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NEUROLOGY AND PRECLINICAL NEUROLOGICAL STUDIES - ORIGINAL ARTICLE

Complex motion series performance differs between previously untreated patients with Parkinson's disease and controls

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Abstract

Motor behaviour in patients with Parkinson's disease is determined with instrumental tests and rating procedures. Results mirror impairment of an individual patient. Objectives were to determine the associations between two kinds of motion series and rating scores in previously untreated 64 patients and to compare outcomes to controls. The line tracing task asks to follow a given path. It measures the needed interval, the number and duration of contacts to the path. The aiming procedure asks to hit contact plates with a pencil and determines the needed time period and the number of accurate, respectively, missed key strokes. Both tests differed between patients and controls. The line tracing task was more sensitive. The line tracing task asks for a complex motion series performance with more cognitive load. The aiming task prompts for a conduction of preponderant simple, repetitive movement series. Only initially, a complex process of aiming is necessary. Performance of complex motion sequences better differs between patients with Parkinson's disease and controls than conduction of simple, repetitive movement series.

Keywords Parkinson's disease · Motor behavior · Line tracing · Aiming

Introduction

Evaluation of patients with Parkinson's disease (PD) includes several procedures. One is clinical evaluation with rating scales, like the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn et al. 1987). Outcomes may be different between various examiners. Scoring outcomes may suffer from insensitivity to subtle modifications and the more general subjective impression of the patient by the rating neurologist (Goetz et al. 2008). Impairment of motor symptoms may additionally be assessed with more objective instrumental test procedures. There are devices, which measure activity of patients over the whole day independent of subjects' concentration on movement performance (Espay et al. 2016; Di et al. 2020; Ricci et al. 2020; Artusi et al. 2020). They are more suitable for at-home testing (Goetz et al. 2008). Alternative approaches are execution of standardised assessments over a short interval. They ask for the performance of a specific motion series (Müller and Harati 2020). This approach prompts the individual to draw the full attention on the test execution. These devices may be employed during an out-patient visit as add on to the neurological examination. Various approaches for quantitative instrumental assessments of motor behaviour have been developed over the years (Lee et al. 2016; Lopane et al. 2018). All these technical methods aim to determine the severity of motor impairment more objectively. Previously untreated PD patients are particularly well suitable for the clinical examination of PD symptoms with an instrumental paradigm, since prior intake of dopamine substituting drugs influences motor behaviour. Need for higher cortical functions and thus dopamine sensitive mesolimbic structures bias the execution of motion sequences (Cools et al. 2019; Nikolaus et al. 2019). High cognitive load demands for attention and motivation and thus influence the value of an employed test. Execution of simple, more automated movement series with a need for low cognitive load was less sensitive for the differentiation between PD patients and matched controls (Müller et al. 2000). An example for

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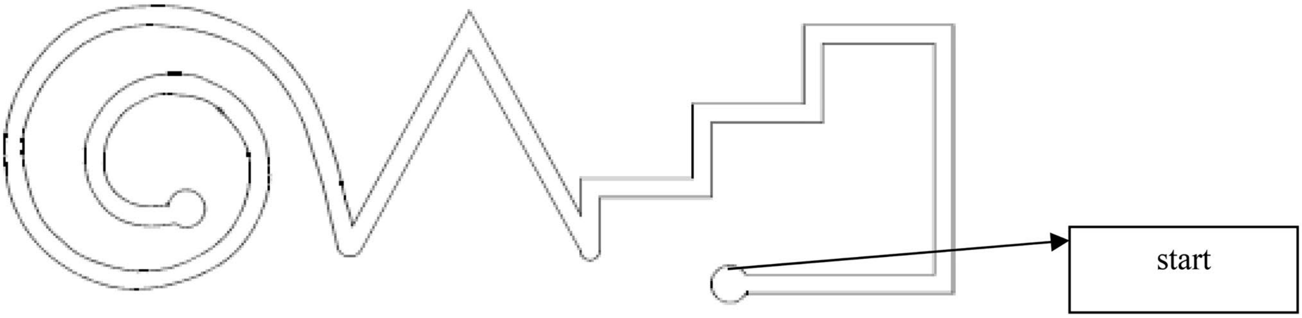

Fig. 1 Graph from the line tracing task (modified from https://psydok.psycharchives.de/jspui/bitstream/20.500.11780/1018/1/Mls.pdf, page 7)

Fig. 2 Graph from the aiming paradigm (modified from https://psydok.psycharchives.de/jspui/bitstream/20.500.11780/1018/1/Mls.pdf, page 7)

a complex movement sequence is the line tracing task. It asks the individual to follow a given path (Fig. 1). Another one is the aiming paradigm (Fig. 2), which prompts the subject to hit a pencil on specific board regions with a certain sequence. Objectives were to determine whether outcomes of aforementioned, standardised, instrumental tests reflect the clinical rating scale scores in PD patients.

