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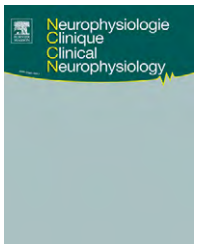

ORIGINAL ARTICLE

Excitability of the lower-limb area of the motor cortex in Parkinson's disease

Excitabilité des aires motrices corticales des membres inférieurs dans la maladie de Parkinson

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Intracortical facilitation;
Dopaminergic substitution therapy

Summary
Objective. — The excitability of the lower-limb area of the motor cortex was investigated in patients with Parkinson's disease (PD) and in control subjects. Our results were compared to literature data assessing upper-limb cortical area. We analysed the effect of dopaminergic substitution therapy (DST).
Methods. — Motor evoked potential (MEP) were assessed with transcranial magnetic stimulation (TMS) in 24 PD patients with (ON) and without (OFF) DST, and nine age-matched controls.
Results. — Resting motor threshold (RMT), active motor threshold (AMT), cortical silent period (CSP), MEP amplitude and area did not differ significantly between groups and medication states. A paired-pulse TMS study revealed normal short-interval intracortical inhibition (SICI) but impaired intracortical facilitation (ICF) in PD OFF, partially normalized under DST. Post-hoc analysis uncovered two opposite effects of DST on MEP amplitude, separating the population in two groups. The paired-pulse study confirmed this division, showing that both groups exhibited distinct intracortical functioning, which was differently influenced by DST.
Conclusions. — The lower-limb motor cortical areas of PD patients essentially exhibited an ICF reduction whereas in upper-limb areas, literature data demonstrated impairment of both SICI and ICF. Our data revealed two groups of patients showing different excitability states and opposite responses to DST.
Significance. — The defective ICF in lower-limb areas could play a key role in the pathophysiology of gait disorders in PD. The fact that two cortical excitability states are inversely influenced by DST may reflect different conditions of denervation and compensatory mechanisms progression.

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MOTS CLÉS
Cortex moteur ;
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Marche ;
Maladie de Parkinson ;
Stimulation magnétique transcranienne ;
Potentiel évoqué moteur ;
Inhibition intracorticale ;
Facilitation intracorticale ;
Traitement dopaminergique substitutif

Résumé
But de l'étude. — Étudier l'excitabilité des aires motrices corticales des membres inférieurs dans la maladie de Parkinson (MP). Les résultats ont été comparés aux données de la littérature existant à propos des aires corticales des membres supérieurs. Nous avons également analysé l'effet du traitement dopaminergique.
Patients et méthodes. — Les potentiels évoqués moteurs (PEM) par stimulation magnétique transcrânienne furent recueillis chez 24 patients parkinsoniens, sous traitement (ON) et sans traitement (OFF), ainsi que chez neuf sujets témoin.
Résultats. — Le seuil d'excitabilité au repos et sous activation, la période de silence central, l'aire et l'amplitude des PEM n'étaient pas modifiés par la pathologie ou le traitement. Le double choc révéla une inhibition intracorticale (ICI) normale et une facilitation intracorticale (FIC) diminuée chez les parkinsoniens OFF, mais partiellement normalisée en ON. L'analyse post-hoc dégagea deux effets opposés du traitement sur l'amplitude des PEM, séparant les patients en deux groupes. Le double choc confirma cette dichotomie, révélant un fonctionnement des réseaux intracorticaux et des réponses au traitement totalement opposés.
Conclusions. — Les aires motrices corticales des membres inférieurs des patients parkinsoniens étudiés présentent principalement une FIC diminuée alors que, selon la littérature, les aires motrices corticales des membres supérieurs présentent une altération à la fois de la FIC et de l'ICI. Nos données révèlent l'existence de deux groupes de patients présentant un fonctionnement intracortical et une dopasensibilité différents.
Pertinence. — Les anomalies de FIC pourraient être impliquées dans la physiopathologie des troubles de la marche dans la MP. Les sous-groupes mis en évidence sont probablement le reflet de différents stades d'avancement de la dénervation dopaminergique et de développement de processus compensatoires.

Introduction

According to physiological modelling [1] and due to its interposition between altered basal ganglia networks and the intact corticospinal tract [13], the motor cortex is functionally involved in the pathophysiology of Parkinson's disease (PD). Imaging studies have highlighted hypoactivity in the supplementary motor area (SMA) and dorsolateral prefrontal cortex (DLPFC) [35,41,19], and hyperactivity in the primary motor cortex (M1), lateral premotor cortex, cerebellum, parietal and occipital lobes [17,43].

Cortical areas have also been investigated using transcranial magnetic stimulation (TMS). Despite some discrepancies, TMS data in PD disclosed an imbalance of cortical excitability towards a state of reduced inhibition, inducing a cortico-motoneuronal hyperexcitability [10]. In this regard, observations of a reduced resting motor threshold (RMT) [9], decreased cortical silent period (CSP), enhanced amplitude of the motor evoked potential (MEP) with target muscle at rest [20], and impaired short-interval intracortical inhibition (SICI) [37,33] are particularly relevant. Facilitatory intracortical processes were also found to malfunction, as PD patients exhibited both a reduced MEP amplitude during voluntary contraction [48] and an impaired intracortical facilitation (ICF) [4]. Antiparkinsonian treatments including dopaminergic substitution therapy (DST), subthalamic nucleus stimulation, and repetitive TMS tend to normalize these electrophysiological abnormalities [10,22]. DST mainly acts on inhibitory processes, lengthening the CSP duration [37,34] and restoring the SICI [33]. Imaging studies confirmed this by showing the reduction of primary motor cortex hyperactivity under DST [19].

Most of these studies investigated the upper-limb motor cortical area. According to a few TMS studies exploring leg muscles of normal subjects, upper- and lower-limb cortical motor areas seem to share similar intracortical mechanisms [12]. However, imaging data indicated that their cortical activation patterns are quite different [31,26,42]. Indeed, hands are most of the time required for volitional or visuo-guided movements whereas lower limbs are rather implied in automatic and self-generated movements. Therefore, it is likely that these two kinds of movement differently recruit the central nervous system [29,18,3]. PD primarily affects automatic movements [28] and, particularly, the gait pattern, with a reduction of walking speed and amplitude of leg movements, giving rise to the characteristic small and shuffling steps, sometimes with freezing [5]. Only one single-pulse TMS study explored a proximal lower-limb muscle in PD patients and found similar abnormalities as those described with hand muscles [46]. In our study, we completed the investigation with a paired-pulse study of lower-limb cortical motor areas. We chose to explore the *tibialis anterior* (TA) muscle, owing to its key role in gait [13,11].

Methods

Subjects

This study was carried out on 24 PD patients (three women, 62 ± 7 years) and nine control subjects (four women, 60 ± 4 years). All the patients were candidates for deep brain stimulation and were therefore very doparesponsive (see Table 1 for clinical details). Their clinical examination was performed in the early morning by the same expert in movement disorders after an overnight DST withdrawal