Deep Brain Stimulation Improves Parkinson's Disease-Associated Pain by Decreasing Spinal Nociception

Pain is a frequent non-motor symptom in patients with Parkinson's disease (PD) with increased pain sensitivity and high impact on quality of life.[1,2] Both dopaminergic treatment and deep brain stimulation (DBS) of the subthalamic nucleus (STN) diminish clinical pain and experimental pain sensitivity.[3,4] Dopamine has been assumed to exert its pain-relieving effects at cortical and spinal levels,[4,5] whereas only cortical effects were described for DBS thus far.[6]

The nociceptive flection reflex (NFR) threshold, reflecting spinal nociception, was assessed during medication *on* (MED-*on*) by the Paintracker (www.dolosys.com): (1) once with the DBS switched ON (DBS-ON); (2) twice with the device switched OFF (DBS-OFF); and (3) once with the device switched ON again (DBS-ON). Automatic threshold determination lasted 5 minutes (30 stimuli with 10-second interstimulus interval). The Paintracker assesses the NFR threshold by using 6.085 times the standard deviation of the noise signal as cut-off within the predefined time frame from 90 to 150 ms for the RIII response (nociceptive reflex).[1] NFR thresholds were determined by logistic regression including the last 11 stimuli.[7] The protocol has been approved by the Institutional Review Board (BASEC ID: 2017:00502). The patients gave their written consent.

The assessment was performed in two female PD patients (48 and 61 years) suffering from an akinetic-rigid subtype for 4 and 12 years. The PD pain classification system score of their PD-associated nociceptive pain was 72/90 and 63/90 before DBS and 0 and 28/90 after DBS implantation (first patient, 1 month after DBS; second patient, 2 years after DBS) (Fig. 1).[2]

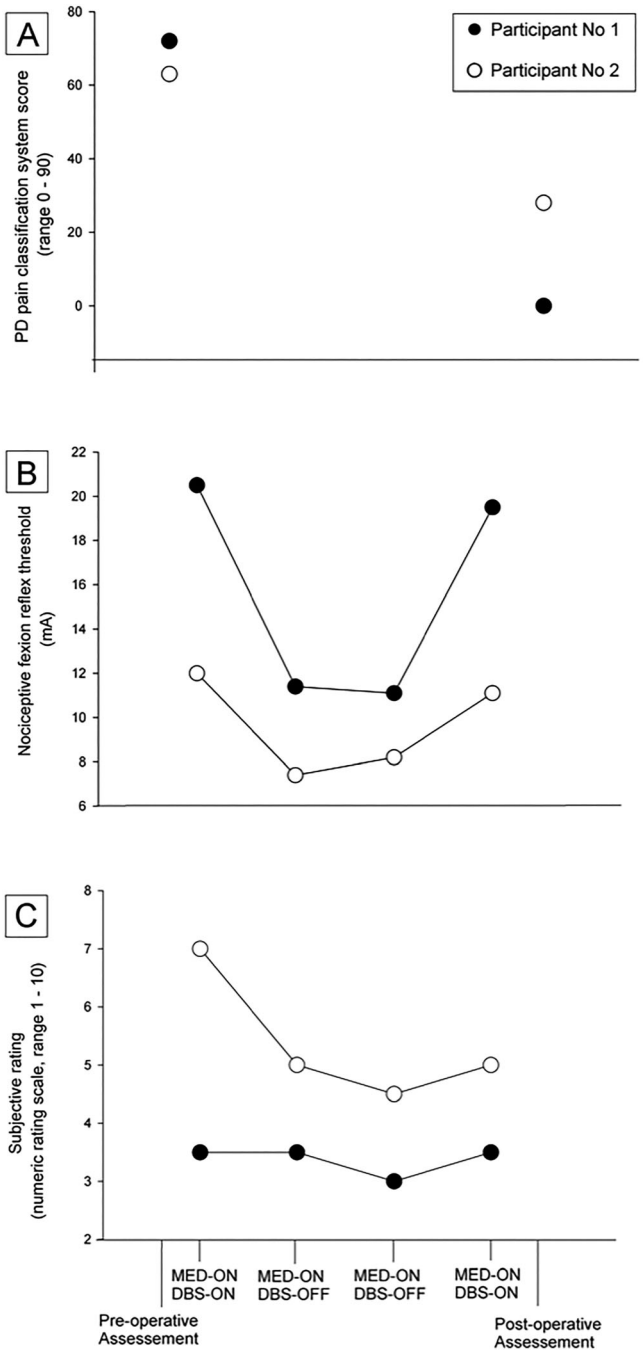

FIG. 1. (**A**) Displays the pre- to postoperative pain assessment in two Parkinson's disease patients. Nociceptive flexion reflex thresholds (**B**) and psychophysical pain ratings (**C**) are shown in a medication *on* and stimulation ON setting (MED-*on*/DBS-ON) and in a medication *on* and stimulation OFF setting (MED-*on*/DBS-OFF).

