

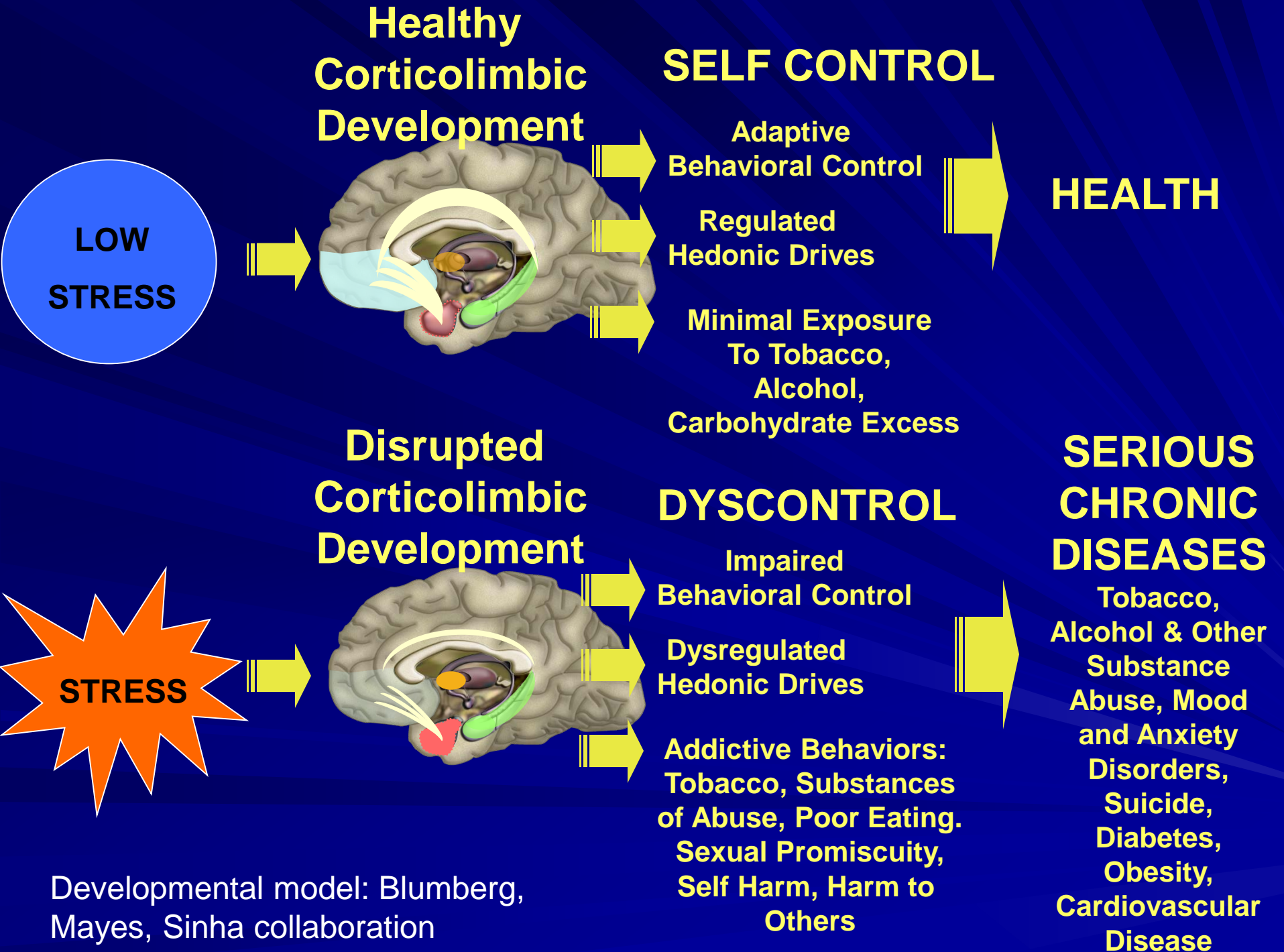


Allostatic Load/Multisystem Indices: Brain Responses that Predict Health Behaviors & Outcomes

RAJITA SINHA, Ph.D.

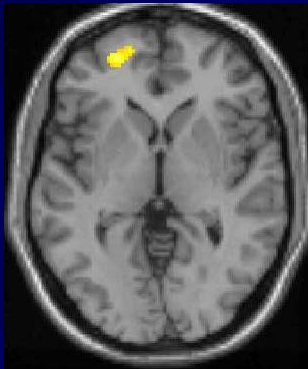
**Professor of Psychiatry, Neurobiology
and Child Study**

Yale University School of Medicine



STRESS AND FRONTAL DEVELOPMENT IN ADOLESCENCE

PFC STRUCTURE (sMRI)



PFC gray matter volume inversely associated with severity of CM

(Edmiston et al, *Arch Ped Adolesc Med*, 2011)

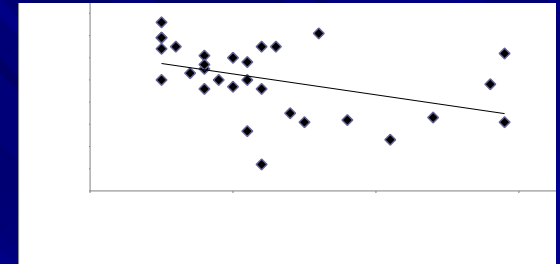
PFC RESPONSE (fMRI)



Inverse association between increase in cortisol on the Trier Social Stress Test and PFC response

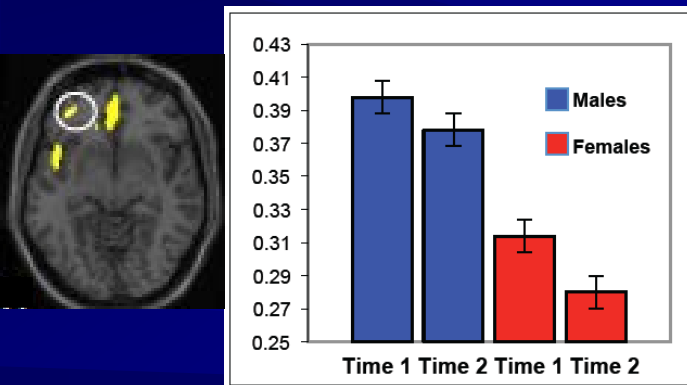
(Liu et al, *JAACAP*, 2012)

PFC FUNCTION



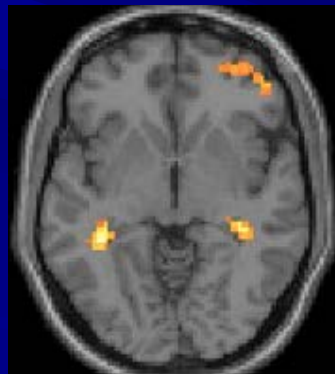
Association between severity of childhood maltreatment and perseverative errors

