

Quantitative Gait Analysis in Parkin Disease: Possible Role of Dystonia

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ABSTRACT: Introduction: Parkin disease (PARK2, OMIM 602544) is an autosomal-recessive early-onset parkinsonism characterized by an early occurrence of lower limb dystonia. The aim of this study was to analyze spatiotemporal, kinematic, and kinetic gait parameters in patients with parkin disease in the *OFF* and *ON* conditions compared to healthy age-matched controls.

Methods: Fifteen patients with parkin disease and 15 healthy age-matched controls were studied in a gait analysis laboratory with an integrated optoelectronic system. Spatiotemporal, kinematic, and kinetic gait parameters at a self-selected speed were recorded in the *OFF* and *ON* conditions. A jerk index was computed to quantify the possible reduction of smoothness of joint movements.

Results: Compared to controls, parkin patients had, either in the *OFF* or in the *ON* conditions, significant reduction of walking velocity, increased step width, and decreased percentage of double support. Kinematic analysis in both conditions showed: increased ankle dorsiflexion and knee flexion at the initial contact; maxi-

mal flexion and increased range of motion in mid stance; increased hip flexion and max extension in stance at pelvis; and increased mean tilt antversion. Kinetics showed increased hip and knee power generation in stance in either condition. The jerk index was increased at all joints both in *OFF* and *ON*. There were no correlations between individual gait parameters and clinical ratings.

Conclusion: Parkin patients have an abnormal gait pattern that does not vary between the *OFF* and the *ON* conditions. Variations recorded with instrumented analysis are more evident for kinematic than kinetic parameters at lower limbs. Severity of dystonia does not correlate with any individual kinematic parameter. © 2016 International Parkinson and Movement Disorder Society

Key Words: parkin disease; kinematics; kinetics; dystonia; gait analysis

Parkin disease (OMIM 602544) is an autosomal-recessive early-onset parkinsonism characterized by diurnal fluctuations, lower limb dystonia, hyperreflexia, and uncommon occurrence of cognitive impairment.¹ The pathological process is usually restricted to the brainstem, and Lewy bodies are rarely

found. Lower limb dystonia is increasingly recognized as a peculiar feature of parkin disease that may also occur as an isolated presenting feature.²

Kinematic and kinetic gait analysis has proven valuable to measure locomotor abnormalities in a number of neurological conditions affecting gait, such as spasticity,³ Parkinson's disease (PD),⁴ ataxia,⁵ vascular encephalopathy,⁶ or hydrocephalous.⁷ In PD, for example, stride length and mean gait velocity are markedly reduced, range of motion (ROM) is largely below normal at all joints, and power generation is reduced at ankle and hip joints.^{4,8} These abnormalities are consistent with a prominent effect of gait akinesia and rigidity and are attenuated by dopaminergic replacement therapy and DBS.⁸

No instrumented data are available on locomotion in parkin disease patients and the influence of specific

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features, such as lower limb dystonia and hyperreflexia, on gait parameters is still undiscovered. Gait analysis is increasingly applied to the study of dystonia syndromes,⁹ and dystonia may contribute to gait abnormalities in parkin disease. We therefore investigated kinetic and kinematic gait variables in a series of parkin disease patients, in the *ON* and *OFF* conditions, and compared them to those of age-matched controls.

Materials and Methods

Fifteen patients with parkin disease (7 men, 8 women) and 15 healthy control subjects (7 men, 8 women) were recruited. The study was approved by the local review board and was carried out according to the Declaration of Helsinki. Inclusion criteria were: genetic diagnosis of parkin disease (with homozygous or compound heterozygous involvement of both alleles; Supporting Table 1); unsupported autonomous gait; and stable dopaminergic medication regimen. Control subjects had no neurological or musculoskeletal abnormality. Exclusion criteria were: unpredictable *OFF* periods (possibly interfering with the test); previous DBS implant; score <23 on the Mini-Mental State Examination; sensory or other medical disorders affecting gait (e.g., visual or musculoskeletal defects); or severe psychological impairment. Two patients who received subthalamic implants were excluded based on these criteria; no other exclusions occurred.

The following demographic and clinical variables were recorded: sex; age at disease onset and at time of evaluation; and motor signs at onset. Motor assessment was performed using the UPDRS motor section.¹⁰ Lower limb dystonia severity was rated using the lower limb severity subscore of the Fahn-Marsden Dystonia Rating Scale (FMDRS)¹¹ in the *OFF* and in the *ON* conditions. Neurological and gait laboratory evaluations were performed in the morning, on 2 different days, in the practically defined *OFF* condition¹² and in the *ON* condition. The levodopa-equivalent daily dose, expressed in milligrams, was obtained by adding to the standard L-dopa dose all dopaminergic medications converted to the relative potency of standard L-dopa.¹³

Kinematic parameters were acquired with a computerized video motion analysis system utilizing eight infrared cameras with a sampling rate of 140 Hz (SMART-D system; BTS Bioengineering, Garbagnate Milanese, Italy). The spatial distribution of the cameras was optimized to yield reliable motion data at the hip, knee, and ankle bilaterally. The motion capture system recorded and processed the locations of passive reflective markers placed at bony prominences according to the Davis protocol,¹⁴ providing anatomic coordinates for the pelvis, thigh, shank, and foot. One set

of data corresponding to the standing position (static data) was recorded in order to calculate the location of joint centers. Ground reaction forces were measured using four force plates (Kistler, Winterthur, Switzerland) embedded in an 8-m walkway, synchronized to the video system and working at a sampling rate of 560 Hz.

