Title

Retention of touchscreen skills is compromised in Parkinson's disease

Authors

Evelien Nackaerts,^a Pieter Ginis,^a Elke Heremans,^a Stephan P. Swinnen,^{b, c} Wim Vandenberghe,^{d, e} Alice Nieuwboer^{a, c}

Affiliation

- a. Research Group for Neurorehabilitation (eNRGy), Department of Rehabilitation Sciences, KU Leuven, Tervuursevest 101, box 1501 Leuven, Belgium
- b. Movement Control & Neuroplasticity Research Group, Department of Movement Sciences, KU Leuven, Tervuursevest 101, box 1501, Leuven, Belgium
- c. Leuven Brain Institute (LBI), KU Leuven, Leuven, Belgium
- d. Department of Neurology, University Hospitals Leuven, Herestraat 49, Leuven, Belgium
- e. Laboratory for Parkinson Research, Department of Neurosciences, KU Leuven, O&N IV Herestraat 49, box 602, Leuven, Belgium

E-mail addresses

evelien.nackaerts@kuleuven.be; pieter.ginis@kuleuven.be; elke.heremans@uhasselt.be;

stephan.swinnen@kuleuven.be; wim.vandenberghe@uzleuven.be; alice.nieuwboer@kuleuven.be

Corresponding author

Evelien Nackaerts

Department of Rehabilitation Sciences

KU Leuven, Belgium

Tervuursevest 101, box 1501, B-3000 Leuven, Belgium

E-mail: evelien.nackaerts@kuleuven.be

Telephone: +32 16 32 93 60

Abstract

Fine motor skill impairments likely have a severe impact on the use of touchscreens in Parkinson's disease (PD). Although recent work showed positive effects of intensive writing training, many questions remained regarding the consolidation of motor learning in PD. The current study examined the effects of PD on practicing the manipulation of touchscreen technology and whether this can lead to 24h-retention and transfer. We developed the Swipe-Slide Pattern (SSP)-task, similar to handling a touchscreen unlock-trace. On day 1, 11 patients and 10 healthy, age-matched controls underwent two consecutive runs of early and late learning (9 x 36 s SSP and 36 s rest). This was followed by a retention test after 24 hours, including the assessment of transfer. Movement time (MT, s), Euclidean distance (ED) and a performance index ($PI=MT/ED$) were compared across the learning phases (early, late, retention and transfer) for both groups. Additionally, a learning, retention and transfer index were compared between groups and correlated to clinical characteristics. Both groups significantly improved in MT and PI across practice. However, while healthy adults showed further improvements after a 24h-retention period, patients presented with impaired retention indices. This was correlated with disease duration, disease severity and performance on a daily life mobile phone task. Finally, transfer to a similar, but untrained pattern was comparable between both groups. Overall, short-term practice of the SSP-task results in improvements for PD patients, albeit with impaired retention. Future work should investigate whether prolonged touchscreen skill training can be retained in motor memory in PD.

Keywords

Parkinson's disease; motor learning; upper limb; retention; transfer

Abbreviations

COV = coefficient of variation; DextQ-24 = Dexterity questionnaire; ED = Euclidean distance; HC = Healthy control; H&Y = Hoehn & Yahr stage; LED = Levodopa equivalent dose; MDS-UPDRS-III = Movement Disorders Society Unified Parkinson's Disease Rating Scale part III; MMSE = Mini-mental state examination; MoCA = Montreal cognitive assessment; MSL = Motor sequence learning; MT = Movement time; MWU = Mann-Whitney U test; PD = Parkinson's disease; PI = Performance index; SSP-task = Swipe Slide Pattern task; VAS = Visual analogue scale

1 Introduction

Rehabilitation forms an important part of therapy for patients with Parkinson's disease (PD) [1], a neurodegenerative disorder mainly affecting the basal ganglia. However, as the basal ganglia, and particularly the striatum, are involved in motor learning, it is not surprising that the ability to learn and refine motor skills is impaired in PD [2, 3]. In healthy adults the associative striatum and its connections are recruited during the early phase of learning [4-8]. In contrast, the sensorimotor network involving dorsolateral putamen is engaged in the consolidation of motor learning [4-8]. This sensorimotor network is already impaired early on in PD [9-11], suggesting that consolidation may be affected. Retention and transfer are two aspects of consolidation, resp. defined as the ability to sustain improvements over time without practice and the capacity to apply the learned skill to a similar but untrained motor task. So far, researchers in PD investigated motor learning abilities mostly using either visuomotor adaptation or motor sequence learning (MSL) paradigms yielding differing results. For visuomotor adaptation tasks, studies consequently showed that retention is impaired in PD despite preserved initial learning [3, 12-15]. For MSL, the literature is less consistent. The majority of studies confirmed that initial learning is relatively intact in PD [16-23]. Some difficulties are present in early learning [24, 25], though this is likely the result of the degree of cognitive demand required for the MSL task. Contrary to visuomotor adaptation, retention of MSL was maintained in both patients and healthy controls when tested after 24 h [21, 24]. However, approximately 1 year after training, retention was impaired in PD, specifically in those with further striatal degeneration [26]. Skill transfer has been shown to be successful in PD patients, though to a smaller extent as for healthy elderly and primarily when the transfer test occurs under the same conditions as training [27, 28]. Overall, these results illustrate the task-specificity of motor learning.

