INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the asymmetrical onset of motor symptoms including, tremor, rigidity, bradykinesia, and postural instability. PD is typically treated with oral dopamine replacement to compensate for the death of dopaminergic neurons in an area of the midbrain referred to as the substantia nigra. Specifically, the substantia nigra projects to other neural structures forming pathways that are responsible for maintaining precision in voluntary movements1. Levodopa remains the primary and most effective dopamine replacement agent, however, participants experience an increasingly shorter period of symptom relief. Many develop motor fluctuations, dyskinesia, and a wide array of psychiatric problems with prolonged use of this medication2. Thus it is important to investigate alternative non-pharmacologic strategies to improve the symptoms of PD.

Speculation exists that vibration therapy may provide relief for symptoms of PD by influencing the abnormal neural rhythms associated with the disease3. The successful function of the basal ganglia is critically dependent on the level of dopamine available to modulate its neural synchrony4. The subthalamic nucleus (STN) can be strongly influential on neuron activity in the basal ganglia. It is hypothesized that the characteristic over-stimulation of the STN that occurs in PD may cause the basal ganglia to be held abnormally in a 15-30Hz oscillatory rhythm5. It may be suggested that the mechanical perturbations of vibration therapy disrupt these hypersynchronized rhythms. Several studies have examined vibration as a potential therapeutic intervention for motor symptoms of PD. Jöbges and colleagues6 administered local vibration to single upper limb muscle groups in individuals with PD experiencing moderate resting tremor, and subsequently found reductions in tremor. The authors suggest that tremor frequency is influenced by manipulating local sensory feedback to a limb. In another study by Haas et al, the investigation was concerned with the effects of vibration using variable stimuli on the whole body of PD participants rather than single muscle groups3. The justification for variable stimuli comes from work by Schultz7 in a series of investigations showing that unpredictability of a stimulus is directly related to dopamine release. By logical extension, if random vibration causes small supplementary releases of dopamine, it may enhance activity of the affected brain circuits. In the experiment by Haas and colleagues3, random unsynchronized vibration (varying in amplitude) was delivered to the feet of PD participants from a platform on the key assumption that the effects would be experienced throughout the whole body. An important feature of the current study is that the vibration is unquestionably experienced throughout the entire body. Haas et al3 found a highly significant improvement of 16.8% in the Unified Parkinson's Disease Rating Scale (UPDRS) motor score (tremor and rigidity scores improved by 25% and 24% respectively). The current study also uses the motor impairment section of the UPDRS as a primary assessment. However, unique to the current study was the creative tactic of videotaping assessments for ensuring rater blindness to the treatment status of the participant. The videotapes were shown in random order at a later date for rating. Quantitative measures were used for gait and bradykinesia, using a pressure sensitive carpet and a grooved pegboard respectively. Changes in parameters such as step length and velocity are important values to investigate in gait analysis because walking of PD participants is normally characterized by slow, short, and shuffling steps. The timing for placement and removal of pegs in a grooved board is a useful standardized measure to evaluate upper limb slowness in initiation and execution of movement

in participants. The present study employs the use of the physioacoustic method to deliver vibrations, as it ensures the delivery of vibration to the entire body, and is a comfortable alternative to other methods of delivering vibration to the body. This is the first study to quantitatively test the effects of the physioacoustic method on motor symptoms associated with PD participants.

Quantitative evidence regarding vibration as a truly effective treatment is limited. The current study serves as an important contribution to this knowledge base given the important enhancements made to the experimental designs of previous studies. The anticipated outcome of this study is that its thorough evaluation of the physioacoustic method will hopefully have a positive impact on the future of vibration therapy as a non-pharmacological mode for symptom relief in PD.

METHODS

Participants

40 individuals diagnosed with idiopathic Parkinson's disease participated in this study with their informed consent. Participants were subdivided into groups according to primary symptom. Hence, there were 20 slow/rigid dominant participants, and 20 tremor dominant participants. The mean (± standard deviation) age was 65.4±9.9 years, and the mean duration of the disease was 6.8±4.8 years. Diagnosis was established by the primary care neurologist. Participants with dementia or other diseases impairing gait or coordination were not admitted to the study, and all subjects had normal or corrected-to-normal vision. To represent their typical day-to-day state, subjects were not withdrawn from their medication and all testing was performed between (10:00am and 4:00pm such that. Some individuals were unable to complete all tasks due to physical incapabilities and/or technical difficulties, which accounts for the different n values of the assessments.

