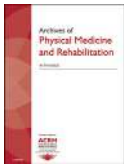
ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2014;95:996-9



BRIEF REPORT

Impact of Physical Exercise on Reaction Time in Patients With Parkinson's Disease—Data From the Berlin BIG Study

Georg Ebersbach, MD,[a] Almut Ebersbach, MD,[a] Florin Gandor, MD,[a] Brigitte Wegner,[b] Jörg Wissel, MD,[c] Andreas Kupsch, MD[d]

From the [a]Movement Disorders Hospital, Beelitz-Heilstätten; [b]Institute of Medical Biometrics and Clinical Epidemiology, Charité University Medicine Berlin, Berlin; [c]Vivantes-Klinikum Spandau, Berlin; and [d]Department of Neurology and Stereotactic Neurosurgery, Otto-von-Guericke-University, Magdeburg, Germany.

Abstract

Objective: To determine whether physical activity may affect cognitive performance in patients with Parkinson's disease by measuring reaction times in patients participating in the Berlin BIG study.

Design: Randomized controlled trial, rater-blinded.

Setting: Ambulatory care.

Participants: Patients with mild to moderate Parkinson's disease (N=60) were randomly allocated to 3 treatment arms. Outcome was measured at the termination of training and at follow-up 16 weeks after baseline in 58 patients (completers).

Interventions: Patients received 16 hours of individual Lee Silverman Voice Treatment-BIG training (BIG; duration of treatment, 4wk), 16 hours of group training with Nordic Walking (WALK; duration of treatment, 8wk), or nonsupervised domestic exercise (HOME; duration of instruction, 1hr).

Main Outcome Measures: Cued reaction time (cRT) and noncued reaction time (nRT).

Results: Differences between treatment groups in improvement in reaction times from baseline to intermediate and baseline to follow-up assessments were observed for cRT but not for nRT. Pairwise *t* test comparisons revealed differences in change in cRT at both measurements between BIG and HOME groups (intermediate: −52ms; 95% confidence interval [CI], −84/−20; $P=.002$; follow-up: 55ms; CI, −105/−6; $P=.030$) and between WALK and HOME groups (intermediate: −61ms; CI, −120/−2; $P=.042$; follow-up: −78ms; CI, −136/−20; $P=.010$). There was no difference between BIG and WALK groups (intermediate: 9ms; CI, −49/67; $P=.742$; follow-up: 23ms; CI, −27/72; $P=.361$).

Conclusion: Supervised physical exercise with Lee Silverman Voice Treatment-BIG or Nordic Walking is associated with improvement in cognitive aspects of movement preparation.

Archives of Physical Medicine and Rehabilitation 2014;95:996-9

Acute effects of exercise on alertness and other cognitive measures have been described in healthy subjects,[1] and physical training has been demonstrated to improve the long-term outcome of cognitive performance.[2] The effect of physical activity on cognitive processing in Parkinson's disease (PD) is receiving growing attention,[3] but clinical studies in this respect are scarce.

Lee Silverman Voice Treatment (LSVT)-BIG is a physiotherapy for patients with PD derived from the widely established LSVT,[4] focusing on training of high-amplitude movements.[5] We have previously reported results from the Berlin BIG study[6] that compared changes in motor performance in 60 patients with mild to moderate PD treated with LSVT-BIG, Nordic Walking, or domestic nonsupervised exercises. Blinded video rating revealed an improvement in Unified Parkinson's Disease Rating Scale motor scores in the BIG group and minor deterioration in the other groups at 16-week follow-up.

Here, we report results of reaction time measurements in patients with PD participating in the Berlin BIG study.

Supported by an unrestricted grant from Deutsche Parkinson Gesellschaft.

No commercial party having a direct financial interest in the results of the research supporting this article has conferred or will confer a benefit on the authors or on any organization with which the authors are associated.

0003-9993/14/$36 - see front matter © 2014 by the American Congress of Rehabilitation Medicine
http://dx.doi.org/10.1016/j.apmr.2013.10.020

Methods

Study design and patients

The Berlin BIG study was a rater-blinded, randomized controlled study that has been described in detail previously.[6] Sixty patients with idiopathic PD referred from local outpatient clinics and office-based physicians to the *Zentrum für ambulante Rehabilitation*, Berlin, were enrolled between June 1, 2008 and May 31, 2009. Patients were randomly allocated by drawing lots to receive LSVT-BIG (BIG), Nordic Walking (WALK), or domestic non-supervised exercise (HOME). Patients allocated to the BIG group received 16 supervised 1-hour sessions (4/wk for 4wk) of a novel high-intensity training aimed at improving movement amplitudes in PD (see Lautenschlager et al[2] for comprehensive description). Patients assigned to the WALK group received 16 supervised 1-hour sessions of Nordic Walking (2/wk for 8wk) in groups of 4 to 6 participants. Patients assigned to the HOME group received a 1-hour instruction of domestic training with practical demonstration and training.

