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Application of continuous relative phase analysis for differentiation of gait in neurodegenerative disease

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ABSTRACT

Continuous relative phase (CRP) is a measure of coordination between two joints, and CRP based analysis is being used to characterise joint or segmental coordination during gait. Postural instability or balancing issue is one of the major motor symptoms of Parkinson's Disease (PD). This study aimed to use CRP variables to distinguish between PD, healthy control (CO) groups, and PD groups divided according to clinical evaluations. The subjects were separated into two groups: healthy controls and Parkinson's disease subjects. Additionally, the PD group was subdivided according to the unified Parkinson disease rating scale (UPDRS) scores: UPDRS 0 and UPDRS 1. Each subject performed the designated walking motor task three times. Four inertial measurement units (IMU) were used to measure movement of the lower limbs. Statistically significant differences in CRP mean, deviation phase (DP), and root mean square CRP (CRP_{RMS}) were found for PD vs CO (right stance, right swing, right mid-stance) and UPDRS 0 vs UPDRS 1 (right stride, left stride, right swing). CRP can be used to separate PD and CO groups, and groups subdivided based on UPDRS score.

1. Introduction

Neurodegenerative disease impairs basic human motor function, such as walking, eating, dressing, or an action as simple as getting up from a chair or bed. Diseases, such as Parkinson's disease (PD), essential tremor, Alzheimer's disease, and Huntington's disease, are neurodegenerative disorders. All these diseases are difficult to treat, and medications can reduce the impact of motor disorders on quality of life.

PD is a neurodegenerative disease from the early-stage and advanced-stage disease with large consequences in quality of life [1]. PD has four cardinal features: rigidity, tremor at rest, postural instability, and akinesia (or bradykinesia) [2].

Bradykinesia of movement is one of the early signs of PD. Rigidity and postural instability emerge in the late stages of disease [3]. PD patients show shortened stride length, stride width, increased stride variability, and reduced walking speed [4]. All motor symptoms can be assessed using the unified Parkinson's disease rating scale (UPDRS). UPDRS is used in clinical trials in patients with PD to assess disease severity. This scale helps assessing motor symptoms and other activities, such as daily life, reasoning, behavior. Assessment of motor symptoms is defined in UPDRS Part III [5], which evaluates language, facial expression, rest tremor, gait, and other motor actions. Each motor task is rated from 0 to 4 (0 – no disorders, 4 – severe disorders).

A motion capture (MOCAP) system or equipment can be used to quantify movement. One of most common MOCAP systems used to capture the human movement is optical motion capture. Optical MOCAP systems have a few limitations [6]. The inertial motion system has become more popular because of its portability. This system usually consists of accelerometers, magnetometers, and gyroscopes, and it is called the inertial measurement unit (IMU). An IMU system can capture the larger-scale motion in an outdoor or indoor environment [7].

Many researchers are concerned with quantifying how the neuromuscular system is organized in individuals who display normal and abnormal gait patterns. The purpose of traditional measures of instrumented gait analysis is to detect pathological gait patterns and help doctors plan surgeries, rehabilitation programs, or select the necessary medications [8]. Traditional gait analysis only measures spatial-temporal parameters, such as stride width, stride length, gait speed, and joint amplitudes during different gait phases.

Coordination is a behavioral aspect of any movement pattern, and an assessment of coordination depends on the quantification of the relative position of the limb over time [9]. Many methods can be used to assess

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coordination between joints and segments: continuous relative phase (CRP) (13), vector coding [11], and discrete relative phase [12].

CRP is considered a measure of coordination between two segments. CRP shows the phase relation between two joints during the cycle of movement [13]. CRP and its variability can be used to separate healthy runners from injured runners [14], patterns of coordination in running and walking [15], and gait analysis [16]. CRP can be used to estimate coordination during different modalities of human locomotion [10,18] in individuals with different movement disorders [19,20].

CRP integrates continuous spatial-temporal data of the segmental movements and estimates the relative phase-relationship level between two joints [10].