Methods

Subjects

64 not previously treated, right handed, idiopathic PD patients and 64 age- and sex-matched controls (deviation tolerance 6 months) were enrolled (Table 1). Individuals with medical conditions, which may affect the outcomes of the performed instrumental tests such as limb paresis, did not participate.

Design

First the rating (W.K.; T.M.) and then the assessments with the devices (standardised sequence: line tracing [first], aiming [second], were performed (technicians). In order to minimise learning and training effects, all PD patients were allowed to practice for one minute on the day before with all instrumental tests.

Table 1 Characteristics of participating PD patients and controls

Patients	
Age	57.77 ± 1.08 years
Sex	27 men; 37 women
HYS	1.89 ± 0.07
UPDRS I	1.28 ± 0.15
UPDRS II	5.7 ± 0.39
UPDRS III	16.47 ± 1.11
UPDRS III arm	10.58 ± 0.67
UPDRS IV	0 ± 0
UPDRS	23.68 ± 1.46
Controls	
Age	57.78 ± 1.07 years
Sex	27 men; 37 women

All data are given as mean ± standard error of means; *HYS* Hoehn and Yahr Scale, *UPDRS I* Unified Parkinson's Disease Rating Scale mental behaviour, *UPDRS II* Unified Parkinson's Disease Rating Scale activities of daily living, *UPDRS III* Unified Parkinson's Disease Rating Scale motor examination, *UPDRS III* Unified Parkinson's Disease Rating Scale motor examination arm (items 20, 21, 22, 23, 24, 25), *UPDRS IV* Unified Parkinson's Disease Rating Scale motor complications

Rating

Patients were scored with the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn et al. 1987).

Instrumental tests

Line tracing

The patient was asked to follow a grooved path with a stylus as exact and fast as possible from the right to the left side first with the right and then with the left hand one time only. The total test duration, the number of contacts and the duration of contacts to the panel interfacing with a computer, which recorded all these parameters, were assessed (Müller et al. 2005). Intervals were determined with 100 ms accuracy. The patients were instructed to execute the task in precise and a quick fashion.

Aiming

Patients were asked to hit 20 small contact plates (diameter 0.5 cm) with a contact pencil from the right to the left side. The 20 plates were located in a straight row with a distance of 0.5 cm between each plate. Initially and at the end of the task, the subject additionally had to tap on big contact plates (diameter 1.5 cm), both of which located in a distance of 0.5 cm from the row with the small plates, to measure to the total time for task performance. The total number of accurate hits was also registered in addition to the total number and the length of missed hits beside the plates. The board was positioned in the middle and the task was carried out with each hand separately, first with the right and then with left hand. The patients were asked to perform this instrumental paradigm as precisely and as quickly as possible.

Statistics

A non-parametric data distribution was shown according to the Kolmogorov–Smirnov test outcomes mainly. Therefore non-parametric tests were only employed for this exploratory analysis. The Mann–Whitney *U* test was employed for comparisons, Spearman rank correlation for correlation analysis. Suitable items of UPDRS part motor examination (III) were selected for calculation of the UPDRS arm score (items: 20, 21, 22, 23, 24, 25) only. Further UPDRS scores were not computed to reduce the number of correlations. Therefore we also only employed computed instrumental test results, which were the computed sum of the right and left upper limb, as handedness and dominance of motor items may interfere with the instrumental task execution. This approach was done to limit the corrections of the significance level, which was set for $p<0.015$ for comparisons and $R<0.4$, $p<0.0001$ for correlations, in this exploratory analysis.

Ethics

The study was approved by the local institutional ethics committees. This investigation was a non-interventional study, i.e., the rules imposed for this observational plan did not interfere with the physician's common therapy. Patient's written informed consent regarding the forwarding and storing of medical data was obtained.

