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# Stochastic resonance therapy in Parkinson's disease

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**Abstract**. *Objective:* To test the effects of stochastic whole body vibration (WBV) we performed a double-blind randomized controlled study.
*Methods:* Patients were allocated either to the experimental or sham group. The experimental group received 5 cycles of stochastic WBV on three days, each cycle consisting of 5 stimulus trains of 60 seconds duration (frequency 6.5 Hz) and 60 seconds resting time between stimuli. Patients allocated to the control group received a sham treatment with 1 Hz. Unified Parkinson's Disease Rating Scale, part III ($UPDRS_{III}$) was performed after treatment at baseline, after the first series on day 1 and on day 5.
*Results:* The reduction of subscores included in UPDRS III relative to baseline served as primary outcome measure. After the five-day course bradykinesia was improved in 14 of 18 patients (77.8%) and postural stability in 8 of 18 (44.4%). Speech and facial expression remained unchanged in both groups. Tremor ($p = 0{,}027$) and postural stability ($p = 0{,}048$) showed a reduction also, but did not reached level of significance ($p < 0{,}01$); $UPDRS_{III}$ sum score was improved by 26,7%.
*Conclusion:* Stochastic whole body vibration may offer a supplementation to canonical physical treatments of PD motor symptoms.

Keywords: Parkinson's disease, whole body vibration, stochastic resonance therapy

## 1. Introduction

Whole body vibration (WBV) is a biomechanical treatment strategy used in professional sports and rehabilitation [2,4,5,18,20,24]. Non-stochastic treatment devices are widely available and numerous benefits have been claimed with regard to general well being, weight-loss and improved health [26]. In contrast to earlier reports however, a recent double-blinded, placebo controlled study in Parkinson's disease (PD) patients found no difference in $UPDRS_{III}$ and several other clinical tests between the non-stochastic WBV and the placebo group [3].

WBV can also be applied as a stochastic (random) vibration pattern. Stochastic resonance therapy (SRT) uses an unsynchronised multidimensional, low impact stochastic stimulus pattern superimposed on a sinusoidal basic activity, generated by a mechanical device [11,13]. The system thus generates unpredictable movements and PD patients retain the ability to react quickly to sudden, unforeseen external cues, despite a severe bradykinesia [21]. Several biomechanics studies suggested, that these stochastic vibratory stimuli

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might modify neuromuscular performance [12]. Interestingly, vibratory stimuli were noticed to ameliorate PD symptoms early in the 19th century and Jean-Martin Charcot introduced a "vibratory chair" to treat PD patients [10].

To test whether stochastic WBV might improve parkinsonian symptoms, we performed a block randomised, double-blind, sham-treatment controlled study in 36 PD patients using a series of 5 stochastic WBV cycles on five consecutive days. Primary outcome measure was the number of responders with a $>$ 20% reduction in UPDRS $_{III}$ relative to baseline [23].

## 2. Methods

### *2.1. Participants*

Thirty-six patients with idiopathic PD at stage 1 to 4 on the Hoehn and Yahr's scale [17] participated in this study [Table 1]. Patients were informed about the test conditions and written consent was obtained from each subject. Patients with dementia, atypical or secondary parkinsonism, nephrolithiasis or relevant orthopaedic diseases (in particular joint injuries) were excluded. Patients agreed not to change medication during the trial and did not participate in any other physical therapy; a strict adherence to timed antiparkinsonian medication was encouraged. None of the patients suffered from severe dyskinesias or random freezing and no wearing-off fluctuations were reported.

### *2.2. Rehabilitation protocol*

We used a double-blind two-group pseudorandomization (block design) with sham treatment serving as control. Patients were randomized with an alternate allocation either to the experimental or sham group using a block design with an AAABBBAAABBB, distribution model (A = experimental; B = sham; first three patients were allocated to experimental group, next three patients to sham group etc.). The protocol was approved by the institutional ethic committee of the University of Bonn (protocol No. 134/08) and the study was conducted in agreement with the principles of Good Clinical Practice and the Declaration of Helsinki.

