

# Biopsychosocial Markers of Risk for Psychopathology During Adolescence

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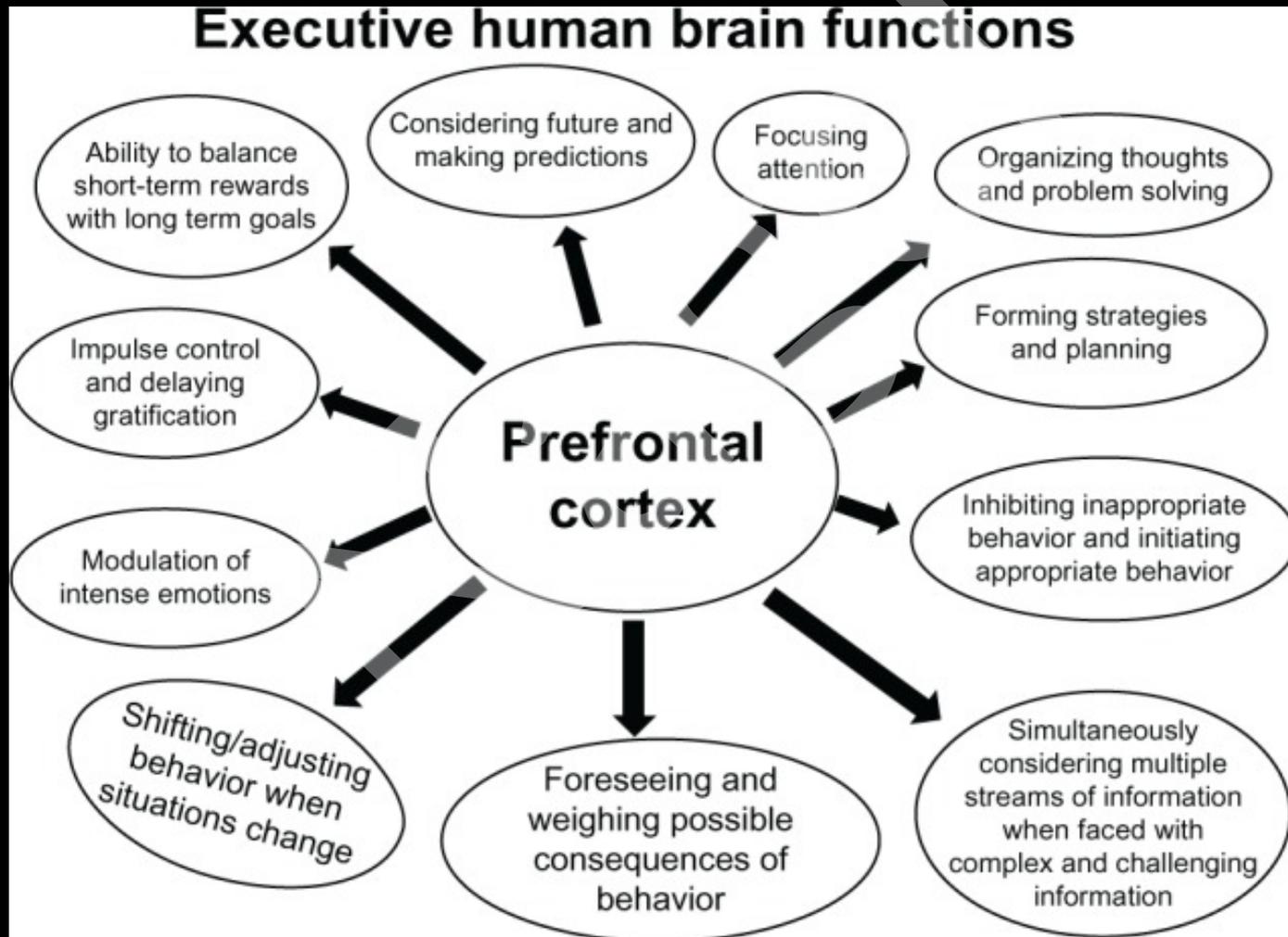
# Disclaimers

- Much of science is based on averages
- Significant findings do not mean that there are not exceptions
- It takes large-scale studies (ongoing) to understand complex interactions between multiple variables within individuals
- Most studies are based on predominantly white, higher SES samples, so generalizability remains limited



