Adolescent Substance Use Disorders, Psychological Regulation, and the Frontoparietal Network

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Outline

- Early study: hippocampus
- Conceptual model
  - Brain maturation and self-control
- Research review
  - Results & limitations
- Conclusions

Adolescent AUD and Hippocampus

Subjects: Matched Groups

- Adolescent AUD (n=12)
- Controls (n=24)

Results

- Hippocampal volume: AUD < Controls
- Hippocampus x AUD duration: r=-.73

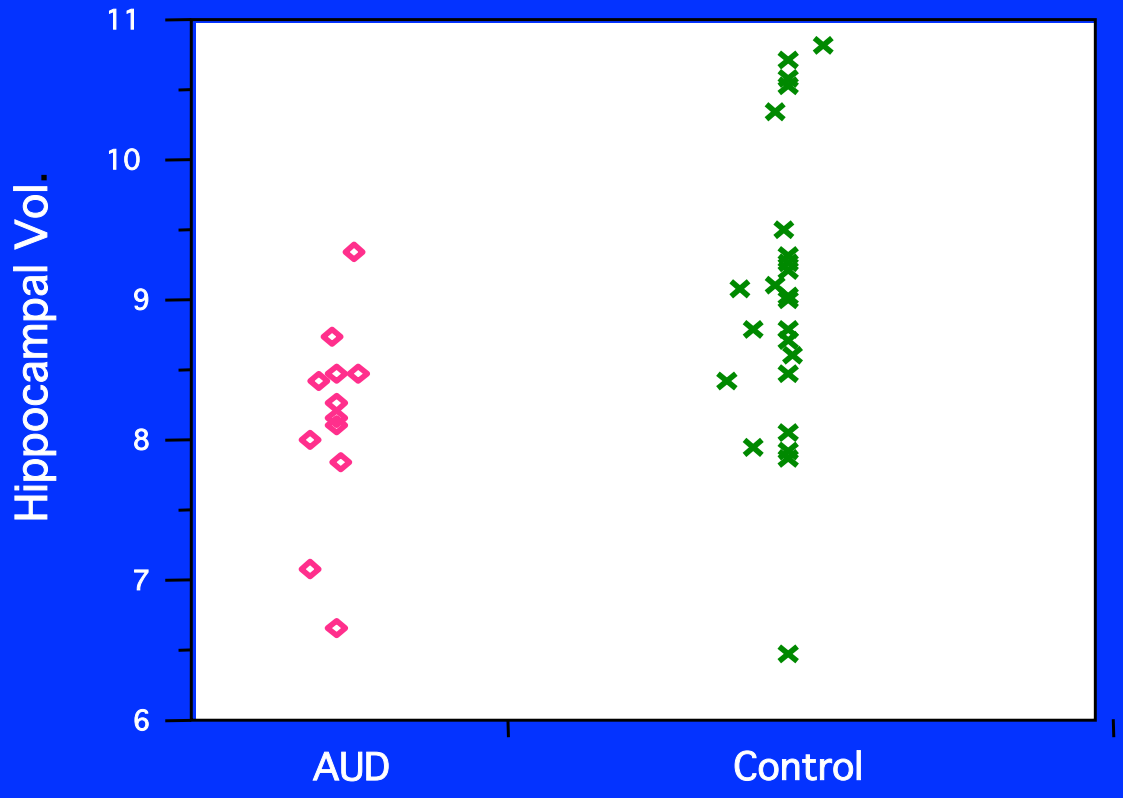
DeBellis, Clark et al. Am J Psychiatry 2000

Hippocampal volume

	left	right
• AUD	4.0 ± 0.4	4.1 ± 0.4
• Controls	4.6 ± 0.6	4.5 ± 0.5

De Bellis, Clark, et al. (2000)

Total hippocampal volumes means (cm^3; ICV adjusted) adolescent onset AUD vs matched controls ($F_{2,33}$= 7.11, p=.01).



Adolescent AUD and Hippocampus

"Replications"

- Nagel, Tapert et al. Psychiat Res 2005
- Negative studies?

Animal studies

- Rats (Nixon & Crews, J Neurochem 2002)
- Non-human primates (Taffe et al. PNAS 2010)

Conclusion

- Teen alcohol use can damage hippocampus
- Dose-response? Vulnerabilities?

Outline

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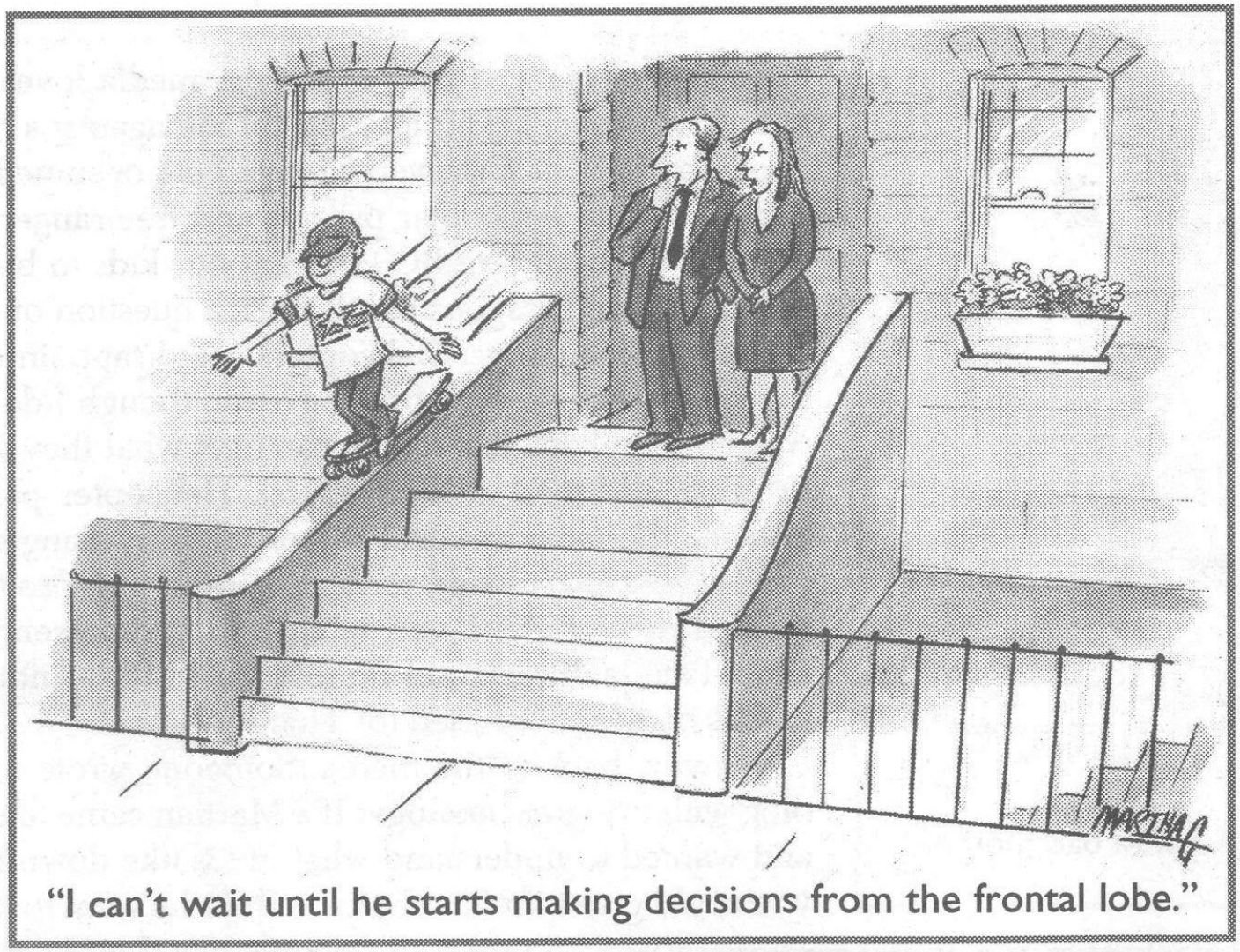
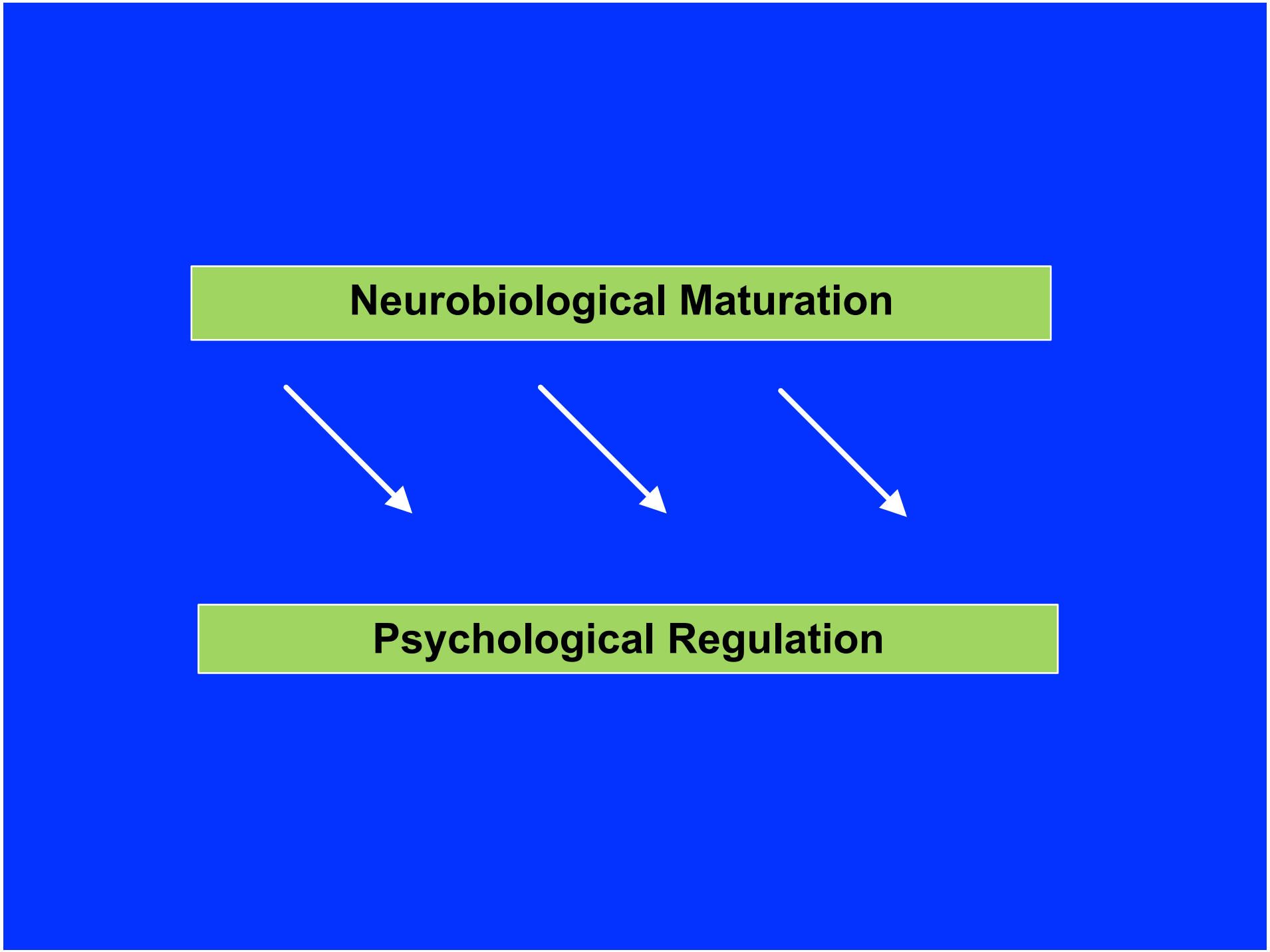
Adolescent-onset SUDs as part of a coherent developmental trajectory