Data collection was performed over two sessions, in the *OFF* and the *ON* conditions, during five overground walking trials at a comfortable self-selected speed, for 8 m each. The most severely affected side was determined based on the patients' dopamine transporter scan and parkinsonian motor features. The left side was considered for healthy subjects. From the five trials, we selected the three that had the most complete kinematic and concurrent kinetic data, from which the average spatiotemporal parameters, sagittal plane kinematics, and kinetics were obtained. An index of jerkiness was computed both for the stance and the swing phase at all joints.¹⁵

Statistical Analysis

Descriptive statistics were computed using Statistica software (version 6.0; StatSoft Inc., Tulsa, OK). Because the Shapiro-Wilk test showed that distribution of data was not normal, nonparametric statistics was adopted: The Mann-Whitney U test was used to compare healthy controls to parkin patients either in the *ON* or in the *OFF* conditions, whereas the Wilcoxon paired test was used to compare the *ON* and the *OFF* states in parkin patients. In order to minimize the possibility of a type 1 error, we set statistical significance at $P < 0.0167$ after Bonferroni correction for multiple comparisons; the standard P value (0.05) was divided by 3, corresponding to the number of performed comparisons (healthy controls vs. parkin *OFF*, healthy controls vs. parkin *ON*, and parkin *OFF* vs. *ON*). An analysis of covariance with a generalized nonlinear model (Wald test) was used to correct for possible influence of different gait speeds between the *OFF* and the *ON* conditions, even when these were not significant. A nonparametric correlation analysis (Spearman rank test) was used to correlate instrumented gait measures with demographic and clinical data (age at onset, disease duration, UPDRS *OFF* and *ON* motor scores, and FMDRS *OFF* and *ON* scores). The minimum P value obtained from the correlation analysis between the clinical data and each instrumented parameter ($p_{\min}$) was calculated.

Results

Clinical Data

Parkin disease patients had a mean age of 50.7 ± 11.5 years, were 166.9 ± 10.9 cm tall, and weighed 71.3 ± 15.2 kg. Healthy controls had a mean age of

TABLE 1. Spatiotemporal parameters

Variables	Control	Parkin OFF	P Value	Parkin ON	P Value	P Value (OFF-ON)
Walking velocity (m/s)	1.39 (0.12)	1.31 (0.22)	0.011 ^a	1.22 (0.20)	<0.001 ^a	0.691
Stride length (m)	1.47 (0.12)	1.34 (0.35)	0.029	1.33 (0.20)	0.005 ^a	0.820
Step width (m)	0.13 (0.02)	0.16 (0.04)	<0.001 ^a	0.15 (0.03)	<0.001 ^a	0.272
Cadence (steps/min)	113.8 (8.6)	114.6 (21.6)	0.594	111.6 (10.0)	0.539	0.683
Double support (%GC)	12.5 (2.2)	9.7 (3.6)	0.012 ^a	9.8 (1.7)	<0.001 ^a	0.820
Single support (%GC)	59.3 (3.6)	58.6 (2.9)	0.967	59.5 (2.6)	0.624	1.000
Duration of GC (s)	1.05 (0.10)	1.05 (0.21)	0.623	1.07 (0.09)	0.345	0.842

Values are median (IQR).

^aP value <0.0167 (significant difference).

GC, gait cycle.

49.2 ± 10.5 years, were 165.7 ± 6.2 cm tall, and weighed 62.7 ± 13.4 kg. The two groups did not differ statistically. Parkin patients had a mean disease duration of 14.7 ± 7.1 years. Their mean UPDRS motor score was 27.7 ± 12.5 in the OFF condition and 15.2 ± 10.6 in the ON condition. The most

affected side was left in 8 patients and right in the remaining 7. Parkinsonian features were of variable severity, overall mild, and prevailed in the upper body (see Video: patient 10).

Lower limb dystonia occurred in most patients with parkin disease (Supporting Table 1). In the OFF

TABLE 2. Kinematic data for control and parkin groups in the OFF and ON conditions

Variables	Control	Parkin OFF	P Value	Parkin ON	P Value	P Value (OFF-ON)
Ankle						
• Initial contact (°)	-1.3 (2.9)	3.5 (7.6)	0.002 ^a	6.4 (8.6)	<0.001 ^a	0.233
• Max dorsiflexion in stance (°)	13.8 (6.5)	14.7 (8.0)	0.744	16.0 (9.3)	0.540	0.977
• ROM during push-off (°)	25.9 (7.9)	23.6 (7.5)	0.325	23.9 (6.3)	0.537	0.427
• Plantarflexion at toe-off (°)	-12.1 (5.7)	-9.6 (11.9)	0.513	-13.0 (6.7)	0.806	0.820
• Max plantarflexion in swing (°)	-14.1 (5.3)	-12.8 (10.3)	0.902	-15.7 (8.5)	0.512	0.363
• Max dorsiflexion in swing (°)	4.3 (6.7)	5.9 (9.6)	0.775	7.9 (6.2)	0.068	0.496
• ROM in swing (°)	18.4 (7.0)	18.6 (5.5)	1.000	19.7 (8.1)	0.061	0.023
• Jerk index in stance (°/s ³)	0.028 (0.003)	0.043 (0.044)	<0.001 ^a	0.039 (0.021)	<0.001 ^a	0.198
• Jerk index in swing (°/s ³)	0.038 (0.002)	0.049 (0.016)	<0.001 ^a	0.040 (0.023)	<0.001 ^a	0.281
Knee						
• Initial contact (°)	6.3 (7.4)	19.5 (6.8)	<0.001 ^a	16.8 (7.6)	<0.001 ^a	0.427
• Max flexion in mid stance (°)	14.7 (11.3)	29.4 (5.7)	<0.001 ^a	27.6 (11.7)	<0.001 ^a	0.334
• Max extension in stance (°)	1.4 (11.7)	8.3 (9.9)	0.004 ^a	6.0 (12.8)	0.055	0.281
• ROM in mid-stance (°)	12.8 (12.6)	23.6 (13.2)	0.002 ^a	24.5 (10.9)	0.001 ^a	0.173
• Flexion at toe-off (°)	38.3 (7.4)	39.5 (8.8)	0.539	38.6 (15.4)	1.000	0.335
• Max flexion in swing (°)	61.3 (8.8)	69.1 (9.6)	0.002 ^a	68.7 (9.4)	0.116	0.281
• Jerk index in stance (°/s ³)	0.019 (0.002)	0.069 (0.037)	<0.001 ^a	0.065 (0.046)	<0.001 ^a	0.233
• Jerk index in swing (°/s ³)	0.033 (0.003)	0.060 (0.032)	<0.001 ^a	0.052 (0.033)	<0.001 ^a	0.776
Hip						
• Flexion initial contact (°)	30.7 (20.8)	42.0 (12.6)	0.010 ^a	40.2 (12.3)	0.021	0.513
• Max hip extension (°)	-12.0 (16.3)	-6.2 (11.2)	0.074	-5.9 (13.9)	0.067	0.955
• Extension/flexion at toe-off (°)	-3.6 (15.8)	1.1 (15.5)	0.055	-0.6 (15.8)	0.217	0.532
• Max flexion in swing (°)	28.8 (19.9)	42.0 (13.7)	0.001 ^a	42.4 (10.4)	0.002 ^a	0.570
• Min rotation (°)	-4.8 (6.4)	-9.7 (11.8)	0.106	-10.1 (8.3)	0.001 ^a	0.820
• Max rotation (°)	19.5 (9.2)	11.5 (16.0)	0.029	14.8 (11.0)	0.026	0.570
• ROM rotation (°)	24.3 (15.2)	20.0 (11.5)	0.713	24.1 (11.0)	0.595	0.088
• Jerk index in stance (°/s ³)	0.007 (0.001)	0.047 (0.026)	<0.001 ^a	0.045 (0.023)	<0.001 ^a	0.570
• Jerk index in swing (°/s ³)	0.008 (0.001)	0.038 (0.020)	<0.001 ^a	0.033 (0.019)	<0.001 ^a	0.650
Pelvis						
• Mean tilt (°)	5.7 (1.6)	9.8 (7.8)	0.005 ^a	11.9 (7.7)	0.005 ^a	1.000
• Range of pelvic tilt (°)	3.3 (8.7)	3.5 (2.1)	0.683	4.0 (1.1)	0.653	0.233
• Range of pelvic rotation (°)	8.9 (5.0)	11.8 (5.5)	0.027	13.3 (7.4)	0.002 ^a	0.020

