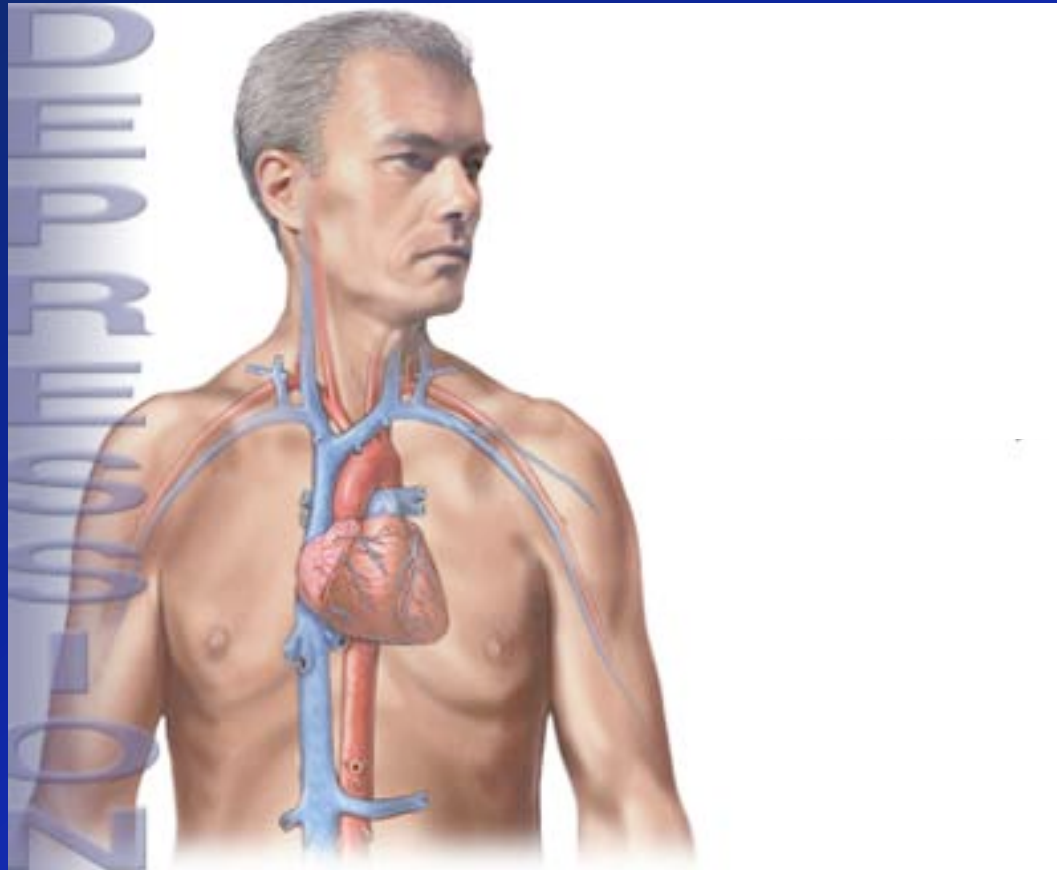


# The Effects of Cardiorespiratory Biofeedback and Dialectical Behavioral Skills Training with Sertraline on Post Myocardial Infarction Major Depression and Low Heart Rate Variability



A Dissertation Presented  
by Priya Chaudhri, M.A.

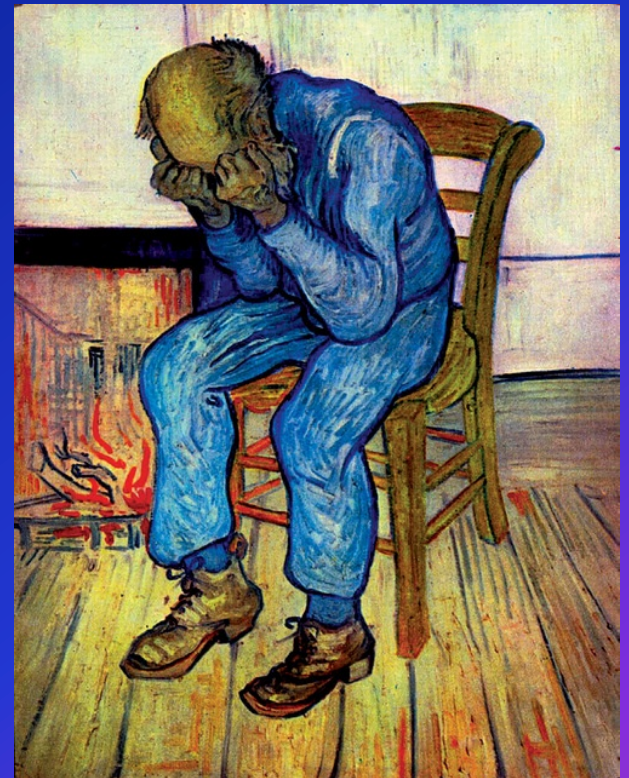
# Cardiovascular Disease

- CVD is the leading cause of morbidity and mortality in the U.S. since the 1940's (AHA, 2005)
- 2,600 people die of CVD in the U.S. each day, which is approximately 1 death every 30 seconds (AHA, 2005)
- This year an estimated 1.2 million Americans will have a new or recurrent coronary attack (WHO, 2006)



# Cardiovascular Disease and Depression

- It is estimated that 40-65 % of MI patients have comorbid depression (AHA, 2005)
- 1 out of 5 MI patients have diagnosable MDD and a quarter have minor depression (Carney et al., 1987)
- Depression is associated with a 2-7 fold elevated risk of cardiac events (Molinari et al., 2006)
- Post-MI depression is associated with a 2-3 fold increased risk for cardiac mortality (van Joost et al., 2004)
- Depression contributes to poor adherence to cardiac rehabilitation (Kessler et al., 1997)



# Depression and ANS Dysregulation

Depression is associated with...

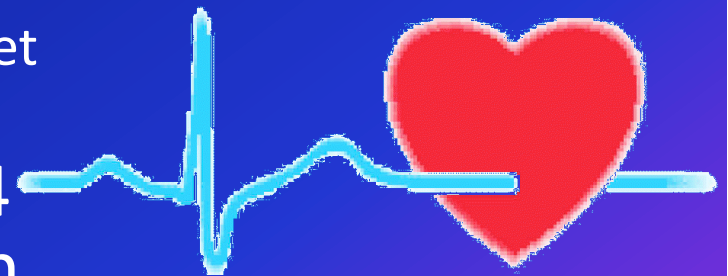
- Elevated heart rate
- Low heart rate variability
- Exaggerated heart rate responses to physical and psychological stressors
- High variability in ventricular repolarization
- Low baroreceptor sensitivity
- Elevated inflammatory response
- Elevated norepinephrine (NE) which increases SNS activity



(Carney et al., 2005)

# CVD and Heart Rate Variability

- HRV is defined as the fluctuations or beat to beat alterations in HR as measured in *ms*
- HRV is the single greatest predictor of morbidity and mortality in CVD patients (Kleiger, et al., 2000)
- Low HRV is associated with a 2-4 fold increased risk of mortality in post-MI patients (Bigger et al., 1993)
- HRV is significantly lower in depressed populations (Carney, et al., 2000)

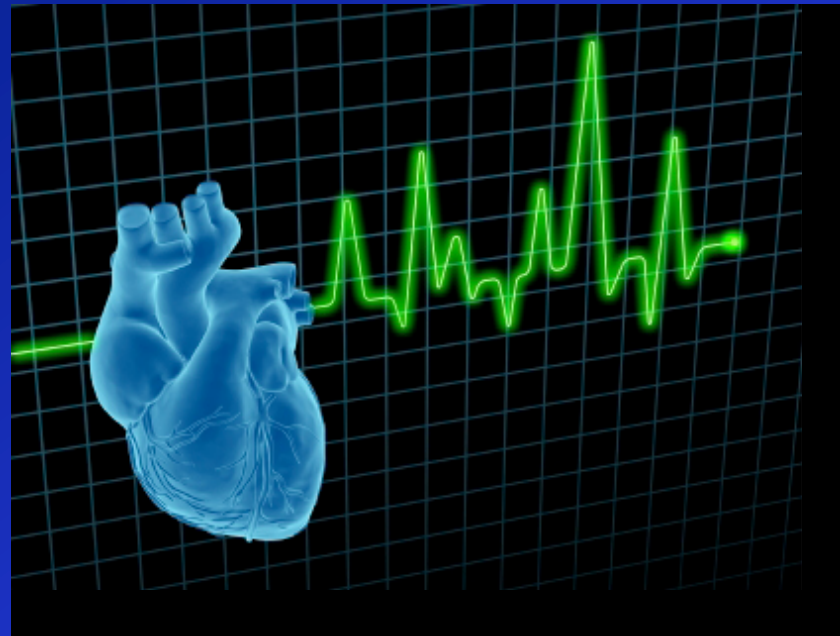


# Limitations of Current Treatment Options

- The current standard of care to treat depression for cardiac patients is SSRI medication, which has been shown to be only 40-60% effective in reducing depressive symptoms. (Carney et al., 2005)
- Beta blockers have been shown to have modest effects on increasing heart rate variability. (Sandrone et al., 1994)
- Although pharmacological treatment has been partially effective for depression and low HRV, there are major concerns with long term consequences, side effects, compliance, and lifetime cost.