- Childhood inattention, impulsive aggression, irritability
- Adolescent SUDs as manifestations of these propensities using available substances
- Adulthood features extend to substances available to adults, social difficulties involve family and work



"I can't wait until he starts making decisions from the frontal lobe."


Neurobiological Maturation
Psychological Regulation

Functional connectivity: Yeo et al. 2011

Methods

- 1,000 subjects
- MRI resting-state functional connectivity
- Identify functionally coupled regions

Result

- 7 functionally coupled networks
- 17 network solution also presented

Yeo et al. (2011) Organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiology

7 cerebral cortex networks

- Frontoparietal
- Limbic
- Dorsal attention
- Ventral attention
- Somatosensory
- Visual
- Default

Frontoparietal Cortex

Anatomy

- Prefrontal cortex
- Posterior parietal cortex
- Anterior cingulate
- Superior longitudinal fasciculus

Frontoparietal Cortex

Functions: “Executive control circuit”

- Working memory
- Selective attention
- Rule-based problem solving
- Goal-directed decision making

Neuroimaging approaches

Macrostructural

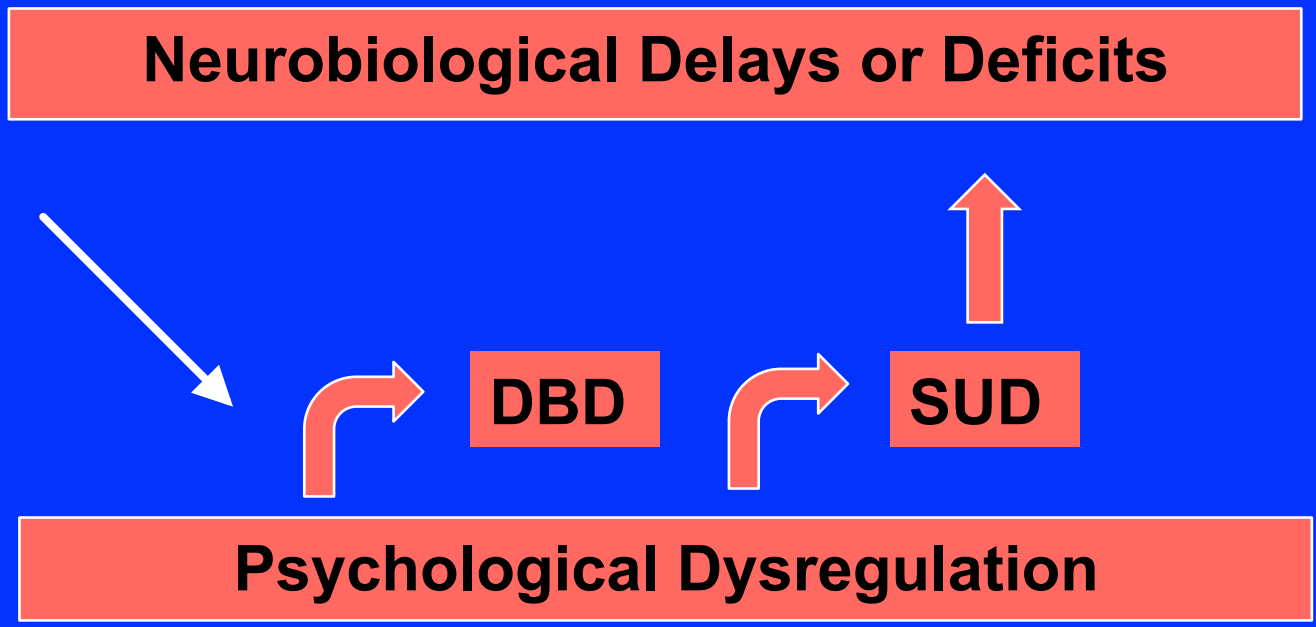
- White matter volumes
- Gray matter volumes

Microstructural: Diffusion Tensor Imaging

- TBSS
- Regional

Functional MRI

- Antisaccade Task


Neurobiological Delays or Deficits
DBD
SUD
Psychological Dysregulation

Macrostructure

Subjects

- Adolescent AUD (n=14)
- Matched controls (n=28)

