

Using Functional Connectivity to Identify Risk For and Consequences of Alcohol Use During Adolescence

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Brain & Behavior: Effects of Alcohol or Risk?

Youth/Adults with AUD

- Impairments in cognition and decision making
- Abnormalities in brain structure
- Abnormal brain response during tasks
- Atypical white matter microstructure
- Atypical cerebellar connectivity

-AND-

-AND-

-AND-

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Youth at risk for AUD

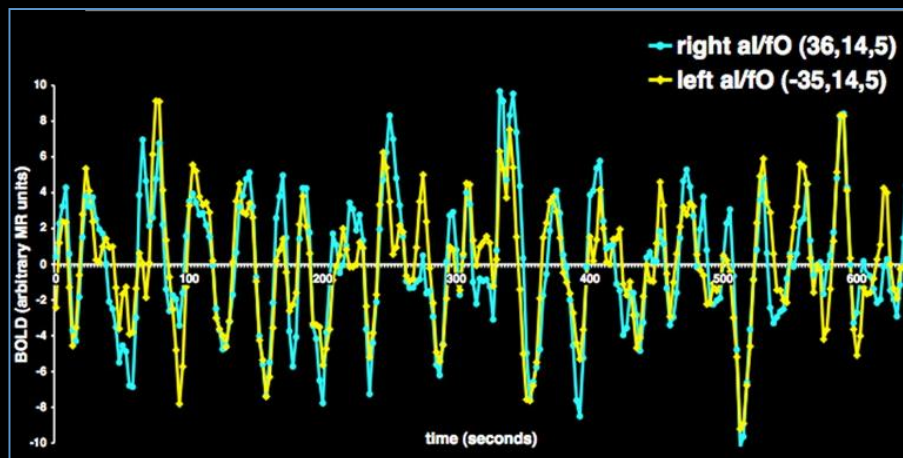
- Impairments in cognition and decision making
- Abnormalities brain structure
- Abnormal brain response during tasks
- Atypical white matter microstructure
- Atypical fronto-cerebellar connectivity during task

Is it possible that premorbid abnormalities in underlying neural circuitry are contributing to increased risk for AUD?

What is Resting State Functional Connectivity (rs-fcMRI)?

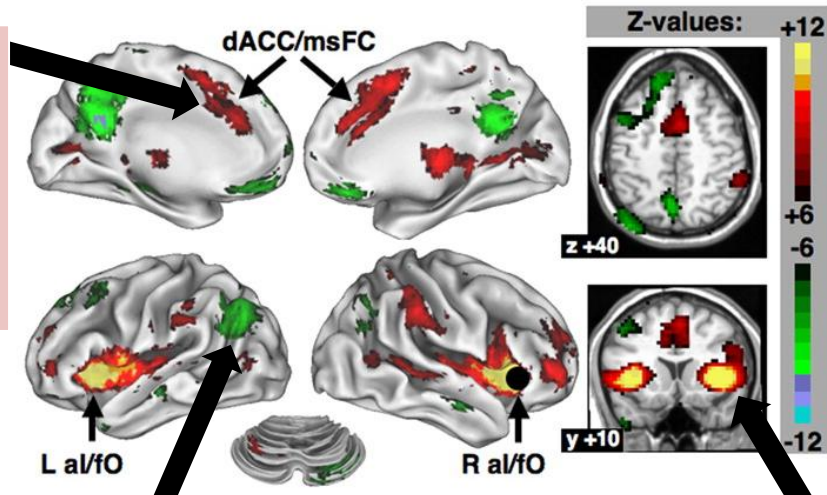
- Rs-fcMRI measures correlated blood oxygen level dependent (BOLD) signal fluctuations between a particular seed region and all other regions in the brain during rest
- Regions whose activity is significantly correlated with the seed region are considered “functionally connected”
- Benefits:
 - Unburdened by experimental design, subject compliance, and task performance
 - Very consistent results across studies; identified “networks”