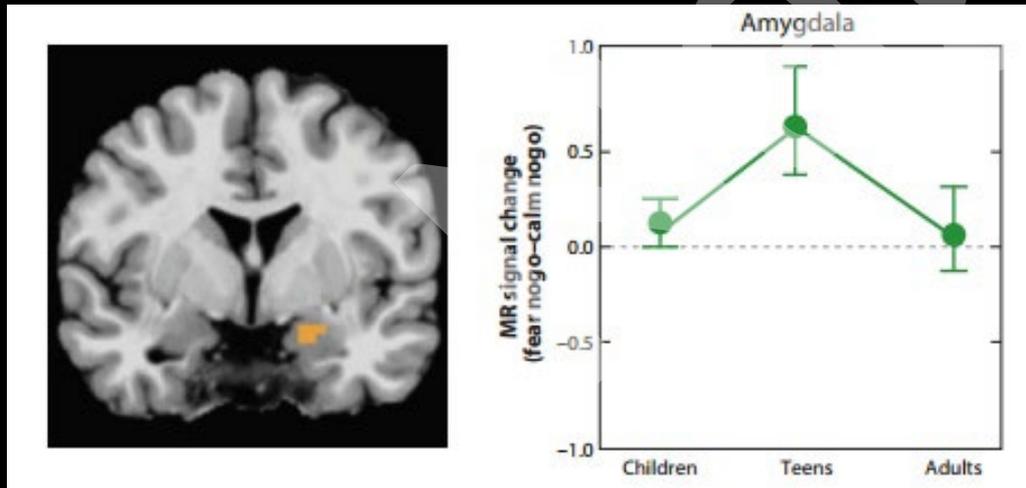


# With Maturation of the Prefrontal Cortex, Executive Functions are Improving



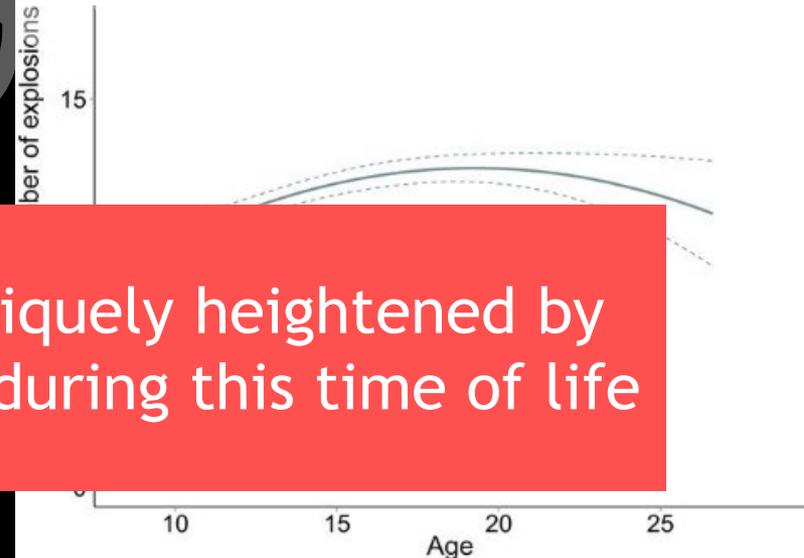
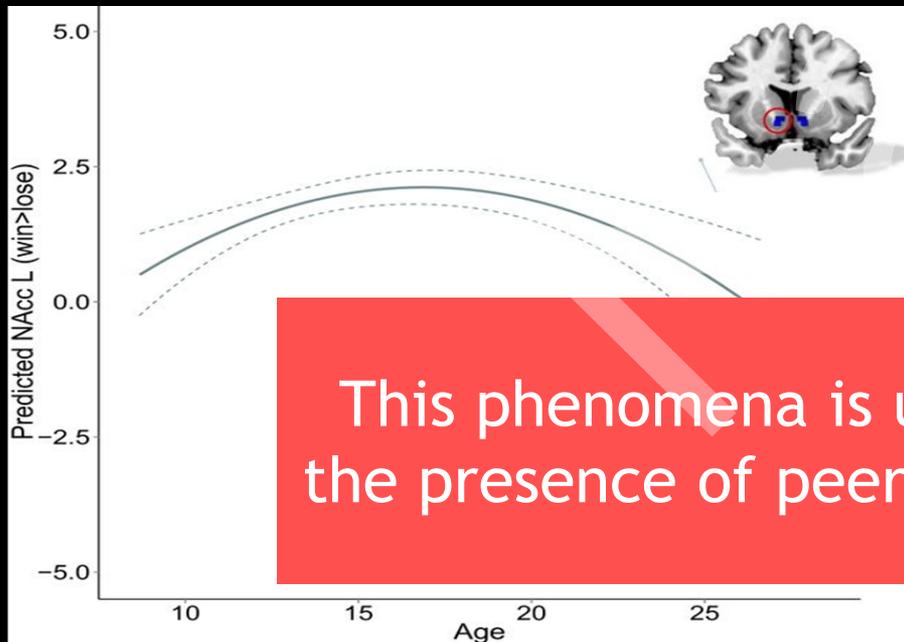
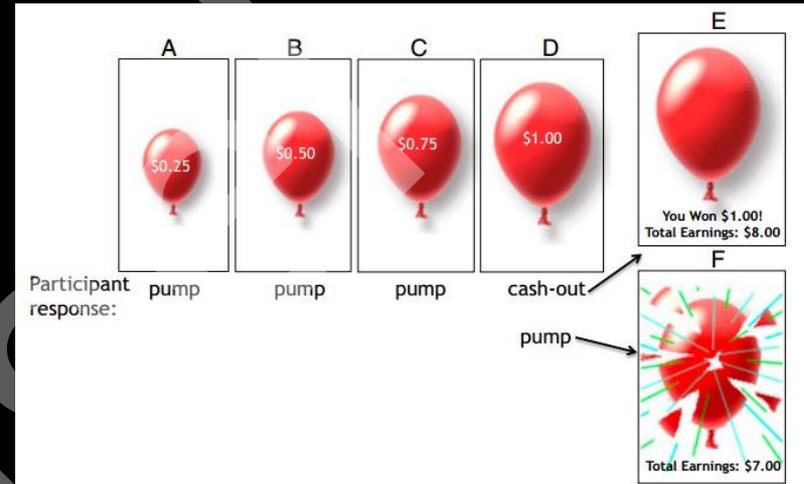
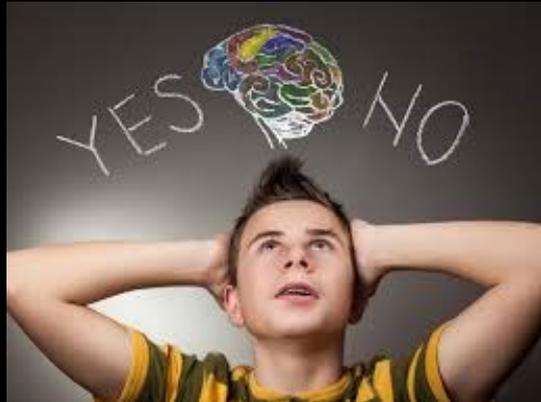
# Adolescents Have Greater Emotional Responsiveness

- Adolescence is a time of increased emotional responsiveness/intensity
- The amygdala is associated with the perception of emotion
- Adolescents show greater amygdalar response to emotional stimuli than children or adults



- Gonadal steroid levels (e.g., testosterone) have been associated with amygdala activity
- Figure from Casey, Annu Rev Psychol 2015

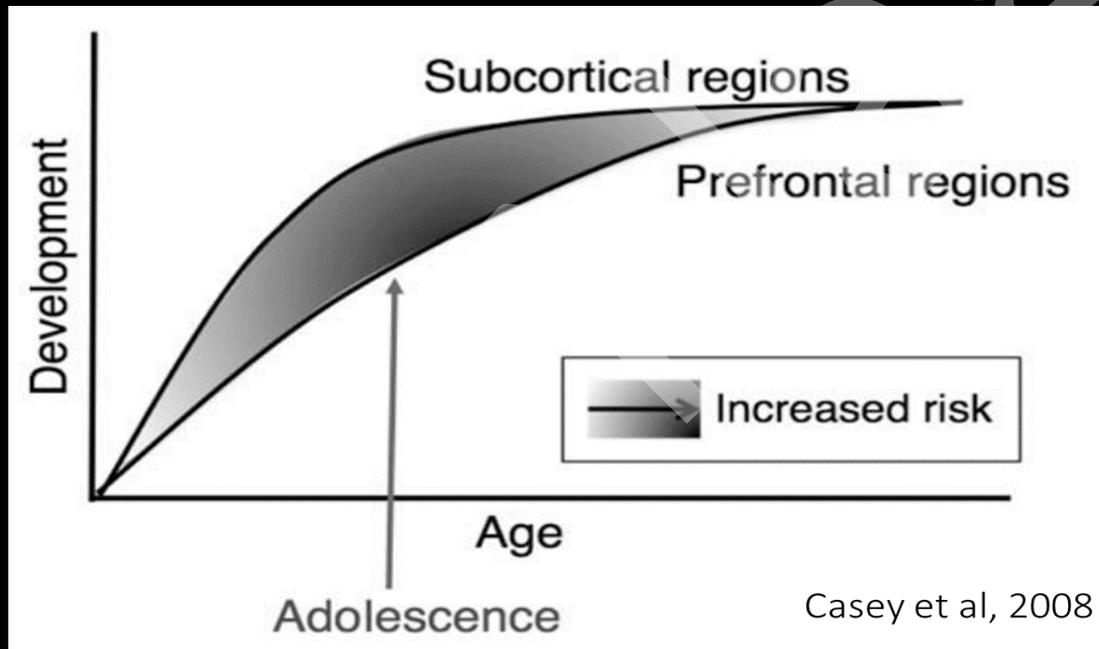
# Adolescents Take More Risks and Their Brain Response to Reward is Heightened



This phenomena is uniquely heightened by the presence of peers during this time of life

