Biomechanical Analysis of Gait Adaptability in Parkinson's Disease

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Abstract: Parkinson's Disease (PD) subjects are less able to adapt gait to fluctuating motor demands in daily life situations than the healthy elderly, e.g. in crowded places, crossing the road, and starting or stopping at traffic lights. Several studies proved gait abnormalities in PD. However, to our knowledge there is currently no biomechanical test that deals with the ability in gait adaptation. The aim of this study was to develop and evaluate a new biomechanical test which proves the adaptability of gait to fluctuating external conditions.

In order to have a reproducible, quantitative gait-test, a treadmill was used, accessed by a special software. The so called adaptability-of-gait test (AOG) changed the treadmill's velocity ballistically and unpredictably for the test subjects. 49 PD-subjects and 10 age-matched controls (HC) participated in the study. In order to subdivide PD subjects in homogeneous groups, we used a cluster analysis. In a first-step of evaluation we focused on differences between PD with moderate (PDM) and severe disease stages (PDS) and HC and examined correlations according to existing, valid tests, e.g. Unified Parkinson Disease Rating Scale (UPDRS) subscales, clinical and biomechanical gait-assessments.

Results showed significant differences in gait-adaptation between the groups. Severe PD had a worse gait adaptation compared to PD moderate and HC. Correlation analysis of the PD sample showed significance differences between the AOG-test and bradykinesia and facial expression, but no significances differences according to conventional clinical gait assessments, e.g. Webster gait-test. We conclude that the AOG-test has potentials to identify a new gait performance: the adaptation of gait.

1. INTRODUCTION

Effective and efficient rehabilitation is based on reliable and valid knowledge of the system parameters (pathology and treatment) that influence motor disturbances. Since gait disturbances in Parkinson's disease (PD) are evident and have a strong impact on quality of life, it is of crucial importance to understand motor control of gait. PD - as one of the most common neurodegenerative diseases [1] - is clinically characterized by the onset of unilateral symptoms with ongoing progression. The cardinal symptoms are resting tremor, muscular rigidity, bradykinesia and postural impairments [2]. Many studies analyzed the gait pattern in PD subjects compared to healthy controls in detail [3]. PD gait is - compared to healthy age-matched subjects - characterized as a slowed gait-speed, with shortened, shuffling, wide based steps, a stooped posture, and a reduced arm swing [4, 5]. Spatiotemporal analysis showed a protracted bipedal phase, a higher cadence and exceeded gait variability as additional pathological signs according to the gait-cycle [3, 6-11].

To quantify kinetic and kinematic gait parameters, different biomechanical methods were used, e.g. a thread-

pulley system, at which threads are attached by Velcro straps to each foot of a subject [6, 12, 13]; force plates embedded in walkways [14] or in a treadmill [15, 16]; 3-D motion analyzing systems [14]; a clinical stride analyzer [7, 14, 17, 18]; force-sensitive shoe-soles [10, 19]; and pressure-sensitive insoles [9, 20, 21].

These methods are also used to get insights into PD pathology. Since the beginning of the systematic gait-analyses in PD, it has been well known that most locomotor parameters are related to the Hoehn and Yahr (H&Y) stages described in the clinical classification [4, 5]. In the early stages of PD, patients' gait already shows a tendency of a reduced cadence and walking speed, which is associated with the cardinal symptom bradykinesia [3]. Coevally gait impairments occur obviously in transitional conditions, e.g. turning during gait [22]. Winogrodzka *et al.* showed that rigidity and bradykinesia limited gait-parameters significantly [23]. Several studies reported that PD subjects compensate their impaired stride length with a higher step frequency, a parameter that is not impaired in PD-gait [6, 9, 17, 24]. All or some of these biomechanical gait parameters may influence the performance in gait-adaptation.

Even if there are several focuses in PD gait studies and the existing methods are proved well, they still cover only a small range of situations and motor demands [3, 14, 25]. In most biomechanical and clinical gait analyses, PD subjects choose their gait parameters themselves (e.g. velocity, step-

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length) or walk with external triggered but constant, chosen velocity. Consequently dynamic requirements, e.g. gait adaptability are low in these test procedures. Various gait studies on the walkway confirmed independently that PD-patients preferred walking speeds between 3.0 and 3.5 km/h [3, 26, 27]. However, several gait-demands take place at slower walking speeds. For example, falls often occur at home and are caused by sudden changes in posture, turning movements of the trunk or by dual tasks [28]. These home activities are accomplished at slower walking speeds [29]. Moreover, gait has to be adapted to urban environmental conditions e.g. pedestrian zones, traffic lights etc. and requires different velocity-ranges. These everyday situations have to be adapted according to external conditions and are characterised by gait parameters that are not chosen freely. Thus, the gait parameters like gait velocity, step frequency or stride length are not constant. They underlie a dynamic process with sudden and unpredictable velocity changes like acceleration, deceleration, stopping and initiating gait. Regarding gait analysis, the diversification of existing clinical and biomechanical methods is required [3]. Even if it is well known that PD subjects have serious exertions with gait adaptability, to our knowledge valid tests are missing to date.

Therefore, the aim of this study was to develop and evaluate a method of biomechanical gait analysis, which analyses the adaptability in gait to fluctuating external conditions. Therefore we developed the AOG-test (AOG stands for adaptability of gait).