Results

Comparisons

PD patients needed longer ($p<0.0001$) intervals than controls for the performance of the line tracing task (Fig. 3). They had more ($p<0.0001$) contacts than the controls (Fig. 4), whereas the duration of contacts to the panel did not differ between both (Table 2). In case of the aiming paradigm only the total needed for task execution differed between patients and controls in contrast to the further determined parameters, such number, respectively, duration,

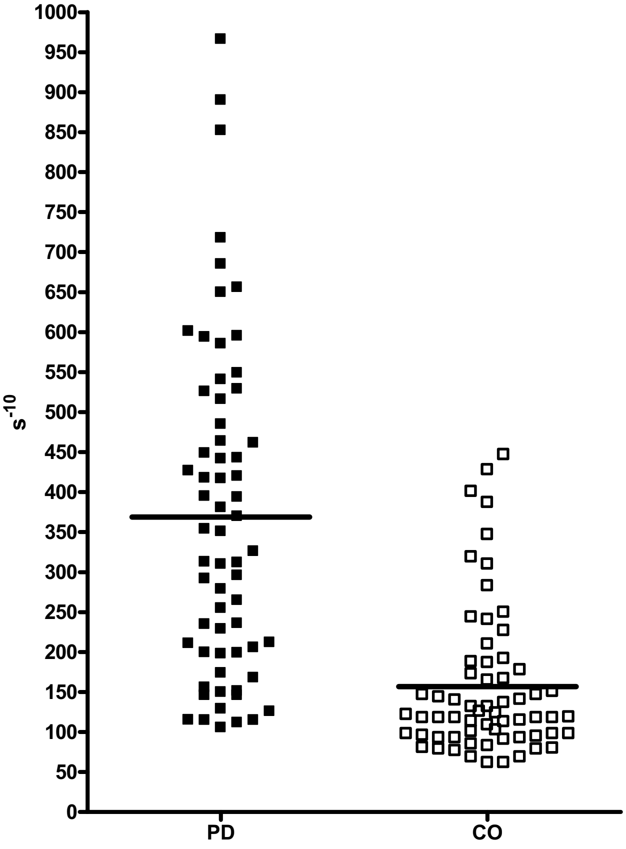

Fig. 3 Duration of line tracing in patients with Parkinson's disease and controls. *PD* Parkinson's disease, *CO* controls (CO), – mean value, *s* seconds

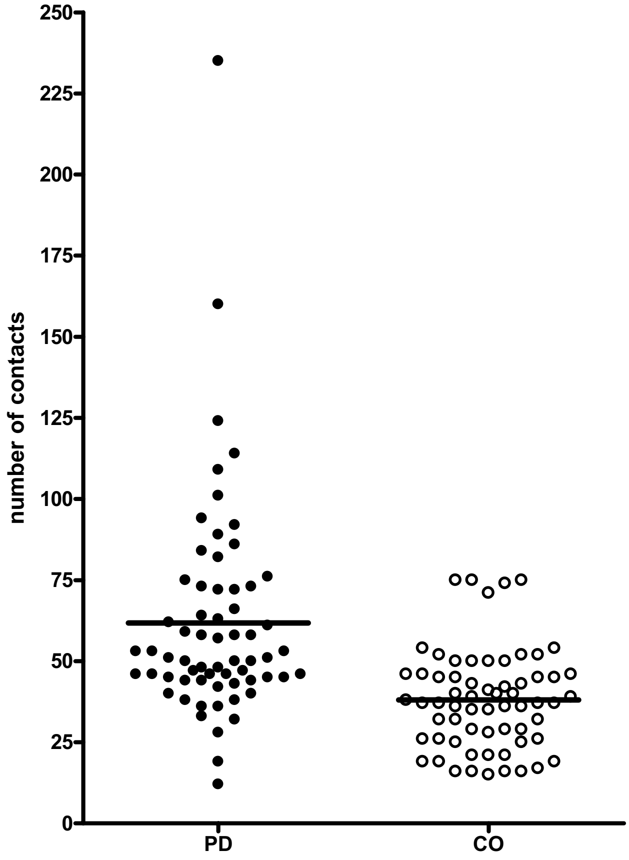

Fig. 4 Number of contacts in the line tracing paradigm in patients with Parkinson's disease and controls. *PD* Parkinson's disease, *CO* controls (CO), - mean value

