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Tonic spinal cord stimulation as therapeutic option in Parkinson disease with axial symptoms: Effects on walking and quality of life

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ABSTRACT

Spinal cord stimulation (SCS) is an effective surgical therapy used for the treatment of chronic neuropathic pain. Tonic SCS is safe and improve not only gait disorders, motor symptoms, but also quality of life in Parkinson patients even with dopa-resistant symptoms with or without associated deep brain stimulation.

Postural instability or gait disorders usually arise in advanced phase in Parkinson disease (PD) and are relatively resistant to treatment. Spinal cord stimulation (SCS) is an effective surgical method of neuromodulation used for the treatment of chronic neuropathic pain [1]. A positive effect of SCS on motor symptoms was reported on isolated cases or small cohorts of PD patients often associated with limb pain or with heterogeneous stimulation protocol [2,3].

We investigated the effect of a standardized Tonic SCS in PD patients with gait disorders 60 days post stimulation.

The monocentric prospective study was approved by the local ethics committee (Cpp Ile de France VIII) and registered at Clinical Trials.gov (NCT02381951). All patients provided signed informed consent. Inclusion criteria were: idiopathic PD for more than 5 years, resistant gait disorders and/or FOG, patients aged 18–80 years old. Patients with atypical parkinsonism, vascular lesions on brain MRI, pregnant, with psychiatric disorders, MMSE < 24, neuropathic pain, abnormal somatosensory evoked potentials, abnormal dorso-lumbar MRI, contra-indication to surgery were excluded. Five patients, including one with deep brain stimulation, were included prospectively and consecutively.

A percutaneous lead (Octrode ™, 3183 St. Jude Medical ©) was inserted into the epidural space on the median line at the T10-T11 level under general anaesthesia and connected to a pulse generator. (EonC ™" -St. Jude Medical ©).

Tonic monopolar stimulation was delivered in a standardized manner at 100 Hz and 300 μs. The amplitude and one active contact were chosen individually just at the threshold of paresthesia in lower limbs. Parameters remain stable during the study.

Endpoints were assessed before surgery in OFF and ON dopa condition and 60 days after SCS with stimulation OFF in OFF and ON dopa condition, and with stimulation ON in OFF and ON dopa condition. ON dopa condition was obtained by the administration of Modopar 125 dispersible® at a dose representing 150% of the usual morning dose. For OFF dopa, drugs were discontinued for at least 12 hours.

The primary evaluation criterion was the change before and after SCS of the stand-walk-sit test (SWS). Patients were blindly assessed by a neurologist (MZ) on the filmed SWS.

Secondary evaluation criteria were: MDS-UPDRS part III, "Freezing of gait" questionnaire (FOG-Q) and PDQ 39.

Paired-sample tests were used for FOG-Q and PDQ-39. Repeated measure analysis of variance was used for MDS-UPDRS. Post-hoc Tukey analyses were performed with Bonferroni corrections afterwards ($p > 0.05$). No tests were performed for variables with missing scores.

The five patients were male, 68.8 yo ± 3.9, MMS 27.6 ± 2.6, 14.8 years ± 7 of disease. Three patients achieved the SWS in OFF dopa and four in ON dopa condition. After SCS all patients achieved the SWS both in ON or OFF dopa condition. Fig. 1A and B shows the results of the 3 patients who successfully performed the SWS under all conditions. Administration of L-Dopa reduced the number of steps by 18%, SCS alone decreased by 12.4% and SCS coupled with of L-Dopa by 20% (Fig. 1A). L-Dopa reduced the duration of SWS by 19.3%, SCS alone decreased by 23.6% and SCS coupled with L-Dopa by 29.8% (Fig. 1B).

With SCS alone, all patients exhibited significant improvement in the MDS-UPDRS score (23.22%), even more marked with dopa (36.8%) (Fig. 1C). The axial signs (items 9 to 13) were significantly improved by SCS alone of 29.8% and by SCS plus dopa by 42.5%.

Difference in FOG-Q scores did not reach significance.

All patients experienced a significant improvement of PDQ39 from 72.2 to 57 ($p = 0.03$). The sub-score of the PDQ39 concerning mobility (1–10) significantly improved from 29.6 to 22.6 ($p = 0.03$) (Fig. 1D). No side effects were observed. At the end of the study, all patients wanted to continue the stimulation.

We now have a follow up of 2 years ± 5 months. After the study, 3 of the 5 patients included retained the initial stimulation parameters as they were considered effective. Another had a pulse duration reduced to 150 ms with an increased stimulation frequency to 190 Hz. For the last patient, the frequency was increased to 200 Hz. We didn't identify a particular phenotype in these two patients. Although not included in the protocol, we assessed the long-term benefit of SCS by the CGI-Improvement scale. The score was evaluated at 2.6 ± 0,5. All patients have chosen to continue the stimulation.

