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Comparing computer-aided therapy with conventional physiotherapy in Parkinson's disease: An equivalence study

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Abstract

Objective: The present study investigated, whether computer-aided therapy in patients with Parkinson's disease is equivalent/non-inferior to conventional Lee Silvermann Voice Treatment (LSVT)-BIG-therapy in respect to motor outcome as measured by the Unified Parkinson's Disease Rating Scale (MDS-UPDRS-III) and quality of life as measured by the Parkinson's Disease Questionnaire (PDQ-39). *Methods:* In this controlled, rater-blinded study, 34 patients were included and 24 patients randomized to train seven standard exercises of the BIG-therapy either by a computer (BeBIG-group) or by a certified LSVT-BIG therapist (ThBIG-group) over four weeks. Equivalence was assessed by comparing the confidence interval of the BeBIG-group to the equivalence margin of the ThBIG-group. *Results:* There were no significant group differences in respect to age, disease duration, L-dopa equivalent daily dose or clinical stage of the disease. Both groups profited significantly from the therapy as demonstrated by an improvement in the MDS-UPDRS-III of 9.17 point in the BeBIG-group and of 8.92 points in the ThBIG-group. There was a non-significant decrease in the PDQ-39 of 9.23 points in the BeBIG-group and 4.23 points in the ThBIG-group. However, equivalence could not be demonstrated as the improvement of the BeBIG-group exceeded the confidence interval of the ThBIG-group. *Conclusion:* Physical training by a computer as well as by a therapist improves motor symptoms and quality of life in Parkinson's disease. Both therapies are not equivalent, superiority of the computerized training can however not be concluded, as the study was only designed to test for non-inferiority. Therefore, computerized training can be considered as an add-on-therapy.

Keywords: Equivalence study, idiopathic Parkinson-Syndrome, computer-aided rehabilitation, LSVT-BIG

INTRODUCTION

In recent years, the evidence for non-pharmacological therapy in the treatment of patients with Parkinson's disease (PD) is growing. However, even though a European survey shows that most patients with PD perceive physiotherapy as very helpful, the access to physiotherapy services varies.[1-3] This is also true for other populations, e.g. in Asia, in which prevalence of PD increases but the access to physiotherapy is insufficient.[4] The main reason for this might be a lack of reimbursement and the missing availability of specialized physiotherapists. This is especially true, as physiotherapy for PD, like the well-established LSVT-BIG-therapy, requires high repetition and frequent therapy by well-trained experts. Computer aided and virtual rehabilitation can provide frequent therapy with feedback and therefore support conventional physiotherapy, as this approach is less expensive and more flexible. In this study we trained a group of patients with PD using a computerized physiotherapy program similar to the LSVT-BIG-therapy (BeBIG-group) and compared them to a group receiving conventional LSVT-BIG-therapy by a well-trained physiotherapist (ThBIG-group). Our goal was to show non-inferiority of the computerized therapy.

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LSVT-BIG therapy

LSVT-BIG therapy has previously been described in detail.[5] The exercises for this treatment (LSVT-BIG) consist of movements with high frequency and big amplitudes of the upper and lower extremities. The LSVT-BIG-therapy is composed of 16 therapeutic one-hour-sessions over four weeks with four sessions per week. Each session is divided into two parts. One part of the treatment consists of seven standardized exercises with multi-directional movements of the extremities. Only this part was computerized in our study. The second part aims to transfer this movements to the daily activities combined with the personal needs of the patient. The goal of LSVT-BIG is to improve the perception and recalibration of the movement.[6]

BeBig System

The Fraunhofer Institute for Open Communication (FOKUS) developed the software and the algorithm of the BeBIG-System. This system is composed of a standard consumer computer, television and a Microsoft Kinect (Figure 1a). Two avatars are displayed on the screen. A therapist demonstrating the exercise and a life-picture of the patient as captured by the Kinect box. Seven exercises were implemented with motion capture. An algorithm compares the movements of the patient with the optimal movement patterns which was implemented by a therapist. Every exercise is visually and auditorily described by the system at the beginning of every exercise. If the movement of the patients differs the movement of the optimal movement, feedback is provided by two colors (red and green) which is overlaid / augmented on the avatar of the patient (Figure 1b and 1c). After every exercise the results in speed, amplitude of movement and posture are presented with bar diagrams (Figure 1d).

The present study investigated whether the seven standardized exercises of the LSVT-BIG therapy trained by a computer (BeBIG-group) are as effective as the same as the exercises trained by a specialized physiotherapist (ThBIG-group).