Resting State Functional Connectivity Magnetic Resonance Imaging (rs-fcMRI)



Temporal fluctuations in BOLD signal from two brain regions

Positive correlation between BOLD signal here and the BOLD signal of the seed region

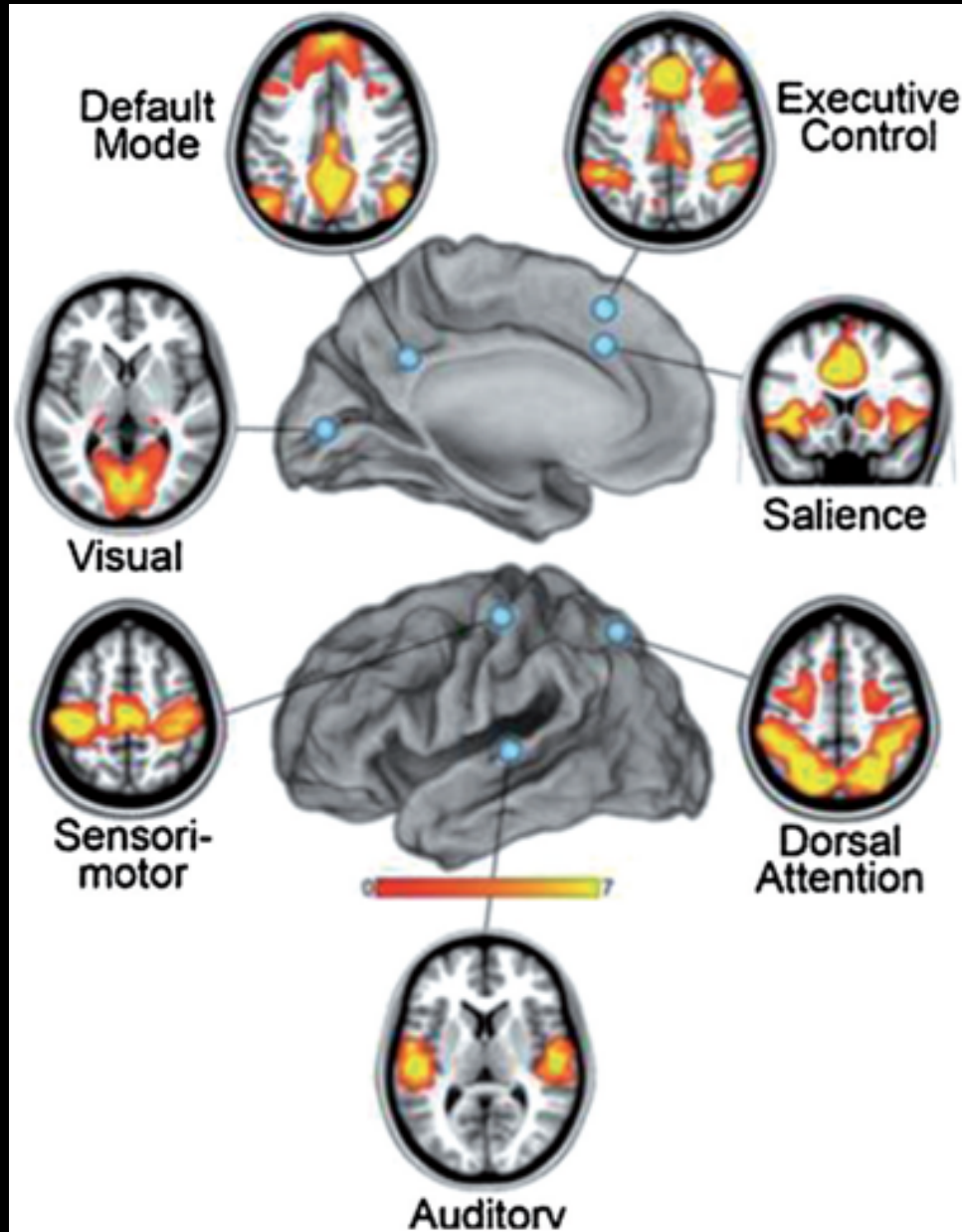


Voxelwise functional connectivity map for a seed region in the right anterior insula/frontal operculum