# Adolescent Vulnerability Hypothesis

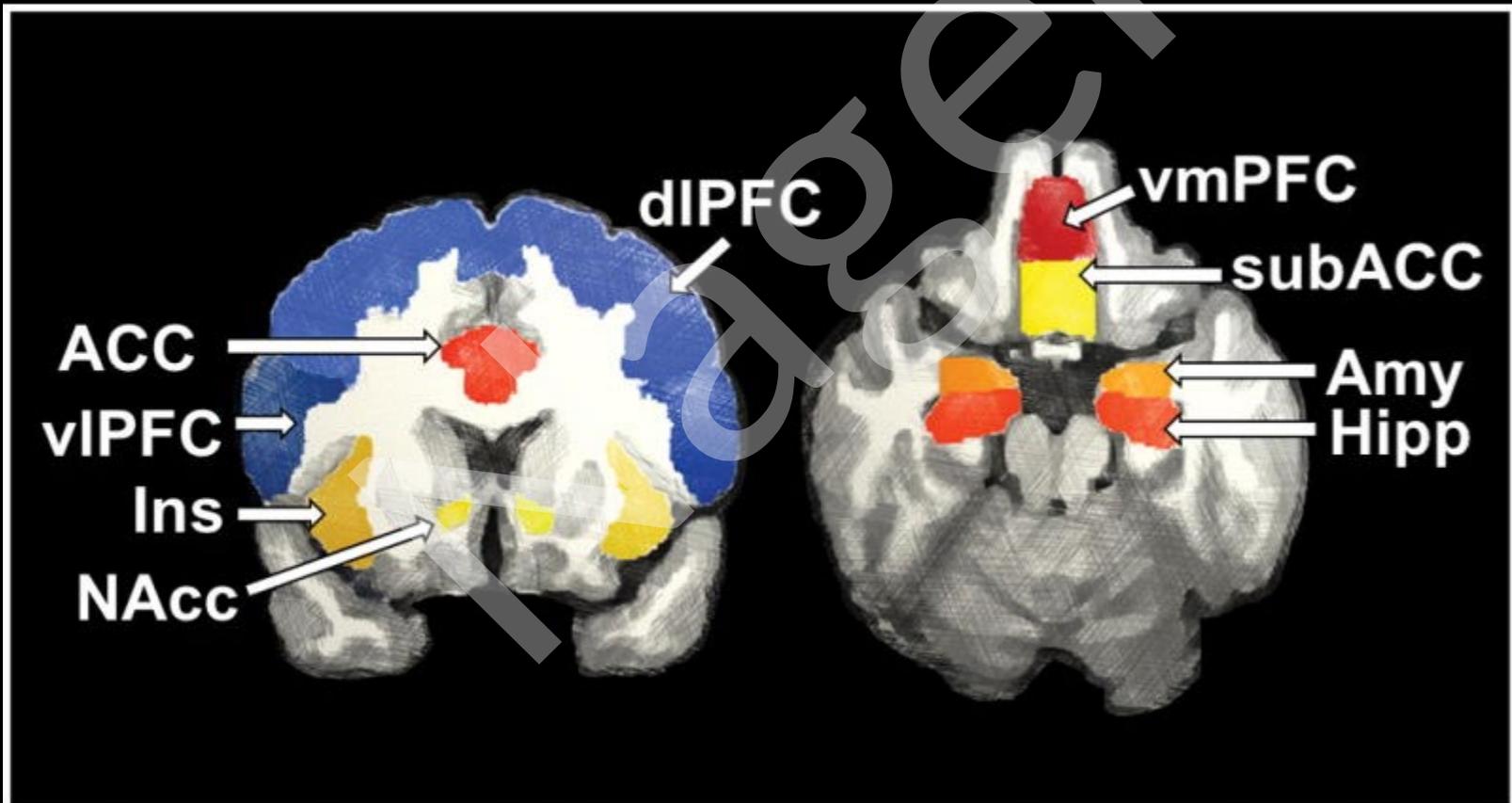
- Due to differential timing of developing neural systems, adolescent behavior may be driven by heightened limbic system (e.g., emotional and reward) responsiveness



# What Do We Know About Mental Illness and Addiction Risk During Adolescence



# Developing Frontolimbic Circuitry is Consistently Implicated in Emergent Psychopathology During Adolescence



# Depression and Suicidality in Adolescents

- In 2019, ~3.8 million adolescents in the U.S. had at

## AAP-AACAP-CHA Declaration of National Emergency in Child and Adolescent Mental Health

Home / Advocacy / Child and Adolescent Healthy Mental Development

CHILDREN'S HEALTH  
The U.S. surgeon general issues a stark warning about the state of youth mental health

December 7, 2021 · 12:44 PM ET

L. CAROL RITCHIE

Los Angeles Times  
SCIENCE  
Suicide rates for U.S. are the highest on record

JOURNAL

SIGN IN

himself. Six More

of deaths clustering in the same town, at the block

among



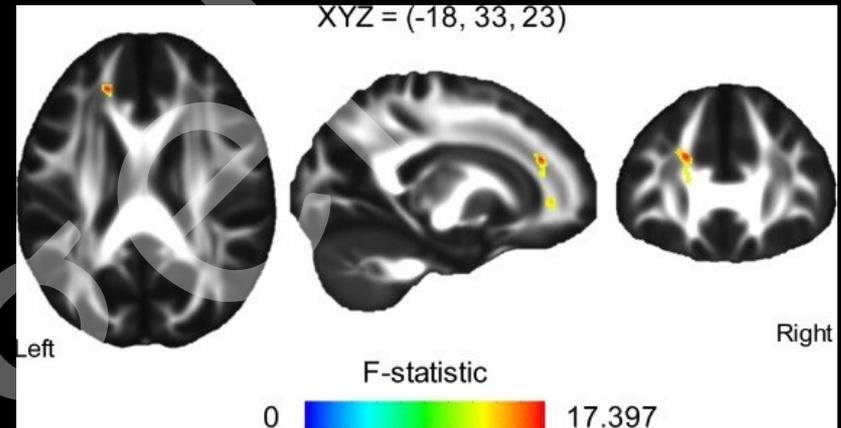
U.S. Surgeon General Vivek Murthy talks to reporters at the White House on July 15.

