Effect of Heart Rate Variability Biofeedback on Myocardial Blood Flow in Patients With Coronary Artery Disease: a Randomized Controlled Pilot Trial

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“Materials that are included in this course may include interventions and modalities that are beyond the authorized practice of mental health professionals. As a licensed professional, you are responsible for reviewing the scope of practice, including activities that are defined in law as beyond the boundaries of practice in accordance with and in compliance with your professions standards.”
Overview

• Introduction to cardiovascular disease
• Discussion of mental stress-induced myocardial ischemia
• Discuss intervention: heart rate variability biofeedback
• Discuss results of paper
• Discuss implications and future efforts

Cardiovascular Disease and Stress

• Cardiovascular disease (CVD) is the number one cause of death in the world
• According to the CDC, an estimated 80% of heart disease deaths can be prevented
• Stress is a major risk factor for heart disease and is blamed for about 1/3 of heart attacks
• Limited options in stress management for clinicians

Mechanisms of Stress and Heart Disease
Stress Can Reduce Cardiac Blood Flow

- Mental stress reduces myocardial ischemia (MSMI)
- Regional blood flow deficits in the heart
- Associated with an increased risk of CVD death

Positron Emission Tomography of the Heart

- Measure real-time blood flow of heart using a radiotracer, Rubidium-82
- Cutting edge software program for measuring real-time blood flow to heart
- Can predict future risk of bad outcomes independently of coronary artery disease

Background – Myocardial Blood Flow

- Mental Stress Myocardial Flow Reserve = myocardial blood flow during stress/rest
Heart Rate Variability: Signals of the Bidirectional Heart Brain Relationship

- Physiological variation in the time interval between heartbeats
- HRV can provide the "common language" between the heart and surrounding nervous system because it is influenced by both of them


Background - Biofeedback

- Heart rate variability biofeedback (HRVB)
  - Wellness practice for improving health through self-regulation of ANS
  - Mindful breathing
  - Loving kindness
  - Heart focus
  - Stress reduction
  - Cultivate focus and energy

- Known treatment for hypertension (Linden et al., Appl Psych. and Biofeedback 2006; 31: 51-63)
- May improve HRV (Del Pozo et al., AHJ 2004; 147(3))
- Increase baroreflex gain (Lehrer et al., Psychosomatic Medicine 2003; 65(5): 795-805)

Emwave 2 device

ANS = autonomic nervous system
BRS = baroreflex sensitivity

Background - Hypothesis

Heart rate variability biofeedback, versus waitlist control, increases mental stress myocardial flow reserve in subjects with coronary artery disease
Methods

- Randomized CAD subjects to HRVB vs. waitlist control (goal 24)
- 6-week hybrid program
  - 3 visits with experienced phone coach
  - 3 in-person visits (in-lab HRVB) with credentialed HRVB trainers (clinical psychologists)
- Recruited from previous study CAD cohort
  - Mental Stress Ischemia Prognosis Study (Hammadah et al., Psychosomatic Medicine 2017; 79(3): 311-7)
  - Oversampled patients with known mental stress-induced myocardial ischemia
  - Randomized prior to enrollment into study

Methods – Myocardial Blood Flow

- Rubidium-82 Positron Emission Tomography
- FDA approved for measuring changes myocardial blood flow in real-time
- Emory Cardiac Toolbox
- Technician blinded to treatment strategy
- Flow computed in 3 vascular territories (LAD, LCX, RCA)
- Images acquired immediately before and after 5-minute mental arithmetic stressor with negative feedback

Sample image from Emory Cardiac Toolbox with Conventional Vasodilator Stress

Methods – Data analysis

- Intent to treat of patients who completed first 2 visits and had imaging data
- Main outcome: mean difference in mental stress myocardial flow reserve from visit 1 to visit 2
  - Secondary outcomes such as mood and vascular measures not presented in current analysis
- T-tests performed to compare group changes
- Multivariate linear regression performed because small sample size and baseline group differences
Results - Study Flow

- Randomized 25 subjects
  - 2 dropped out because could not make appointments due to life changes
- 23 subjects completed visits 1 and 2
- 21 subjects had complete imaging data (imaging data corrupted on 2 of them)
  - 12 in HRVB arm
  - 9 in wait-list control arm

Results - Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>HRVB</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Age, years</td>
<td>66 (5)</td>
<td>64 (8)</td>
</tr>
<tr>
<td>Female</td>
<td>42%</td>
<td>33%</td>
</tr>
<tr>
<td>Black Race</td>
<td>58%</td>
<td>33%</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>17%</td>
<td>11%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>33%</td>
<td>44%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>67%</td>
<td>100%</td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>136 (23)</td>
<td>128 (19)</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>77 (10)</td>
<td>72 (8)</td>
</tr>
<tr>
<td>Heart rate, beats per minute</td>
<td>61 (10)</td>
<td>56 (9)</td>
</tr>
<tr>
<td>Lifetime major depression</td>
<td>30%</td>
<td>20%</td>
</tr>
<tr>
<td>Lifetime posttraumatic stress disorder</td>
<td>8%</td>
<td>13%</td>
</tr>
<tr>
<td>Medical stress-related myocardial inclusions</td>
<td>54%</td>
<td>50%</td>
</tr>
<tr>
<td>History of coronary artery bypass surgery</td>
<td>8%</td>
<td>33%</td>
</tr>
</tbody>
</table>

Results: Myocardial Blood Flow – Control Arm

Change in Myocardial Blood Flow from Rest to Stress in Waitlist Control Arm
Results: Myocardial Blood Flow – HRVB Arm

![Graph showing change in myocardial blood flow from rest to stress in HRVB Arm]

Results – Mental Stress Myocardial Flow Reserve

![Graph showing change in mental stress myocardial flow reserve from Visit 1 to Visit 2]

*All p-values for age, race, sex, systolic blood pressure, heart rate, hypertension, smoking, diabetes, lifetime depression, history of bypass surgery, Gensini score, and baseline mental stress myocardial blood flow were unadjusted.

Results - Other

- No differences between visits or groups for heart rate, blood pressure, or double product (heart rate x blood pressure).
- No change in outcome when normalizing myocardial blood flow for blood pressure x heart rate during each session (rest, stress).
Limitations and Strengths

- **Limitations**
  - Small pilot study
  - Many baseline differences > 10%
  - Limited generalizability to CAD
  - Prognostic and/or clinical value of mental stress myocardial flow ratio unknown

- **Strengths**
  - Evaluate direct cardiac impact of stress and HRVB

Conclusions

- HRVB increases mental stress myocardial flow reserve by 16%
  - 3% non-significant increase in waitlist controls
  - Treatment group differences not significant (p=0.16)
  - Adjusted group differences significant (28% increase, p<0.001)
- The clinical significance of these findings are not clear
  - Mechanisms (autonomic, inflammatory, neurologic)
  - Symptoms and long-term outcomes
- Encouraging for larger trial to answer additional questions

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