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Kinematic angular parameters in PD: Reliability of joint angle curves and comparison with healthy subjects

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Abstract

Background: Most previous biomechanical studies of Parkinson's disease (PD) have been restricted to the description of spatiotemporal parameters and certain peak values for angular parameters. The reliability of joint angle curves and comparisons with control data are of major interest in PD, since variability in gait cycle timing is a feature of this pathology.
Methods: We used a video motion analysis system to record kinematic, spatiotemporal and angular parameters in 32 'off-drug' PD patients. The reliability of the patients' lower limb joint angle curves in the sagittal plane were analysed using the intra-class correlation coefficient (ICC), together with fast Fourier transform (FFT) analysis and hierarchical classification for discarding deviant curves. Lastly, we compared average curves (using a mixed model and the bootstrap method) for the less-affected and more-affected sides of PD patients and then compared the patient data with the results from 30 age-matched controls.
Results: The ICC-based procedure was easily applicable. Only 9.4% and 12.5% of the patients' hip and knee curves (respectively) were deemed to be unreliable. However, the PD patients' very high cycle-to-cycle variability in the sagittal plane ankle curves prevented us from applying to this joint. For the knee joint, the curves for the most disabled patients (who walked at below 0.5 m/s) were not reliable. We did not find any differences between the less and more disabled sides. The differences between patient and control curves concerned the double-support time during the stance phase and the time point for maximum knee flexion during the swing phase. Patients and controls differed in terms of the hip extension phase, with lower values in PD.
Conclusion: We have developed the use of validated statistic tools for unambiguously comparing PD patients and controls in terms of joint angle curve differences.

Keywords: Parkinson's disease; Gait; Reliability; Variability; Bootstrap

1. Introduction

Many biomechanical studies have reported on spatiotemporal gait parameters in Parkinson's disease (PD) [1–7] but only some have focused on angular parameters. A reduction in the angular excursion of lower limb joints was noted in parkinsonian syndromes [8,9]. These results have been confirmed by several studies in PD [3,10–15]. In the off-drug condition, the total sagittal plane excursions (TSPEs) were lower than control values, L-Dopa only improving the maximum knee joint flexion during the swing phase [3]. It has also been reported that the TSPEs in ''on drug'' severely impaired PD patients is about 70% of the control value [10]. In contrast, any significant decrease in TSPEs of proximal joints (hip and knee) was observed in 'on drug' patients with a mean UPDRS score of 16.1 [13]. The variability of angular gait parameters in PD has also been studied [14,16]. Patients

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showed great stride-to-stride variability in TSPEs [14]. This high variability makes it difficult to detect consistent trends when analysing several trials in a given patient [11].

The above-mentioned studies were limited to evaluation of certain numerical values that are supposedly representative of joint angle curves (e.g. initial contact, maximum extension and flexion, TSPE, etc.). This is important for a rapid overall evaluation but analysis of just a few points on the curve is not representative of the curve as a whole and some parts of the curve are thus not taken into account. Moreover, even though peak values simplify analysis and facilitate data interpretation, they usually occur at slightly varying times within the gait cycle (due to inter-individual variability) and thus can explain the observed discrepancies between the mean peak values and what is really present in the curve as a whole [17]. Variability in angle joint curves makes it difficult to draw any conclusions concerning analysis of a set of curves recorded in a given session. Hence, an 'average' curve which is representative of the patient would facilitate angular gait analysis. We have developed statistical tools for gait curve analysis [18,19]; our initial problem was to estimate the reliability of the curves recorded for a given subject and then select those which can legitimately be used to build an 'average' curve—a representative guide for a given patient and session. These tools were based on the use of intra-class correlation coefficients (ICCs) to assess curve reliability. In the present paper, we first focused on the application of this method to PD patients, in view of the significance of stride-to-stride variability in this pathology.

PD is clinically characterized by tremor, rigidity and akinesia that are generally asymmetric. Indeed, gait asymmetry itself could have a direct effect on joint angle curves but no significant differences were found between sides in 'on drug' patients [15]. In the second part of the present study, we sought to determine whether or not the more-affected and the less-affected sides in PD patients differed in terms of joint angle gait curves; this aspect is particularly important when seeking to compare curves between patients and control subjects. If the right and left curves indeed differ, one cannot legitimately pool the data and compare the resulting ''average'' PD patient curve with a control curve.