In this study, we investigated the impact of PD on the retention and transfer of a novel motor skill directly relevant for daily life, namely performing tasks on a touchscreen that resembles smartphone or tablet use, thereby requiring dexterity. We defined dexterity in accordance with the International Classification of

Functioning, Disability and Health (ICF) as “fine hand use, performing the coordinated actions of handling objects, picking up, manipulating and releasing them using one's hand, fingers and thumb, such as required to lift coins off a table or turn a dial or knob” [29]. The preservation of dexterity is not trivial for PD patients [30, 31] and becomes more vital with the increasing importance of smartphone applications for both patient follow-up [32-35] and rehabilitation [36, 37]. Though the ability to use smartphones in PD is often assumed [38], it was shown that impaired dexterity hinders the interaction of patients with touchscreen handheld devices [39]. Moreover, if PD patients will need to use mobile-health technology successfully in the future, the robust acquisition of these skills needs to be addressed in rehabilitation programs. Hence, we aimed to understand the impact of PD on touchscreen skill learning. Therefore, we developed the Swipe-Slide Pattern (SSP)-task, in which participants have to learn a sequence of continuous swiping/sliding movements. We hypothesized that both healthy adults and PD patients would be able to learn the SSP-task, but that 24h-retention and transfer would be more compromised in PD. We also predicted that disease severity would be associated with these difficulties.

2 Methods

2.1 Participants

Eleven PD patients and 10 healthy, age-matched controls (HC) were tested. Inclusion criteria for PD patients were: diagnosis of PD according to the United Kingdom PD Society Brain Bank criteria [40]; Hoehn and Yahr (H&Y) stage I to III in the on phase of the medication cycle with right-sided impairment for patients in H&Y I [41]; and Mini-Mental State Examination (MMSE) ≥ 24 [42]. The exclusion criteria for both groups were: upper-limb problems other than those related to PD; other medical or psychiatric disorders that could interfere with the protocol; and people who play games on a touchscreen-operated device on a daily basis. All patients were tested in the on phase of the medication cycle (± 1 h after medication intake). The study design and protocol were approved by the local Ethics Committee of the

KU Leuven and were in accordance with the code of Ethics of the World Medical Association (Declaration of Helsinki, version 2013). After complete explanation of the study protocol, written informed consent was obtained from all participants prior to participation in the study.

2.2 Experimental procedure

All participants underwent a two-day testing procedure with practice of the Swipe-Slide Pattern (SSP) task. On day 1, two consecutive runs were performed, each consisting of nine task blocks (each 36 s) and an equal amount of rest. On day 2, all participants had a 24h-retention test, consisting of: (i) a run containing the learned pattern (6 blocks); and (ii) a run including a new pattern to assess transfer (9 blocks). All participants were tested at the same time of day on both test days. At the end of each day, participants indicated fatigue caused by the SSP-task on a visual analogue scale (VAS).

On day 1, all participants additionally underwent a set of cognitive and motor skill tests, including the MMSE, Montreal Cognitive Assessment (MoCA) [43], Dexterity questionnaire (DextQ-24) [44] and a mobile phone task. For the latter, participants had to tap a pre-defined telephone number on a standard smartphone and the required amount of time to complete the task was measured. Three trials were performed. Disease characteristics were evaluated using H&Y staging [41] and the Movement Disorders Society Unified Parkinson's Disease Rating Scale part III (MDS-UPDRS-III) [45] on medication. Finally, the levodopa equivalent dose (LED) was calculated.

2.3 Swipe-Slide Pattern (SSP) task

The SSP-task required finger movements to unlock a touchscreen device. Participants learned a pre-defined pattern, visible in the upper left corner of the screen during actual task performance to reduce cognitive load (**Figure 1**). Additionally, participants were able to see the lines they were drawing. The pattern began in the middle of a nine-circle configuration and consisted of connecting six different circles. Participants were instructed to form the patterns as quickly and accurately as possible. To avoid over-

emphasis on accuracy and to obtain fluent movements, the minimal requirement was to touch the within-circle surface. Hence, participants were not required to make movements from the exact center of one circle to the exact center of the next circle. Also, participants were told to move their hand without lifting the finger stylus from the screen to maintain the online trace and to return to a fixed starting point (i.e. the middle circle) when the pattern was completed. After reaching the starting point again, the pattern was erased and participants continued making the same pattern for the duration of the trial (36 s). The SSP-task was performed on a custom-made tablet, incorporating a resistive touchscreen in a 4-wire set-up (Fujitsu Components Europe, Hoofddorp, The Netherlands). Unpublished pilot work in healthy young adults revealed measurement errors when using the set-up without a finger stylus. Hence, a commercially available finger stylus (Nintendo®) was used to standardize performance (**Figure 1**).

