Title: **Vibration Impact on Parkinson's Tremor**

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Vibration Impact on Tremor

STUDY DESIGN:

We will perform a two-group, randomized, longitudinal study exploring the feasibility and impact of the RM Band vibration device on tremor of participants who suffer from Parkinson's disease (PD). This study will be a single session study with participants randomly assigned to one of two dose levels. PD patients will be recruited and randomized into either Group A (low dose) or Group B (high dose). Target enrollment for Group A and B is 15 participants each.

STUDY VISIT PROCEDURE:

We will prescreen volunteers by phone or in the clinic for eligibility criteria (we are requesting partial waiver for recruiting purposes only). We will be obtaining names, contact information, and diagnosis from the registry to identify potential participants and reach out to them to determine if they are interested in participating. A member of the Parkinson Movement Disorder Center (PMDC) research registry staff shall pre-screen the registry for ID possible participants and will transmit the contact information to the staff of this study. Our study staff will contact the volunteer, explain the study, and determine if they wish to be scheduled for a screening visit. Informed consent will be obtained at that screening visit prior to any further assessments. After the informed consent is signed, the Mini Mental State Exam (MMSE) will be administered by the study coordinator to determine final eligibility to the study. Individuals with MMSE <24 will be excluded from the study.

Before study intervention start, we will confirm that the participant is in the "on" state, defined as when their medication is working, per confirmation from subject. If the participant is due to take their Parkinson's medications, they will be asked to take them, and then the study will begin approximately 30 minutes later to allow the medication a chance to work. If the participant confirms that they are not in their "on" state and they are not due to take their medication, we will wait an additional 30 minutes and if the participant still is not in the "on" state, we will reschedule the visit. If the participant confirms their medications are working the study will begin.

DATA COLLECTION:

Data will be collected at baseline (prior to vibration start), during treatment (after 5 minutes of vibration start and with vibration still turned on), and after vibration is stopped to assess the duration of effect. Vibration stimulation will last a total of 20 minutes.

Baseline data includes: (1) demographics (date of birth, sex); (2) disease descriptors (date of Parkinson's diagnosis, medication list, medical history, tremor history, and Movement Disorder Society Unified Parkinson Disease Rating Scale (MDS UPDRS) parts II-IV to assess the total burden of motor PD symptoms as well as their impact on activities of daily living for the prior two weeks; and (3) Tremor Rating Scale.

Estimated time to complete is 30 minutes. Demographics and disease descriptors will be obtained directly from patient, confirmation of diagnosis will be confirmed from medical records.

During treatment and post treatment data collection includes: (1) MDS UPDRS – part III only (motor assessment), and (2) Tremor Rating Scale. The time to complete these two assessments is estimated to be 15 minutes.

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During and after vibration study the participant will be asked qualitative questions about the stimulus and apparatus including: How are you feeling? Do you have any pain? What does the vibration sensation feel like? Is it tolerable? How does the arm band itself feel? Is it comfortable? Are you having any unexpected sensations in your arm or fingers? Anything else you would like to comment on? RESEARCH

MEASUREMENTS:

The MDS UPDRS and the Tremor Rating Scale will be administered by the research coordinator under the supervision of the medically responsible PI or designee and will be videotaped, de-identified, and later evaluated by the PI (blinded to the participant's vibration frequency assignment) who will score the performance tests.

1) Movement Disorder Society - Unified Parkinson Disease Rating Scale (MDS UPDRS) - parts II-IV (Goetz, Tilley, Shaftman, Stebbins, Fahn, Martinez-Martin …. & LaPelle, 2008). All items are rated using a scale of 0 = normal to 4 = severe. Only Part III (Motor evaluation) will be repeated during vibration and post intervention data collection times and will take approximately 5 minutes to complete.

2) Clinical Rating Scale for Tremor – (Fahn, Tolosa, & Marin, 1988).