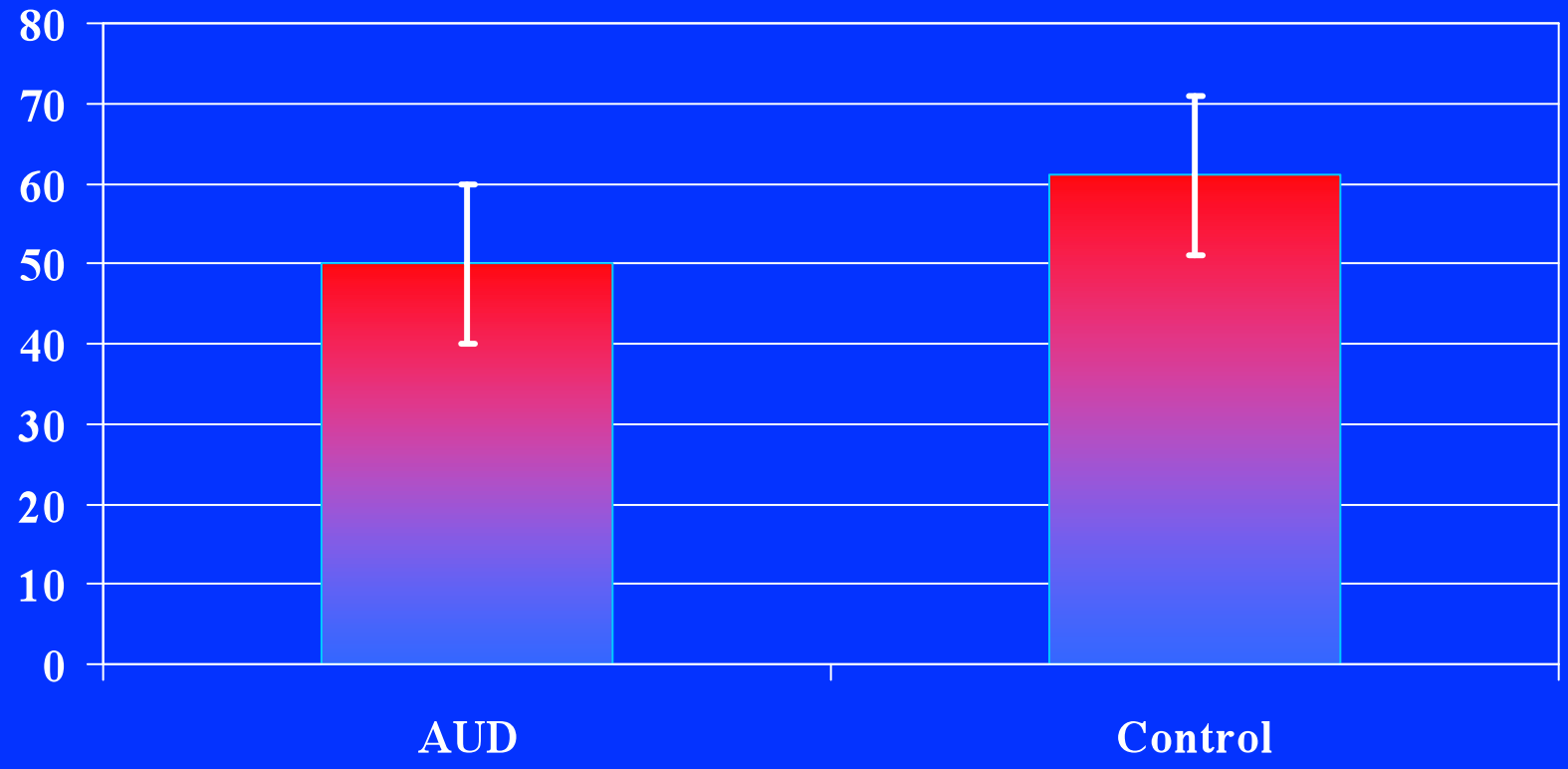
Results

- PFC white matter volume
- PFC gray matter volumes
- PFC gray x maximum drinks

  R= -0.78 (n=14), p<.001

DeBellis, Clark et al. ACER 2006

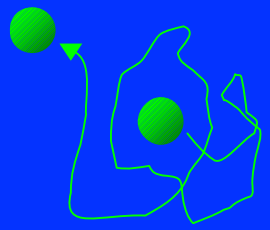
Prefrontal white matter volumes in adolescents (mean cm3 ± SD)



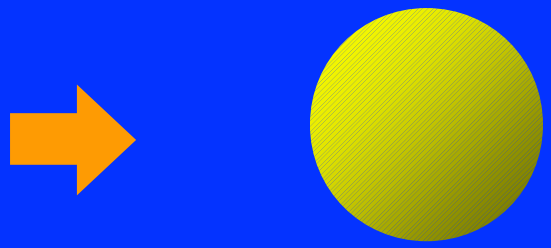
De Bellis, Clark, et al. ACER (2005)

