Parkinsonism and Related Disorders 15 (2009) 359–364

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

# Dyskinesia-induced postural instability in Parkinson's disease

Stéphane Armand [a], Theodor Landis [b], Roman Sztajzel [b], Pierre R. Burkhard [b,*]

[a] Kinesiology Laboratory, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland
[b] Department of Neurology, Geneva University Hospitals and Faculty of Medicine, 1211 Geneva 14, Switzerland

ARTICLE INFO

*Article history:*
Received 21 April 2008
Received in revised form 9 July 2008
Accepted 18 August 2008

*Keywords:*
Dyskinesia
Parkinson's disease
Postural instability
Gait
Posturography
Sway

ABSTRACT

Parkinson's disease (PD) patients may complain of unsteadiness and impaired balance not only when OFF, but also while being ON with levodopa-induced dyskinesia (LID), yet influence of LID upon postural stability has not been specifically examined. In this study, we addressed this issue using static and dynamic posturography in patients with advanced PD and typical LID. Relevant postural stability parameters were measured on force platforms when patients were OFF and ON, either in quiet standing or when performing leaning tasks designed to stress postural stability. Simultaneously, LID was assessed clinically using a dyskinesia rating scale of severity and subjective unsteadiness was computed. Displacement of the net center of pressure (COPnet), range of COPnet in the mediolateral and antero-posterior directions and 95% confidence ellipse area for both feet were measured as indicators of postural stability and used for comparison analyses. We found a significant increase of COPnet displacement in all tasks up to 556% (mean: 125 ± 165%) when patients were ON with dyskinesia compared to the OFF state. In about half of the patients, this increase was marked and correlated with subjective unsteadiness while ON. There was a good correlation between the clinical scores of dyskinesia severity and most COPnet values. Patients demonstrated a tendency to sustain their weight on the foot less affected by dyskinesia, probably as a compensatory mechanism. Our results suggest that LID may compromise balance and independently contribute to postural instability in advanced PD.



## 1. Introduction

Postural instability (PI) is one of the most common and disabling features of advanced Parkinson's disease (PD), which, together with gait impairment [1], leads invariably to repeated falls [2], increased morbidity, reduced quality of life, progressive handicap, high institutionalization rate [3] and eventually an increased mortality risk [4]. Causes of PI in PD involve many distinct, albeit closely related factors, including alterations of balance control mechanisms, rigidity and static posture abnormalities, gait impairment, autonomic dysfunction particularly orthostatic hypotension, impairment of visuo-spatial tasks and anxiety-related fear of falling [5]. Static and dynamic posturography techniques using force platforms have long been used to assess balance in PD [6–16] and have elucidated a number of specific pertubatory and compensatory mechanisms that may be concomitantly engaged in altering postural stability. Early in the course of PD, body sway during quiet stance appears to be reduced as a result of increased body stiffness [3]. This strategy leads to a narrowing of the center of gravity, at the cost of altering and slowing adaptative responses to dynamic balance perturbations. Later, this tendency tends to invert and spontaneous body sway increases in all directions [6]. In addition, automatic or voluntary postural adjustment mechanisms to external destabilizing perturbations become impaired in several ways: the amplitude of motor responses to spontaneous or induced instability is inappropriate, the sequence of these responses is altered and their delay is prolonged [3]. Finally, it has been shown that modifications of sway characteristics may be central in the pathophysiology of PI in PD. Indeed, PD patients exhibit an abnormal tendency to increase not only the antero-posterior sway as a result of their stooped posture [6], but also the mediolateral sway possibly in relation with the asymmetrical distribution of parkinsonian signs [6,8,17]. The latter is highly correlated with disease severity and risks of falling [17].

While most posturographic studies on PI in PD have examined sway parameters in the ON and OFF states [8,9,11,13,18,19], very few have paid attention to the potential influence of levodopa (LD)-induced dyskinesia (LID), one of the clinical hallmarks of ON state in PD, upon balance and postural stability. Rocchi et al. [10,13] found an increased postural sway in PD patients with no or minor LID and Guehl et al. [9] mentioned that PD patients with LID increase COP parameters but these last authors did not detail their findings. However, a significant impact of LID upon sway parameters may be suggested by a number of clinical observations: (1) PD patients tend

* Corresponding author. Tel.: +41 22 372 83 09; fax: +41 22 372 83 32.
*E-mail address:* pierre.burkhard@hcuge.ch (P.R. Burkhard).