METHOD

Subjects

Thirty-four patients with PD were included in the study. The following inclusion criteria were applied: diagnosis of idiopathic Parkinson's disease with mild to moderate symptoms (Hoehn & Yahr I-III), no restrictive cardiovascular

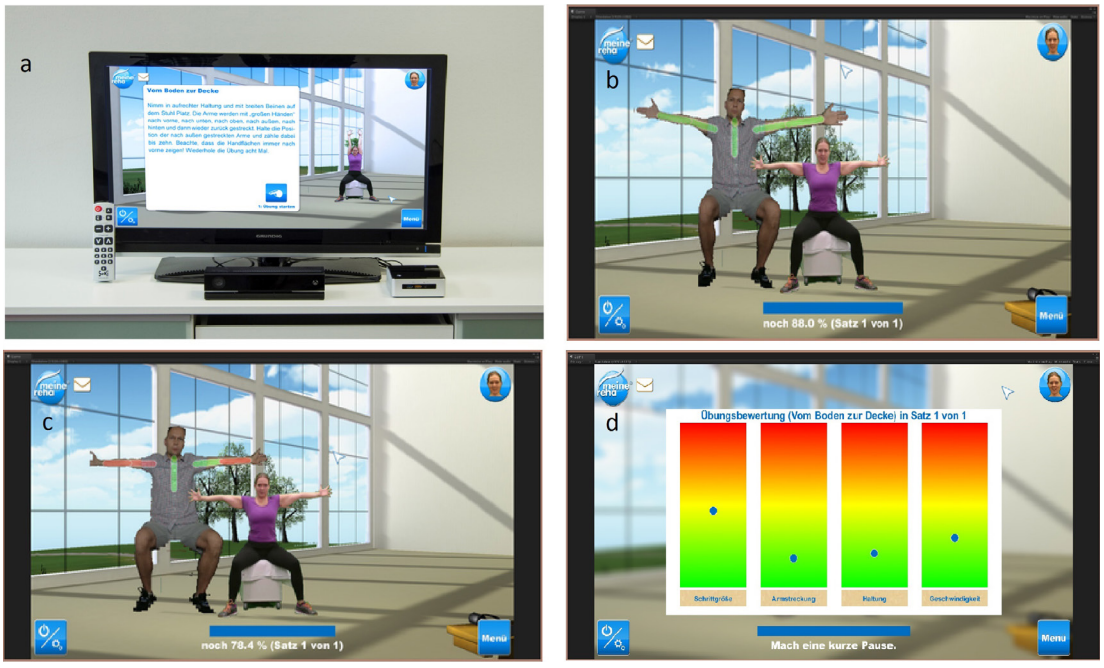

Figure 1. a: shows the hardware components including the Kinect-box and the TV-screen showing the avatar of the therapist and the instructions for the patients; b: shows the therapist and the patient as avatars with positive (green) feedback; c: negative feedback (red); d: feedback screen after each exercise to size of steps, amplitude of arm movement, position and speed.

diseases and the ability to give informed consent (Mini Mental Status ≥ 24 Points). Exclusion criteria, dementia, depression (Becks Depression Inventory II (BDI-II)) or other severe psychiatric symptoms, high risk of fall (Performance-Oriented Assessment of Mobility; POMA ≥ 21). The patients were enrolled between October 2016 and September 2018. The study was conducted in Passauer Wolf Centre of Movement Disorders and Rehabilitation Centre Bad Gögging. The study was approved by the local ethics committee and all subjects gave informed consent. Subjects were allocated by a randomization list to one of the groups.[7] According to the list, 15 patients were assigned to the BeBIG-group and 19 to the ThBIG-group.

Of the 34 patients enrolled 10 patients discontinued the study, all because the stay in the rehabilitation facility was not extended because of economic reasons and the full therapy over four weeks could therefore not be delivered.

Intervention

This study compared two interventions; seven standard exercises of the BIG-therapy trained by a computer (BeBIG-group) to the same exercises trained by a certified LSVT-BIG therapist (ThBIG-group). All subjects received conventional LSVT-BIG-therapy with a therapist over four sessions of each 60 minutes in the first week. Each session consisted of a first part (30 minutes) in which seven standardized exercises were trained and a second part (30 minutes) consisting of an individualized transfer-training of the learned movement in daily activities. After the first week patients were randomized to one of the two groups. In the BeBIG-group the patient trained the seven standardized exercises of part one with a computer system receiving instruction and feedback on a monitor. In the ThBIG-group the patient was trained by a certified therapist. The second part of the BIG-therapy consisting of the transfer-training was conducted equally in both groups by a physiotherapist. Both groups received four sessions of training over three additional weeks. Both groups received the same amount of therapy. The therapy was in addition to the regular rehabilitation program provided.