2.4 Data processing and statistical analysis

A touch-sensitive tablet (13 x 10 cm) was used to record xy-coordinates at a sampling rate of 200 Hz and with a spatial resolution of 32.5 μm . Patterns were filtered at 7 Hz with a 4th-order Butterworth filter and further processed using MATLAB R2016b (The Mathworks, Natick, Massachusetts, USA). A visual inspection for correctness was also implemented. Our primary outcome measure was the time necessary to complete the pattern, i.e. movement time (MT, s). In addition, the Euclidean distance (ED), i.e. the deviation between the ideal pattern and the pattern formed, was calculated as a measure of accuracy. For both MT and ED, a coefficient of variation (COV, %) was determined by dividing the within-subject standard deviation by the average. Secondly, a performance index (PI), taking into account both movement time and accuracy, was computed, with a lower PI indicating better performance. Finally, to capture the learning process across time, three metrics were calculated for MT, ED and PI in analogy with the work of Manuel *et al.* [13].

1. The learning index, representing the acquisition phase: $\frac{(Late - Early)}{Early} \times 100$

2. The retention index, characterizing 24h-offline learning: $\frac{(Retention-Late)}{Late} \times 100$
3. The transfer index, signifying transfer of learning: $\frac{(Transfer-Late)}{Late} \times 100$

For all three indices, a negative value indicates improvements.

We excluded one patient from further analysis, as this patient regularly touched the screen with the other fingers while performing the task with the right index finger, rendering the data inadequate for processing.

Data were analyzed using SPSS software (version 24 SPSS, Inc., Chicago, IL, USA) with significance levels of $\alpha < 0.05$. Depending on the data distribution and equality of variances, either a parametric independent samples t-test or non-parametric Mann-Whitney U (MWU)-test was performed to compare general characteristics, baseline performance on the SSP-task (i.e. block 1) and baseline performance on the mobile phone task between both groups. For gender, a Chi-squared test was performed. Spearman correlations were used to correlate baseline performance on the SSP-task and mobile phone task with each other and with clinical characteristics (age, MoCA, DEXTQ-24, disease duration, LED and MDS-UPDRS-III). The learning, retention and transfer index of MT, ED and PI were compared between patients and controls using a MWU-test and Spearman correlations were used to correlate these to clinical characteristics (age, MoCA, DEXTQ-24, disease duration, LED and MDS-UPDRS-III) and to baseline performance on the mobile phone task. Finally, a repeated measures ANOVA was performed, with group as a between-subject factor (PD or HC) and time as a within-subject factor (early learning (block 1-9), late learning (block 10-18) and retention (block 19-24)) to assess retention effects. For transfer, a mixed model ANOVA was performed with between-subject factor group (PD or HC) and within-subject factor test (retention or transfer). Both analyses were done for MT, ED, COV_{MT} , COV_{ED} and PI. As the sphericity assumption was violated for the repeated measures ANOVA, Greenhouse-Geisser corrected p-values are reported. In case of significant differences, post hoc analyses were carried out using Bonferroni tests.

3 Results

3.1 Participants

Demographics and clinical characteristics are specified in **Table 1**. Patients and healthy controls did not differ significantly, except for a higher score on the DEXTQ-24 in PD patients, indicating worse fine motor skills ($Z = -3.732; p < 0.001$).

3.2 Baseline performance

Baseline performance on the SSP-task did not differ between PD patients and HC (**Table 1**). Performance on the mobile phone task, however, was worse in PD patients ($Z = -2.345; p = 0.019$) (**Table 1**). Exploring the validity of the touchscreen outcomes, there was a trend toward a correlation between a slower performance (i.e. higher MT) on the SSP-task and a slower performance of the mobile phone task across participants ($r_s = 0.403; p = 0.078$). Moreover, in PD patients, a slower performance and worse accuracy of the SSP-task correlated with a higher score on the MDS-UPDRS-III (i.e. worse disease severity) (*resp.* $r_s = 0.788; p = 0.007; r_s = 0.652; p = 0.041$).

3.3 Learning the SSP-task in PD and HC

3.3.1 From early learning to retention

Repeated measures ANOVA revealed a main effect of time for MT, COV_{MT} and PI (*resp.* $F = 22.635, p < 0.001; F = 12.103, p = 0.001; F = 18.288, p < 0.001$) (**Figure 2**). Post hoc analyses revealed that both from early to late learning and from early learning to retention participants showed a decrease in MT (both $p < 0.001$), COV_{MT} (*resp.* $p < 0.001$ and $p = 0.095$) and PI (both $p < 0.001$), suggesting better performance. There were no further changes from late learning to retention.

For PI, there was a strong tendency towards an interaction between group and time ($F = 3.075; p = 0.063$). Exploratory post hoc analyses showed a decrease in PI in HC from early learning to late learning

($p = 0.013$) and to retention ($p = 0.001$), with a tendency to further decrease from late learning to retention ($p = 0.099$), suggesting better performance. In PD patients, PI decreased from early to late learning ($p = 0.001$), though there was only a tendency towards a decrease from early learning to retention ($p = 0.059$) and no difference between late learning and retention ($p = 0.952$). Additionally, only at retention PD patients tended to have a higher PI than HC ($p = 0.082$). Details on all non-significant main and interaction effects can be found in **Suppl. Table A1**.

The number of patterns formed throughout training and fatigue at the end of training on day 1 did not differ between groups (resp. **Suppl. Table A2 & A3**).