The mechanisms accounting for the effect of SCS are unknown but, from accumulated experience with the use of SCS in the management of chronic pain, it is known that the pathways most probably activated by SCS are the superficial fibers of the dorsal columns [4]. Fuentes et al. suggested that the prokinetic effect of SCS is mediated through activation of lemniscal and brainstem ascending pathways to thalamic

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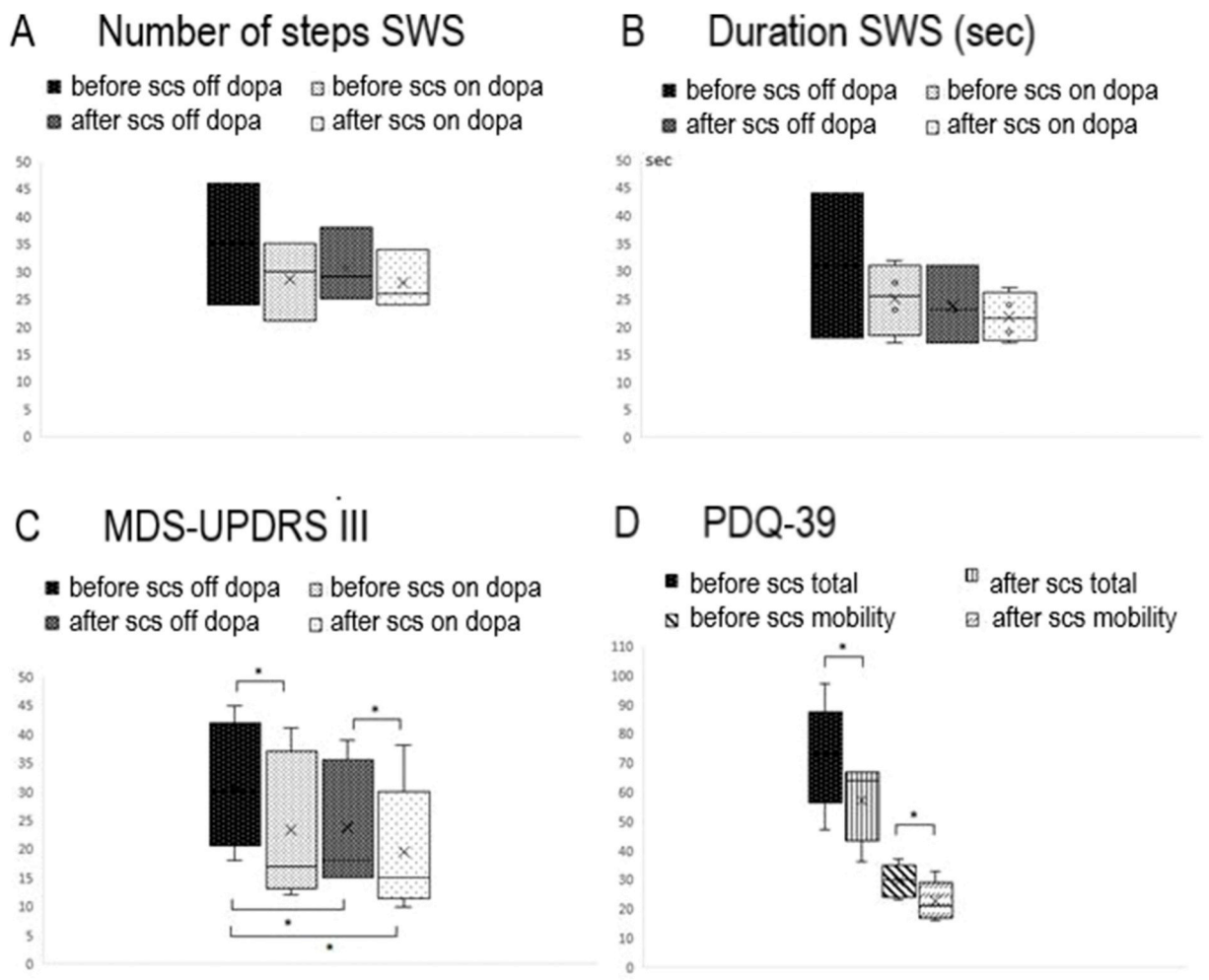

Fig. 1. Fig. 1A and B: Changes in SWS: stand-walk-sit test. Due to the severity of the gait trouble only 3 of the patients achieved the SWS ON and OFF dopa. Fig. 1A: Dopamine reduced the number of steps by 18%, Spinal Cord Stimulation (SCS) alone decreased by 12,4% and SCS coupled with dopamine by 20%. Fig. 1B: Dopamine reduced the duration of SWS by 19,3%, SCS alone decreased by 23,6% and SCS coupled with dopamine by 29.8%. With SCS alone, all patients exhibited significant improvement in MDS-UPDRS (Unified Parkinson Disease Rating Scale) by 23.22%. Fig. 1C Changes in MDS-UPDRS before and after SCS at day 60. With SCS alone, all patients exhibited significant improvement in the MDS UPDRS score (23.22%), even more marked with dopa (36.8%). Fig. 1D Changes in PDQ 39. After 60 days of SCS, PDQ39 improved of 21%, with the mobility sub-score (items 1 to 10) improving by 23.6%.

nuclei, cerebral cortex and brain stem nuclei contributing to initiation of movement [5].

In conclusion, tonic SCS is safe and effective to improve gait disorder, motor symptoms and quality of life in Parkinson patients. This effect cannot be explained to the relief of pain as we included only painless patients. Complementary studies are needed to establish possible correlations between patient characteristics and optimal stimulation parameters and to investigate the neurophysiological changes occurring at different SCS parameters.

Potential conflict of interests

The authors declare that they have no potential conflicts of interest in relation to this article.

Disclosure

The author has no conflicts of interest relevant to this study.

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