# Study Objective

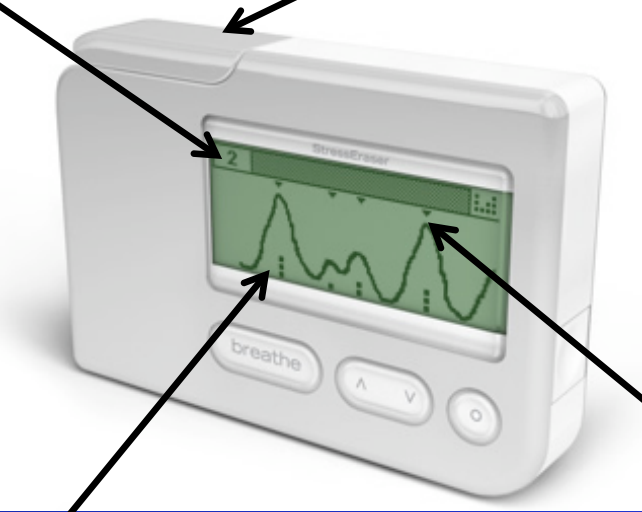
To examine the efficacy of cardiorespiratory biofeedback with dialectical behavioral therapy (DBT) in conjunction with sertraline medication for the treatment of major depressive disorder and low heart rate variability in post-MI patients.



# The StressEraser, Helicor, Inc.

Infrared Finger Sensor

**Daily Points**  
Every time a point is obtained it is added in the left hand corner. The goal is to get 2 or 3 squares continuously in order to reach the daily goal of 50-100 pts.



**Pulse Rate Wave**  
Reflects the activity of the nervous system or RSA and represents the spontaneous rhythmic increase and decrease of the heart rate.

Squares tell you whether you are relaxed...

- 3 squares = 1 point
- 2 squares = ½ point
- 1 square = 1 point



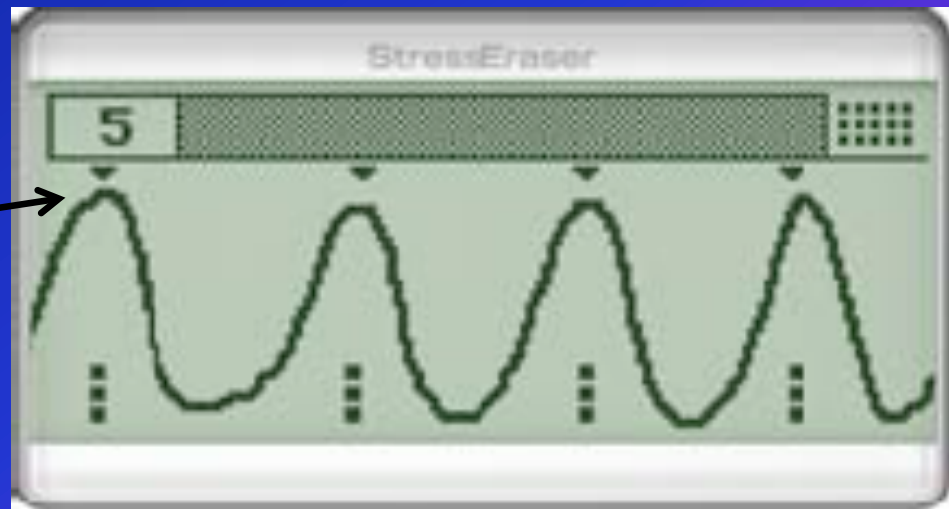
## Strained Breathing

An indicator of poor baroreceptor functioning, strained breathing or emotional stress



## Synchronized Comfortable Breathing

Synchronized breathing at less than 6.5 breaths per minute.



# Dialectical Behavioral Therapy

- **Traditional DBT** (1 x week for 2.5 hours)
- **4 Modules of Treatment:**
  - \* Mindfulness Skills
  - \* Interpersonal Effectiveness Skills
  - \* Distress Tolerance Skills
  - \* Emotion Regulation Skills
- **DBT Skills Training for this study** (1 x week for 1.5 hours)
- **3 Modules of Treatment:**
  - \* Mindfulness Skills
  - \* Distress Tolerance Skills
  - \* Emotion Regulation Skills

# Treatment Protocol

## Experimental Group

### Cardiorespiratory Biofeedback

20 minute daily practice of StressEraser device

### Dialectical Behavioral Skills Training

90 minute weekly DBT group

### Antidepressant Medication

sertraline treatment

## Control Group

### Antidepressant Medication

sertraline treatment

# *Hypotheses*

**Hypothesis 1:** Participants in the experimental group would show a greater decrease in depressive symptoms at post-treatment and follow-up relative to the antidepressant control group.

**Hypothesis 2:** Heart rate variability, as measured by SDNN, LF/HF ratio, VLF would improve more at post-treatment and follow-up for the experimental group, than the control group.

**Hypothesis 3:** Participants in the experimental group would show greater improvements in mindfulness and emotion regulation scores at post-treatment and follow-up relative to the antidepressant control group.

**Hypothesis 4:** The experimental group would demonstrate a significant correlation with StressEraser biofeedback points and improvements in depression scores at post-treatment and follow-up.

**Hypothesis 5:** Decreases in depression scores would be mediated by improvements in mindfulness, emotion regulation and SDNN at post-treatment and follow-up.

# Measurements

## Psychological

Depression Interview and Structured Hamilton (DISH)

Beck Depression Inventory II (BDI-II)

Difficulties in Emotion Regulation Scale (DERS)

Five Facet Mindfulness Questionnaire (FFMQ)

## Heart Rate Variability

Standard Deviation of Normal-Normal Beats (SDNN)

Low Frequency/ High Frequency Ratio (LF/HF)

Very Low Frequency (VLF)

## Weekly Logs

Medication Log

Breathing Log

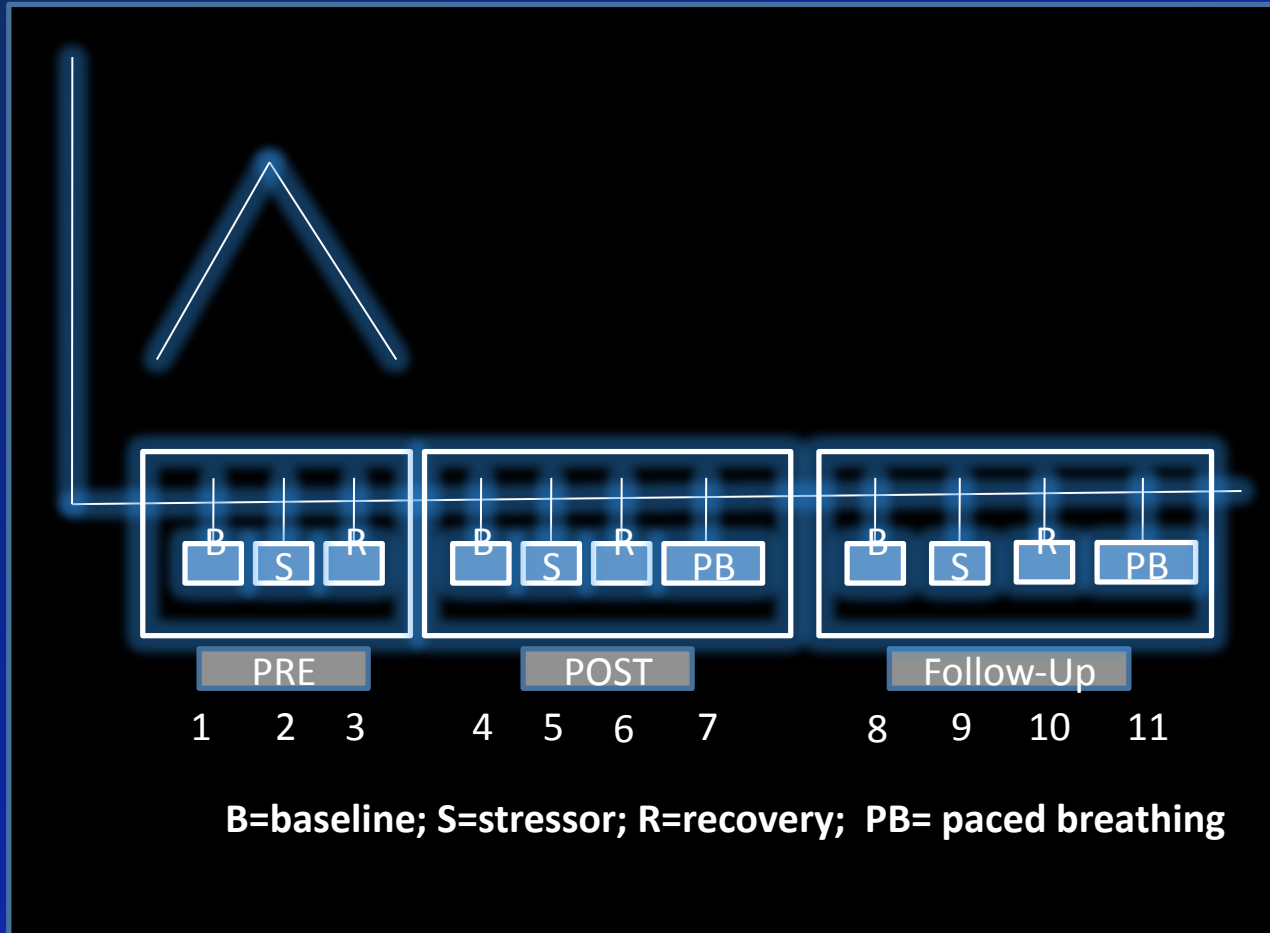
## Assessment Periods

Baseline (Week 1)

Post-Treatment (Week 8)

Follow-Up (Week 12)

# Physiological Measurement of HRV



**Baseline:** 10 min (listened to travel log)

**Stressor:** 2 minute serial 7 test

**Recovery:** 3 minute recovery (sitting quietly)

**Paced Breathing:** 5 min of 6 BPM breathing

## Inclusion Criteria

- Documented CVD and MI.
- Absence of recent cardiac events (MI < 2 months) and medications changes in the 4 weeks prior to the first treatment visit.
- A primary diagnosis of Major Depressive Disorder, as assessed by a DISH Hamilton score of 18 or greater, with low risk of suicide defined by a BDI score of less than 2 on question # 9.
- Stabilized on sertraline medication (at least 4 weeks) prior to study.
- Stable cognitive functioning based on the Mini-Mental Status Exam (MMSE).

