Defrosting Parkinson's disease: exploring the neural correlates of freezing of gait.

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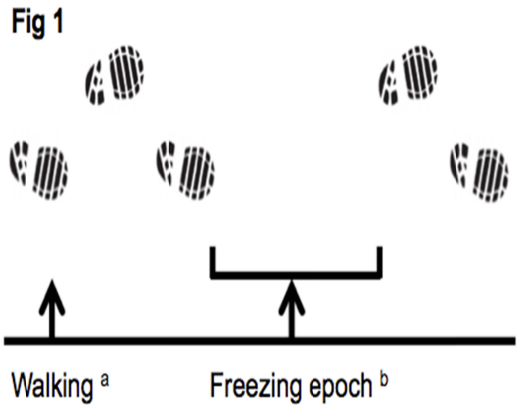
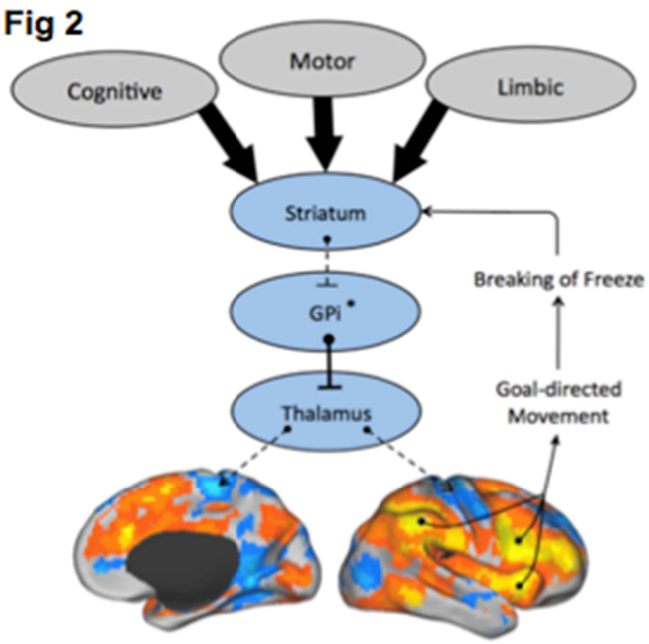
Background: Freezing of gait (FOG) is a devastating symptom of advanced Parkinson's disease (PD), however the neural correlates of this phenomenon remain poorly understood (Shine, 2011). To date, a major impediment to our understanding has been the lack of a paradigm allowing for direct neuroimaging of the freezing phenomenon.



Methods: In this study, 16 patients with PD and FOG underwent fMRI whilst performing a virtual reality (VR) gait task in their clinical 'Off' state. We then compared the BOLD correlates of normal 'walking' (Fig 1[a]) within the VR task with epochs of time when the footstep pattern paused for longer than twice the patient's modal footstep latency (Fig 1[b]). Data were analysed in an epoch design in the General Linear Model using SPM8 software.

Findings: 'Walking' (Fig 1[a]) through the VR environment was associated with increased BOLD response in the primary sensorimotor regions whereas freezing behaviour (Fig 1[b]) was associated with hypo-activation in these regions and increased bilateral activation in the prefrontal and posterior parietal cortices. Furthermore, freezing behaviour was associated with decreased activation in the head of the caudate and thalamus bilaterally.

Interpretation: These results strongly support a recently proposed model of freezing of gait (Lewis, 2009), which proposed that FOG is due to dysfunction within competing yet complimentary neural networks, which lead to a loss of function in the striatum and a subsequent increase in the synchronous firing of inhibitory output structures of the basal ganglia (Fig 2).



References: Shine, J. M., Naismith, S. L. and Lewis, S. J. G. et al. The pathophysiological mechanisms of freezing of gait in Parkinson's disease. 2011. *J Clin Neurosci*. 18(9):1154-7.

Lewis, S. J. G. and Barker, R. A. A pathophysiological model for freezing of gait in Parkinson's disease. 2009. *Parkinsonism Relat Disord*; 15(5):333-8.