- Suicide is the leading cause of death among

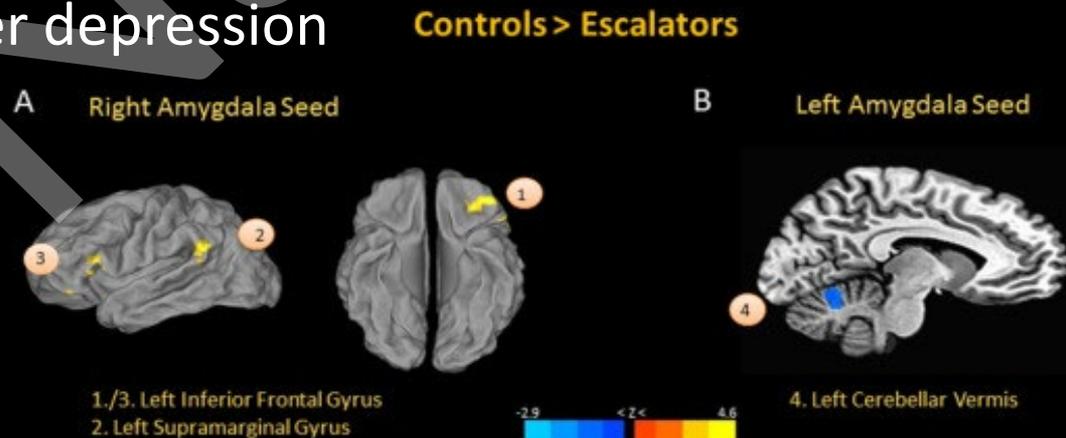
\* After an initial drop  
CDC.GOV

# Initial Studies of Brain Predictors of Risk for Depression During Adolescence

- Reduced integrity of prefrontal structural connections in the brain are associated with greater risk for emerging depression
- Reduced functional fronto-amygdalar connectivity is associated with greater depression symptoms over time

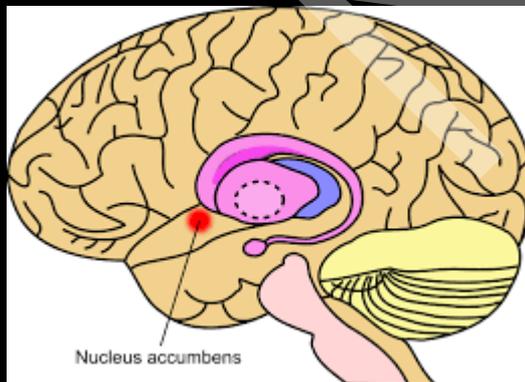
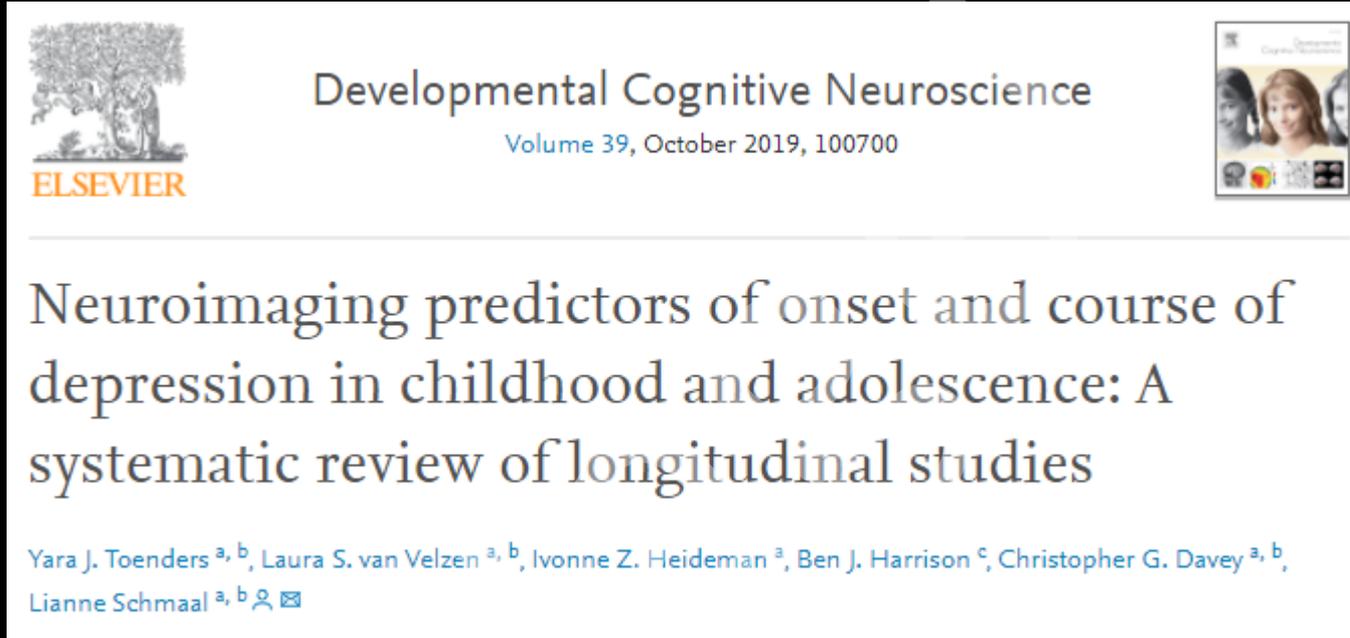


Kliamovich et al., 2021 Psychiatry Res Neuroimaging



Sheuer et al., 2017 Psychiatry Res Neuroimaging

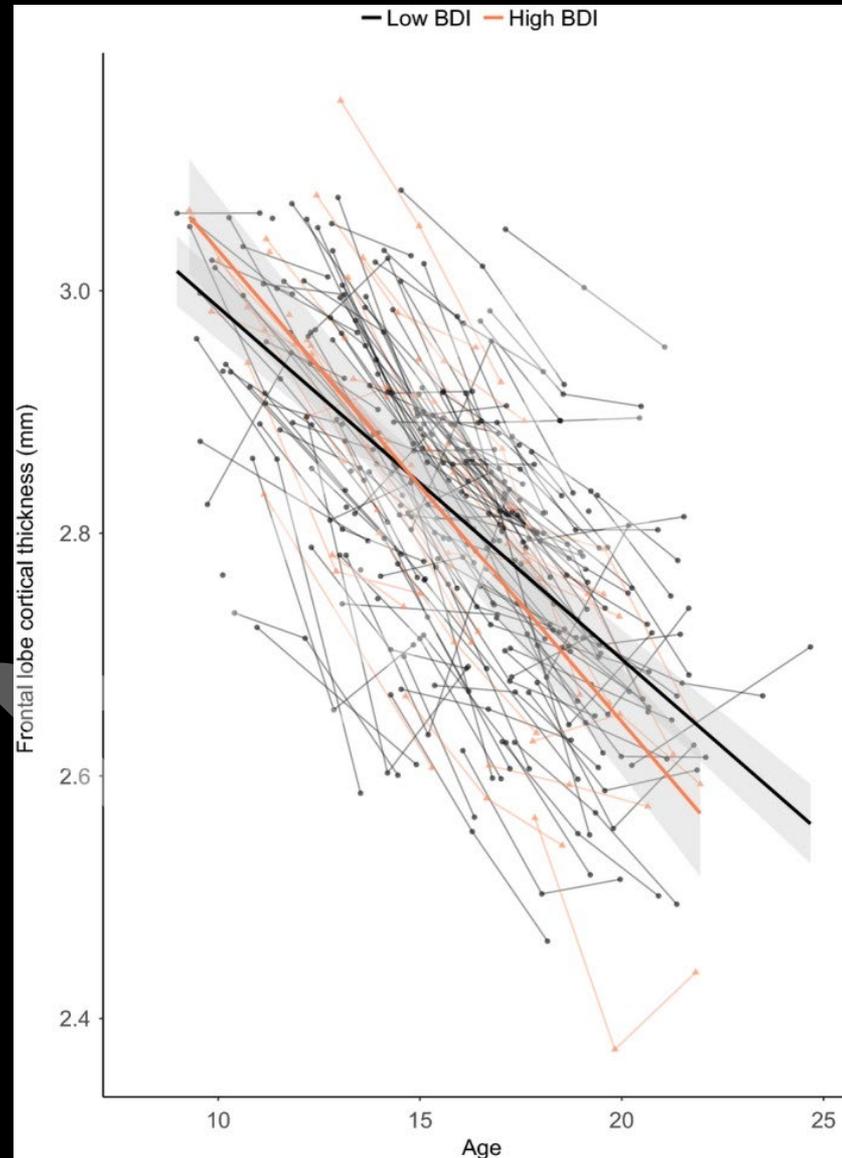
# Brain Predictors of Risk for Depression



