LETTER TO THE EDITOR

Does dominant pedunculopontine nucleus exist?

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Sir,
We read with great interest the paper by Fling et al. (2013) recently published in Brain. In this imaging study, patients with Parkinson’s disease with freezing of gait (FOG), without FOG, and age-matched controls were studied with diffusion tensor imaging to identify group and inter-hemispheric differences of tract quality and quantity in the pedunculopontine nucleus (PPN) network. Interestingly, patients with Parkinson’s disease with FOG had significantly less right PPN tract volume in terms of absolute values and ratio with the left side (i.e. greater laterality index) compared to patients without FOG. Furthermore, solely in the Parkinson’s disease with FOG group, linear regression analysis significantly correlated greater lateralization of PPN tract volume with poorer performance in action inhibition tasks. The authors concluded that right hemispheric circuitry might be uniquely involved in the pathophysiology of FOG (Fling et al., 2013). In keeping with these findings, clinical evidence from the DATATOP cohort supports the notion that patients with left-onset Parkinson’s disease have a moderately increased risk for future development of FOG (Giladi et al., 2001). Moreover, recent studies have pointed to the right hemispheric network involved in visuospatial navigation as an important determinant in the pathophysiology of FOG (Cremers et al., 2012; Peterson et al., 2014).

Keeping all these aforementioned considerations in mind, we have carried out further analysis of patients with Parkinson’s disease who received unilateral PPN deep brain stimulation (DBS) to determine whether the outcome of stimulation was related to the implanted side. This analysis is a post hoc analysis of the same sample of patients with Parkinson’s disease published by Moro et al. (2010) in Brain, which demonstrated that unilateral PPN DBS improves falls. We compared the clinical data of left PPN DBS patients versus right PPN DBS patients. There were three patients in each category, and we looked at the changes in motor performance 3 months post-surgery and 12 months post-surgery compared to baseline. These two groups of patients (left versus right, respectively) did not seem to differ at baseline in terms of gender (three males versus two males), age at disease onset (50.0 ± 5.2 versus 49.3 ± 8.3 years), disease duration at surgery (15.3 ± 5.5 versus 15.7 ± 8.1 years), UPDRS-III OFF medication (40.0 ± 5.1 versus 35.8 ± 7.3), UPDRS-III ON medication (20.3 ± 0.6 versus 16.5 ± 6.1), UPDRS-II OFF medication (22.2 ± 2.3 versus 25.0 ± 3.0), UPDRS-II ON medication (9.7 ± 2.5 versus 12.7 ± 2.5), and specific UPDRS items assessing axial symptoms (Fig. 1). Interestingly, compared to right PPN DBS patients, we found that left PPN DBS patients presented an improvement in many axial symptoms and particularly at 12 months in the stability and gait items of the UPDRS-III in the OFF-medication condition as well as in the stability item ON medication.

Our findings are in keeping with Fling et al.’s (2013) results, possibly indicating that the left PPN plays a compensatory role in the pathophysiology of the right PPN network in Parkinson’s disease. In keeping with this hypothesis, we also found—in a preliminary PET study—that left unilateral PPN stimulation caused increased thalamic perfusion bilaterally by an equal degree, suggesting that the stimulation of one hemisphere may suffice for clinical efficacy (Strafella et al., 2008). Another PET study in
three PPN DBS patients (of whom two had left implant) found significant increases of regional CBF in subcortical structures bilaterally and predominantly in the right cortex (Ballanger et al., 2009). An alternative explanation for the 12-month difference in the two groups of patients is that the decline of axial symptoms was faster in patients with left-dominant parkinsonism (who therefore underwent right PPN DBS). However, this is actually in contrast with a recent study showing that left-sided onset is associated with long disease and ambulatory Parkinson’s disease survival (Munhoz et al., 2013).

In conclusion, these preliminary results encourage us to further explore the concept of a ‘dominant PPN’ in future studies enrolling larger cohorts of patients, a concept already proposed for subthalamic DBS (Castrioto et al., 2011). In spite of PPN having extensive bilateral projections, patients with Parkinson’s disease currently undergo bilateral procedures; therefore, it would be impactful to determine whether unilateral surgery can yield the same degree of clinical benefit, exposing patients to fewer risks.

References


