

Supplemental Digital Content 3:

Part 1 - Principle Component Analysis for Physical Function

Part 2 - Exponential Curve-Fitting

Part 3 - Mixed-Effects Regression Procedures

Predicting Motor Sequence Learning in People with Parkinson Disease

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Part 1 - Principal Component Analysis (PCA) for Physical Function

To obtain an estimate of participants' baseline physical function, the following variables were entered into a principal component analysis (PCA): off-medication MDS-UPDRS scores, mean self-selected gait speed, mean fast gait speed, mean 4SST time, and mean mini-BEST score. Visual inspection of a "scree" plot showed one principal component with an Eigenvalue >1 . Referred to as *PC1*, this principal component had a total Eigenvalue of 2.93, explaining 58.59% of the initial variance (the other Eigenvalues were, $PC2 = 0.78$, $PC3 = 0.69$, $PC4 = 0.43$, $PC5 = 0.17$). The component matrix showed that mean fast gait speed positively loaded on *PC1* ($r = 0.89$), as did mean self-selected gait speed ($r = 0.87$) and mean mini-BEST scores ($r = 0.67$); off-medication MDS-UPDRS scores ($r = -0.70$) and mean 4SST negatively loaded on *PC1* ($r = -0.66$). As such, the latent variable of *PC1* appears to be a reliable measure of physical function, with more positive *PC1* values indicating better physical functioning across a range of scales. The inter-relationships among the constituent measures, and their relationship to physical function is shown in Figure S3-1.

We conducted regression analyses to examine the effects of *PC1* on response times at Retention 1 and Retention 2, in order to check the validity of the relationship between *PC1* and the SRTT. Among the included participants (repeating $n=23$, random $n=19$), for both random and repeating sequences, less impaired participants (higher *PC1* scores) showed significantly faster response times on both retention tests and the pretest. In sum, *PC1* appears to be a valid measure of physical function (given the number of measures of physical function that load on this factor) and the SRTT is sensitive to individual differences in physical function (given the relationship between SRTT performance and *PC1* scores).

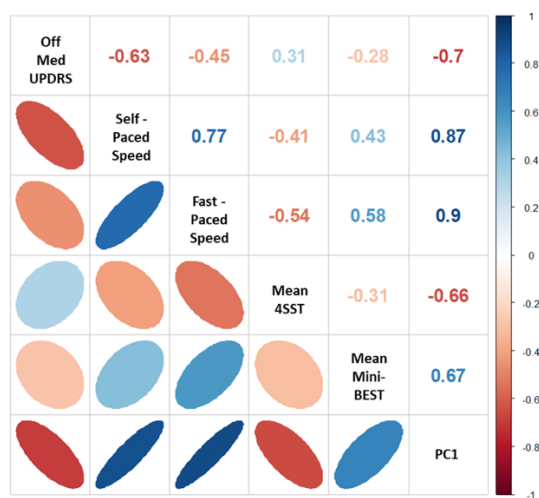


Figure S3-1. Correlation matrix showing the relationship between all of the constituent measures and the first principal component, *PC1*. The off-left diagonal shows the 95% confidence ellipse and the off-right diagonal shows the correlation coefficient (Pearson's r) for each bivariate comparison. Mini-BEST: Mini Balance Evaluation Systems Test. 4SST: Four Square Step Test. Self-paced speed and fast-paced speed refer to gait speeds, respectively. UPDRS: Movement Disorders Society sponsored version of the Unified Parkinson Disease Rating Scale (referred to in the manuscript as *MDS-UPDRS*).

Part 2 - Explanation of Exponential Curve-Fitting Procedures

Three parameter exponential curves were fit using the dose-response analysis package of Ritz, Baty, Streibig, & Gerhard (2015), specifically the “*drm()*” function. Parameters in the function are estimated based on the minimization of the negative log-likelihood. Models were fit separately for the random and repeating sequences, with average response time as a function of total trial number (across all days). This excluded the first block of trials (trials 1-6) which were considered pretest performance for each participant. Thus, trial numbers ran from 7-108.

Data Exclusions

To understand the reasons for our exclusions, it is helpful to understand how the exponential decay parameters relate to one another. The typical skill acquisition pattern of rapid performance improvement during early practice followed by eventual stable performance, is shown in Figure 1C of the manuscript, and is reliably modelled by a negative decay constant, R (also referred to as the *acquisition rate* parameter in the manuscript), and a positive change constant, C . In this typical case, the negative sign of the decay constant, R , is correctly interpreted as exponential decay; however, if the sign of the change constant, C , is switched from positive to negative, then the same negative decay constant, R , should then be interpreted as exponential growth (the resultant curve can be visualized by inverting Figure 1C's curve over a horizontal axis). Therefore, the correct interpretation of the decay constant, R , depends on the sign of the change constant, C .