Treatments

The vibrations were delivered using a method called the physioacoustic method. This method is an arm chair run by software that produces and controls sound vibrations from its six strategically placed speakers to allow the whole body to experience its effects (see figure 1). Because sound is changes in air pressure, the method is reliant on the external distribution of tactile receptors throughout the body, and the internal resonance of vibrations in the body's tissues. To ensure correct resonance frequencies, the software uses frequencies to cause the sound to vary about a fixed pitch, a technique called scanning. This results in a pulse-like sensation that causes a traveling sound pressure in the body facilitating circulation8. Vibration treatments were administered in 5 series lasting one minute each with one minute rest periods between each series. When sitting in the chair, participants were instructed to close their eyes and relax as much as possible with their legs reclined and uncrossed. Lower legs, thighs, buttocks, lower back, and upper back were to be in contact with the surface of the chair at all times.

Insert figure 1 about here

Assessments

Qualitative

Participants were first assessed using a segment of the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS). The UPDRS is a standardized diagnostic tool that gauges the nature of the disease progression and effectiveness of treatment plan9. The scale is categorically organized by mental effects, limitations in activities of daily living, complications of treatment, and motor impairments. Only a subset of the motor impairment scale was used and then rated by

an experienced evaluator. Videotaping the assessments allowed the rater to be completely blinded to the treatment status of each participant, with no cues as to which experimental group the individual belonged. For the videotaped assessment, participants were rated for tremor, finger tapping, leg agility, posture, and ability to arise from a seated position, corresponding to items 20-23 and 26-28 on the UPDRS. The only subset that could not be rated with videotapes was the rigidity component which was also completed by the same blinded rater for each assessment. The overall rigidity score is a sum of UPDRS rigidity scores for all four limbs and the neck.

Quantitative

The quantitative assessment segment was two-fold. First, each participant was required to walk in a straight line at a normal pace down a pressure-sensitive carpet that was run by software (GAITRite®, CIR Systems, Inc., Clifton, New Jersey). This carpet measured several parameters regarding the gait of the individual and five trials were completed for each assessment block. The dependent measures of interest were velocity and step length for both right and left feet. The second quantitative assessment was the timing of a grooved pegboard task to indicate the severity of the bradykinesia. **This grooved pegboard is a manipulative dexterity test consisting of 25 holes with randomly positioned slots. Pegs with a key along one side must be rotated to match the hole before they can be inserted.** Participants were timed for the placement and the removal separately, and these were added together for a total time of task. Both placement and removal tasks are considered to be fine motor tasks, however the placement of pegs requires more precision. Therefore, while removal is considered a primary measure of motor speed, the placement task better represents a measure of visual-motor speed10. This task is an efficient way to represent several reach, place and grasp tasks encountered with common daily living.

Procedure

In each test session, two participants were studied in a parallel crossover design and were randomly assigned to one of two treatment groups. All participants were assessed at baseline, after vibration treatment, and after the control period. The difference between the groups (table 1) was the order of the vibration treatment and control period, in which group A received the vibration session first, and the rest period second, while group B received the rest period first and the vibration session second.

The parallel crossover design was used for the purpose of counterbalancing practice effects and fatigue across assessments. In addition the crossover design allows us to gauge the duration of the benefit given the treatment's effectiveness. In group A, the participant receives the vibration treatment first and the rest period second, the expected result would be for improvement in the second assessment. If this effect were to last longer than approximately 30 minutes, we would expect to see a carry over effect in the third assessment which is completed after the rest period. However, in group B when participants receive a rest period first and a vibration session second, there should only be an improvement in the third assessment, prior

Statistical Analysis

Group A and group B results were submitted to separate repeated measures ANOVAs for each parameter of assessment. Whether it be tremor-dominant or slow/rigid-dominant, the participant's dominant symptom was also included as a between groups variable in each ANOVA in the event that individuals were affected differently by the treatment because of their dominant symptom. In the analyses for step length and velocity, trial number was included as a

within-subjects variable in the event that it contributed to the overall variance between assessments. ANOVAS for UPDRS scores of tremor, finger-tapping, leg agility, posture, sitting-to-standing ability, and rigidity, as well as pegboard times were conducted as follows: 2 Dominance (tremor, rigid) X 3 Assessment (Baseline, Post Vibration, Post Rest Period)..Steplength and velocity were submitted to repeated measures ANOVAs as 2 Dominance (tremor, rigid) X 3 Assessment (Baseline, Post Vibration, Post Rest Period) X 5 Trials. For main effects, Tukey's Honest Significant Difference post hoc tests were conducted to determine if the effects of vibration treatment differ significantly from the effects of the rest period with an alpha level of 5%.