The test procedure was based on the following preconditions: 1) test-reliability, -objectivity and -accuracy; 2) the test results have to be accessible immediately; 3) the testing procedure should ensure a high patient safety; 4) the test procedure should be usable in clinical infrastructures with limited space and human resources. In order to realise the above mentioned, we decided to use a treadmill for the AOG-test, keeping in mind that the validity of the gait-pattern on the treadmill is diversely discussed [30, 31]. Several significant differences are reported between overground- and treadmill walking [30], e.g. EMG profiles [32-34], ground reaction forces [35, 36] or inter limb synchronicity [30]. Carpinella *et al.* observed that treadmill walking might be regulated through a different 'motor set' [30]. In addition, treadmill walking might require greater attentional demands and a more constant supraspinal control [37]. Other authors argue that the kinematic patterns [32, 34, 38] and gait biomechanics [36] are highly similar between both walking conditions and therefore treadmill walking can be transferred to overground walking.

To evaluate the AOG-test, we focused on gait differences between PD and healthy controls (HC). Additionally, we analyzed connections between the new AOG-parameters with established biomechanical and clinical gait parameters and the cardinal symptoms.

2. METHODS

2.1. Subjects

We recruited subjects from the Parkinson Clinic Bad Nauheim (Germany) and several PD support groups. The ethic committee of the Justus Liebig University of Giessen (Germany) granted ethical approval of the study. All included subjects had a diagnosis of idiopathic PD, disease severity of Hoehn and Yahr stage I-III (H&Y) and were able to walk on a treadmill. We performed all evaluations while the subjects were pharmaceutically "on". Volunteers were screened in a personal interview and a neurological examination. Age-matched control subjects were recruited from the community. PD subjects' marriage partners were also required.

Descriptive information was examined for subjects' characteristics (age and sex) and disease severity. With respect to the heterogeneous structure of PD, we used cluster analysis (see statistical analysis) in order to subdivide groups. We compared the performance in adaptation of gait between these groups, conctrely named PD moderate (PDM) and PD severe (PDS) *(Tab. 1)*. In correlation analysis we focused on the pathological differences of gait in PD, assuming, that HC results would have ceiling effects in the tests e.g. Webster-test, biomechanical gait analysis.

2.2. Clinical Assessments

2.2.1. UPDRS Scales

The Unified Parkinson's Disease Rating Scale (UPDRS) is the standard and the most commonly used clinical assessment in PD [39]. The four subscales focus on I mentation, behaviour and mood; II activities of daily life (ADL); III: clinical assessed motor score and IV: H & Y stadium and assessment of other complications according to advanced disease.

Subscore indices of motor function were determined from the UPDRS motor score (III) [39], to compare standardised clinical assessments with the AOG-test results.

- *Subscore cranial* includes the items 'speech' and 'facial expression',

- *subscore tremor* includes the items 'tremor at rest' and 'action or postural tremor of hands',

- *subscore rigidity* includes the items 'rigidity' and 'finger taps',

- *subscore bradykinesia* includes the items 'hand movements', 'rapid alternating movements of hands', 'leg agility' and 'body bradykinesia' and 'hypokinesia',

- *subscore gait and posture* include the items 'arising from chair', 'posture', 'gait' and 'postural stability'.

2.2.2. Webster Gait-Test

Patients were asked to walk a distance of 12m in their common walking velocity, and a distance of 24m with a turn after 12m. The time was taken for the 12m distance and the 24m distance [40].

2.3. Biomechanical Gait Assessment

2.3.1. Spatiotemporal Gait Assessment

To get spatiotemporal gait-parameters in constant gait velocities, a treadmill with two independently functioning force platforms was used. The treadmill was used for velocity-standardization and comparison to the AOG-test (*v [km/h]:* 1.5, 1.8, 2.1, 2.4, 2.7 and 3.0). Vertical ground-reaction-force (GRF) of left and right foot-contact gave

Table 1.   Subject Characteristics

	n	Age (y)	Sex (f/m)	UPDRS	UPDRS Part III	H & Y	L-Dopa (Yes/No)	LED (mg/d)	Disease Duration (m)
PDM	16	59.06 (8.02)	6/10	27.66 (5.82)	14.41 (4.34)	2.06 (.61)	10/6	251.25 (252.21)	56.1 (35.7)
PDS	20	63.1 (8.58)	13/7	42.48 (6.88)	25.78 (3.92)	2.43 (.37)	12/8	201.25 (198.1)	62.9 (59.1)
HC	8	63.88 (9.0)	4/4						

Values are means (±SD). UPDRS: Unified Parkinson Disease rating Scale; H & Y: Hoehn & Yahr; L-Dopa: Levodopa; LED: Levodopa Dose

information about parameters e.g. stride-length, stride time, double-stance time, stance- and swing time. The variables stride-length and stride time are intercorrelated, because of the constant velocity of the treadmill. Spatiotemporal gait-parameters were quantified using GRF-graphs within 10 strides of 30 seconds. Stride time and stride-length were quantified using spectral analysis (FFT, Hamming-window).

