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The Effects of Cognitive Training of Prefrontal Functions in Patients with Parkinson's Disease

Martina Piefke[1*], Hannah Vogel[1] and Stefan Troche[2]

[1]*Faculty of Health, Neurobiology and Genetics of Behavior, Witten/Herdecke University, Germany*
[2]*Institute of Psychology, Bern University, Switzerland*

Abstract

The treatment of cognitive impairments in individuals with Parkinson's disease (PD) poses a challenge on the therapy of the disorder. The current study examines the effects of a computer based cognitive training in patients with PD. 13 individuals with PD (3 females, 10 males) and 16 healthy controls (8 females, 8 males) participated in the study. They underwent a 6 week cognitive rehabilitation program, focusing on attention, working memory, and executive functions. We measured (i) pre- and post-training cognitive performance with standard neuropsychological tests and (ii) improvement in the training tasks across the intervention. In both groups, performance improved significantly within all training modules ($p<.001$). A significant increase of performance was evident from pre to post-intervention untrained neuropsychological measures of working memory ($p<.001$). Moreover, correlational analyses showed that enhancement in each trained task was accompanied by improvement in the same cognitive domain in untrained neuropsychological tests. To our knowledge this study is the first providing evidence for a transfer of cognitive improvement in trained tasks to untrained neuropsychological measures in patients with PD. We propose that patients with PD will benefit from the inclusion of cognitive training in medical treatment of the disorder.

Keywords: Neuropsychological training • Working memory • Executive functions

Abbreviations

(ANOVA) Analysis of Variance; (BAI) Beck Anxiety Inventory; (BDI) Beck Depression Inventory; (CERAD) Consortium to Establish a Registry for Alzheimer's Disease; (CG) Control Group; (DA) Divided Attention; (DST) Digit Span Test; (MMSE) Mini Mental State Examination; (PAH) Plan a Holiday; (PD) Parkinson's Disease; (PFC) Prefrontal Cortex; (PG) Parkinson Group; (RCT) Randomized Controlled Trial; (RehaCom) Cognitive Training Software Rehacom Hasomed Company; (TMT) Trail Making Test; (WOME) Training Module Working Memory.

Introduction

Cognitive impairment in Parkinson´s disease (PD) is a widespread and serious problem. Symptoms such as mental retardation, disturbances of action and strategy planning or memory and orientation disorders are, besides motoric major symptoms, commonly reported in the context of PD [1-4]. Cognitive functions associated with the prefrontal cortex (PFC) such as executive functions, working memory and attention rank among the most severely impaired competences [4-7]. Cognitive deficits have been demonstrated in 20%-40% of individuals with PD even at initial stages of the disease [8-10] and range up to 57% five years after diagnosis [11].

Empirical findings concerning the aetiology of cognitive impairment in patients with PD are heterogeneous [7,10]. Fronto-striatal dysfunctions, which derive from a lack of dopamine and result in impaired of executive functions and attention are frequently reported [2,4,7,11,12]. According to Pagonabarraga et al. [13], functional alterations in the dorsolateral PFC may lead to specific deficits in attention, working memory and executive functions.

To date, research on treatment methods of PD has predominantly addressed motor symptoms [14]. Research on neuropsychological assessment as well as non-pharmacological and cognitive treatment options for individuals with PD is rare [15,16]. In clinical routines, neuropsychological methods are also rarely applied. However, cognitive training is considered as a profitable method within the therapy of various neurological disorders. As an example, the implementation of cognitive training is a common and efficient clinical practice in the treatment of stroke and traumatic brain injury [17,18]. Most frequently, memory [19] and executive functions [17,20] are affected. Therapeutic objectives, cognitive profiles, and needs of patients with PD are highly comparable to those of patients with other neurological disorders, who are treated neuropsychologically in clinical routines. Accordingly, it is reasonable to assume that patients with PD will also profit from neuropsychological assessment and cognitive training [17].