Assessment procedures and outcome parameters

The primary outcome was change of the motor symptoms of PD as measured using the motor part of the Unified Parkinson Disease Rating Scale (UPDRS-III).[8] All patients were assessed during ON-medication condition. The secondary outcome was quality of life as assessed by the PDQ-39.[9,10] Both assessments were performed before and after the four weeks of therapy by a blinded neurologist. The equivalence of both groups was tested. The ThBIG-group was the reference group, the BeBIG-group was the intervention group. Further assessments were the Mini Mental Status Test (MMST)[11,12], the Performance-Oriented Assessment of Mobility (POMA) and the BDI-II.[13,14] An equivalence is established if the confidence interval of the BeBIG Group lies between the equivalence margin, which was calculated with the reference group. If the confidence interval lies above or below the equivalence margin, equivalence is not established.

Data analyses

The data were analyzed after completion of the investigations. Descriptive statistics (mean, standard deviation), Student t-test for normally distributed baseline was calculated. The calculation of the equivalence was done with the Two-One-Sided Test (TOST). The results are presented with confident intervals and were analyzed with the statistical language R and the Graphical User Interface Rstudio.[15,16]

Equivalence margin

The equivalence margin was established with the lower confidence interval of the results of the reference group (ThBIG). This approach was considered, because no placebo-controlled trial was conducted with LSVT-BIG therapy. Therefore we followed the recommendation of the guideline on the choice of the non-inferiority margin.[16] The equivalence margin for the PDQ-39 is ± 0.46 Points and for UPDRS-III ± 2.4 Points.

The study was approved by the Ethics committee of the Landesärztekammer Bayern (16094). Written informed consent was obtained from all participants.

RESULTS

Only 24 subjects out of the 34 patients, who were included, completed the four week of training, as 10 subjects had to withdraw earlier. All subjects withdrew because the rehabilitation treatment was discontinued for economic reasons. Of the remaining subjects, 12 were randomized to the ThBIG Group and 12 subjects to the BeBIG group.

Of all participants 9 (37.5 %) were female and 15 (62.5%) male subjects. The average age of the subjects was 56.04 ± 7.18 years. Subjects

Table 1: Demographic data of the study.

	sum		ThBIG		BeBIG		
	x	±	x	±	x	±	p-value
Age	56.0	7.18	53.8	4.28	58.2	8.88	0.14
Years since diagnosis	3.3	2.60	3.5	2.58	3.2	2.72	0.76
Hoehn and Yahr stage	1.9	0.66	1.8	0.71	2.1	0.58	0.30
LEDD mg/d	519.6	269.11	470.7	325.30	568.5	200.95	0.39
BDI	7.3	5.04	7.8	5.67	6.9	4.52	0.69
POMA	24.6	3.36	25.5	2.81	23.8	3.74	0.21
UPDRS-III	27.2	13.66	24.0	14.59	30.5	12.43	0.25

Note: Values are means and standard derivation with comparison of both group with a t-test.

were relatively mildly affected with an average Hoehn and Yahr stage 1.94 ± 0.66, average disease duration of 3.33 ± 2.72 years and a MDS-UPDRS III of 27.25 ± 13.66. At the time of inclusion out of the 34 patients randomized, 5 patients in the ThBIG-group and 2 patient in the BeBig group reported motor fluctuations up to 25% of the day according to the MDS-UPDRS. All participants were treated with dopaminergic medication and an average Levodopa equivalence dose (LEDD) of 468.25 mg/d ± 250.65 mg/d at the beginning of the study. During the study the LEDD was slightly adjusted for medical reasons in some patients to an LEDD of 519.58 mg/d ± 269.11 mg/d. The adjustment of the LEDD differed slightly between both groups. The average LEDD increased from 394.17mg/day to 470.67mg/day in the ThBIG-group and from 542.33mg/day to 568,5mg/day in the BeBIG-group. No patient was severely depressed as measured by the BDI (Table 1). Both groups did not differ significantly in these demographic and clinical parameters as demonstrated in Table 2. According to the therapy protocol all subjects were to receive four treatment units per week over four weeks and therefore a total of 16 treatments. A few treatments were missed for holidays or sick leave of the therapist resulting in an average number of treatments for the participants of 15 ± 1.56 treatment units. Subjects of the ThBIG-group participated in 14.58 ± 1.68 treatment units, subjects of the BeBIG-group participated in 15.42 ± 1.38 treatment units. This difference in treatment units was not significant between both groups (p = 0.2).