RESULTS

All participants tolerated the treatment well with no report of pain, dizziness, or discomfort. Symptom category namely, tremor-dominant or slow/rigid-dominant was included as a between groups variable, but showed no comparable differences in any assessment category.

Rigidity

Figure 3 shows the mean UPDRS scores for rigidity in the group that received vibration first and a rest period second (group A). There was a significant effect of treatment status ($F_{(2,34)} = 3.36$; $p= 0.046$) for the UPDRS score such that rigidity decreased for both post-vibration and post-rest period assessments. Post-hoc confirmed that there were rigidity improvements similar in both the post-vibration and post-rest period conditions. Rigidity scores were also significantly different between the treatments in group B, the group that received a rest period first and a vibration session. The UPDRS rigidity score decreased significantly in the post vibration assessment ($F_{(2,36)} = 10.35$; $p<0.001$). Post hoc analyses show that post vibration assessments in group A are significantly different from baseline ($p= 0.049$) but did not differ from post-rest period assessments ($p=0.141$). In group B, post vibration assessments differed significantly from both baseline ($p< 0.001$) and post rest period assessments ($p< 0.003$).

FIGURE #3
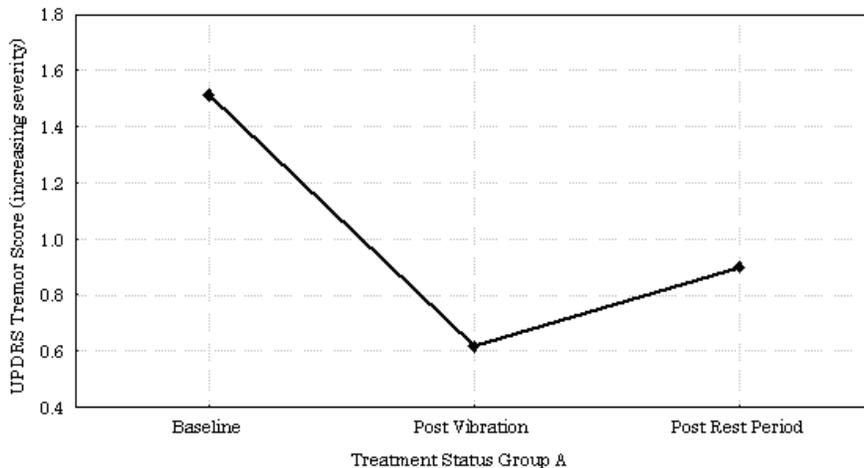
Tremor

Figure 4 shows the mean UPDRS scores for tremor in the group receiving treatment before rest. There was a significant effect of treatment ($F(2,34) =8.3$; p= 0.002) for the UPDRS score, such that it decreased in both post-vibration and post-rest period assessments. Tremor UPDRS scores failed to reach a level of significance between assessments in group B ($F(2,32)=2.38$; p= 0.109). Post hoc analyses show that baseline assessments in group A are significantly different from post vibration assessments (p< 0.001) and from post-rest period assessments (p< 0.021).. In group B, there were no significant post hoc analyses.
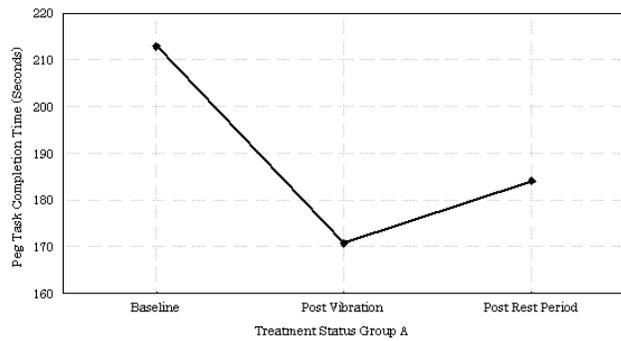

FIGURE #4

Other UPDRS Measures
The UPDRS measures for finger tapping, leg agility, posture, and arising from a seated position all failed to reach a level of significance.

