



## Sacral nerve stimulation improves gait in Parkinson's disease



### Introduction

Neurogenic overactive bladder is frequently present as a manifestation of autonomic dysfunction in patients with Parkinson's disease (PD). Sacral nerve stimulation (SNS), which delivers low-amplitude electrical stimulation via a lead to the sacral nerve accessed from the S3 foramen, is an established treatment of urinary incontinence, high urinary frequency and urinary retention [1]. Here, we report our findings that SNS unexpectedly improved gait in a patient with PD.

### Case report

A 56-year old man was diagnosed with PD seven years before his initial visit with us. He received bilateral DBS of the globus pallidus pars interna (Gpi) five years after PD diagnosis because of progressive motor disability and response fluctuations. The dyskinesias improved postoperatively but his pre-existent gait disturbances (hypokinetic gait and freezing of gait (FOG) that manifested in both ON/OFF state) did not improve and were resistant to all adjustments of dopaminergic medication or DBS settings (as recommended by conventional protocols) [2,3]. At home, he experienced FOG at least once daily with a duration of around 30 seconds, which seriously affected his quality of life. FOG episodes usually appeared at movement onset, during turning, when crossing narrow passages or when he was anxious. Nine years after the diagnosis of PD, neurogenic bladder dysfunction developed, as reflected by dysuria, frequent urination and incomplete emptying. These symptoms caused anxiety which in turn further worsened his FOG. To reduce the need for intermittent catheterization, he received bilateral SNS. A single electrode (Interstim<sup>®</sup> model 3889-28; Medtronic, Minneapolis, MN) was inserted bilaterally into the sacral foramen (S3). We selected the sacral nerve root that provided the best perineal motor response and ipsilateral big toe response. Subsequently, the lead was connected to an external stimulator (Medtronic Interstim<sup>®</sup> 3625) set at the maximal subsensory threshold (1.9 V, 16 Hz, 210 ms). Medication and Gpi DBS parameters remained unchanged. Urine retention disappeared after three days of SNS; the residual urine volume decreased from 230 ml to 30 ml. The lead was subsequently connected to an internal pulse generator (Medtronic Interstim<sup>®</sup> II 3058) and placed in a subcutaneous pocket over the hip under local anesthesia (Fig. 1). The internal pulse generator was programmed to elicit a low-threshold perianal sensory response with 15 minutes on and 15 minutes off as a 30 min loop. The patient described a constant paranesthesia in the perineum during the 'on' state of SNS, but this was not rhythmic in nature. Interestingly, the patient's gait performance improved when the nerve stimulator was switched on (video). Improvement was observed within

minutes of stimulation onset and slowly deteriorated again in hours after SNS was switched off, suggesting a carry-on effect of the stimulation. In the three months after SNS treatment, he experienced an improvement in frequency and duration of FOG at home which was consistently present throughout the day. The patient reported substantially more confidence in executing daily tasks and an improved quality of life.

Supplementary video related to this article can be found at <https://doi.org/10.1016/j.brs.2019.03.074>.

Three possible mechanisms might explain how SNS improved FOG in this patient. First, SNS-induced paresthesias may have increased arousal, thereby supporting a shift from automated to more goal-directed control of gait [4]. In this patient, we applied 15 minutes on and 15 minutes off cycle mode in each impulse generator, so tolerance for the sensation of paresthesias did not occur. Second, as anxiety is a strong provoking factor for FOG [5], SNS might have improved gait indirectly, by reducing the stress and anxiety that accompanied the neurogenic bladder dysfunction. Third, and more speculatively, SNS may have partially corrected disruptions in spinal cord networks, similar to what has been suggested as the possible underlying working mechanisms for spinal cord stimulation (SCS) [6,7]. More specifically, the pedunculopontine nucleus (which plays a key modulatory role in gait) might then be modulated by SNS, via ascending pathways from the spinal cord [8].