*__Correspondence to:__ Prof. Dr. Veit Mylius, Department of Neurology, Center for Neurorehabilitation, 7317 Valens, Switzerland; E-mail: veit.mylius@kliniken-valens.ch

Relevant conflicts of interest/financial disclosures: J.H.B. is the former owner of the www.dolosys.com company, the manufacturer of the Paintracker device. V.M., K.W., D.B., D.C.d.A., G.K., J.B., and F.B. report no disclosures relevant to the manuscript.

Funding agency: No specific funding was received for this work.

Received: 16 September 2023; **Revised:** 26 October 2023; **Accepted:** 2 November 2023

Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.29666

In an MED-*on* and DBS-ON setting, the NFR threshold was 20.5/12 mA (first/second patient) and in the MED-*on*/DBS-OFF setting 11.4/7.4 mA and 11.1/8.2 mA, respectively. After switching DBS-ON again, a threshold of 19.5/11.1 mA was measured. This corresponds to a mean NFR threshold increase of 44% and 32%, respectively. The stimuli were rated with an average of 3.5/6 on a numeric rating scale (NRS; 1–10) with DBS-ON and 3.25/4.75 with DBS-OFF. With DBS-ON and medication-*off*, the second patient had a NFR threshold of 7 mA with a corresponding pain report of 6/10 (second patient only).

Here, we present the first observation of DBS effects on spinal nociception in two PD patients with DBS-responsive PD-associated nociceptive pain. Therefore, besides the effects on the somatosensory cortex, the modulation of pain in DBS-responsive patients extents to the spinal level.[6] Because the patients were assessed in the MED-*on* and dopamine exerts its effects also at the spinal level,[4] we hypothesize additive effects on descending inhibitory control. The amount of NFR threshold increase (DBS-ON compared to DBS-OFF) may serve as indicator for DBS programming to treat PD-associated nociceptive pain.

We overcame the problem of increased muscle tone because of inactivating DBS by assessing the NFR directly after turning the DBS OFF and by using a new device allowing for comfortable stimulation. Verbal pain reports in both conditions and results obtained in DBS-ON condition both, before, and following the DBS-OFF condition, underline the validity of our observations.

Acknowledgments: We thank our patients for their participation and patience during the application of the NFR. Open Access funding enabled and organized by Projekt DEAL.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Veit Mylius, MD,[1,2,3*] Jan Harald Baars, MD,[4] Karsten Witt, MD,[5,6] David Benninger, MD,[7] Daniel Ciampi de Andrade, MD, PhD,[8] Georg Kägi, MD,[2,9] Julien F. Bally, MD,[7] and Florian Brugger, MD[2]

[1]*Department of Neurology, Center for Neurorehabilitation, Valens, Switzerland,* [2]*Department of Neurology, Kantonsspital St. Gallen, St. Gallen, Switzerland,* [3]*Department of Neurology, Philipps University, Marburg, Germany,* [4]*Department of Anesthesia, Klinikum Neubrandenburg, Neubrandenburg, Germany,* [5]*Department of Neurology, School of Medicine and Health Sciences, Research Center Neurosensory Science, University of Oldenburg, Oldenburg, Germany,* [6]*Department of Neurology, Evangelic Hospital Oldenburg, Oldenburg, Germany,* [7]*Service of Neurology, Department of Clinical Neurosciences, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland,* [8]*Center for Neuroplasticity and Pain (CNAP), Department of Health Science and Technology, Faculty of Medicine, Aalborg University, Aalborg, Denmark, and* [9]*Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland*

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Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

V.M.: 1ABC, 2A, 2B, 2C, 3A, 3B
J.H.B.: 1C, 2B, 2C, 3B
K.W.: 1C, 2C, 3B
D.B.: 1B, 1C, 2C, 3B
D.C.D.: 2C, 3B
G.K.: 1B, 2C, 3B
J.F.B.: 1B, 1C, 2C, 3B
F.B.: 1B, 1C, 2A, 2B, 2C, 3B.

Financial Disclosures of all authors (for the preceding 12 months)

V.M. received a research grant from BIAL, speaker's honoraria from Zambon and Abbvie, congress organization support from Zambon, AbbVie, and Everpharma, and congress fees from Zambon. J.H.B. reports no disclosures. K.W. receives speaker fees from STADAPHARM, BIAL, and Boston Scientific. He is an advisory board member for STADAPHARM. He received grants from the German Research Society and STADAPHARM. D.B. is supported by the Swiss National Science Foundation. He received speaker's honoraria from BIAL and travel grants from BIAL and Merz. D.C.d.A. is supported by a Novo Nordisk Grant NNF21OC0072828, and European Research Council grant 101087925. G.K. reports no disclosures. J.F.B. received speaker's honorary from Merz, BIAL, and AbbVie and congress fee from Merz. F.B. reports no disclosures.