In the third and last part of the present study, we compared the average curve for the PD group to the average control curve and then sought to identify the parts of the gait cycle where there is a significant difference between PD patients and control subjects.

2. Patients and methods

2.1. PD patients

We studied 32 right-handed patients (20 men, 12 women) classified as suffering from PD according to the United Kingdom Parkinson's Disease Brain Bank (UKPDBB) 1989 criteria. The more-affected side (defined by tremor, rigidity and/or akinesia) was the right side for 12 patients and the left side for 16 patients. Four subjects did not show a lateral predominance. The characteristics of the patients are reported in Table 1. All patients had been medication-free for at least 12 h prior to testing.

Table 1
Characteristics and gait parameters in PD patients, compared with controls (using the Mann and Whitney U test for unpaired comparisons)

	PD		Controls		
	Mean	S.D.	Mean	S.D.	p
Age (years)	62.7	9.7	62.2	4.3	NS
Disease duration (years)	12.9	3.6			
UPDRS (motor)	45.3	11.7			
Walking speed (m/s)	0.67	0.25	1.26	0.16	<0.001
Cadence (steps/min)	104.46	18.63	115.18	8.31	<0.05
Stride length (m)	0.76	0.24	1.31	0.10	<0.001
Stride time (s)	1.19	0.25	1.05	0.08	<0.05
Single support/double-support	1.18	0.49	1.86	0.59	<0.001

2.2. Controls

Thirty healthy elderly control subjects (same gender ratio) were recruited from amongst the participants in a community project for senior citizens. A screening examination indicated that all control subjects were clinically normal, especially in terms of neurological and musculoskeletal parameters.

2.3. Methods

2.3.1. Gait data collection

Gait measurements were automatically recorded by means of a video motion system (the VICON system from Oxford Metrics, Oxford, England) featuring six infrared cameras and a sampling frequency of 50 Hz. Thirteen spherical, retro-reflective markers (2.5 cm in diameter) were used to define different segments of the pelvis and lower limbs. We used the VICON® software's lower body model (''Plug-in Gait'').

2.3.2. Assessment of gait function

The subjects (in underwear and bare-footed) walked at their normal speed. For each cycle, spatiotemporal gait measurements were determined. Joint angle curves in the sagittal plane were generated using VICON Polygon® software. For each subject and each body side, a minimum of seven gait cycles were obtained (mean $\pm$ S.D.: 14.3 $\pm$ 5.1). Data were expressed as a percentage of the gait cycle (from 0% to 100% in 2% steps, i.e. a total of 51 values).

2.4. Data analysis

2.4.1. Gait curve reliability in PD patients

By using a total of 64 curve beams (32 patients $\times$ 2 sides), we computed the ICC in order to determine whether or not the patients' gait curves were reliable [18]. Briefly, let r be the number of gait curves in the studied beam (r curves for a given patient and for a given side). The ICC of the r curves can be interpreted as the proportion of the variance due to the time-to-time variability in the total variance of the r curves. When the r curves are very similar, the ICC value is close to 1, indicating good reliability. In contrast, when the r curves are scattered, the ICC value is nearer to 0.

The ICC_m cut-off value (i.e. a beam with an ICC value greater than ICC_m is regarded as being reliable) was determined by studying the distribution of the 32×2 ICCs. We computed 64 ICC values and estimated the probability density function (PDF) using a Gaussian kernel. When the beam was not reliable ($ICC < ICC_m$), we discarded the deviant curves using multivariate analysis. For the beam in question, the data underwent an FFT in order to reduce the spread of the variables (51 values for each of the r curves). Each curve was then analysed according to the finite Fourier sum corresponding to the first p harmonics. Selection of the number of harmonics was based on examination of the distribution of the mean of the squared errors computed from the sample as a whole (32×2 curve beams). We then performed a hierarchical cluster analysis of the r curves represented by the p harmonics. Lastly, on the basis of the cluster tree, the deviant curves were deleted until the ICC was greater than ICC_m. The gait of a subject was considered to be reproducible when a minimum of four curves for each body side yielded an ICC value greater than ICC_m.