Clinically, the CRP method has been used to distinguish coordination differences between pathological and healthy movements as well as the rehabilitation training effects, such as stroke, sports injuries, and knee osteoarthritis [16,19,20]. The variability of joint coordination can be estimated using the deviation phase (DP). A high DP indicates more variable coordination between two joints [21]. CRP is commonly used to study the more affected side of the body (either left or right), but there are no studies that examine both sides and use of CRP variables in disease diagnosis or disease assessment-based clinical scales.

This study aimed to use CRP variables to distinguish between PD and healthy control (CO) groups and PD groups divided according to clinical evaluations (UPDRS). CRP variables are derived using IMU data that was collected from IMU sensor attached on to two body segments (thigh and shank) and both sides of the body (right and left).

2. Materials and methods

2.1. Subjects

The data for lower limb kinematics was recorded at Vilnius University Hospital' Santaros Klinikos' Centre of Neurology, under medical personnel's supervision. The research included two groups of subjects: PD subjects and healthy control (CO) subjects. The PD group was additionally subdivided in two according to UPDRS scores: UPDRS 0 and UPDRS 1. We evaluated the distribution of PD groups, according to UPDRS, to find quantitative differences in disease severity. The numbers 0 and 1 indicate the severity of the disease. Demographic data for all groups are presented in Table 1. UPDRS 0 and UPDRS 1 groups were determined after clinical examination of patients. Gait difficulty was defined as 0 (normal gait) and 1 (walks slowly, may shuffle with short steps, but no festination or propulsion), and no major difficulties were found. The purpose of this subdivision was to test the hypothesis that CRP variables can be used to differentiate between subjects according to gait severity assessment and to find a quantitative estimate within these groups.

CRP variables provide diagnostic information that will allow them to be applied in clinical practice. The subdivision of gait cycle into smaller phases (stride, swing, stance, mid-stance (MS), early stance (ES), and late stance (LS)) will help identify which phase of the gait cycle has the most impaired coordination.

The inclusion criteria for the PD group were as follows: the person must be an adult, have a disease severity according to the Hoehn and Yahr scale from 2 to 3, and walk without assisting devices. The exclusion criteria included other diseases that affect the performance of movement. The inclusion criterion for the CO group was as follows: participant did not have any injuries or illnesses that would affect movement. All procedures performed were in accordance with the local (Vilnius University Hospital' Santaros Klinikos') ethical committee and the 1964 Helsinki declaration.

Table 1
Subject demographic data.

Group	n	Age (mean ± SD)	Total UPDRS score (mean ± SD)	UPDRS III score (mean ± SD)
PD	13	61.05 ± 11.21	39.17 ± 16.43	26.45 ± 10.25
CO	12	57.83 ± 7.58	–	–
UPDRS 0	8	62.24 ± 7.45	40.25 ± 15.64	26.19 ± 9.11
UPDRS 1	5	64.33 ± 6.45	49.95 ± 12.67	34.29 ± 6.97

2.2. Equipment, motor task, and data collection

We used wireless IMU (Shimmer Research, Dublin, Ireland) to measure motor tasks. Four IMUs were attached on to the subject's limbs using mounting straps (Fig. 1).

The kinematic data of the IMU was sampled at a frequency of 51.2 Hz and stored on a laptop using Bluetooth for processing.

Motor task consisted of walking five meters in a straight line, with a marked start and end. The participants were instructed to follow a verbal command to start the walking. All participants repeated the motor task a total three times at their selected comfortable speed.

2.3. Data processing

The MATLAB software (The Mathworks Inc., Natick, MA) was used to process kinematic data. The raw angular velocity signal was filtered using a low-pass Butterworth filter with a cut-off frequency of 5 Hz. The gyroscope signal before and after filtering is shown in Fig. 2.

To calculate joint angles, we used numerical integration methods. The data was filtered with a first-order Butterworth high-pass filter with a cut-off frequency of 0.5 Hz to reduce the integration drift.

The characteristic point of the shank angular velocity related to the heel-strike during gait was determined using built-in MATLAB functions and a customised algorithm for gait events detection. Stride was characterised as a gait cycle between two characteristic points. One stride was normalised to 100 % of the gait cycle using spline.

