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Identifying Behavioural Changes due to Parkinson's Disease Progression in Motor Performance Data

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Abstract: Parkinson's disease (PD) is a progressive nervous system disorder that affects movement. PD has a severely negative impact on the quality of life of patients and their caregivers. The timing of treatment depends, amongst others, on the quantification of patients' motor performance. To date, the resolution used in scaling motor performance is too low to detect subtle behavioral changes over time. This paper investigates if 'longitudinal' datasets of motor performance data obtained from tracking tasks can detect behavioural changes in motor performance data representative for PD symptoms. Such longitudinal data were approximated using a combined data-set based on 50 trials of collected experiment data from 25 healthy participants (age range 55-75 years), augmented with 25 bootstrapped samples scaled to represent 'Mild' or 'Severe' motor performance degradation. An approach based on general linear regression models was tested for its capacity to detect the adverse trends in typical tracking task metrics (K_p , τ , ζ_{nms} , ω_{nms} , $RMSe$, and $RMSu$). Overall, it was found that with this approach in at least 50% of all participants, a simulated change in motor behaviour was successfully detected, a number that may increase to 97% for the most sensitive metric (ζ_{nms}) and consistent participant data. This indicates that the developed approach is promising towards the development of more objective and detailed monitoring of disease progression and treatments in PD patients.

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Keywords: Pursuit tracking, Parkinson's disease, trend detection, diagnostics, linear regression

1. INTRODUCTION

In Parkinson's disease (PD), it is especially the loss of motor skills (i.e., eye-hand coordination) that affects patients' quality of life (Lees et al., 2009; De Boer, 2015). PD causes a decrease in dopamine-producing neurons of the Basal Ganglia that hampers communication in the brain, especially in the motor area, and causes symptoms such as slowness of movement (bradykinesia), postural instability, and tremors (Lees et al., 2009; De Lau and Bretelet, 2017). Key to early detection and fine-tuned treatment of motor symptoms to restore patients' quality-of-life, is the accurate quantification and semi-continuous monitoring of patients' motor performance (Lees et al., 2009).

In current clinical practice, motor and non-motor PD symptoms are tested mainly through questionnaires (Gelb et al., 1999), whose results are translated into a five-stage Unified Parkinson's Disease Rating Scale (UPDRS) (Goetz, 2012), with only a very coarse resolution in both *symptom severity*, as well as *time*. An alternative approach, which has received considerable attention in a research context, is to directly measure motor performance and its degradation with the use of *tracking tasks*; manual control tasks where a dynamic system is continuously

perturbed by forcing functions and controlled by a human controller (Flowers, 1976; Hufschmidt and Lucking, 1995; Soliveri et al., 1997; Oishi et al., 2011; Jones and Ivan, 1989; Pool et al., 2022). While tracking tasks have indeed proven to reveal differences in motor performance between healthy controls and PD patients, their true effectiveness for monitoring motor symptom progression in individual patients has, to the best of our knowledge, never been explored. A key challenge for using tracking task data for functional diagnostics is that motor performance is generally characterized by a number of different metrics (e.g., performance metrics, human control model parameters (Mulder et al., 2018)), meaning that the detection of degraded motor performance is a multivariate problem. Furthermore, performance in tracking tasks inherently shows significant, and strongly participant-dependent, day-to-day variation, which needs to be adequately accounted for to reliably detect adverse trends in disease progression.

This paper focuses on using trend analysis with multivariate linear regression models (Chandler and Scott, 2011) for identifying behavioural changes in individuals' motor performance data due to PD. To approximate a clinical longitudinal data set, an experiment with 25 healthy participants aged between 55-75, who each performed 50

trials of a pursuit tracking task on a large touchscreen with both their dominant and non-dominant hands, was used to collect representative ‘motor symptom free’ reference data. Participants’ control dynamics in the tracking task were quantified with a fitted human control model (Mulder et al., 2018). To simulate a reduction in motor performance, the experiment data was augmented with bootstrapped PD data, where trends in human control model parameters as representative for PD, based on earlier research (Pool et al., 2022), were implemented. For augmented data sets representative for ‘‘Mild’’ and ‘‘Severe’’ motor skill loss, the accuracy with which behavioural changes in motor performance data can be detected using trend analysis techniques was directly assessed.

