Allostatic Load/Multisystem Indices: Brain Responses that Predict Health Behaviors & Outcomes

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Healthy Corticolimbic Development

- Self Control
  - Adaptive Behavioral Control
  - Regulated Hedonic Drives
  - Minimal Exposure To Tobacco, Alcohol, Carbohydrate Excess

Healthy Corticolimbic Development

- Dysocontrol
  - Impaired Behavioral Control
  - Dysregulated Hedonic Drives
  - Addictive Behaviors: Tobacco, Substances of Abuse, Poor Eating, Sexual Promiscuity, Self Harm, Harm to Others

Serious Chronic Diseases
- Tobacco, Alcohol & Other Substance Abuse, Mood and Anxiety Disorders, Suicide, Diabetes, Obesity, Cardiovascular Disease

Low Stress

Developmental model: Blumberg, Mayes, Sinha collaboration
STRESS AND FRONTAL DEVELOPMENT IN ADOLESCENCE

**PFC STRUCTURE (sMRI)**
- PFC gray matter volume inversely associated with severity of CM

**PFC RESPONSE (fMRI)**
- Inverse association between increase in cortisol on the Trier Social Stress Test and PFC response
  (Liu et al, *JAACAP*, 2012)

**PFC FUNCTION**
- Association between severity of childhood maltreatment and perseverative errors
  (Spann et al, *Child Neuropsychology*, 2011)

**Sup Frontal**
- Association between response to emotionally ambiguous faces and severity of CM
  (Bick et al, under review)


**Sex-related longitudinal changes associated with CM**
(Cox et al, in preparation)
Childhood Trauma and Substance Abuse Effects in Adults:

Vam Dam et al., JAMA Psychiatry, 2014
Early Trauma, Trauma related Brain Volume and Substance Relapse Severity

Vam Dam et al., JAMA Psychiatry, 2014
Cumulative Stress/Adversity Checklist (CAC - from Turner et al., 1998; 2003; 2008)

The CAC is a 20 minute structured interview that asks about events experienced in lifetime, how often and first and last age of experiencing that event:

• **Major Life Events**: e.g. abandonment, divorce/separation, loss of child, parents substance abuse, relationship difficulties.

• **Life Traumas**: loss of home, witnessing or being in an accident, and in violent situations, sexual, physical and emotional abuse, being shot, assaulted, tortured, being in combat, losing someone to violence.

• **Recent Life Events (past year)**: Accidents, illnesses, loss of child, trouble with law, pregnancies/abortion/miscarriages, school drop-out, financial crisis, school or work failures, work and relationship problems, living problems.

• **Chronic Stressors**: sense of being overwhelmed with life, unable to manage life problems, difficulties with job, living, finances relationships, conflicts, loneliness, unfulfilled desires, problems with children, living, etc.
High cumulative stress reduces brain tissue in prefrontal neurons/regions that regulate stress

*Ansell et al. (2012) Biol Psychiatry*

Cumulative Stress related to lower brain volume in a community cohort (p<.001)

*Radley et al. (2006) Cerebral Cortex*

Stress-related neuronal atrophy in animals

*Ansell et al. (2012) Biol Psychiatry*
Higher cumulative stress is associated with lower mean gray matter volume (GMV; $p<.001$, FWE corrected)

Controlling for age, sex, and total intracranial volume ((whole-brain voxel-based morphometry analysis)

*Ansell et al., Biol Psychiatry, 2012*
Higher Cumulative Adversity Predicts Greater Neural Responses to Acute Emotional Stress (N=75)

Hi/lo Cumulative Stress Effects on Brain Response to Acute Emotional Stress (N=50)

Seo et al., Neuropsychopharmacology, 2013

p<.05 WBC
Brain Responses to Stress is Associated with Health Symptoms on the Cornell Medical Index

A. Medial OFC

B. Right Hippocampus

C. Medial OFC & Hippocampus

$r = -.42$
$p < 0.01$

$r = .37$
$p < 0.01$

$r = -.36$
$p = 0.01$
Corticostriatal-Limbic Activation During Emotional Stress in Healthy Individuals

I. Stress Imagery Provocation

II. Emotional Pictures Provocation

Seo et al., Neuropsychopharm, 2013

Sinha Lab - unpublished
Disrupted Neural Response to Stress and Relaxed Scenarios in Recovering Alcoholics (AD)s versus Controls (HC) (p<.01 WBC)

Seo et al., JAMA Psychiatry, 2013
Neural Correlates of Days of Alcohol Used During Follow-up (p<.01 WBC)
Stress Pathophysiology in the Brain: Predicting Health Outcomes

Brain responses to high cumulative adversity and to acute subjective stress.

Using different paradigms, subject samples and multiple outcome measures, we see remarkable similarity in ventromedial PFC dysfunction that predicts stress-related health behavior outcomes.

Adversity and trauma-related effects on hippocampus also predict health symptoms.

Can we develop these measure as biomarkers?