2.3.2. The AOG-Test

2.3.2.1. AOG-Test Apparatus

In order to realise the test setting, we used a slat-style treadmill with a ball bearing design (Woodway®). Compared to a conventional treadmill, this treadmill accelerates immediately and with low friction. The subjects had the task to walk in a constant position that was marked at the treadmill's handrail (Fig. **1a**). They were instructed that the treadmills velocity will change unpredictably. The feasible velocities were tested before (see 2.3.1), an incremental encoder with a cable-belt-system was used to measure the subject's position (Fig. **1b**, **c**). We used a standardised test setting with a self-programmed software in order to transmit data bit-serially to the treadmill's serial-interface. The AOG-test had a significantly good test-retest reliability between two independent gait trials in HC (r=0.747; p<0.05).
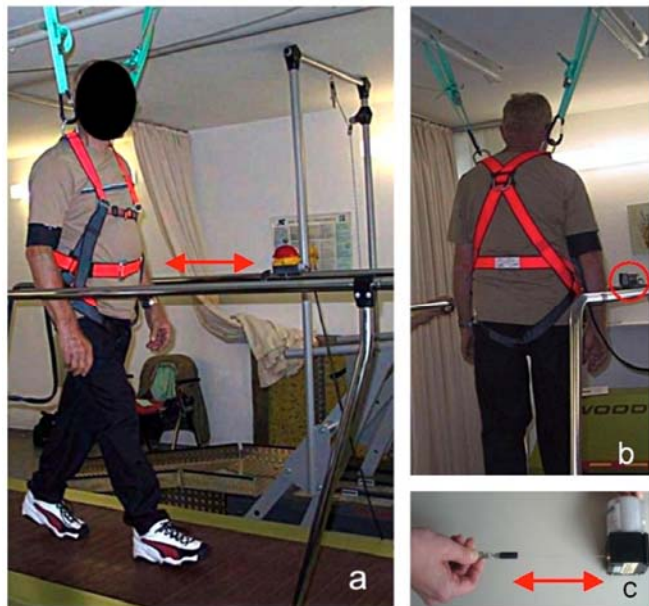

Fig. (1). (**a**, **b**, **c**) PD patient walking on the treadmill with security belt, **a**. Side view, **b**. back view, **c** Incremental encoder.

The test-velocities were set in the range between 1.2 and 3.8 km/h. We decided to change the velocity every 8-seconds according to the following assumptions: the PD subjects should be able to react adequately to new gait conditions. If velocity would change more often, the reaction pattern might be biased, since velocity-compensation strategies eg. Bradykinesia or dyskinesia could superpose each other, e.g. studies found hyperstability of walking coordination that leads to difficulties in adapting to a single velocity change during gait on a treadmill [45]. These sequential operations might be overlapping [41]. The total testing-time was set to 5.30 minutes, to avoid physical fatigue. A velocity increment >8 Seconds might have started external cueing effects [19] and the total testing time would have risen. The type of modification (acceleration or deceleration) and the different velocity changes were standardised and called AOG-test (Fig. **2a**, **b**, upper trace). These modifications could not be anticipated by the subjects.

2.3.2.2. AOG Data Analysis

To analyze the data of the AOG-test, the following presumptions were taken. In a cybernetic view the overall performance can be regarded as a linear velocity-compensation in terms of

velocity-changing ─ sensor identification ─ motor reaction ─ ready for the next perturbation.

A limitation of this view is that the AOG-performance is neither a single, nor an ad-hoc reaction. In fact, a linear analyzing-strategy would distort the presented phenomenon. Spectral analysis (FFT, Hamming window) was used, to analyze patterns in the subjects-position changes due to the fluctuating velocities. We quantified the spectral-diagram to enable insights in the different operations, e.g. overcompensatory gait conclusions, delayed compensation or long term compensation.

For quantifying the overall results (AOG-all) the whole position-over-time-graph of the subjects was taken (Fig. **2a**, **b**, lower trace) and integrated after FFT. For more detailed information about time-related performance in gait adaptability, we split the FFT-graph into four frequency bands to relate time dependent differences of gait-adaptation (AOG I-IV, Fig. **3A-C**). Therefore we divided the upper spectral graph into four sub sequences: AOG I reflects 7-18 velocity changes in the test, AOG II reflects 3-7 changes, AOG III reflects 2-3 changes and AOG IV reflects 1-2 changes. For example, a high value in AOG I represents a more frequent change in position of the subject over the whole test. A higher value in AOG IV represents changes of the subject nearly every 8-seconds. Data acquisition and evaluation, e.g. spectral analysis were conducted with DasyLab 8.0®.
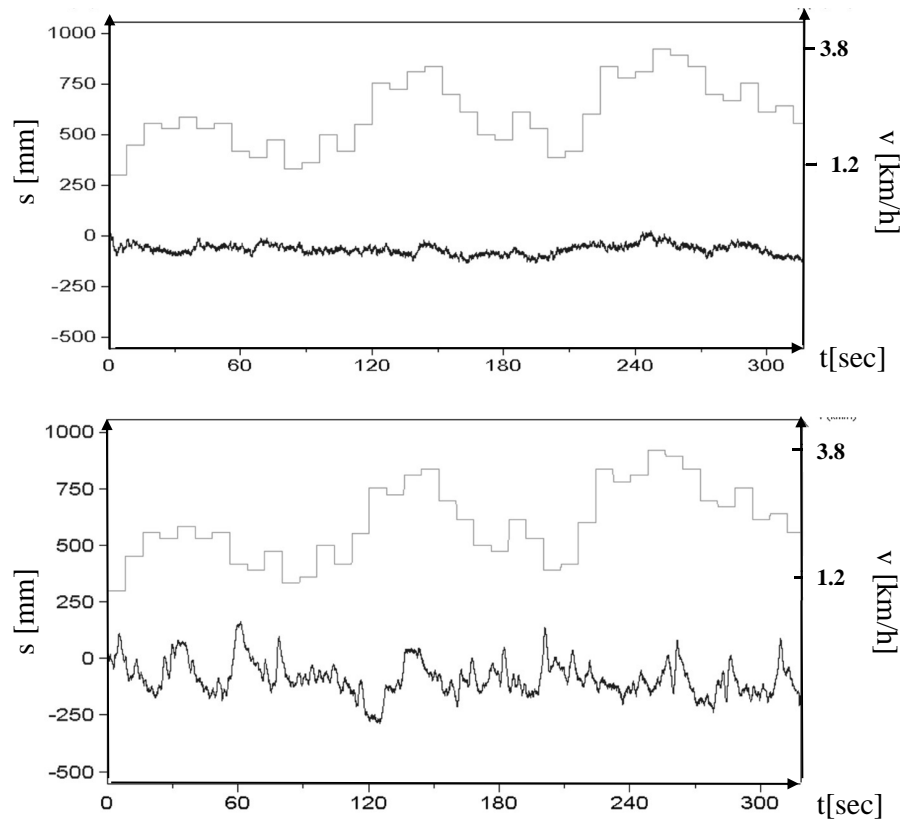
Fig. (2). (**a**, **b**) Different examples of gait adaptation at the AOG-test: Fig. (**2a**, **b**) show different gait adaptations according to the AOG test. The upper traces show the treadmill's velocity, the lower traces show the subject's position on the treadmill. The subject's position in graph a) represents a good gait-adaptability. The subject in graph b) represents a higher variance in gait-adaptability, thus the subject's position varies between plus/minus 20 cm according to the subject's starting-position.