3.3.2 From retention to transfer

The mixed model ANOVA revealed a main effect of test for ED, COV_{ED} , COV_{MT} and PI (resp. $F = 7.853$, $p = 0.012$; $F = 6.351$, $p = 0.021$; $F = 9.352$, $p = 0.007$; and $F = 6.221$, $p = 0.023$) (**Figure 3**). Results revealed that participants performed the pattern more accurately and with less variability in MT and ED during retention compared to transfer. However, the PI was higher during the retention test, suggesting worse overall performance. Details on all non-significant main and interaction effects can be found in **Suppl. Table A1**.

3.4 The SSP-task across time - Indices

The MWU-test comparing PD patients and HC revealed no significant difference for either the learning or transfer index (see **Suppl. Table A4**). For the retention index on the other hand, a deterioration was found for both MT and PI in PD patients compared to HC (resp. $Z = -2.343$, $p = 0.019$; $Z = -2.343$, $p = 0.019$) (**Figure 4A-B**), confirming the above described difficulties with retention in PD. For ED no significant differences were found (see **Suppl. Table A4**).

The correlation analysis revealed a slower performance on the mobile phone task correlated with a higher retention index for both MT (**Figure 4C**) and PI, suggesting worse retention, across participants (resp. $r_s =$

0.531; $p = 0.016$; $r_s = 0.513$; $p = 0.021$). In patients, a longer disease duration correlated with a higher MT-retention index ($r_s = 0.884$; $p = 0.001$). Additionally, a higher score on the MDS-UPDRS-III, suggesting worse disease severity, correlated with a higher PI-retention index ($r_s = 0.720$; $p = 0.019$) (Figure 4D).

For the transfer index, similar correlations were found. A slower performance on the mobile phone task correlated with a higher transfer index for MT and PI, i.e. worse transfer, across participants (*resp.* $r_s = 0.670$; $p = 0.001$; $r_s = 0.457$; $p = 0.043$). Additionally, a higher score on the MDS-UPDRS-III correlated with a higher MT-transfer index ($r_s = 0.770$; $p = 0.015$).

No correlations were found with age, cognitive test outcomes, manual dexterity or LED.

4 Discussion

We investigated whether PD patients were able to perform and learn a swiping pattern similarly to age-matched healthy controls. Overall, both groups were equally able to perform the SSP-task and showed similar early learning. However, patients presented with impaired retention indices, while HC showed further improvements after a 24h-retention period. The retention deficits in PD were correlated with disease duration, disease severity and performance on the mobile phone task, i.e. tapping a telephone number. Surprisingly, transfer to a similar, but untrained pattern, was comparable between groups. Worse transfer was, however, related to a more severe disease and compromised performance on the mobile phone task.

4.1 Impaired retention in PD

The current study revealed that while healthy elderly maintained and even improved their performance on the SSP-task after 24 hours, PD patients did not. This is in line with previous studies investigating visuomotor adaptation learning in PD [3, 12-15]. Moreover, difficulties with retention were related to a

longer disease duration and worse disease severity, similar to what was found by Manuel *et al.* [13]. Contrary to other MSL studies [21, 24, 26], retention was compromised in our study. This can be attributed to the difference in task specifications, as the SSP-task combined characteristics from MSL with a strong visuomotor coupling, as is required in visuomotor adaptation studies. As such, participants did not learn a sequence of discrete finger movements, but rather a pattern requiring a continuous finger movement while making use of visuomotor processing. Hence, the SSP-task reflected a degree of complexity relevant for daily life touchscreen use. Despite its relative complexity, it is unlikely that the observed retention difficulties can be attributed to cognitive load, as the required pattern was visible at all times during task performance and therefore not dependent on memory. Moreover, no correlations were found between the retention index and cognitive tests, though this may be attributed to the fact that we did not include patients with cognitive impairments. Future research should include a broader patient sample to investigate the influence of cognition on the SSP-task into more depth. Worse retention was correlated with a poorer baseline performance of the mobile phone task, supporting the idea that the SSP-task is relevant for picking up learning deficits of smartphone use. Importantly, differences in retention between PD and HC cannot be ascribed to a difference in amount of training or fatigue at the end of practice on day 1, as the number of patterns during learning and VAS scores did not differ significantly between groups.

4.2 Preserved acquisition and transfer in PD

In line with our hypothesis and some previous studies [13-23], we found that both PD patients and HC were equally able to learn the SSP-task. Research has shown that patients likely use compensatory attentional networks to achieve this [22, 23]. Moreover, both patients and HC exhibited transfer to an unknown pattern, though this was accompanied by greater variability in performance. This greater variability may have prevented us from obtaining significant differences, as our study was at risk for generating false negatives due to the small sample size. So far, the literature mainly documented impairments of transfer in PD indicating loss of flexible application of what was learned [27, 28]. However,

PD patients did show transfer for a functional reach task depending on the context [27] and from cued to uncued handwriting [46]. However, transfer from practiced writing exercises to daily life was limited and no comparison was made with healthy elderly [46]. Overall, these differences in the literature are likely the result of the type of transfer that was tested. Finally, our correlation analysis revealed that transfer is more limited in patients with a worse disease severity and poorer baseline performance on the mobile phone task, as possible markers of reduced flexibility to adapt motor skills. This is analogous to what we found for retention and suggests consolidation problems as the disease progresses. Future research is therefore necessary to clarify transfer capacities in PD and how basal ganglia pathology contributes to this.

