

Mental Stress and CAD

- Stress: Chronic and Acute
- Lab induced Mental Stress induced myocardial ischemia: Background
- LAB Induced Mental Stress: Methods and detection techniques
- Recent Research Findings by our group
- Recent relevant research findings by our group
- Meditation based research in CAD patients
- Mindfulness Based Stress Reduction in CAD patients – A Randomized Clinical Trial at University of Florida, Gainesville, FL.

Chronic Stress

Chronic Stress

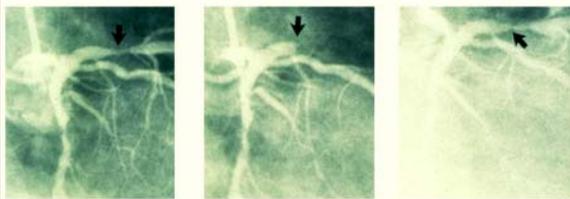
- DEPRESSION AND VITAL EXHAUSTION
- ANXIETY
- SOCIAL SUPPORT
- TYPE A BEHAVIOR PATTERN (TABP), HOSTILITY AND ANGER
- WORK STRESS
- MARITAL STRESS

Acute Stress: Epidemiology

- Multicenter Investigation of the Limitation of Infarct Size (MILIS): 48% had Emotional triggers out of which the most common was emotional upset (14%).
- 1981 Athens earthquake: Incidence of cardiac deaths rose from the normal average of 2.6 deaths per day to an average of 5.4, with a peak of 8 deaths per day.
- 1994 Los Angeles earthquake, San Francisco earthquake of 1989, 1991 Iraq war: Increased incidence of MI and SCD.

Acute Stress: LAB

Case Study: Acute Stress Constricts Diseased Coronary Arteries--A Possible Mechanism for Mental Stress Ischemia



Baseline Mental Stress Recovery

(From Papademetriou et al:AHJ, 1998)

BACK GROUND / MENTAL STRESS

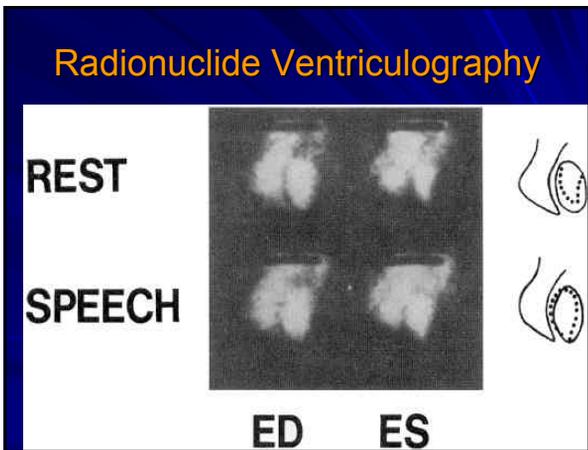
- Can be induced by lab stressors in a substantial subset (30-70%) of CAD patients
- Usually silent (asymptomatic)
- Occurs at lower heart rate threshold than standard exercise testing
- Often not detected by ECG markers in the laboratory
- Requires an imaging modality to detect ischemia

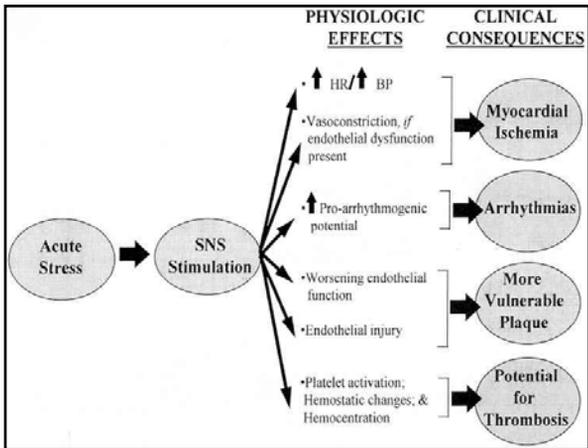
Mental Stress Tasks

- Mental arithmetic
- Stroop Color-Word task
- Public Speaking Task
- Recall of angry events (Mittleman et al)

Detection Techniques

- | | |
|---|---|
| ■ Radionuclide ventriculography | Measure
Markers of
Myocardial
Ischemia |
| ■ Echocardiography | |
| ■ Assessment of left ventricular changes by either a stationary probe and ambulatory VEST | <ul style="list-style-type: none"> •Wall motion •Perfusion •ECG •Chest pain |
| ■ Positron emission tomography | |
| ■ 99m Tc-sestamibi myocardial perfusion tomography | |