(Spann et al, *Child Neuropsychology*, 2011)



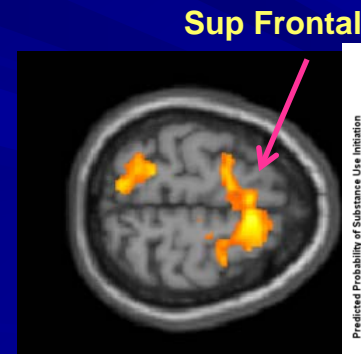
Sex-related longitudinal changes associated with CM

(Cox et al, in preparation)

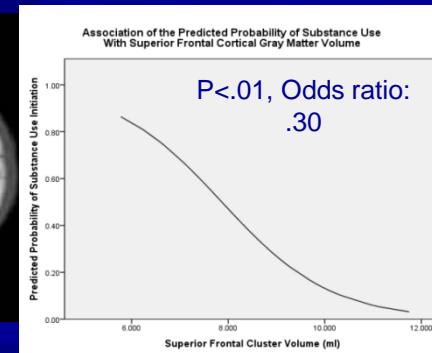


Association between response to emotionally ambiguous faces and severity of CM

(Bick et al, under review)

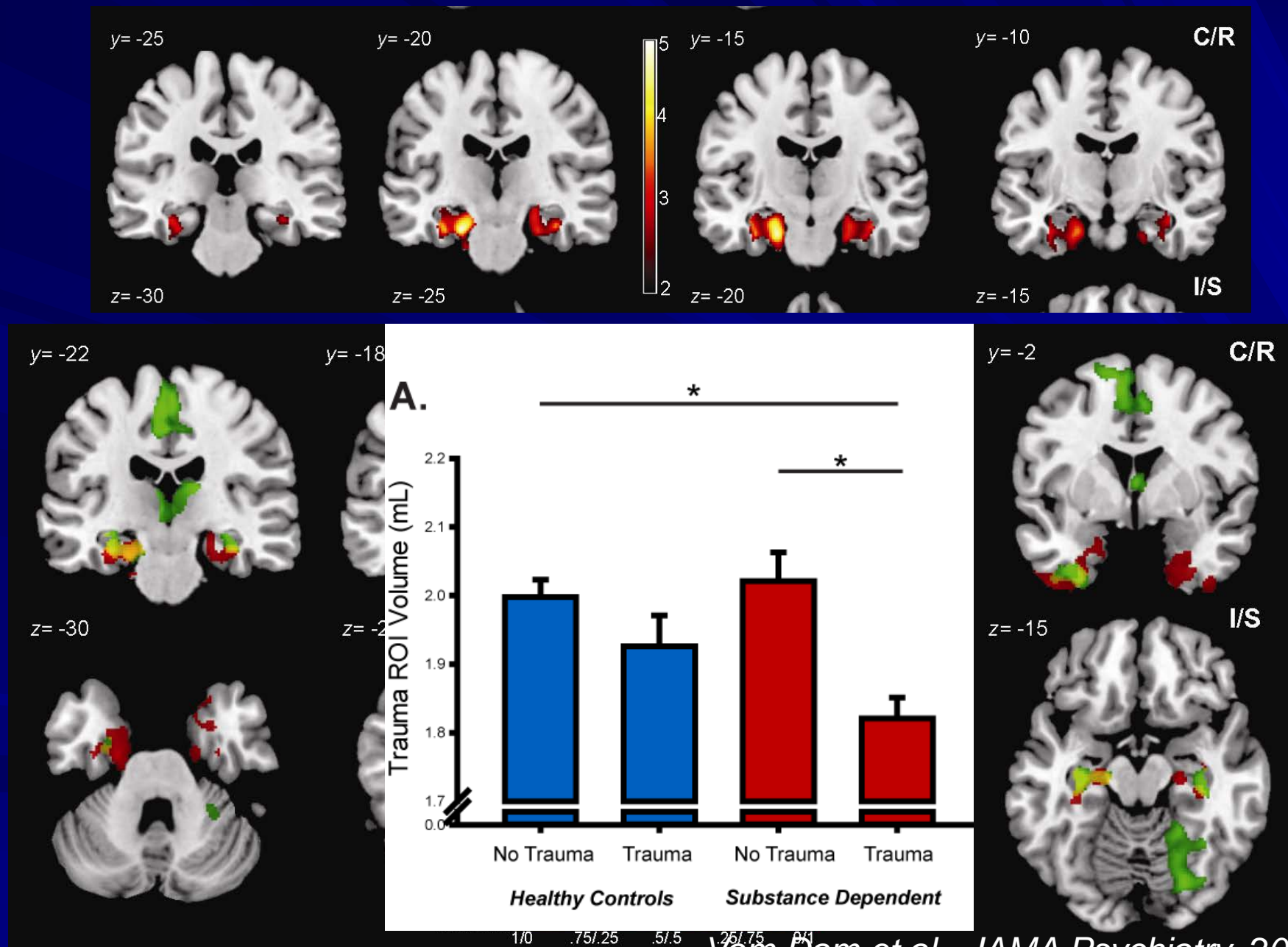


Sup Frontal

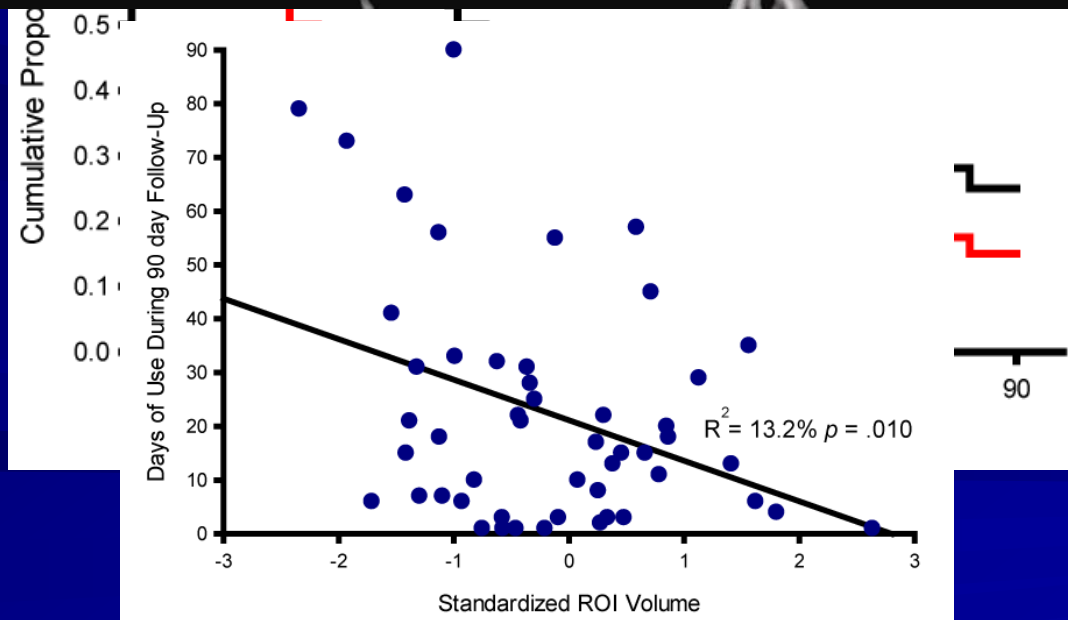
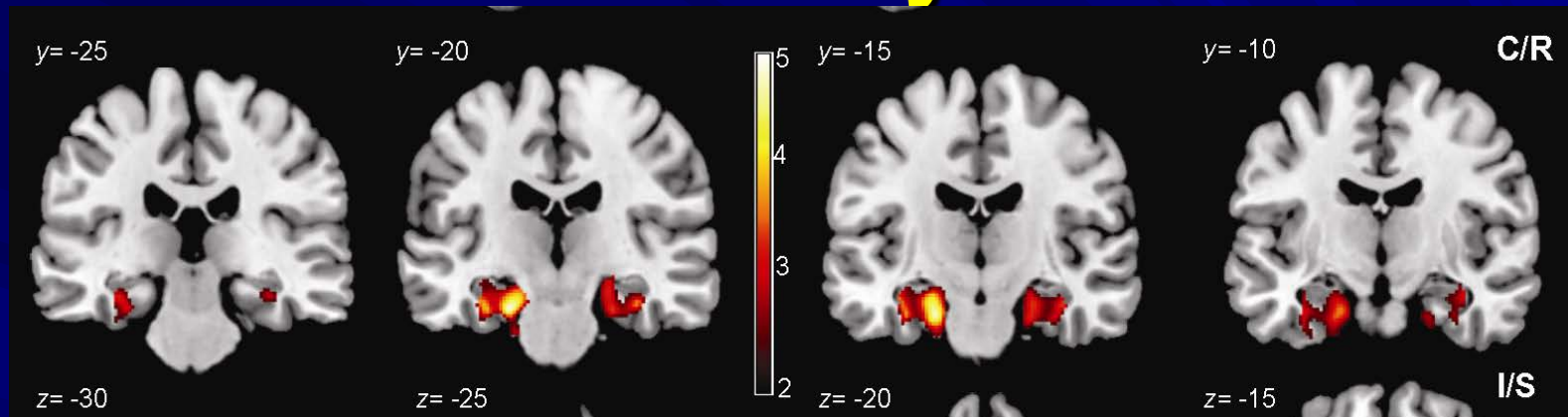


High stress related lower frontal brain volume predicts future substance use behaviors, *Biol Psychiatry* 2013