These preliminary observations provide cautious initial evidence that SNS might be a safe approach to improve both FOG and urinary retention in patients with advanced PD. Our findings must now be replicated in a larger study with longer follow-up.

### Author contributions

Collecting video data: L.B.W.  
 Video rating: J.N., L.B.W.  
 Surgery: Y.X.P, B.M.S, D.Y.L.  
 Statistical analysis: C.C.Z.  
 Drafting the manuscript: C.C.Z, L.B.W.  
 Critical comments: J.N., B.R.B., D.Y.L.

### Disclosures

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**Fig. 1.** A posteroanterior X-ray image illustrates the deep brain stimulation and sacral nerve stimulation systems.

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### References

- [1] Peters KM, Kandagatla P, Killinger KA, Wolfert C, Boura JA. Clinical outcomes of sacral neuromodulation in patients with neurologic conditions. *Urology* 2013;81:738–44. <https://doi.org/10.1016/j.urology.2012.11.073>.
- [2] Nonnekes J, Snijders AH, Nutt JG, Deuschl G, Giladi N, Bloem BR. Freezing of gait: a practical approach to management. *Lancet Neurol* 2015;14:768–78. [https://doi.org/10.1016/S1474-4422\(15\)00041-1](https://doi.org/10.1016/S1474-4422(15)00041-1).

- [3] Picillo M, Lozano AM, Kou N, Puppi Munhoz R, Fasano A. Programming deep brain stimulation for Parkinson's disease: the toronto western hospital algorithms. *Brain Stimul* 2016;9:425–37. <https://doi.org/10.1016/j.brs.2016.02.004>.
- [4] Gilat M, Ligia Silva de Lima A, Bloem BR, Shine JM, Nonnekes J, Lewis SJG. Freezing of gait: promising avenues for future treatment. *Park Relat Disord* 2018;52:7–16. <https://doi.org/10.1016/j.parkrelidis.2018.03.009>.
- [5] Martens KAE, Hall JM, Gilat M, Georgiades MJ, Walton CC, Lewis SJG. Anxiety is associated with freezing of gait and attentional set-shifting in Parkinson's disease: a new perspective for early intervention. *Gait Posture* 2016;49:431–6. <https://doi.org/10.1016/j.gaitpost.2016.07.182>.
- [6] Samotus O, Parrent A, Jog M. Spinal cord stimulation therapy for gait dysfunction in advanced Parkinson's disease patients. *Mov Disord* 2018;33:783–92. <https://doi.org/10.1002/mds.27299>.
- [7] Fuentes R, Petersson P, Siesser WB, Caron MG, Nicoletis MAL. Spinal cord stimulation restores locomotion in animal models of Parkinson's disease. *Science* 2009;323(80):1578–82. <https://doi.org/10.1126/science.1164901>.
- [8] de Andrade EM, Ghilardi MG, Cury RG, Barbosa ER, Fuentes R, Teixeira MJ, et al. Spinal cord stimulation for Parkinson's disease: a systematic review. *Neurosurg Rev* 2016;39:27–35. <https://doi.org/10.1007/s10143-015-0651-1>.

Chencheng Zhang

Department of Functional Neurosurgery, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Linbin Wang

Department of Functional Neurosurgery, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Yixin Pan

Department of Functional Neurosurgery, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Bomin Sun

Department of Functional Neurosurgery, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Jorik Nonnekes

Radboud University Medical Center, Donders Institute for Brain, Cognition and Behavior, Department of Rehabilitation, Nijmegen, Netherlands

Bastiaan R. Bloem

Radboud University Medical Center, Donders Institute for Brain, Cognition and Behavior, Department of Neurology, Nijmegen, Netherlands

Dianyou Li\*

Department of Functional Neurosurgery, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

\* Corresponding author. Department of Functional Neurosurgery, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China.

E-mail address: [ldy11483@rjh.com.cn](mailto:ldy11483@rjh.com.cn) (D. Li).

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