2.4. Statistic Analysis

2.4.1. Cluster Analysis

Calculations of statistical data are based on an initial cluster analysis (squared Euclidian distance, ward method) in order to split patients into homogeneous groups. The factors for division were the 14 single variables of the UPDRS motor examination: speech, facial expression, tremor at rest, action or postural tremor of hands, rigidity, finger taps, hand movements, rapid alternating movements of hands, leg agility, body bradykinesia, hypokinesia, arising from chair, posture, gait and postural stability. The resulting groups were divided in parkinson disease moderate (PDM) and parkinson disease severe (PDS) and compared to healthy controls (HC).

2.4.2. ANOVA

Normality of the AOG-data was proven by using the non-parametric Kolmogorov-Smirnov test (K-S test). A one-way analysis of variance (ANOVA) and post-hoc analysis (LSD) were calculated to get information about group differences.

2.4.3. Correlation Analyses

A correlation analyses was done only for the PD group data.

Pearson's correlation coefficient was used to evaluate the association between dynamic gait variables and AOG frequency and non frequency-weighted parameters.

Spearman's correlation coefficient was used to evaluate the association between AOG parameters and the clinical features. A *p*-value of less than 0.05 (two-tailed) was considered statistically significant. All statistical analyses were performed using SPSS 19.0®.

3, RESULTS

All subjects performed the task without complications. Subjects were excluded from data analysis, when touching the handrail for safety reasons (4 PD), in sudden Off-state (1 PD); and because of several reasons (6 PD; 2 HC). The data of thirty-eight PD- and eight HC subjects were analyzed.

3.1. ANOVA Results

3.1.1. AOG-Overall

ANOVA detected significant group differences for AOG-all results. Post-hoc analysis showed that PDS performed significantly worse compared to PDM and HC. Between PDM and HC no statistical differences became evident (Fig. **4**).

3.1.2. AOG-Overall

Table **2** summarizes the data of the frequency-weighted performance in AOG I-IV. ANOVA showed significant differences in AOG II and a statistical trend in AOG III between the groups. Post-hoc analysis showed that PDS performed significantly worse compared to PDM in AOG II and in AOG III. PDS performed significantly worse than HC
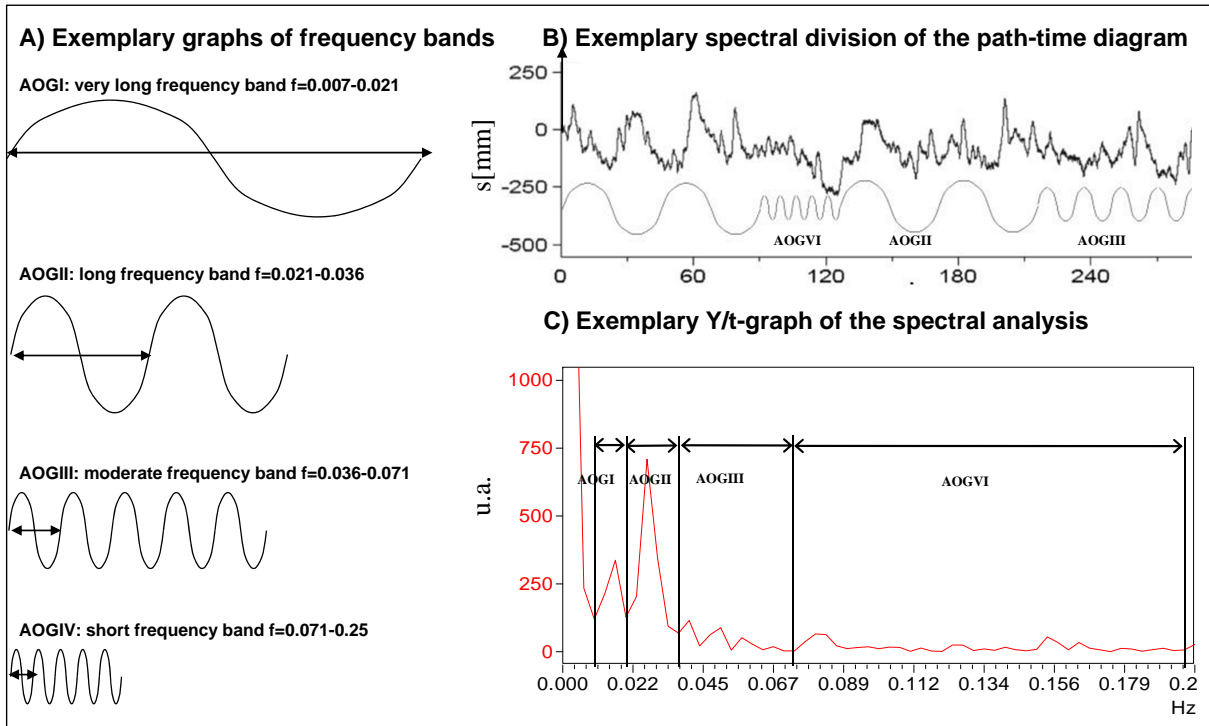
Fig. (3). A) Exemplary graphs of frequency bands AOG I: very long frequency band, AOG II: long frequency band, AOG III: moderate frequency band, AOG IV: short frequency band; **B**) Exemplary spectral division of path-time diagram; the spectral analysis divides a signal into sinus-frequency bands over the whole signal. this example shows a very simple idea, of how a complex signal can be divided into different sinus-signals. **C**) Exemplary Y/t graph of the spectral analysis We quantified the Power Spectral Density (PSD)-spectrum by integrating a) non-frequency weighted (AOG) and b) frequency-weighted after splitting the function into four frequency bands (AOG I-IV).