Although not yet incorporated into standard treatment guidelines, cognitive training has been evaluated in clinical studies of PD. A randomized controlled trial (RCT) by Petrelli et al. [21] did not reveal cognitive improvement, but stable levels of cognitive performance in the intervention group, following a 6 week training of attention, memory, and executive functions. Effects lasted across a 12 month follow up period. In contrast, the control group (CG) showed progressively decreasing cognitive performance. Another RCT demonstrated improved performance of attention, speed of information processing, verbal fluency and executive functions in PD patients of the intervention group following a four week cognitive training [22]. In a further study, a computer based cognitive training program was applied in patients with PD across a 7 week period. Results show evidence for a significant improvement in memory and learning after training [23]. Naismith et al. [23] argue that cognitive training may help patients with PD to acquire adaptive and/or compensatory cognitive strategies and that it can therefore be applied as a viable tool to improve cognitive functioning in individuals with PD. Due to its proven efficacy, various authors currently propose the implementation of cognitive training in the standard treatment of PD [17,22,24].

It needs to be considered, however, that Glitzer and MacDonald demonstrate in a systematic review that cognitive training results mainly in short term

***Address for Correspondence:** Martina Piefke, Department of Neurobiology and Genetics of Behavior, Witten/Herdecke University, Germany, Email: martina.piefke@uni-wh.de*

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and moderate enhancements of cognitive functions in patients with PD [7]. Although results should be treated with care due to methodological deficiencies and insufficient comparability of the reviewed studies, evidence for long term stability of training effects is lacking, to date.

Available data show a necessity of further research on the efficacy of cognitive training in patients with PD [7,25,26]. The present study aims at evaluating the impact of a 6 week computer based cognitive training program on cognitive capacities of patients with PD and a healthy control group. In particular, we focus on the training of attention, working memory, and executive functions.

To our knowledge, this is the first study applying a computer based cognitive training with standard neuropsychological pre-post intervention measures in patients with PD and a matched control group. We hypothesized that the implementation of a cognitive training program over a 6 week period leads to significant improvement in all study participants in tasks of attention, working memory, and executive functions. Moreover, we expected that performance enhancement does not only occur within the trained tasks, but that it also transfers to untrained neuropsychological tasks requiring the same cognitive abilities. Moreover, we assessed putative differences in depression and anxiety at the beginning and the end of the training period [27-29]. We assumed that experiences of competence and self-efficacy, originating from successful completion of training tasks, may lead to notable reductions of depression and anxiety scores in patients with PD.

Methods

Participants

Thirteen patients with PD [Parkinson group (PG)] and sixteen control subjects without PD [control group (CG)] were included in the study. Patients and control subjects were subgroups of participants of a long term study (across three years) on changes of neuropsychological capacities of patients with PD. All participants gave written consent prior to participation. Eleven PG participants completed the intervention study successfully. Two PG participants abandoned study participation ahead of schedule due to health and family related demands. All participants of the CG completed the entire intervention study. Using a matched pair design, participants in both groups were matched individually for age, gender, and education (Table 1). Exclusion criteria for the cognitive rehabilitation study were diminished intelligence (Intelligence Quotient (IQ) ≤ 80), dementia (Mini Mental State Examination (MMSE) ≤ 24), as well as severe neurological and heart diseases at the time of enrolment in the study. Sample characteristics are illustrated in Table 1. The study is in accordance with the current version of the Declaration of Helsinki of the World Medical Association. It was approved by the ethics committee of Witten/Herdecke University.

Table 1. Sample characteristics of Parkinson and control group (PG and CG).

	PG	CG	p
Age	M [a]=71.30 years (age range: 51-86, SD [b]=8.59)	M=69.93 years (age range: 57-82, SD=6.51)	.020
Sex	3 women; 10 men	8 women; 8 men	.501
Education	high school graduation n=6, higher education n=4	high school graduation n=10, higher education n=9	.191
IQ [c]	M=106.15 (IQ range: 97.5-115; SD=4.25)	M=105.46 (IQ range: 87-121; SD=10.16)	.843
MMSE [d] values	M=29.06, SD=0.95	M=29.12, SD=0.80	.783
Note: [a] M=mean value. [b] SD=standard deviation. [c] IQ=intelligence quotient. [d] MMSE=Mini Mental State Examination.			