We will use Part A, items 1 – 14 for analysis of tremor over time. The range of score for these items is 0 – 56. All items are rated on a scale of 0 = normal to 4 = severely abnormal. Total time to complete the Scale for Tremor assessment is 10 minutes.

3) Objective measurement of tremor –

This device will allow us to objectively measure tremors of both the right and left arms (a device will be worn simultaneously on each wrist) of the Parkinson's disease patients. This is being used as an experimental outcome measure to gather more quantitative tremor data such as frequency and amplitude using compact accelerometers and gyroscopes cased within the small light weight watch-like device. The objective tremor measuring device will be worn and will be recording 5 minutes before vibration is turned on, throughout vibration treatment to assess impact of vibration on tremor, and for approximately five minutes post treatment data collection to assess for possible carry over effects.

INTERVENTION:

The RM Band (Resonate Forward LLC)is a small, untethered device that is attached to a soft elastic arm band. Inside the band are small vibration motors that deliver vibration like that of a cell phone on vibration mode. Through the controller inside the small box we can "set" the amplitude and frequency of the vibration. The armband is placed on arm that is more effected by tremor (determined by investigator). If both arms are equally effected, then the participants dominant arm will be used. Once the RMBand is in place, the vibration will be set at the frequency dictated by randomized group assignment. The amplitude duty cycle will be set so that the participant can feel the vibration. If the participant cannot feel the vibration, we will note it and continue with the study. Data collection will follow based on above description.

DATA ANALYSIS PLAN:

Descriptive statistics will be used to characterize participants: frequencies for categorical variables, mean/standard deviation for normally distributed continuous variables, and median/interquartile range

for continuous variables with skewed distributions. Because of the exploratory nature of this pilot intervention study, no adjustment for multiplicity is planned with alpha set at 0.05 for determining significance. The analysis plan for each aim will be discussed separately.

Aim 1: To determine the impact of vibration delivered by the RMBand on parkinsonian tremor pre (baseline), during, and post vibration intervention. It is anticipated that a linear mixed effects model (Brown & Prescott, 2006; Verbeke & Molenberg, 2000; Vonesh & Chinchilli, 1997) will be used to test the group effect (low frequency vs. high frequency) as well as testing the effect each frequency across time (pre, during and post). The general form of the mixed linear model is given by $y = XB + ZU + e$, where y is the observed data vector (e.g., stress), X is a known design matrix, B is a vector of unknown fixed effects, Z is a known design matrix, U is a vector of unknown random effects, and e is a vector of unknown random errors. This model will include random effect for participant (represented by ZU in the equation), and fixed effects for group and time (represented by XB in the equation). The model is flexible enough to model potential cofactors including demographic or disease descriptors. Modeling assumptions such as normality and homoscedasticity will be checked for each model. In the case of non-normal data, a transformation (such as a log-transformation) will be used to normalize the data. Analyses will be performed using SAS software, specifically PROC MIXED and JMP.

Aim 2: To evaluate the safety and tolerability of the RMBand vibration device applied to the arm of the person with Parkinson's disease tremor. Safety and tolerability of the RMBand will be ascertained by qualitative questions such as: How are you feeling? Do you have any pain? What does the vibration sensation feel like? Is it tolerable? How does the arm band itself feel? Is it comfortable? Are you having any unexpected sensations in your arm or fingers? Anything else you would like to comment on? Answers to these questions will be tabulated by group and across groups.

SAMPLE ADEQUACY:

The overarching goal of this pilot study is to obtain good estimates of means and variances of the three research measures (MDS UPDRS, Tremor Rating Scale & watch device) at pre, during and post vibration therapy change over time within each of the 2 groups. van Belle (2008) proposed that a minimum of 12 subjects is needed to calculate confidence intervals based on a t-statistic with n-1 degrees of freedom, based on the fact that confidence interval half-width decreases rapidly up to n=12, at which point the decrease is less dramatic. Thus, the proposed sample size of 15 subjects per group should be adequate to estimate means and variances to assess group differences and trends over time.