Phase plane of the two joints for CRP calculation was constructed from the normalised angular velocity versus angle [22]. Angular data were normalised between −1 and 1 for each gait cycle [17]:

$$\theta_i^{'} = \frac{2 \cdot [\theta_i - min(\theta_i)]}{max(\theta_i) - min(\theta_i)} - 1 \tag{1}$$

where $\theta^{'}$ is the normalised angle, θ is the original angle, and i is a data point in the gait cycle.

A similar technique was used for angular velocity normalisation, but keeping zero velocity at the origin of the phase plane [17]:

$$\omega_i^{'} = \frac{\omega_i}{max[max(\omega_i), max(-\omega_i)]} \tag{2}$$

where $\omega^{'}$ is the normalised angular velocity, ω is the angular velocity, and i is a data point in the gait cycle.

Phase plane plots are shown in Fig. 3. The next step in phase angle calculation is as follows:

$$\phi(i) = tan^{-1}\left(\frac{\omega^{'}(i)}{\theta^{'}(i)}\right) \tag{3}$$

where $\omega^{'}(i)$ is the normalised angular velocity and $\theta^{'}(i)$ is the normalised angle.

Phase angles were calculated from flexion and extension movements from the knee and thigh segments.

The CRP curve in Fig. 4 was derived for the left and right hip-knee combination from the absolute value of the difference between the phase angles of the right and left hip and knee at every point during the gait cycle:

$$\mathrm{CRP}(i) = \Phi_{hip}(i) - \Phi_{knee}(i) \tag{4}$$

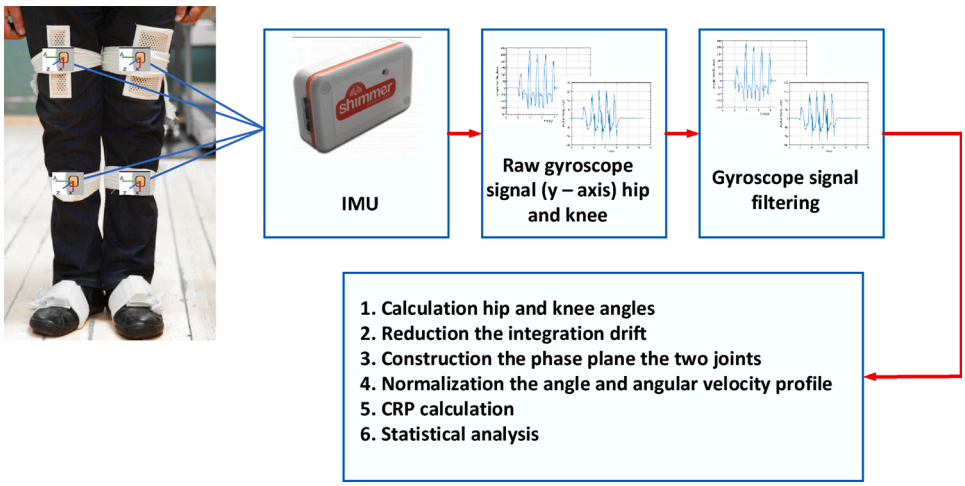

Fig. 1. Placement of IMU sensors on the extremity and data processing algorithm.

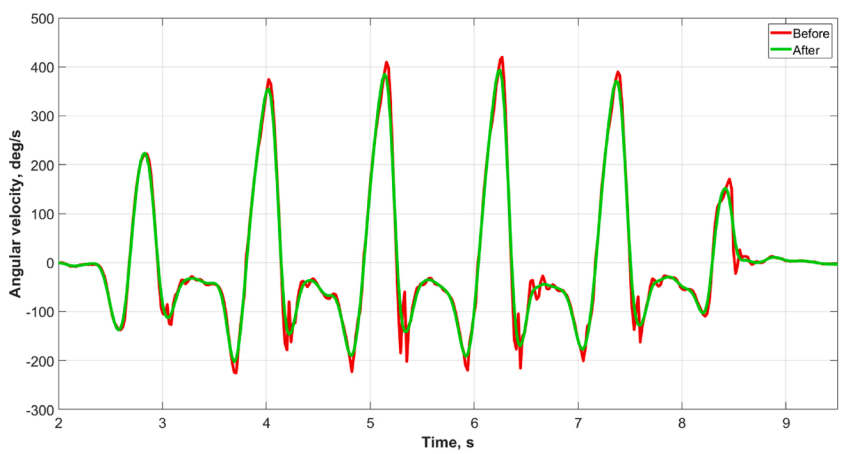

Fig. 2. Angular velocity of shank before and after low-pass filtering.