within AOG II. There were no significant differences for any frequency-weighted performance between the groups PDM and HC. Overall, the performance in gait adaptation in AOG II and III decreased from HC, to PDM, to PDS. AOG I and AOG IV did not differ between the groups.

3.1.3. Gait Dynamics in PD Patients

Table **3** shows the biomechanical gait parameters of all PD patients according to the spatiotemporal gait variables. These values were used for the correlation analyses.

3.2. Correlation Results

Table **4** summarizes the correlations between the parameters of the AOG-test and clinical parameters of the UPDRS test e.g. motor function, clinical gait analysis and biomechanical gait analysis.

AOG-all parameters showed correlations to UPDRS, UPDRS part III and a correlation to bradykinesia and cranial parameters. There was no correlation between AOG-all parameters and levodopa-dosage, freezing, falls, fluctuations, sensory dysfunction or dyskinesia. The webster-
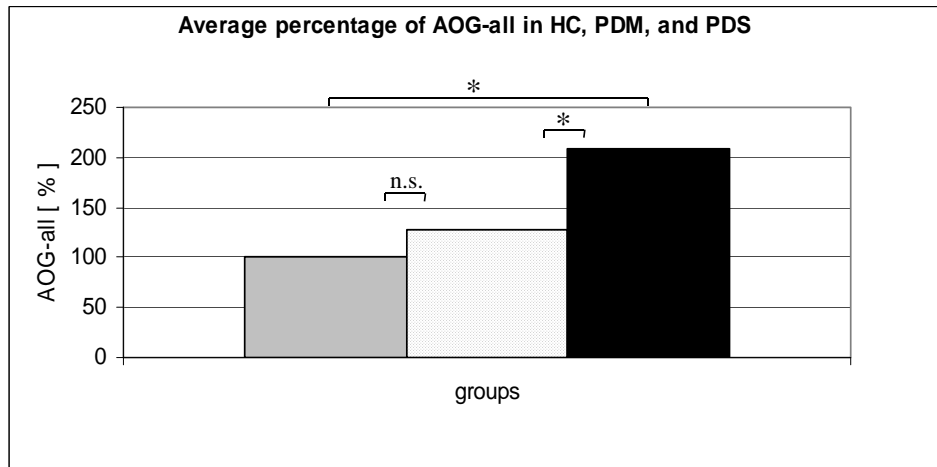

Fig. (4). Average percentage of non-frequency weighted performance in HC (grey bar), PDM (dotted bar) and PDS (black bar) (*: p<0.05; n.s: not significant).

gait test had no correlations according to any AOG-parameters. The spatiotemporal gait parameters e.g. double support time, stance phase or cycle time did not correlate with any AOG parameter.

Table 2. Outcome Measures

	Mean (SD)	ANOVA, Between Group, *p* Value	ANOVA, Post-Hoc, Pairwise Comparisons, *p* Value
AOG-all PDM PDS HC	1.73 (1.11) 2.82 (1.64) 1.35 (0.76)	0.015*	PDM *vs* PDS 0.021* PDS *vs* HC 0.012* PDM *vs* HC 0.51
AOG I (148-60sec) PDM PDS HC	0.93 (1.07) 1.36 (1.10) 0.48 (0.27)	0.104	
AOG II (60-28sec) PDM PDS HC	0.23 (0.12) 0.61 (0.42) 0.30 (0.16)	0.002**	PDM *vs* PDS 0.001** PDS *vs* HC 0.02* PDM *vs* HC 0.595
AOG III (28-14sec) PDM PDS HC	0.25 (0.13) 0.44 (0.33) 0.30 (0.23)	0.069*t*	PDM *vs* PDS 0.026* PDS *vs* HC 0.174 PDM *vs* HC 0.653
AOG IV (14-4sec) PDM PDS HC	0.33 (0.13) 0.41 (0.17) 0.27 (0.24)	0.129	

Results of ANOVA (analysis of variance) and post-hoc analysis according to AOG-all (parameter for the gait performance Adaptability-of-gait at the whole testing time) and AOGI-IV (subsequent parameters for the gait performance Adaptability-of-gait) between the groups PDM (Parkinson moderate), PDS (Parkinson severe) and HC (healthy control).
p<=0.01**
p>0.01-0.05*
0.01<p<0.05t.