4.3 Impaired touchscreen use in PD

Finally, we explored difficulties in using touchscreens in PD. Patients performed worse on the mobile phone task compared to healthy elderly. Although the SSP-task assesses different aspects of touchscreen use, there was a strong tendency towards a correlation between both tasks. The use of the finger stylus during the SSP-task may have improved movement accuracy and fluency for PD patients, thereby concealing difficulties experienced in daily life. Nevertheless, SSP performance was related to disease severity, though a larger sample size across disease stages is required to substantiate our findings and assess the impact of these deficits in daily use of touchscreens. What is more, it will be interesting to capture these deficits in future generations of patients, who have learned and automatized touchscreen skills at an earlier age.

4.4 Study limitations

The results of this study need to be interpreted against the risk of type II errors due to sample size. Nevertheless, we found significant and consistent results pointing to retention deficits in an ecological task. Patients were tested in the optimally medicated state. While this best reflects daily life situations, research has shown that dopaminergic medication can influence motor learning [47-49]. Finally, the SSP-

task focused on the motor skills required to navigate an unlock-trace screen of a smartphone. However, many more skills are required for daily use such as finger pressure, repetitive sliding, cognitive switching and multitasking. All of these skills need careful future study to truly understand the impact of PD on touchscreen utilization.

5 Conclusion

Overall, results of the current study support previous findings that the initial stages of motor learning are relatively preserved in PD and further extend the knowledge on retention impairments using a task that is relevant for daily use of a smartphone. Future work should address whether prolonged touchscreen skill training can improve retention capacities in PD.

6 Acknowledgments

We want to express our gratitude to all participants in this study. We thank Ir. Marc Beirinckx for developing the tablet and providing technical support and Dorien Hunin for contributing to data processing.

7 Funding

E. Nackaerts is a postdoctoral researcher funded by the KU Leuven research fund [grant number PDM/17/197] and Research Foundation Flanders – FWO [grant number 12F4719N]. W. Vandenberghe is a Senior Clinical Investigator of the FWO. This project was supported by the Fund Druwé-Eerdeken [grant 2018] of the King Baudouin Foundation.

8 References

1. Abbruzzese, G., et al., *Rehabilitation for Parkinson's disease: Current outlook and future challenges*. Parkinsonism Relat Disord, 2016. **22 Suppl 1**: p. S60-4.

2. Felix, K., et al., *Upper Extremity Motor Learning among Individuals with Parkinson's Disease: A Meta-Analysis Evaluating Movement Time in Simple Tasks*. Parkinson's disease, 2012. **2012**: p. 589152.
3. Marinelli, L., et al., *The many facets of motor learning and their relevance for Parkinson's disease*. Clin Neurophysiol, 2017. **128**(7): p. 1127-1141.
4. Coynel, D., et al., *Dynamics of motor-related functional integration during motor sequence learning*. Neuroimage, 2010. **49**(1): p. 759-66.
5. Doyon, J., et al., *Contributions of the basal ganglia and functionally related brain structures to motor learning*. Behav Brain Res, 2009. **199**(1): p. 61-75.
6. Doyon, J. and H. Benali, *Reorganization and plasticity in the adult brain during learning of motor skills*. Curr Opin Neurobiol, 2005. **15**(2): p. 161-7.
7. Fogel, S.M., et al., *fMRI and sleep correlates of the age-related impairment in motor memory consolidation*. Hum Brain Mapp, 2014. **35**(8): p. 3625-45.
8. Lehericy, S., et al., *Distinct basal ganglia territories are engaged in early and advanced motor sequence learning*. Proc Natl Acad Sci U S A, 2005. **102**(35): p. 12566-71.
9. Bruck, A., et al., *Striatal subregional 6-[18F]fluoro-L-dopa uptake in early Parkinson's disease: a two-year follow-up study*. Mov Disord, 2006. **21**(7): p. 958-63.
10. Morrish, P.K., G.V. Sawle, and D.J. Brooks, *Regional changes in [18F]dopa metabolism in the striatum in Parkinson's disease*. Brain, 1996. **119** (Pt 6): p. 2097-103.
11. Nurmi, E., et al., *Rate of progression in Parkinson's disease: a 6-[18F]fluoro-L-dopa PET study*. Mov Disord, 2001. **16**(4): p. 608-15.
12. Bedard, P. and J.N. Sanes, *Basal ganglia-dependent processes in recalling learned visual-motor adaptations*. Exp Brain Res, 2011. **209**(3): p. 385-93.

