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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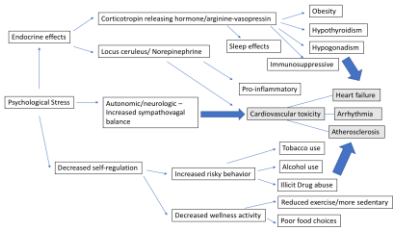
Overview

- 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

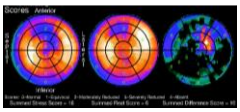
- Cardiovascular disease (CVD) is the number one cause of death in the world
- According to the CDC, an estimated 80% of heart disease deaths can be prevented
- Stress is a major risk factor for heart disease and is blamed for about 1/3 of heart attacks
- Limited options in stress management for clinicians

Mechanisms of Stress and Heart Disease

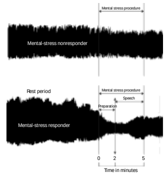


Stress Can Reduce Cardiac Blood Flow

- Mental stress-induced myocardial ischemia (MSIMI)
  - Regional blood flow deficits in the heart
  - Speech stressor (usually mild) used
  - Associated with 2x increased risk of CVD death



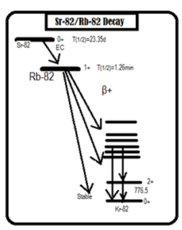
Heart scan showing reduced regional blood flow during stress



Reduced blood flow in finger after stress challenge

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



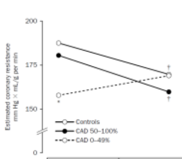
Background – Myocardial Blood Flow

- Mental Stress Myocardial Flow Reserve = myocardial blood flow during stress/rest

	Rest	Mental stress	Dipyridamole
CAD patients (n=10)			
Mean blood pressure (mm Hg)	93 (4)	107 (13)*	93 (13)
Heart rate (bpm)	58 (8)	66 (9)*	73 (12)*
Rate-pressure product	7766 (1787)	10 215 (2436)*	9471 (1847)*
Coronary flow reserve			
0–49% stenosis		1·1 (0·3)†	2·0 (0·7)†
50–100% stenosis		1·3 (0·3)‡	1·8 (0·7)†
Absolute MBF (mL/min per g)			
0–49% stenosis	0·65 (0·25)†	0·68 (0·20)	1·20 (0·30)†
50–100% stenosis	0·61 (0·26)†	0·75 (0·24)*	1·01 (0·34)†‡
Controls (n=5)			
Mean blood pressure (mm Hg)	94 (13)	106 (11)*	101 (10)*
Heart rate (bpm)	68 (7)	79 (9)*	91 (10)*
Rate-pressure product	8507 (818)	10 963 (843)*	12 024 (1295)*
Coronary flow reserve		1·5 (0·9)	2·8 (0·9)
Absolute MBF (mL/min per g)	0·52 (0·11)	0·80 (0·52)*	1·48 (0·54)*

Values presented as mean (SD). *p<0·05 (versus rest), †p<0·05 (versus control group), ‡p<0·05 (versus 0–49% stenosis group).

Haemodynamic and myocardial blood flow (MBF) data at rest, during mental stress, and during dipyridamole in patients with coronary artery disease and controls



Changes in estimated coronary resistance with mental stress in patients with coronary artery disease in regions with significant (50–100%) and non-significant (0–49%) epicardial stenosis, and in controls
*p<0·05 (versus controls), †p<0·05 (versus rest).

Arrighi *et al.,* Lancet 2000; 356: 310-1

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

http://www.saintphonie.be/en_syscardresp.php

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

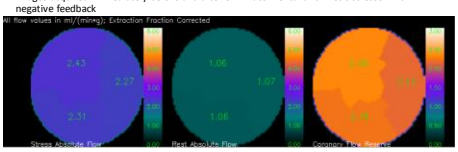
Heart rate variability biofeedback, versus waitlist control, increases mental stress myocardial flow reserve in subjects with coronary artery disease

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



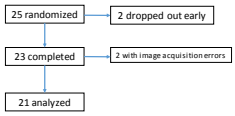
Sample image from Emory Cardiac Toolbox with Conventional Vasodilator Stress

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

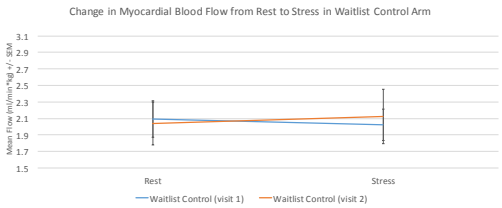
- Randomized 25 subjects
  - 2 dropped out because could not make appointments due to life changes
  - 23 subjects completed visits 1 and 2
  - 21 subjects had complete imaging data (imaging data corrupted on 2 of them)
    - 12 in HRVB arm
    - 9 in wait-list control arm



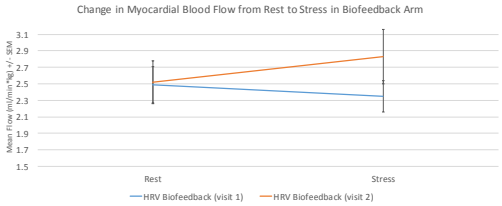
Results - Baseline Characteristics

	HRVB	Control
n	12	9
Age, years	66 (5)	64 (8)
Female	42%	33%
Black Race	58%	33%
Current Smoker	17%	11%
Diabetes	33%	44%
Dyslipidemia	67%	100%
Systolic BP, mmHg	136 (23)	128 (19)
Diastolic BP, mmHg	77 (10)	72 (8)
Heart rate, beats per minute	61 (10)	56 (9)
Lifetime major depression	42%	22%
Lifetime posttraumatic stress disorder	8%	11%
Mental Stress Induced Myocardial Ischemia	58%	67%
Conventional Stress Induced Myocardial Ischemia	58%	78%
History of coronary artery bypass surgery	8%	33%

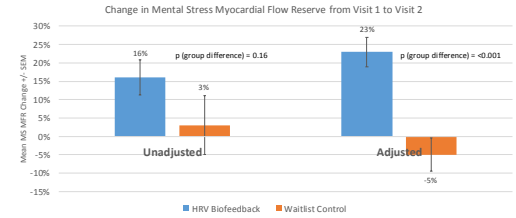
Results: Myocardial Blood Flow – Control Arm



Results: Myocardial Blood Flow – HRVB Arm



Results – Mental Stress Myocardial Flow Reserve



*adjustment for age, race, sex, systolic blood pressure, heart rate, hyperlipidemia, smoking, diabetes, lifetime depression, history of bypass surgery, CAD severity (Gensini score), baseline mental stress myocardial blood flow ratio

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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