For the exponential curves, the model failed to converge for one participant's random-sequence curve, and another participant's decay parameter was an extreme outlier (with a value of essentially zero, it was >25 standard deviations different from the other scores). As such, both participants were excluded from the random sequence analyses. Furthermore, exponential curves actually showed negative change for 4 participants' performance on repeating trials and 6 participants' performance on random trials. Because the interpretation of the decay constant, R , depends on the sign of the change constant, C , we excluded these participants from the mixed-effects regressions so that all analyses focused on participants who improved over time. Importantly, these exclusions also make our analyses more similar to past work by Wadden et al.¹ Interestingly, Wadden et al. did not report any exclusions or adjustments to their decay/change constants, suggesting that all participants reliably improved over time in that study. It is not clear exactly why our change curves would differ from Wadden et al., but our sample was drawn from a different population (PD versus stroke) and our task had different demands (a lower extremity standing postural stepping serial reaction time task versus a seated upper extremity continuous tracking task). Therefore, multiple factors (e.g., task difficulty, “fatigue,” and a different patient population with different impairments) could contribute to these different skill acquisition patterns. However, in order to make the interpretation of our decay constants comparable to Wadden et al., we decided to exclude participants whose performance worsened during practice.

Part 3 - Mixed-Effects Regression Models

We tested a series of mixed-effects regression models, separately, for both the repeating sequence and random sequences. Models were compared based on the Akaike's Information Criterion (AIC) with an a priori threshold of a two-point reduction of the AIC. In the event that two models fell within the two-point threshold, the simpler model was chosen as the better explanation of the data. The dependent variable for all models was the difference between pretest performance and performance on retention tests. This difference score was chosen to represent learning given the high correlation between pretest and retention tests ($r_{\text{rand}} = 0.84$, $r_{\text{repeat}} = 0.87$), and the correlation between pretest performance and PC1 ($r_{\text{rand}} = 0.68$, $r_{\text{repeat}} = 0.67$). This multicollinearity meant that pretest performance and PC1 could not be included as predictors in the same model; thus the difference score approach was preferable. Details of the fixed-effects and random-effects for each of the models are presented below:

- **Model 01:** Random-effect of subject. Fixed-effect of retention test (Retention 1 versus Retention 2).
- **Model 02:** Random-effect of subject. Fixed-effects of retention test and PC1.
- **Model 03:** Random-effect of subject. Fixed-effects of retention test, PC1, and decay rate (R).
- **Model 04:** Random-effect of subject. Fixed-effects of retention test, PC1, decay rate (R), and medication status (ON medication versus OFF).
- **Model 05:** Random-effect of subject. Fixed-effects of retention test, PC1, decay rate (R), and all two-way and three-way interactions.

All variables were either contrast-coded (if categorical) or mean-centred (if continuous) prior to analysis. As such, the intercept represents the average amount of learning (i.e., the change from pretest to retention tests) and a statistically significant positive intercept indicates significant learning (see Table 2 in the manuscript). Model fit statistics for the repeating sequence are shown in Table S3-2 and model fit statistics for the random sequences are shown in Table S3-3. All models were fit using maximum-likelihood estimation.

Table S3-2. Model fit statistics for the repeating sequence.

Model	Deviance	AIC	df	RanEff SD	Residual SD
M01	-102.31	-94.31	4	0.096	0.044
M02	-104.84	-94.84	5	0.090	0.044
M03*	-108.70	-96.98	6	0.082	0.044
M04	-109.96	-95.96	7	0.079	0.044
M05	-115.43	-95.43	10	0.082	0.039

The asterisk (*) denotes the best fitting model based on the change in the AIC. "RanEff SD" is the standard deviation for the random effect of subject. "Residual SD" is the standard deviation of the model's residuals (i.e., random errors).

Table S3-3. Model fit statistics for the random sequences.

Model	Deviance	AIC	df	RanEff SD	Residual SD
M01	-97.87	-89.87	4	0.100	0.031
M02	-100.37	-90.37	5	0.093	0.031
M03	-102.00	-90.00	6	0.089	0.031
M04*	-106.51	-92.51	7	0.079	0.031
M05	-103.70	-83.70	10	0.089	0.030

The asterisk (*) denotes the best fitting model based on the change in the AIC. “RanEff SD” is the standard deviation for the random effect of subject. “Residual SD” is the standard deviation of the model’s residuals (i.e., random errors).

References

1. Wadden KP, Asis K, Mang CS, et al. Predicting Motor Sequence Learning in Individuals With Chronic Stroke. *Neurorehabil Neural Repair*. 2017;31(1):95-104.