Childhood Trauma and Substance Abuse Effects in Adults:



Early Trauma, Trauma related Brain Volume and Substance Relapse Severity



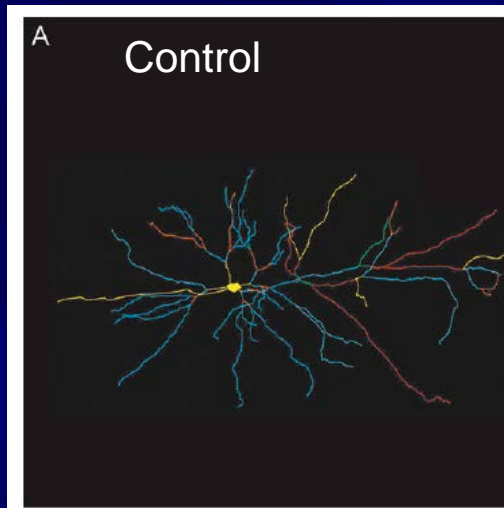
Cumulative Stress/Adversity Checklist (CAC

- from Turner et al., 1998; 2003; 2008)

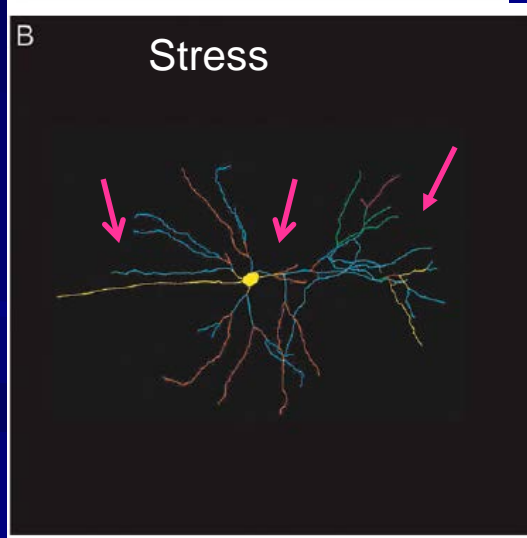
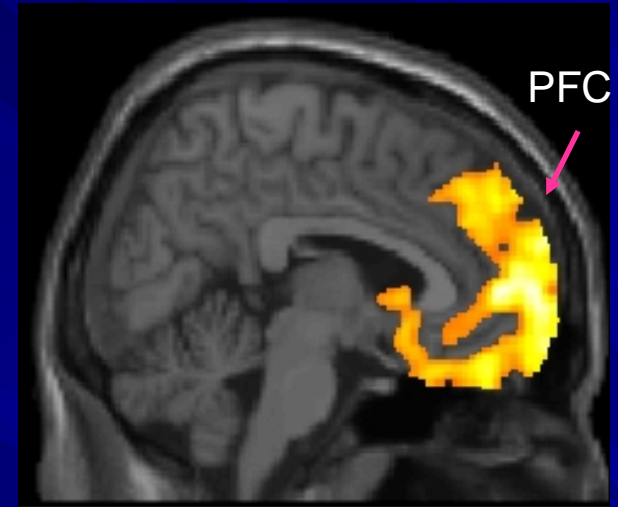
The CAC is a 20 minute structured interview that asks about events experienced in lifetime, how often and first and last age of experiencing that event:

- **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.