Diffusion Tensor Imaging

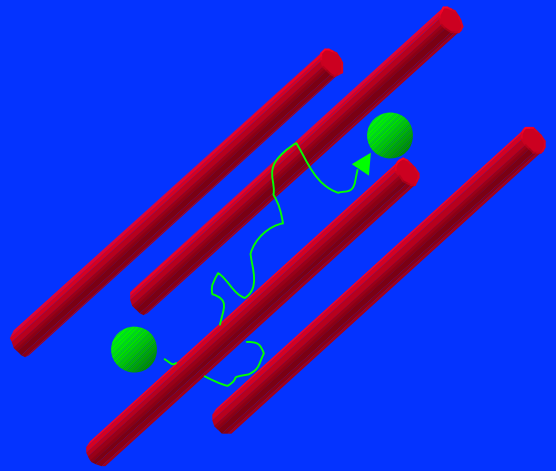
Free diffusion



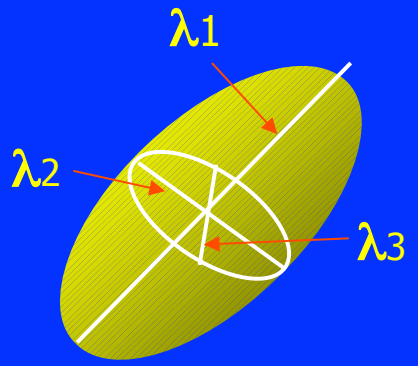
Isotropic diffusion

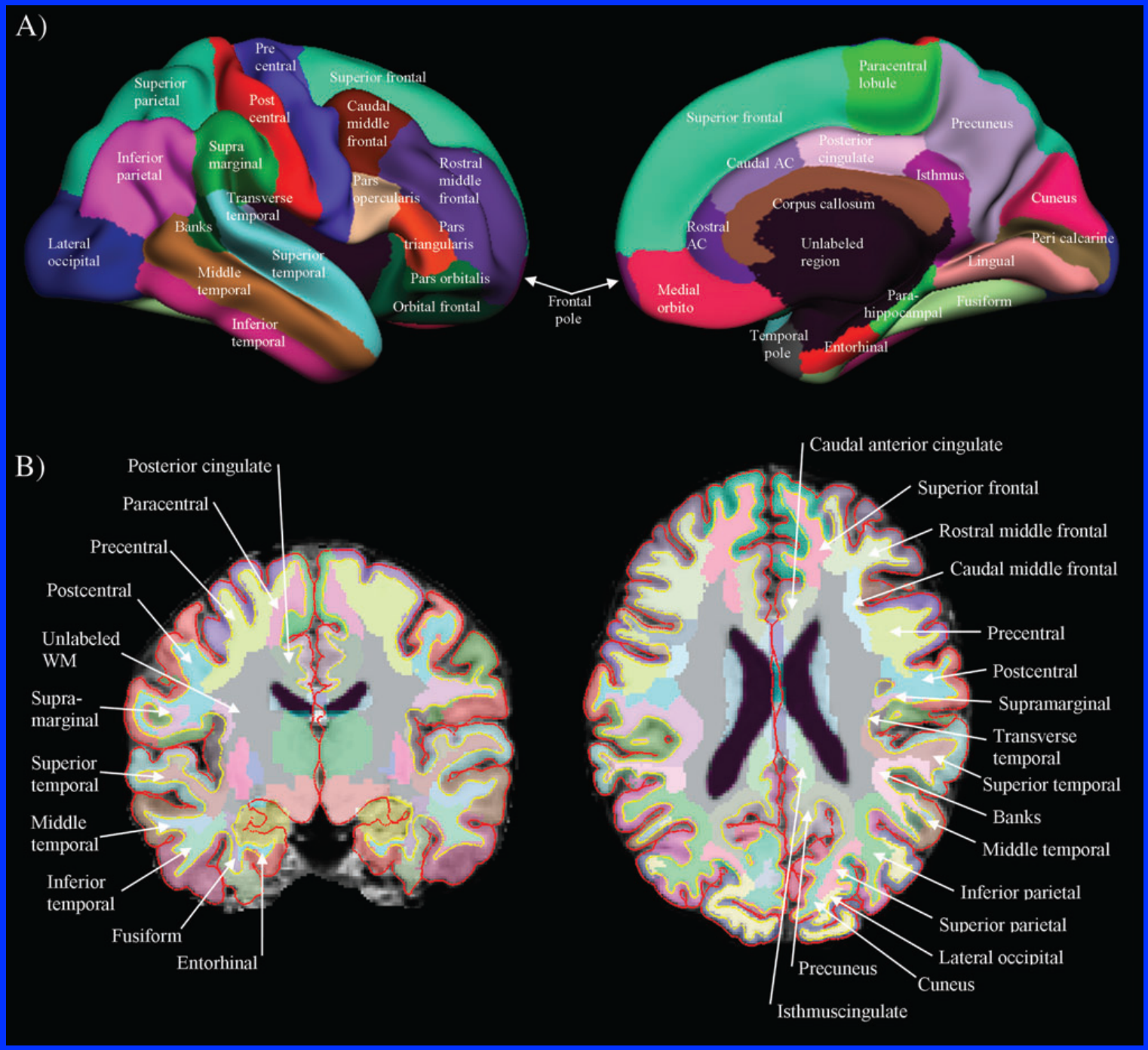


Restricted diffusion



Anisotropic diffusion




A)
Pre central
Superior frontal
Superior parietal
Post central
Caudal middle frontal
Supra marginal
Inferior parietal
Rostral middle frontal
Pars opercularis
Transverse temporal
Banks
Pars triangularis
Lateral occipital
Superior temporal
Middle temporal
Pars orbitalis
Orbital frontal
Inferior temporal
Frontal pole
Paracentral lobule
Superior frontal
Precuneus
Posterior cingulate
Caudal AC
Isthmus
Cuneus
Corpus callosum
Rostral AC
Unlabeled region
Peri calcarine
Lingual
Medial orbito
Para-hippocampal
Fusiform
Temporal pole
Entorhinal
B)
Posterior cingulate
Paracentral
Precentral
Postcentral
Unlabeled WM
Supra-marginal
Superior temporal
Middle temporal
Inferior temporal
Fusiform
Entorhinal
Caudal anterior cingulate
Superior frontal
Rostral middle frontal
Caudal middle frontal
Precentral
Postcentral
Supramarginal
Transverse temporal
Superior temporal
Banks
Middle temporal
Inferior parietal
Superior parietal
Lateral occipital
Precuneus
Cuneus
Isthmuscingulate

Neurodevelopmental Maturation

- n =142
- Stratification
  - Age: 12: 24%; 13: 23%; 14: 27%; 15: 26%
  - Gender: males: 47%; females: 53%
  - Race: White: 73%; AA: 27%
- Other characteristics
  - Alcohol use: 12: 3%; 13: 13%; 14: 29%; 15: 27%
  - Binges: 12: 0%; 13: 3%; 14: 3%; 15: 5%
  - AUD: n=1; Other SUD (cannabis): n=3
  - Parental AUDs: 38%

Regional DTI FA x age (ages 12-15)

Region	r
• Prefrontal	.24*
• Cingulate	.23*
• Parietal	.21*
• Temporal	.25*

*significant @ p<.05

DTI FA Microstructure: TBSS

Subjects

- Adolescent SUD (n=24)
- Matched Controls (n=12)