Values are median (IQR).

^aP value <0.0167 (significant difference).

Max, maximum; Min, minimum.

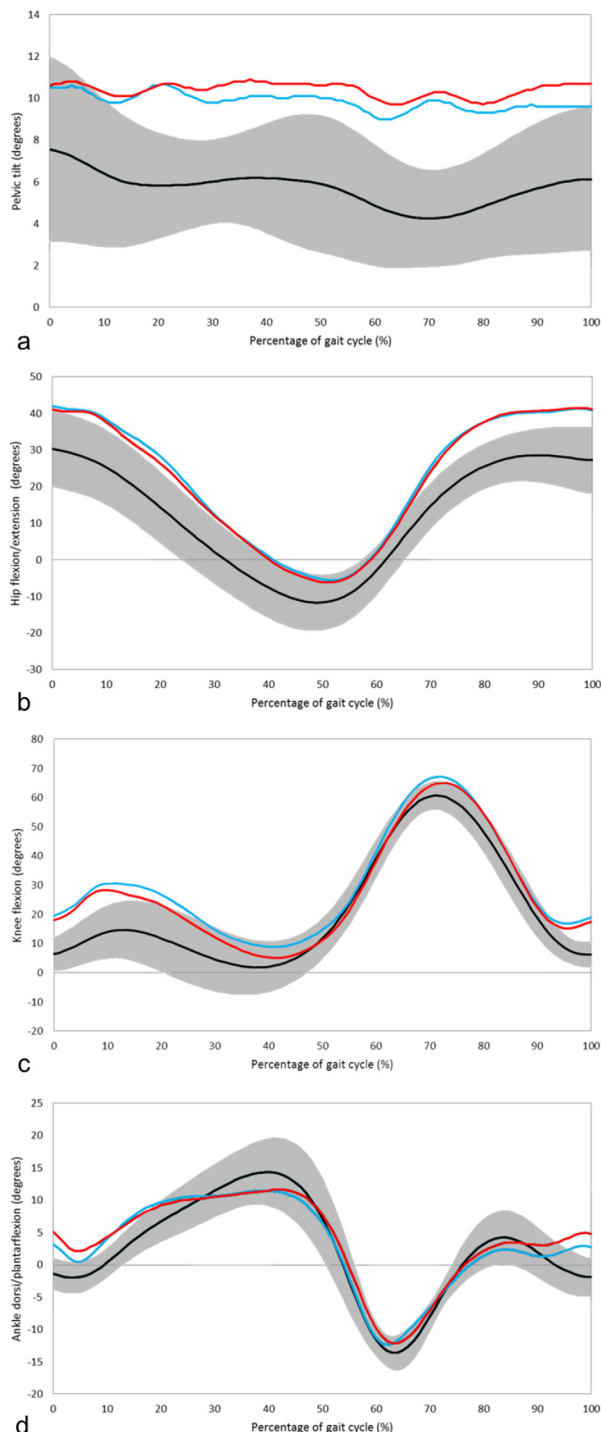


FIG. 1. Mean sagittal kinematic curves of pelvis (A), hip (B), knee (C), and ankle (D) in patients with parkin disease. Blue lines indicate the OFF condition, red lines the ON condition; control values are shaded in gray. The parameters recorded in parkin patients lie out of the boundary of normal range at pelvis, knee, and hip and within the boundary of normal range at ankle, where there is an abnormal curve morphology in the stance phase. Anterior tilt of the pelvis is more increased in the ON condition. At the hip, there is increased flexion at initial contact, stance phase, and swing either in OFF or ON. At the knee, there is increased flexion at initial contact, with more evident loading response and swing in OFF. [Color figure can be viewed at wileyonlinelibrary.com.]

condition, 9 patients had lower limb dystonia while walking: 8 scored 1 at FMDRS and had a slight foot torsion; 1 patient scored 2 at FMDRS and had mild torsional dystonia. The remaining 6 patients had no dystonia (score 0). In the ON condition, 11 patients were found to have dystonia: 8 scored 1, 2 scored 2, and 1 scored 3 at FMDRS. In 5 patients, the FMDRS score worsened by 1 point from OFF to ON; in 10, the score remained unchanged. In no patients was the FMDRS score improved from OFF to ON.

The features of dystonia were assessed in the OFF and in the ON conditions. Patients scoring 1 had mild abnormalities, particularly at ankle joints, producing a plantarflexion rebound during the stance phase and a mild torsion in the swing phase (see Video: patient 14); occasionally, a mild torsion of hips and pelvis was also observed; these features were more marked in the ON condition, but were often present in OFF as well. Patients scoring 2 had torsion dystonia at all joints with some nondisabling interference with gait (see Video: patient 9 in ON). No patient scored 3 or 4 at FMDRS in OFF, whereas 1 scored 3 in ON (see Video: patient 6).

Instrumented Data

A comparison of spatiotemporal gait parameters of parkin patients in the OFF condition with those of controls showed that patients had a slower walking velocity, larger step width, and a shorter double support phase within the gait cycle (Table 1). In the ON condition, patients had the same differences compared to healthy controls, and also a shortened stride length. Spatiotemporal gait parameters in ON did not differ from those recorded in OFF.