## Exclusion Criteria

- Not between the ages of 20-85, met the criteria for Class IV Congestive Heart Failure, had a pacemaker, and/or pregnant.
- Exceeded a daily consumption of 830 milligrams of caffeine.
- Presence of any physical conditions or medications that make heart rate variability uninterruptible.
- Coronary intervention within the past 2 months.
- Serious comorbid medical condition that may affect depression levels (i.e. hypothyroidism, diabetes).
- Practiced weekly yoga or meditation .



# Demographics

- **60** Total Participants
- **34** Males
- **26** Females
- **55** = Mean Age
- **50%** Caucasian
- **70%** Married
- **70%** College education

# Statistical Analyses

## Primary Analyses

Multi-level Modeling was implemented using hierarchical linear modeling (HLM). A random intercept HLM model was used to analyze the psychological measures (HAM-D, BDI-II, DERS, FFMQ). An unstructured HLM model using random intercept and random slope was used to analyze heart rate variability (SDNN), (LF/HF ratio), (VLF) across three measurement conditions (baseline, stressor, and recovery). To assess the potential impact of missing data, a random effects pattern-mixture analysis was implemented with a binary missing data variable (all participants versus completers) which was entered as a predictor in the random regression model.

## Mediation Analyses

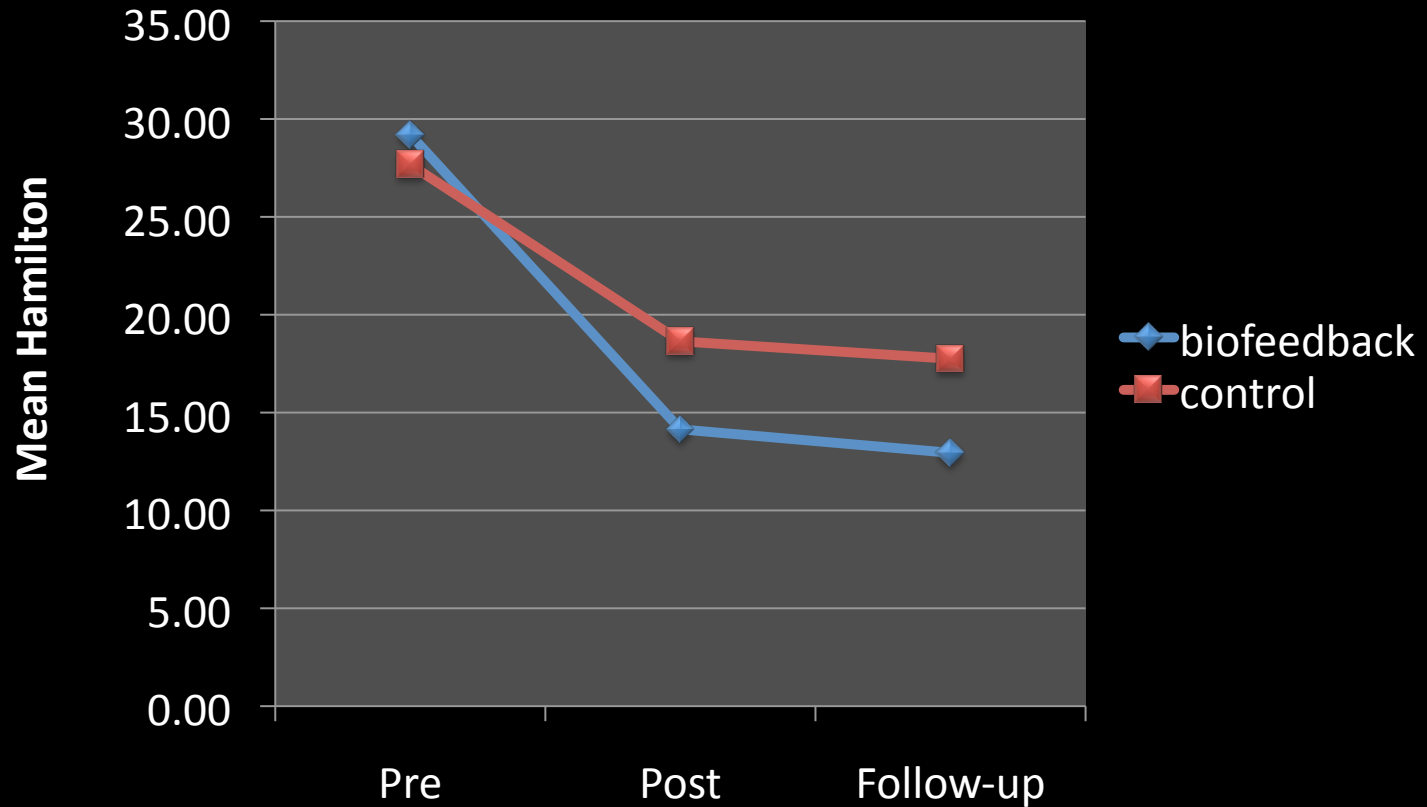
Structural equation modeling (SEM), Sobel mediation test.

## Correlation Analyses

Pearson correlation tests.

# Results of the Study

## Hamilton Scores Across Time ( N = 60)



### HLM Analysis of Hamilton Scores Across Time

All Participants ( N = 60)

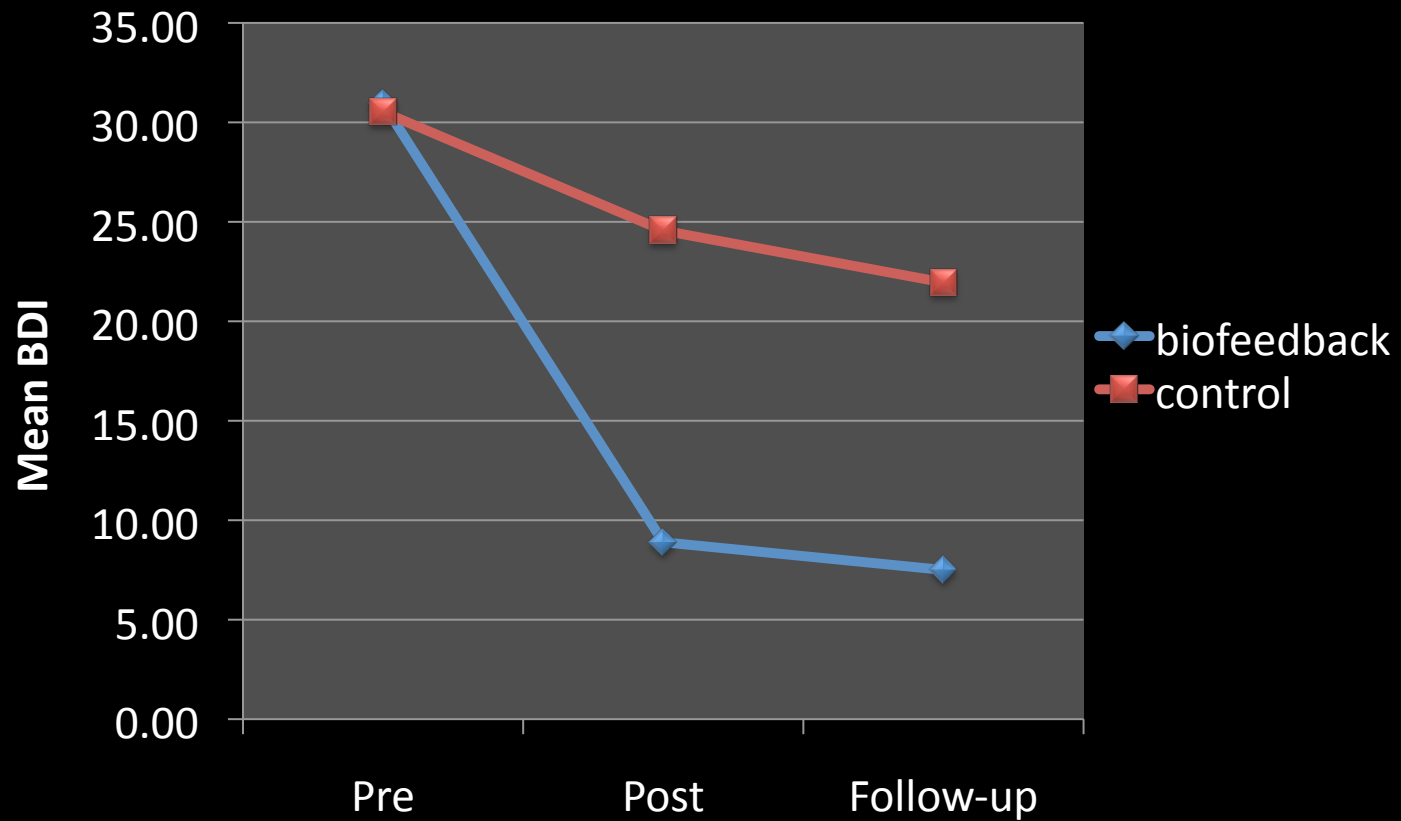
	<u>Est.</u>	<u>SE</u>	<u>p &lt;</u>	
Time x Treatment	-3.20	1.12	.006	**
Dropout x Time x Treatment			.591	