2. EXPERIMENT

2.1 Tracking Task

The human motor performance data for this study were gathered using a horizontal-axis pursuit tracking task, similar to that used in previous research with PD patients (Pool et al., 2022; Flowers, 1976). The task was performed on a touch screen (Dell P2341T), see Fig. 1, and participants wore touchscreen gloves to reduce friction between finger and the screen. In pursuit tracking the participant is asked to reduce the error e between the system output y (blue dot) and the target signal f_t (black circle), as shown in Fig. 2. This means participants controlled the blue dot so that it was positioned on the black circle at all times. To ensure sufficient measurable excitation of participants the neuromuscular dynamics, the blue dot’s response to touch inputs had single integrator controlled dynamics, i.e., $8/s$. The controlled dynamics gain was heuristically tuned such that finger movements were within reasonable limits.



Fig. 1. Experiment test set-up.

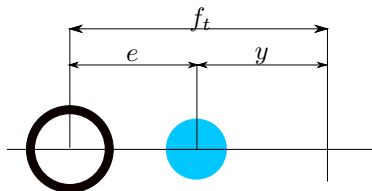


Fig. 2. Pursuit display

A quasi-random multisine forcing function f_t was used in the tracking task. The signal was identical to that used in earlier research (Büskens et al., 2019) and defined as the sum of $N_f = 11$ sines, i.e., $f_t(t) = \sum_{k=1}^{N_f} A_f(k) \sin(\omega_f(k)t + \phi_f(k))$. The frequencies ω_f of the multisine were all integer multiples of the base frequency,

i.e., $\omega_f(k) = 2\pi n_f(k)/T_m$, where T_m indicates the measurement time. This signal, for which the detailed settings are listed in Table 1, covered the whole region of interest in human behaviour dynamics. Tracking runs lasted a total of 50 s, of which the first 9.04 s were run-in time.

Table 1. Multisine target signal settings.

n_f	ω_f [rad/s]	A_f [deg]	ϕ_f [rad]
4	0.614	1.079	7.239
7	1.074	0.776	0.506
13	1.994	0.391	7.860
19	2.915	0.225	8.184
29	4.449	0.117	9.012
37	5.676	0.082	6.141
43	6.596	0.066	6.776
53	8.130	0.051	6.265
79	12.118	0.035	4.672
109	16.720	0.028	2.672
157	24.084	0.024	8.009

2.2 Participants

As listed in Table 2, the participants were 25 healthy adults in the age range of 56–75 years ($\mu = 66.88$ years, $\sigma = 6.77$ years), coinciding with the average age of symptom onset in PD (Lees et al., 2009). This elderly participant population without any neurological impairments shows similar, though slightly better, visuomotor performance than PD patients on Levodopa treatment (Hufschmidt and Lucking, 1995), which provides a good baseline for our analysis. Minor deficiencies related to natural neurological degeneration and ageing, such as slowness of movement, were allowed. All participants signed a consent form. The experiment was approved by TU Delft’s Human Research Ethics Committee (HREC) under application number 982.

2.3 Procedures

To approximate longitudinal clinical data, the experiment was spread over 5 days. On the first day, participants received a detailed briefing and were asked to perform a Mini Mental State Examination (MMSE) to assess their cognitive functioning (Tombaugh and McIntyre, 1992). A motor performance baseline is defined using a previously developed dedicated test procedure (De Boer, 2015), measuring reaction time and eye-hand coordination. On all five days, participants performed the tracking task with both their dominant (D) and non-dominant (ND) hand. Participants always first performed five practice trials with each hand, to re-acquaint themselves with the task. On the first day, this training was extended if needed, until participants showed convergence to a stable control behavior. After training, 10 measurement trials for each hand were performed on all days (20 trials/day). D and ND trials were alternated and balanced across participants to mitigate any learning and fatigue effects. Short breaks were taken frequently to lessen hand and eye fatigue.

2.4 Data analysis

For all trials, the time traces of the target signal f_t , participants’ touchscreen input u , the resulting controlled dynamics output y (i.e., the position of the blue dot in

Table 2. Overview of participant information.