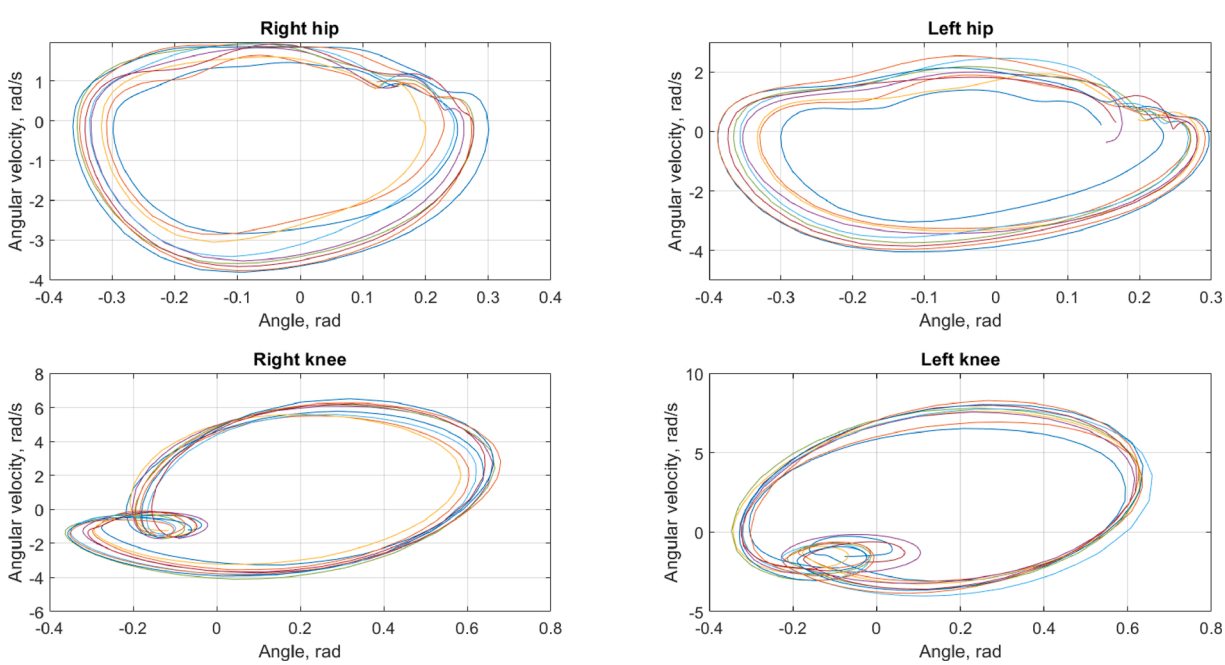

Fig. 3. Hip and knee joint phase plane plots for the control group.