Kinematic variables of parkin patients in OFF revealed several differences with respect to healthy controls at each joint angle during the gait cycle (Table 2; Fig. 1). Parkin patients had: increased ankle dorsal flexion at initial contact; increased knee flexion at initial contact and in the loading response; decreased knee extension in stance; increased knee range of motion in stance and increased max flexion in swing; increased hip flexion at the initial contact; increased maximal hip flexion in swing; and increased pelvis antversion throughout the gait cycle ($P < 0.0167$ for each comparison).

Kinematic parameters of parkin patients in ON revealed the same differences from controls, as reported in OFF, apart from: knee maximum (max) extension in stance and max flexion in swing; hip flexion at initial contact; and increased hip intrarotation and range of pelvic rotation, which did not differ from controls ($P < 0.0167$).

Correction of all data for gait speed by means of covariate analysis revealed that the above differences were still significant. No kinematic differences

TABLE 3. Kinetic data for control and parkin groups in the *OFF* and *ON* conditions

Variables	Control	Parkin <i>OFF</i>	<i>P</i> Value	Parkin <i>ON</i>	<i>P</i> Value	<i>P</i> Value (<i>OFF-ON</i>)
Ankle						
Joint moment (Nm/kg)						
• Moment at loading response	−0.05 (0.07)	−0.15 (0.24)	0.043	−0.15 (0.20)	0.174	0.334
• Max moment in mid and terminal stance	1.44 (0.23)	1.33 (0.27)	0.049	1.28 (0.32)	0.014 ^a	0.570
• Minimum moment in pre-swing	0.01 (0.12)	0.02 (0.22)	0.539	0.06 (0.15)	0.037	0.955
Power (W/kg)						
• Generation at pre-swing	3.61 (3.24)	2.77 (0.90)	0.461	2.62 (1.27)	0.461	0.363
• Absorption at loading response	−0.65 (0.42)	−0.40 (0.46)	0.029	−0.34 (0.18)	<0.001 ^a	0.570
Knee						
Joint moment (Nm/kg)						
• Max flexion moment in stance	−0.37 (0.27)	−0.60 (0.23)	<0.001 ^a	−0.50 (0.49)	0.037	0.394
• Max extension moment in stance	0.49 (0.64)	0.69 (0.39)	0.097	0.59 (0.42)	0.512	0.570
Power (W/kg)						
• Max power generated in stance	0.45 (0.74)	1.03 (0.46)	<0.001 ^a	1.07 (0.51)	<0.001 ^a	0.532
• Max power absorbed in late stance	−1.58 (2.42)	−0.82 (0.79)	0.267	−0.72 (0.30)	0.567	0.609
Hip						
Joint moment (Nm/kg)						
• Max flexion moment in stance	−0.97 (0.56)	−0.62 (0.43)	0.011 ^a	−0.64 (0.35)	0.024	0.496
• Max extension moment in stance	1.03 (0.42)	1.18 (0.45)	0.250	1.08 (0.23)	0.486	0.733
• Max abduction moment in stance	0.69 (0.66)	0.94 (0.16)	0.061	0.85 (0.26)	0.161	0.363
Power (W/kg)						
• Max power generated in stance	1.06 (0.10)	1.60 (0.95)	0.012 ^a	1.30 (0.77)	0.012 ^a	0.495
• Max power absorbed in late stance	−0.82 (0.80)	−0.61 (0.61)	0.325	−0.63 (0.32)	0.486	0.955

Values are median (IQR).

^a*P* value <0. 0167 (significant difference).

Max, maximum.

between the *ON* and the *OFF* conditions were found ($P < 0.0167$).

The jerk index calculated on angular displacement of all joints showed significantly larger values in parkin patients compared to controls (either in *OFF* or in *ON*), indicating a reduced smoothness of joint flexion-extension movement. No significant difference between *OFF* and *ON* was found at any joint.

Kinetic parameters in *OFF* revealed that, compared to controls, patients had: increased max knee flexion moment in stance and maximum knee power generation in stance; decreased maximal hip flexion moment in stance and increased max hip power generation in stance ($P < 0.0167$ for each comparison; Table 3; Fig. 2).

Kinetic parameters in *ON* showed, compared to controls, the same abnormalities of power production at hip and knee joint measured in *OFF*, and also a reduced ankle max moment in mid and terminal stance (push-off phase) and a reduced ankle power absorption at loading response.

With reference to kinetic parameters, no significant differences were detected between *ON* and *OFF*.

Clinical-Instrumented Correlations

There was no meaningful correlation of instrumented parameters and variables with the following clinical data: age at onset ($p_{\min} = 0.194$), disease duration ($p_{\min} = 0.057$), UPDRS motor score *OFF*

($p_{\min} = 0.117$), UPDRS motor score *ON* ($p_{\min} = 0.122$), FMDRS *OFF* ($p_{\min} = 0.407$), and FMDRS *ON* ($p_{\min} = 0.071$).

When mean sagittal kinematic curves of hip, knee, and ankle were grouped by FMDRS scores, it was observed that patients scoring 0 plotted within the normal range only at ankle either in *OFF* or in *ON*. Otherwise, all groups were outside the normal range, with FMDRS score 2 patients plotting quite farther from normal than the other two groups. Comparison of FMDRS scores in *OFF* and *ON* showed no statistical difference (Supporting Table 1). Furthermore, curve shapes had an irregular profile either in stance or in swing phases that, on average, worsened from *OFF* to *ON* (Fig. 3).