Inclusion criteria comprised diagnosis of PD according to UKPD Brain Bank Criteria, Hoehn and Yahr stages I to III, outpatient treatment, and stable medication 4 weeks before inclusion. Exclusion criteria encompassed dementia, severe depression, disabling dyskinesias, and comorbidities affecting mobility or ability to exercise. The local ethics committee (Ärztekammer Brandenburg) approved the study, and written informed consent was obtained from each subject.

Assessment procedures

The primary efficacy measure was the difference in rater-blinded Unified Parkinson's Disease Rating Scale-III score changes between treatment groups from baseline to follow-up at 16 weeks. Secondary outcome variables included Timed Up and Go test and time required to walk 10 meters.

Reaction times were assessed while patients were in the medication ON state using the Testbattery for Attentional Performance 2.2[a] at baseline, immediately after the termination of active intervention (week 4 in BIG and HOME and week 8 in WALK), and at follow-up 16 weeks after baseline. The Testbattery for Attentional Performance subtest for alertness was applied in which 2 tasks measure noncued reaction time (nRT) and cued reaction time (cRT). The subtest "Alertness" has been validated in healthy subjects and patients with different neurological disorders.[7] During the measurement of nRT, participants were seated facing a computer screen with their dominant hand placed comfortably on a response switch. They were then required to press the switch immediately after the appearance of a visual stimulus (white cross on a black computer screen). For the assessment of cRT, the imperative visual stimulus was preceded by an acoustic warning signal. Two blocks comprising 20 presentations of a stimulus were performed for each condition in an ABBA sequence (starting with 2 nRT series, followed by 2 cRT series).

We calculated the difference in mean values between baseline and intermediate assessments and between baseline and follow-up assessments for nRT and cRT, respectively. On an exploratory basis, these differences were then compared between treatment groups using 2-factorial repeated-measures analysis of variance (ANOVA) (3 groups × 2 measurements). If the overall comparison revealed significant effects, pairwise ANOVA was performed. In addition, 1-way ANOVA and pairwise *t* tests were applied to compare changes in reaction times from baseline to intermediate and from baseline to follow-up between treatment groups. The alpha level was set at .05, and outcome analyses were conducted on a per-protocol basis using SPSS software.[b]

List of abbreviations:

ANOVA	**analysis of variance**
CI	**confidence interval**
cRT	**cued reaction time**
LSVT	**Lee Silverman Voice Treatment**
nRT	**noncued reaction time**
PD	**Parkinson's disease**

Results

Of 60 patients randomly assigned to treatments, 58 subjects completed the study (fig 1) and were available for follow-up at 16 weeks: BIG (n=20), WALK (n=19), and HOME (n=19). No significant differences in age, disease duration, and levodopa equivalence dose were found between the groups. Weekly unsupervised exercise time in addition to supervised therapy in BIG and WALK groups did not differ between groups (see Ebersbach et al[6] for further details).

Outcome of primary and secondary motor assessments has been reported previously.[3] Mean values of reaction times are given in table 1.

Analysis of change in reaction times applying 2-factorial repeated-measures ANOVA indicated differences between groups for cRT ($P=.008$, $F=5.27$) but no effect of measurement ($P=.926$, $F=.009$) or group×measurement interactions ($P=.550$, $F=.604$). Pairwise comparisons detected differences between BIG and HOME groups ($P=.005$, $F=9.144$) and between WALK and HOME groups ($P=.01$, $F=7.474$) but not between BIG and WALK groups ($P=.452$, $F=.578$). One-way ANOVA showed differences in change in cRT between treatment groups at intermediate ($P=.030$, $F=3.758$) and follow-up ($P=.013$, $F=4.709$) assessments.

At the intermediate assessment, mean cRT was reduced by −47 ms (95% confidence interval [CI], −68/−25) in the BIG group and by −56 ms (CI, −111/−1) in the WALK group. In the HOME group, the mean change in cRT was 5 ms (CI, −20/30). At final assessment, the changes compared with baseline were −41 ms (CI, −70/−11) for BIG, −64 ms (CI, −106/−21) for WALK, and 14 ms (CI, −28/57) for HOME groups (fig 2). Within-group comparisons showed that changes were significant for BIG ($P=.001$, $F=9.7$) and WALK ($P=.015$, $F=5.5$) groups but not for the HOME group ($P=.79$, $F=.24$).