Participant	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
Age	56	58	75	75	72	74	73	74	75	58	64	64	64	61	67	70	72	62	60	58	69	75	68	72	56
Sex	f	m	f	f	f	m	f	f	m	m	f	f	m	f	f	f	f	m	f	f	m	f	f	f	f
Handedness	r	r	r	r	r	r	r	l	r	r	r	r	r	r	r	r	r	l	r	r	r	r	r	r	r

Fig. 2), and the tracking error e were measured. From these signals, normalized root mean square (RMS) values of e and u were calculated, i.e., $RMS_e = \text{RMS}(e)/\text{RMS}(f_t)$ and $RMS_u = \text{RMS}(u)/\text{RMS}(f_t)$. High values of RMS_e and RMS_u indicate bad tracking performance (large errors) and high control activity, respectively. It should be noted that $RMS_e < 1$ indicates successful error attenuation, while for $RMS_e > 1$ participants amplify errors and do worse than when no inputs u would have been given (for which $RMS_e = 1$). Furthermore, the e and u signals were used to estimate a model of participants' control dynamics using a time-domain fitting method, see (Lugtenborg, 2020) for details. For this, the model defined in Eq. (1) was used, which is a well-known model for describing control dynamics in compensatory, as well as pursuit, tasks with single integrator control dynamics (Mulder et al., 2018). Using this approach, we obtained estimates of a participant's control gain K_p , time delay τ , and neuromuscular damping ratio and natural frequency (ζ_{nms} and ω_{nms} , respectively) for all measurement trials.

$$H_p(s) = K_p e^{-s\tau} \frac{\omega_{nms}^2}{s^2 + 2\zeta_{nms}\omega_{nms}s + \omega_{nms}^2} \quad (1)$$

3. TREND ANALYSIS

3.1 Data preparation

Learning trend removal In this paper, the measured 50 trials of participant data are used as a 'symptom-free' reference for detecting (simulated) changes in motor performance representative for PD progression. While the pursuit task was designed to be learned quickly (Pool et al., 2022), and hence no strong learning trends were expected, any learning trend that still existed in our participants' data was removed for further analysis. Learning trends were detected by fitting a linear regression model (using MATLAB's *mvregress* function), which was subtracted from all measured metrics in case a significant linear trend was present. This correction was applied to 64%, 48%, 54%, 28%, 84% and 68% of the data for K_p , τ , ζ_{nms} , ω_{nms} , RMS_e , and RMS_u , respectively. Fig. 3 shows an example of the learning trend removal (for Participant 25, D) with a clear increasing trend in the measured K_p data (yellow) that is removed in the corrected data set (blue).

Participant inclusion criteria Prior to collecting the experiment data, we defined a set of inclusion criteria, see Table 3, for our participants' data to meet to be representative of measurements of healthy and motivated individuals. For example, participants were expected to achieve $RMS_e < 1$, i.e., better performance than would be achieved without providing any input (for which $RMS_e = 1$ by definition, see Section 2). Furthermore, for the cognitive functioning assessment using the MMSE, all participants were expected to score ≥ 26 (no cognitive decline, (Tombaugh and McIntyre, 1992)). Indeed, all our partici-

pants had an MMSE score of 26 or higher. Finally, reaction time and tapping performance metrics from the performed eye-hand coordination tests of De Boer (2015) contributed to the inclusion criteria. Of the 25 tested participants, only 15 (i.e., 60%) were found to meet our inclusion requirements. This group, in the remainder of this paper referred to as the '*high performance*' participants, had the same age range as the complete sample, however, the average age was almost three years younger ($\mu = 64.07$ years).

Table 3. Participant inclusion criteria.

Inclusion metric	Accepted range
RMS_e [-]	≤ 1
MMSE [-]	≥ 26
Reaction time simple tap [s]	≤ 0.4
Reaction time screen touch [s]	$0.8 \leq \delta \leq 1.2$
Reaction time space release [s]	$0.2 \leq \delta \leq 0.4$
Taps per second [-]	≥ 4

Table 4. Parameter ranges for Mild/Severe PD.