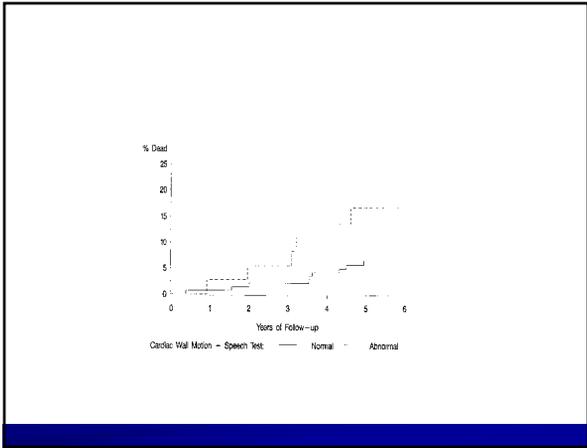
Mental stress ischemia: Mechanisms

- Decreased cardiac supply
 - Epicardial coronary vasoconstriction (e.g., Yeung et al. NEJM: 1991)
 - Impaired dilation of coronary microcirculation (e.g., Dakak et al. AJC: 1995)
- Increased cardiac demand (hemodynamic responses to stress)

Lab Induced Mental Stress ischemia as a Prognostic Factor

Studies Assessing Prognostic Relation of Inducible Mental Stress Ischemia to Clinical Events

STUDY	N	FOLLOW-UP LENGTH	RR of MS+ / MS-
Jain et al. AJC 1995; 76:31.	30	2 yr	2.5
Krantz et al. AJC:1999	85	3 yr	2.2
Jiang et al. JAMA, 1996	126	2 yr	2.6



**Recent Research Findings from
our group**

Detection and reproducibility of mental stress-induced myocardial ischemia with Tc-99m sestamibi SPECT in normal and coronary artery disease populations.

CK Kim, BA Bartholomew, ST Mastin, VC Taasan, KM Carson, DS Sheps

Methods

- A total of 40 patients were enrolled in this study: 19 patients with CAD and typical-angina or reversible ischemia (positive exercise treadmill study or positive adenosine thallium study) and 21 normal control subjects underwent mental stress testing as well as myocardial perfusion imaging.

■ The subjects were given a speaking task, and SPECT imaging was subsequently performed. Two experienced readers compared mental stress imaging with a resting image using a 20-segment cardiac model.

Results

- 16 out of 19 (84%) had ischemia.
- On repeat testing 12 out of 16 (75%) had ischemia.
- The mean number of new or worsened perfusion defects attributable to mental stress was 3.5, with a mean severity of 1.7.
- None of the 21 normal control subjects had evidence of mental stress-induced myocardial ischemia.

Mental Stress-Provokes Ischemia In Some Coronary Artery Disease Patients Without Exercise / Adenosine Induced Ischemia

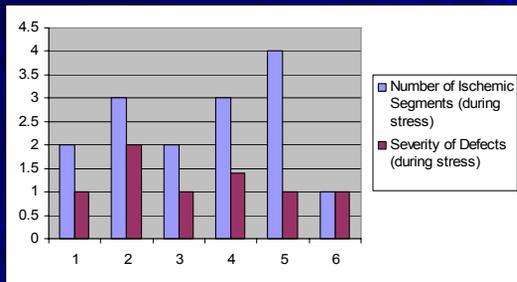
SRIKANTH RAMACHANDRANI, Michelle L. Ruby, RN, Courtney Butler, RN, Roger B. Fillingim, Ph.D, Carsten M. Schmalfuss, MD, FACC, Susan P. McGorray, Ph.D, Gary R. Cooper, MD, FACC, David S. Sheps, MD, FACC, University of Florida, Gainesville, FL, Malcolm Randall VA Hospital, Gainesville, FL