Bradykinesia

Figure 5 shows the mean time in seconds for the peg task completion in group A by assessment. There was a significant effect of treatment status ($F(2,32) = 5.24$; $p = 0.011$) for the peg board task such that completion time decreased for both post-vibration and post-rest period assessments. Peg task completion time was also significantly different between the treatments in group B (see figure 5) with the peg board task time decreasing in the post vibration assessment ($F(2,36) = 11.2$; $p < 0.001$).

FIGURE
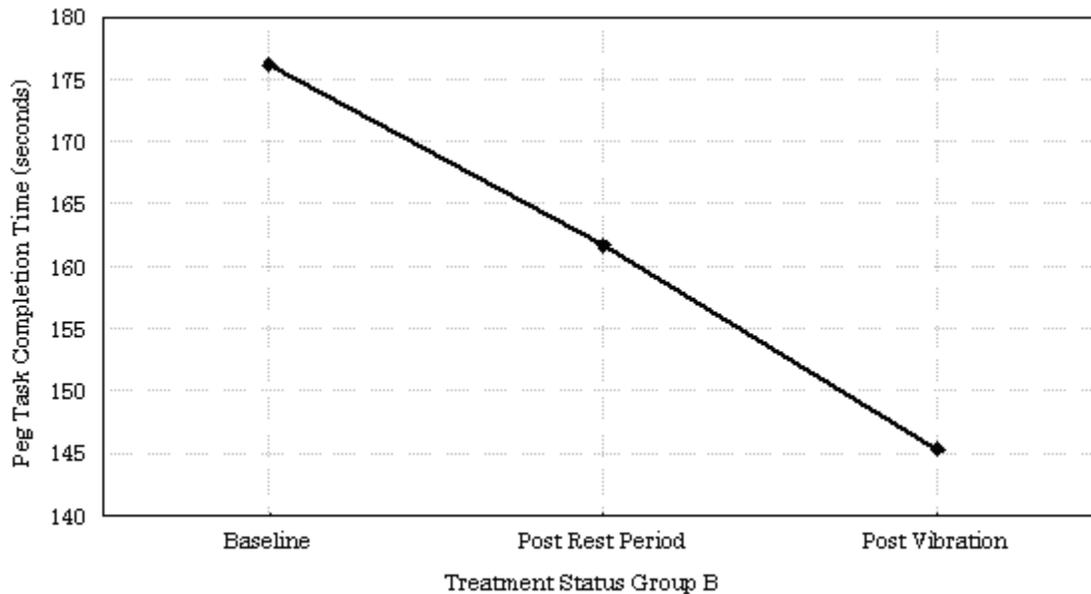
#5

Post hoc analyses show that post vibration assessments in group A are significantly different from baseline ($p = 0.008$) but did not differ from post-rest period assessments ($p = 0.565$). In group B, post vibration assessments differed significantly from both baseline ($p < 0.001$) and post rest period assessments ($p = 0.039$).

Step Length

Step length was not significantly different across the assessments in Group A ($F(2, 36) = 0.386$, $p = 0.982$), however, group B did show a significant effect of treatment status ($F(2,32) = 4.26$; $p = 0.023$) for the step length such that it was increased for the post-vibration assessment (see figure 6).
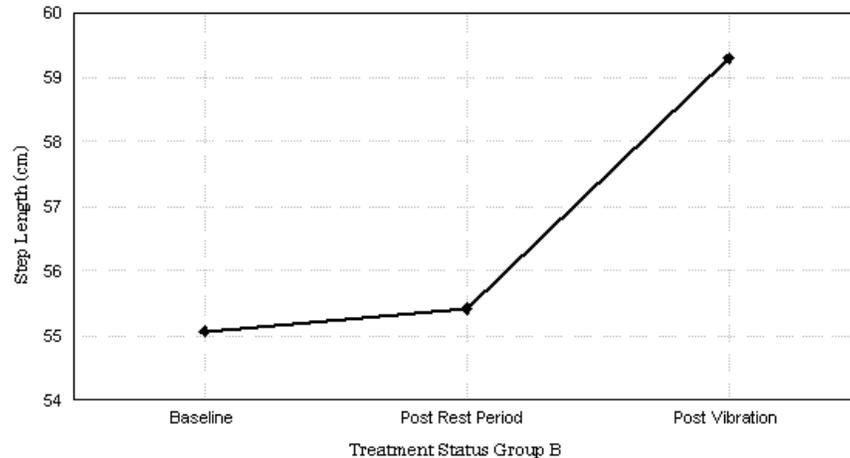
FIGURE #6