\* (p<.05)

\*\* (p<0.01)

\*\*\* (p<.001)

## BDI Scores Across Time ( N = 60)



### HLM Analysis of BDI Scores Across Time

All Participants ( N = 60)

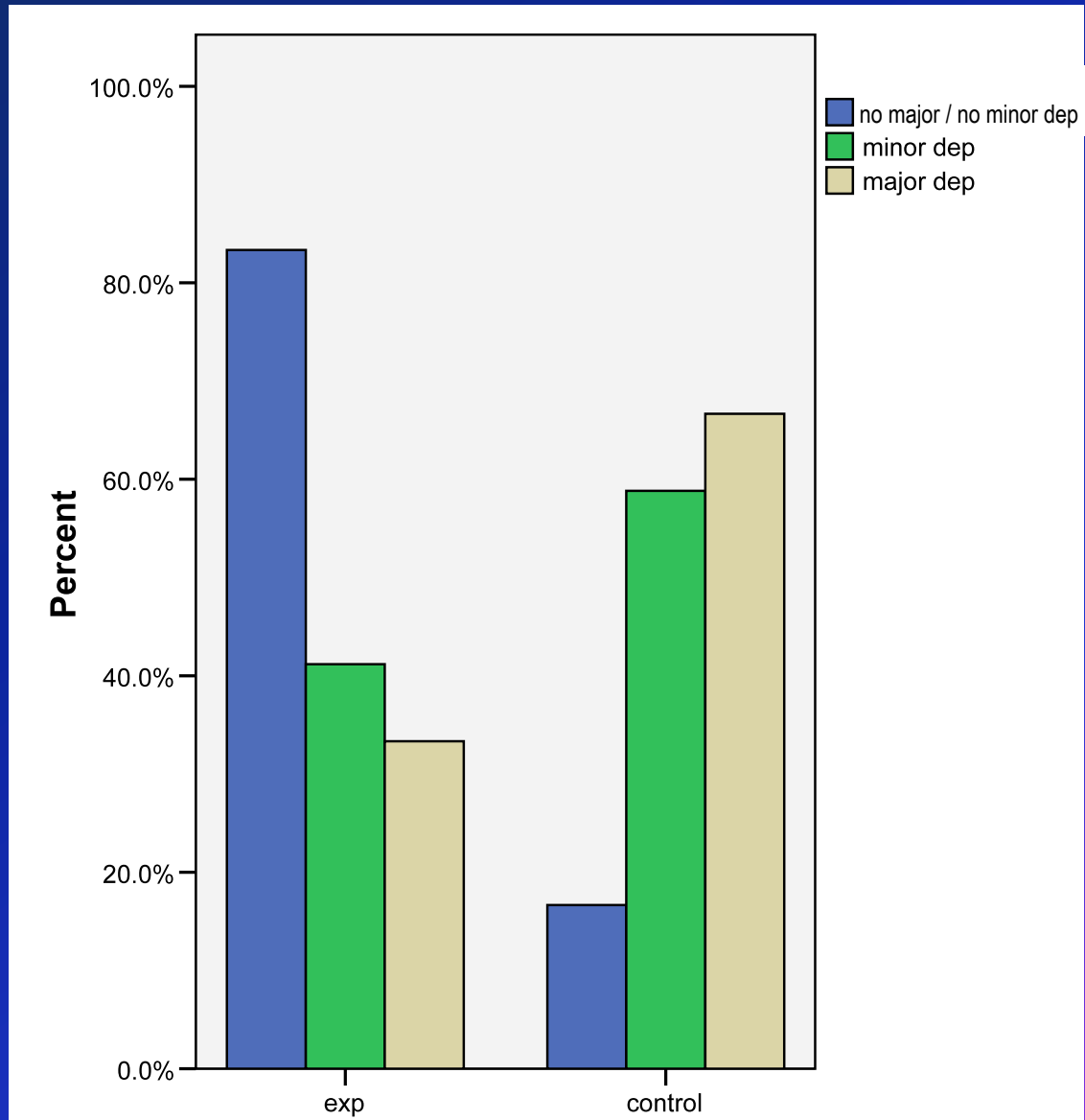
	<u>Est.</u>	<u>SE</u>	<u>p &lt;</u>
Time x Treatment	-8	1.6	<.0001***
Dropout x Time x Treatment			0.002 *

\* (p<.05)

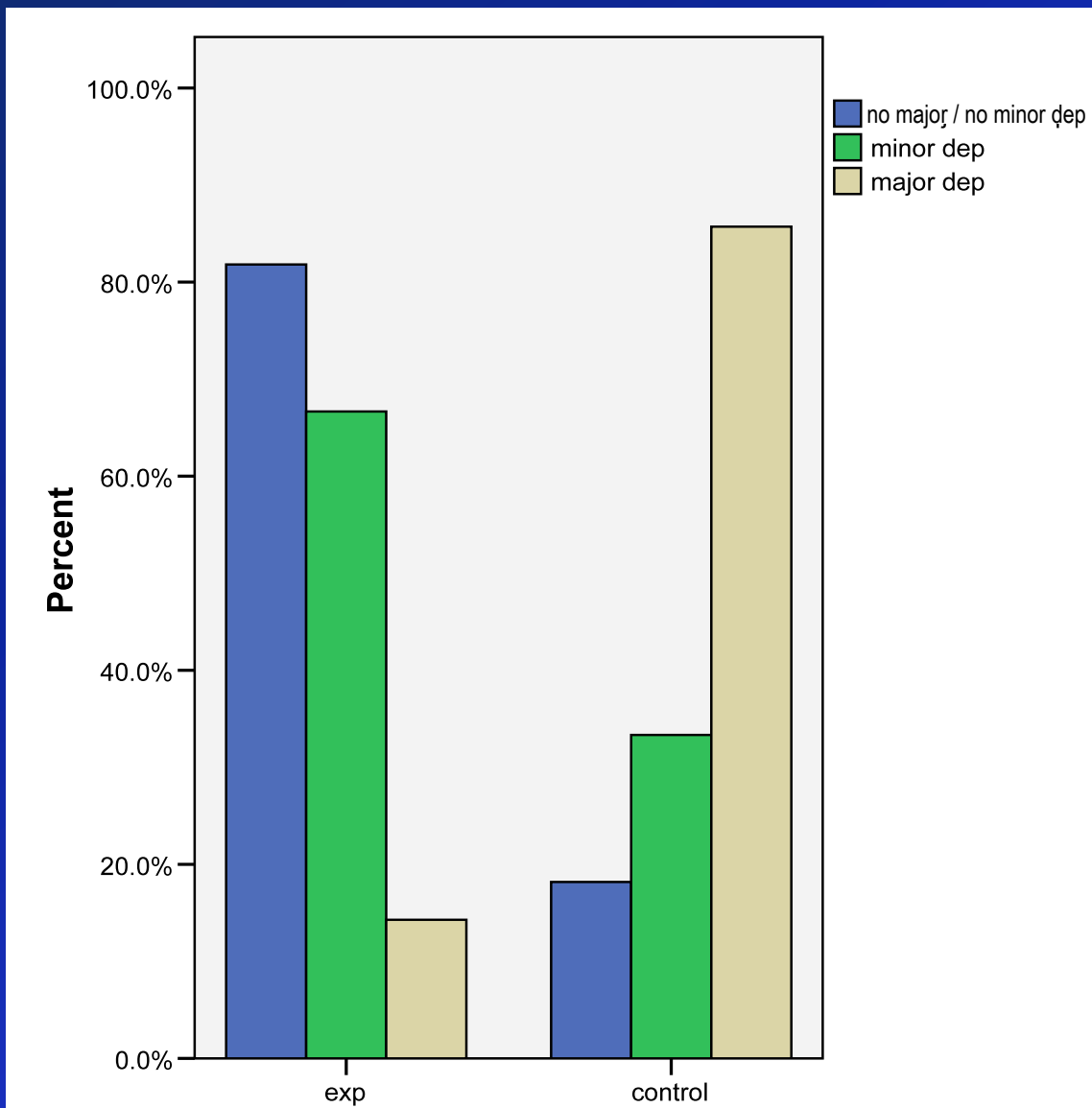
\*\* (p<0.01)

\*\*\* (p<.001)