Subjects with non-reproducible curves were discarded from the analysis. Reproducible curves from patients or controls were pooled to build the respective average curves.

2.4.2. Comparison between the more-affected and less-affected sides in PD

We used a mixed linear model (analysis of variances with both fixed and random effects) to compare the PD subgroups (i.e. more-affected side vs. less-affected side).

The fixed effects were side (two levels: less-affected vs. more-affected), time (51 levels) and time–side interaction. The subject effect was considered to be random and we chose a first-order, autoregressive covariance pattern to take into account the dependency between the repeated measurements. Our choice of this model was based on the likelihood ratio test [20]. We computed the confidence band for the difference between the means (CBDM) (more-affected–less-affected) using the bootstrap method described in [18]. The latter is superior to the standard method (which involves computing a confidence interval at each time point by applying a Gaussian approximation) because it (i) does not presuppose a Gaussian distribution for the data and (ii) takes into account the correlations between the repeated measurements.

The CBDM provides a graphical check of the mixed model test: if the X axis is included in the CBDM, then there is no difference between the two sides. Depending on this result, data from more-affected and less-affected sides were pooled for subsequent analysis and a subject was characterized by the average of the two curves.

2.4.3. Comparison between PD patients and controls

The comparisons between average curves for independent groups (PD vs. controls) were performed using the linear mixed model. The fixed effects were time (51 levels), group (two levels) and time–group interaction, with subject as the random effect. As above, we choose a first-order autoregressive covariance pattern model. Comparisons for each time point (a post hoc analysis) were performed using the CBDM (the confidence band for the mean in the control group minus the mean in the PD group) computed using the bootstrap method, as described above. Time points where the horizontal line at zero exceeds the CBDM indicate the significant differences between the two groups.

3. Results

3.1. Description of spatiotemporal parameters in the study population (Table 1)

Gait speed was significantly lower in the PD group, with clearly subnormal values for stride length and, to a lesser extent, cadence. Furthermore, the double-support time was higher in PD.

3.2. Reliability of gait curves in C and PD groups (Table 2)

For the hip, knee and ankle curves of PD and control subjects, the mean (median) ICC values were reported in Table 2. In PD, the reliability of hip and knee curves was high enough to apply the whole procedure contrary to the ankle curves. Indeed, nearly 50% of the ICC values of the ankle curves were below 0.8—the minimum level for reliability of a single numerical measurement. Fig. 1 represents an estimation of the probability distribution

Table 2
Reliability of gait curves for hip, knee and ankle joints in Parkinson's disease patients and controls

	Controls	PD
Hip, mean ICC (median)	0.98 (0.99)	0.95 (0.98)
Hip, minimum ICC	0.74	0.56
Knee, mean ICC (median)	0.97 (0.98)	0.96 (0.98)
Knee, minimum ICC	0.67	0.68
Ankle, mean ICC (median)	0.91 (0.95)	0.76 (0.82)
Ankle, minimum ICC	0.73	0.18
Hip, ICCm	0.96	0.94
Knee, ICCm	0.95	0.90
% of unreliable beams[a] (hip)	1.66% (1 out 30×2)	9.37% (6 out of 32×2)
% of unreliable beams[a] (knee)	6.66% (4 out of 30×2)	12.5% (8 out of 32×2)

Intra class correlation coefficients (ICCs) were computed to assess reliability of the curves. ICCm was the cut-off value under which the curve beams were regarded as being unreliable before multivariable analysis. Then fast Fourier transform (FFT) was performed with hierarchical cluster analysis in order to discard the deviant curves of the unreliable beams and a new ICC was computed for each beam. NB: Two patients have unreliable beams for both hip and knee joints.