Table 2 Comparison of instrumental test outcomes between patients and controls

	Patients	Controls	*p*
Line tracing contacts	61,75 ± 4,20	38,09 ± 1,91	< 0.0001
Line tracing duration of contacts	91,10 ± 6,89	74,53 ± 3,87	Ns
Line tracing total duration	368,9 ± 25,78	156,8 ± 11,62	< 0.0001
Aiming missed hits	5,47 ± 1,06	4,92 ± 0,52	Ns
Aiming duration of missed hits	3,67 ± 0,96	2,57 ± 0.46	Ns
Aiming total interval	231,1 ± 8,01	181,8 ± 5,89	< 0.0001
Aiming number of accurate hits	40.02 ± 0,29	40 ± 0,02	Ns

ns not significant, *p p* value, for further abbreviations see legend to Table 1

respectively, number of missed and accurate hits (Fig. 5, Table 3).

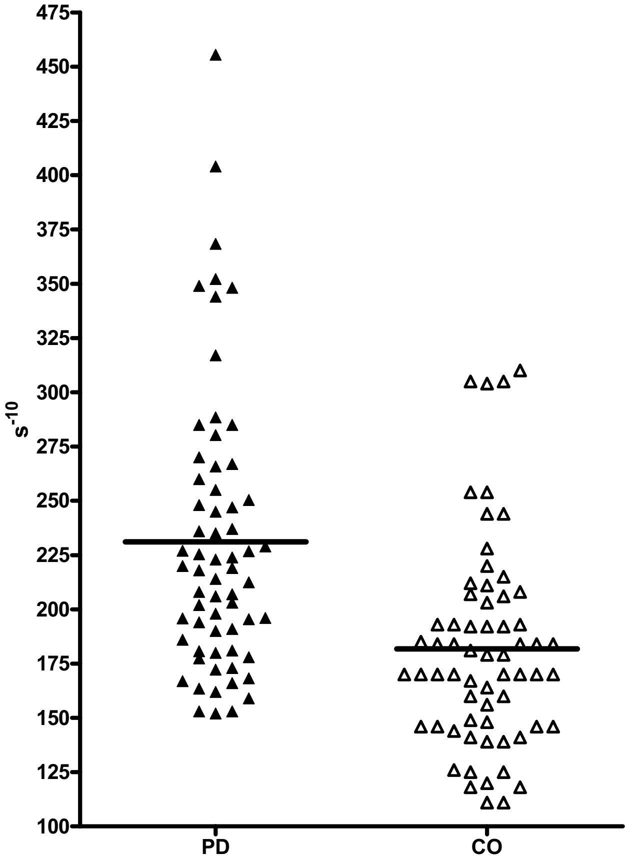

Fig. 5 Interval needed for the aiming task in patients with Parkinson's disease and controls. *PD* Parkinson's disease, *CO* controls (CO), - mean value, *s* seconds

Correlation analysis

Table 3 only shows the significant outcomes in PD patients. The total interval needed for line tracing was related to the number of contacts. The duration of contacts associated with the number of contacts, UPDRS, UPDRS III, UPDRS III arm, UPDRS activities for daily living (II) and the interval needed for the aiming task performance. This outcome of the aiming procedure correlated with UPDRS and UPDRS III. The number and duration of missed hits of the aiming paradigm correlated to each other. UPDRS scores were closely associated to each other with the exception of UPDRS I (mental behaviour). There was no impact of age or sex in the PD cohorts. Table 4 describes the outcomes in the controls. Results of the instrumental tests correlated to each other and were age dependent.