The experimental group received 5 cycles of stochastic WBV on 3 days (Monday = day 1- Wednesday-Friday = day 5), each cycle consisting of 5 stimulus trains of 60 seconds duration (frequency 6.5 Hz) and 60 seconds resting time between stimuli. Patients allocated to the control group received a sham treatment with 1 Hz, the lowest frequency available on the SR-Zeptor® device (Human Mobility, Germany) which was used to generate stochastic whole body vibration. Each participant was treated separately at similar daytimes. During treatment, the patient stood with shoes on two moving platforms, one for each foot allowing separate and unsynchronised multidimensional (forward/back, right/left, up/down) vibrations applied to both feet. Hereby the patient is unhinged permanently, but learns quickly to respond to these stimuli. During the treatment all participants adopted a semi-squat position [22].

Table 1
Characteristics of patients at baseline

| | Sham ($n = 17$) | Experimental ($n = 19$) |
|---|---|---|
| Male/Female | 14/3 | 15/4 |
| Age (years) | $68.6 \pm 4.04$ | $70.1 \pm 4.27$ |
| Hoehn and Yahr stage | $2.47 \pm 0.4$ | $2.76 \pm 0.4$ |
| UPDRS$_{III}$ score | $23.12 \pm 10.28$ | $26.94 \pm 10.2$ (n.s.) |

Values are expressed as mean $\pm$ SD; UPDRS. Unified Parkinson's Disease Rating Scale.

UPDRS$_{III}$ [6] was performed approximately 15 minutes after treatment by a blinded rater (OK) at baseline (pre), after the first series on day 1 (post 1) and on day 5 (post 5). The difference between baseline and treatment was measured by total UDPRS$_{III}$ score and subscores of the UDPRS$_{III}$ representing speech and facial expression (items 18 and 19), tremor (items 20 and 21), rigidity (item 22), bradykinesia (items 23–26, 31), arising from chair (item 27), posture (28), gait (29) and postural stability (30). A paired t-test was used for the calculation of differences between baseline and day 5 within each group (within group analysis). To evaluate putative effects of a single treatment session we also tested the differences between baseline and day 1 as a secondary outcome feature.

### *2.3. Data analysis*

The effect of vibration was assessed by comparing data of the treatment group and the sham group. For the calculation of differences we performed ANOVA. The level of significance was set at $p < 0{,}05$ for evaluation of the UPDRS$_{III}$ sum scores. For subscores of UPDRS$_{III}$ we used a Bonferroni correction resulting in $p < 0{,}01$.

To test if the number of responders with a $>$ 20% reduction in UPDRS III relative to baseline is significant we used the Fisher's Exact Test. The sample size