13. Manuel, A.L., et al., *Resting-state connectivity after visuo-motor skill learning is inversely associated with offline consolidation in Parkinson's disease and healthy controls.* Cortex, 2018. **106**: p. 237-247.
14. Marinelli, L., et al., *Learning and consolidation of visuo-motor adaptation in Parkinson's disease.* Parkinsonism Relat Disord, 2009. **15**(1): p. 6-11.
15. Nicastro, N., et al., *Consolidation of a Learned Skill Correlates with Dopamine SPECT Uptake in Early Parkinson's Disease.* J Clin Neurol, 2018. **14**(4): p. 505-512.
16. Doyon, J., et al., *Role of the striatum, cerebellum, and frontal lobes in the learning of a visuomotor sequence.* Brain Cogn, 1997. **34**(2): p. 218-45.
17. Kwak, Y., et al., *L-DOPA changes ventral striatum recruitment during motor sequence learning in Parkinson's disease.* Behav Brain Res, 2012. **230**(1): p. 116-24.
18. Muslimovic, D., et al., *Motor procedural learning in Parkinson's disease.* Brain, 2007. **130**(Pt 11): p. 2887-97.
19. Stefanova, E.D., et al., *Visuomotor skill learning on serial reaction time task in patients with early Parkinson's disease.* Mov Disord, 2000. **15**(6): p. 1095-103.
20. Stephan, M.A., et al., *Motor sequence learning performance in Parkinson's disease patients depends on the stage of disease.* Brain Cogn, 2011. **75**(2): p. 135-40.
21. Terpening, Z., et al., *The contribution of nocturnal sleep to the consolidation of motor skill learning in healthy ageing and Parkinson's disease.* J Sleep Res, 2013. **22**(4): p. 398-405.
22. Wu, T., P. Chan, and M. Hallett, *Effective connectivity of neural networks in automatic movements in Parkinson's disease.* NeuroImage, 2010. **49**(3): p. 2581-7.
23. Wu, T. and M. Hallett, *A functional MRI study of automatic movements in patients with Parkinson's disease.* Brain, 2005. **128**(Pt 10): p. 2250-9.

24. Dan, X., et al., *Motor Sequence Learning and Consolidation in Unilateral De Novo Patients with Parkinson's Disease*. PLoS One, 2015. **10**(7): p. e0134291.
25. Ghilardi, M.F., et al., *The differential effect of PD and normal aging on early explicit sequence learning*. Neurology, 2003. **60**(8): p. 1313-9.
26. Doyon, J., et al., *Role of the striatum, cerebellum and frontal lobes in the automatization of a repeated visuomotor sequence of movements*. Neuropsychologia, 1998. **36**(7): p. 625-41.
27. Onla-or, S. and C.J. Winstein, *Determining the optimal challenge point for motor skill learning in adults with moderately severe Parkinson's disease*. Neurorehabilitation and neural repair, 2008. **22**(4): p. 385-95.
28. Sidaway, B., et al., *Contextual Interference Can Facilitate Motor Learning in Older Adults and in Individuals With Parkinson's Disease*. J Mot Behav, 2016. **48**(6): p. 509-518.
29. World Health Organization (WHO), *International classification of functioning, disability and health, ICF*. Geneva, 2001.
30. Gebhardt, A., et al., *Poor dopaminergic response of impaired dexterity in Parkinson's disease: Bradykinesia or limb kinetic apraxia?* Mov Disord, 2008. **23**(12): p. 1701-6.
31. Pohar, S.L. and C. Allyson Jones, *The burden of Parkinson disease (PD) and concomitant comorbidities*. Arch Gerontol Geriatr, 2009. **49**(2): p. 317-21.
32. Arora, S., et al., *Detecting and monitoring the symptoms of Parkinson's disease using smartphones: A pilot study*. Parkinsonism Relat Disord, 2015. **21**(6): p. 650-3.
33. Lakshminarayana, R., et al., *Using a smartphone-based self-management platform to support medication adherence and clinical consultation in Parkinson's disease*. NPJ Parkinsons Dis, 2017. **3**: p. 2.

34. Lee, C.Y., et al., *A Validation Study of a Smartphone-Based Finger Tapping Application for Quantitative Assessment of Bradykinesia in Parkinson's Disease.* PLoS One, 2016. **11**(7): p. e0158852.
35. Zhan, A., et al., *Using Smartphones and Machine Learning to Quantify Parkinson Disease Severity: The Mobile Parkinson Disease Score.* JAMA Neurol, 2018. **75**(7): p. 876-880.
36. Ellis, T.D., et al., *Comparative Effectiveness of mHealth-Supported Exercise Compared With Exercise Alone for People With Parkinson Disease: Randomized Controlled Pilot Study.* Phys Ther, 2019. **99**(2): p. 203-216.
37. Ginis, P., et al., *Feasibility and effects of home-based smartphone-delivered automated feedback training for gait in people with Parkinson's disease: A pilot randomized controlled trial.* Parkinsonism Relat Disord, 2016. **22**: p. 28-34.
38. Espay, A.J., et al., *A roadmap for implementation of patient-centered digital outcome measures in Parkinson's disease obtained using mobile health technologies.* Mov Disord, 2019. **34**(5): p. 657-663.
39. Nunes, F., et al., *User interface design guidelines for smartphone applications for people with Parkinson's disease.* Universal Access in the Information Society, 2016. **15**(4): p. 659-679.
40. Hughes, A.J., et al., *Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases.* J Neurol Neurosurg Psychiatry, 1992. **55**(3): p. 181-4.
41. Hoehn, M.M. and M.D. Yahr, *Parkinsonism: onset, progression and mortality.* Neurology, 1967. **17**(5): p. 427-42.
42. Folstein, M.F., S.E. Folstein, and P.R. McHugh, *"Mini-mental state". A practical method for grading the cognitive state of patients for the clinician.* Journal of psychiatric research, 1975. **12**(3): p. 189-98.

