Heart Rate Variability Biofeedback in the Treatment of Major Depression

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Statement of the Problem: Depression

• The most common mood disorder
• One of the world’s most burdensome and costly diseases
• Despite their efficacy, current treatment paradigms have substantial limitations and drawbacks, including:
  – Significant residual symptoms
  – Unpleasant and deleterious medication side effects
  – Prohibitive treatment costs
Autonomic Nervous System Functioning and Depression

• ANS dysfunction is increasingly being implicated in the etiology of MDD, as characterized by:
  – Sympathetic predominance
  – Parasympathetic Impairment
• Decreased parasympathetic modulation has been attributed to altered vagus (10th cranial) nerve activity
  – Attenuated heart rate variability (HRV) at the respiratory frequency (respiratory sinus arrhythmia (RSA)) is one index of this dysfunction
The Vagus Nerve: Pathway to the Limbic System
The Vagus Nerve, Emotions and Polyvagal Theory

• Nucleus Ambiguus (NA)
  ▪ Nerve branch of vagus responsible for RSA
  ▪ NA projections are influenced by cortical, subcortical, and adjacent brain stem nuclei (i.e., limbic system, anterior cingulate cortex, medial and dorsal prefrontal cortex, etc) that are associated with arousal, attention, emotion, and communication

• Polyvagal Theory (Porges, 1995, 2003)
  – RSA reflects homeostatic adaptability and the capacity of warm-blooded animals to self-regulate
  – RSA indexes the ability of the CNS to regulate emotional responding, thus serving as an indicator for emotion regulation functioning and psychopathology
HRV/RSA and Depression Link: Empirical Support

- Much of the recent literature has been consistent with the hypothesis of RSA attenuation in MDD
  - A meta-analysis (Rottenburg, 2007) found depressed patients to have significantly attenuated RSA levels
  - Nahshoni, et al., 2004, found MDD patients indistinguishable from heart transplant recipients with regards to HRV levels
  - Su, et al., 2009 found MDD and RSA to have a common genetic pathway
HRV Biofeedback

- Individuals trained in HRV BFB have consistently been shown to produce higher magnitude RSA oscillations—even at the outset of training (Vaschillo, 1984; Vaschillo, et al., 2002)—as a method of improving autonomic homeostasis.
- RSA is augmented through slow, deep breathing (Wilhelm, 2004).
- When one breathes at their resonance frequency (approx. 6 breaths/min), chances in BP and HR are in phase (simultaneous), and this generates the highest amplitude RSA oscillations possible.
HRV Biofeedback for Depression: Notable Studies

- In an open label study by this lab (Karavidas, et al., 2007) a 10-session RSA bfb protocol was found to significantly decrease MDD sx, on both the BDI-II and the HAM-D in 11 depressed individuals.

- In an open label study by Siepmann, et al., 2008, a 2 week, 6-session RSA bfb protocol was found to significantly decrease MDD sx on the BDI-II in 14 depressed individuals.
HRV Biofeedback for Depression
Research: Limitations

- Methodological limitations of extant literature include:
  - No control group
  - Case study design
  - Open-label study design
  - ***Lack of placebo biofeedback control as comparison

- Thus, the current literature has limited internal validity
Current Study: Goals

• A preliminary efficacy RCT study to follow-up the study by Karavidas, et al., 2007
  
  – *Primary Goal:* evaluate efficacy of HRV biofeedback in the treatment of depression
  
  – *Secondary Goal:* evaluate tolerability and viability of sham biofeedback control protocol
Current Study: Hypotheses

• Main Hypotheses:
  – **H1**: Participants who complete the HRV biofeedback intervention will experience greater improvement in depression symptoms than those assigned to the sham control condition.
  – **H2**: Improvements in depression exhibited by the biofeedback intervention group will persist at 1 month post-treatment.
  – **H3**: There will be a greater percentage of clinical response to the biofeedback intervention as compared to the sham, with clinical response defined as a reduction of at least 50% on HAM-D scores from baseline to fu2, or a final score ≤ 10 on HAM-D.
Methods

• **Participants**: 11 individuals meeting DSM-IV criteria for MDD completed the study

• **Location**: Psychopharmacology division/Physiology Lab at UMDNJ-UBHC

• **Recruitment Procedures**: recruited using flyers, pamphlets, and informational from UMDNJ-UBHC population, UMDNJ-RWJMC practices, and surrounding communities in Middlesex County (esp. Piscataway, Highland Park, and New Brunswick)
Methods

• **Inclusion Criteria:**
  – 18-75 years old
  – MDD dx as defined by SCID
  – English fluency

• **Exclusion Criteria:**
  – No MDD dx
  – Dx of any other disorder besides MDD, dysthymia, or anxiety disorder
  – Active grieving
  – Certain medical dx that posed risk (i.e., heart arrhythmias, HTN, DM)
  – Suicide risk
  – Use of any psychiatric medications
  – Involvement in concurrent psychotherapy
  – Substance use/abuse
# Demographic Characteristics of the Study Sample

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<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
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<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>64%</td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
<td>36%</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
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<tr>
<td>18-25</td>
<td>4</td>
<td>36%</td>
</tr>
<tr>
<td>31-40</td>
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<tr>
<td>41-50</td>
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</tr>
<tr>
<td><strong>Ethnicity</strong></td>
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<tr>
<td>Caucasian</td>
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<td>55%</td>
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<tr>
<td>Hispanic</td>
<td>1</td>
<td>9%</td>
</tr>
<tr>
<td>Asian</td>
<td>4</td>
<td>36%</td>
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## Protocols: HRV Biofeedback vs. Credible Sham