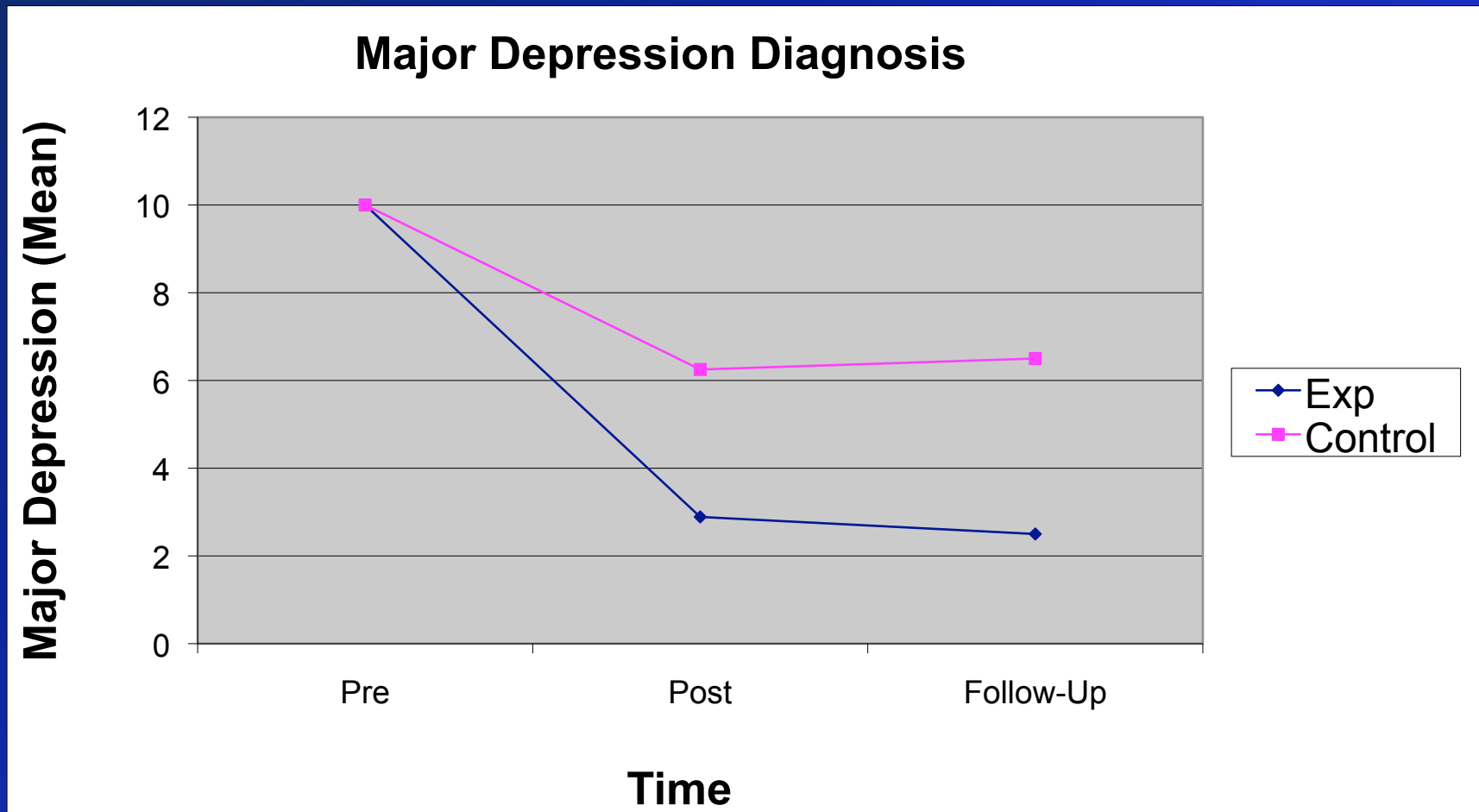
# DISH Depression Diagnosis Frequency Distribution at Post-Treatment



# DISH Depression Diagnosis Frequency Distribution at Follow-Up



# Major Depressive Disorder Across Time (N = 60)



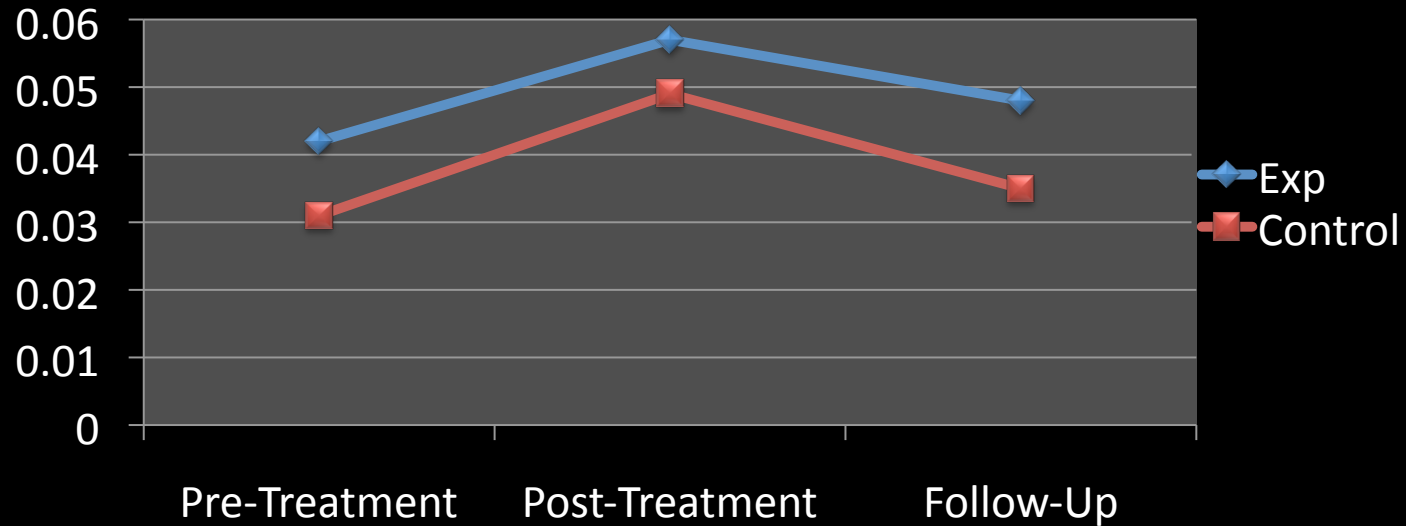


# HLM Analysis of Heart Rate Variability

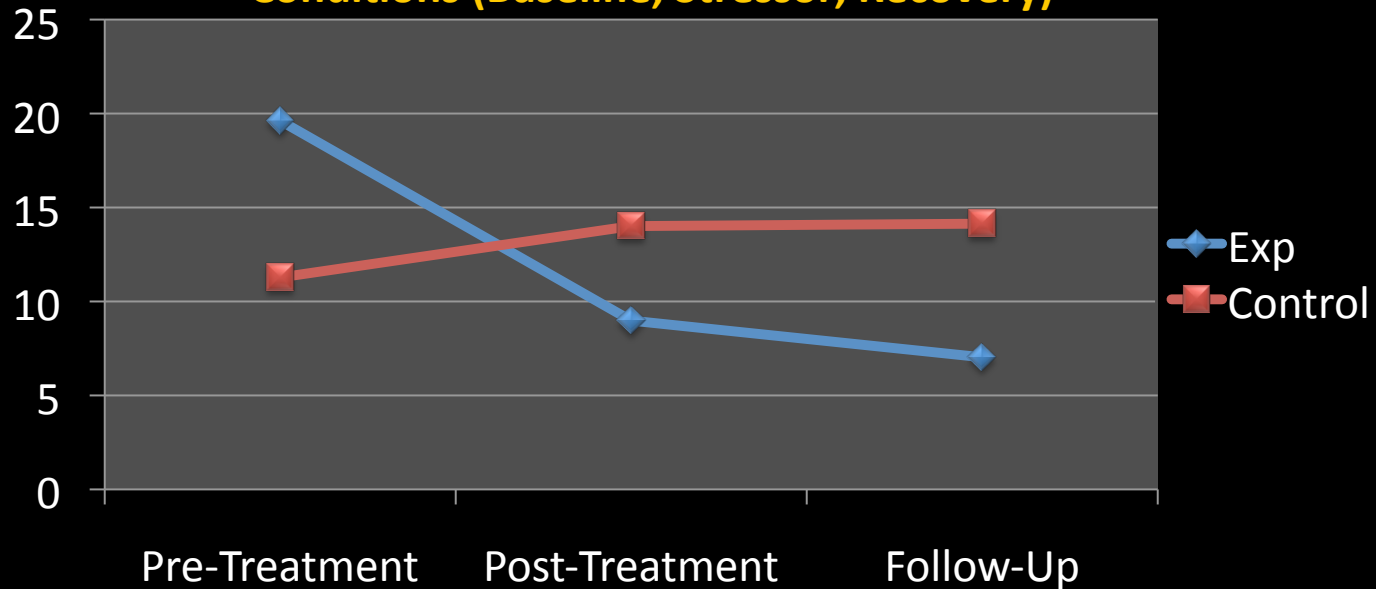
SDNN	Est.	SE	p <
<b>Stressor</b>			
Time X Treatment	0.009	0.005	0.055 $\gamma$
Dropout X Time X Treatment			0.134
<b>Recovery</b>			
Time X Treatment	12.696	4.555	0.004**
Dropout X Time X Treatment			0.138
<b>LF/HF Ratio</b>			
<b>Stressor</b>			
Time X Treatment	0.051	0.403	0.213
Dropout X Time X Treatment			0.138
<b>Recovery</b>			
Time X Treatment	0.362	0.479	0.453
Dropout X Time X Treatment			0.590
<b>VLF</b>			
<b>Stressor</b>			
Time X Treatment	0.374	2.441	0.879
Dropout X Time X Treatment			0.144
<b>Recovery</b>			
Time X Treatment	8.383	2.437	0.001***
Dropout X Time X Treatment			0.130