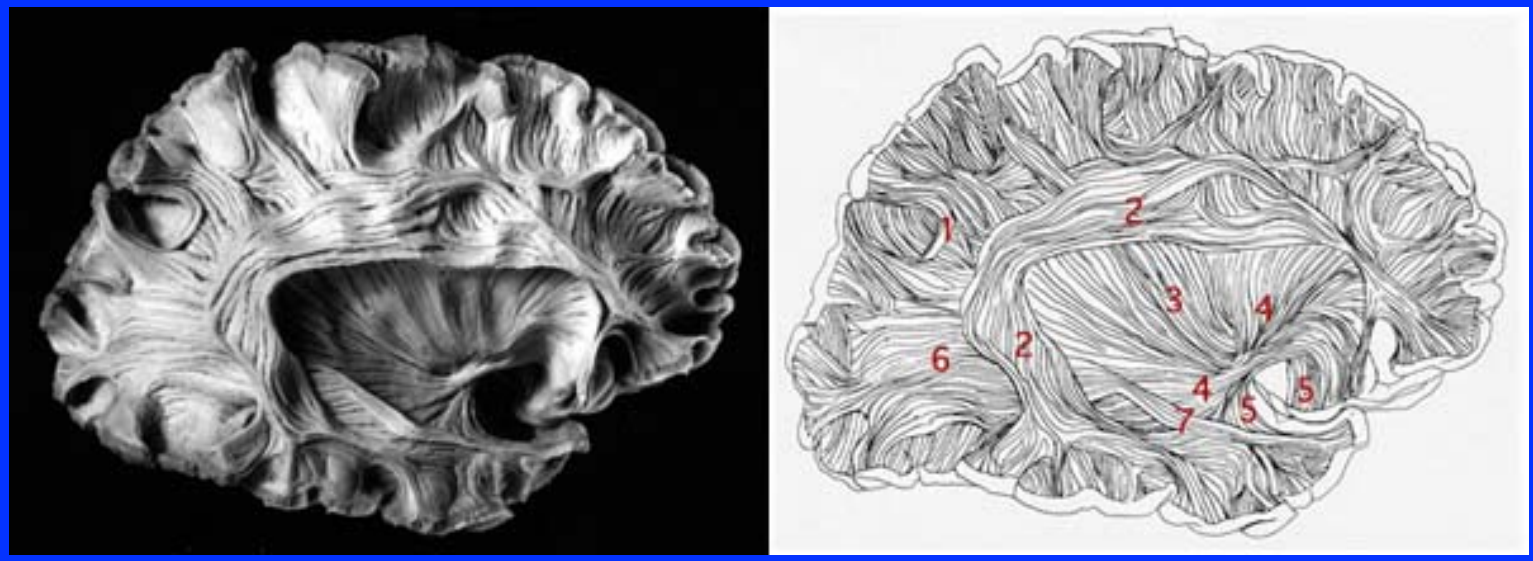
MRI Analysis: TBSS

Results

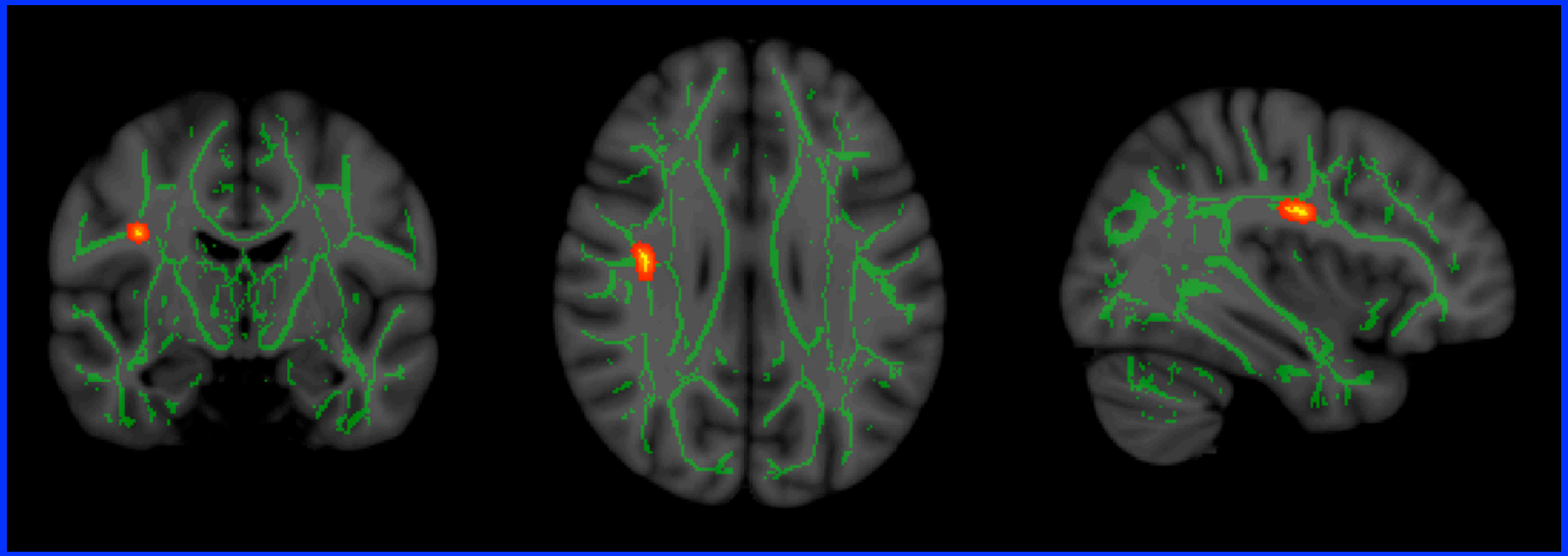
- SLF FA: SUD< Controls
- Females greater difference than males

Thatcher, Clark et al. DAD 2010

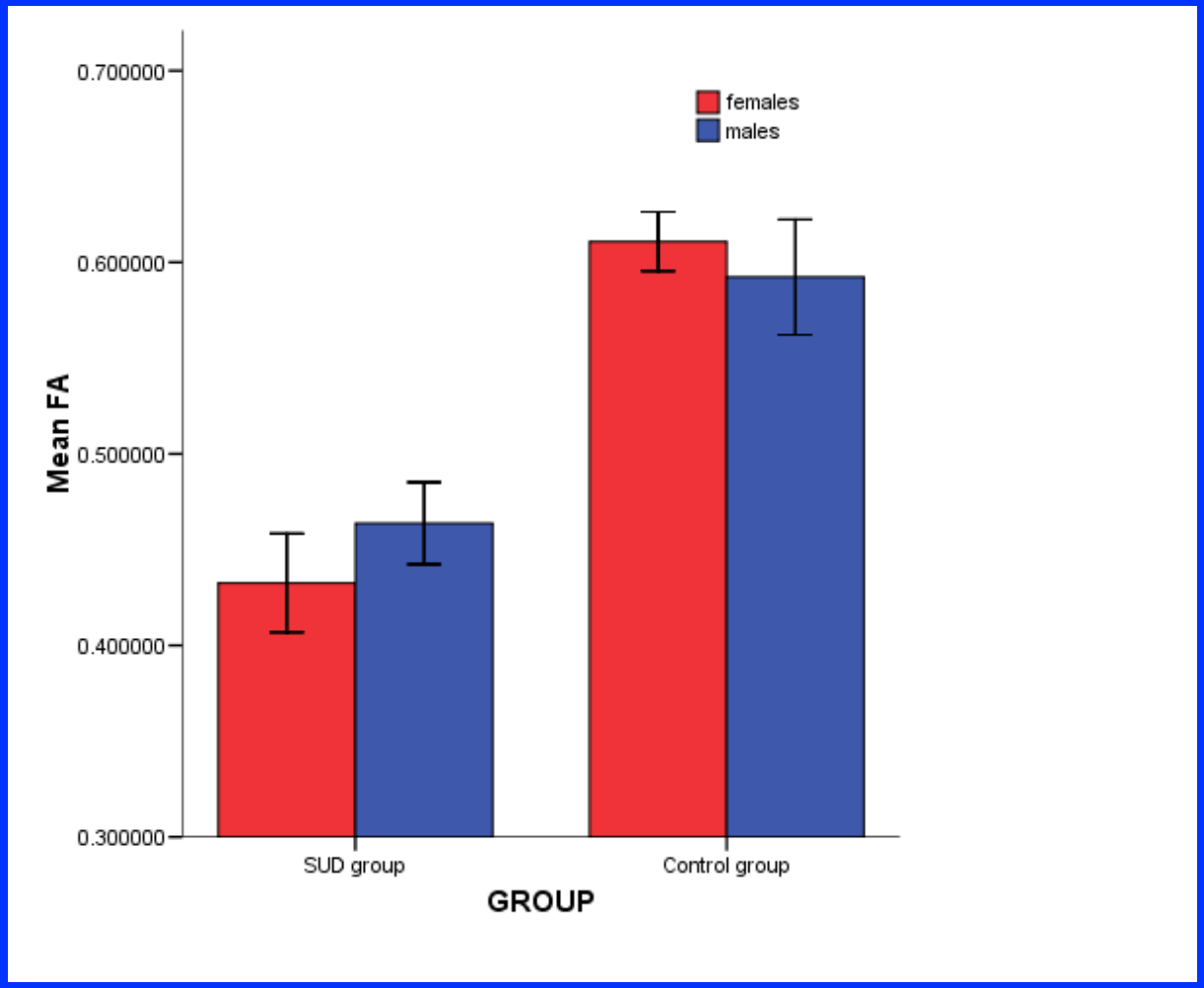
Longitudinal fasciculus



White Matter Microstructure in Adolescents with SUDs



Thatcher, Clark et al (July 2010) Drug and Alcohol Dependence


0.700000
0.600000
0.500000
0.400000
0.300000
Mean FA
females
males
SUD group
Control group
GROUP

DTI FA Microstructure: Regional

Subjects: ages 14-19 years old

- Adolescent SUD (n=35)
- Matched Controls (n=20)