Discussion

Measured features of both instrumental tests differed between patients and controls. Both instrumental tests have in common that initiation and conduction of a precise and

Table 3 Correlation analysis in PD patients

Variable 1	Variable 2	*R*	*p*
Lline tracing total duration	Line tracing contacts	0.48	< 0.0001
Line tracing duration of contacts	Line tracing contacts	0.43	0.0004
Line tracing duration of contacts	UPDRS	0.54	< 0.0001
Line tracing duration of contacts	UPDRS II	0.43	0.0004
Line tracing duration of contacts	UPDRS III	0.54	< 0.0001
Line tracing duration of contacts	UPDRS III arm	0.52	0.0006
Line tracing duration of contacts	Aiming total interval	0.65	< 0.0001
UPDRS	Aiming total interval	0.42	0.0006
UPDRS III	Aiming total interval	0.44	0.0006
Aiming missed hits	Aiming duration of missed hits	0.86	< 0.0001
UPDRS II	UPDRS	0.87	< 0.0001
UPDRS III	UPDRS	0.96	< 0.0001
UPDRS II	UPDRS III	0.75	< 0.0001
UPDRS III arm	UPDRS	0.85	< 0.0001
UPDRS III arm	UPDRS II	0.68	< 0.0001
UPDRS III arm	UPDRS III	0.86	< 0.0001

P p value, *R* Spearman rank correlation coefficient, for further abbreviations see legend to Table 1

Table 4 Correlation analysis in the controls

Variable 1	Variable 2	*R*	*p*
Line tracing contacts	Line tracing total duration	0.72	< 0.0001
Line tracing duration of contacts	Line tracing total duration	0.65	< 0.0001
Line tracing contacts	Age	0.5	< 0.0001
Line tracing duration of contacts	Age	0.53	< 0.0001
Line tracing total duration	Age	0.45	0.0002
Aiming total interval	Line tracing total duration	0.46	0.0002
Aiming missed hits	Aiming duration of missed hits	0.89	< 0.0001
Aiming total interval	Line tracing duration of contacts	0.65	< 0.0001
Aiming total interval	Line tracing total duration	0.45	0.0002
Aiming total interval	Age	0.75	< 0.0001

P p value; *R* Spearman rank correlation coefficient

aimed movement sequence is necessary. Performance of these motion series asks for considerable load in the cognitive domains attention and concentration (Cools et al. 2019). More components of the line tracing task differed between PD patients and controls compared with the aiming task. Line tracing asks for continuous execution of an aimed motion series with a necessary permanent focus on movement execution. In the case of aiming, an initiation of an aimed and precise movement is warranted, whereas the component of the movement sequence for performance of hitting the board is a simple, automated motion with need for low cognitive load only. In particular, number of errors and duration of errors in the line tracing task mirrors the functional capacity for continuity of execution of aimed and thus precise movement series. They ask for additional involvement of higher dopamine sensitive brain structures, such as the mesolimbic system (Cools et al. 2019). Thus, a more continuous and higher cognitive load with additional involvement of midbrain is necessary for completion of the line tracing task. In contrast the aiming paradigm only involves these higher brain functions only transiently during the initiation of the aiming process to hit the plate, whereas the remaining movement sequence has a repetitive character with lower cognitive effort (Cools et al. 2019). Accordingly, number of accurate or missed hits and their duration reflect a simply structured movement with low need for cognitive load. In other words, the aiming paradigm mainly asks for execution of a simple movement component, which is hitting the board in contrast to the single carrying out of the line tracing task, which is complex during the whole period of task performance (Müller et al. 2020). Both have in common the velocity of task execution as an important feature. Accordingly, the movement speed dependent component of the total interval needed for the aiming task execution differed between patients and controls similar to the total time period necessary for completion of the line tracing paradigm. Instrumental test results correlated to each other and were related to the UPDRS scores to a certain extent. The missing impact of age on instrumental outcomes in the patients in contrast to the controls is the consequence of altered movement behaviour due to the disease process. We emphasise that these instrumental tests are not specific for PD and a certain overlap of test outcomes exists between patients and controls. A limitation is that assessment of both instrumental does not determine the rate of failures, i.e., contacts to the path or missed hits, during performance of the whole movement sequence. Therefore we cannot comment on putative peaks of failed motion sequences, i.e., at the beginning or at the end of the measurement. The applied instrumental tests in this trial ask to focus on a specific task performance during a specific interval similar to the rating procedure, whereas wireless, patient-worn sensors or smart phone mobile apps monitor severity of PD symptoms throughout the whole day (Dai et al. 2013; Espay et al. 2016).

In conclusion, we show that performance of both instrumental tests is execution speed dependent and differs between patients and controls. The value of the more complex line tracing task is superior to the preponderant simple aiming paradigm with its repetitive character. Therefore this investigation confirms that instrumental assessment of complex motion series better differentiate between PD patients and controls than measurement of simple movement sequences.

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