Blunted reward-related response is one of the only consistent findings to emerge



# Emerging Depression is Associated with Accelerated Frontal Lobe Cortical Thinning



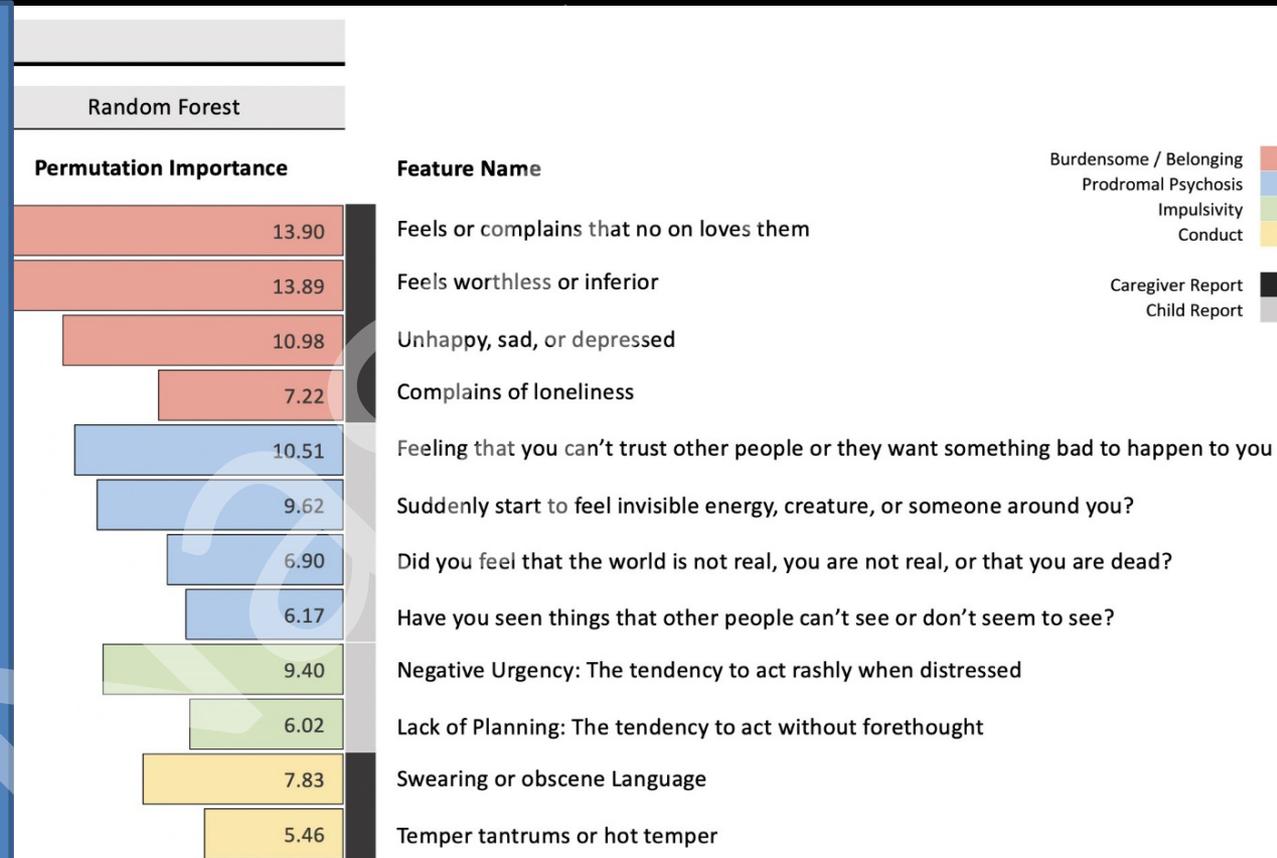


# What About Psychosocial Risk Predictors?

Neurologist

# Psychosocial Risk for Suicidality in ABCD at Age 9-10 - Machine Learning Prediction

- Compared to controls (n=10,060), we were able to classify suicidal ideators (n=1,116) using demographic and with an area-under-the-curve (AUC) of 0.70.
- Using features of importance identified, we were able to classify suicidal attemptors with an AUC of 0.77.



- Future studies in the lab are working to understand physiological signals that point to worsening suicidality

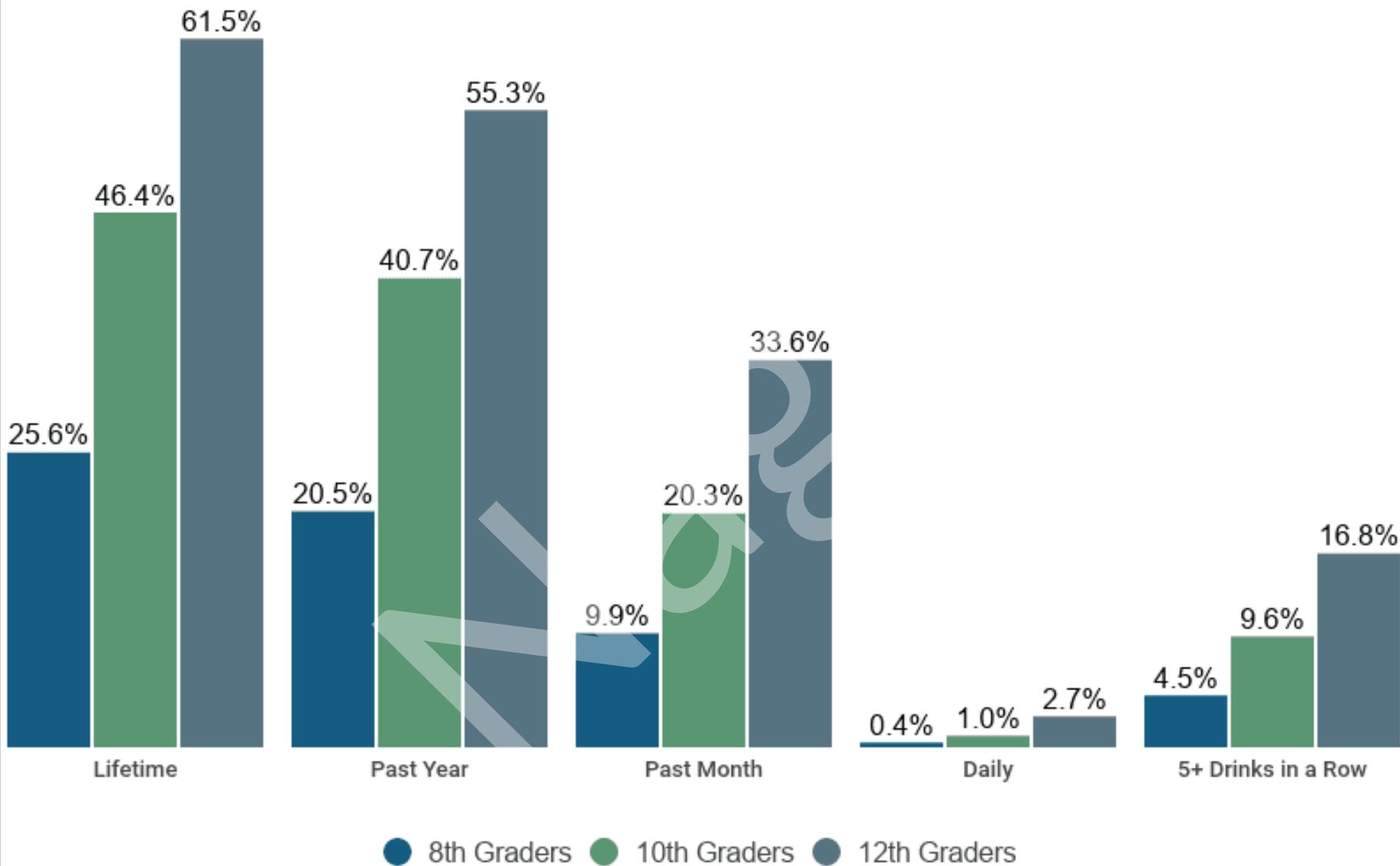
# Summary of Depression/Suicide Findings