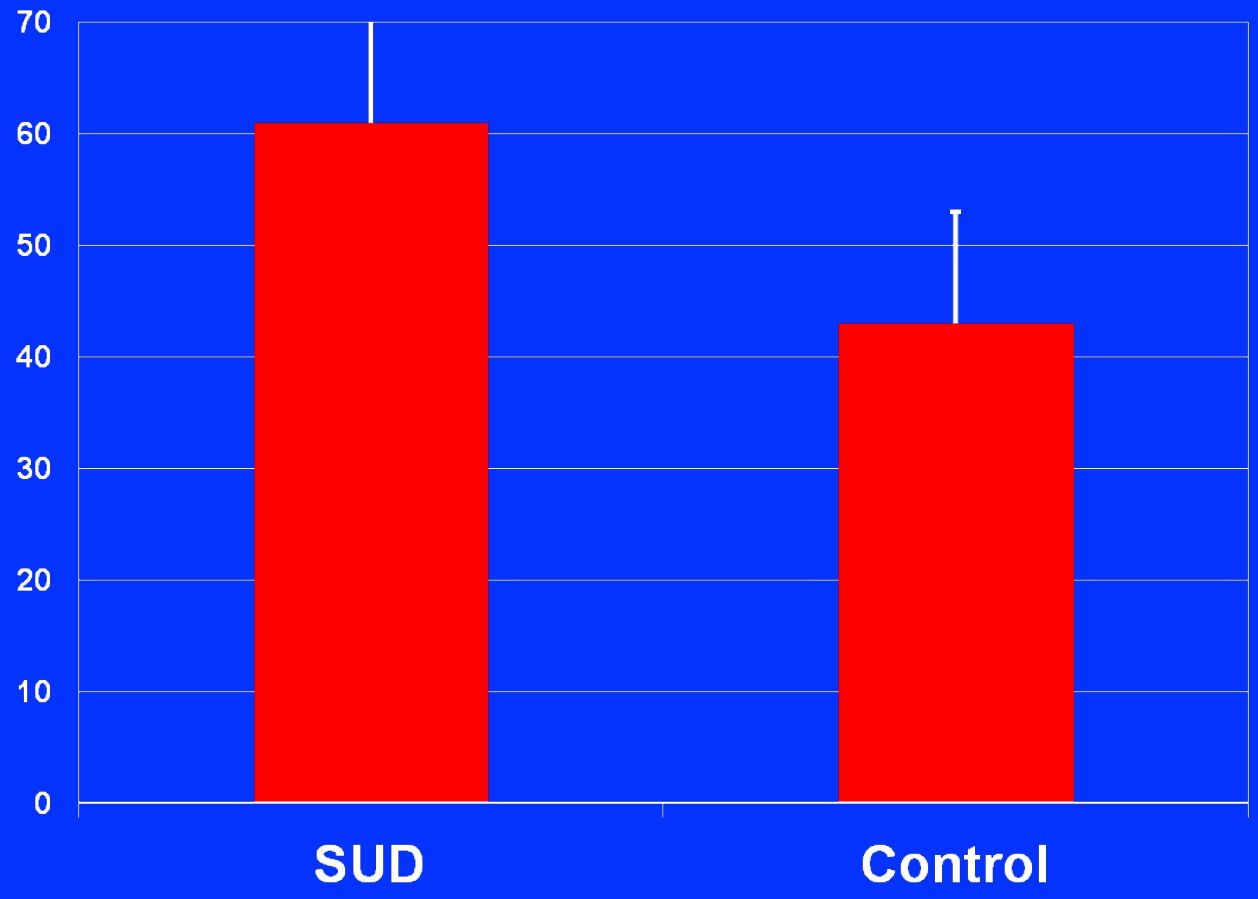
MRI Analysis: FreeSurfer

Measures

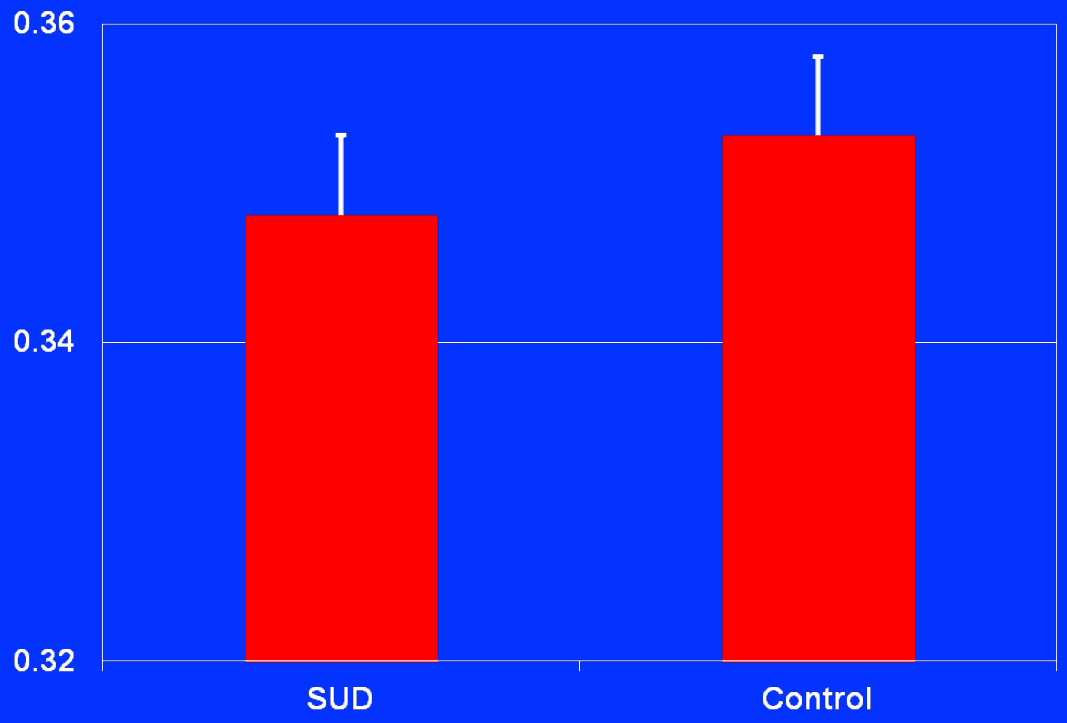
- Behavior Rating Inventory of Executive Function
- Regional white matter volumes
- Regional white matter DTI FA