\* significant (p<0.05); \*\*significant (p<0.01); \*\*\* significant (p<0.0001);  $\gamma$  statistical trend

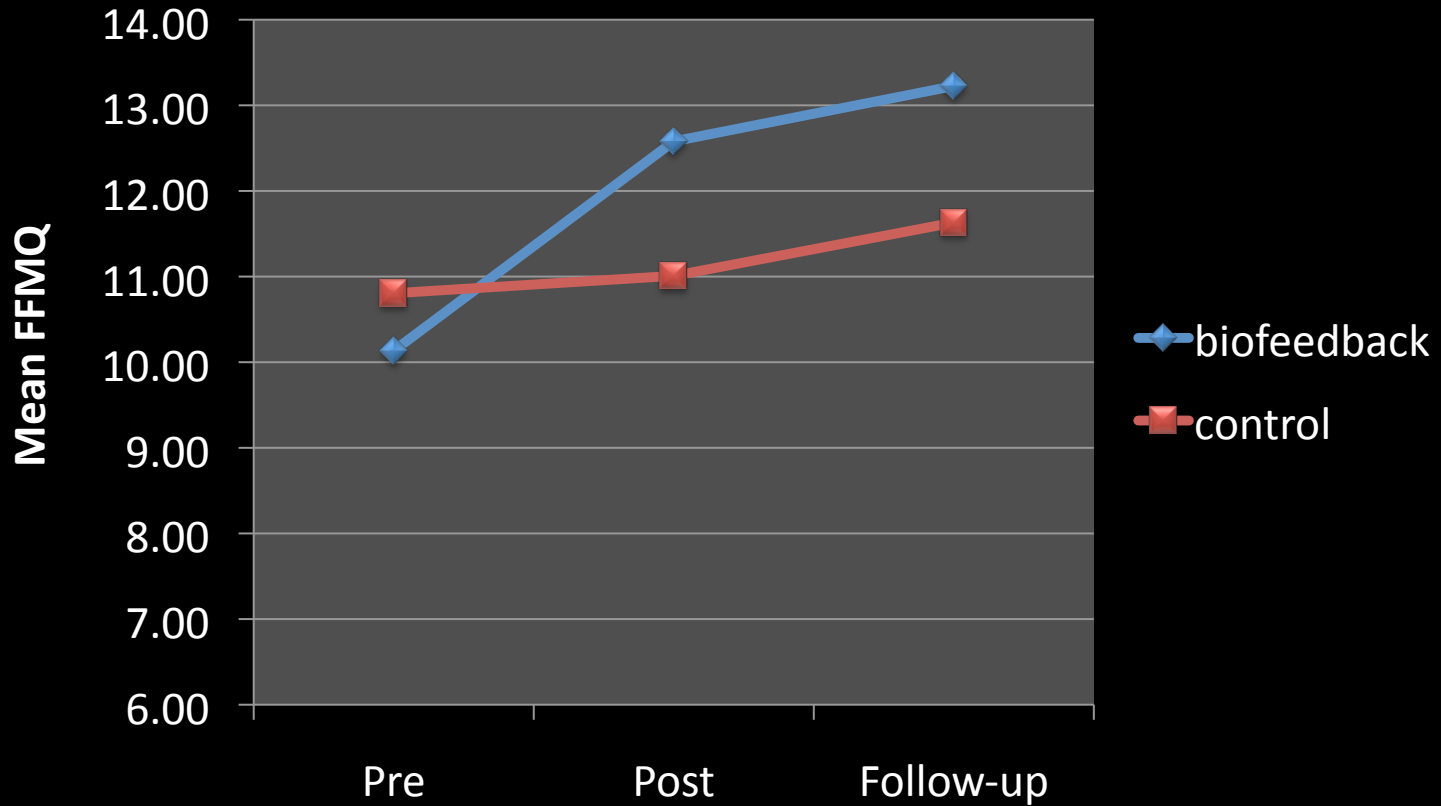
### Standard Deviation of Normal-Normal Beats (SDNN) Mean Across All Measurement Conditions (Baseline, Stressor, Recovery)



### Very Low Frequency (VLF) Mean Across All Measurement Conditions (Baseline, Stressor, Recovery)



## FFMQ Scores Across Time ( N =60)



### HLM Analysis of FFMQ Scores Across Time

All Participants ( N = 60)

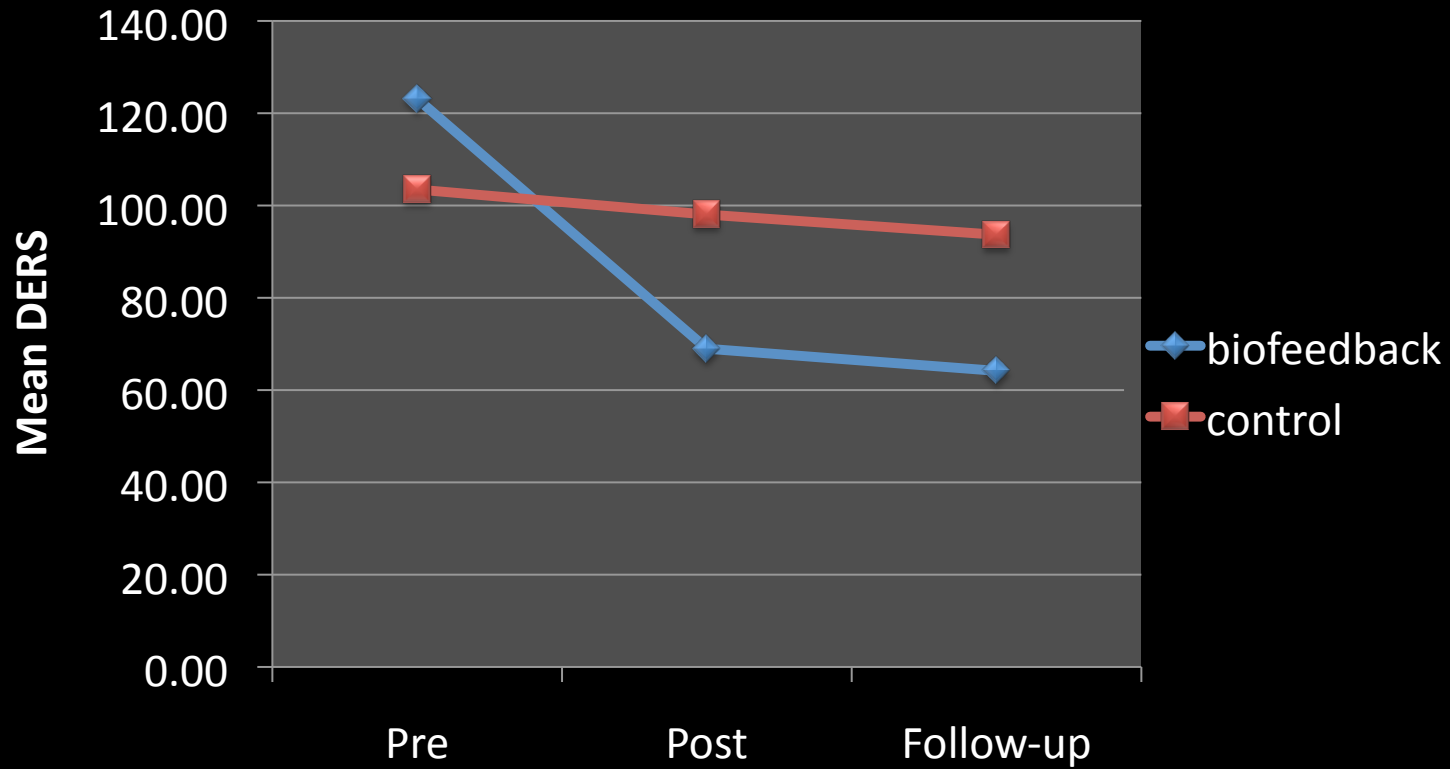
	Est.	SE	<i>p</i> <
Time x Treatment	0.28	0.05	<.0001 ***
Dropout x Time x Treatment			.132

\* (p<.05)

\*\* (p<0.01)

\*\*\* (p<.001)

## DERS Scores Across Time (N = 60)



### HLM Analysis of DERS Scores Across Time

All Participants ( N = 60 )

	Est.	SE	<i>p</i> <	
Time x Treatment	28.00	3.68	<.0001	***
Dropout x Time x Treatment			.150	