METHODS

Demographics

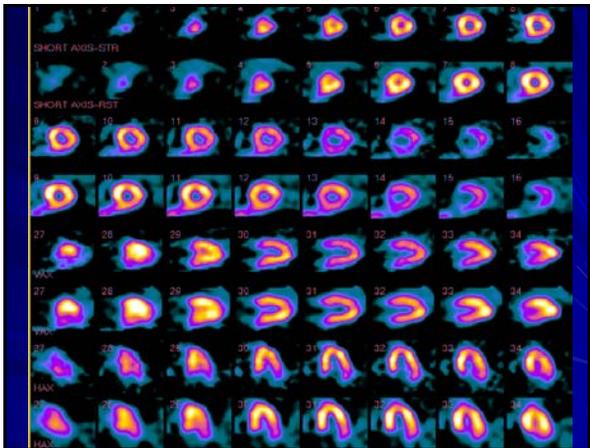
- Number of Patients: 14 patients (10 males, 4 females)
- Mean age: 65.2 Years
- History of CAD: (S/P MI 7%, PTCA/Stents 85%, CABG 28%)
- Medications: (78% on beta blockers, 21% on calcium blockers, and 14% on nitrates)
- History of HTN: 29%
- History of Diabetes mellitus: 28%
- History of Hyperlipidemia: 100%

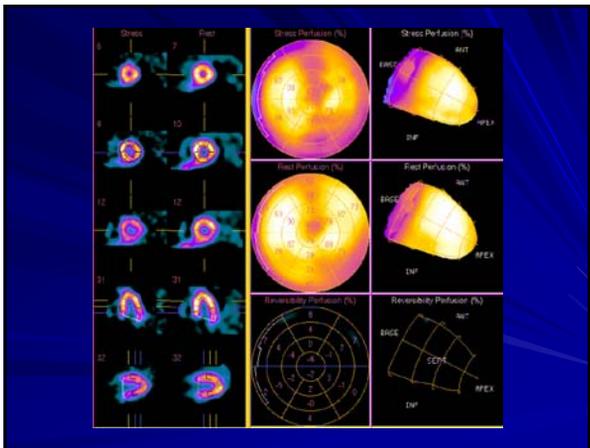
Nuclear Imaging Results



RESULTS HEMODYNAMICS

Resting		Patients (n=14)
Systolic BP (mm hg)	129.8 ± 3.5*	
Diastolic BP (mm hg)	75.6 ± 1.8*	
Heart Rate (Beats/minute)	63.9 ± 2.9*	
Stress		* All changes from rest to peak stress (p<0.0001)
Systolic BP (mm hg)	191.2 ± 5.9*	
Diastolic BP (mm hg)	102.8 ± 2.2*	
Heart Rate (Beats/minute)	85.7 ± 3.9*	





Previous Relevant Meditation
Research

Meditation

- In another study relaxation training compared to control condition, was found to decrease premature ventricular contractions in ischemic heart disease patients, especially during sleep.
- Heart rate variability, an important predictor for ischemia, also was found to increase with meditation in one study.
- A recent study of heart rate variability suggests that meditation might increase parasympathetic activity, as demonstrated by an increase in HF power spectral activity during an acute relaxation/meditation period in normal subjects even after controlling for respiration.
- The concept that the long term use of relaxation/ meditation might alter SNS activity is supported by a study which demonstrated that 6 months of daily relaxation led to changes in the standard deviation of RR with deep breathing and decreases in tachycardia with the valsalva maneuver.

Meditation

Patel and others reported 4 controlled trials in which he tested a meditation-based individual psychoeducational therapy which has consistently obtained larger and more durable improvements than any other nonpharmacological hypertensive therapy.

After between 6 to 12 weeks of treatment, patients in the meditation program consistently demonstrated strong improvements in systolic (SBP) and diastolic (DBP) blood pressure, and these changes were much larger than improvements in control situations. Follow-ups at 1 and 4 years showed continued maintenance of improvements, as well as significantly reduced coronary events versus the disease education condition.

**MINDFULNESS BASED STRESS
REDUCTION
&
MYOCARDIA ISCHEMIA**

INTRODUCTION

Blumenthal et al has conducted the only published stress management vs. exercise vs. usual care intervention study for stress-induced ischemia. Although the stress management condition demonstrated the strongest effects, there was no control for the potential therapeutic effects of attention.

Meditation-based interventions have reliably demonstrated the efficacy of meditation to reduce blood pressure as well as increase parasympathetic activity.

INTRODUCTION

Mindfulness meditation specifically teaches skills that reduce self-perceived stress reactions by not only inducing the 'relaxation response' but by also revealing moment to moment patterns of chronic hyperreactivity.