- Patterns of developing frontolimbic (emotion) and frontostriatal (reward) circuitry, as well as the default mode network, are important in risk for depression and internalizing symptoms
- Psychosocial predictors also play an important role in depression and suicide risk
- Work has yet to be done to determine associations between these brain and psychosocial risk factors and how they interact to inform symptom trajectories

# What About Risk for Addiction?

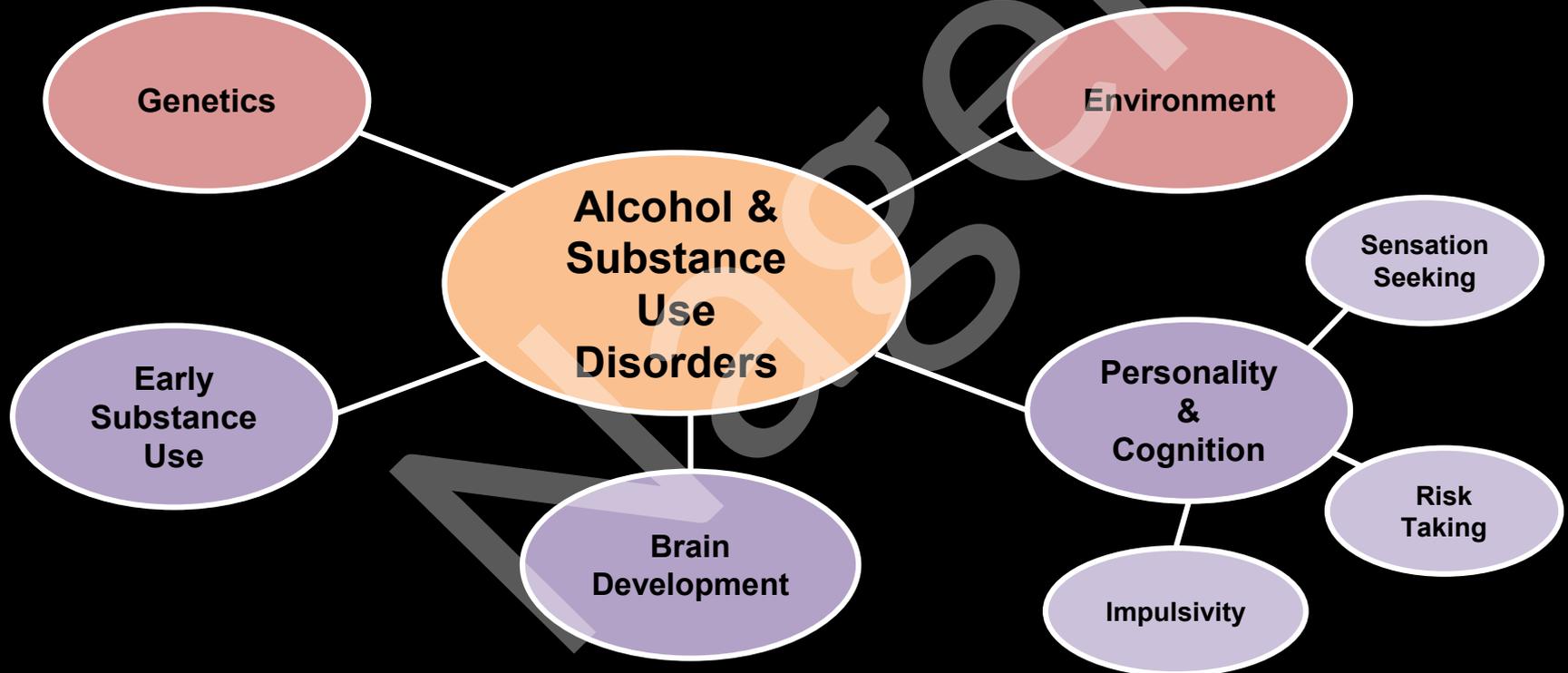


# Youth Alcohol Abuse

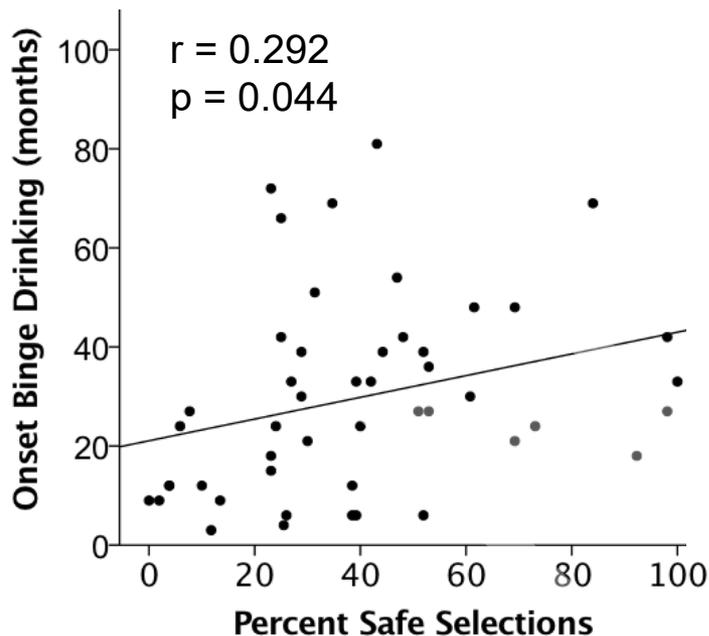


\*Reported usage at any point throughout 2020.