[a] After FFT and hierarchical cluster analysis for each beam to eliminate deviant curves.

function (PDF, using a Gaussian kernel) of the ICCs for the patient and control hip, knee and ankle curves. For the patients' curves that were not reliable, FFT was performed. The values of the means of the squared errors did not decrease significantly when the number of harmonics exceeded five for the knee and four for the hip, for both body sides. Each curve was then analysed in terms of the finite Fourier sum corresponding to the first four harmonics for the hip and the first five for the knee. For each beam, hierarchical cluster analysis was used to eliminate deviant curves and a new ICC was then computed. The results of this process are reported in Table 2.

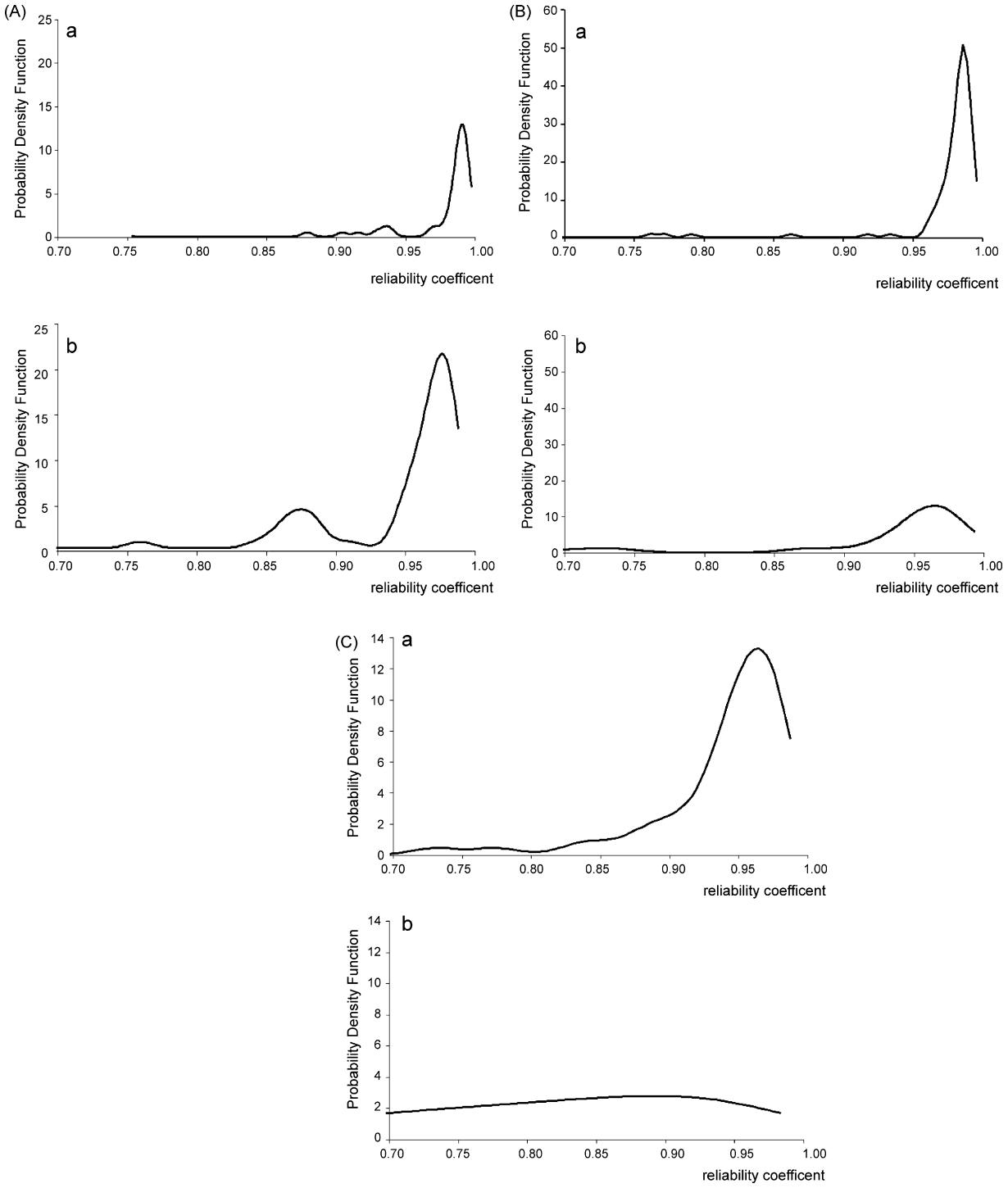

Fig. 1. Estimation of the probability distribution function (PDF) using a Gaussian kernel. (A) Hip in controls (a) and PD subjects (b). For example, the PDF values increased strongly above 0.96 for controls. Consequently, the ICC_m value was set at 0.96. (B) Knee in controls (a) and PD subjects (b). (C) Ankle in controls (a) and PD subjects (b).

