THE BIOPSYCHOSOCIAL MODEL OF RISK FOR DEPRESSION

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What distinguishes individuals who develop depression following a life stressor from those that do not?
Outline

- Introduction to the literature
- **Study 1**
  - *Part 1*- Cortisol secretion in depressed and at-risk adults
  - *Part 2*- Stress sensitivity and risk for depression
- **Study 2**- Characterization of the stress sensitive phenotype
- **Study 3**- Interventions for stress sensitivity
- Racial Differences in HPA Axis Functioning
- Future Directions
Depression

- Second most burdensome disease in terms of disability-adjusted life years by 2020 (Global Burden of Disease Study, 2010)
- Lifetime incidence is 20% in the US and yearly prevalence between 8-12% in the UK (Kessler et al., 2005, NCS-R, The Office for National Statistics Psychiatric Morbidity report, 2001)
- Annual salary-equivalent costs of depression related lost productivity in the U.S. exceeds $33 billion.
- In the UK, around 10 billion pounds in terms of yearly costs for treatment of depression are reported
Diathesis Stress Models

DIATHESIS
- Genes
- Cognitive Style
- HPA Axis Dysregulation
- Personality Style
- Early Adversity
- Personality Type
- Chronic Stress
- Stressful Life Events
- Mood Reactivity to Stress

Stress

DEPRESSION
The Biopsychosocial Model of Stress Sensitivity and Risk for Depression

High NA
Low PA

Personality Style

HPA Axis Functioning

Mood Reactivity

Sensitivity to Stress

Depression
HPA Axis

**NODES**
- CNS
- Pituitary
- Adrenal

**NETWORK**
- CRH
- AVP
- Delayed Integral
- Rapid Rate-Sensitive

**FEEDBACK**
- (-) synthesis
- (+) synthesis
- (-) synthesis

**synthesis**
- ACTH
- CORTISOL

**release**
- storage pool
- no storage
Cortisol Reactivity to an Acute Stressor

![Graph showing cortisol levels over time with a stressor event highlighted. The graph indicates an increase in cortisol levels following the stressor event.](image-url)
# Past Research

<table>
<thead>
<tr>
<th>Diurnal Cortisol Secretion</th>
<th>At-Risk for Depression</th>
<th>Currently Depressed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher waking cortisol</td>
<td></td>
<td>High flat pattern</td>
</tr>
<tr>
<td>Large CAR</td>
<td></td>
<td>High waking</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Large CAR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low evening</td>
</tr>
<tr>
<td>Cortisol Reactivity</td>
<td>?</td>
<td>Slow return to baseline</td>
</tr>
</tbody>
</table>
STUDY 1-PART 1
Cortisol Secretion in Depressed and At-Risk Adults

Dienes et al., 2013, PNEC
Hypotheses

- Depressed and at-risk participants will have the following when compared to controls:
  - Higher diurnal cortisol on average
  - High waking
  - Larger CAR
  - Flatter slope of diurnal cortisol secretion
  - Slower recovery to baseline following a psychosocial laboratory stressor
Sensitivity to Stress
Personality Style
Mood Reactivity

HPA Axis Functioning

High waking cortisol, large CAR, high flat diurnal pattern, slow recovery post stressor for at-risk and depressed

High NA Low PA

Sensitivity to Stress
Depression
Participants

- 57 women ages 18-23
- 24.6% Caucasian, 26.3% Asian/Pacific Islander, 19.3% Hispanic, 7.0% Middle Eastern, 5.3% Indian, 7.0% Biracial, 1.8% African American

Exclusion Criteria

- Heavy smokers, steroid medication use, pregnancy, serious medical condition
- Generalized anxiety disorder, dysthymic disorder, panic disorder, obsessive-compulsive disorder, psychotic symptoms, psychoactive substance abuse, post-traumatic stress disorder, anorexia and bulimia nervosa
Initial Interview

- Modified SCID (Structured Clinical Interview for DSM-IV: First et al., 1995)
- Life Stress Interview (Hammen et al., 1987)
- Early Adversity Questionnaire (Cohen et al., 2004)
- Beck Depression Inventory II (Beck et al., 1996)
Groups

- **Depressed**
  
  (N=15)