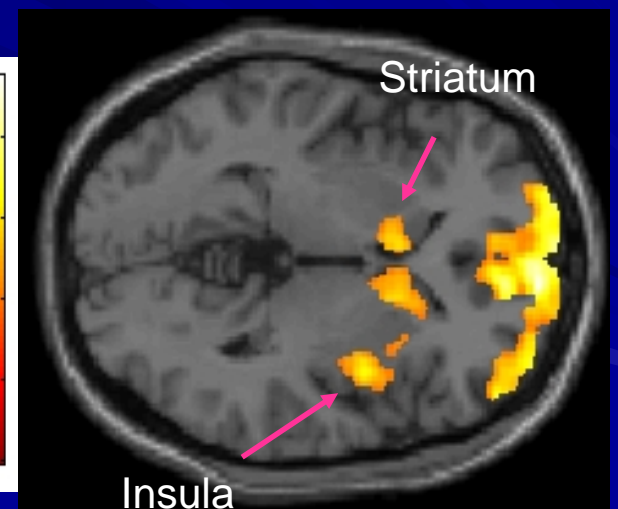
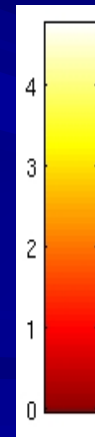
High cumulative stress reduces brain tissue in prefrontal neurons/regions that regulate stress



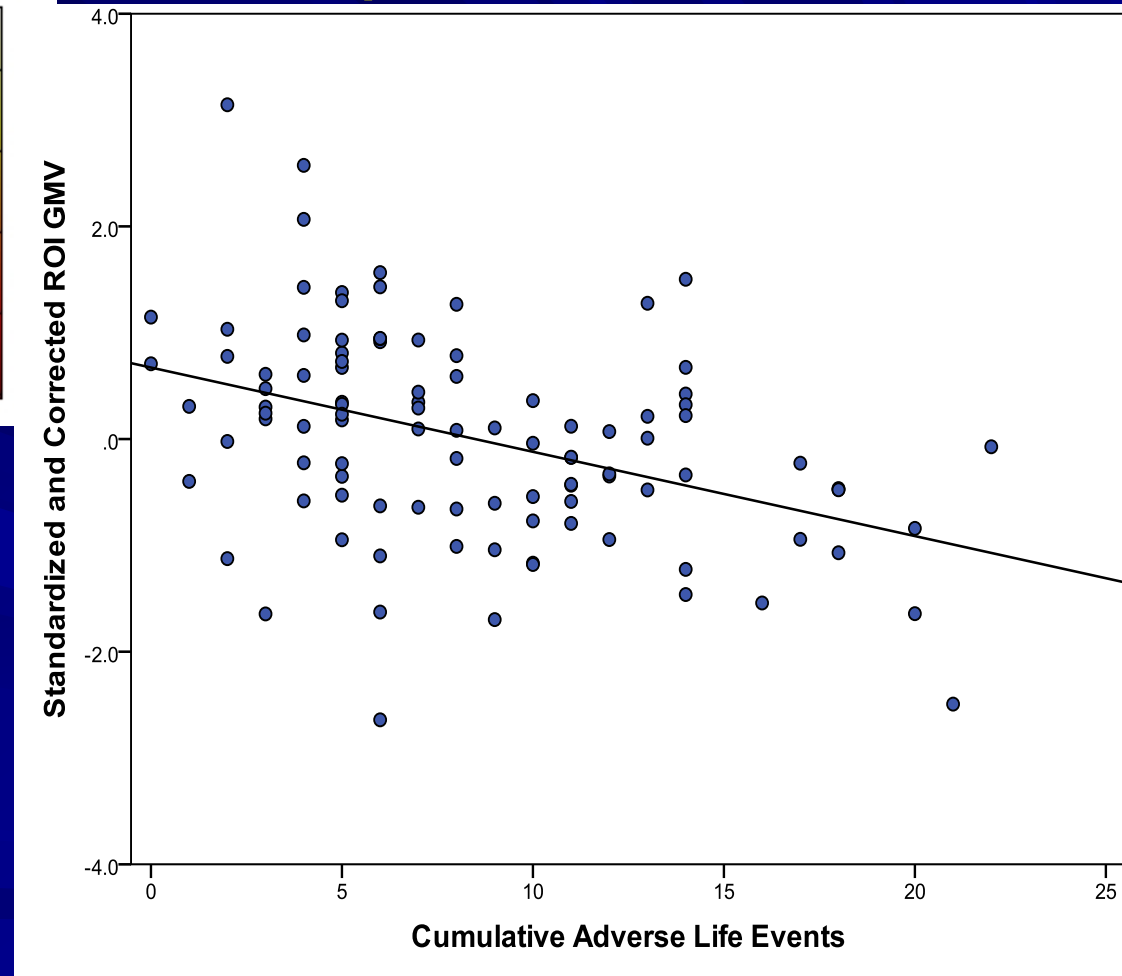
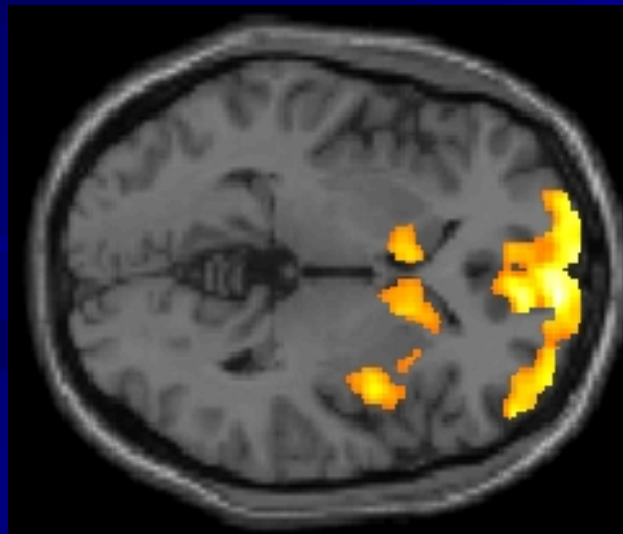
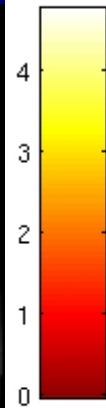
Cumulative Stress
related to lower
brain volume in a
community cohort
($p < .001$)



Stress-related
neuronal
atrophy in
animals



Higher cumulative stress is associated with lower mean gray matter volume (GMV; $p < .001$, FWE corrected)