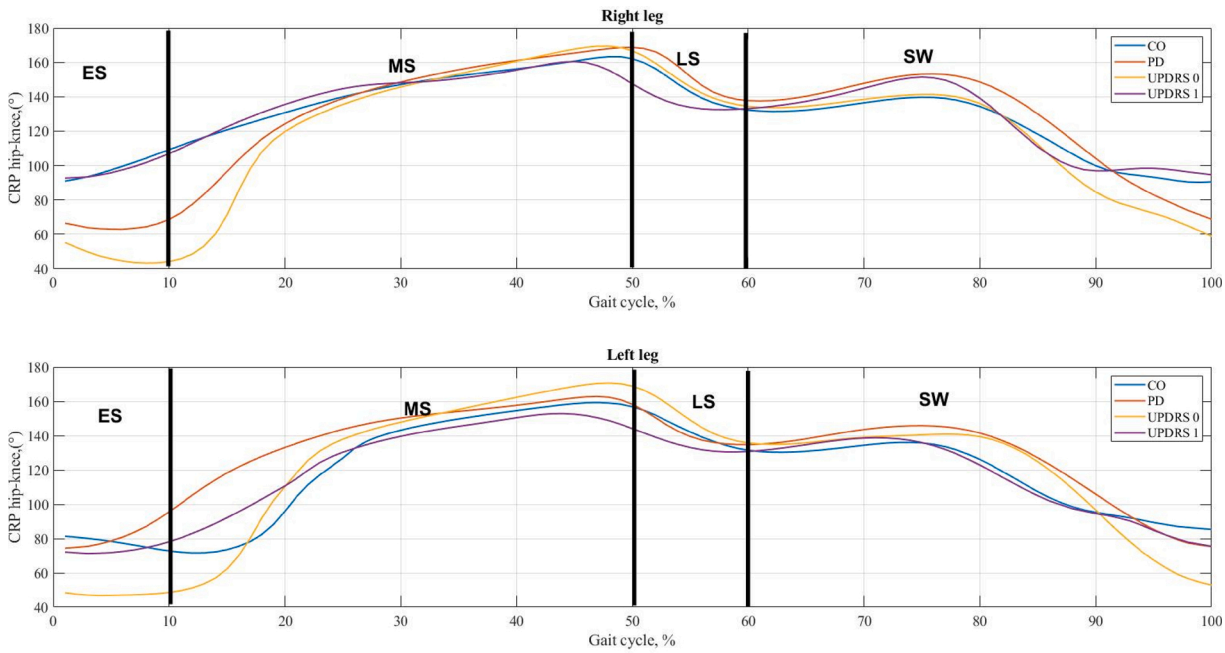

Fig. 4. CRP hip-knee throughout the gait cycle: ES–early stance; MS–mid-stance; LS–late stance; SW–swing phase.

where $\Phi_{hip}(i)$ is the phase angle of the hip, and $\Phi_{knee}(i)$ is the phase angle of the knee at data point i in the gait cycle.

Dependent variables were the angle of the right and left knee and hip joints in these gait stages: stride, swing, stance, early stance (ES) (0–10 %), mid-stance (MS) (10–50 %), and late stance (LS) (50–60 %). CRP patterns were analysed using the root mean square (CRP_{RMS}), mean value of the CRP (CRP_{mean}), and deviation phase (DP). DP is the average standard deviation, calculated from the CRP curve over the right and left stride, swing, stance, ES, MS, and LS during the gait cycles (Fig. 4).

Large DP values indicate high coordination variability between two joints [17]. The mean values of the CRP during each phase (right and left stride, swing, stance, ES, MS, LS) were calculated to investigate the coordination pattern in a specific gait phase. The root mean square was calculated to investigate CRP variability.

CRP variability was used as a metric to separate two groups of subjects and assess PD severity according to UPDRS clinical assessment (UPDRS III motor task 29). This motor task 29 is gait and is evaluated from 0 to 4 (0: normal gait; 1: walks slowly; 2: walks with difficulty; 3: severe disturbance of gait; 4: cannot walk at all) [23]. Each subject was classified according to the following clinical assessment: UPDRS 0 and UPDRS 1.

2.4. Statistical analysis

A Shapiro–Wilk's test was used to test data distributions. Normally distributed data were compared with a one-way ANOVA (post-hoc test Bonferroni). Statistical analyses were performed using SPSS (Version 22.00 IBM Corp., USA).

3. Results

The statistically significant differences ($p < 0.05$) between the CO and PD groups and groups determined according to the UPDRS score are presented in Tables 2 and 3.

CRP and CRP variability can be used to separate two groups, namely PD from CO. However, in this study, only a few parameters were found to be sensitive enough to separate these groups: right mid-stance CRP mean ($p = 0.030$), right mid-stance CRP_{RMS} ($p = 0.022$), right swing DP ($p = 0.038$), and right stance CRP mean ($p = 0.045$).

In groups determined according to UPDRS (UPDRS 0 vs UPDRS 1), we found more statistically significant differences: right swing CRP mean ($p = 0.045$), right swing CRP_{RMS} ($p = 0.048$), right stride CRP mean ($p = 0.033$), right stride CRP_{RMS} ($p = 0.049$), left stride DP ($p = 1.2 \times 10^{-5}$), and left stride CRP_{RMS} ($p = 0.017$).