More detailed information can be seen in the relations between the AOG frequency-weighted-parameters (AOG I-IV). The total UPDRS score has the strongest correlation with the AOG II-parameter (r=0.631; *p*<0.01) and significant but moderate correlations to AOG-III. Motor function correlated moderately with AOG II-IV (*r*>0.4; *p*<0.01). The subscales of motor function showed highly-significant correlations between AOG-II and rigidity, bradykinesia and cranial parameters. No correlation between gait and posture variables and AOG-frequency-weighted-parameter, as well as the tremor variable were detected. A moderate correlation was seen between H & Y-stage and AOG, AOG II-III (*r*=0.39; *p*<0.05).

The frequency-weighted AOG I correlated not at all. Stride time showed for the velocities 1.5-2.1km/h (*r*=0.44; *p*<0.01) and significant moderate correlations for the velocities 2.4 and 2.7 km/h (*r*>0.32; *p*<0.05). Between step length and AOG III-parameter was a moderate negative relationship for all velocities (from *r*=-0.35 to -0.43; *p*<0.05) was detected.

4, DISCUSSION

The aim of this study was to develop and evaluate a method of biomechanical gait analysis which investigates the adaptability in gait to fluctuating external conditions: the AOG-test. Within our novel gait-test, velocities change periodically, but the magnitude and time of acceleration are unpredictable for the subjects. The test represents spontaneous adaptations during repetitive movements and therefore the adaptation through an ongoing process (walking). The AOG-test excludes start-stop situations e.g. gait-initiation, walk-to-stand, as well as chronic adaptation-processes in the context of learning.

The main outcome is that the AOG-test identifies differences between PD-patients and HC according to the performance of gait adaptation. The results of AOG-all (performance in gait adaptation) of the group 'PD severe' (PDS) were significantly worse compared to the group 'PD moderate' (PDM) and 'healthy controls' (HC) (Table **2**). Furthermore, AOG-all of PDM was 28% worse than HC, but the results did not reach significance (Fig. **4**). These results indicate, that the performance in gait adaptation gets worse during disease progression (Table **1**). This goes in line with most locomotor parameters. Gait parameters are related to the stages of the disease described in the clinical classification [3-11, 22].

To get detailed information about the causing gait differences, we correlated the AOG-test with existing, valid gait assessments and the UPDRS test. We found predominant no correlation between the AOG-test and these biomechanical or clinical tests, except one significant strong

Table 3. Gait Dynamics of the Study Population (PD, n=36)

Velocity (km/h)	Step Length (m)	Stride Time (s)	Stride Time Variability (%)	Double Stance (ms)	Swing Time Left (ms)	Swing Time Right (ms)
1.5	.60 (.10)	1.43 (.25)	5.63 (2.22)	233 (69)	484 (105)	475 (102)
1.8	.69 (.11)	1.35 (.22)	5.53 (2.73)	203 (49)	513 (242)	519 (241)
2.1	.76 (.11)	1.29 (.19)	5.63 (2.88)	185 (47)	453 (88)	457 (106)
2.4	.83 (.11)	1.24 (.17)	5.33 (3.04)	183 (53)	434 (84)	438 (73)
2.7	.91 (.11)	1.2 (.15)	4.84 (2.64)	173 (50)	436 (63)	418 (81)
3.0	.96 (.12)	1.16 (.16)	5.41 (2.72)	166 (36)	438 (103)	420 (114)

Table entries are means (SD).

Table 4.   **Correlation Between AOG Non Frequency Weighted and Frequency-Weighted Performance and UPDRS Subscales and Other Parkinsonian Features, Gait Parameter, Webster Gait Test and Gait Dynamics**

Parkinsonian Features	AOG	AOG II (60-28sec)	AOG III (28-14sec)	AOG IV (14-4sec)
UPDRS Part III	0.45**	0.63**	0.43**	0.46**
Sub Cranial	0.45**	0.59**	0.21 n.s.	0.18 n.s.
Sub Tremor	0.07 n.s.	0.02 n.s.	0.06 n.s.	-0.01 n.s.
Sub Rigidity	0.26 n.s.	0.46**	0.4*	0.40*
Sub Bradykinesia	0.44**	0.54**	0.36*	0.33*
Sub Gait&Posture	0.14 n.s.	0.23 n.s.	0.23 n.s.	-0.00 n.s.
Parkinsonian Features				
Levodopa dose	0.17 n.s.	0.09 n.s.	0.17 n.s.	0.26 n.s.
Freezing	0.08 n.s.	0.14 n.s.	-0.56 n.s.	-0.22 n.s.
falls	-0.02 n.s.	0.09 n.s.	-0.08 n.s.	-0.09 n.s.
sensory dysfunction	-0.28 n.s.	-0.18 n.s.	0.02 n.s.	-0.11 n.s.
Webster Gait Test				
Webster12	0.09 n.s.	0.05 n.s.	-0.01 n.s.	0.06 n.s.
Webster24	0.12 n.s.	0.11 n.s.	-0.39 n.s.	0.11 n.s.
Stride Time				
1.5 (km/h)	-0.31 n.s.	-0.31 n.s.	-0.43	0.05 n.s.
1.8 (km/h)	-0.34 n.s.	-0.31 n.s.	-0.43 *	0.05 n.s.
2.1 (km/h)	-0.29 n.s.	-0.28 n.s.	-0.43 *	0.02 n.s.
2.4 (km/h)	-0.22 n.s.	-0.24 n.s.	-0.43 *	0.02 n.s.
2.7 (km/h)	-0.18 n.s.	-0.14 n.s.	-0.38 *	0.06 n.s.
3.0 (km/h)	-0.25 n.s.	-0.17 n.s.	-0.31 n.s.	0.02 n.s.
Step Length				
1.5 (km/h)	-0.3 n.s.	-0.31 n.s.	-0.43*	0.05 n.s.
1.8 (km/h)	-0.34 n.s.	-0.32 n.s.	-0.43 *	0.04 n.s.
2.1 (km/h)	-0.3 n.s.	-0.28 n.s.	-0.43*	0.02 n.s.
2.4 (km/h)	-0.24 n.s.	-0.23 n.s.	-0.43 *	0.01 n.s.
2.7 (km/h)	-0.19 n.s.	-0.15 n.s.	-0.39*	0.05 n.s.
3.0 (km/h)	-0.22 n.s.	-0.16 n.s.	-0.35 *	0.06 n.s.