Region negatively correlated with the seed region

Dosenbach, 2008

seed region



AR Whitfield-Gabrieli S, Ford JM. 2012.
 Annu. Rev. Clin. Psychol. 8:49–76

Adapted from Raichle 2011

Sample Demographics

	FHP (N = 47)	FHN (N = 50)
Age	14.57 (1.31)	14.34 (1.28)
Pubertal Status ^a	3.66 (.98)	3.48 (.87)
IQ ^b	111.19 (9.90)	113.28 (11.32)

	Emergers (N = 7)	Controls (N = 7)
Age at Baseline	14.15(.61)	14.00(.76)
Pubertal Status ^a	3.57(.79)	3.29(.76)
IQ ^b	110.29(8.67)	108.57(7.09)

^a Pubertal Development Scale, ^b WASI (2-subtest)

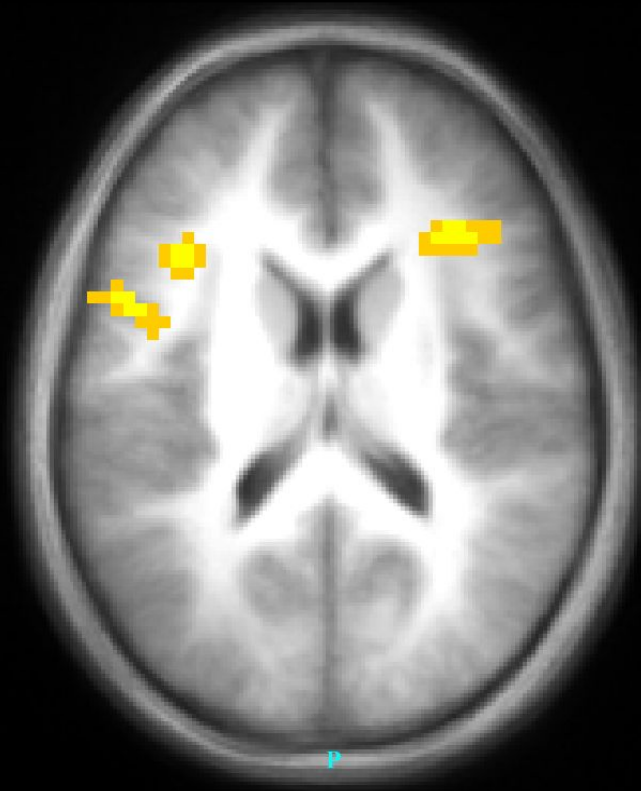
Emergers:

- Binge alcohol use prior to 16 years of age (Mean age of binge = 15.17)