43. Nasreddine, Z.S., et al., *The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment.* Journal of the American Geriatrics Society, 2005. **53**(4): p. 695-9.
44. Vanbellingen, T., et al., *Reliability and validity of a new dexterity questionnaire (DextQ-24) in Parkinson's disease.* Parkinsonism Relat Disord, 2016. **33**: p. 78-83.
45. Goetz, C.G., et al., *Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results.* Mov Disord, 2008. **23**(15): p. 2129-70.
46. Nackaerts, E., et al., *Relearning of Writing Skills in Parkinson's Disease After Intensive Amplitude Training.* Mov Disord, 2016. **31**(8): p. 1209-16.
47. Beigi, M., et al., *Levodopa medication improves incidental sequence learning in Parkinson's disease.* Neuropsychologia, 2016. **93**(Pt A): p. 53-60.
48. Kwak, Y., et al., *Effect of dopaminergic medications on the time course of explicit motor sequence learning in Parkinson's disease.* J Neurophysiol, 2010. **103**(2): p. 942-9.
49. Ruitenberg, M.F.L., et al., *Sequence learning in Parkinson's disease: Focusing on action dynamics and the role of dopaminergic medication.* Neuropsychologia, 2016. **93**(Pt A): p. 30-39.

9 Tables

Table 1: Demographics and clinical characteristics			
	PD (N = 10)	HC (N = 10)	P-value
Age (years)	67.5 ± 6.2	63.6 ± 6.7	0.194
Gender (M/F)	4 / 6	6 / 4	0.800
MMSE (0-30)	28.2 ± 1.6	29.2 ± 0.9	0.107
MoCA (0-30)	28.0 (24.5, 29.3)	28.0 (27.0, 29.0)	0.739
DEXTQ-24 (24-96)	29.0 (25.8, 32.0)	24.0 (24.0, 24.0)	< 0.001
Disease duration (years since diagnosis)	5.9 ± 4.0	-	-
H&Y (II/III)	8 / 2	-	-
Disease dominance (R/L)	8 / 2	-	-
LED (mg/day)	358.7 ± 172.4	-	-
MDS-UPDRS-III (0-132)	25.8 ± 10.9	-	-
Mobile phone task (s)	9.0 (8.1, 12.0)	7.4 (6.5, 8.3)	0.019
Baseline SSP performance			
– MT (s)	7.41 ± 3.43	7.79 ± 4.23	0.828
– COV _{MT} (%)	27.23 ± 17.96	29.31 ± 10.09	0.766
– ED	3.53 ± 1.05	3.41 ± 0.97	0.791
– COV _{ED} (%)	13.92 ± 8.42	17.70 ± 9.72	0.391
– PI (%)	2.16 ± 0.99	2.24 ± 0.86	0.830
Mean ± Standard deviation or median (IQR) are displayed depending on normality of the data			
Abbreviations: PD = Parkinson's disease; HC = healthy controls; M = male; F = female; MMSE = Mini-Mental State Examination; MoCA = Montreal Cognitive Assessment; DEXTQ-24= Dexterity questionnaire; H&Y = Hoehn and Yahr stage; LED = Levodopa Equivalent Dose; MDS-UPDRS-III = Movement Disorders Society sponsored revision of the Unified Parkinson's Disease Rating Scale part III; SSP = Swipe Slide Pattern; MT = movement time; COVMT = coefficient of variation of movement time; ED = Euclidean distance; COVED = coefficient of variation of Euclidean distance; PI = performance index.			

10 Figures and captions

Figure 1: The Swipe-Slide Pattern task. Participants first looked at an instruction screen for 3 s, showing the pre-defined to-be-learned pattern. When the pattern disappeared, participants started producing the pattern for the remaining 33s using the provided finger stylus. During this period, the pattern remained visible in the upper left corner of the screen.

Figure 2: Performance on the Swipe-Slide Pattern task during early learning, late learning and retention.

(A) Trial by trial learning curve for movement time; (B) Changes in movement time; (C) Changes in variability of movement time; and (D) Changes in performance index. Data are presented as group means ($\pm$ standard deviation), as well as individual data points. (*) $p < 0.10$; *** $p < 0.001$

Figure 3: Comparison of the Swipe-Slide Pattern task between retention and transfer test. (A) Euclidean distance; (B) Variability in Euclidean distance; (C) Variability in movement time; and (D) Performance index. Data are presented as group means ($\pm$ standard deviation), as well as individual data points. * $p < 0.05$; ** $p < 0.01$

Figure 4: The learning, retention and transfer index. (A) Differences between PD and HC for movement time (MT); (B) Differences between PD and HC for performance index (PI); (C) A positive correlation between the retention index for MT and performance on the mobile phone task; and (D) A positive correlation between the retention index for PI and the MDS-UPDRS-III. Data are presented as group means ($\pm$ standard deviation), as well as individual data points. * $p < 0.05$