$p <= 0.01$**.
$0.01 < p < 0.05$*.
$p > 0.05$ n.s.

correlation with UPDRS bradykinesia and cranial subscale and moderate correlations with step frequency and step-length (see Table **4**). Based on the fact that this study is of exploratory character, we decided to discuss strong and moderate correlations according to the AOG-test, to get first indications.

4.1. Differing Gait Task

In this study we used conventional clinical gait tests e.g. the UPDRS-test and the Webster gait-test, for comparison with the AOG-test. The UPDRS 'gait and posture' subscale includes the tasks 'standing up from a sitting position', 'the pull-test' (retropulsion-test) posture and 'gait in constant, self selected walking speed'. Gait is only one variable of four,

which is examined over a short distance with constant velocity. By contrast, the AOG-test focusses on gait adaptation over a longer time and distance. Thus, the missing correlation to the 'gait and posture subscore' certified our presumption to have a completely different assessment-task in the AOG-test. This might explain the lack of correlation between the UPDRS 'gait and posture'-subscore and the adaptation of gait. Brusse *et al*. complain, that there is low evidence that the UPDRS-test adequately measures walking, mobility performance or comfortable and fast gait speeds [42].

These results are resembled by Turbanski *et al*. according to postural control. They also found no correlations between the UPDRS subscore 'gait and posture' and static or dynamic

biomechanic tests for postural control. They concluded that the reliable retropulsion-test gives an insight into one phenomenon, and the dynamic test for postural control to another phenomenon. Nevertheless, both tests are important for the evaluation of postural control mechanisms in PD [43].

We took this into account, and used other qualitative (UPDRS), semi-quantitative (Webster-gait test) and quantitative gait analyses (AOG and biodynamic gait assessment). Others like the TUG (timed get up and go-test), BBS (Berg Balance-Scale), FGA (Functional Gait Assessment) can also be used to measure gait performance [15, 42]. The Webster-test represents a gait task with initiation and constant gait elements at comfortable walking velocity and a turn. Although, the test inherits velocity changes, no correlation with the AOG-test can be seen. This might also be attributed 60 differing tasks. The Webster-gait test has feedforward processes while the AOG-test is characterized by an unpredictable feedback regulation. Also, gait has to be adapted more frequently than in the Webster-gait test and other common clinical gait assessments.

4.2. Adaptation of Gait and Bradykinesia

Insights into the dominating parameters of gait adaptation get visible by examining the correlation with the cardinal symptom bradykinesia. Bradykinesia includes the terms hypokinesia and akinesia. Several studies analyzed and described the influence of hypokinesia to gait [3, 7, 17, 18]. Hypokinesia refers to slow movements e.g. slowed gait velocity and smaller amplitudes e.g. shortened step length [41]. Akinesia is defined as a poverty of spontaneous movements, like sudden changes in gait velocity or facial expression [41].

Both hypokinesia and akinesia can be part of the gait adaptation process. Continuous slow and short stepped gait reasoned by hypokinesia would have caused a back drift on the treadmill during the AOG-test, in particular during the fast velocities and the positive velocity changes (+0.5km/h) in the test. This would have caused a higher, probably significant value in AOG-IV, representing difficulties in adapting to one, respectively two velocity steps. Controversially, a back drift might also have been compensated and balanced through the tests velocity-time sequence (see Fig. **2**). We chose a range of treadmill-velocities between 1.2 and 3.8 km/h which lies beneath the average gait-velocity of PD patients at this age and disease stadium. So we assume, that hypokinesia should play a subordinate role in the AOG-test, explaining the lack of the correlation.

Another aspect was described by Morris *et al.* [44]. They argued, that gait hypokinesia is responsible for an impaired stride length, so that PD subjects compensate their impaired stride length with a higher stride time, a parameter that is not impaired in PD-gait [6, 9, 17, 24]. Stride time might have compensated the reduced step length during the whole AOG-test. According to some velocity steps in the AOG-test, this regulation-pattern seems to get critical in several adaptation situations, referred to the subjects constant position on the treadmill, like the correlation between AOG III and stride length and stride time shows. Stride length and stride time seem not to be able to compensate the fluctuating gait-velocities adequately. Nevertheless, the results have moderate correlations in all velocities.

