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Editorial

Theta rhythms may support executive functions in Parkinson's disease with freezing of gait

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Freezing of Gait (FOG) in Parkinson's disease (PD) is an unpredictable disorder causing the sudden inability to lift the foot from the floor while walking (Nutt et al., 2011). FOG is frequently responsible for falls and injuries owing to ineffective stepping associated with forwarding projection of the trunk. The episodic nature and the influence from multifactorial variables suggest that FOG arises from functional disruption of a widespread network rather than reflecting the structural impairment of a specific cortical or subcortical motor area in PD (Bharti et al., 2019).

Recent studies investigating brain networks dynamics underlying FOG have raised the hypothesis that abnormal oscillatory rhythms in several cortical and subcortical structures may contribute to the pathophysiology of this motor disorder in PD (Anidi et al., 2018; Handojoseno et al., 2015; Pozzi et al., 2019; Shine et al., 2014; Syrkin-Nikolau et al., 2017). For instance, experimental studies examining intracranial recordings of local field potentials (LFPs) in PD patients who received surgical procedures for deep brain stimulation (DBS) have demonstrated prolonged beta oscillations (13–30 Hz) in the subthalamic nucleus (STN) during FOG occurrence (Anidi et al., 2018). Still, during FOG episodes, the concurrent registration of STN-LFPs and scalp electroencephalography (EEG) has disclosed significant decoupling of oscillations in STN and locomotor cortical areas such as the supplementary motor area, primary motor cortex and parietal cortex, in patients with PD (Pozzi et al., 2019).

Despite the observation of abnormal oscillations in motor networks, it is important to note that FOG crucially reflects also cognitive and emotional factors (Nutt et al., 2011). Indeed, it is known that PD patients with FOG (PD + FOG) typically manifest variable degrees of cognitive impairment, prominently in executive and visuospatial abilities (Heremans et al., 2013). In agreement with clinical and behavioural evidence, neuroimaging studies in PD + FOG have confirmed structural and functional impairment of widespread brain regions associated with fronto-striatal and fronto-parietal networks (Bharti et al., 2019). So far, however, the possible pathophysiological role of abnormal oscillations in brain regions responsible for executive and visuospatial abilities has never been explored in PD + FOG.

The present volume of *Clinical Neurophysiology* includes the study by Gérard et al. (2022), who used high-resolution EEG (hrEEG) to investigate functional connectivity changes underpinning executive dysfunction in PD + FOG. The authors used the "dynamic phase-locking value" method to measure phase relationships between oscillatory signals recorded from different cortical areas, during the execution of the Attention Network Test (ANT), a standardized task assessing attentional networks, including alerting, orienting, and executive control components (Fan et al., 2009). Concerning behavioural measures, PD + FOG showed longer reaction times and lower accuracy in response to visual stimuli than PD patients who never manifested FOG (PD-FOG) and healthy subjects (Gérard et al., 2022). This finding fits in well with previous studies demonstrating prominent executive dysfunction associated with FOG in PD (Amboni et al., 2008; Heremans et al., 2013). Regarding neurophysiological measures, hrEEG disclosed greater coherence in the theta-band (4–8 Hz) in frontotemporal-occipital networks in PD + FOG than controls. The abnormal oscillatory activity prominently occurred at around 400–600 ms after target presentation, thus suggesting the main involvement of frontal network nodes implied in the decision-making phase of the ANT (Gérard et al., 2022). Theta rhythms have been traditionally related to different mental processes, including arousal state, attentiveness and active cognition (Hoffmann et al., 2015). Previous experimental investigations in animals have demonstrated the role of theta-band synchronization in the dynamic processing of information between distant cortical brain areas (Jones and Wilson, 2005; Siapas et al., 2005). Also in humans, theta-band rhythms primarily in the prefrontal cortex and interconnected cortical regions have been associated with the dynamic central networking responsible for executive abilities (Mizuhara and Yamaguchi, 2007). Accordingly, the high theta-band synchronization in frontotemporal-occipital networks in PD + FOG reported by Gérard et al. (2022) may reflect a compensatory activation of visual and attentional networks to support executive control during the visual attentional task. Further fostering this hypothesis, connectivity changes in PD + FOG were positively associated with the cognitive performance assessed through the Montreal cognitive assessment (MoCA). However, since the authors did not examine possible correlations between neurophysiological and behavioural measures (i.e., performance at the ANT), it cannot be excluded that functional connectivity changes were associated with cognitive subsets other than those related to executive functions in PD + FOG.

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A further relevant result of the study by Gérard et al. (2022) concerns the prominent involvement of the frontotemporal-occipital networks in the left hemisphere in PD + FOG. This finding fits in well with previous neuroimaging studies showing greater impairment of the right hemisphere in PD + FOG (Bharti et al., 2020), thus further supporting the potential compensatory role of left cortical areas through increased activity of specific networks.

Overall, by highlighting the neural correlates associated with executive processes in PD + FOG, the study by Gérard et al. (2022) fosters the pathophysiological hypothesis of the "interference/cross-talk model" that points to the functional competition of multimodal networks, including those responsible for cognitive, motor and limbic functions, as a possible mechanism underlying FOG in PD (Lewis and Barker, 2009). However, several methodological points should be considered when examining the observations of Gérard et al. (2022). Indeed, the rather small cohort of enrolled subjects may be responsible for the lack of significant differences in brain network dynamics between PD + FOG and PD-FOG. Also, since patients have been evaluated only when under L-Dopa (i.e., ON state), some network activity changes may have been missed owing to the known impact of the dopaminergic therapy on brain functional connectivity as well as on FOG in PD (Suppa et al., 2017).

In conclusion, the study by Gérard et al. (2022) provides new relevant information on the role of theta rhythms in enhancing executive functions in PD + FOG while performing a visual-attentional task. Accordingly, based on these findings, future studies should test whether supporting the functional coupling of frontotemporal networks through the modulation of cortical rhythms at a theta frequency would improve executive control during attentional tasks in PD + FOG.

Conflict of interest statement

None of the authors have potential conflicts of interest to be disclosed.

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Alessandro Zampogna
Valentina D'Onofrio
Department of Human Neurosciences, Sapienza University of Rome, Italy

Antonio Suppa *
Department of Human Neurosciences, Sapienza University of Rome, Italy

IRCCS Neuromed Institute, Pozzilli, IS, Italy

* *Corresponding author at: Department of Human Neurosciences, Sapienza University of Rome and IRCCS Neuromed Institute, Viale dell'Università 30, 00185, Rome, Italy.*
E-mail address: antonio.suppa@uniroma1.it

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