Research design

The PG and the CG were examined neuropsychologically before and after the cognitive intervention. Accordingly, a pre- and post-test study design was applied. Additionally, a combined within and a between subject design [30] was used to determine (i) improvement within each group and (ii) putative differences in neuropsychological diagnostics and training effects between groups. The study plan included baseline measures, pre-intervention neuropsychological tests, a 6 week cognitive training period, and post-intervention neuropsychological tests. Baseline measures were accomplished about six months before the pre-intervention tests. Post-intervention tests took place not later than seven days after completion of the intervention. Pre- and post-test included only paper and pencil versions of neuropsychological standard instruments.

Target parameters

Attention, working memory, and executive functions were defined as independent target parameters, as neuropsychological impairments in patients with PD have been reported predominantly for these cognitive domains [4,6,7].

Baseline, pre- and post intervention measures

For baseline, pre- and post intervention tests, the Consortium to Establish a Registry for Alzheimer's Disease Plus (CERAD; including Trail Making Test (TMT) A and B) [31,32], subtest four of the LPS (LPS 4) and the digit span test (DST; forward, backward, and total; Wechsler Memory Scale – Revised) [33] tests were applied. The TMT predominantly measures executive functions as well as dimensions of attention, which are crucial for the successful use of executive functions [34]. A further device for measuring executive functions was the LPS 4 was also used to estimate intelligence.. The DST served to assess working memory. The Beck Depression Inventory II (BDI II) [35,36] and Beck Anxiety Inventory (BAI) [37,38] were applied to assess depression and anxiety levels.

Computer based cognitive training

The software "RehaCom" by the Hasomed Company (Magdeburg, Germany; www.hasomed.de) was used for cognitive training. The efficacy of RehaCom and comparable programs has been examined by various studies for a broad variety of diseases such as Alzheimer's disease [39], stroke [40], and traumatic brain injury [41].

Attention, working memory, and executive functions were trained by corresponding RehaCom training modules. Study participants accomplished the training tasks across six weeks, with five training sessions per week. Two non-adjacent days without training per week were chosen by each participant individually. Training took place at the volunteers' homes. It included three different tasks of the RehaCom training program: training of attention (Divided Attention 2; DA), working memory (Working Memory; WOME), and executive functions (Plan a Holiday; PAH) see Figure 1. To ensure a gradually increasing training structure as well as a minimum of 20 training units of each training task [42], DA and WOME were trained throughout the entire 6 week training period, whereas PAH training started from the third training week on. Each task was trained for 10 min on each

training session. On average, participants trained DA for about M=24.38 days (SD=7.99; range 1-30 days), WOME for M=24.59 days (SD=7.77; range 3-30 days) and PAH for M=14.87 days (SD=6.84; range 0-20 days).

Figure 1

Figure 1. (a) Example view of the task Divided Attention 2 (DA). Participants are required to drive a car and react to several visual and auditory stimuli simultaneously, such as signals originating from dashboard, rear-view mirrors or navigation system. (b) Example view of the task Working Memory (WOME). Participants have to memorise and sort playing cards. The number of cards increases with time. (c) Example view of the task Plan a Holiday (PAH). The aim is to complete a number of activities in a specific order successfully. Participants are therefore demonstrated a city map and asked to visit demanded spots according to a given priority and timetable.

Statistical analyses

All statistical analyses were conducted with the software Statistical Package for the Social Sciences (SPSS, version 24.0; https://www-01.ibm.com/software/de/stats24/). Descriptive statistics were calculated for all available data. For assessing improvements in cognitive performance within and between groups, a repeated measures analysis of variance (ANOVA) was accomplished. To check the requirements of an ANOVA-normal distribution of data and sphericity-a Kolmogorov-Smirnov and a Mauchly's test were conducted beforehand. In case of lacking sphericity, a Greenhouse-Geisser respective Huynd-Feldt correction was applied to adjust the degrees of freedom. Missing data was approximated by mean value substitutions of the corresponding items. Boxplots were created to detect deviating data. Values, located more than three interquartile ranges from the end of a box were labelled as outliers and excluded from analysis. Two ANOVAs were run separately: changes between baseline, pre- and post-tests as well as performance changes on RehaCom tasks were assessed. For the latter, an average performance index was calculated for each participant, training task and training week respectively. To adjust outcomes for multiple comparisons, a Bonferroni correction was accomplished. In the event of significant results, a Bonferroni Post Hoc test was applied to provide specific information on which results significantly differed from each other. Significant results of non-parametric data were reviewed by means of a Wilcoxon test. To examine possible interrelations between test outcomes and whether performance in pre- and post-tests correlated with performance in the respective computer based intervention tasks, Pearson (for normally distributed data) and Spearman correlations (for not normally distributed data) were calculated. Differences between results in pre- and post-tests were correlated with differences between the performance index of the first training session and the averaged performance index of the last three training days of the respective cognitive tasks.

