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Levodopa effect on electromyographic activation patterns of tibialis anterior muscle during walking in Parkinson's disease

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ABSTRACT

Previous studies have reported that patients with Parkinson's disease (PD) show, in the "off medication" state, a reduced activation of tibialis anterior (TA) in the late swing–early stance phase of the gait cycle. In PD patients the pathophysiological picture may cause differences among the stride cycles. Our aims were to evaluate how frequently TA activity is reduced in the late swing–early stance phase and if there is a relationship between the TA pattern and the clinical picture.

Thirty PD patients were studied 2 h after Levodopa administration ("on-med") and 12 h after Levodopa wash-out ("off-med"). They were evaluated by the Unified Parkinson's Disease Rating Scale (UPDRS III) and surface electromyography of TA and gastrocnemius medialis (GM). The root mean square (RMS) of the TA activity in late swing–early stance phase (RMS-A) was normalized as a percent of the RMS of the TA activity in late stance–early swing (RMS-B).

RMS-A was reduced in 30% of patients in the "off-med" condition. Within these patients, the percentage of stride cycles with reduced RMS-A, ranged between 28% and 83%. After Levodopa intake, no stride cycle showed reduced RMS-A. Patients with reduced RMS-A had a lower UPDRS III total score in the "on-med" rather than in the "off-med" condition ($p = 0.02$).

Our data confirm and extend previous observations indicating that, in "off-med" the function of TA is impaired in those patients clinically more responsive to Levodopa. TA activation is reduced in a relatively high percent of gait cycles in the "off-med" state. Since the variability of TA activation disappears after Levodopa administration, this phenomenon could be the expression of an abnormal dopaminergic drive.

1. Introduction

Parkinson's disease (PD) is a neurodegenerative disorder characterised by bradykinesia, rigidity, resting tremor, and postural instability [1,2]. Levodopa remains the most effective drug for this condition. The degree of response to pharmacological treatment significantly affects patients' health [3,4]. Some patients respond remarkably to Levodopa administration, while others have only modest benefits [3,5,6]. Gait disturbance is one of the major problems in PD. The walking pattern is characterised by reduced velocity, increased stance phase duration, shorter stride length [7,8], start hesitation, freezing, festination [9], and reduced activation of some lower limb muscles [10]. Cioni et al. [10] found that tibialis anterior (TA) activity, recorded by surface electromyography (sEMG), was absent or reduced during the late swing–early stance phase of the gait cycle when patients were in the "off" state, while in the "on" state, TA activity improved [10]. The same improvement in TA activation during early stance phase has been demonstrated after subthalamic nucleus (STN) stimulation [11]. These findings regarding TA activation were obtained by calculating the mean values over a number of gait cycles [10,11]. However, the pathophysiological condition and the degree of response to therapy, may cause differences among the stride cycles, namely stride length, step length and double-support time [12,13]. Consequently, the activation of individual muscles might change from one stride to another. We hypothesized that an evaluation of different gait cycles might be useful to better understand the influence of Levodopa on lower limb muscles activations. Since the

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Table 1
Main demographic features of the Parkinson's disease sample.

	Total ($n=30$)	Referred improvement ($n=10$)	No referred improvement ($n=20$)	p Value
Age (years)	70.7 ± 5.5	65.3 ± 2.3	73.8 ± 4.1	<0.001
Gender (M/F)	12/18	4/6	8/12	ns
Age at onset (years)	58.9 ± 11.5	61.3 ± 12.1	59.6 ± 12.8	ns
Disease duration (years)	5.8 ± 1.4	6.2 ± 1.5	6.7 ± 1.3	ns
L-dopa dose (mg/day)	537 ± 258	579 ± 267	494 ± 248	ns
LDED (mg/day)	547 ± 230	621 ± 263	473 ± 196	ns

distal muscles of the lower limbs are mainly impaired [10,11,14], we evaluated the Levodopa effect on the TA and gastrocnemius medialis (GM) activations during different gait cycles. We focused mainly on TA because the presence of a phase-specific reduction in the amplitude of TA activations is relevant both for theoretical and clinical issues. In fact, a better definition of the phase dependent modulation of TA activations [10,11] could provide insight into motor control mechanisms during locomotion. Moreover, the abnormal activation of TA in the late swing–early stance phase [10,11], a crucial phase for adequate placement of the foot, might be a factor of stumbling with an increased risk of falling [15]. Our aims were: (1) to evaluate if an abnormal pattern of TA activation is constantly present in the late swing–early stance phase during the "off" state, (2) if there is a relationship between the abnormal pattern of TA and the clinical condition evaluated by the Unified Parkinson's Disease Rating Scale (UPDRS) part III or with slow walking speed, which is present also in other pathologies [16–18] and (3) if TA impairment in swing/stance phase is specifically linked to striatal dopamine deficiency. We also recorded GM activation in order to collect some additional information on spatial–temporal activation patterns of antagonist muscles.