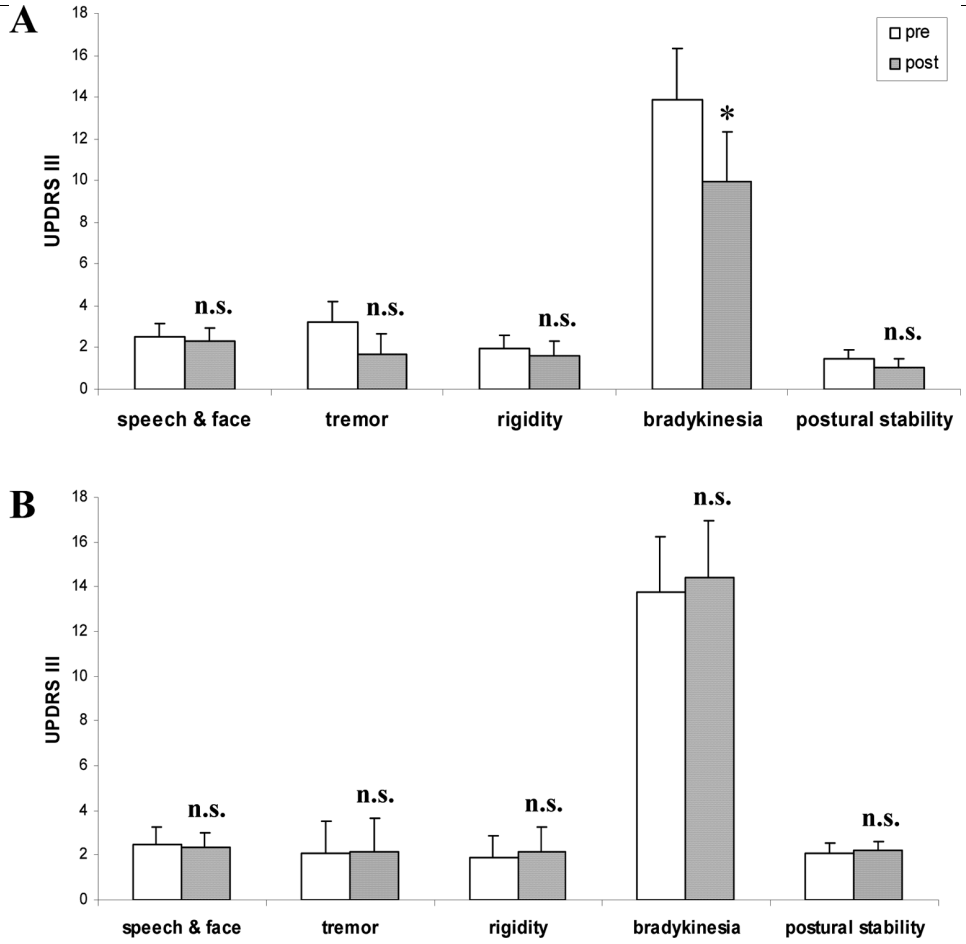


Fig. 1. Effect of whole body vibration in experimental and sham treated group. **A.** Unified Parkinson's Disease Rating Scale (UPDRS) III subscore of bradykinesia showed significant improvement ($^*p < 0{,}05$) in comparison of baseline (pre) to UPDRS III subscores after 5 days of treatment (post). No significant difference of speech, facial expression, tremor, rigidity or postural stability was detectable. **B.** In the sham treated group none of the subscores examined changed. N.s. means no significant difference.

was determined at $n = 17$ using the recommendations described by Dupont and analyses were performed "as intended treated" [7].

## 3. Results

Seventeen patients with idiopathic PD were allocated to the sham group, 19 to the experimental group. One patient of the experimental group aged 77 years withdrew from the study on day 3 due to novel pain in his knees; thus 35 PD patients completed the trial. Mean Hoehn and Yahr stage was $2.5 \pm 0.4$ in the sham and $2.8 \pm 0.4$ in the experimental group (a single patient was stage IV). Accordingly, clinical severity evaluated by UPDRS scores was lower in the sham treated group although not significantly ($\text{UPDRS}_{III}$: 23 vs. 27, Table 1, Fig. 1).

In the experimental group, four patients showed stage 1 in Hoehn and Yahr stage scale, 11 patients stage 2, three patients stage 3 and no patient stage 4, whereas in the sham group one patient with stage 1, 15 patients with stage 2, one patient with stage 3 and no patient with stage 4 was seen. Greatest improvement of $\text{UPDRS}_{III}$ within the experimental group exhibited patients with stage 3 (improvement in $\text{UPDRS}_{III}$ sum score was 29,31%), patients with stage 2 improved by 27,6% and patients with stage 1 by 22,6%.

Upon completion of the five-day course a significant greater number of responders was observed for bradykinesia and postural stability in the treatment group ($p =$ 0,00002 and 0,0029, respectivly; Fisher's Exact Text; Table 2). Bradykinesia improved in 14 of 18 patients

Table 2
Percentage of responders in sham and treatment group on day 5

| | Sham ($n = 17$) | Treatment group ($n = 18$) |
|---|---|---|
| Tremor | 18% (*3 of 17*) | 50% (*9 of 18*) # |
| Bradykinesia | 6% (*1 of 17*) | 78% (*14 of 18*)** |
| Postural stability | none | 44% (*8 of 18*)* |

** $p = 0{,}00002$; * $p = 0{,}0029$; # $p = 0.075$ Fisher's Exact Text. Responder was defined as $> 20\%$ reduction in UPDRS $_{III}$ subscore relative to baseline.