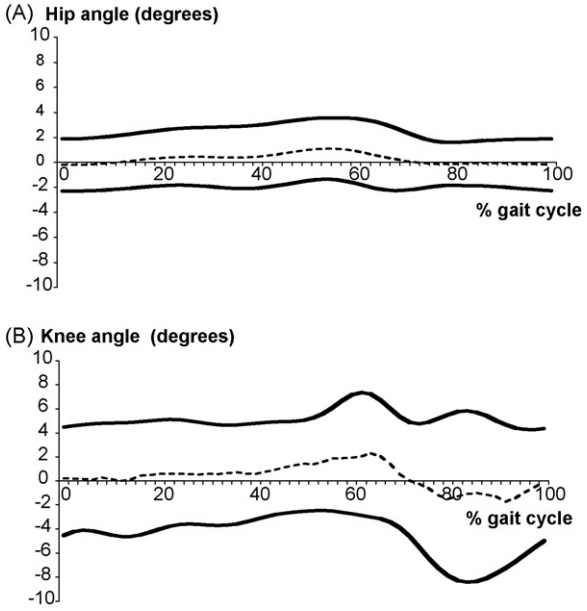

Fig. 2. Confidence band for the difference between the means of two sides (more-affected minus less-affected) computed using the bootstrap method. The dotted line represents the difference between the means. The *X* axis fell within the confidence band, meaning that there was no difference between the two sides. Hip angle (A) and knee angle (B) joints.

3.3. Comparisons between the more-affected and less-affected sides

In controls, no side effects or side × time interactions were observed for any of the joints analysed. For PD patients, this analysis was performed on the patients who presented a clinical difference between the two sides and whose curves were judged to be reliable (24 patients for the knee and 25 patients for the hip). No side × time interaction was observed ($p = 0.99$ for the knee and for the hip) and there were no statistically significant differences between the gait curves on the less-affected and more-affected sides ($p = 0.85$ for the knee and for the hip).

The bootstrap CBDM confirmed these results, since the *X* axis fell within the confidence band (Fig. 2).

3.4. Comparisons between PD patients and control subjects

We observed a significant group × time interaction ($p < 0.0001$), meaning that the two groups differed in terms of the time course of their respective curves. The average curves and confidence intervals for PD patients and controls are shown in Fig. 3. The bootstrap method was used to validate these results: The significantly different times when comparing PD and control subjects correspond to values on the *X* axis that do not fall within the CBDM and are also represented in Fig. 3.

4. Discussion

4.1. Reliability of angle joint curves in gait in PD

The present study's first aim was to assess the reliability of joint curves in the sagittal plane during gait in PD patients. The ICC-based procedure was clearly applicable for hip and knee joints but not for ankle joints. It is worth thinking about the reasons that could render joint angle curves unreliable for a given patient or session. Several hypotheses may be proposed:

- An increase in gait curve variability may characterize the most impaired patients and therefore decrease gait curve reliability in these individuals.
- Gait in PD is often characterized by freezing of gait (FOG), which is considered as a late-onset feature, but that may also occur in the very early stages [21]. Stride-to-stride variability increases markedly in patients presenting FOG. PD patients who experience FOG display abnormal cadence and stride length for the three steps prior to freezing. Moreover, even during FOG-free gait, PD patients with a history of FOG show higher stride-to-stride variability than with patients who have never suffered from the phenomenon [22].
- A technical incident (marker loss, an abnormal curve generated by the software, false determination of heel-off and heel contact times by the investigator, etc.) could also account for unreliable curves.
- Taking into account too few cycles for each patient could also explain higher curve variance and thus unreliability (although this is not applicable to our study).

