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

<table>
<thead>
<tr>
<th></th>
<th>Left</th>
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<tbody>
<tr>
<td>AUD</td>
<td>4.0 ± 0.4</td>
<td>4.1 ± 0.4</td>
</tr>
<tr>
<td>Controls</td>
<td>4.6 ± 0.6</td>
<td>4.5 ± 0.5</td>
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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

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

Psychological Dysregulation

DBD

SUD
Macrostructure

Subjects
• Adolescent AUD (n=14)
• Matched controls (n=28)

Results
• PFC white matter volume
• PFC gray matter volumes
• PFC gray x maximum drinks
  \[ R = -0.78 \text{ (n=14), } p<.001 \]

DeBellis, Clark et al. ACER 2006
Prefrontal white matter volumes in adolescents
(mean cm3 ± SD)

Diffusion Tensor Imaging

Free diffusion

Restricted diffusion

Isotropic diffusion

Anisotropic diffusion
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%
<table>
<thead>
<tr>
<th>Region</th>
<th>r</th>
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<tbody>
<tr>
<td>Prefrontal</td>
<td>.24*</td>
</tr>
<tr>
<td>Cingulate</td>
<td>.23*</td>
</tr>
<tr>
<td>Parietal</td>
<td>.21*</td>
</tr>
<tr>
<td>Temporal</td>
<td>.25*</td>
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*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
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
Prefrontal FA by DTI
<table>
<thead>
<tr>
<th>Region</th>
<th>r</th>
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</thead>
<tbody>
<tr>
<td>Prefrontal</td>
<td>-.30*</td>
</tr>
<tr>
<td>Parietal</td>
<td>-.36**</td>
</tr>
</tbody>
</table>

*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: \( r = -0.49^{**} \)
- Parietal FA x 6-mo RAPI: \( r = -0.42^{**} \)

Chung, Clark et al. Psychol Addictive Behav 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
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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