Results

Baseline, pre- and post intervention measures

The repeated measures ANOVA of baseline, pre- and post-test data revealed significant improvement on DST forward ($F(1.79, 41.22)=5.91$, $p=.003$, $n=25$), backward ($F(2,44)=4.52$, $p=.008$, $n=24$) and total ($F(2,44)=11.56$, $p<.001$, $n=24$). Bonferroni corrected pairwise comparisons demonstrated that differences between baseline and post-tests were significant on DST forward (baseline: M=8.10, SD=1.92; post-test: M=9.58, SD=1.80), backward (baseline: M=5.69, SD=1.45; post-test: M=7.06, SD=1.95) as well as total (baseline: M=14.00, SD=3.06; post-test: M=16.87, SD=3.48). Significant pre- to post-test differences were apparent only in DST forward (pre-test: M=8.32, SD=2.41; post-test: M=9.58, SD=1.80) and total (pre-test: M=15.00, SD=3.05; post-test: M=16.87, SD=3.48). As data of DST forward were non-parametric, significance of results was reviewed and confirmed by a Wilcoxon test (baseline to post-test: $z=-3.71$, $p<.001$, $n=27$ and pre- to post-test: $z=-3.06$, $p=.001$, $n=27$). Group mean values differed significantly from each other in DST backward in favour of the CG ($p=.026$). Table 2 shows the average differences between baseline, pre- and post-training measures. The average differences between baseline, pre- and post-tests in DST forward and DST total are illustrated in Figure 2.

Figure 2

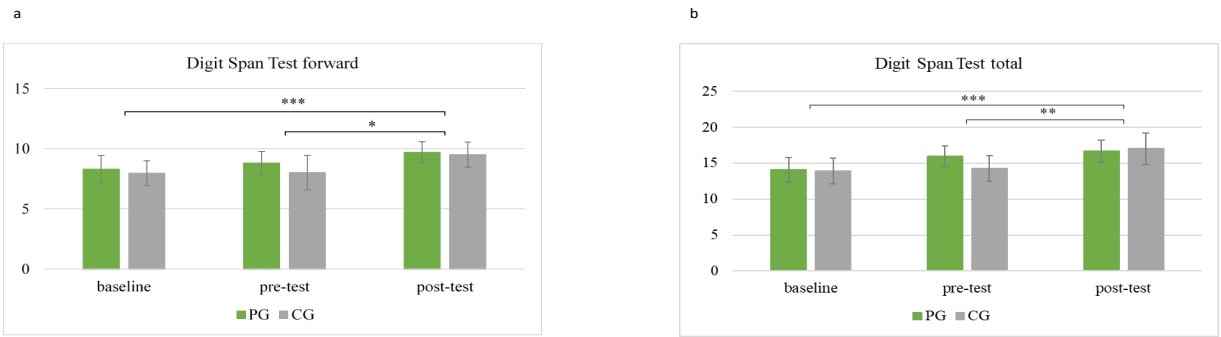

Figure 2. Average performance of Parkinson and control group (PG and CG) in baseline, pre- and post-tests in Digit Span Test (a) forward and (b) total. Mean values and 95% confidence intervals. *p<.05. **p<.01. ***p<.001.

Table 2. Average performance of Parkinson and control group (PG and CG) in baseline, pre and post-tests.