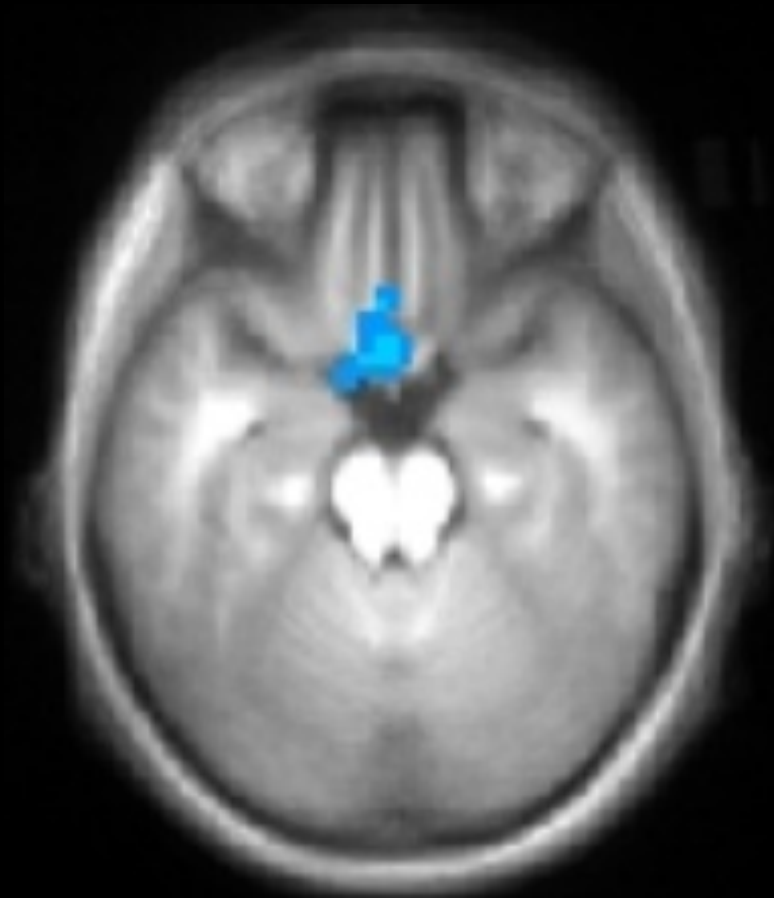
Controls:

- Substance-naïve until at least 16 years of age (Mean age of controls = 16.77)

FHP Youth Show Less Segregation Between Nucleus Accumbens (NAcc) and Prefrontal Cortex