Pairwise *t* test comparisons revealed differences in change in cRT at both measurements between BIG and HOME groups (intermediate: −52ms; CI, −84/−20; $P=.002$; Cohen's *d*, 1.1; follow-up: 55ms; CI, −105/−6; $P=.030$; Cohen's *d*, 0.7) and between WALK and HOME groups (intermediate: −61ms; CI, −120/−2; $P=.042$; Cohen's *d*, 0.7; follow-up: −78ms; CI, −136/−20; $P=.010$; Cohen's *d*, 0.9). There was no difference between BIG and WALK groups (intermediate: 9ms; CI, −49/67; $P=.742$; Cohen's *d*, 0.1; follow-up: 22ms; CI, −27/72; $P=.361$; Cohen's *d*, 0.3).

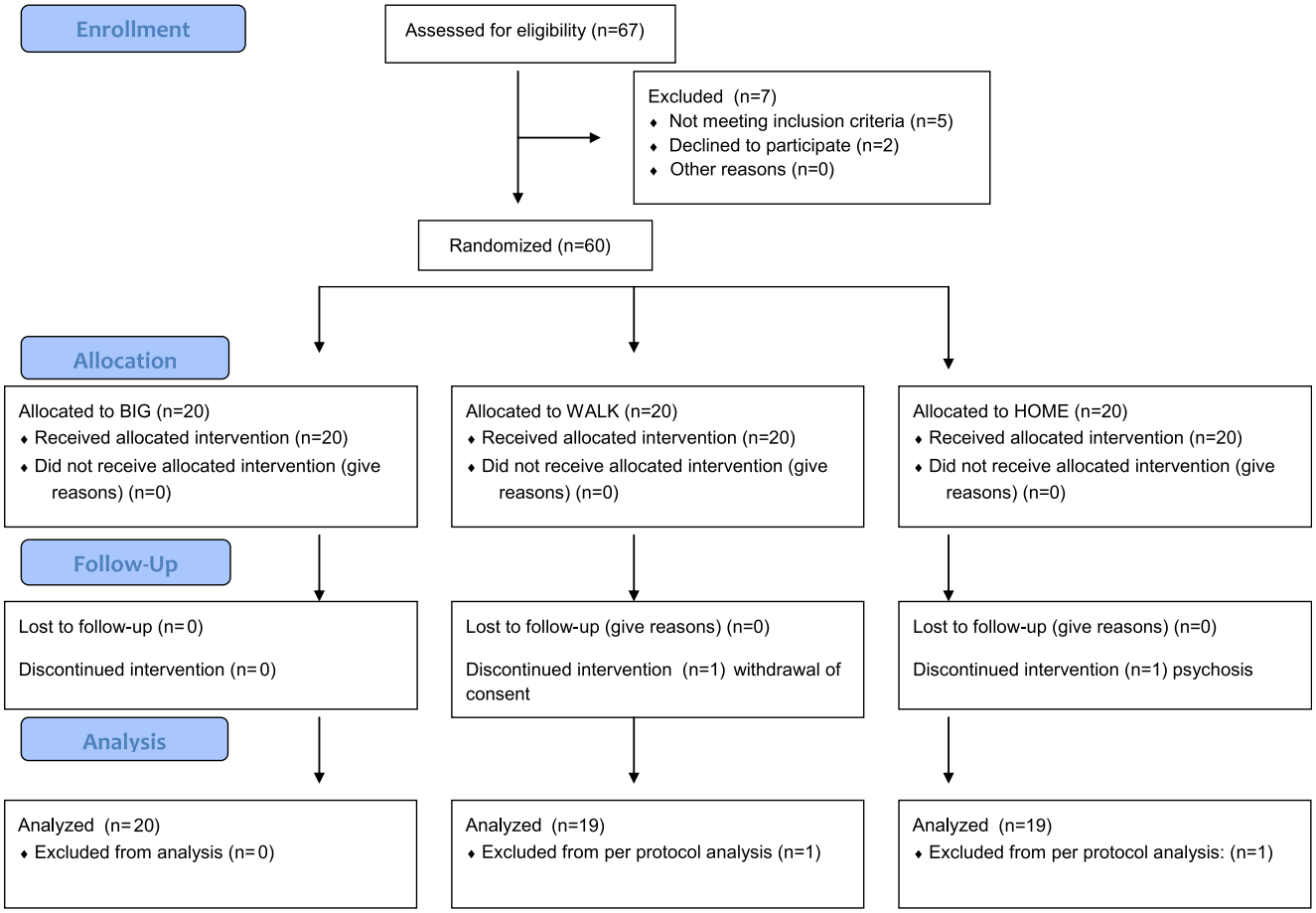


Fig 1 Consolidated Standards of Reporting Trials diagram showing the disposition of patients.