Discussion

This study describes the spatiotemporal, kinematic, and kinetic variables of gait in patients with parkin disease in the *OFF* and *ON* conditions. These patients had lower limb dystonia involving different joints that still allowed unsupported and efficacious gait and, on average, did not present marked reduction of joint power production. Overall, the motor expression of parkin disease is characterized by an excess of movement at lower limbs in the *OFF* and, particularly, in the *ON* condition, as demonstrated by the larger than

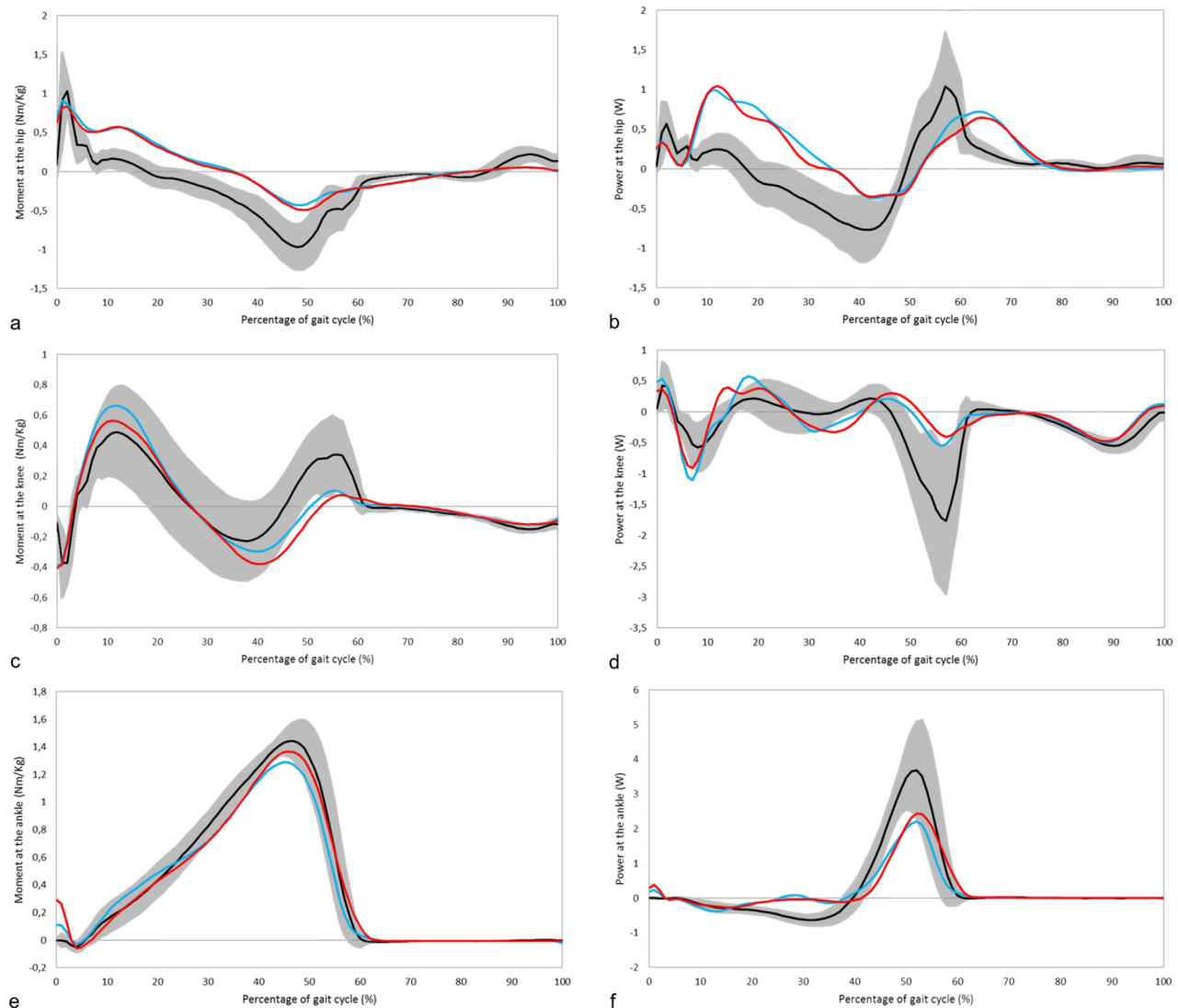


FIG. 2. Mean sagittal kinetic curves of hip (A and B), knee (C and D), and ankle (E and F) moment (left column) and power (right column) in patients with parkin disease. Blue lines indicate the OFF condition, red lines indicate ON; control values are shaded in gray. Hip and ankle parameters are evidently outside the normal range. The main kinetic abnormalities are recorded at hip and consist in increased internal extensor moment associated with increased hip power generation in initial stance. [Color figure can be viewed at wileyonlinelibrary.com.]

normal range of pelvic rotation, hip intrarotation, and knee ROM in the mid stance.

Although parkin disease has some parkinsonian features, the locomotor abnormalities observed in parkin patients in the OFF condition indicate only few changes that resemble, although with smaller figures, those observed in the PD OFF state, namely, reduced mean velocity and stride length and increased step width.^{16,17} Conversely, several dissimilarities between parkin and PD patients were notable. Parkin patients had reduced percentage of double support, a shift of knee displacement toward greater flexion during the whole gait cycle, with an increased knee ROM in stance and increased hip and knee flexion and ankle dorsiflexion at initial contact. Kinetic parameters in OFF also differentiated parkin disease patients who had increased power generation at hip and knee com-

pared to controls. Differently from PD patients, parkin patients did not show a reduction of power generation at the ankle during push-off when compared to healthy subjects.

Another difference is that in PD, abnormal kinematic and kinetic gait parameters recorded in the OFF condition tend to normalize when patients switch to ON,⁸ a feature not observed in gait analysis of parkin patients. Particularly, dystonia did not disappear or attenuate in ON, and even increased at hip and pelvic joints, a feature that may have affected UPDRS scores assessing gait and the lower limbs. These observations raise the question of whether UPDRS is an appropriate measure for patients with parkin disease; particularly in the ON condition, this scale does not pick some features of parkin disease that may thus escape clinical rating. Besides, there is a lack of a validated rating