Carels et al. have reported that CAD patients who are high emotional responders (with increased stress reactivity) demonstrated higher (2.5-3.9) odds ratios for laboratory mental stress and ambulatory myocardial ischemia as compared to low emotional responders. This finding further supports the hypothesis that MBSR will reduce stress-induced ischemia, as MBSR skills specifically alter emotional reactivity.

Hypothesis

150 Patients will be randomized in 2:2:1 ratio to MBSR, Education and Usual care groups. First randomized controlled trial of MBSR treatment for mental stress induced myocardial ischemia in patients with CAD.

In comparison to either of the control conditions, significantly more CAD patients in the mindfulness meditation condition will

1. Demonstrate reductions in mental stress induced ischemia.
2. Increased heart rate variability during ambulatory ECG monitoring
3. Report greater improvement in quality of life
4. Sustained positive results at the end of three months

Inclusion Criteria

- At least 18 years old.
- **Confirmed CAD** : The clinical diagnosis of coronary disease will be defined by the presence of at least 1 of the following :
 - **Abnormal coronary angiogram**, abnormal IVUS, or abnormal flow reserve.
 - **Documentation of one of the following**:
 1. Elevated Troponin lab values typical for myocardial infarction
 2. ECG that shows q-wave abnormalities.
 3. Nuclear scan that demonstrates a fixed wall motion abnormality consistent with an old MI.
 4. > 95% probability of coronary disease according to the criteria o Diamond and Forrester.
 5. Radionuclide study, dobutamine or exercise echocardiographic study consistent with stress-induced ischemia (development of segmental wall motion abnormalities or reversible perfusion defects on radionuclide imaging and/or wall motion abnormalities or systolic thickening abnormalities on stress echocardiographic exam)

Exclusion Criteria

- Current pregnancy or probability of pregnancy during the duration of the 12-week study.
- Diagnosis of unstable angina in the prior 2 months.
- Presence of other severe, complicating medical problems that will significantly shorten the patients' life expectancy such that they will not be expected to live for the 12 weeks of this study.
- Presence of serious psychopathology
- With existing meditation practice.
- Weighs over 400 pounds

Methods

Baseline and Post Intervention PHYSIOLOGICAL AND PSYCHOLOGICAL PROCESS MEASURES

- Radionuclide Procedures: Gated Myocardial Perfusion Imaging
(after mental stress speech task)
- 24 HOUR HOLTER
- Demographic Information

Methods Contd

Psychological Battery

- The Brief Symptom Inventory (BSI)
- Hostility The Cook-Medley Hostility Scale (CMHS)
- Depression Beck Depression Inventory (BDI-II).
- Anxiety The State-Trait Anxiety Inventory, (STAI)
- Optimism Revised Life Orientation Test (LOT-R).
- Anger The State-Trait Anger Expression Scale (STAXI)
- Health Survey The SF-36
- Daily Stress Diaries

EXPERIMENTAL PROTOCOL

Interventions	* * * * * * * *	
48hr Holter	*	*
Daily Diaries	* *	* * * *
Randomization	*	
Psychological Battery	*	* *
SPECT Imaging	* *	* *
Screening Interview	*	
Weeks	-2 -1	1 2 3 4 5 6 7 8 9 10 11 12 0 0
Assessment	Pretreatment	Posttreatment 3 mo

DATA ANALYSES

- Preliminary analyses will test for group differences in age, race, education, social-economic status, marital status and illness-related variables (i.e., duration of CAD, smoking, hypertension, previous CABG, PTCA, or MI). Three distinct statistical approaches will be applied. An analysis of covariance (ANCOVA), Multivariate analysis of covariance (MANCOVA), Multilevel model analyses.
- We evaluated the power available with the proposed 150 patients to ascertain 25-30% reductions in the number of mental stress-induced perfusion defects with the proposed 60/60/30 sampling design.
- Power estimates to detect a significant difference across groups are .92 for 30% reductions with effect sizes of .32 and .80 for 25% reductions with effect sizes of .26.

Mental Stress and CAD

- Stress: Chronic and Acute
- Lab induced Mental Stress induced myocardial ischemia: Background
- LAB Induced Mental Stress: Methods and detection techniques
- Recent Research Findings by our group
- Recent relevant research findings by our group
- Meditation based research in CAD patients
- Mindfulness Based Stress Reduction in CAD patients – A Randomized Clinical Trial at University of Florida, Gainesville, FL.