4. Discussion

This study aimed to compare coordination during different gait phases in PD patients with healthy controls (CO) and determine CRP-based metrics for differentiation between CO and PD groups.

Comparison of CO and PD groups revealed higher values of CRP_{mean} and CRP_{RMS} in CO groups, which shows that both joints (hip and knee)

Table 2
Mean, deviation phase, and root mean square of CRP variability in PD and CO groups.

Parameter	Group	Mean	SD	95 % Confidence Interval for the Mean		Minimum	Maximum	F	*p* values
				Lower Bound	Upper Bound				
Right mid stance CRP mean (°)	CO	143.61	5.08	123.25	155.58	133.67	168.39	5.321	0.030
	PD	138.32	8.20	128.24	149.63	136.77	153.38		
Right mid stance CRP_{RMS} (°)	CO	145.59	4.33	126.48	150.45	157.69	153.34	6.049	0.022
	PD	141.13	6.39	136.32	148.33	129.69	150.28		
Right swing DP (°)	CO	23.13	2.38	19.25	25.13	18.73	33.81	5.807	0.038
	PD	25.79	4.42	22.15	28.79	22.80	30.17		
Right stance CRP mean (°)	CO	131.64	3.90	126.69	135.58	122.17	140.54	4.236	0.045
	PD	126.43	9.28	123.23	129.46	121.31	136.73		

Table 3
Mean, deviation phase, and root mean square of CRP variability in UPDRS groups.

Parameter	Group	Mean	SD	95 % Confidence Interval for the Mean		Minimum	Maximum	F	*p* values
				Lower Bound	Upper Bound				
Right swing CRP mean (°)	UPDRS 0	133.24	11.95	123.62	135.52	119.01	138.46	4.65	0.045
	UPDRS 1	122.54	6.25	119.45	128.48	115.31	130.92		
Right swing CRP_{RMS} (°)	UPDRS 0	135.53	12.85	125.45	139.58	123.55	140.25	4.68	0.048
	UPDRS 1	125.41	6.07	118.25	131.25	119.44	135.55		
Right stride CRP mean (°)	UPDRS 0	131.81	4.28	124.69	134.15	125.18	141.02	5.91	0.033
	UPDRS 1	123.08	7.21	118.65	128.08	115.64	133.04		
Right stride CRP_{RMS} (°)	UPDRS 0	134.97	5.69	124.48	137.13	125.98	144.79	4.85	0.049
	UPDRS 1	127.31	6.32	119.13	131.94	120.31	134.46		
Left stride DP (°)	UPDRS 0	4.23	0.93	2.19	6.58	2.24	6.24	5.64	0.000012
	UPDRS 1	6.95	2.71	3.25	7.28	3.06	10.15		

are moving in phase. Lower CRP_{mean} and CRP_{RMS} we found in PD groups. Lower CRP_{RMS} values was founded in [24]. Lower CRP_{RMS} values in the middle swing phase indicates that subjects in the PD group have impaired control of hip and knee joints in this gait phase.

During different gait phases in CO groups, lower DP values indicated less coordination impairment than in PD groups during the right swing phases, which suggests that coordination in this gait phase is more affected. Higher DP values indicate the coordination variability is higher between the hip and knee joints. The values obtained correspond to those given in the literature [17].

While analysing PD groups divided according to UPDRS, we found higher values of CRP_{mean} and CRP_{RMS} for UPDRS 0 and lower values for UPDRS 1, which indicates that as the severity of the disease increases, CRP values decrease, and this implies that the two joints will move differently during different gait phases.

The analysis showed that CRP variables are more suitable for assessing the severity of disease than distinguishing between PD and CO groups. Therefore, CRP is more appropriate for assessing disease severity. The values of CRP variables obtained allowed distinction between UPDRS 0 and UPDRS 1 groups.

Therefore, we conclude that IMU can be used in clinical studies and to evaluate movement coordination using the CRP metric. The CRP metric can be used to differentiate between different study groups and groups determined according to UPDRS. CRP parameters will be used in the diagnostic system being developed.

Declaration of Competing Interest

The authors report no declarations of interest.

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