Parameter	Mild PD	Severe PD
K_p [-]	$-0.5 < \delta < 0$	$-0.9 < \delta < 0$
τ [s]	$0 < \delta < 0.02$	$0 < \delta < 0.07$
ζ_{nms} [-]	$0 < \delta < 0.2$	$0 < \delta < 0.31$
ω_{nms} [rad/s]	$0 < \delta < 3$	$0 < \delta < 5$

3.2 Data augmentation

For our analysis, the (corrected) measured data (50 trials) from all participants and both hands was augmented with 25 additional 'simulated' data points representative for PD symptoms, see Fig. 4. 25 augmented PD trials were chosen as a representative upper limit, after which symptoms would certainly be detected. The augmented data for K_p , τ , ζ_{nms} , and ω_{nms} were generated from each participant's measured data using bootstrapping methods (Chandler and Scott, 2011) and then offset with a bias δ that matched observed changes in PD (Pool et al., 2022). The corresponding RMS_e and RMS_u data were generated by simulating the tracking task with the augmented parameters in the human control model of Eq. (1). This considered sudden variation in PD symptom severity is representative for good and bad control days or the influence of treatment (i.e., 'on/off moments' (Lees et al., 2009)).

Two different severity ranges for the PD data offset δ were defined, representative of 'Mild' and 'Severe' motor skill loss. For these Mild and Severe cases, the parameter δ values were randomly selected from the ranges in Table 4, which are based on the average and most extreme early-stage PD data measured by Pool et al. (2022), respectively. Fig. 4 shows examples of the combined experimental and augmented data for the same K_p example data also shown in Fig. 3. In Fig. 4, the blue markers indicate the corrected measured data, while the green and red markers show Mild and Severe augmented data points, respectively.

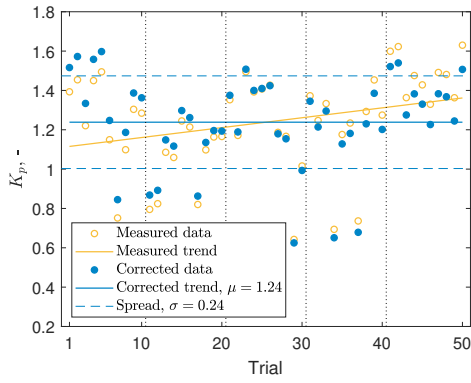


Fig. 3. Example of learning trend removal for K_p , Participant 25, D

3.3 Trend detection

Statistical trend analysis methods can be used to separate underlying behavioural patterns from noise (Chandler and Scott, 2011). For the application considered in this paper, monotonic trends are expected (i.e., a consistent decline in motor performance due to PD) in human control behavior metrics that will show considerable day-to-day variation (i.e., noisy data). For detecting monotonic trends in noisy data, the use of linear regression models as defined in Eq. (2) are generally preferred and most powerful (Chandler and Scott, 2011). In Eq. (2), y_t represents a control behavior metric sequence (e.g., K_p) across a certain time interval, the predictor variable x_t is the corresponding time variation, β_0 and β_1 are the regression's intercept and slope parameters, and ε_t represents the fit error. For our analysis, we fitted linear regressions to each metric separately using least squares estimation. A t-test was used to check if a significant linear trend was present, i.e., we tested the null hypothesis $H_0 : \beta_1 = 0$, which when rejected indicates that a significant trend exists.

$$y_t = \beta_0 + \beta_1 x_t + \varepsilon_t \quad (2)$$

For testing the sensitivity of this trend detection method we compare two cases: 1) a fixed data window size of 50 trials that moves over the augmented data set, and 2) a 'full' window size that always uses all available past data. For both cases, sensitivity is tested by incrementally moving over the simulated PD data per sample, giving a total of 26 different test windows. Examples of 'full' window size regressions over the complete augmented dataset (Window 26) are shown in Fig. 4. With a fixed window size the detection is less strongly biased by a large amount of baseline data (blue markers in Fig. 4), hence it is expected that an initial decline in performance is detected earlier. A more extensive analysis in (Lugtenborg, 2020), including smaller window sizes (which only provided negligibly quicker detection at reduced consistency), shows that the optimal fixed window size is 50 data points.

