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Attention modulation during motor preparation in Parkinsonian freezers: A time–frequency EEG study

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HIGHLIGHTS

- EEG oscillations can be studied during attentional processes and motor preparation.
- Parkinsonian patients with freezing of gait did not display beta desynchronization.
- Post-discrimination processing was impaired in parkinsonian patients with freezing of gait.

ABSTRACT

Objective: To investigate the cortical integration of attentional stimuli during motor preparation in parkinsonian patients with freezing of gait (FoG, $n = 12$) or without freezing of gait ($n = 13$), and in aged-matched healthy controls ($n = 13$). We hypothesized that interference between attention and action in freezers would be revealed by differences in cortical modulation during this dual task.
Methods: Attention during step preparation was modulated by means of an auditory oddball discrimination task. EEG oscillations in different frequency bands were measured for the attentional stimulus and the motor stimulus.
Results: Over the 500 ms following the sound, low-frequency power increased in all three groups. This was followed by a power decrease in mid-range frequencies after both target and standard sounds in the healthy controls and in the non-FoG group. In contrast, EEG oscillations in the beta band were impaired in the FoG group, who notably failed to display event-related desynchronization after perceiving the sound.
Conclusions: An attentional stimulus was able to trigger event-related desynchronization before motor preparation in the non-FoG group but not in the FoG group.
Significance: In the FoG group, stimulus discrimination was maintained but the coupling between attention and motor preparation was impaired.

1. Introduction

1.1. Why is it useful to study the links between attention and motor preparation in Parkinson's disease (PD) in general and in freezing of gait (FoG) in particular?

In PD, FoG is a major health concern because of its impact on quality of life (Ellis et al., 2011) and the increased risk of falls (Bloem et al., 2004). Attention is a cognitive process that allows humans to prioritize stimuli according to the situation and to

Abbreviations: APA, anticipatory postural adjustment; ERD, event-related desynchronization; ERP, event-related potential; ERSP, event-related spectral power; ERS, event-related synchronization; FoG, freezing of gait; HC, healthy controls; LEDD, levodopa equivalent daily dose; PD, Parkinson's disease; UPDRS, Unified Parkinson's Disease Rating Scale.

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adjust their response accordingly (Raz and Buhle, 2006; Corbetta et al., 2008). In fact, attention has a role in the occurrence of FoG, as evidenced by (i) the critical impact of external stimuli on this phenomenon (Nanhoe-Mahabier et al., 2012), (ii) the attentional impairments described in patients with FoG ("freezers") (Amboni et al., 2008; Naismith et al., 2010; Vandenbossche et al., 2011, 2012; Shine et al., 2013; Tard et al., 2015) and (iii) the occurrence of this phenomenon in the event of basal ganglia overload, such as when the patient has to deal with several motor and cognitive inputs (Lewis and Barker, 2009; Shine et al., 2011). Even in parkinsonian patients without FoG, attention has a greater influence on motor preparation and execution than in healthy elderly people; this is because damage to the basal ganglia (which are involved in motor program selection) leads to the impairment of internal, automated planning (Hallett, 1990; Takakusaki et al., 2008). Indeed, attentional impairment has often been described in parkinsonian patients (Brown and Marsden, 1988; Wright et al., 1990; Richards et al., 1993; Sharpe, 1996; Dujardin et al., 2013) and especially in freezers (Shine et al., 2013; Tard et al., 2015). Attentional impairment is particularly apparent during dual-task conditions (Brown and Marsden, 1991; Woollacott and Shumway-Cook, 2002; Canning, 2005; Yogev et al., 2005), although the interplay between attention and motor preparation has not been fully characterized. In previous work, we looked at how the attentional load affected motor preparation. We chose to study step initiation because the latter is often affected by motor blocks (in 86% of freezers (Giladi et al., 1992)) and combines motor, cognitive and emotional aspects of movement preparation and execution (Takakusaki et al., 2008). Thus, studying step initiation enables one to explore the impact of attentional information on motor preparation. We found that performing an attentional task prior to step initiation was associated with abnormal release of the loaded motor program during the motor preparation phase (i.e. before motor execution) (Tard et al., 2014). These unwanted, abnormal, anticipatory postural adjustments (called pre-APAs) were observed more frequently in freezers than in non-freezers and were particularly frequent when the cognitive load was high (in an attentional oddball paradigm) – reflecting a lack of motor inhibition during motor preparation (Tard et al., 2014). However, the time course of cortical oscillations between attentional stimulus and motor preparation in parkinsonian patients with or without FoG (as a guide to the cortical mechanisms linking attention and motor preparation) has yet to be studied. Our starting hypothesis was that the attentional load could modify cortical oscillations during motor preparation and would thus provide us with information on the successively involved processes.