For example, of the six PD subjects who had unreliable knee joint curves before the FFT was used to select and discard deviant curves, four had suffered from the disease for many years (14, 15, 16 and 17 years, respectively) and showed high UPDRS III scores (over 50). One presented camptocormia with severe scoliosis. These patients displayed dramatically low gait speeds (below 0.5 m/s) but none had a history of FOG and none presented FOG during our trials. No marker loss was recorded. For just one trial in one patient, incorrect identification of heel-off and toe-off points and heel contact times was evidenced. These cycles were considered as deviant when applying the FFT with hierarchical classification of the harmonics. The fact that the method is not applicable for these patients who walked at less than 0.5 m/s limits the use of the bootstrap method for building an 'average' curve. Indeed, it is now established that very low gait speed can increase stride-to-stride variability, even in normal subjects [23].

4.2. Comparisons between less-affected and more-affected sides in PD

We did not find any differences between the curves for the less-affected and more-affected sides in PD. Asymmetry of

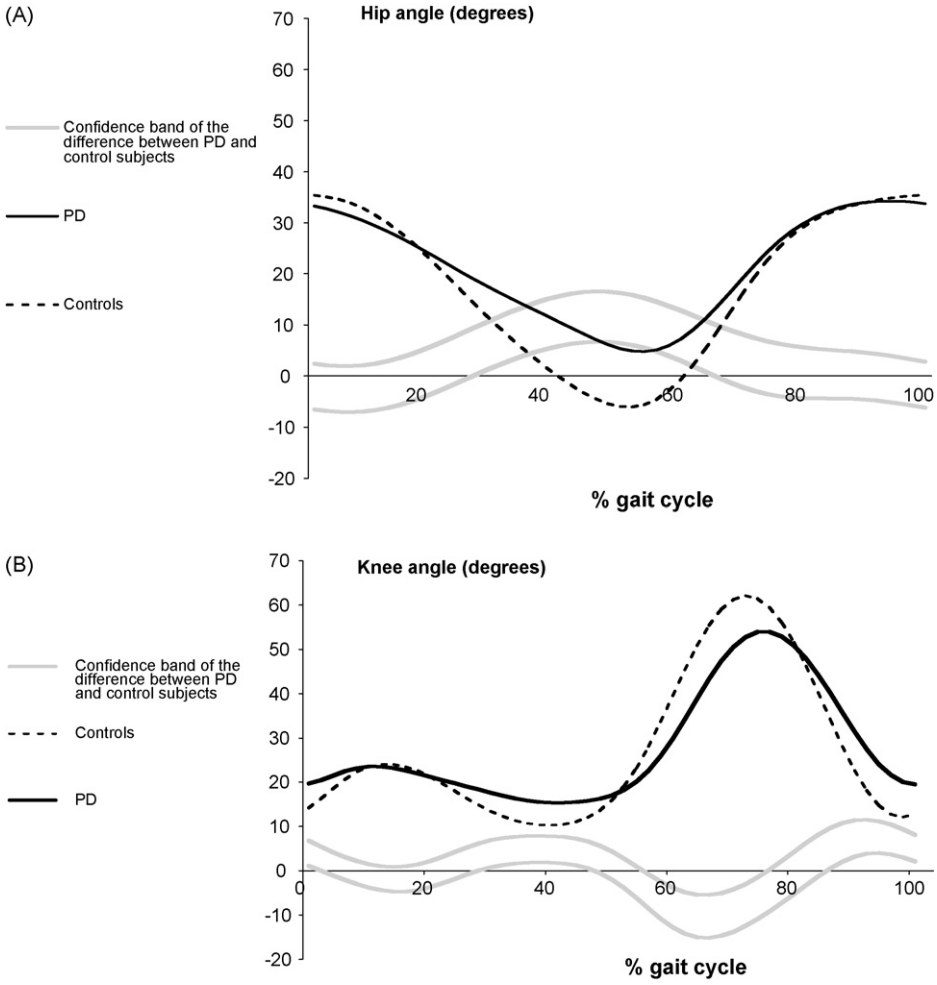

Fig. 3. Average curves for PD patients (dark line) and control subjects (dotted line), together with the confidence band for the difference between the means (CBDM) of the two groups (grey line). The CBDM was built using the bootstrap method. The times at which the *X* axis falls outside the CBDM are those for which differences between patients and control subjects exist. Hip (A) and knee (B) joints.

gait in parkinsonian syndromes has been demonstrated using symmetry factors [8,24]. In this latter study, gait asymmetry was not correlated with asymmetry of the clinical symptoms. Moreover, the presence of significant gait asymmetry for angle joints in PD was not confirmed in another study [15].