1353-8020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.parkreldis.2008.08.007

to fall more often in the ON state, and less while OFF, presumably in relation with improved mobility and increased ambulatory time provided by dopaminergic agents [20]; (2) some dyskinetic PD patients occasionally complain of instability, poor balance and falls which they spontaneously relate to ON periods with dyskinesia, the symptoms improving when LID wanes [21,22]; (3) it has been well established that LID usually start and, in some patients, remain more prominent in the lower extremities compared to other body parts [22,23]; (4) similarly to parkinsonian signs, LID are asymmetrically distributed and usually more severe on the side more affected by parkinsonism [24], this asymmetry possibly contributing to PI. We therefore hypothesized that the presence of LID in the ON state may modify sway parameters to such an extent that it may significantly worsen PI. To test this hypothesis, we conducted a prospective, clinical and posturographic study in 11 patients with advanced PD exhibiting dyskinesia when under LD and compared various sway parameters, scores of dyskinesia severity and clinical data related to PI in the ON and OFF states.

## 2. Patients and methods

Eleven PD patients hospitalized in the Neurology Department of our institution for therapeutic adjustments were selected and enrolled in the study. Inclusion criteria were as follows: (1) fulfilment of the UKPDSBB criteria for PD, including LD responsiveness and at least a 30% difference between the ON and OFF UPDRS motor scores; (2) presence of motor fluctuations and typical peak-dose LID; (3) conventional antiparkinsonian therapy excluding amantadine, clozapine, deep brain stimulation or past pallidotomy or thalamotomy; (4) absence of significant psychiatric condition, cognitive decline or dementia that may prevent patients to understand or perform the required tasks; (5) absence of significant medical, rheumatic or orthopaedic condition that may independently influence posturographic parameters. Available data from a group of 12 age-matched, neurologically intact subjects (hospital staff members) selected from our laboratory database, were used for control purposes.

For each patient, two recording sessions were conducted during their hospital stay, once while the patient was OFF (after a 12-h, overnight period without medication) and once while the patient was ON which, for the purpose of this study, required clinically obvious dyskinesia to be present. During each session, a UPDRS part III, a Hoehn and Yahr staging and a dyskinesia rating scale (DRS) were administered by a neurologist trained in movement disorders (PRB) at the time of posturography recordings. A modified version of the abnormal involuntary movements scale (AIMS) was used, in which selected body parts (head, trunk, right and left upper and lower limbs) were assessed individually by means of a 4-point rating of dyskinesia amplitude (0 = no dyskinesia, 1 = mild, 2 = moderate, 3 = severe dyskinesia) yielding a maximum score of 18 points. Patients were also specifically asked to ascertain whether they felt subjectively unsteady at the time of the recording sessions (yes/no). A Shellong test was performed to exclude orthostatic hypotension (defined as a drop of mean blood pressure of 20 mmHg and more between a lying and upright position at any time over a 10-min recording) as a potential confounding factor. Posturography recordings were performed by investigators blinded to clinical data (SA and YB). PD patients and controls were standing barefoot with each foot on an individual force plate (Kistler type 8291B11 and charge amplifier 9865B). Position of the feet were kept identical on the force plates during the whole session, practice was permitted prior to data collection and a 1-min rest was allowed between sessions. Participants were asked to perform the following tasks: (1) 30-s standing at rest; (2) 30-s leaning movements of the body forward; and (3) 30-s leaning backward with the ankles as pivot joints. The signal from each force plate was A/D converted (12 bit), sampled at 104.17 Hz and stored (Bioware 2.0, Kistler) for further off-line processing and computation with a MatLab adapted software. Data were low pass filtered at 7.5 Hz. The location of the center of pressure (COP) on each plate (right COP and left COP) and with the 2 plates taken as a single one (COPnet) were computed and expressed in the resting position and during forward and backward leaning tasks. The following COPnet parameters, computed for 20-s (the first and last 5-s periods were removed) were used as main variables: length (expressed in mm), antero-posterior (AP) range (mm), medio-lateral (ML) range (mm) and 95% confidence ellipse area ($mm^2$). Illustrative examples of posturographic recording are shown in Fig. 1 where a patient with mild dyskinesia (upper panel A) is compared with a patient with severe dyskinesia (lower panel B). Data did not follow a normal distribution according to the Kolmogorov–Smirnov test. Statistical analyses (SPSS 15.0) were thus performed using the Wilcoxon signed-rank test to compare these variables with and without LID and the Spearman rank correlation coefficient to evaluate the relationship between posturographic (plate forms) and clinical (DRS scores) parameters. Statistical significance was set at $p < 0.05$.