Analysis of nRT revealed no difference in group ($P=.122$, $F=2.191$), measurement ($P=.693$, $F=.157$), or interactions ($P=.230$, $F=1.51$) and no treatment effects at intermediate ($P=.199$, $F=1.665$) and follow-up ($P=.159$, $F=1.904$) assessments.

Discussion

In the present exploratory study, the modalities of physical exercise affected cRT in patients with PD. Subjects assigned to Nordic Walking and LSVT-BIG showed a sustained improvement in cRT, whereas no changes were observed in subjects assigned to domestic training without supervision. The total amount of active training was higher in supervised groups (WALK and BIG) because weekly domestic training time did not differ between groups. Improvement in reaction times can thus be attributed to supervised physical exercise, confirming the importance of direct supervision in the rehabilitation of patients with PD previously described in a study of Ridgel et al.[8] In contrast to the improvement in Unified Parkinson's Disease Rating Scale motor scores seen only with LSVT-BIG (one-to-one exercise), reduction in reaction times occurred to the same extent following Nordic Walking (group treatment). Individual face-to-face interaction with the therapist and choice of physical exercise may thus not be as crucial for the improvement in reaction times as for the amelioration of bradykinesia.

Significant effects were demonstrated for cRT but not for nRT, suggesting that a shorter preparatory phase between the presentation of an acoustic preparatory cue and an imperative go-signal was crucial for faster reactions. This finding points to nonmotor effects of LSVT-BIG and Nordic Walking exercise, mainly concerning the domains of phasic alertness and attention. Phasic alertness represents an increased readiness to respond to a signal that is neurophysiologically accompanied by activation in bilateral thalamus, anterior cingulate, and bilateral supplementary motor area.[9] In a recent study,[2] 24 weeks of exercise resulted in an improvement in cognitive abilities in subjects with memory deficits. Acute effects of physical exercise on some cognitive

Table 1 nRT and cRT (ms)

Condition	Group	Baseline	Intermediate	Follow-Up
nRT	BIG	385±100	349±73	364±115
	WALK	405±156	383±118	356±120
	HOME	335±56	341±82	342±105
cRT	BIG	377±79	330±64	337±90
	WALK	388±136	339±71	325±80
	HOME	315±57	320±80	330±114

NOTE. Values represent mean ± SD.

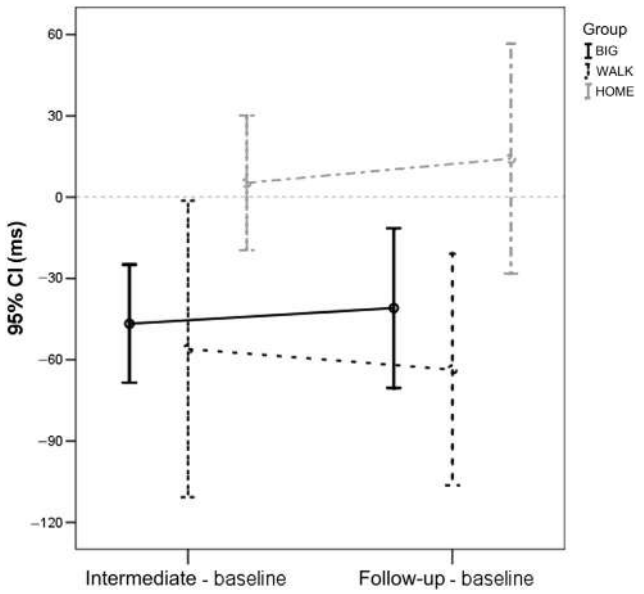


Fig 2 Mean change in cRTs (ms) from baseline assessment to intermediate assessment and from baseline assessment to follow-up assessment in BIG (black solid line), WALK (black dotted line), and HOME (gray dotted line) groups. Improvements in cRT (negative values reflecting shorter reaction time) were found at intermediate and follow-up assessments for BIG and WALK groups.

measures have also been reported in PD. Ridgel et al[10] found passive cycling to improve performance in the Trail Making Test. Muller and Muhlack[11] reported reduction in reaction time after active cycling. The present study is in line with these findings, but it is the first to compare different treatment modalities and to reveal sustained effects after 8 to 12 weeks.

