Sir,

We appreciate the thoughtful comments and additional contributions from Lam and colleagues with regards to our recent manuscript in Brain, which demonstrated substantial asymmetry of structural connectivity strength within the locomotor network of individuals with Parkinson’s disease who experience freezing of gait (FOG+) (Fling et al., 2013). Specifically, we reported reduced white matter tract volume between the right pedunculopontine nucleus (PPN) and the midline of the right frontal cortex, assessed by diffusion tensor imaging. This was in contrast to those patients with Parkinson’s disease who did not have freezing issues and age-matched controls. In addition, this asymmetric reduction of the right hemisphere’s locomotor network was strongly related to inhibitory cognitive control, a process that is uniquely lateralized to the right hemisphere (Aron, 2007). In their letter, Lam and colleagues report how the PPN asymmetry results from our study are supported by post hoc analysis of PPN DBS data previously collected by Moro et al. (2010). The authors present data demonstrating that left PPN stimulation presented an improvement in axial symptoms 12 months post-surgery in comparison with right PPN stimulation. Due to strong bilateral projections, the authors suggest that the less involved, left PPN has the potential to serve a compensatory role in the pathophysiology of FOG+
dominant pedunculopontine nucleus exist?

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et al., 2014). Similar to our recent interpretation, other researchers have pointed to poorer performance on tasks requiring cognitive inhibition and conflict resolution within this population (Shine et al., 2013; Cohen, et al., 2014). While this sub-domain of cognitive control is clearly differentially affected in those who experience FOG, there is also an historical body of literature that supports a dominant role of the right hemisphere in gait itself.

Dating back to the seminal work of Geschwind (1965), left hemispheric lesions are often associated with bilateral limb apraxia, whereas whole body movements are largely unaffected. Following stroke, right hemiparetics (in whom the right hemisphere was uninjured) progressed more rapidly and achieved higher levels of functional mobility following gait training (Cassvan et al., 1976). Further, Rapcsak et al. (1993) suggested that the right hemisphere is preferentially involved in programming and executing familiar, automated movements (e.g. locomotion). These findings may be explained by a right hemisphere dominance in body schema, spatial orientation (Wolpert et al., 1998), and proprioceptive control (Goble and Brown, 2008). Taken together, these studies indicate that the right hemisphere may play a preferential role in controlling axial, whole body movements like gait, and that dysfunction within this hemisphere leads to greater mobility impairments. The differential loss of fibre tracts within the right locomotor network of Parkinson’s disease individuals who are FOG+ in combination with the promising results in Lam and colleagues’ Letter to the Editor further underscores the importance of the right hemisphere’s role in gait.

It is possible that the lack of improvement in right PPN stimulation that Lam et al. observed is due to reduced structural connectivity within the right hemisphere’s locomotor network. As a result of reduced white matter connectivity, the nervous system is
likely at a disadvantage to transmit stimulation and may provide strong rationale for left PPN stimulation. This interpretation must be taken with caution as recent work from our group demonstrates bilateral alterations in functional communication within the locomotor network of FOG+ patients (Fling et al., 2014). Our findings of unilateral structural loss, but bilateral changes in functional communication underscore the complex pathophysiology of FOG. Future studies will benefit from studying additional clinical populations with similar behavioural phenomena such as vascular parkinsonism and frontal gait disorders (Nutt et al., 2011).

References