This study was approved by the ethics committee of our department and patients were required to sign an informed consent form before enrolment.

## 3. Results

The PD population included 8 males and 3 females, aged 64.6 years (range: 55–81 years), whereas the control population included 8 males and 4 females, aged 65.4 years (range 51–79 years, $p = 0.702$). All PD patients had advanced disease (mean disease duration: 12 years, ranging from 6 to 25 years, OFF Hoehn and Yahr stage: 3–4) and were being treated with various regimens of standard and slow-release LD/carbidopa or LD/benserazide, COMT inhibitors and dopamine agonists (not detailed). Demographics and relevant clinical data of individual PD patients, including OFF and ON UPDRS III scores, OFF and ON Hoehn and Yahr stages, and DRS scores, are detailed in Table 1. Response to LD was marked in most, as demonstrated by a mean 58% improvement of the UPDRS motor scores and a 51% change of the Hoehn and Yahr stage. Subjectively, about half (6/11; P4, P5, P7–P9, P11) of the patients complained of unsteadiness in upright position that was only present or clearly increased when ON compared to OFF. The Shellong test was negative in all patients but it is noteworthy that 5 of 11 patients were treated with midodrine 5–20 mg daily for symptomatic orthostatic hypotension. DRS scores were strongly associated with clinical symptoms of PI, particularly when lower limbs were considered, all but one patient (P4) who complained of unsteadiness while ON showing lower limbs DRS score above 4 (maximum score for lower limbs: 8). There was an excellent correlation between the side where parkinsonism was more marked and that where dyskinesia dominated, with 10 of 11 patients showing a predominance of both parkinsonism and dyskinesia on the same side (Table 1).

### 3.1. Comparison of the COPnet parameters between ON (with dyskinesia) and OFF (without dyskinesia) states

At rest, there was a statistically significant difference of COPnet length between the non-dyskinetic ($371.4 \pm 106.7$ mm) and the dyskinetic state ($888.4 \pm 704.2$ mm, $p = 0.004$), as shown in Table 2

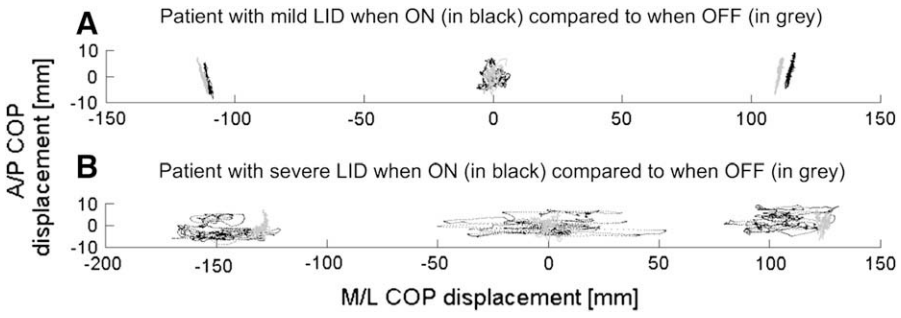


**Fig. 1.** Illustrative examples of COPnet, COP right and COP left displacement and trajectory of PD patient in ON (in black) and OFF (in grey) conditions. (A). Patient with mild LID; (B). Patient with severe LID.