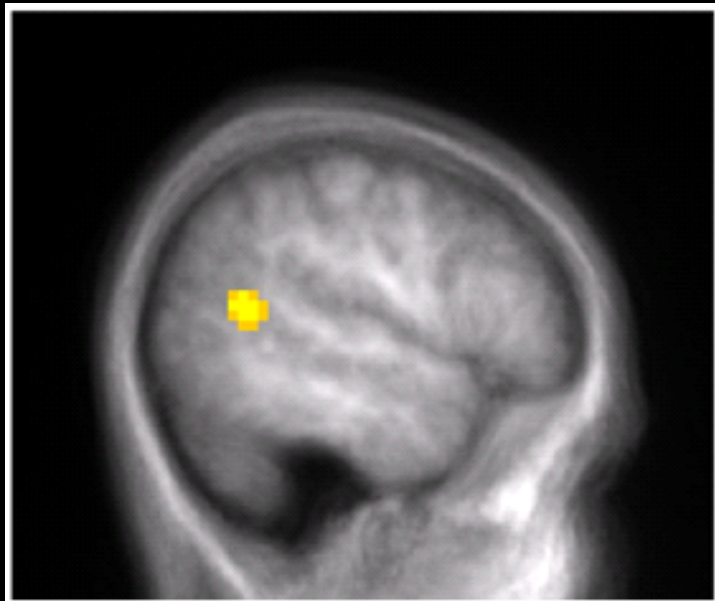


FHP Youth Show Less Integration Between Right NAcc and Orbitofrontal Cortex

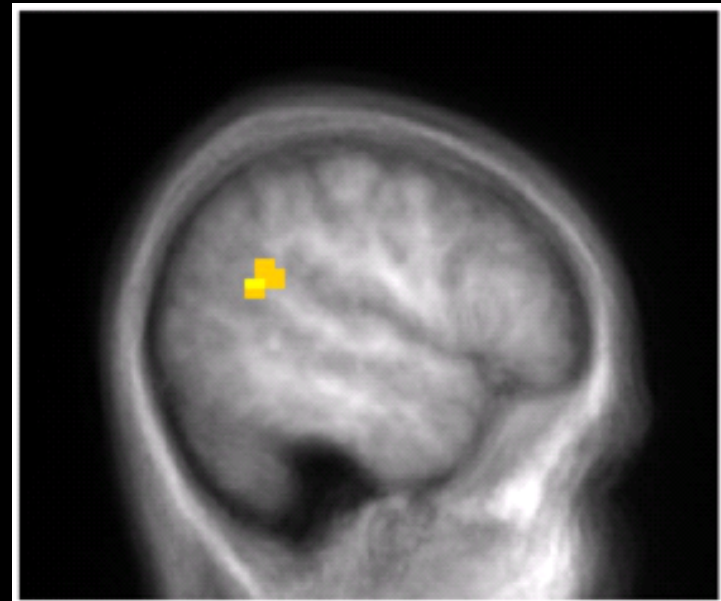


NAcc Connectivity with Superior Temporal Lobe

Both FHP youth and baseline activity of young bingers demonstrate less negative connectivity (less segregation) between the right NAcc and right superior temporal lobe

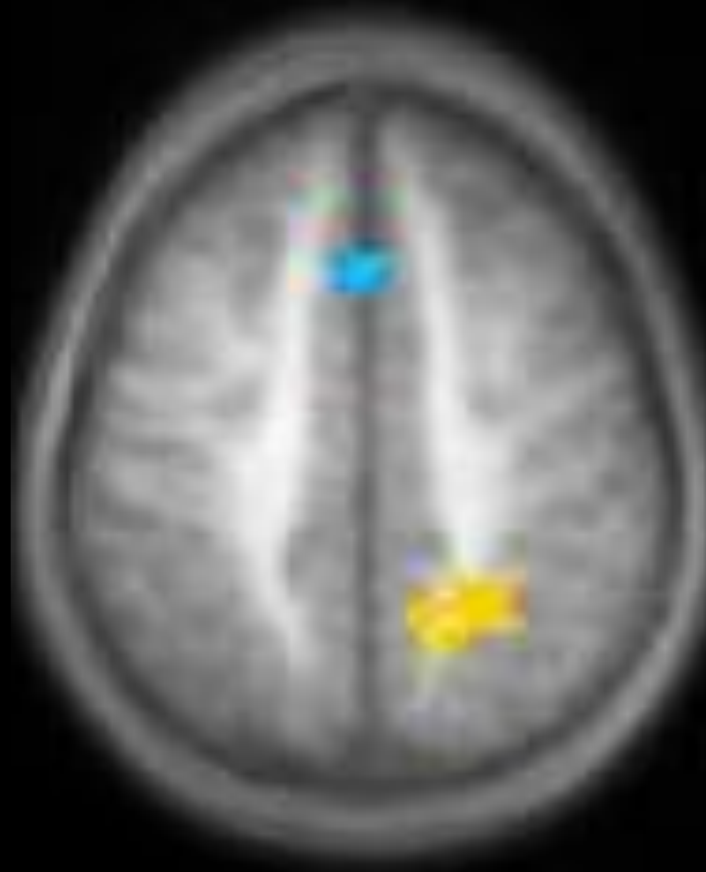


FHP > FHN



Emerging young bingers >
older non-using controls

Early Bingers Show Reduced Segregation Between NAcc and Default Mode Network at Baseline



What Happens to Connectivity After Binge-Level Alcohol Use?