Akinesia might explain differences in gait adaptation. Changes of velocity (+/-) during the AOG-test are getting

critical, because akinetic PD patients have a poverty of spontaneous movements in both directions: undershooting movements during a positive velocity change, overshooting movements during a negative velocity change. Further studies found hyperstability of walking coordination that leads to difficulties in adapting to a single velocity change during gait on a treadmill [45]. Winogrodzka *et al*. showed that rigidity and bradykinesia limited gait-parameters significantly in PD patients, depending on the degeneration of the dopamine system. They analyzed the ability to adapt to single, signalized velocity-change on the treadmill. Bradykinesia was significantly associated with the coordination of arm and leg movements during this walking-task (velocity change plus and minus 0.8km/h between 0.6 and 5.4 km/h, one signalized step every 60-second), so that the gait adaptation was retarded. They conclude that the extent of degeneration of the dopamine system was associated with a limited adaptive ability in movement coordination [23]. This goes in-line with our study, where bradykinesia correlated with the AOG parameters (moderately), and the progression in PD (highly).

Interesting in this context is the significantly high correlation (r=0.59; p<0.000) between AOG II and the cranial subscale. In our study the items 'speech' and 'facial expression' show the highest association of all analyzed parameters to the AOG-test. The high correlation between the cranial-subscale and the AOG-test might be caused by akinesia, because both are caused by poverty of spontaneous movements [41, 46]. Cantiniaux *et al*. were the first who studied correlations between speech and gait parameters. Their quantitative examination of gait and speech parameters correlated significantly in HC and PD subjects [47]. They found parallels in the regulation of gait and speech in HC and PD subjects. Walking velocity and speech velocity, as well as step length and the so-called ISD (time interval between two pauses) significantly correlated, levodopa dependent. Furthermore, the rhythmic-parameter of gait and speech: walking cadence and the so-called SPIR (Speech Index of Rhythmic) correlated (negative) significantly in HC and in PD off-stage and could not be influenced with levodopa. Speech or facial expression and gait are both complex mechanisms in different non-dopaminergic structures [47]. Cantiniaux *et al*. bring out the possibility of a speech rhythm generator comparable to the gait rhythm generators that are well-known through numerous studies regarding spinal cord injuries (human and animal based). Repeated rhythmic stimulation of the lower extremities leads to the activation of the so called central-pattern-generators (CPG) [48], which are networks of spinal nerve cells that work self-sufficient after activation and lead to a rhythmic and functional activation of agonistic and antagonistic leg muscles during gait [49-51]. Nevertheless they are bound to proprioceptic and exteroceptic afferences. So even if priorities change within the integration of sensoric modalities, the processing of proprioceptic information should still play a major role during the generation of a rhythmic gait pattern. In humans the discreteness of the CPG is influenced by supraspinal areas [52]. A major structure of the supraspinal regulation is the *mesencephylic locomotor region* (MLR) which is connected with the pedunculopontine nucleus (PPN) *via* colineric neurons [53]. The PPN is sending sensoric feedback to the basal ganglia [54] as well as efferences to the spinal cord. The PPN shows a rhythmic activity which is controlled through cerebellar paths. In PD-patients a reduced amount of cells in the PPN was found in postmortem [48, 55]. Because the neurons of the PPN are

dopamin-independent, a degeneration of the PPN neurons could be one of the causes for dopamin-resistent PD-symptoms, like freezing of gait, postural instability or sleep disorders [56].

Relating to our study where all PD-patients were tested pharmaceutically "on", the significant worse gait adaption of the PDS-group in the AOG-test could possibly be caused by a malfunction of this dopamin-independent interaction. In consequence of a nerve cell loss in the PPN, the supraspinal efferences from the PPN to the CPG could potentially be defective when state changes of velocity take place. It seems that an ongoing adaptation of the gait velocity is not possible, because the feedback with the basal ganglia is limited as well in the worse affected group PDS. A further hint for this explanation gives the results of Getrost [57] in an additional study with the AOG-test. He found pecularities regarding PD-patients with freezing of gait (FOG) relating to the adaptability of gait in comparison to patients without FOG and patients with dyskinesia.

In summary: the AOG-test clearly makes restrictions in gait adaption apparent. Yet the underlying pathologic mechanisms or interfaces became not fully evident. Our analyzation of data and literature brings us to considerations that a defective gait adaptability is potentially associated with akinesia and/or dopamin-independent alterations in the sensorimotor integration between PPN and CPG.

5. CONCLUSION

It is obvious, that the gait task intentionally differs from the conventional gait-tests. Gait adaptation seems to refer partly to the cardinal symptom bradykinesia, but the main influencing part is still unclear. Thus, the AOG-test obviously exposes different phenomena we cannot allocate yet. Several explanations are possible, e.g. impaired sensorimotor integration, hypokinesia, akinesia or levodopa induced dyskinesia. Further evaluation processes are necessary to improve the diagnostics like different patient groups (freezer/non-freezer; "on"/"off" state) or additive assessments (speech and cognitive variables, e.g. attention). There also seems to be a potential of the AOG-test as a therapy strategy. Different studies have already shown that deviance based gait training and treadmill training are effective interventions to improve pathological gait [58, 59]. The AOG-test combines those two approaches and could be useful as a training tool.

To our knowledge, this is the first test that explores the adaptability of gait. The detected parameters are not represented in the usual biomechanical and clinical gait assessments to date. Whereas it is a well known difficulty of PD subjects to adapt to changing gait conditions (e.g. at crowded places). We conclude, that the AOG-test seems to measure a new and important factor in gait-regulation and might represent a dynamic gait-task that detects gait deficits influenced by akinesia and/or a dopamin-independent phenomenon relying on a defective processing in the gait rhythm.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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