1.2. What types of information can cortical EEG oscillations provide?

Brain oscillations in parkinsonian patients have been studied during attentional processes and during motor preparation processes but not during a task that combines both aspects. Firstly, brain oscillations in the various frequency bands within the EEG power spectrum have recently been used to study cortical responses to attentional stimuli (Fan et al., 2007; Cahn et al., 2013). In an auditory oddball paradigm (i.e. the detection of an infrequent target sound among a series of frequent, standard sounds), healthy subjects showed early, alpha-band event-related synchronization (ERS) during sensory encoding and late, alpha-band event-related desynchronization (ERD) (Cahn et al., 2013).

Secondly, brain oscillations are also associated with motor preparation; alpha–beta ERD is characteristic of activated cortical areas that are ready to process information. Indeed, premotor beta ERD is observed before movement onset (i.e. during motor preparation or execution) and is correlated with greater cellular excitability in the thalamocortical system (Pfurtscheller and Andrew, 1999; Neuper et al., 2006). Hence, beta ERD is related to the preparation of functionally appropriate motor responses in general and motor selection in particular. In contrast, post-movement beta ERS is also observed during movement termination (van Wijk et al., 2012) and reflects idling of the motor network (Cassim et al., 2001). This beta ERS may correspond to the deactivation or active inhibition of the sensorimotor cortex (Zhang et al., 2008). Taken as a whole, these findings suggest that beta oscillations have a role in active immobilization (defined as a "status quo" condition) (Engel and Fries, 2010) and are involved in the pathogenesis of bradykinesia. Indeed, alterations in the beta and theta bands across occipital and parietal areas have been observed during FoG episodes when turning (Handojoseno et al., 2012). EEG dynamics may also predict FoG episodes, using time–frequency analyses (Handojoseno et al., 2015) or connectivity analyses (Ardi Handojoseno et al., 2014).

The objective of the present study was to explore the cortical processes that occur in the time window between (i) the presentation of a stimulus on which attention is focused and (ii) motor execution. We postulated that attention can modulate cortical oscillations during motor preparation. Accordingly, we investigated attention-motor preparation coupling during a dual-task paradigm in parkinsonian patients with or without FoG.

2. Materials and methods

The FoG group ($n = 12$), non-FoG group ($n = 13$) and healthy controls (HCs, $n = 13$) were defined according to the objective criteria presented below.

2.1. Subjects

Twenty-five patients with PD (diagnosed according to Gibb's criteria (1988)) were recruited from the active case file in the Movement Disorders Department at Lille University Medical Center (Lille, France). Patients were classified as freezers (forming the FoG group, $n = 12$) or non-freezers (the non-FoG group, $n = 13$), depending on their response to item 3 of Giladi et al.'s FoG questionnaire (2000). For all patients, the presence or absence of FoG in the "off-drug" condition was checked during a FoG trajectory (Snijders et al., 2008).

The EEG was recorded after patients had received their usual dopaminergic medications (i.e. in the "on-drug" state). The FoG and non-FoG groups of patients were matched for motor severity disease according to their Unified Parkinson's Disease Rating Scale (UPDRS) motor score (Fahn S, Elton RL, and members of the UPDRS development committee. (1987)). Thirteen age-matched HCs also participated in the study. The exclusion criteria for both parkinsonian patients and HCs included the inability to walk even a few steps unaided, the presence of neurological disorders other than PD, the presence of dementia (according to the DSM IV criteria (American Psychiatric Association, 1994) or a major depressive disorder (again according to the DSM IV criteria), and the use of electrical deep brain stimulation. Furthermore, HCs were excluded if they presented signs of parkinsonism or had rheumatologic or orthopedic diseases that perturbed gait.

The study was approved by the local investigation review board (*CPP Nord-Ouest IV*, reference 2009-5656-A00821) and sponsored by Lille University Medical Center. Each participant gave his/her prior, written, informed consent to participation in the study.

2.2. Experimental design and task

As described elsewhere (Tard et al., 2014), the experimental task featured an auditory preparatory stimulus (S1) and an imper-