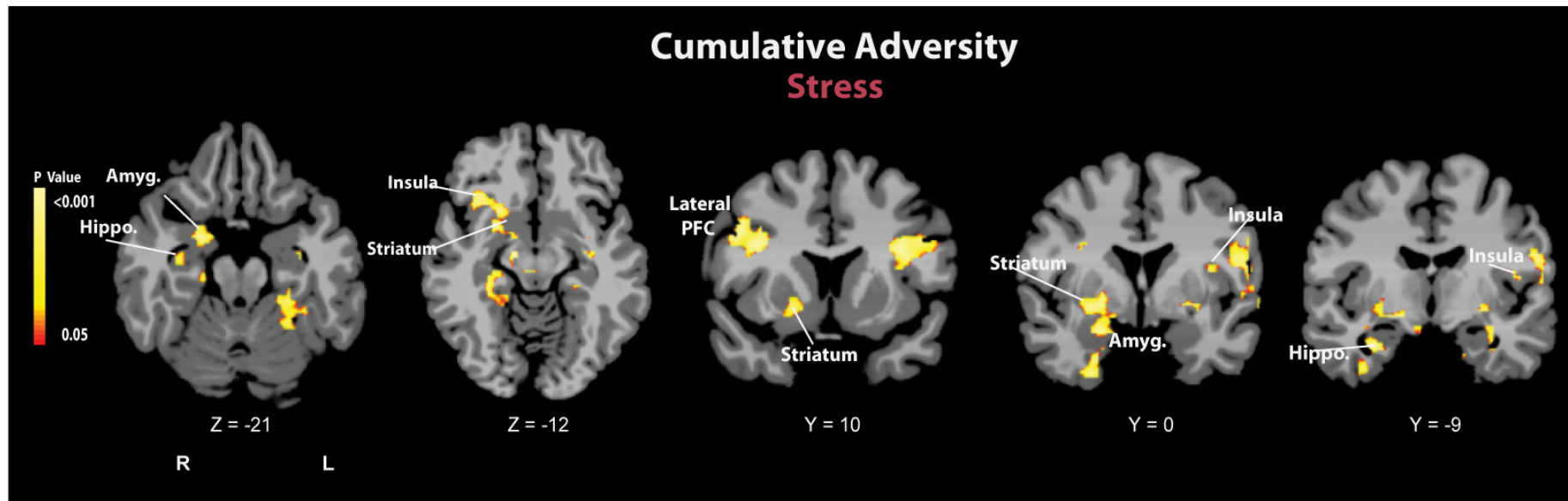


Controlling for age, sex, and total intracranial volume
((whole-brain voxel-based morphometry analysis)

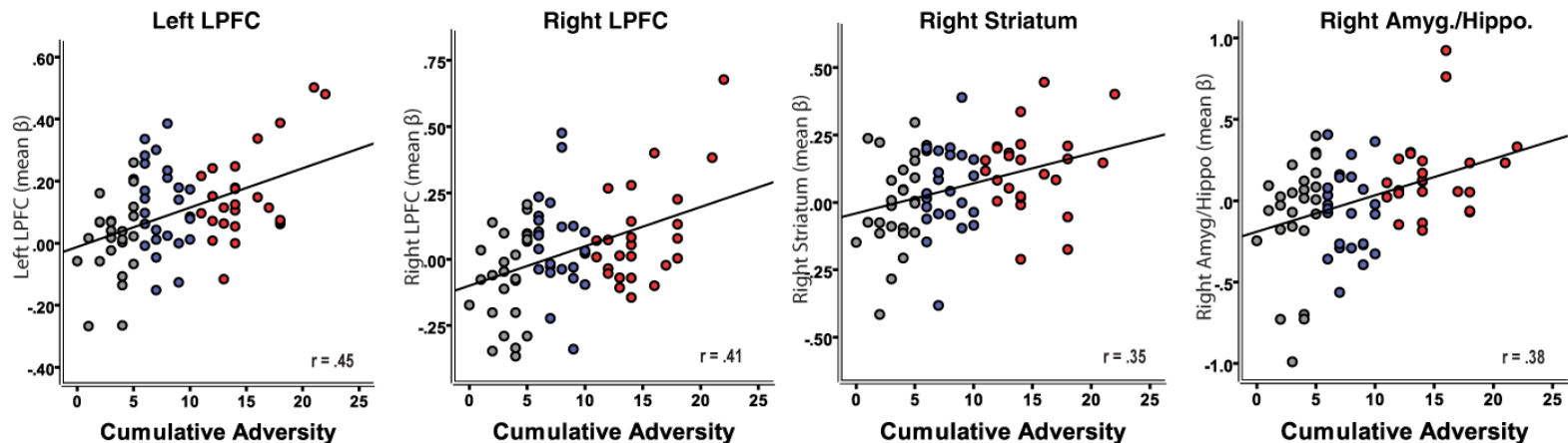
Ansell et al., Biol Psychiatry, 2012

Higher Cumulative Adversity Predicts Greater Neural Responses to Acute Emotional Stress (N=75)

a.



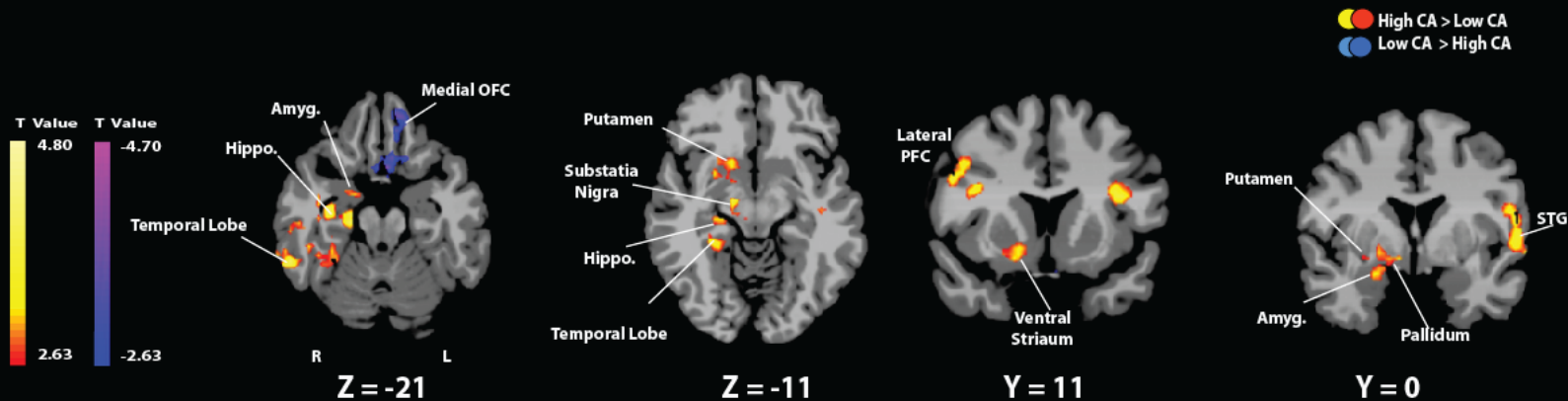
b.



