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## Comment on: “A Transatlantic Viewpoint on the Role of Pallidal Stimulation for Parkinson's Disease”

We read the viewpoint by Drs. Boogers and Fasano with interest.<sup>1</sup> We agree that the target globus pallidus internus (GPi) could have been underused compared with subthalamic nucleus (STN) in deep brain stimulation (DBS) practice for patients with Parkinson's disease (PD), as the published data so far has been largely on STN DBS. Besides the many reasons to endorse a more frequent use of GPi in the future as mentioned in the article,<sup>1</sup> there is also a potential benefit of using GPi for the important and challenging axial symptoms as we would like to emphasize here. The symptoms of postural instability and gait disability (PIGD) were analyzed in a meta-analysis article comparing GPi with STN DBS at medication *off* and *on* status over time.<sup>2</sup> It was found that GPi is superior to STN DBS on PIGD in the long term use of DBS at medication *on* status.<sup>2</sup> Swallowing

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function is another major axial symptom (although much less studied than gait and balance) where GPi DBS has demonstrated superiority to STN, as reflected in a relatively large size study and a more recent systematic review on the effect of DBS on swallowing function,<sup>3,4</sup> particularly at medication *on* status,<sup>3,4</sup> which is also strikingly similar to the conclusion on the effect of GPi compared with STN DBS on PIGD.<sup>2</sup>

Axial symptoms are major causes of morbidity and mortality and poor quality of life in patients with PD, particularly in the advanced disease stage or after long-term DBS therapy,<sup>2,4,5</sup> when they become more and more prominent, but less and less responsive to the dopaminergic medications and DBS therapy, likely because they are largely due to deficits caused by non-dopaminergic mechanisms.<sup>6</sup> It is hard to tell whether the worsening of axial symptoms is because of disease progression, DBS stimulation related side effects (possibly less so in GPi given its much larger size than STN), medication changes (given the significant reduction of the dopaminergic medications post-surgically in patients with STN, but not much in GPi DBS), or the combination of all. This, along with the favorable effect of GPi DBS on mood, cognitive function, and dyskinesia compared with STN DBS,<sup>1,7</sup> would further suggest that GPi should be more frequently used, particularly also as mentioned that the journey post implantation could be different or more challenging for STN, and that we need to make our decision based on real world data, which can also be affected by the currently implicit selection bias of the targets.<sup>1</sup> The possible superiority of GPi DBS on the important challenging axial symptoms of gait, balance, and swallowing function here could possibly further motivate an increased use of GPi,<sup>2,4</sup> which will help us to gather more information on the use of GPi and yield a better assessment and selection of the targets for DBS in the future. ●

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### Data Availability Statement

Data sharing not applicable – no new data generated.

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## Reply to: Comment on: A Transatlantic Viewpoint on the Role of Pallidal Stimulation for Parkinson's Disease

We thank Xie and Warnke for their comment<sup>1</sup> on our viewpoint,<sup>2</sup> in which they raise a possible additional benefit of deep brain stimulation (DBS) targeting the globus pallidus internus (GPI) compared to the subthalamus (STN). Xie and Warnke<sup>1</sup> reference a few different studies showing that postural instability, gait disorder, and swallowing function have a better outcome in cohorts receiving GPI DBS as opposed to STN.<sup>3–5</sup> Our clinical experience is aligned with these findings. Interestingly, one of these studies investigated the impact on axial motor function of unilateral GPI versus unilateral STN DBS.<sup>4</sup> Nowadays, especially when targeting the STN, bilateral procedures have become the standard-of-care, even if staged. Therefore, we argue that the safety profile of GPI is even more beneficial when considering bilateral procedures.

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**Key Words:** deep brain stimulation, Parkinson's disease, subthalamic stimulation, pallidal stimulation

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It is well recognized that axial motor function plays a major role in determining the mood and quality of life of PD patients. Perhaps not surprisingly, a systematic literature review, meanwhile published, concluded that these metrics are more favorable in patients undergoing GPI DBS compared to STN DBS.<sup>6</sup> Specifically, the authors concluded that the GPI cohort demonstrated a greater improvement in terms of Beck Depression Inventory as well as depression and anxiety subscores of the Hospital Anxiety and Depression Scale. Moreover, after a follow-up of 6 months or more, both cohorts showed an improvement in the Parkinson's Disease Questionnaire 39 (PDQ-39), although a larger effect was seen when targeting the GPI. A similar trend was seen in the emotions subscore of PDQ-39.

In conclusion, the points raised by Xie and Warnke<sup>1</sup> further strengthen the main message of our viewpoint, namely that patient-centered and patient-reported outcomes are essential when assessing the effect of DBS in people with PD. ●

### Data Availability Statement

Not applicable.

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