	Baseline M (SD)		Pre-test M (SD)		Post-test M (SD)				
Scale	PG	CG	PG	CG	PG	CG	p factor	p group	p factor x group
TMT A	44.82 (14.89)	38.54 (7.65)	43.73 (15.81)	45.31 (18.08)	41.55 (10.16)	40.53 (15.56)	.218	.338	.190
TMT B	98.10 (25.22)	82.54 (28.63)	91.10 (33.45)	93.38 (38.97)	107.70 (35.30)	91.13 (42.16)	.144	.214	.110
DST for	8.30 (1.83)	7.96 (2.03)	8.80 (1.55)	8.00 (2.85)	9.70 (1.42)	9.50 (2.06)	.003** a,b	.256	.383
DST back	5.80 (1.23)	5.62 (1.63)	7.20 (1.40)	5.21 (2.39)	7.00 (1.15)	7.10 (2.40)	.008** a	.118	.026*
DST total	14.10 (2.73)	13.93 (3.38)	16.00 (2.31)	14.29 (3.38)	16.70 (2.45)	17.00 (4.15)	<.001*** a,b	.325	.109
LPS 4	105.86 (9.60)	107.96 (10.58)	105.45 (8.91)	106.70 (9.72)	108.32 (11.65)	110.37 (13.60)	.097	.319	.483
BDI II	11.73 (5.64)	5.85 (6.60)	9.91 (7.53)	5.31 (5.90)	11.73 (5.39)	4.40 (5.67)	.242	.005** c	.192
BAI	11.45 13.82)	9.31 (10.40)	14.55 (9.52)	9.00 (9.26)	15.00 (7.44)	8.60 (8.20)	.366	.068	.276

Note: TMT A=Trail Making Test A; TMT B=Trail Making Test B; DST for=Digit Span Test forward; DST back=Digit Span Test backward; DST total=Digit Span Test total; LPS 4=Leistungsprüfsystem subtest four; BDI II=Beck Depression Inventory II; BAI=Beck Anxiety Inventory. [a] significant performance difference between baseline and post-test. [b] significant performance difference between pre and post-test. [c] superiority of the control group. * p<.05. **p<.01. ***p<.001.

Computer based neurocognitive intervention

Significant performance improvement during the cognitive intervention was apparent in all applied training modules (DA: F(2.31, 62.40)=31.64, p factor<.001, p group=.005, p factor x group<.001, n=29; WOME: F(2.15, 57.97)=37.61, p factor<.001, p group=.011, p factor x group=.017, n=29; PAH: F(1.22, 32.97)=35.98, p factor<.001, p group=.002, p factor x group<.001, n=29) see Figure 3. Significant group differences favouring the CG were found in DA (p<.001), WOME (p=.016) and PAH (p<.001).

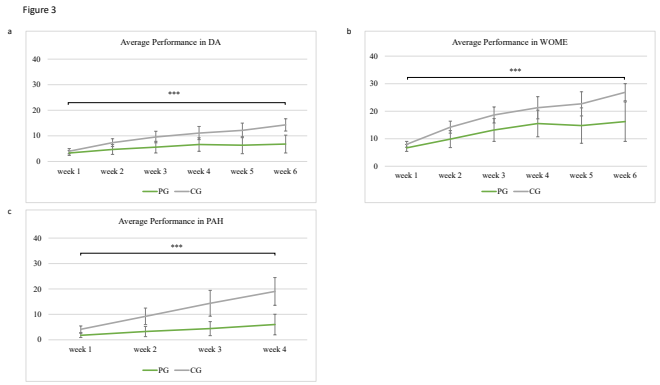

Figure 3. Average performance per week in (a) Divided Attention (DA), (b) Working Memory (WOME) and (c) Plan a Holiday (PAH; training started at the third week of the intervention period). Mean values and 95% confidence intervals. PG=Parkinson group; CG=control group. ***p<.001.

Correlations of improvement in training modules and pre- and post-intervention measures

Evidence for significant correlations was observable between the improvement in WOME and pre-post improvement in DST total (r=.440, p=.028, n=25) as well as between the improvement in PAH and pre-post improvement in TMT B (r=-.479, p=.013, n=26). Both correlations correspond to a small to medium positive (WOME and DST total) and negative (PAH and TMT B) effect [43].