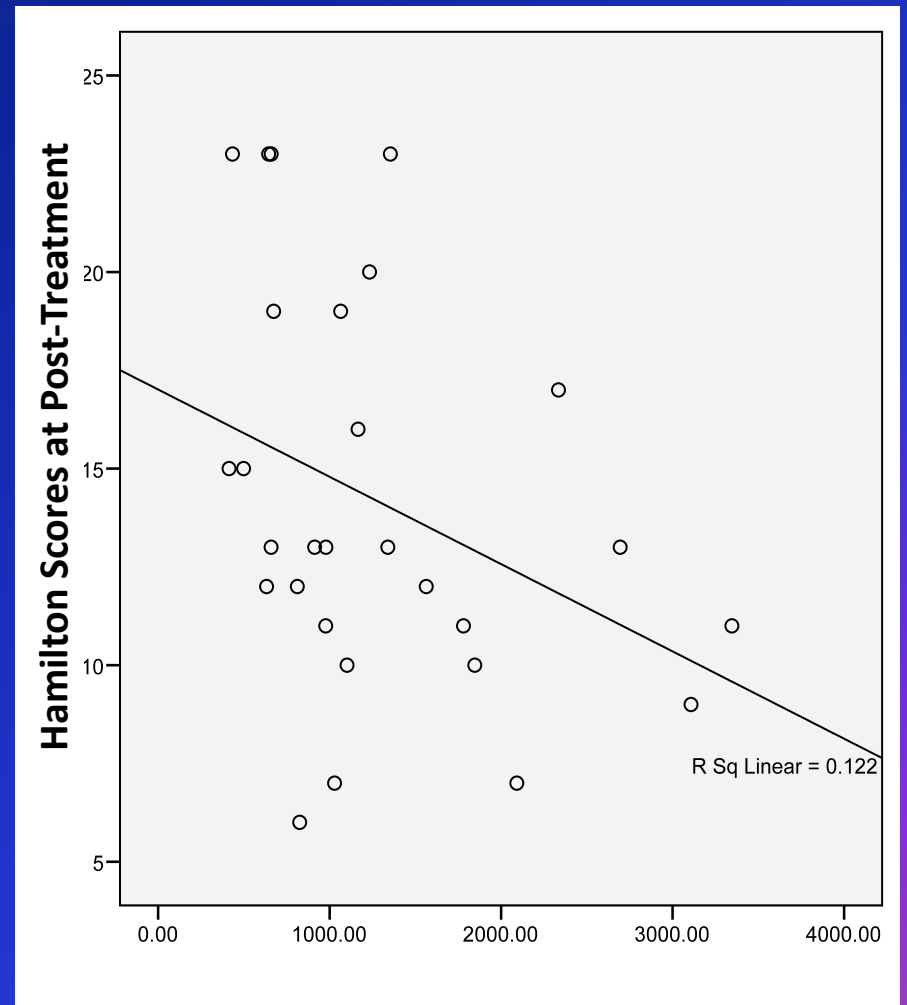
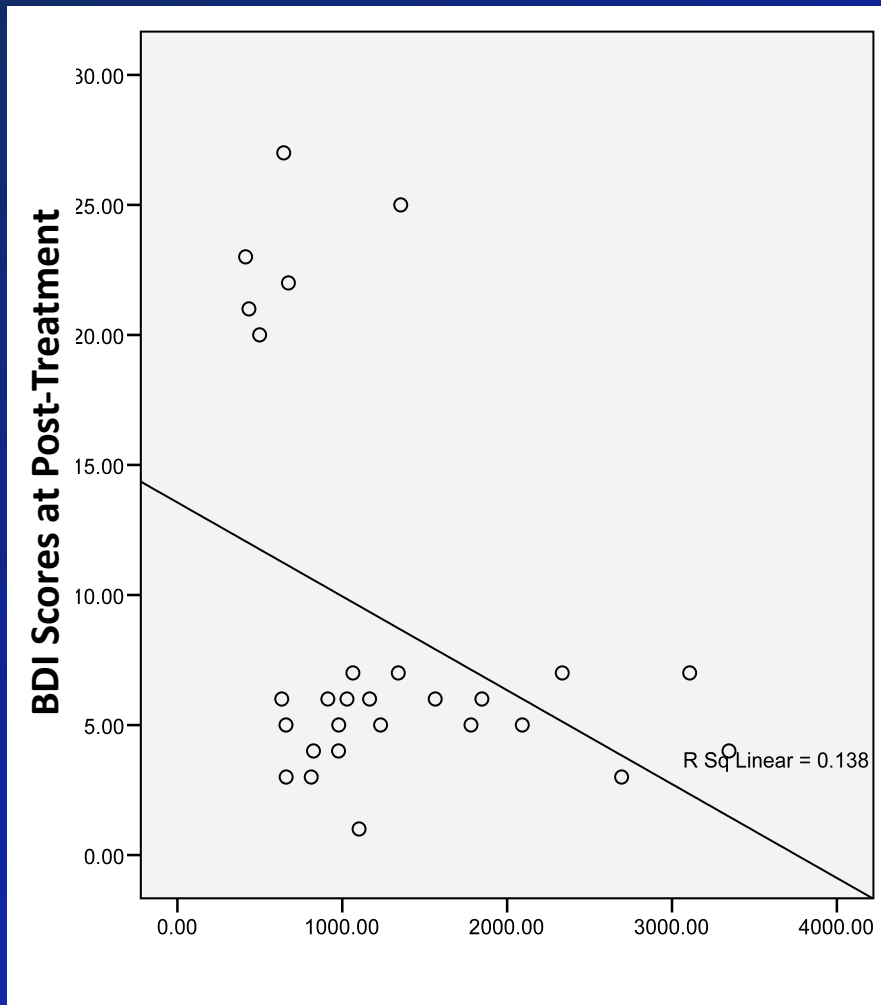
\* (p<.05)  
 \*\* (p<0.01)  
 \*\*\* (p<.001)

## StressEraser Points Correlation with Depression Outcomes

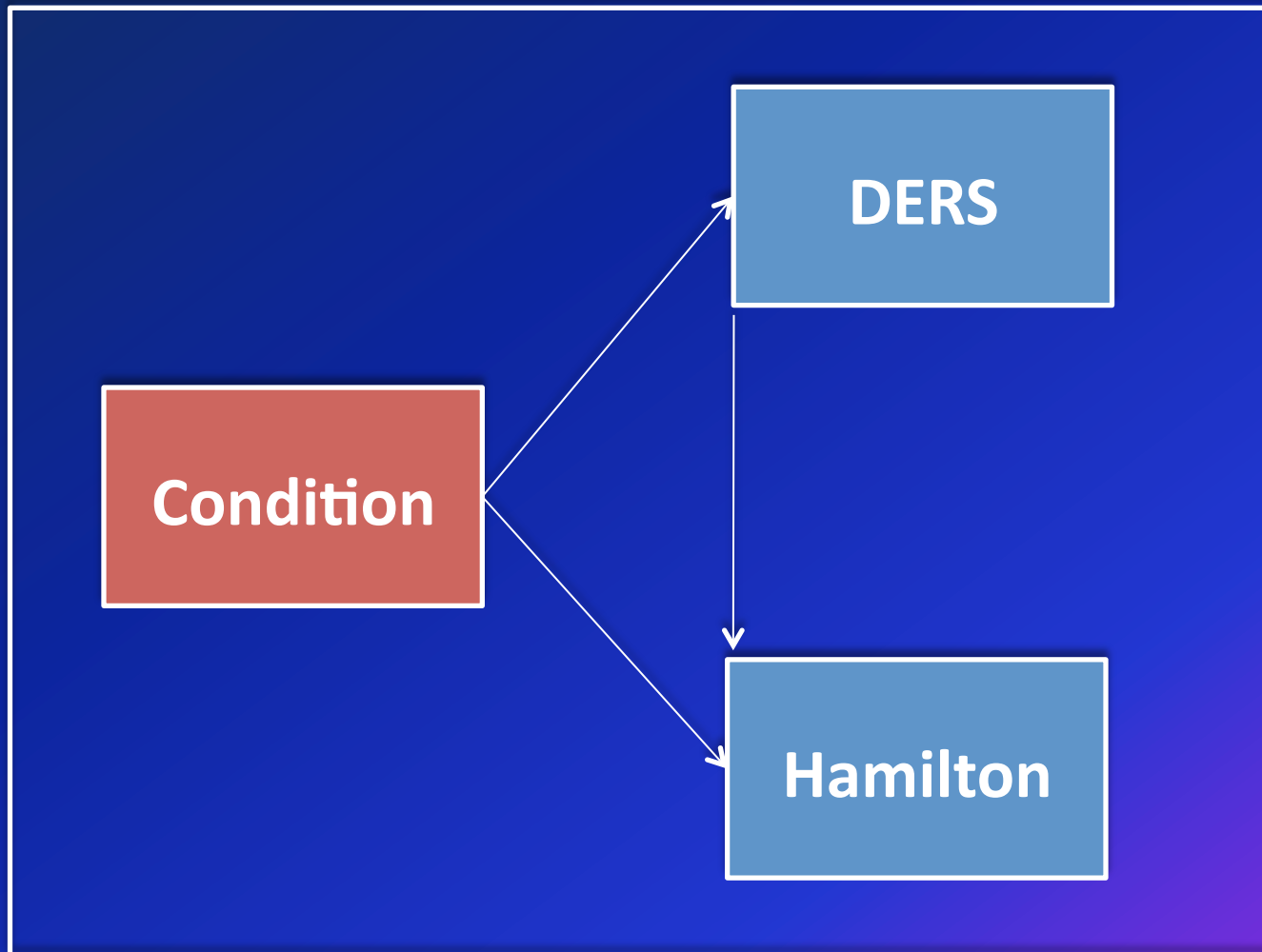
	Pearson Correlation	<i>p</i> value	n
BDI Post-Treatment	-0.371	.052 $\gamma$	28
BDI Follow-Up	-0.535	.022 *	18
Hamilton Post-Treatment	-0.349	.069 $\gamma$	28
Hamilton Follow-Up	-0.476	.040 *	18