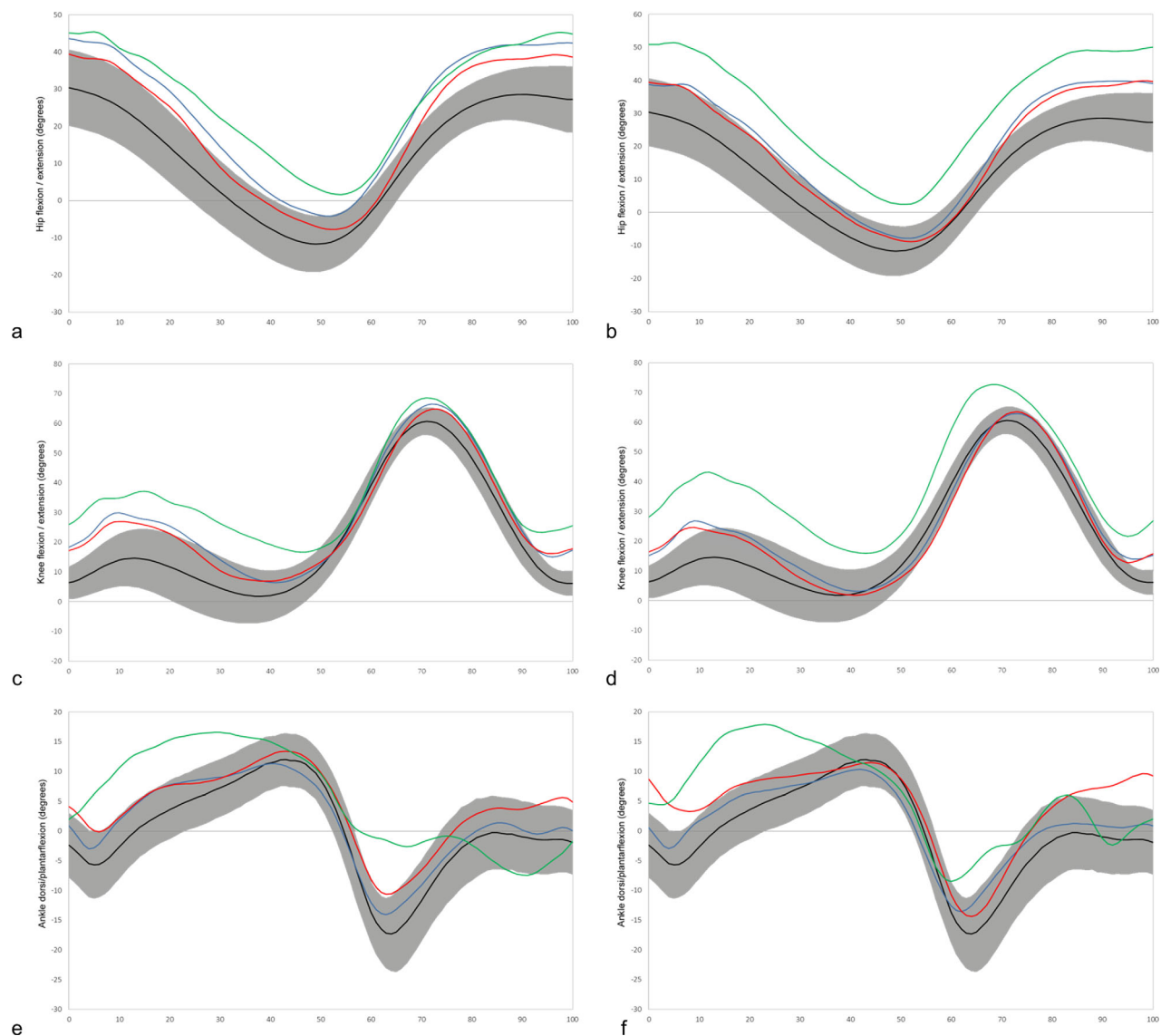


FIG. 3. Mean sagittal kinematic curves of hip (A and B), knee (C and D), and ankle (E and F) in patients with parkin disease, grouped by dystonia severity according to FMDRS score (blue, FMDRS 0; red, FMDRS 1; green, FMDRS 2). Left column OFF condition, right column ON condition. Comparison of FMDRS scores in OFF and ON showed no statistical difference (Supporting Table 1). [Color figure can be viewed at wileyonlinelibrary.com.]

scale for lower limb and gait dystonia¹⁸; we used the FMDRS that was originally designed for generalized isolated dystonia. The development of new rating scales specific for dystonia in PD and other disorders is a still unmet need. Notwithstanding, we were able to show that dopaminergic replacement therapy did not improve spatiotemporal parameters in parkin patients; it rather increased dystonia, particularly at hip and pelvis. This observation is in keeping with a recent report of L-dopa-resistant gait abnormalities in classical PD patients, particularly those with postural instability.¹⁹

Some peculiar abnormalities of gait parameters observed in parkin disease patients, particularly increased ankle plantar flexion and excessive knee flexion, may thus be the instrumented expression of the prominent dystonic features observed in these

patients that are specifically activated by gait. This is reflected by the observation of an abnormal morphology of kinematic curves at hip, knee, and, particularly, ankle (see Fig. 3). An increased jerk index, indicating a reduced movement smoothness at a given joint, may also be considered a possible instrumented index of dystonia. This index may possibly be more sensitive than the FMDRS. Patients scoring 2 at FMDRS had more evident kinematic abnormalities at all joints compared to patients who scored 1 or 0. Those who scored 0, however, did not have normal kinematic curves: They all displayed, in at least one joint, the abnormal jerkiness observed in patients who had overt dystonia (Supporting Figs. 1, 2, and 3, where data for individual patients are reported). The present observation therefore suggests that kinematic analysis may detect some subtle abnormalities not appreciated by

clinical scores. A formula incorporating different kinematic variables, rather than any individual parameter, will probably be needed to build an instrumented quantitative measure of dystonia.

Regrettably, no kinematic data are available for isolated dystonia syndromes, such as DYT1. There are two case reports on combined dystonia syndromes. In one study, postural and kinetic gait parameters were assessed before and after DBS in a patient with DYT3 dystonia.⁹ In this study, no kinematic parameters of lower limbs are reported; dystonia prevailed in the trunk and lower limbs; but, because there are no data on lower limb joints, direct comparisons with our results cannot be sketched. In another study, the spatial-temporal and kinematic gait parameters were analyzed in *OFF* and *ON* in a patient with DYT5 dystonia. The effect of L-dopa was dramatic, as expected, in this dopa-responsive condition.

Further evaluations are therefore needed to describe the kinematic and kinetic features of patients with isolated or combined dystonia syndromes. Inherited dystonias provide a natural test field for instrumented movement analysis, notwithstanding some inevitable limitations. The relatively small sample size is characteristic of rare conditions, such as parkin disease. Furthermore, although homogeneity of data is provided by a common genetic diagnosis (all patients in this study had bi-allelic mutations in the PARK2 gene), it may be argued that different mutations may underpin a degree of genetic heterogeneity.