- **At-risk** (high NA, low PA)
  
  (N = 20)

- **Control** (high PA, low NA)
  
  (N = 22)
## Cortisol Sampling

**Daily sampling** - 4 samples a day for 5 days; wakening, 30 min, 8 hours and 11 hours post wakening

**Trier Social Stress Test (TSST; Kirschbaum et al., 1993)** – Baseline sample, 5 min prep, 5 min speech task, 5 minute math task, immediate post-task sample, 10 min, 25 min, and 40 min post task samples (total 5 samples)

<table>
<thead>
<tr>
<th>Prep</th>
<th>ST</th>
<th>MT</th>
<th>10 min</th>
<th>15 min</th>
<th>15 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>
## Psychosocial Variables

<table>
<thead>
<tr>
<th></th>
<th>Control (N = 22)</th>
<th>At-risk (N = 20)</th>
<th>Depressed (N = 15)</th>
<th>Total (N = 57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety Sx*</td>
<td>36.4%</td>
<td>65.0%</td>
<td>80%</td>
<td>57.9%</td>
</tr>
<tr>
<td>Early Adversity*</td>
<td>54.6%</td>
<td>90%</td>
<td>73.3%</td>
<td>71.9%</td>
</tr>
<tr>
<td>Total Chronic Stress*</td>
<td>19.4 ± 2.58</td>
<td>21.9 ± 3.08</td>
<td>23.7 ± 3.27</td>
<td>21.4 ± 3.38</td>
</tr>
<tr>
<td>BDI-II* (M ± SD)</td>
<td>4.39 ± 3.30</td>
<td>6.10 ± 5.48</td>
<td>18.0 ± 7.67</td>
<td>8.57 ± 7.86</td>
</tr>
</tbody>
</table>

* Groups significantly different at p < 0.05  
Note: Subscripts indicate groups that are not significantly different from each other
Statistics

Hierarchical Linear Modeling

- **Diurnal cortisol**-Three level model, samples within days within persons for diurnal cortisol.

Level 1: \( \text{LNCORT} = b_{00} + b_{01}(\text{TIME}) + b_{02}(\text{TIMESQ}) + b_{03}(\text{MORNRISE}) + r \)

Level 2: \( b_{00} = g_{00} + g_{01}(\text{WAKETIME})_j + u \)

Level 3: \( g_{00} = d_{00} + d_{01}(\text{GROUP})_j + d_{02}(\text{BIOBEH})_j + d_{03}(\text{PSYCHOSOC})_j + e_j \)

- **TSST**-Two level model, samples within persons.

Level 1: \( \text{LNCORT} = b_{0j} + b_{1j}(\text{MIN12}) + b_{2j}(\text{MIN23}) + b_{3j}(\text{MIN35}) + e_{ij} \)
Mean Diurnal Cortisol Secretion

Salivary Cortisol (um/dl)

Time of Day

- control
- at-risk
- depressed

* p < 0.05
# TSST Psychosocial Variables

<table>
<thead>
<tr>
<th></th>
<th>Control (N = 21) (M ± SD)</th>
<th>At-risk (N = 20) (M ± SD)</th>
<th>Depressed (N = 13) (M ± SD)</th>
<th>Total (N = 54) (M ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embarrassed during speech*</td>
<td>2.95 ± 1.99a</td>
<td>4.94 ± 1.91b</td>
<td>4.25 ± 2.06ab</td>
<td>3.93 ± 2.13</td>
</tr>
<tr>
<td>Eye contact during speech*</td>
<td>4.71 ± 1.49a</td>
<td>3.13 ± 1.36</td>
<td>5.14 ± 1.29a</td>
<td>4.33 ± 1.61</td>
</tr>
<tr>
<td>Voice steady during speech*</td>
<td>4.48 ± 1.17ab</td>
<td>3.63 ± 1.20b</td>
<td>4.75 ± 1.45a</td>
<td>4.28 ± 1.32</td>
</tr>
<tr>
<td>Fidgety during speech*</td>
<td>3.38 ± 1.63a</td>
<td>5.06 ± 1.73</td>
<td>3.50 ± 1.23a</td>
<td>3.94 ± 1.71</td>
</tr>
<tr>
<td>Voice steady during math*</td>
<td>4.81 ± 1.17a</td>
<td>3.56 ± 1.63b</td>
<td>4.64 ± 1.65ab</td>
<td>4.37 ± 1.54</td>
</tr>
<tr>
<td>Difficulty of the experience*</td>
<td>2.38 ± 1.07a</td>
<td>3.25 ± 1.07b</td>
<td>3.00 ± 1.18ab</td>
<td>2.85 ± 1.15</td>
</tr>
<tr>
<td>Tense*</td>
<td>2.76 ± 1.22a</td>
<td>3.75 ± 1.16b</td>
<td>3.21 ± 1.19ab</td>
<td>3.24 ± 1.25</td>
</tr>
</tbody>
</table>