Post hoc analyses show that post vibration assessments in group B are significantly different from baseline assessments (p=0.033). The post vibration assessment failed only differed slightly from post-rest period assessments (p≈0.05) which indicates a high variation in scores. In group A, there were no significant post hoc analyses.

Velocity
The other parameter of interest in gait analysis was velocity, in which there was no main effect of treatment. Velocity was the only quantitative measure to not reach a level of significance.

DISCUSSION

Our objective was to complete a thorough, quantitative analysis of the effectiveness of whole body vibration as a potential treatment for motor symptoms of PD. Although previous investigations have also supported the idea that vibration therapy is an effective mode of symptom relief, the thoroughness in quantitative gait and functional upper limb assessments of the current study is unprecedented. The current method permitted effective delivery of vibration throughout the whole body. The parallel crossover design we employed allows to counterbalance the effects of fatigue and practice in our assessments, as well determines if there is a difference between vibrating in the chair and simply sitting in the chair.

For several motor symptoms, significant improvements were linked to the vibration treatment, while the control condition (post-rest) led to small, insignificant changes as compared to the baseline assessment. In light of this evidence, the beneficial effects of vibration therapy have not been more apparent. Vibration therapy in general is a relatively untouched area of research, and the current study has unprecedented efficiency and accuracy through biomechanical analyses and a parallel cross over design. Despite being the gold standard for PD assessments, the UPDRS carries with it a high degree of subjectivity. By videotaping as much of the assessment as possible, and having the recordings rated at another date, the rater is entirely blinded from the biases of knowing the participant's treatment status. In addition, quantitative testing using GAITRite technology and the grooved peg board test largely enhances the ability to detect functional outcomes that may be more relevant to activities of daily living rather than evaluating a change in only symptoms of participants.

In summarizing the results, no major symptom category is left untouched. UPDRS scores for tremor and rigidity both improved. The other subsets of the UPDRS scales namely posture, sitting to standing scores, and leg agility did not reach a level of significant improvement.

However, this is likely because these scores were naturally less severe initially. Therefore, unlike tremor and rigidity, there was little room for improvement in the first place.

The GAITRite carpet was able to provide the study with accurate and unbiased parameters indicating the improvement in step length. Both practice effects and fatigue can be factors in the quality of the walking. However, the crossover design controls for these effects by reversing the order of the vibration session and rest periods in group A and B. Step to step variability may be of interest to look at in future studies as this may be an important diagnostic tool in evaluating impaired gait. A large step to step variability may reduce the experimenter's ability to detect improvements in step length as a trend in a large group of participants. Also, the grooved peg board test requires more complex visual-motor coordination than most bradykinesia assessments. Although practice and fatigue may play a role in the participant's completion speed, it is ultimately one of the most efficient assessments for bradykinesia available. Even with the crossover design, the pegboard completion times were shown to decrease in post vibration assessments, in correspondence with the decrease in bradykinesia.

The most significant limitation associated with the study was the unexpected duration of benefits and the timescale for assessments. It was obvious in group B that the post rest period assessments should not differ significantly from the baseline assessments, and that post vibration assessments should be significantly different from both baseline and post rest period assessments. However, in group A it was unknown as to whether there would be carry-over effects of the treatment into the post rest period assessment since the vibration therapy was administered beforehand. Evidently, in all tests that showed significant effects of the treatments in group A, namely the bradykinesia, rigidity and tremor, post hoc analyses revealed carry over effects of the treatment in each post rest period assessment. In response to this finding, the long-term benefits of vibration therapy are worth looking into in future studies.