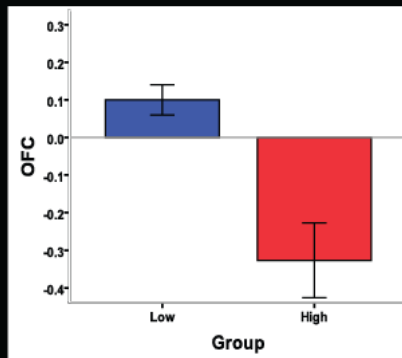
Seo et al, Cumulative adversity sensitizes neural responses to acute stress. *Neuropsychopharmacology* (2013)

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

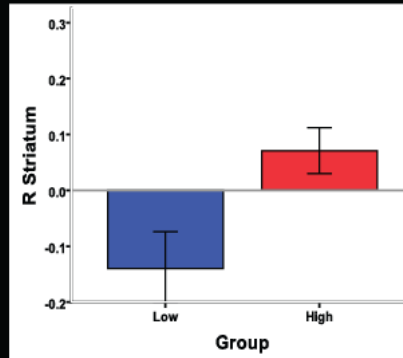
High CA vs. Low CA



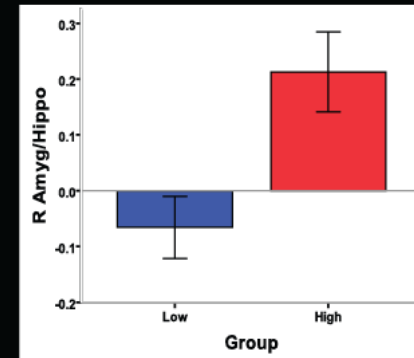
Medial OFC



Striatum

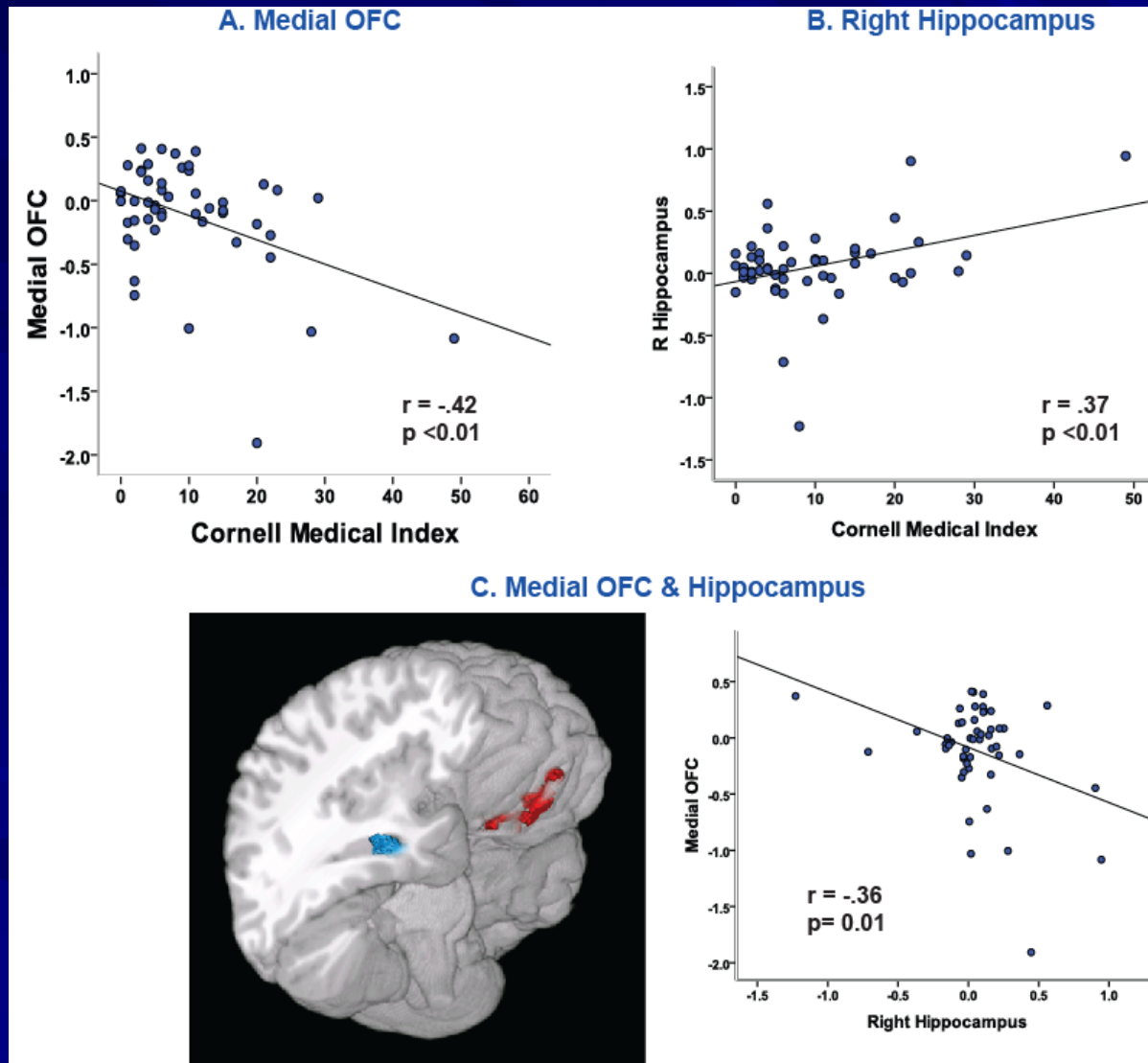


Amyg/Hippo