11 Supplementary tables

Supplementary table A1: Overview of all main and interaction effects for the group x time analysis			
Effect	F-value	p-value	Partial Eta squared
From early learning to retention			
	MT		
Main effect of group	0.985	0.334	0.052
Main effect of time	22.635	<0.001*	0.557
Interaction between group & time	1.299	0.282	0.067
	COV_{MT}		
Main effect of group	0.376	0.547	0.020
Main effect of time	12.203	0.001*	0.402
Interaction between group & time	0.136	0.810	0.007
	ED		
Main effect of group	0.047	0.830	0.003
Main effect of time	0.697	0.469	0.037
Interaction between group & time	0.306	0.678	0.017
	COV_{ED}		
Main effect of group	0.523	0.479	0.028
Main effect of time	0.320	0.720	0.017
Interaction between group & time	1.988	0.154	0.099
	PI		
Main effect of group	0.667	0.425	0.036
Main effect of time	18.288	<0.001*	0.504
Interaction between group & time	3.075	0.063*	0.146
From retention to transfer			
	MT		
Main effect of group	3.322	0.085	0.156
Main effect of test	0.247	0.625	0.014
Interaction between group & test	0.039	0.846	0.002
	COV_{MT}		
Main effect of group	0.552	0.467	0.030
Main effect of test	7.853	0.012*	0.304
Interaction between group & test	0.621	0.441	0.033
	ED		
Main effect of group	0.031	0.863	0.002
Main effect of test	6.351	0.021*	0.261
Interaction between group & test	0.362	0.555	0.020
	COV_{ED}		
Main effect of group	3.321	0.085	0.156
Main effect of test	9.352	0.007*	0.342
Interaction between group & test	1.009	0.328	0.053
	PI		
Main effect of group	3.357	0.084	0.157
Main effect of test	6.221	0.023*	0.257
Interaction between group & test	1.008	0.329	0.053
* = reported in main text			
Abbreviations: MT = movement time; COV _{MT} = coefficient of variation for movement time; ED = Euclidean distance; COV _{ED} = coefficient of variation for Euclidean distance; PI = performance index			

Supplementary table A.2: Number of patterns per trial			
	PD (N = 10)	HC (N = 10)	p-value
	LEARNED PATTERN		
Trial 1	3.5 (3.0, 6.0)	4.0 (3.0, 5.5)	0.912
Trial 2	5.5 (4.0, 9.0)	7.0 (6.0, 9.0)	0.481
Trial 3	7.0 (5.0, 9.8)	8.0 (6.0, 9.8)	0.579
Trial 4	8.0 (7.0, 9.8)	8.5 (7.0, 11.0)	0.579
Trial 5	9.5 (7.3, 10.0)	9.0 (7.3, 11.0)	0.739
Trial 6	9.0 (7.5, 10.8)	9.5 (7.5, 10.8)	0.684
Trial 7	9.5 (7.5, 10.8)	9.5 (7.5, 10.8)	0.796
Trial 8	9.5 (6.8, 12.0)	10.5 (7.5, 11.0)	0.853
Trial 9	11.0 (7.8, 11.8)	10.0 (8.3, 11.0)	0.912
Trial 10	10.0 (6.8, 11.8)	10.0 (9.3, 10.8)	0.796
Trial 11	11.5 (7.5, 12.0)	10.0 (8.5, 13.3)	1.000
Trial 12	11.0 (8.0, 12.0)	10.0 (8.5, 13.3)	0.971
Trial 13	11.0 (8.3, 12.8)	10.5 (9.3, 14.0)	0.971
Trial 14	10.0 (8.5, 12.8)	10.0 (9.3, 12.5)	0.971
Trial 15	10.5 (8.5, 12.0)	11.0 (9.3, 13.3)	0.796
Trial 16	11.0 (9.0, 11.8)	11.0 (10.0, 13.3)	0.739
Trial 17	11.5 (8.3, 12.0)	11.0 (8.5, 14.0)	0.791
Trial 18	11.0 (7.8, 12.8)	11.0 (8.5, 14.0)	0.739
Trial 19	8.0 (4.3, 11.0)	10.0 (8.3, 11.0)	0.280
Trial 20	10.5 (6.0, 13.0)	12.0 (10.3, 13.5)	0.353
Trial 21	11.0 (7.5, 14.0)	12.5 (11.3, 13.8)	0.393
Trial 22	11.5 (7.5, 14.0)	12.5 (11.3, 14.8)	0.247
Trial 23	11.0 (9.3, 13.8)	12.5 (10.3, 14.8)	0.315
Trial 24	10.5 (7.8, 12.8)	11.5 (11.0, 14.0)	0.218
Median (IQR) are displayed, with p-values from a Mann-Whitney U test.			
Abbreviations: PD = Parkinson's Disease; HC = healthy controls.			

Supplementary table A.3: Fatigue measured using a VAS.			
	PD (N = 10)	HC (N = 10)	p-value
VAS (0-10)	0.8 (0.5, 4.0)	0.7 (0.3, 2.4)	0.436
Median (IQR) are displayed, with p-values from a Mann-Whitney U test.			
Abbreviations: PD = Parkinson's Disease; HC = healthy controls, VAS = visual analogue scale.			

Supplementary table A.4: overview of all main effects of group for the indices		
	Z-value	p-value
	MT	
Learning index	0.000	1.000
Retention index	-2.343	0.019*
Transfer index	-1.663	0.105
	ED	
Learning index	-0.227	0.853
Retention index	-1.890	0.063
Transfer index	-0.680	0.529
	PI	
Learning index	-0.151	0.912
Retention index	-2.343	0.019*
Transfer index	-1.512	0.143
* = reported in main text		
Abbreviations: MT = movement time; ED = Euclidean distance; PI = performance index		