<table>
<thead>
<tr>
<th>HRV Biofeedback (10 weeks)</th>
<th>Sham Respiratory Training (10 weeks)</th>
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<tr>
<td><strong>Baseline Assessment</strong> (structured clinical interview and outcome measures)</td>
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<tr>
<td><strong>Session 1</strong>: Intro to method and initial estimate of resonance frequency; collection of physio data and outcome measures; home practice</td>
<td><strong>Session 1</strong>: Intro to method and initial estimate of &quot;designated frequency&quot; <em>(an inert, spontaneous breathing rate)</em>; collection of physio data and outcome measures; home practice</td>
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<td><strong>Session 2</strong>: HRV biofeedback training (20 minutes); home practice</td>
<td><strong>Session 2</strong>: Sham biofeedback training (20 minutes); home practice</td>
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<td><strong>Session 3</strong>: Review of pursed lips/abdominal breathing with long exhalation</td>
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<td><strong>Session 4</strong>: Continued practice with technique; physio data and outcome measures; home practice</td>
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<td><strong>Session 5 (wk 7)</strong>: collection of physiological data and outcome measures</td>
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<td><strong>Session 6 (wk 10)</strong>: collection of physiological data and outcome measures</td>
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Sham Respiratory Protocol

- **Session 1: Introduction to the Method and Obtaining Initial Estimate of “Designated” Frequency**
  - Baseline breathing
  - Breathing with pacer
  - Determine designated frequency (11-15 BPM)
  - Breathing at designated frequency
  - Baseline recording
  - Home practice

- **Session 2: Beginning of Sham Biofeedback**
  - Breathing at DF
  - Breathing at DF with pursed lips and abdominal breathing
  - Practicing breathing at DF with lips and ab. Breathing
  - Repeat
  - Home Practice

- **Session 3 & 4: Review of Pursed Lips Abdominal Breathing with Longer Exhalation**
  - Breathing at DF
  - Breathing at DF thinking about stressor and increasing HF/decreasing VLF
  - Breathing at DF with pacer
  - Same as above
  - Home Practice
Cont’d Methods

- **Equipment**: J&J Engineering I-330-C2 physiograph unit; Heart Math Freeze Frame; Respitrace

- **Primary Outcome Measures**: HAM-D

- **Exploratory Outcome Measures**: BDI-II, SF-36, CAS, BSSI, BHS, CEQ, & CCPRQ

- **Statistical Analysis**: repeated measures mixed model analysis for outcome measures; pairwise t-test, where applicable; Chi-square for categorical variables
Results

• **Group Equivalence at Baseline**: One-way ANOVA and Chi-square revealed no significant group differences.

• **Main Analysis of Outcome Measures**: main effects for time for BDI and HAM-D scores were significant; however, main effects for treatment group were not.

• **Exploratory Analyses**: main effects for time for CAS, and energy level, emotional well-being, and social functioning (SF-36) were significant; however, main effects for treatment group were not. Main effects for time and tx. group were not signf. for all other measures.
Discussion: Findings and Explanatory Hypotheses of Current Study

- **Biofeedback and Depression:**
  - No significant difference in the degree of improvement in depression sx between participants in the sham vs. intervention group was found
    - These finds reflect other extant studies
    - Variations in treatment compliance?
    - Too small an N?
    - The rigor of our credible sham control?
  - Participants in both groups experienced significant improvement in depression sx over time
    - Regression to the mean?
    - Natural course of the disease?
    - Unintentionally therapeutic elements? (i.e., focusing on breathing as distraction)

- **Biofeedback, Anxiety & Health/Wellbeing:**
  - No significant group differences, but significant main effects for time for anxiety, social/emotional functioning, and energy level
    - Regression to the mean?
    - Caused by improvements in depression over time?
Credibility, Expectancy, and the Feasibility of the Sham Control

- The placebo-controlled design is deemed ideal, as it rules out incidental, common factors—allowing treatment specificity of the purported active ingredients to be optimally ascertained.

- The current sham placebo control was structurally indistinguishable from the biofeedback protocol, in that:
  - both utilized the respiratory biofeedback format
  - both used the same number of training sessions
  - both utilized the same session length

- One strategy commonly employed to evaluate the adequacy of placebo controls is to derive this empirically from ratings of credibility and expectation.
Credibility, Expectancy, and the Feasibility of the Sham Control

• Our analyses found no significant differences between groups on CEQ scores, suggesting that the control and intervention protocols were essentially equivalent with respect to participants’ perceptions of how logical, believable, and effective the respective protocols were.

• That there were no reported complaints of discomfort or adverse side effects among individuals assigned to either protocol is an important consideration as well with regards its tolerability.

• Thus, the credible sham respiratory control protocol utilized in the current study has been found to be an effective and feasible placebo control for utilization in HRV/RSA biofeedback research.
Summary

• Irrespective of group assignment, participants experienced significant improvements in the symptoms of depression, anxiety, and various indicators of general health over the 10-week study course.
• Factors such as regression to the mean, natural disease course, and extraneous therapeutic elements may account for this.
• No significant differences on depression scores, or any other outcome measures, were found between groups. However, the study had limited power to detect significant differences, due to its very small sample size.
• Thus definitive conclusions regarding the efficacy of HRV biofeedback in the treatment of depression cannot be drawn from the results of the present study.
• Other hypothesized factors that may account for this include use of placebo control and variable treatment compliance.
• An important finding of the present study was that the credible sham respiratory protocol developed by this laboratory was an effective, viable, and tolerable placebo control comparison.
Conclusions

• The efficacy of HRV biofeedback as an alternative or adjust treatment modality for depression may be established in future studies, with the implementation of improved experimental design.

• Future studies would benefit from employing a sham respiratory protocol similar to the one developed for this study.