# Risk Factors for Alcohol and Substance Use Disorders



# Adolescents Who Make More Risky Selections Start Binge Drinking Sooner



## High Risk/Reward Condition

$r = 0.228$

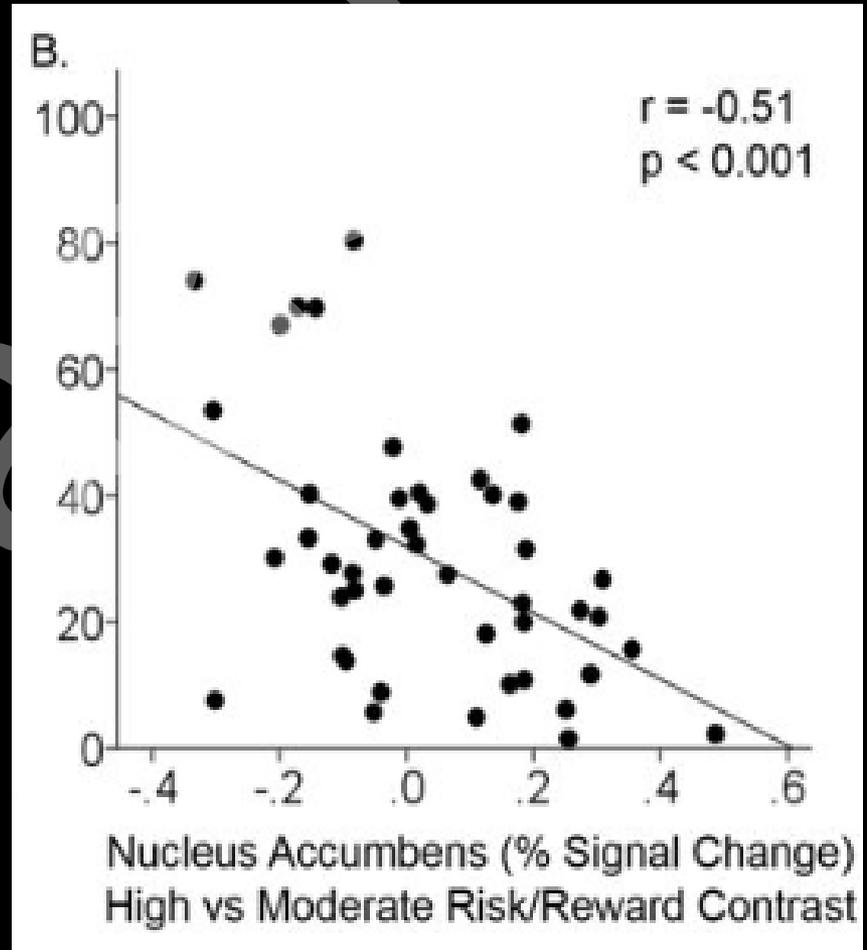
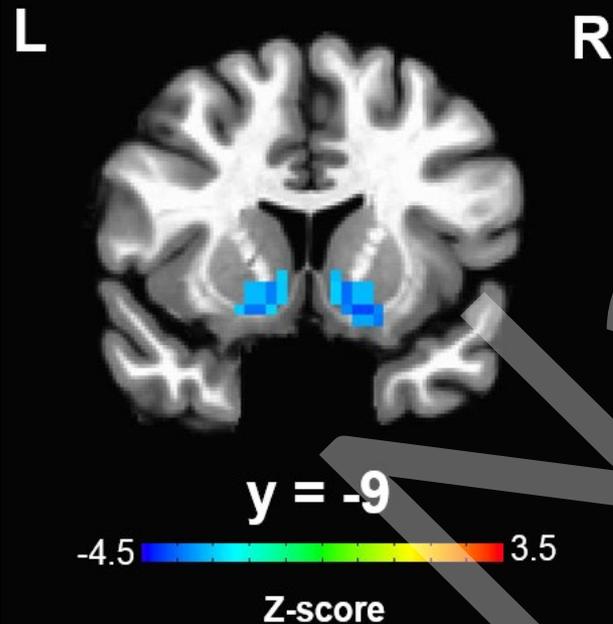
$p = 0.119$

## Moderate Risk/Reward Condition

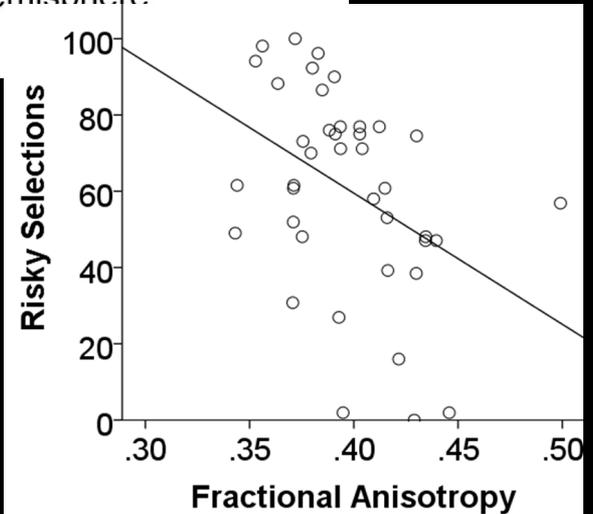
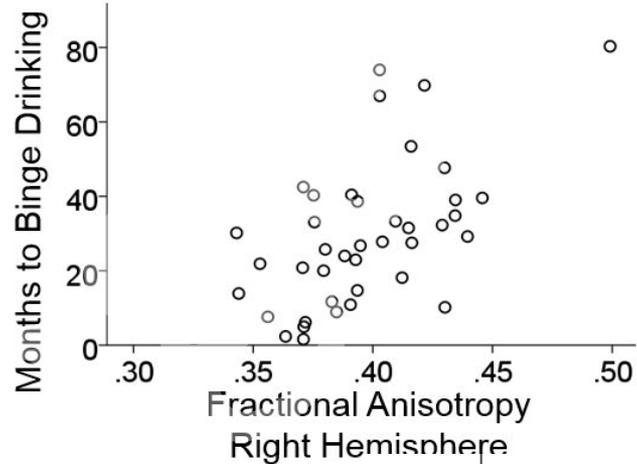
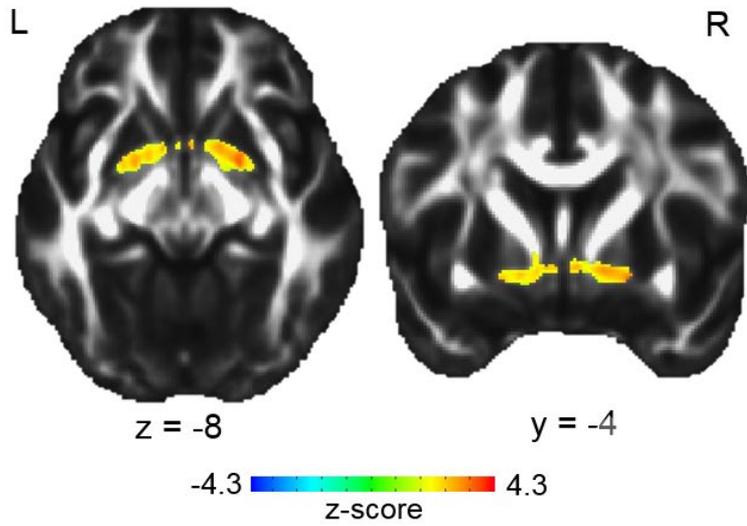
$r = 0.309$