The study of quantitative movement analysis in dystonia is at its dawn. Parkin disease provides an interesting model for performing clinical-instrumented correlations aimed at detecting the motor components involved in the phenomenology of gait. We suggest here that, in this model, lower limb dystonia influences more kinematic than kinetic parameters of gait and that the clinical severity of dystonia does not correlate with any individual variable. Dystonia affecting the upper body is also worth being studied with instrumented analysis. Standardized automatic and voluntary motor tasks may be assessed in upper body regions. Kinematic parameters and specific indexes of movement jerkiness computed on different body regions will allow to identify features for the instrumented detection and assessment of dystonia.

Legend to the Video

Video: Video clips show the variable phenomenology of dystonia. Patient 10: Moderate parkinsonian gait is observed in *OFF*; in the *ON* condition, parkinsonian features disappear; grade 1 dystonia is observed in either condition. This patient had a prominent improvement of the UPDRS motor score from *OFF* to *ON* (Supporting Table 1). Patient 1: In the right foot

and hip, a grade 1 dystonia is observed in *OFF*; grade 1 dystonia is also observed in *ON*, at mildly increased velocity. Patient 14: In the right foot and hip, a grade 1 dystonia, associated with an increased pelvis rotation, is observed in *OFF*; grade 1 dystonia in the lower limb is also observed in *ON*. Patient 9: Mild parkinsonian features and grade 1 dystonia of the left foot with increased ankle plantarflexion in stance are observed in *OFF*; grade 2 dystonia is observed in *ON* with increased left ankle dorsiflexion in swing. Patient 6: In the right lower limb, a grade 2 dystonia, more evident at hip and knee joints, is observed in *OFF*; grade 3 dystonia is observed in *ON*, prominent at hip, knee, and also ankle joint. ■

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Supporting Data

Additional Supporting Information may be found in the online version of this article at the publisher's web-site.

Quantitative gait analysis in parkin disease: possible role of dystonia

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Supplementary online material

This supplement provides individual data to complement the main text. Supplementary table 1 reports individual demographic and clinical data of patients and controls. Supplementary figures 1, 2 and 3 describe the individual variability of sagittal kinematic curves in patients.

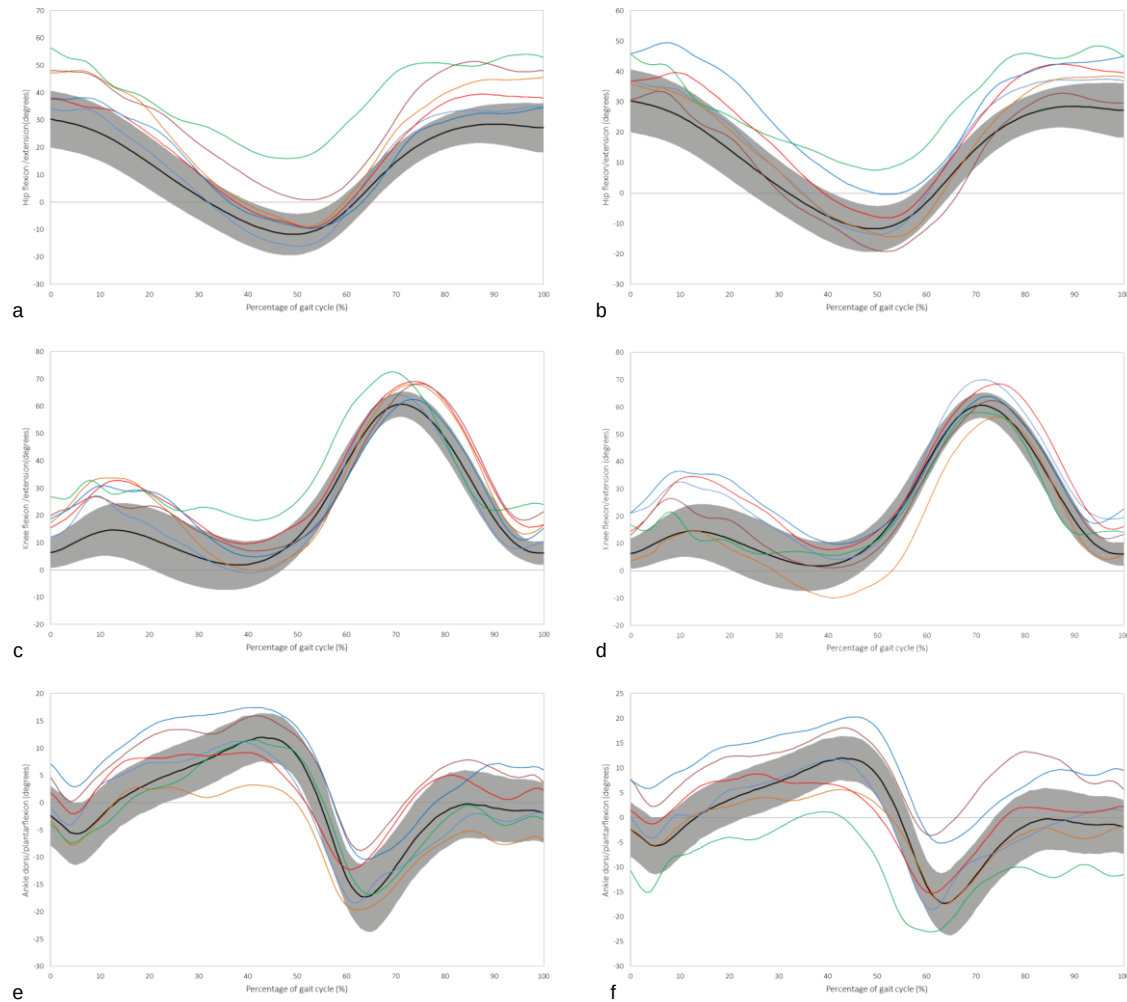
Supplementary Table 1. Demographic and clinical features of individual patients in this series. Mean values $\pm$ SD are reported in the bottom line.