4.3. Comparison of knee and hip joint angles in gait in PD patients and controls

In the third part of the present study, we compared the PD group with the control group. Hip extension was lower during late stance phase in PD. This could explain the decrease in stride length observed in 'off drug' PD patients but gait speed was very different in the two groups. For the knee, we found that the double-support time differed significantly during the stance phase. During the swing phase, the time points corresponding to maximum knee flexion in the sagittal plane were significantly different. The double-support phase corresponds to a posture where balance seems to more easily maintained. A decrease in maximum knee flexion during the swing phase could be related to mechanical constraints, since rigidity plays an important role in PD. Indeed, muscle stiffness influences the natural oscillatory properties of the swing limb, as confirmed in upper motor neuron syndrome patients [25]. Our results confirm the visual description of curves made by Lewis et al. [11].

4.4. Reliability of the ankle

The procedure described in the present work is not applicable to the ankle joint. One of the reasons is that the ankle curve is too variable in this 'off-drug' PD population. However, ankle gait curves are also less reliable than hip and knee curves in controls (mean ICCs; hip: 0.98; knee: 0.97; ankle: 0.91). The presence of predominantly distal 'off-dystonia' in patients might explain the difference with other joints but this phenomenon does not explain reliability differences in controls.

4.5. Methodological considerations

One of the aims of the present work was to assess reliability of curves in a population of patients who display great stride-to-stride variability. We conclude that the method presented here efficiently removes outliers that are not representative of the patient's gait. One could argue that this method suppresses intra-individual variability. However, the aim of our method is not to study gait variability *per se* (since it can be evaluated by using the coefficient of variation, for example). The method presented here assesses reliability of the curves of a given patient and enables a comparison of his/her 'average' curve with that of another session or population in a very easy and methodologically valid way.

5. Conclusion

By using validated statistical tools, we are now able to compare PD patients and controls in terms of joint angle differences. This procedure makes it easier to determine the influence of therapy on gait in a given by comparing the subject's average curve to average gait curves for populations of PD patients and controls [19]. When applied under appropriate conditions, these tools appear to be applicable to both single cases and groups. One of the limitations is that building an average curve is impossible for the most severe patients who walked at less than 0.5 m/s (who are fortunately a minority) and comparisons of single curves should be preferred for these latter.