Clark et al. Addiction 2011

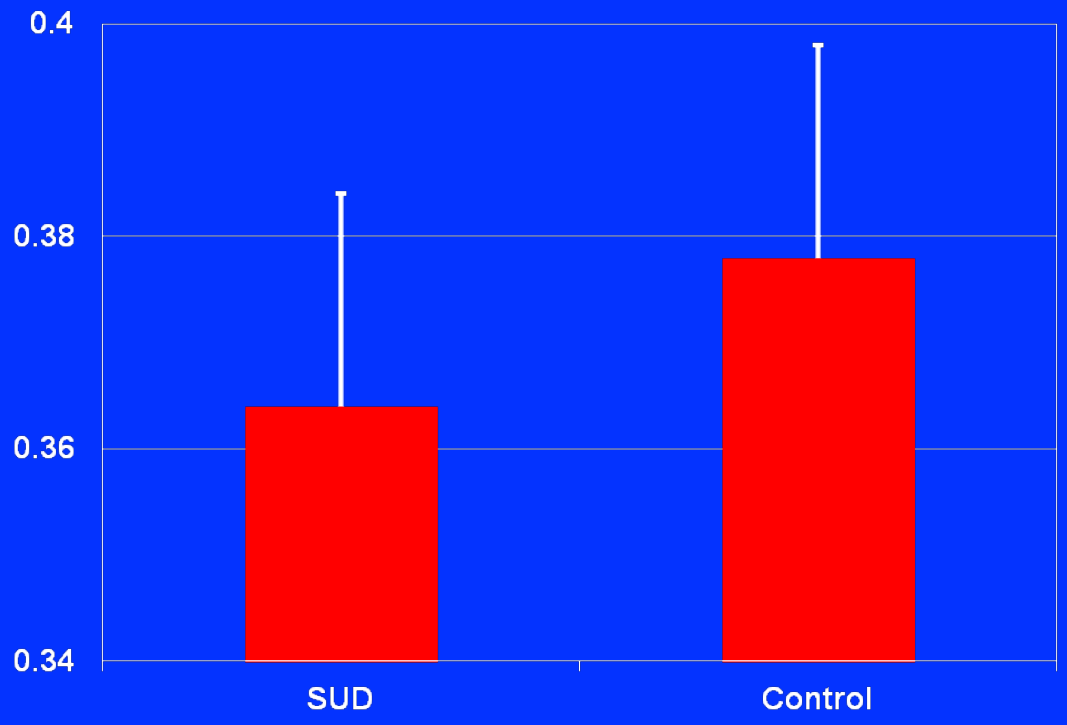
BRIEF scores



Prefrontal FA by DTI



Parietal FA by DTI



Regional DTI FA x BRIEF

Region	r
• Prefrontal	-.30*
• Parietal	-.36**

*significant @ p<.05; **<.01

DTI FA and Treatment Outcome

Subjects: Adolescents SUD ages 14-18

Intensive Outpatient SUD Program

MRI Analysis: FreeSurfer

Measures

- Baseline regional white matter DTI FA
- 6-month Rutgers Alcohol Problem Index

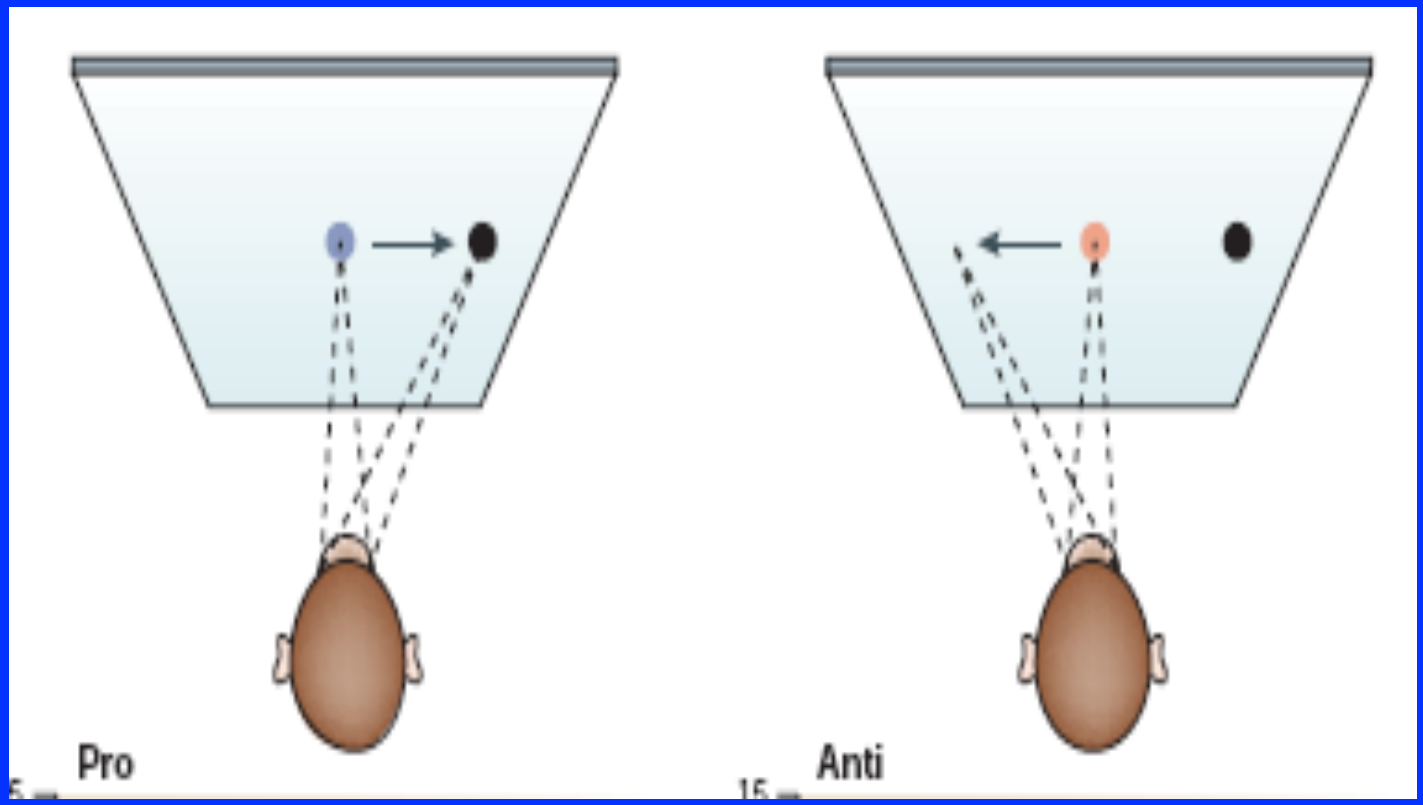
Results

- PFC FA x 6-mo RAPI: r= -.49**
- Parietal FA x 6-mo RAPI: r= -.42**

Chung, Clark et al. Psychol Addictive Beh 2012

Behavioral regulation: Anti-saccade task

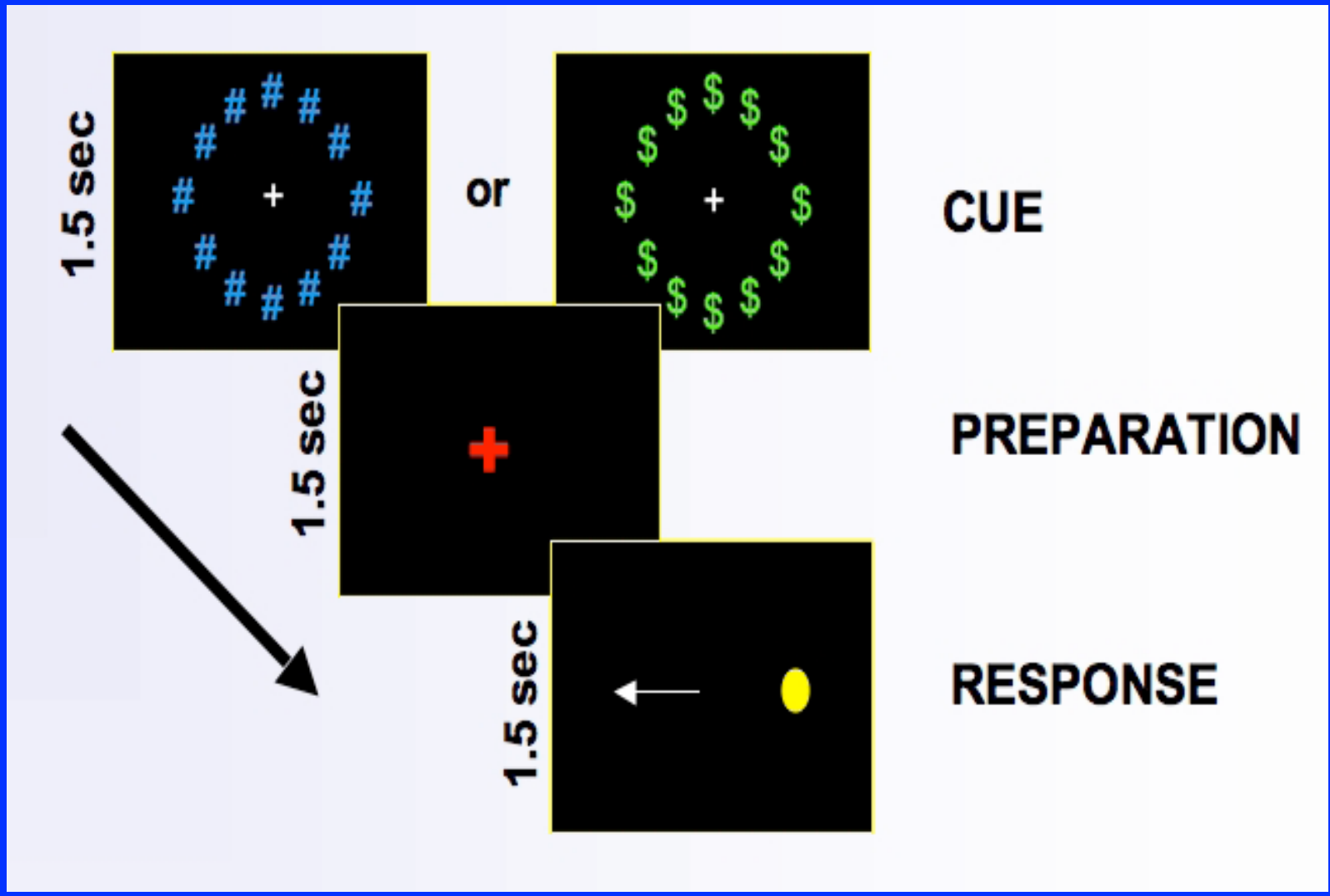
Look to the “mirror” location of the target