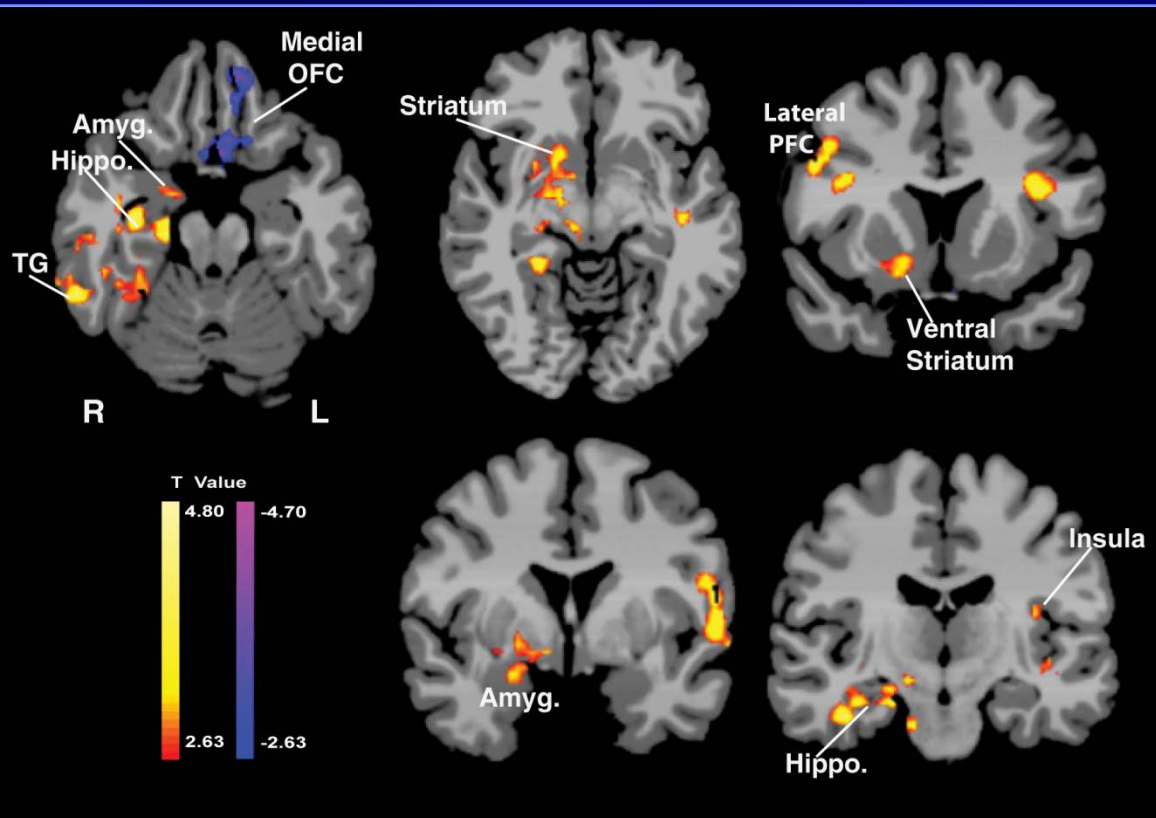
$p < .05$ WBC

Brain Responses to Stress is Associated with Health Symptoms on the Cornell Medical Index

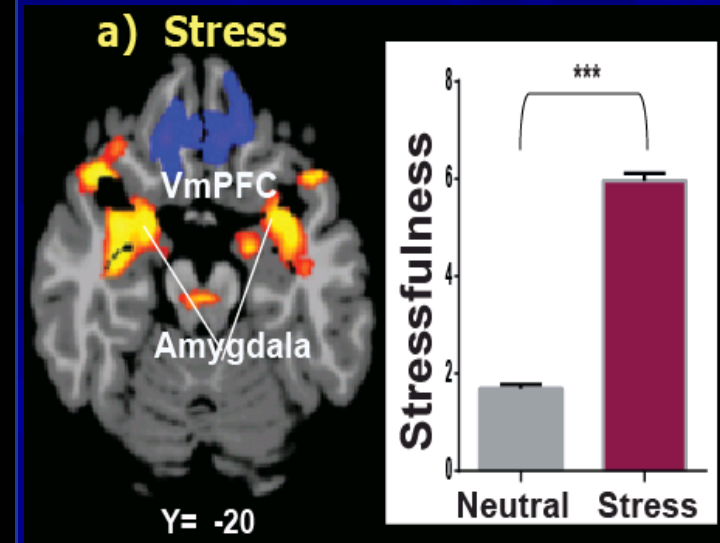


Corticostriatal-Limbic Activation During Emotional Stress in Healthy Individuals

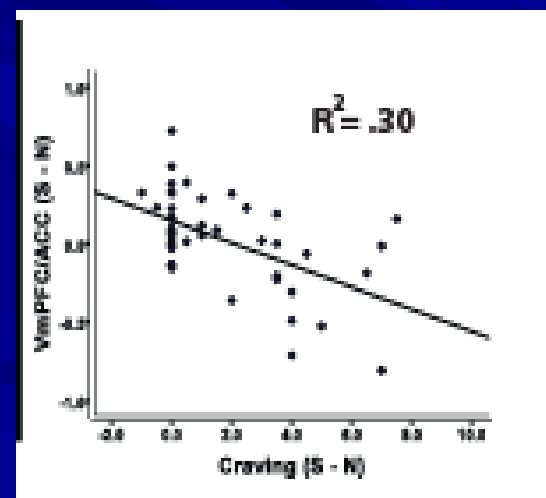
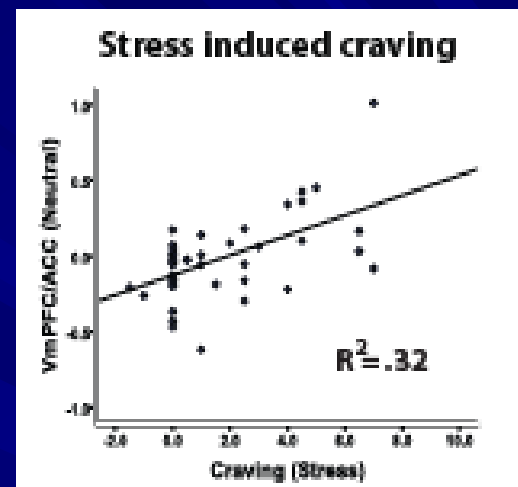
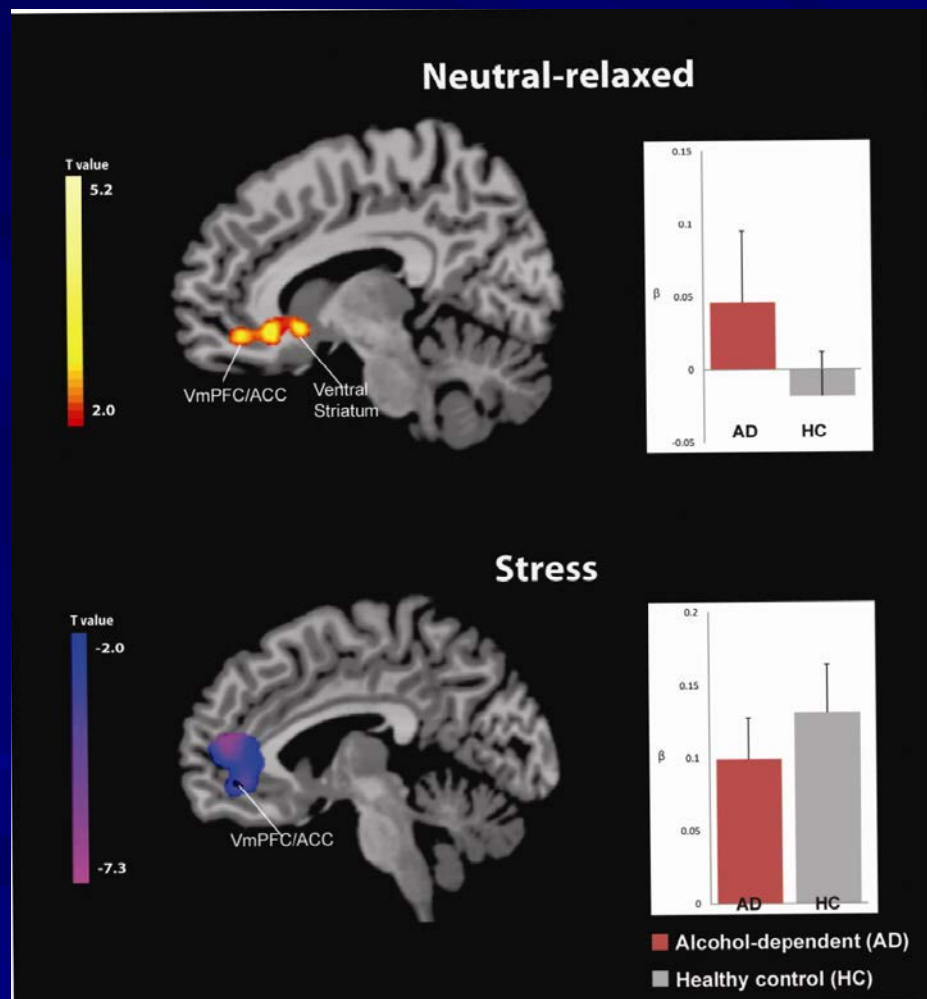
I. Stress Imagery Provocation