* Groups significantly different at p < 0.05
Note: Subscripts indicate groups that are not significantly different from each other
Mean Cortisol Secretion: TSST

* p < 0.05
Mean Negative Mood During TSST Recovery

* p < 0.05
Diurnal cortisol for depressed vs. controls were mainly in keeping with prediction and community research.

Higher waking levels but not CAR for the at-risk group compared to controls.

Rapid cortisol reactivity for the at-risk group compared to the depressed group-resilience and/or sensitivity to threat?
STUDY 1-PART 2

Mood Reactivity to Naturalistic and Laboratory Stressors and the Relationship Between Cortisol and Mood Reactivity
Sensitivity to Stress

High waking cortisol, large CAR, high flat diurnal pattern, slow recovery post stressor

HPA Axis Functioning

Personality Style

Mood Reactivity

Greater mood reactivity to stress, stronger relationship between mood and cortisol reactivity

Depression

High NA
Low PA

Greater mood reactivity to stress, stronger relationship between mood and cortisol reactivity
Hypotheses

Greater severity of stress will predict increased negative mood, especially for depressed and at-risk participants compared to controls.

There will be a significant relationship between elevated cortisol secretion and increased mood reactivity to daily naturalistic stressors.

Depressed and at-risk participants will have a stronger relationship between cortisol and mood reactivity to both naturalistic and laboratory stressors compared to controls.
Procedure

- Daily Diary (Computerized, nightly before bed for 2 weeks, 5 min)
  - The Multiple Adjective Affect Checklist (MAACL)
  - Stressful Events Checklist
- Momentary PANAS filled out at each point of diurnal cortisol sampling and across the TSST
Statistics

Hierarchical Linear Modeling

Two level model – Days within persons for daily diary.

Level 1: \( \text{LNCORT} = b_{00} + b_{01}(\text{Time}) + r \)

Level 2: \( b_{00} = g_{00} + g_{01}(\text{GROUP})_j + g_{02}(\text{BIOBEH})_j + g_{03}(\text{PSYCHOSOC})_j + u_j \)
Daily Mood and Stress

The depressed group had elevated negative mood and reported greater severity of stress on a daily basis than both the at-risk and control groups.

The at-risk group had a significant decrease in negative mood with increased reported stress compared to the depressed group, but did not differ significantly from the control group.
Equation Model of Mood and Stress

Average Stress Rating

Negative Mood

- ND
- AR
- CD
Negative Mood, Stress and Diurnal Cortisol

Overall, a flatter, or more positive, slope of diurnal cortisol secretion was predictive of increased emotional reactivity to stress.

There were no significant differences among the groups in the relationship among negative mood, stress, and cortisol
Diurnal Cortisol and Mood at Time of Sampling

- The depressed group had significantly less of an increase in cortisol secretion with an increase in negative mood compared to the at-risk and control groups for diurnal cortisol secretion.

- The three groups differed significantly in the relationship between cortisol and negative mood in response to the TSST. The depressed group had the strongest relationship between cortisol secretion and negative mood.
Regression Lines for Negative Mood and Diurnal Cortisol at Time of Sampling

Salivary Cortisol

Control
At-risk
Depressed

Negative Mood
Depressed Group

- Low cortisol secretion
- High cortisol secretion

- Percent in Category
- Low negative mood
- High negative mood

Low negative mood: Low cortisol secretion (30%)
Low negative mood: High cortisol secretion (45%)
High negative mood: Low cortisol secretion (55%)
High negative mood: High cortisol secretion (65%)
Discussion

- Depression and major stressful life events
- At-risk group and reactivity/resilience
STRESS GENERATION AND HPA AXIS FUNCTIONING
Stress Generation

Hypothesis: Dependent events and interpersonal events will significantly predict diurnal cortisol secretion, whereas achievement events will not.

