plane. The mean trajectories in the four conditions (S-M-, S+M-, S-M+, S+M+) are superimposed. Shaded area is the range of variability (+/- 1 SD) of control subjects. This patient presents larger effects with STN alone than with L-dopa alone.

The single subject analysis showed that 8 patients out of 10 presented a general improvement of the walking pattern and a significant increase of speed (with respect to the basal condition) when stimulation was applied. One of the two residual subjects, although not showing significant changes in gait parameters, presented an improvement of the mobility and of the correct forward inclination of the trunk. Among the eight patients who showed significant improvements in walking, three of them presented larger effects with STN stimulation (see for example fig. 1), three with L-dopa and two did not show significant differences between the two treatments.

Discussion

High frequency electrical stimulation of the subthalamic nucleus provides significant improvement in gait features of patients with idiopathic PD. The main improvements found in the present study are: an increase of stride length and of walking speed, an increase of ROM of lower limb joints, a recovery of a more physiologic mobility and postural attitude of the trunk, and an increase of the power production peak at push off. In most cases such improvements are similar or even greater than those associated to L-dopa treatment, and do not present the negative secondary effects of the pharmacological approach. For some of the parameters considered, an additional effect was found.

Due to the presence of additive and synergistic effects, we conclude that the mechanisms of action of the two treatments are likely different and that, in most cases, the optimal effect can be obtained when an adequate dosage of L-dopa is added to the STN stimulation. Finally, this study highlighted the importance of the multifactorial analysis of movements in the comprehension and differentiation of treatments' effect and, in some cases, in the optimisation of drug dosage.

References

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