Discussion

The current study demonstrates that the implementation of a computer based cognitive training program over a 6 week period results in significant improvements in attention, working memory and executive functions in patients with PD and healthy controls within the trained tasks. Furthermore, training leads to significantly improved performance in untrained working memory tasks. Correlational analyses revealed that enhancement in cognitive training comes along with specifically enhanced capabilities within the same cognitive domain in untrained neuropsychological tests. To our knowledge, the current study is the first demonstrating a transfer of improvement of working memory in a specific trained task to standard neuropsychological measures of overall working memory capacity in patients with PD.

Results of the repeated measures ANOVA showed that the neurocognitive intervention significantly improved the performance of individuals in PG and CG on the trained modules DA, WOME and PAH. Importantly, the results demonstrated significant (DST forward and backward) to highly significant (DST total) enhancement of working memory in both the PD and the control group. As improvements in DST forward and total were observable between all times of measurement except baseline to pre-test, the data show evidence that achieved progress traces back to the cognitive intervention. Thus, the presented results provide strong support for our hypothesis that enhanced performance in the WOME training task can be transferred to untrained standard neuropsychological measures of working memory tasks. Despite some main differences between the tasks (e.g., complexity, sensory modalities and response demands) they share basic cognitive abilities, which could be enhanced by the cognitive intervention.

Individual working memory capacity has long been assumed to be unchangeable. However, current research yielded promising results regarding its trainability [44-46]; for a review see [47]. A meta-analysis by Weicker et al. [42] dealt with the efficacy of working memory training in brain injured patients. The authors reported a moderate improvement of performance in untrained working memory tasks after the training intervention. Although cognitive profiles of individuals with traumatic brain injury and PD are sometimes comparable, and training interventions in both patient groups target basic mechanisms of neuroplasticity [17], a transfer of results needs to be treated with caution. Evidence for the efficacy of a specific working memory training in individuals with PD is provided by París et al. [22] who reported a significant improvement in standardized working memory tests following a 4 week cognitive intervention. This intervention was implemented to improve diverse cognitive domains including attention, working memory, executive functions, and visuospatial abilities. Improvement in those domains was measured by a battery of neuropsychological tests. Note, the authors do not report whether statistical

analyses were corrected for multiple comparisons such that the reliability of the statistical significance remains unclear. In general, previous studies focused on the overall enhancement of cognitive functions in individuals with PD rather than the improvement of a specific cognitive domain such as working memory. The general usefulness of cognitive training in individuals with PD is addressed in a meta-analysis of Glitzer and MacDonald [7]. The results of their meta-analysis indicate a moderate improvement of cognitive abilities following neuropsychological training interventions in patients with PD. In contrast, our present data demonstrate considerably high cognitive gains from the training intervention, in particular, in both trained and untrained working memory tasks. The implementation of the WOME as a module of neuropsychological rehabilitation in patients with PD can therefore be considered as a promising approach to the enhancement of overall working memory functions.

Further evidence for a transfer of cognitive improvement from the specific trained task to overall working memory and attention capacities is derived from the correlational analyses. Enhanced performance in the WOME and PAH tasks was related to the pre-post improvement in DST total and TMT B. This transfer of training success supports the assumption of training induced neuroplasticity and related changes in brain activity following cognitive training. These do not only build up the neural basis for performance in the specific trained task, but rather for a spectrum of cognitive functions belonging to a more general cognitive domain such as working memory or attention [44,45,48].

Pre-post changes in TMT A and LPS 4 were non-significant in both the PD and the CG. As the constructs of these neuropsychological instruments target executive functions, attention, and intelligence, the absence of a transfer from trained tasks to these standard measures may at least in part be due to the low neuropsychological specificity of these pre-post testing instruments. A further explanation can be derived from differences in the duration of the training period. PAH was trained for 14.87 days on average. According to a meta-analysis on the efficacy of cognitive training programs [42], the number of training units is a crucial factor for successful training. However, the meta-analysis focused on training programs of working memory such that the data can only be considered as reference values for training concepts for other cognitive domains such as executive functions. It is also important to note that the TMT is a speed test requiring intact motor abilities of at least the hand and upper extremities. Due to motor impairments of patients with PD, the test may therefore be confounded in this patient group. However, this argument does not explain absence of TMT training effects in the CG.