4. RESULTS

4.1 Healthy participant experiment data

Dominant and non-dominant hand control All participants performed the experiment with both their dominant

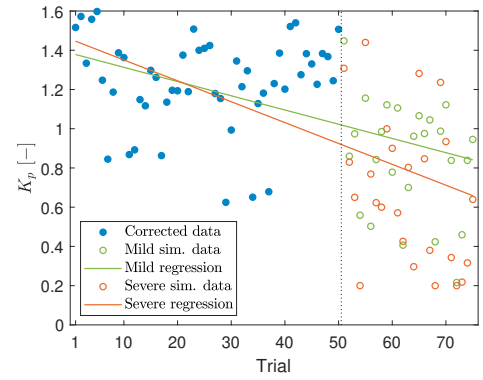


Fig. 4. Example of mild vs severe symptom trend analysis for K_p , Participant 25, D

(D) and non-dominant (ND) hands. As expected, significant differences ($p \leq 0.01$) were found between D and ND data for all metrics except τ and ω_{nms} . For ND control, increased K_p and reduced ζ_{nms} were found, while $RMSe$ and $RMSu$ both increased. Overall, these differences are consistent with the expected inferior motor performance for ND. For details, please refer to (Lugtenborg, 2020).

Day-to-day variation A crucial aspect of motor performance data that needs to be accounted for in disease progression is that all tracking task metrics will show considerable day-to-day variations, e.g., see Fig. 4. Table 5 shows an overview of the average (μ) and variation (σ) of the corrected data for all participants and metrics for dominant hand control (D). Despite the observed differences in control behaviour, the variation in all metrics for D and ND control is found to be equivalent. Table 5 shows that participants neuromuscular parameters (ζ_{nms}

Table 5. Measured mean and standard deviation for all metrics and all participants (D).

#	K_p [-]		τ [s]		ζ_{nms} [-]		ω_{nms} [rad/s]		$RMSe$ [-]		$RMSu$ [-]	
	μ	σ	μ	σ	μ	σ	μ	σ	μ	σ	μ	σ
1	0.90	0.20	0.33	0.12	0.33	0.15	6.6	3.7	1.03	0.20	1.33	0.26
2	1.39	0.26	0.30	0.06	0.25	0.10	11.1	3.1	0.77	0.13	1.38	0.18
3	0.12	0.10	0.35	0.22	0.08	0.08	10.8	7.5	2.07	0.57	1.19	0.38
4	0.23	0.16	0.48	0.31	0.08	0.09	8.6	6.8	3.39	1.23	2.22	0.56
5	1.00	0.31	0.46	0.19	0.32	0.20	7.0	4.3	1.73	0.29	2.63	0.50
6	0.62	0.25	0.38	0.17	0.50	0.21	8.2	5.0	1.38	0.30	1.15	0.25
7	0.75	0.24	0.47	0.15	0.41	0.24	10.8	7.2	1.41	0.38	1.41	0.20
8	0.95	0.33	0.45	0.16	0.32	0.20	8.9	3.3	1.58	0.34	2.02	0.22
9	1.18	0.27	0.36	0.07	0.30	0.20	10.5	3.3	1.05	0.34	1.60	0.24
10	1.14	0.24	0.25	0.06	0.65	0.20	10.1	2.7	0.84	0.13	1.17	0.12
11	0.88	0.54	0.31	0.14	0.51	0.31	8.5	5.0	1.13	0.16	1.60	0.19
12	0.46	0.24	0.43	0.22	0.42	0.31	8.3	6.0	1.56	0.29	1.17	0.21
13	1.05	0.17	0.31	0.07	0.52	0.17	6.2	1.9	0.87	0.10	1.15	0.09
14	0.50	0.34	0.54	0.29	0.15	0.12	6.7	5.4	2.24	0.48	2.06	0.57
15	0.74	0.23	0.28	0.09	0.42	0.21	10.2	4.6	1.24	0.19	1.21	0.13
16	0.75	0.36	0.34	0.14	0.52	0.28	9.1	5.8	1.29	0.22	1.33	0.28
17	0.44	0.22	0.56	0.28	0.21	0.14	6.6	6.1	2.46	0.84	2.25	0.44
18	1.36	0.16	0.24	0.11	0.47	0.16	8.3	3.7	0.72	0.08	1.24	0.14
19	1.20	0.18	0.31	0.07	0.35	0.13	8.5	2.9	0.85	0.20	1.27	0.16
20	1.07	0.14	0.28	0.11	0.40	0.15	7.4	3.2	0.87	0.07	1.23	0.12
21	1.34	0.31	0.28	0.06	0.60	0.20	9.3	2.8	0.94	0.14	1.47	0.15
22	0.92	0.27	0.40	0.13	0.45	0.25	10.4	3.7	1.40	0.36	1.62	0.20
23	1.33	0.32	0.33	0.12	0.45	0.22	8.4	3.5	0.96	0.16	1.54	0.23
24	1.22	0.39	0.39	0.14	0.28	0.13	5.5	2.7	1.32	0.23	2.53	0.69
25	1.24	0.24	0.29	0.06	0.56	0.19	11.9	3.7	0.79	0.09	1.15	0.15
μ	0.91	0.26	0.37	0.14	0.38	0.19	8.7	4.3	1.36	0.30	1.56	0.27
%		28.4		38.8		48.9		49.5		22.2		17.1