(78%), postural stability in 8 of 18 (44%) and tremor in 9 of 18 (50%).

Comparing the UPDRS$_{III}$ subscores of the sham group with the treatment group after day 5, a significant decrease was observed for bradykinesia ($p = 0{,}01$) and postural stability ($p = 0{,}0015$), but not for rigidity, tremor and speech and facial expression (comparison between groups, one-way ANOVA; not shown).

A within group analysis revealed no significant change to baseline in the sham-treated group but an improvement of tremor ($p = 0.027$), bradykinesia ($p = 0.001$) and postural stability ($p = 0.048$) in the treatment group (Fig. 1, Table 3). Using the Bonferroni correction level of significance was set at $< 0{,}01$. The UPDRS$_{III}$ sum score improved by 26,7% in the treatment group comparing baseline to score of day 5 ($p = 0{,}028$, Fig. 2). Comparing UPDRS$_{III}$ sum score between the sham group at day 5 with the sum score of the treatment group of day 5 no significance was reached ($p = 0{,}097$; Fig. 2).

We further analyzed whether a single treatment train had any effect and somewhat surprisingly found that tremor, rigidity and bradykinesia decreased in the experimental group on day 1 after the first series of $5 \times 60$ seconds of stochastic WBV (Table 3). Bradykinesia improved considerably, while the effect on rigidity was less prominent and was not sustained upon completion of the treatment course.

Severe adverse events were not reported. The only mild adverse event was novel pain in the knees of a single individual. Three patients in the treatment group complained about transient muscle soreness on day 2 or later, another about lower back pain on day 3, all resolving shortly after.

## 4. Discussion

We found a beneficial effect of stochastic WBV on key features of PD in this first sham-treatment controlled double-blinded study. After repetitive application of 5 cycles of stochastic WBV on 3 consecutive days, a significant number of responders was found for bradykinesia and postural stability. The extent of improvement of bradykinesia in the treatment group was evident in comparison to the sham-treated group (intergroup analysis) and to baseline (within group analysis). More severely affected patients appeared to gain the greatest benefit of WBV. But this conclusion is limited due to small sample sizes of the subgroup analysis. Effects on tremor were highly variable between individuals. The UPDRS sum score showed significant improvement in the within group analysis, but not in the intergroup analysis.

With regard to the observed degree of improvement in our study, placebo effects which can account for as much as 30% have to be considered [6]. To avoid such placebo effects, the sham condition was chosen with care to provide an identical experimental setting. Both inter-group and within-group comparisons yielded significant improvements in the treatment group only. The observed effects should be clinically relevant, especially as postural instability usually shows insufficient response to dopaminergic therapy and confers a high risk of falls not only in daily life but also in the perioperative period when falls contribute significantly to increased morbidity and mortality of PD patients [19].

It is interesting to note, that in their original comments, Charcot and co-workers, who claimed a therapeutic effect of vibration on PD symptoms, too, reported very similar effects of vibratory therapy [10]. They observed changes after the fifth or sixth treatment session with regard to "less stiffness and walking improvement" while tremor was less prominently influenced.

Data in the literature on contemporary vibratory therapies are scant and conflicting: although in an early study non-stochastic vibration using a 25 Hz stimulation (15 min./each, twice a day) was reported to be effective in PD patients [8], the recent study of Arias et al. found no difference of UPDRS and other movement related scores between the experimental group treated with non-stochastic vibration and the placebo group [3]. Case reports and cohort studies suggested a benefit from single series of stochastic WBV in PD patients [15].