$p = 0.033$

# Adolescents with Greater Reward Activation in the Brain During Risk Appraisal Start Binge Drinking Sooner



# Adolescents with Less Integrity in Structural Connections Start Binge Drinking Sooner and Take More Risks

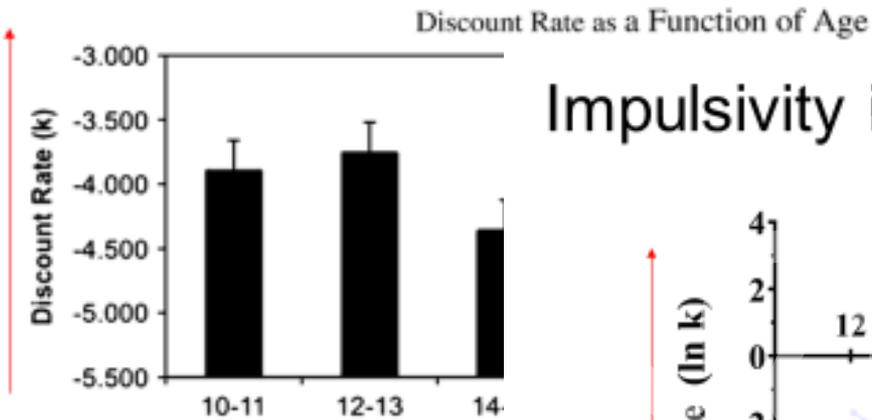


# Adolescents with Greater NAcc Volume Report Greater Alcohol Use 2 Years Later



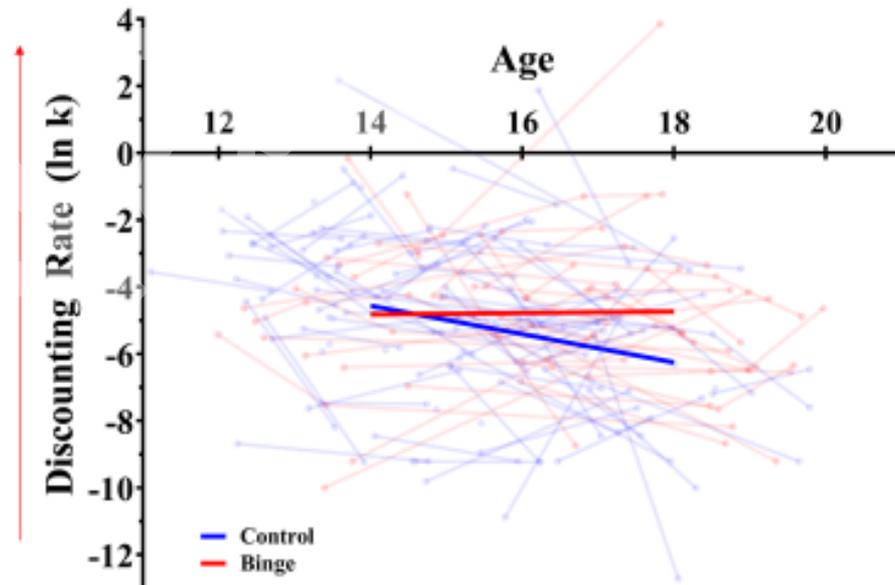
# Early Alcohol Use Thwarts Normative Development of Executive Functioning

## Impulsivity Decreases with Age



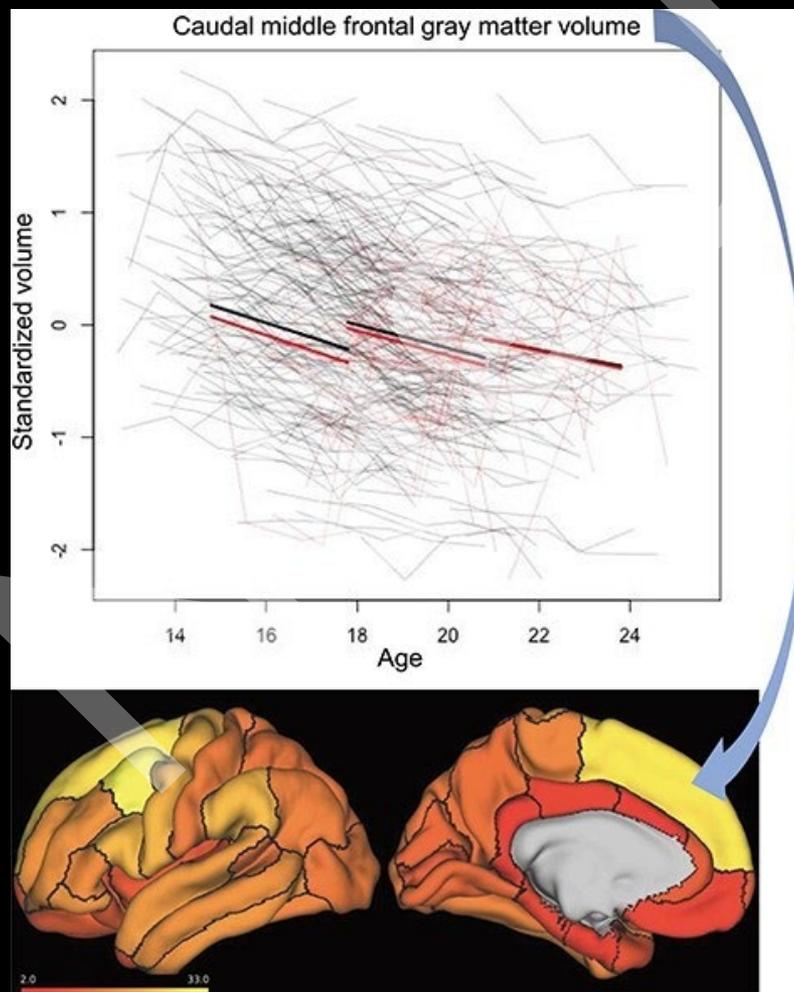
Steinberg et al., *Child Dev*, 2009

## Impulsivity in Adolescent Binge Drinkers



Jones, Steele, & Nagel., *Addiction*, 2017

# Younger Adolescent Binge Drinkers Show a Greater Difference from Non-Drinkers in Gray Matter Volume Decline



# Summary of Risk for Alcohol Use Disorders/Addiction Findings

- Patterns of developing frontostriatal (reward) circuitry are important in identifying risk for alcohol use and addiction
- Individual differences in personality (e.g., risky decision making) play an important role in addiction risk and relate to the developing brain
- Early alcohol use relates to subsequent behavior and brain development that may further perpetuate risk

# Conclusions & Next Steps

- Adolescents is a time of significant maturation and the timing of the development of different brain systems render it a time of vulnerability
- Developing regions of the brain and the connectivity between them (e.g., prefrontal cortex and reward/emotion regions) show markers of risk prior to the development of mental health problems, making them promising targets for intervention
- These *transdiagnostic* biomarkers, combined with known psychosocial risks, provide opportunities to better intervene prior to the development of mental illness
- Large, longitudinal studies and big data efforts are crucial to determine which risk markers are most predictive of risk (as well as resilience) for which individuals

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