No significant differences on PDQ-39 and UPDRS-III were measured on exclusion between both groups (t-test), the results are shown in Table 2.

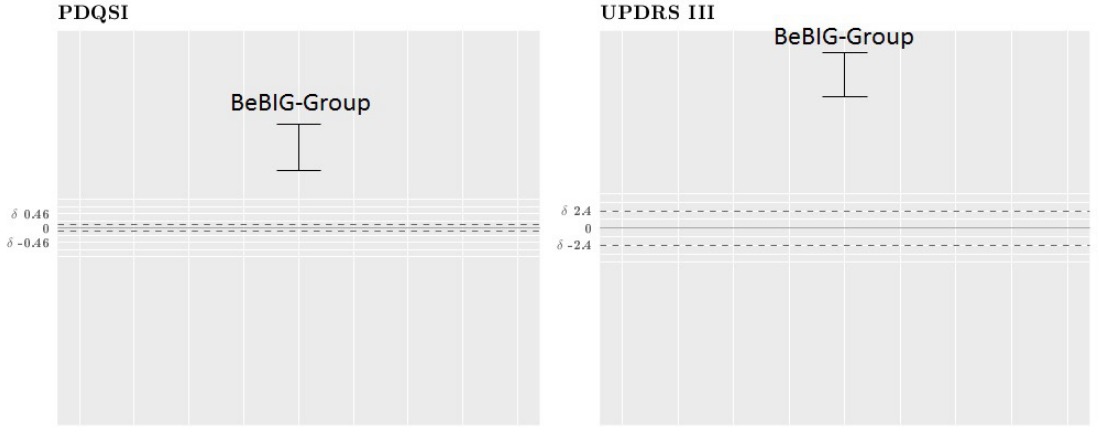

Figure 2. The equivalence margin (dotted lines) established with the lower confidence interval of the results of the reference group (ThBIG) are exceeded by the BeBIG group, demonstrating non-inferiority of the computer-aided therapy for the PDY-39 as well as for the MDS-UPDRS-III.

Table 2: Outcome motor assessment and quality of life.

	ThBIG					BeBIG						
	T1		T2			T1		T2				
	x	±	x	±	Δ	x	±	x	±	Δ	t-Test p-Value	TOST-p-Value
	17.69	10.74	13.46	11.30	-4.2	20.50	10.41	11.27	8.27	-8.3	0.34	0.74
PDQ-39												
Mobility	13.75	16.80	9.8	14.4	-4.0	16.27	15.11	5.62	7.47	-7.5	0.11	0.88
Activities	19.44	16.89	14.58	14.6	-4.9	20.14	14.85	5.90	6.27	-6.3	0.06	0.99
Emotional well being	22.92	17.27	18.06	16.9	-4.9	15.97	12.91	13.54	16.87	-2.43	0.26	0.81
Stigma	21.88	24.79	15.62	23.3	6.2	15.10	21.73	9.90	17.77	-5.21	0.37	0.74
Social support	6.25	10.13	11.11	18.9	+4.9	8.33	15.49	7.58	15.12	-0.76	0.78	0.99
Cognitions	17.71	13.80	9.38	10.2	-8.3	22.92	21.87	13.54	17.24	-9.38	0.80	0.71
Communication	11.81	16.07	9.03	13.0	-2.8	31.25	21.06	6.94	8.58	-24.31	0.46	0.84
Bodily discomfort	27.78	17.88	20.14	22.0	-7.6	34.03	22.88	27.78	18.91	-6.25	0.61	0.90
UPDRS-III	24.00	14.59	15.08	9.57	8.9	30.50	12.43	21.33	7.82	-9.17	0.6	0.85

Changes from baseline to follow up between inclusion (T1) and exclusion (T2) and both group. Comparison with t-test and TOST of the primary outcome (UPDRS III) and secondary outcome (PDQ-39 with subtests). The equivalence margin was conducted with the lower confidence interval of the results of the reference group (ThBIG). Values are means and standard derivation

T-tests comparing the values of the MDS-UPDRS-III and PDQ-39 at the beginning and the end of the study show improvement of motor symptoms and quality of life during the treatment period of four weeks in both groups. The motor symptoms as measured by the MDS-UPDRS-III improved in the BeBIG-group by 9.17 points and the ThBIG-group by 8.92 points. This change of the MDS-UPDRS-III was significant in both groups (ThBIG-group $p = 0.01$) (BeBIG-group $p = 0.00$). The quality of life also improved in both groups over the treatment period as shown by a decrease in the PDQ-39 of 9.23 points in the BeBIG-group and 4.23 points in the ThBIG-group. The decrease in both groups, however, was not significant (BeBIG-group $p = 0.17$), (ThBIG-group $p = 0.07$).