Binge Drinking Reduces Connectivity Between NAcc and Prefrontal Cortex



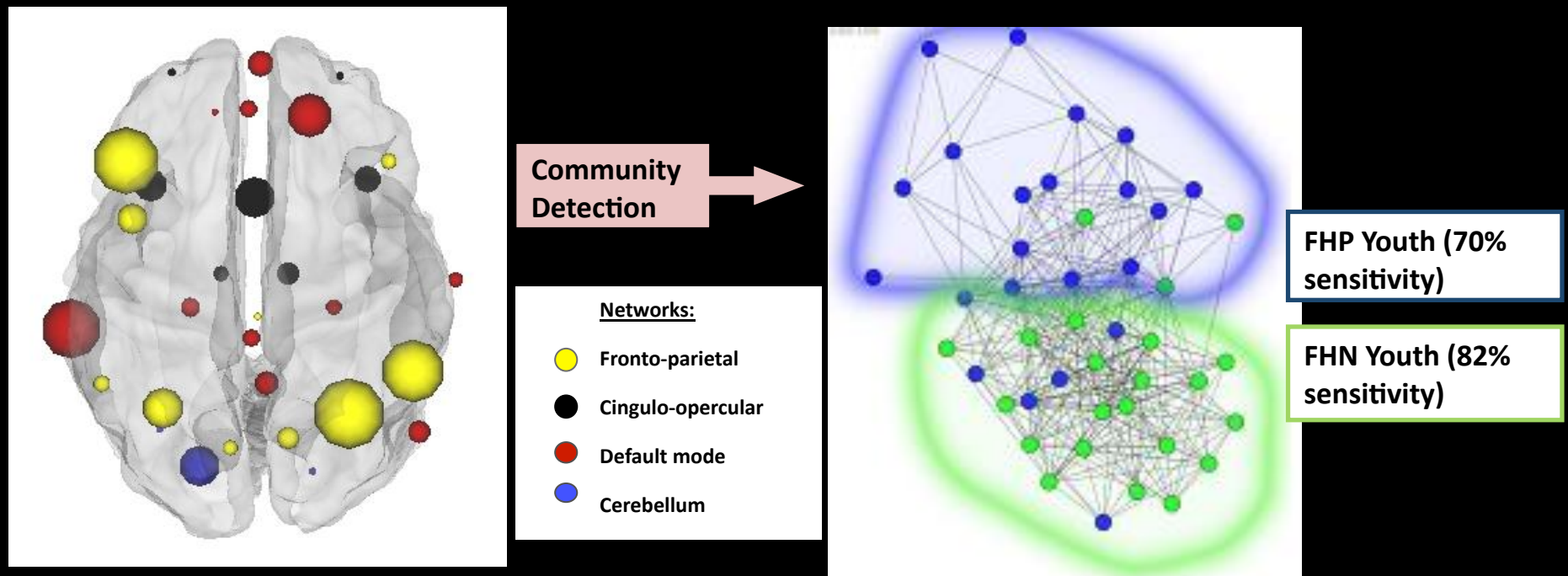
Binge drinking sample (≥ 3 binges/3 months: $N=9$; mean age at revisit = 16.11 ± 1.12)

What Else Can Be Done
With rs-fcMRI Data?

Rs-fcMRI Patterns Can Distinguish FHP and FHN Youth

Based on the cross-correlation of 52 previously-identified regions-of-interest for each subject (smaller preliminary sample):

- Identified the 200 connections that best differentiated FHP and FHN youth; most prominent differences seen in the fronto-parietal network (see below)
- Comparing every subject's connection values, a distance matrix shows how similar any one subject is to any other subject, based on these 200 connections
- Using community detection analyses, we show that FHP and FHN youth can be separated into groups based on connectivity differences



*Summed connection weights (z-scores) for 200 connections to respective regions

Conclusions

- FHP youth and youth who emerge early into binge drinking show altered connectivity of the NAcc
- Differences in functional connectivity, particularly in fronto-parietal circuitry, can differentiate FHP and FHN groups
- Results suggest that abnormalities in neural circuitry may exist prior to alcohol use onset
- Adolescent binge-drinking alters NAcc functional connectivity
- Given the role of brain networks in subserving executive and emotional/appetitive functioning, premorbid abnormalities in related circuitry may heighten the risk for developing an AUD

Limitations & Future Directions

- Results are preliminary
- Future studies will examine associations between atypical functional connectivity and behavior
- Important to continue to prospectively examine how brain functioning changes after initiation of alcohol use, as well as to determine which of these premorbid abnormalities are predictive of use
- Important to integrate rs-fcMRI findings with other measures (e.g., neuropsychological functioning, structural connectivity, etc.) to identify risk phenotypes

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