2. Methods

2.1. Definition of cases

We prospectively enrolled 30 consecutive patients with idiopathic PD who were referred to Don Gnocchi Foundation for rehabilitation. All the patients were treated with Levodopa, associated or not, to dopamine agonist drugs. Presence of PD diagnosis and Levodopa treatment were the two inclusion criteria. The patients were not selected according to the presence/absence of tremor and/or bradykinesia. The patients came from different neurological centres where the diagnosis was made and the pharmacological therapy decided. All patients gave their written consent to participate in the study which was approved by the Don Gnocchi Foundation ethics committee. Table 1 illustrates the demographic features of our sample. All patients were evaluated twice, on different days, in the morning:

1) 2 h after the administration of the usual Levodopa dosage ("on-med")
2) at least 12 h after Levodopa and agonist drugs wash-out ("off-med").

Before the "on-med" evaluation, the patients answered the following "yes" or "no" motor ability question: "Does your walking ability improve after Levodopa intake?"

A neurologist filled in the UPDRS part III [19,20] which assesses motor performance (lower scores mean a better function). The physician did not know if the patients were in "on-med" or "off-med" state and was not aware of the patients' answer to the motor ability question.

After the neurological evaluation, two technicians performed sEMG of GM and TA.

2.2. Electromyographic evaluation

Activity of TA and GM was recorded bilaterally using bipolar surface electrodes (16-channels Delsys equipment). The sampling frequency was 8 kHz. Electrodes were placed over the muscle belly of TA and over the centre of GM at 5–6 cm below its cranial origin [21]. We recorded the location of the electrodes, along with some anatomical structures, on a stocking in order to facilitate the correct reproduction of the placement. To identify the heel strike and the toe off instants, we used two pressure sensors for each foot: one under the great toe and one under the heel. The heel strike and the toe off instants were identified by the onset and the return to baseline of the respective pressure curves (considering a threshold of 2% of the maximal value of the curves) (Fig. 1). All patients walked along the distance of 10 m at least twice for each day of evaluation. Walking speed was recorded by a chronograph. The first two and last two strides of each 10 m trial were discarded to focus only on steady state.

A neurologist evaluated the sEMG without knowing:

1) if the patient was in the 'off-med' or in the 'on-med'
2) if the patient reported a subjective improvement after Levodopa administration
3) the variation of the UPDRS III scores after taking Levodopa.

The processing of sEMG signals was done according to a previously reported procedure [22]. A high-pass filter with a cut-off frequency of 50 Hz was applied to remove movement artefacts and then the linear envelope was computed by means of signal rectification and low-pass filtering at 7.5 Hz. We used the Delsys software to process the raw sEMG. Fig. 1 shows an example of an EMG linear envelope of TA activity in a normal subject. The root mean square (RMS) of the enveloped EMG signal of the two TA bursts (late swing–early stance phase and the late stance–early swing phase bursts) was computed over time intervals of 0.05 s across the peak of activation. The RMS value of the TA burst in the late swing–early stance phase

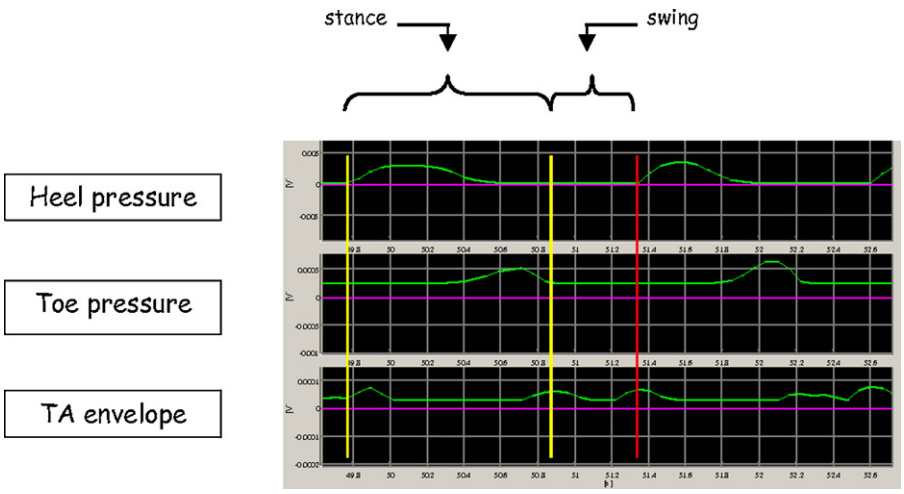

Fig. 1. An example EMG linear envelope of TA activity during one stride in a normal subject.