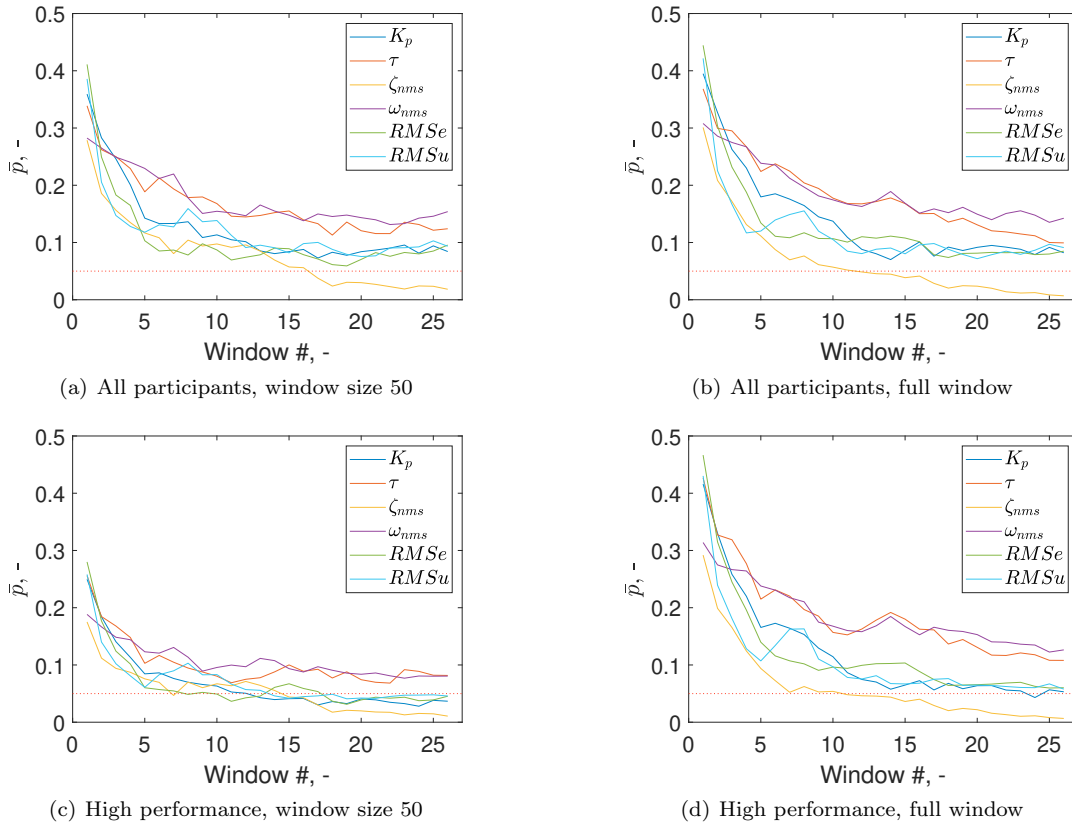


Fig. 5. Average trend detection p -values as a function of data window number for both a fixed window size of 50 and the ‘full’ window, and for all participants as well as only the high-performance group (‘Severe’ dataset).

and ω_{nms}) show the largest day-to-day variation of nearly 50% compared to their means. On average, RMS_e (22%) and RMS_u (17%) show the least day-to-day variation.