Procedure: Life Stress Interview (Hammen et al., 1987)
- Events rated 3 or higher across the two weeks
- Objective stress rating teams
- Dependency, Interpersonal, Achievement
STUDY 2

Stress Sensitivity and Cortisol Secretion
Sensitivity to Stress

Personality Style

High NA, Low PA

Mood Reactivity

HPA Axis Functioning

High waking cortisol, rapid rise and recovery in cortisol secretion in response to a stressor

Negative self evaluation, and quick recovery in negative mood following the TSST

Depression
Objectives

- Replication and improved methodology
- Further characterization of stress sensitive individuals to determine factors that might be associated with
  - High waking levels of cortisol
  - Rapid rise in cortisol in response to the TSST
  - Quick recovery in negative mood following the TSST
Factors Associated With the Stress Sensitive Phenotype

- Early Adversity
- Emotion Regulation
- Personality Variables
- Coping Style
- Anxiety comorbidity
- Chronic and Episodic Life Stressors—number, type, duration, dependency
Procedure

- Prescreening
- Initial Interview: SCID, LSI-6 months
- Questionnaire Packet
- Diurnal Cortisol Sampling
  - CAR-0, 30, 60 min post waking
  - 12 hours post waking
- TSST
Measures

- Life Experiences Questionnaire (Gibb et al., 2001)
- Early Adversity Questionnaire (EAQ; Cohen et al. 2004)
- State-Trait Anxiety Inventory (STAI-T and STAI-S: Spielberger, 1983)
- IPIP Neuroticism Scale
- BIS/BAS Scales (Carver & White, 1994)
- Difficulties in Emotion regulation Scale (DERS; Gratz & Roemer, 2004)
- Multidimensional Perfectionism Scale (MPS: Hewitt et al., 1991)
- Ways of Coping (Revised)
- BDI-II
Demographics

Gender

- Male: 33%
- Female: 67%

Race

- Caucasian: 33%
- African American: 42%
- Latino/Hispanic: 13%
- Asian/Pacific Islander: 7%
- Indian: 2%
- Other: 3%
STUDY 3
Interventions for Stress Sensitivity
Group CBT Intervention for Stress Reduction

- The CAR was compared pre and post a four week group CBT intervention for stress reduction for eleven participants.
- Three of the eleven participants were deemed compliant based on negative CAR profiles.
- AUCi was significantly lower post intervention for compliant participants, though if all participants are included in analyses the decrease is not significant.
CAR Pre and Post Intervention

- **Day 1**
- **Day 2**

The graph shows the comparison between pre and post intervention levels over time, with two lines representing different days.
RACIAL DIFFERENCES IN HPA AXIS FUNCTIONING
Relationship among race, discrimination and cortisol secretion

Differences in diurnal cortisol secretion have been found among racial groups, but there is less research on racial differences in response to the TSST

- Study 1
- Study 2
Study 1: Mean Cortisol Secretion in Response to the TSST by Group
Study 2: Mean Lifetime Discrimination Scores

GEDS Lifetime Score

Race

AA  30.5

C   19.3
Study 2: Cortisol Secretion Across the TSST

![Cortisol Secretion Graph]

- **Cortisol (um/dl)**
- **Minutes**
- **Caucasian**
- **African American**

The graph illustrates cortisol secretion levels across the Trier Social Stress Test (TSST) for Caucasian and African American participants. The cortisol levels are measured in units of micrograms per deciliter (um/dl) and are plotted against time in minutes. The graph shows a peak cortisol response around the 30-minute mark, with subsequent decline over time.
Future Directions

- Longitudinal study stress sensitive individuals to determine if they develop depression
- Experience Sampling Methodology to investigate mood and cortisol reactivity to naturalistic stress in stress sensitive individuals
- Treatment study to determine if several interventions (self compassion, mindfulness meditation) can reduce biopsychosocial stress sensitivity in individuals at-risk for depression
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