Several possibilities present themselves with respect to future investigations. The rationale for choosing the frequencies and durations for this study were based on a very limited selection of previous studies as well as individual testimony. To keep in the mind that this is the first study to quantitatively test the effects of the physioacoustic method on PD participants, is to realize that there are a number of other frequencies and durations that could be chosen for a treatment plan. In planning the study, it was also unknown how long benefits would last in the event of treatment success. Future studies should seek to measure the benefits over a longer time scale, and subsequently work to lengthen this benefit. Since participants were subjected to only ten minute treatments, by logical extension increasing the duration of treatment sessions, and possibly the number of treatments may be the next step in lengthening the beneficial effects.

Finally, the current study attempted to compare subjects based on their dominant symptom, however there was no apparent relationship between greater treatment success and primary symptom. Studies involving individuals with PD are limited by the fact that PD is pathologically heterogeneous across participants, and the variation in how participants responded to the treatment is currently beyond the scope of explanation for a study of this nature. Sources for this variation should be explored in greater detail.

In summary, although vibration therapy may not be at the stage in which it can be regarded as an exclusive treatment for PD, the results of the study strongly suggest its application as an important adjunct to medication.)

REFERENCES

[1]   S. S. Rao, L. A. Hofmann, and A. Shakil, "Parkinson's disease: diagnosis and treatment," *Am Fam Physician*, vol. 74, pp. 2046-54, 2006.

[2]   K. H. Deane, D. Jones, E. D. Playford, Y. Ben-Shlomo, and C. E. Clarke, "Physiotherapy for patients with Parkinson's Disease: a comparison of techniques," *Cochrane Database Syst Rev*, pp. CD002817, 2001.

[3]   L. Dixon, D. Duncan, P. Johnson, L. Kirkby, H. O'Connell, H. Taylor, and D. Kho, "Occupational therapy for patients with Parkinson's disease," *Cochrane Database Syst Rev*, pp. CD002813, 2007.

[4]   C. T. Haas, S. Turbanski, K. Kessler, and D. Schmidtbleicher, "The effects of random whole-body-vibration on motor symptoms in Parkinson's disease," *NeuroRehabilitation*, vol. 21, pp. 29-36, 2006.

[5]   M. Cassidy, P. Mazzone, A. Oliviero, A. Insola, P. Tonali, V. Di Lazzaro, and P. Brown, "Movement-related changes in synchronization in the human basal ganglia," *Brain*, vol. 125, pp. 1235-46, 2002.

[6]   R. Levy, P. Ashby, W. D. Hutchison, A. E. Lang, A. M. Lozano, and J. O. Dostrovsky, "Dependence of subthalamic nucleus oscillations on movement and dopamine in Parkinson's disease," *Brain*, vol. 125, pp. 1196-209, 2002.

[7]   E. M. Jobges, J. Elek, J. D. Rollnik, R. Dengler, and W. Wolf, "Vibratory proprioceptive stimulation affects Parkinsonian tremor," *Parkinsonism Relat Disord*, vol. 8, pp. 171-6, 2002.

[8]   W. Schultz, "Predictive reward signal of dopamine neurons," *J Neurophysiol*, vol. 80, pp. 1-27, 1998.

[9]   A. A. Q. J. Johnson, "Effects of Exercise on Movement Disorders," *I forget*, vol. 2, 2007.

[10]   P. Lehikoinen, *The Physioacoustic Method*. Kalamazoo, MI: Next Wave Inc, 1990.

[11]   S. Fahn, Elton. R., "Unified Parkinson's Disease Rating Scale," *Recent Developments in Parkinson's Disease*, vol. 2, pp. 153-163, 293-304, 1987.

[12]   P. J. Bryden and E. A. Roy, "A new method of administering the Grooved Pegboard Test: performance as a function of handedness and sex," *Brain Cogn*, vol. 58, pp. 258-68, 2005.

[13]   S. Farmer, "Neural rhythms in Parkinson's disease," *Brain*, vol. 125, pp. 1175-6, 2002.

[14]   M. Rivlin-Etzion, O. Marmor, G. Heimer, A. Raz, A. Nini, and H. Bergman, "Basal ganglia
          oscillations and pathophysiology of movement disorders," *Curr Opin Neurobiol*, vol. 16, pp. 629-
          37, 2006.

[15]   H. Nakamura, T. Moroji, S. Nohara, and A. Okada, "Activation of cerebral dopaminergic systems
          by noise and whole-body vibration," *Environ Res*, vol. 57, pp. 10-8, 1992.