High-intensity exercise has been shown to improve corticomotor excitability in PD.[12] Acute effects could be mediated by catecholamine release, whereas exercise-induced increases in brain-derived neurotrophic factor may account for more persistent improvement.[1] Long-term effects of increased brain-derived neurotrophic factor concentration include neuroplastic changes, which may aid cognition[3] and relate to improved endogenous dopamine release into limbic and central motor structures.[13]

Notably, no improvement in reaction times was described for acute challenges of levodopa,[14] suggesting that exercise may have effects on nonmotor measures that are not elicited by medication.

Study limitations

We cannot exclude a ceiling effect in the HOME group because baseline reaction times were shorter in this group. Furthermore, no additional assessments of executive function, such as working memory or set shifting, were applied. Further studies are needed to explore the potential of physical exercise to improve cognitive function in patients with PD.

Conclusion

Supervised physical exercise with LSVT-BIG or Nordic Walking is associated with an improvement in cognitive aspects of movement preparation.

Suppliers

a. Testbattery for Attentional Performance; PSYTEST Psychologische Testsysteme, Kaiserstrasse 100, D-52134 Herzogenrath, Germany.
b. SPSS, Inc, 233 S Wacker Dr, 11th Fl, Chicago, IL 60606.

Keywords

Exercise; Parkinson's disease; Reaction times; Rehabilitation

Corresponding author

Georg Ebersbach, MD, Fachkrankenhaus für Bewegungsstörungen/Parkinson, Paracelsusring 6a, 14547 Beelitz-Heilstätten, Germany. *E-mail address:* ebersbach@parkinson-beelitz.de.

References

1. McMorris T, Hale BJ. Differential effects of differing intensities of acute exercise on speed and accuracy of cognition: a meta-analytical investigation. Brain Cogn 2012;80:338-51.
2. Lautenschlager NT, Cox KL, Flicker L, et al. Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: a randomized trial. JAMA 2008;300:1027-37.
3. Ahlskog JE. Does vigorous exercise have a neuroprotective effect in Parkinson disease? Neurology 2011;77:288-94.
4. Ramig LO, Sapir S, Fox C, Countryman S. Changes in vocal loudness following intensive voice treatment (LSVT) in individuals with Parkinson's disease: a comparison with untreated patients and normal age-matched controls. Mov Disord 2001;16:79-83.
5. Farley BG, Fox CM, Ramig L, Farland DC. Intensive amplitude-specific therapeutic approaches for Parkinson's disease. Topics Ger Rehabil 2008;24:99-114.
6. Ebersbach G, Ebersbach A, Edler D, et al. Comparing exercise in Parkinson's disease—the Berlin LVST-BIG study. Mov Disord 2010; 25:1902-8.
7. Zimmermann P, Fimm B. A test battery for attentional performance. In: Leclerq M, Zimmermann P, editors. Applied neuropsychology of attention: theory, diagnosis and rehabilitation. London: Psychology Pr; 2002. p 110-51.
8. Ridgel AL, Vitek JL, Alberts JL. Forced, not voluntary, exercise improves motor function in Parkinson's disease patients. Neurorehabil Neural Repair 2009;23:600-8.
9. Nagai Y, Critchley HD, Featherstone E, Fenwick PB, Trimble MR, Dolan RJ. Brain activity relating to the contingent negative variation: an fMRI investigation. Neuroimage 2004;21:1232-41.
10. Ridgel AL, Kim CH, Fickes EJ, Muller MD, Alberts JL. Changes in executive function after acute bouts of passive cycling in Parkinson's disease. J Aging Phys Act 2011;19:87-98.
11. Muller T, Muhlack S. Effect of exercise on reactivity and motor behaviour in patients with Parkinson's disease. J Neurol Neurosurg Psychiatry 2010;81:747-53.
12. Fisher BE, Wu AD, Salem GJ, et al. The effect of exercise training in improving motor performance and corticomotor excitability in people with early Parkinson's disease. Arch Phys Med Rehabil 2008;89:1221-9.
13. Petzinger GM, Fisher BE, Van Leeuwen JE, et al. Enhancing neuroplasticity in the basal ganglia: the role of exercise in Parkinson's disease. Mov Disord 2010;25:S141-5.
14. Molloy SA, Rowan EN, O'Brien JT, McKeith IG, Wesnes K, Burn DJ. Effect of levodopa on cognitive function in Parkinson's disease with and without dementia and dementia with Lewy bodies. J Neurol Neurosurg Psychiatry 2006;77:1323-8.