\* ( $p < .05$ )  
 $\gamma$  ( $p < .10$ ), statistical trend

## StressEraser Points Correlations with Depression Outcomes at Post-treatment



# Mediation Path Analysis Model



# Mediators to Improvements in Depression Outcomes

	Unstandardized Regression Coefficient	Standard Error	Z Score
<b>Post-Treatment</b>			
<b>(N =53)</b>			
DERS on Hamilton	-1.32	0.74	-1.80
DERS on BDI	-1.53	0.44	-3.46*
FFMQ on Hamilton	0.72	0.4	1.81
FFMQ on BDI	0.20	0.23	0.85
SDNN on Hamilton	-0.27	0.37	-0.74
SDNN on BDI	-1.48	0.38	-3.92*
<b>Follow-Up</b>			
<b>(N =30)</b>			
DERS on Hamilton	-4.33	1.11	3.90*
DERS on BDI	-5.35	1.52	-3.53*
FFMQ on Hamilton	1.31	0.65	2.01*
FFMQ on BDI	-0.91	0.64	-1.42
SDNN on Hamilton	-1.33	0.68	-2.07 *
SDNN on BDI	-1.46	0.36	-3.90 *

\* Significance is (Z>1.96) or (Z<-1.96)



**Summary of Descriptive Data for  
all Outcome Variables**

		<i>Pre-Treatment</i> ( <i>n</i> = 60)		<i>Post-Treatment</i> ( <i>n</i> = 53)		<i>Follow-Up</i> ( <i>n</i> = 30)		<i>Slope</i>	<i>Effect Size</i> <i>Post-Treatment</i>
		<i>M</i>	<i>(SD)</i>	<i>M</i>	<i>(SD)</i>	<i>M</i>	<i>(SD)</i>		
<i>Hamilton</i>	Exp	29.2	(4.47)	14.14	(5.05)	12.94	(3.64)	-8.9 ***	1.4
	Con	27.67	(4.64)	18.64	(4.92)	17.75	(4.67)	-5.7 ***	1.0
<i>BDI</i>	Exp	30.95	(8.69)	8.89	(7.71)	7.5	(6.99)	-12.6 ***	1.5
	Con	30.53	(6.33)	24.56	(5.56)	21.95	(6.64)	-4.5 ***	0.8
<i>FFMQ</i>	Exp	10.13	(1.96)	12.58	(1.92)	13.23	(1.23)	0.32 ***	1.3
	Con	10.81	(1.7)	11.01	(1.76)	11.63	(1.26)	0.04	0.4
<i>DERS</i>	Exp	123.13	(16.54)	68.96	(20.42)	64.17	(15.00)	31.7 ***	1.5
	Con	103.47	(19.92)	98.04	(19.01)	93.67	(15.14)	-3.7	0.5
<i>SDNN</i> <i>Across phases</i>	Exp	0.042	(0.012)	0.057	(0.020)	0.048	(0.016)	1.30 **	-0.9
	Con	0.031	(0.020)	0.049	(0.021)	0.035	(0.019)	0.0046	-0.9
<i>LF/HF</i> <i>Across Phases</i>	Exp	2.39	(1.79)	1.89	(0.95)	1.21	(0.71)	-0.225	0.4
	Con	1.86	(1.03)	2.32	(1.26)	1.94	(1.32)	0.297	-0.4
<i>VLF</i> <i>Across Phases</i>	Exp	19.62	(9.21)	8.98	(4.13)	7.03	(8.63)	-8.40 ***	1.6
	Con	11.28	(10.88)	14.01	(7.84)	14.14	(11.99)	-0.303	-0.3

\* significant (p<0.05); \*\*significant (p<0.01); \*\*\* significant (p<0.0001); γ statistical trend

## Time x Treatment Interaction Effects

Measures	Slope Differences	p Value	Effect Size
Hamilton	-3.20	.006 **	1.0
BDI	-8.00	<.0001 ***	2.0
FFMQ	0.28	<.0001 ***	0.9
DERS	28.00	<.0001 ***	1.6
SDNN			0.6
Baseline	-0.003	.848	
Stressor	0.0093	.055 $\gamma$	.....
Recovery	-0.0019	.004 **	
LF/HF Ratio			0.3
Baseline	0.4704	.316	
Stressor	0.0508	.213	.....
Recovery	0.3616	.453	
VLF			0.7
Baseline	8.4248	.013 *	
Stressor	0.3744	.879	.....
Recovery	8.3827	.001 **	

\* significant (p<0.05); \*\*significant (p<0.01); \*\*\* significant (p<0.0001);  $\gamma$  statistical trend

# Conclusions

- This study revealed that the cardiorespiratory biofeedback and DBT oriented skills training in conjunction with sertraline resulted in a significantly larger improvement in depression severity, depression diagnosis, and heart rate variability at post-treatment compared to the control group, and this effect was maintained at follow-up. In addition, the experimental group showed a significantly larger improvement in emotion regulation and mindfulness scores across time.

**Why Did The Experimental  
Group Have Better Outcomes?**

# Reasons For Drop Out

Categories	Post-Treatment (N=53)		Follow-Up (N=30)	
	Experimental Group	Control Group	Experimental Group	Control Group
Time Conflict	2	1	7	4
SSRI Discontinued	0	1	4	5
Disinterested	0	1	0	4
Cardiac Reoccurrence	0	2	1	5
		n = 7		n = 30

# Group Equivalence

The results of this study cannot be explained by the following confounds at baseline:

- **Depression diagnosis and severity**
- **Medications**
- **Gender**
- **Age**
- **Ethnicity**
- **Socioeconomic status**
- **Participants' treatment expectancies**

Although the patterns of dropout may have biased the results for the BDI at follow-up, there was no evidence that the Hamilton, heart rate variability, emotion regulation, and mindfulness results were affected by dropouts.

# Better Outcomes May Be Attributed To .....

## **DBT Skills**

- \* Emotion regulation
- \* Distress tolerance
- \* Mindfulness
- \* Behavioral activation

## **Improved Heart Rate Variability**

- \* Cardiorespiratory biofeedback
- \* Breathing retraining

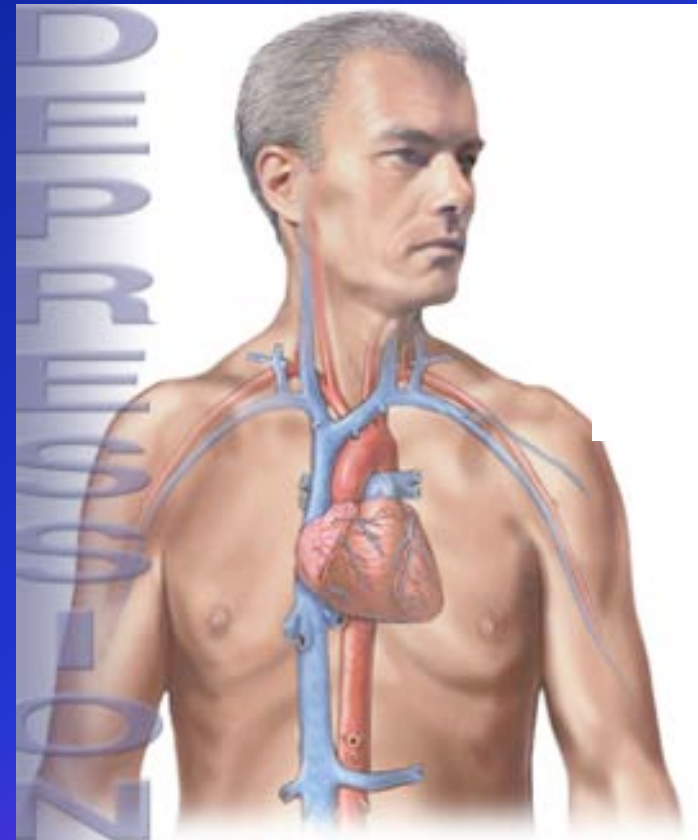
## **Self-Efficacy**

- \* Empowerment



# Clinical Implications

- Decreases in depression and increases in HRV can improve ANS regulation----which may reduce risk of cardiac morbidity and mortality
- Decreases in physiological reactivity to stressors and improved recovery from it may also protect against the development or worsening of CVD
- Better adherence to cardiac rehabilitation
- More attentive to behavioral risk factors (tobacco /alcohol use, physical inactivity, poor diet)
- Improved emotional and physical health
- Improved quality of life and self-efficacy
- Improved mindfulness and emotion regulation may prevent relapse rates with future depressive episodes
- It is noteworthy that the control group had more drop outs attributed to cardiac reoccurrence.



# Acknowledgements

## Committee

Dr. Milton Brown, Ph.D.

Dr. Richard Gevirtz, Ph.D.

Dr. Ray Gandhi, M.D.

Dr. Sharon Foster, Ph.D.

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## Research Assistants

Amy McKinney

Christina Huang

Mishaneh Marjani



# Post Hoc Mediation with Individual Mindfulness Facets to Improvements in Depression Outcomes

Individual Facets of FFMQ	<i>p</i> Values	
	Hamilton	BDI
observing	.163	.159
describing	.124	.107
acting with awareness	.077 $\gamma$	<b>.045*</b>
non-judging of inner experience	<b>.025*</b>	<b>.028*</b>
non-reactivity to inner experience	.070 $\gamma$	<b>.049*</b>

\* significant ( $p < 0.05$ );  $\gamma$  statistical trend

# Post Hoc Mediation with Individual Subscales for DERS to Improvements in Depression Outcomes

<b>Individual Subscales of DERS</b>	<i>p</i> Values	
	<b>Hamilton</b>	<b>BDI</b>
non-acceptance of emotional responses	0.837	0.984
difficulties engaging in goal directed behavior	0.590	0.571
impulse control difficulties	0.509	0.936
lack of emotional awareness	0.918	0.805
limited access to emotion regulation strategies	0.678	0.517
lack of emotional clarity	0.990	0.316