Conflicts of Interest

None

References

[1] Blin O, Ferrandez AM, Serratrice G. Quantitative analysis of gait in Parkinson patients: increased variability of stride length. J Neurol Sci 1990;98:91–7.
[2] Morris ME, Iansek R, Matyas TA, Summers JJ. The pathogenesis of gait hypokinesia in Parkinson's disease. Brain 1994;117:1169–81.
[3] Azulay JP, Van Den Brand C, Mestre D, Blin O, Sangla I, Pouget J, et al. Automatic motion analysis of gait in patients with Parkinson disease: effects of levodopa and visual stimulations. Rev Neurol (Paris) 1996;152:128–34.
[4] Defebvre L, Krystkowiak P, Blatt JL, Duhamel A, Bourriez JL, Perina M, et al. Influence of pallidal stimulation and levodopa on gait and preparatory postural adjustments in Parkinson's disease. Mov Disord 2002;17:76–83.
[5] Krystkowiak P, Blatt JL, Bourriez JL, Duhamel A, Perina M, Blond S, et al. Effects of subthalamic nucleus stimulation and levodopa treatment on gait abnormalities in Parkinson disease. Arch Neurol 2003;60:80–4.
[6] Krystkowiak P, Blatt JL, Bourriez JL, Duhamel A, Perina M, Kemoun G, et al. Chronic bilateral pallidal stimulation and levodopa do not improve gait in the same way in Parkinson's disease: a study using a video motion analysis system. J Neurol 2001;248:944–9.
[7] Krystkowiak P, Delval A, Dujardin K, Bleuse S, Blatt JL, Bourriez JL, et al. Gait abnormalities induced by acquired bilateral pallidal lesions: a motion analysis study. J Neurol 2006;253:594–600.
[8] Knuttson E. An analysis of parkinsonian gait. Brain 1972;95:475–86.
[9] Murray MP, Sepic SB, Gardner GM, Downs WJ. Walking patterns of men with parkinsonism. Am J Phys Med 1978;57:278–94.
[10] Mitoma H, Hayashi R, Yanagisawa N, Tsukagoshi H. Characteristics of parkinsonian and ataxic gaits: a study using surface electromyograms, angular displacements and floor reaction forces. J Neurol Sci 2000;174:22–39.
[11] Lewis GN, Byblow WD, Walt SE. Stride length regulation in Parkinson's disease: the use of extrinsic, visual cues. Brain 2000;123:2077–90.
[12] Morris M, Iansek R, McGinley J, Matyas T, Huxham F. Three-dimensional gait biomechanics in Parkinson's disease: evidence for a centrally mediated amplitude regulation disorder. Mov Disord 2005;20:40–50.
[13] Sofuwa O, Nieuwboer A, Desloovere K, Willems AM, Chavret F, Jonkers I. Quantitative gait analysis in Parkinson's disease: comparison with a healthy control group. Arch Phys Med Rehabil 2005;86:1007–13.
[14] Delval A, Krystkowiak P, Blatt JL, Labyt E, Dujardin K, Destee A, et al. Role of hypokinesia and bradykinesia in gait disturbances in Huntington's disease: a biomechanical study. J Neurol 2006;253:73–80.
[15] Peppe A, Chiavalon C, Pasqualett P, Crovato D, Caltagirone C. Does gait analysis quantify motor rehabilitation efficacy in Parkinson's disease patients? Gait Posture 2007;26:452–62.
[16] Hausdorff JM, Cudkowicz ME, Firtion R, Wei JY, Goldberger AL. Gait variability and basal ganglia disorders: stride-to-stride variations of gait cycle timing in Parkinson's disease and Huntington's disease. Mov Disord 1998;13:428–37.
[17] Sadeghi H, Allard P, Shafie K, Mathieu PA, Sadeghi S, Prince F, et al. Reduction of gait data variability using curve registration. Gait Posture 2000;12:257–64.
[18] Duhamel A, Bourriez JL, Devos P, Krystkowiak P, Destée A, Derambure P, et al. Statistical tools for clinical gait. Gait Posture 2004;20:204–12.
[19] Duhamel A, Devos P, Bourriez JL, Preda C, Defebvre L, Beuscart R. Functional data analysis for gait curves study in Parkinson's disease. Stud Health Technol Inform 2006;124:569–74.
[20] Brown H, Prescott R. Applied mixed model in medicine. Chichester: John Wiley & Sons; 1999. pp. 212–214.
[21] Giladi N, McDermott MP, Fahn S, Przedborski S, Jankovic J, Stern M, et al., Parkinson Study Group. Freezing of gait in PD: prospective assessment in the DATATOP cohort. Neurology 2001;56:1712–21.
[22] Hausdorff JM, Schaafsma JD, Balash Y, Bartels AL, Gurevich T, Giladi N. Impaired regulation of stride variability in Parkinson's disease subjects with freezing of gait. Exp Brain Res 2003;149:187–94.
[23] Kang HG, Dingwell JB. Separating the effects of age and walking speed on gait variability. Gait Posture. September 1, 2007 [Epub ahead of print].
[24] Plotnik M, Giladi N, Balash Y, Peretz C, Hausdorff JM. Is freezing of gait in Parkinson's disease related to asymmetric motor function? Ann Neurol 2005;57:656–63.
[25] Holt KG, Obusek JP, Fonseca ST. Constraints on disordered locomotion. A dynamical systems perspective on spastic cerebral palsy. Hum Mov Sci 1996;15:177–202.