Stochastic WBV might exert a yet unappreciated effect on parkinsonian symptoms, which is not achieved with non-stochastic stimuli. The underlying mechanism of stochastic WBV leading to a putative better motor control and postural stability, however, are not fully understood. Although it has been hypothesized, that impaired proprioceptive regulation in PD is related to abnormal muscle stretch reflexes, no improve-

Table 3
Subscore decrease of UPDRS III after experimental treatment at day 1 and 5

| UPDRS III subscores | Day 1 | $P$ | Day 5 | $P$ |
|---|---|---|---|---|
| Speech and face | $+0.05 \pm 0.53$ | 0.66 | $-0.2 \pm 1.00$ | 0.36 |
| Tremor | $-1.6 \pm 2.03$ | 0.033 | $-1.55 \pm 1.88$ | 0.027 |
| Rigidity | $-0.4 \pm 0.8$ | 0.041 | $-0.4 \pm 0.98$ | 0.187 |
| Bradykinesia | $-2.8 \pm 2.79$ | 0.005 | $-3.9 \pm 3.20$ | 0.0007 |
| Arising from chair | $-0.16 \pm 0.62$ | 0.26 | $-0.11 \pm 0.67$ | 0.49 |
| Posture | $-0.11 \pm 0.47$ | 0.33 | $-0.22 \pm 0.64$ | 0.16 |
| Gait | $-0.05 \pm 0.41$ | 0.57 | $-0.16 \pm 0.61$ | 0.26 |
| Postural stability | $-0.38 \pm 0.84$ | 0.068 | $-0.38 \pm 0.77$ | 0.048 |

p-values from paired t-test; "Tremor" is the combined value of tremor at rest and action tremor. Level of significance was $p < 0{,}01$.

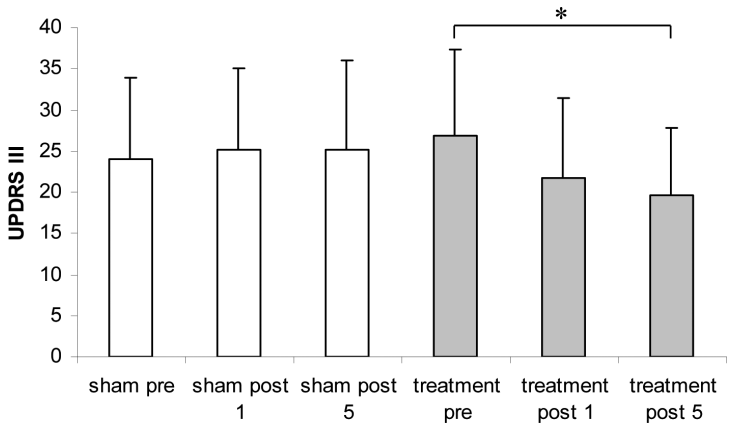


Fig. 2. Effect of whole body vibration in experimental and sham treated gruop. Unified Parkinson's Disease Rating Scale (UPDRS) III sum scores exhibited significant improvement ($^*p < 0{,}05$) in comparison of baseline (treatment pre) to UPDRS III after 5 days of treatment (treatment post 5). Within the sham treated group UPDRS III scores were unchanged. Comparing UPDRS III of the sham group at day 5 with the treatment group of day 5 no significance was detectable.

ment of proprioceptive performance of PD patients after stochastic WBV has become evident [14]. Several studies using somatosensory evoked potentials (SEP), propulse inhibition and event-related potentials provided data on central abnormalities of sensorimotor integration in PD [reviewed in 1]. Afferent stochastic cues may inhibit the neuronal $\beta$-activity believed to underlie bradykinesia. Similarly, visual cues have been shown to modulate cortical activation related to gait, which might improve the processing of input information [27]. Additionally, stochastic WBV may exert external cues improving central motor control [16]. The abnormal synchronous oscillating activity related to tremor on the other hand might be less prone to modulation.

In conclusion, we demonstrated the efficacy of stochastic WBV on bradykinesia and postural stability in PD patients. It remains to be determined whether the observed effects are maintained over time and what treatment regimen, i.e. how many treatment series in a given time period might provide the best long-term benefit.

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