II. Emotional Pictures Provocation

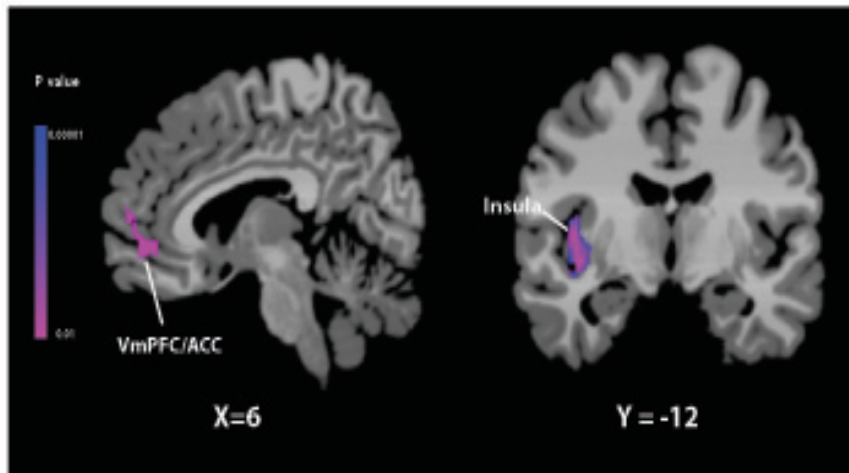


Disrupted Neural Response to Stress and Relaxed Scenarios in Recovering Alcoholics (AD)s versus Controls (HC) ($p < .01$ WBC)

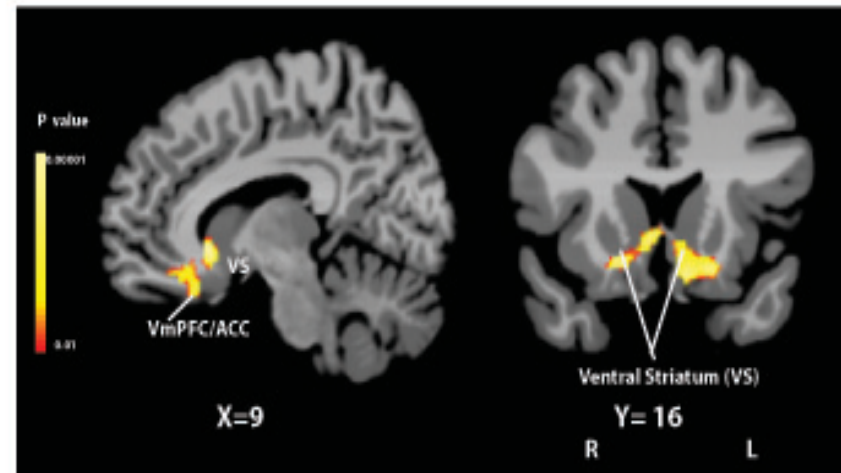


Neural Correlates of Days of Alcohol Used During Follow-up ($p < .01$ WBC)

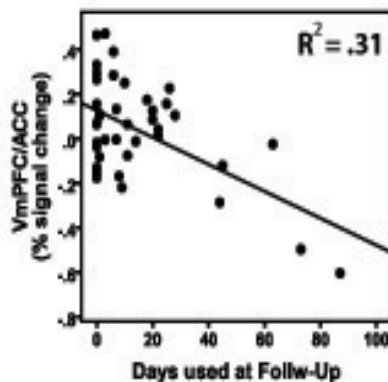
a. Stress (S)



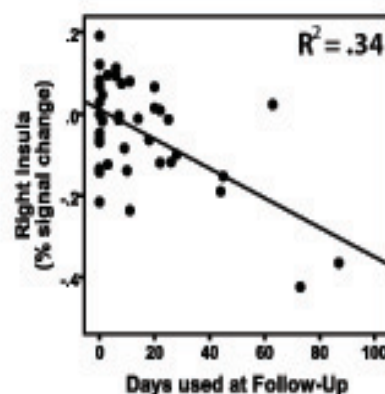
b. Neutral (N)



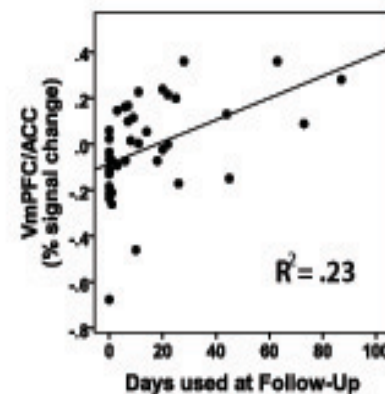
VmPFC/ACC (S)



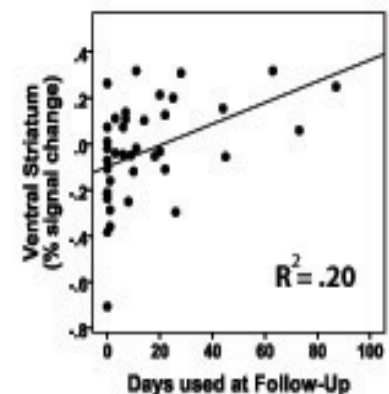
Right Insula (S)



VmPFC/ACC (N)



Ventral Striatum (N)



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?