Patient /gender	Age at on- set	Disease duration	Age	Lower limb dystonia FMDRS score		UPDRS motor score		LEDD (mg)	Parkin gene mutations
				OFF	ON	OFF	ON		
1/M	34	9	43	1	1	33	10	400	deletion exons 4, 5 homozygous
2/M	35	18	53	0	0	16	10	125	p.T903C and duplication exon 3
3/M	33	14	47	1	1	27	11	650	ivs11+1homozygous
4/F	34	18	52	1	2	26	13	650	deletion exon 2 and deletion exon 3
5/F	20	24	44	0	0	27	12	80	p.R275W and deletion of exon 3
6/M	44	16	60	2	3	15	11	100	p.R275W and deletion exons 3, 4
7/M	20	22	42	0	1	12	6	290	p.G1459A and deletion exon 2
8/F	65	8	73	0	1	30	11	400	p.R275W and deletion of exon 1
9/M	35	15	50	1	2	22	9	400	p.L211N and p.P437L
10/F	33	10	43	1	1	43	27	440	deletion exon 3 homozygous
11/M	21	31	52	1	1	59	48	515	deletion exon 6 homozygous
12/F	49	7	56	0	0	35	21	100	p.R275W and deletion of exon 5
13/F	11	11	22	0	0	11	7	300	p.R275W and deletion of exons 6, 7
14/F	38	12	50	1	1	28	13	133	p.AT34T and deletion exon 3
15/F	30	5	35	1	1	32	19	170	deletion exon 3 homozygous
<i>All pa- tients</i>	<i>33.5 $\pm$13.1</i>	<i>14.7 $\pm$7.1</i>	<i>48.1 $\pm$11.5</i>	<i>0.7$\pm$0.7</i>	<i>1.1$\pm$0.9</i>	<i>27.7* $\pm$12.5</i>	<i>15.2* $\pm$10.6</i>	<i>316.9 $\pm$196.5</i>	

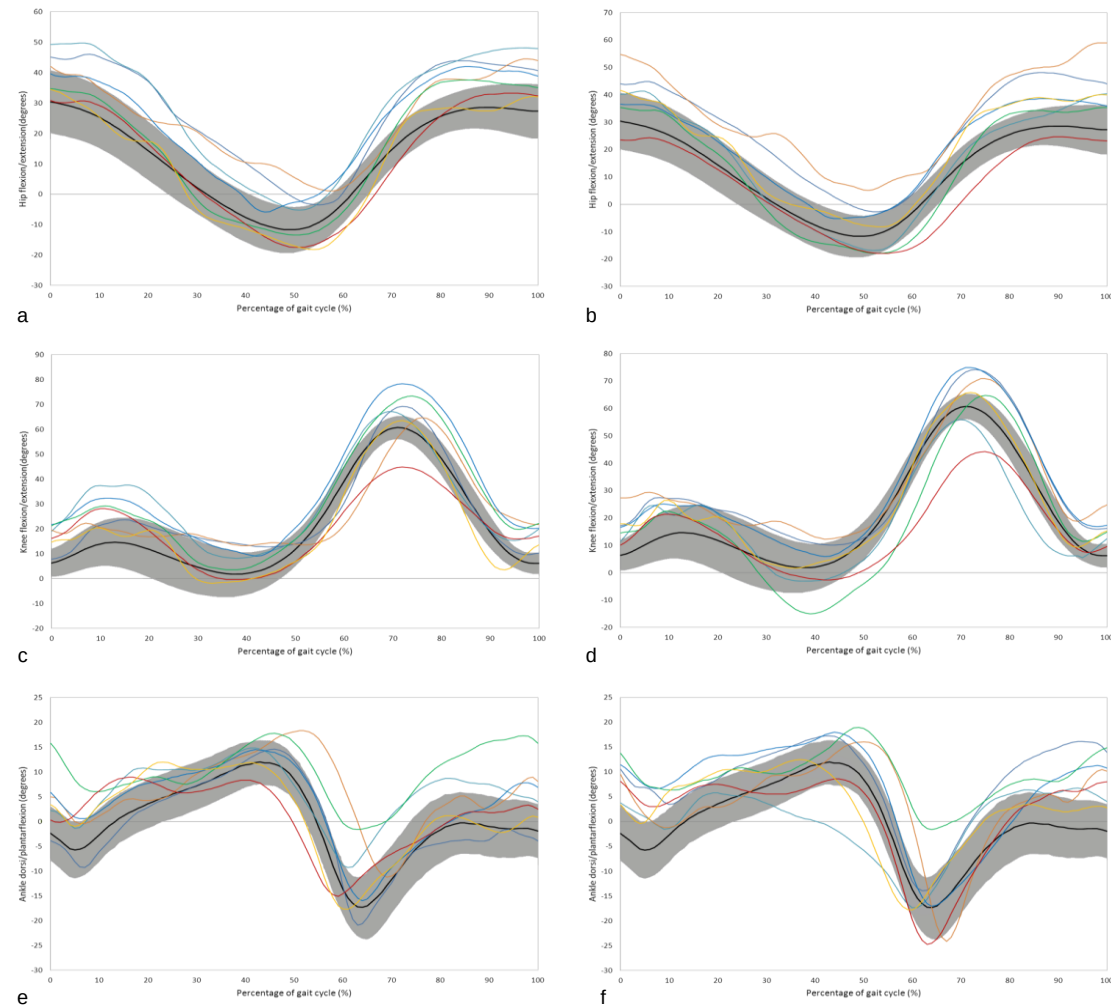
Abbreviations: FMDRS, Fahn-Marsden dystonia rating scale; LEDD, levodopa-equivalent daily dose; UPDRS, Unified Parkinson disease rating scale.

FMDRS dystonia severity subscores: 0, No dystonia present; 1, Slight dystonia, but not causing impairment, clinically insignificant; 2, Mild dystonia, walks briskly and unaided; 3, Moderate dystonia, severely impairs walking or requires assistance; 4, Severe. Unable to stand or walk on involved leg. An asterisk * means statistically significant difference between *OFF* and *ON* conditions ($P < 0.05$).

Supplementary Figure 1. Individual variability of sagittal kinematic curves in patients with parkin disease scoring 0 at FMDRS at hip (a, b), knee (c, d) and ankle (e, f), Left column represents the *OFF* condition, right column is the *ON* condition. Abnormal curve morphology is more marked in *ON* than in *OFF*. Differences are particularly evident in the ankle (f).



Supplementary Figure 2. Individual variability of sagittal kinematic curves in patients with parkin disease scoring 1 at FMDRS at hip (a, b), knee (c, d) and ankle (e, f), Left column represents the *OFF* condition, right column is the *ON* condition.



Supplementary Figure 3. Individual variability of sagittal kinematic curves in patients with parkin disease scoring 2 at FMDRS at hip (a, b), knee (c, d) and ankle (e, f), Left column represents the *OFF* condition, right column is the *ON* condition.