The aim of this study was to demonstrate non-inferiority of the BeBIG-group to the ThBIG-group as measured by the MDS-UPDRS-III (primary outcome) and the PDQ-39 (secondary outcome). The calculation of the equivalence was done with the Two-One-Sided Test (TOST). However, equivalence of both groups could not be shown neither for the MDS-UPDRS-III nor for the PDQ-39. As demonstrate in Figure 1, the BeBIG group shows in the MDS-UPDRS-III as well as in the PDQ-39 superiority to the ThBIG group. Further analysis of the subdomains of the PDQ-39 showed similar results for mobility, activities of daily living, emotional wellbeing, stigma, social support, cognitions and bodily discomfort but not for the subdomain communication.

DISCUSSION

The aim of this study was to demonstrate non-inferiority of a computer aided physiotherapy program similar to the LSVT-BIG-therapy (BeBIG-group) compared to a group receiving conventional LSVT-BIG-therapy by a well-trained physiotherapist (ThBIG-group). Therefore, a randomized controlled, blinded-assessor, clinical trial was conducted on 34 patients with mild to moderate PD during an inpatient rehabilitation. Our goal was to reproduce the LSVT-therapist guided therapy in our computerized version as closely as possible. However the computerized version gives only standardized instructions and feedback, while a physiotherapist obviously could individualize the interaction with the patient. The results shows that the computerized physiotherapy program similar to the LSVT-BIG-therapy has at least the same effect as the conventional physiotherapy. These results however do not grant the conclusion that the computerized physiotherapy is more effective than the conventional therapy as the study was designed only to test for non-inferiority. Interestingly however the BeBIG-group was on average older and more severely affected than the ThBIG-group even though this difference did not reach significance. It might be speculated that the benefit for the BeBIG-group might have been even bigger, if they were of identical clinical and demographic parameters. Another reason for the positive benefit in the BeBIG-group might be the high motivation by a newly developed computerized system as many patients were very enthusiastic about the computer system.

A limitation of the study is the small sample size and the relatively high dropout. Out of the 34 patients included in the study only 24 could be trained for the full period of four weeks. The reason for the dropout in all cases was that the health provider in our setting usually grant an inpatient rehabilitation for three weeks and additional time must be requested. If this request was declined, the four weeks of the study could not be fulfilled. Patients, who did not fulfill the four weeks of therapy for these administrative reasons had to be excluded from our analysis. This explains the high dropout rate due to administrative circumstances. As the LSVT-BIG-treatment in both groups was delivered during an inpatient program, the environment and daily routines were fairly controlled over the four weeks period.

However the subjects of both groups also received additional exercises treatments. This additional treatment was mostly consisting of speech-therapy, aerobic training and non-activating massage therapy. The amount of the additional treatment was not included in the analysis as a confounding variable. Therefore the effect of the additional treatment cannot be assessed.

It also has to be noted that only patients with mild to moderate clinical symptoms were included in the study and that the average age (56.04 ± 7.18 years) of the participants is lower than the average age of patients with PD in the general population. It is most likely that patients with more severe symptoms and/or elderly might benefit more from a conventional physiotherapy. Furthermore we did not present the entire conventional LSVT-BIG-Therapy in a computerized version. Over the entire four weeks, only the first 30 minutes of the hourly unit consisting of seven standardized exercises was computerized, while the second half of the therapy session, in which the new-

learned movements are individually transferred into daily routines was in both groups conducted by a physiotherapist. The computerized therapy could therefore reduce the contact time of the physiotherapist with the patient by 50%.

In conclusion, this study shows that computer-aided rehabilitation in patients with mild to moderated PD can have a similar effect as conventional training. In this study the computerized therapy was part of a more extensive physiotherapy program similar to the LSVT-BIG-program. From this study we cannot conclude that computerized therapy can replace conventional physiotherapy, it can however contribute to a more extensive physiotherapeutic training if access to physiotherapy services is not given due to lack of reimbursement or limited availability of specialized physiotherapists.

DISCLOSURE

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