4.2 Trend analysis

Metric sensitivity Based on the equivalent day-to-day variation observed in the D/ND data, both sets of data were used for our analysis of trend analysis sensitivity. Furthermore, for brevity, this section will mostly focus on the ‘Severe’ augmented PD dataset, see Section 3.2. Table 6 shows the percentage of cases where a significant trend was detected in the full augmented dataset for the different metrics, both across all participants and the ‘high performance’ group. Table 6 shows that except for ω_{nms} a significant trend was detected in at least 50% of participants. In earlier research (Pool et al., 2022), especially K_p , ζ_{nms} and RMS_e showed clear differences between healthy controls and PD patients. Here, K_p and ζ_{nms} show the highest detection rates of 66% and 96%, respectively, when all participant data is considered; numbers that increase to 77% and 97% for the ‘high performance’ group. However, in our analysis, only 34% of the analyzed augmented data sets showed a significant trend in all three PD-related metrics. In future work, we plan to improve on the overall sensitivity of the trend detection using more advanced (nonlinear) regression methods.

Trend analysis sensitivity To evaluate the trend detection’s sensitivity to picking up on a sudden transition in motor performance representative of PD, two differ-

Table 6. Percentage of participants with a trend ($p < 0.05$) for the ‘Severe’ dataset.

Parameter	K_p	τ	ζ_{nms}	ω_{nms}	RMS_e	RMS_u
All participants	66%	64%	96%	46%	50%	58%
High performance	77%	53%	97%	50%	53%	73%

ent ‘windowing’ approaches explained in Section 3.3 are compared. Fig. 5(a) and 5(b) show the average p -values for all 26 data windows across all participants when using a fixed window size of 50 samples and for an increasing ‘full’ window, respectively. Fig. 5(c) and 5(d) show the same results, but for the ‘high performance’ participants only. The dashed horizontal red lines in all figures mark the considered p -value significance threshold, i.e., $p \leq 0.05$. Consistent with Table 6, comparison of the different sets of results in Fig. 5 shows that K_p , ζ_{nms} , RMS_e , and RMS_u consistently have the lowest p -values and thus provide the most sensitive detection. When all participants are considered (Fig. 5(a) and 5(b)), the full window approach requires slightly less PD data points for \bar{p} to approach the significance threshold. When only the more consistent high-performance participants are considered, the added sensitivity of the fixed window size of 50 samples provides far superior results. For example, Fig. 5(c) shows that for K_p , ζ_{nms} , and RMS_e significant trends are detected at Window 6-10, i.e., after only 6-10 augmented PD data points are present in the 50-point detection window.

Symptom severity While so far not presented, both ‘Mild’ and ‘Severe’ augmented PD data-sets were gen-

erated as explained in Section 3.2. To show the trend detection method's sensitivity to symptom strength, Fig. 6 compares the detection p -values for both data-sets for the final 'full' window (i.e., across all 75 augmented data-set samples). The boxplots show the variation across participants and D/ND, while the dashed horizontal red line marks the significance threshold. Fig. 6 shows that for all metrics the trend detection is less effective (higher p -values) for the 'Mild' data. Especially K_p , τ , ζ_{nms} and ω_{nms} show notably lower p -values for the 'Severe' data, and trend detection that is much more consistent (less spread) between participants. Still, Fig. 6 shows that even for the 'Mild' data-set key metrics such as K_p and ζ_{nms} are sufficiently sensitive to detect deteriorated motor performance for the majority of tested samples.

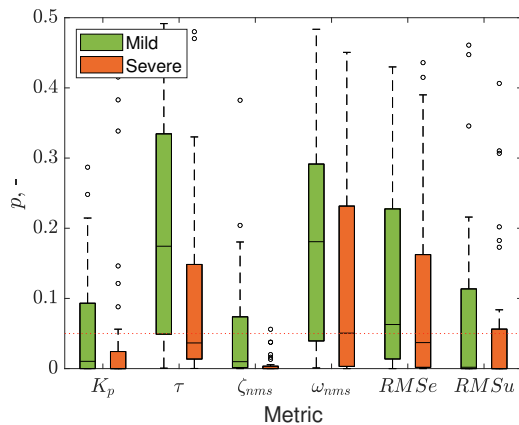


Fig. 6. Trend analysis p -values for 'Mild' and 'Severe' augmented PD data ('full' window of size 75, high-performance participants).