Regarding attention, results did not reveal significantly improved performance from pre- to post-tests. Contrary to our results, results of Parí s et al. [22] suggest that the implementation of a 4 week cognitive training may lead to improvement in untrained attention tasks in individuals with PD (but see the statistical restriction mentioned above). In our study, the applied pre- and post-intervention measures did not exclusively assess attention, but a combination of attention and executive functions. Therefore, we cannot disentangle to what extent enhanced attention and executive performance from the training were transferred to untrained tasks requiring attention. Further studies investigating effects of neuropsychological training in patients with PD effects should therefore include specific tests of attention, such as the Brief Test of Attention [49], to examine the attentional gains following training. As this test does not require manual dexterity, it may be considered as an appropriate instrument for assessing attention in individuals with PD.

Our results did not reveal significant pre-post training changes in anxiety and depression in either group. Our hypothesis suggesting an improvement of emotional states in response to cognitive training is therefore not corroborated by the data. This finding is in line with previous studies by París et al. [22] and Edwards et al. [50], who also reported unaltered mood following a cognitive intervention. Possibly, absence of improved emotional state traces at least in part back to participants' dissatisfaction with their own training performance. In our cognitive intervention, performance feedback given by the software itself focused on committed errors and was therefore predominantly negative (especially within the DA task). In a debriefing, participants reported that they subjectively perceived this kind of feedback as discouraging and frustrating rather than motivating. This idea is supported by empirical evidence for a relationship between positive feedback and both the magnitude of test performance and improved mood after a computer training [51]. Martocchio and Webster conducted a field experiment in which patients accomplished a microcomputer training and were given feedback on their performance. Feedback was either positive or negative and randomly assigned to participants (i.e., independent of their actual performance). It also needs to be taken into consideration that BAI and BDI measures target changes in anxiety and depression within the previous seven (BAI) and fourteen days (BDI). As post-tests were conducted up to one week after the end of the cognitive training, changes of levels of anxiety and depression during the whole training period were not continuously assessed. In future studies, it would be interesting to measure participants' emotional states every week during the training intervention. Suitable instruments for continuous measures of training related changes of mood could be the Visual Analog Mood Scales [52] or the Profile of Mood States Questionnaire [53]. Both tests assess positive and negative emotional states (e.g., satisfaction, anger) and therefore allow determining relative increases or decreases in positive and negative emotions.

The current study has some limitations. In particular, the sample size was small such that the statistical power of data analysis rather low. Moreover, we did not control for age at PD onset, disease duration, and medication. Especially medication should be addressed in future research as a variety of studies demonstrated that dopaminergic medication alters performance in cognitive tasks. Effects of dopaminergic medication differ depending on the specific task demands and the basal level of dopamine function in cortico-striatal areas [54,55]. However, since patients with PD need to be treated pharmacologically, the medication confound cannot be eliminated from neuropsychological studies in this patient group. A further limitation relates to repeated testing during the course of the study. Although the DST, the TMT, and the LPS 4 are relatively robust against learning effects, we cannot completely exclude that learning effects in standard neuropsychological tests occurred across baseline, pre- and post-intervention measures. However, the high level of cognitive interference induced by the training intervention should have helped to prevent or at least minimize learning effects across repeated neuropsychological testing. Finally, no follow up measurement was carried out to examine the stability of training effects. Future study should include regular follow up neuropsychological measures to assess the stability and vulnerability of training effects across time and in response to changes of medication, mood, and events that are relevant for the patients' health and social situation.

Conclusion

In conclusion, our data show clear evidence that individuals with PD can achieve a considerable improvement in working memory following a computer based cognitive training intervention. Cognitive improvement does not only occur in the trained, but also in untrained tasks. This study provides strong evidence for a transfer of improvement in the trained tasks to standard neuropsychological measures. Our data thus provide valuable information on the treatability of PD related cognitive impairment beyond pharmacological therapy. Since neurocognitive interventions are medically and psychologically efficient approaches with economically cost effective requirements, we recommend the inclusion of a PD specific cognitive training in medical treatment routines of the disorder.

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Conflicts of Interest

All authors declare that they have no conflict of interest.

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