PRO-SACCADE **ANTI-SACCADE**

Munoz & Everling, 2004

Antisaccade Task: Reward & Neutral Trials



Geier, Luna et al (2010) Cerebral Cortex

Adolescent SUD and AS Task

Subjects: Matched Groups

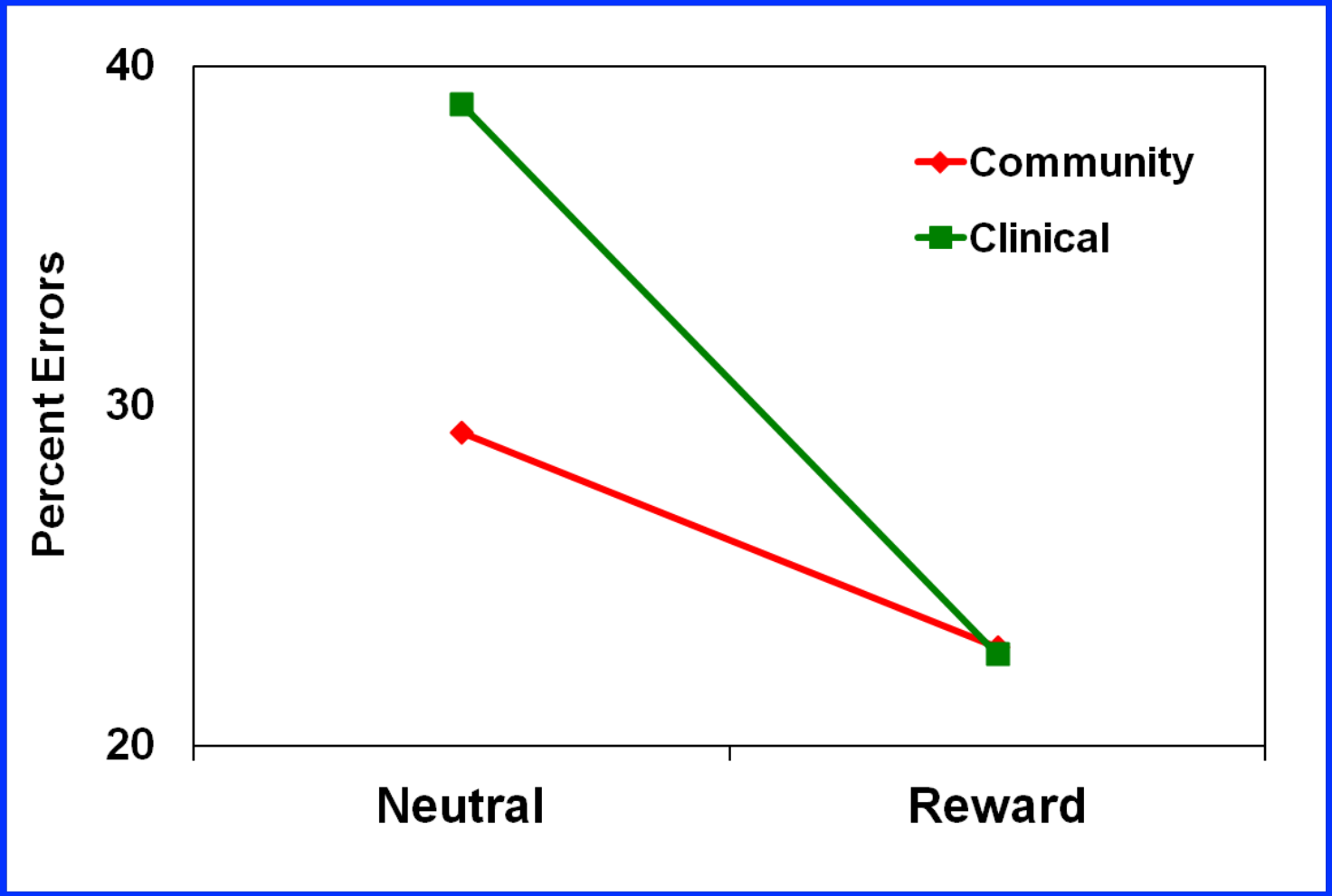
- Adolescent SUD (n=12)
- Controls (n=12)

Results

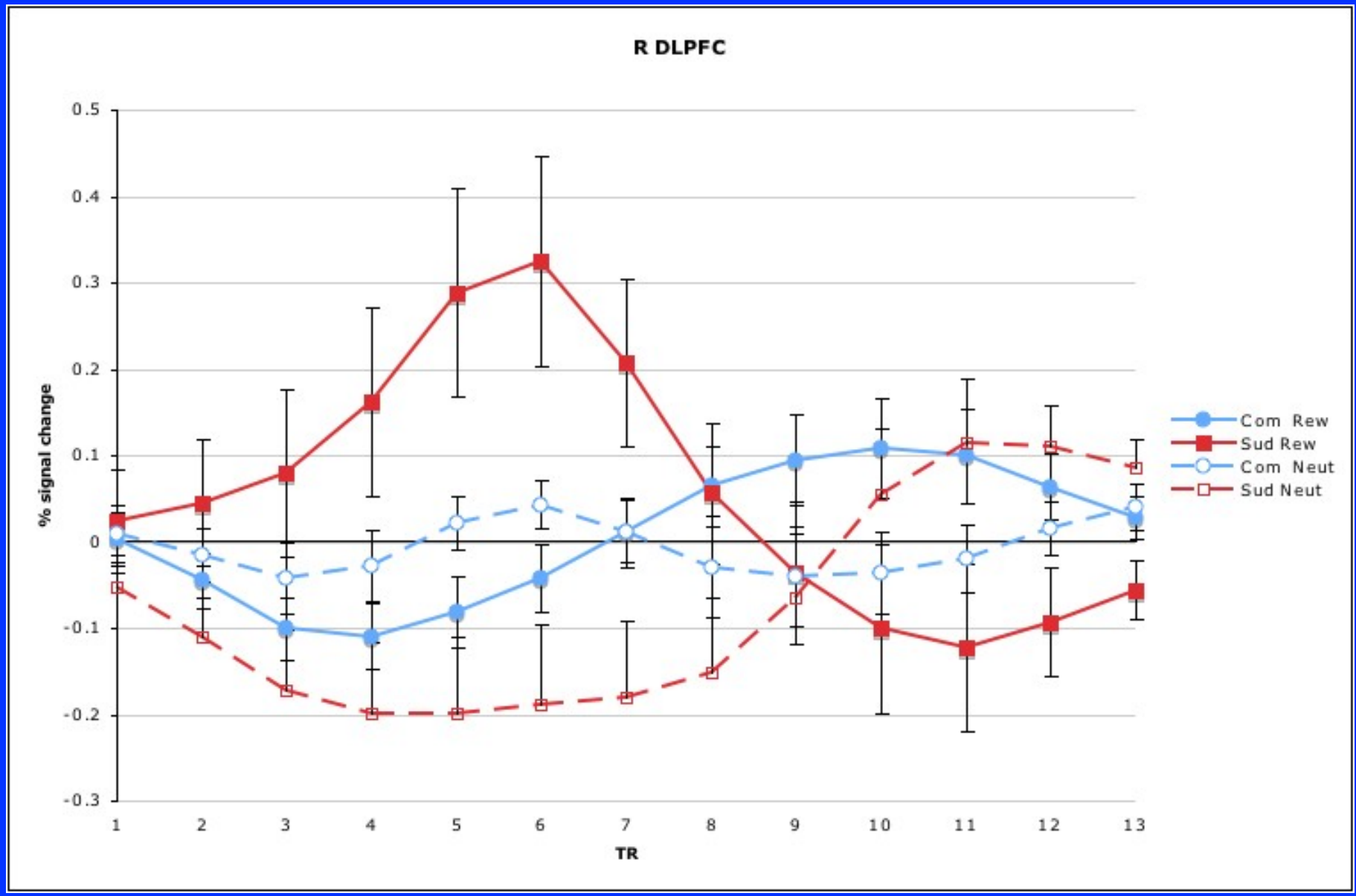
- % correct
  - SUD group: neutral < reward
  - Controls: neutral vs reward not sig different
- Prefrontal activation differences

Chung, Clark et al. DAD 2011

Behavioral Data: Antisaccade Error Rate



Chung, Clark et al. Drug & Alcohol Dependence 2011


R DLPFC
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
% signal change
1
2
3
4
5
6
7
8
9
10
11
12
13
TR
Com Rew
Sud Rew
Com Neut
Sud Neut

Adolescent SUD & frontoparietal network

- Smaller PFC white matter volume
- Disorganized white matter
  - PFC, Parietal cortex, SLF
- Deficits in executive function correlate with disorganized PFC & Parietal WM
- Disorganized PFC and Parietal WM predicts poorer treatment outcome
- Behavioral inhibition task

  Less PFC activation - neutral condition (worse performance)

  More PFC activation - reward condition (normal performance)

Conclusions

- High risk teens may have brain maturation deficits
- Teens can have substance induced brain deficits
- While studies not definitive, teen abstinence is safest option
- Short-term incentives enhance abstinence
- SUD teens achieving abstinence remain vulnerable

Further Reading

Clark, Chung, Pajtek, Zhai, Long & Hasler

Neuroimaging methods for adolescent substance use disorder prevention science.

Prevention Science 2013

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