5. CONCLUSION

This paper presents a proof-of-concept for the application of trend analysis using linear regressions to detect changes in control behavior and motor performance data due to Parkinson's disease (PD). Based on pursuit tracking data collected from 25 healthy participants in the age range of 55-75 years, augmented data-sets of typical tracking task metrics (K_p , τ , ζ_{nms} , ω_{nms} , $RMSe$, and $RMSu$) including a simulated sudden degradation representative for 'Mild' and 'Severe' PD symptoms were generated. Using linear regression models for detecting these changes showed that for the control gain K_p , the neuromuscular damping ratio ζ_{nms} , and participants' tracking performance $RMSe$, a trend was detected in at least 50% of participant data-sets. Furthermore, for the more consistent ('high performance') participant data, using a sliding window with 50 data points for trend detection accuracy is most effective, resulting in significant trend detections after only 6-10 PD data-points. Finally, while detection accuracy was worse for the 'Mild' data-set compared the 'Severe', for specific metrics (e.g., K_p and ζ_{nms}) the approach was still reasonably effective. Overall, the proposed approach is capable of detecting behavioural changes in at least half of the population, which shows its potential for further development towards a diagnostic tool that would enable more objective and personalised disease assessment and symptom monitoring in PD patients.

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REFERENCES

- Büskens, J., Pel, J.J.M., and Pool, D.M. (2019). Effects of multisine signal bandwidth on eye movement dynamics. In *Proc. of the 14th IFAC Symp. on Analysis, Design and Eval. of Human-Machine Sys., Tallinn, Estonia*.
- Chandler, R. and Scott, E. (2011). *Statistical methods for trend detection and analysis in the environmental sciences*. John Wiley & Sons, Ltd, Chichester, UK.
- De Boer, C. (2015). *Visuomotor Integration in Neurodegenerative Brains*. Ph.D. thesis, Erasmus University Rotterdam, Neuroscience Department.
- De Lau, L. and Breteler, M. (2017). Epidemiology of Parkinson's disease. *J. of Neural Transmission*, 124(8).
- Flowers, K. (1976). Visual 'closed-loop' and 'open-loop' characteristics of voluntary movement in patients with Parkinsonism and intention tremor. *Brain*, 99(2).
- Gelb, D., Oliver, E., and Gilman, S. (1999). Diagnostic criteria for Parkinson's disease. *Archives of Neurology*, 56(1), 33–39.
- Goetz, C. (2012). Unified Parkinson's Disease Rating Scale (UPDRS) and Movement Disorder Society Revision of the UPDRS (MDS-UPDRS). In *Rating Scales in Parkinson's Disease: Clinical Practice and Research*. Oxford University press.
- Hufschmidt, A. and Lucking, C. (1995). Abnormalities of tracking behavior in Parkinson's disease. *Movement Disorders*, 10(3), 267–276.
- Jones, R. and Ivan, M. (1989). Tracking tasks and the study of predictive motor planning in Parkinson's disease. In *Proc. of the IEEE Engineering in Medicine and Biology Society Conference*, 1055–1056.
- Lees, A., Hardy, J., and Revesz, T. (2009). Parkinson's disease. *Lancet*, 373(9680), 2055–2066.
- Lugtenborg, L.A. (2020). *Identifying Behavioural Changes due to Parkinson's Disease Progression in Motor Performance Data*. Master's thesis, TU Delft.
- Mulder, M., Pool, D., Abbink, D., Boer, E., Zaal, P., Drop, F., van der El, K., and van Paassen, M. (2018). Manual control cybernetics: State-of-the-art and current trends. *IEEE Trans. on Human-Machine Sys.*, 48(5), 468–485.
- Oishi, M., Talebifard, P., and McKeown, M. (2011). Assessing manual pursuit tracking in Parkinson's disease via linear dynamical systems. *Annals of Biomedical Engineering*, 39(8), 2263–2273.
- Pool, D.M., De Vries, R.J., and Pel, J.J.M. (2022). Quantifying motor skills in early-stage parkinson's disease using human controller modeling. In *Proc. of the 15th IFAC Symposium on Analysis, Design and Evaluation of Human-Machine Systems, San Jose (CA), USA*.
- Soliveri, P., Brown, R., Jahanshahi, M., Caraceni, T., and Marsden, C. (1997). Learning manual pursuit tracking skills in patients with Parkinson's disease. *Brain*, 120(8).
- Tombaugh, T. and McIntyre, N. (1992). The mini-mental state examination: A comprehensive review. *Journal of the American Geriatrics Society*, 40(9), 922–935.