Developmental trajectories of reward and habitual brain circuits are differentially linked to alcohol use in youth

Petrie DJ, Parr AC, Foran W, Calabro F, Luna B

Department of Psychiatry, University of Pittsburgh,Pittsburgh, PA

Introduction

- Prominent theories of addiction suggest that an imbalance between reward-driven, goal-directed, and habitual behaviors is associated with the progression to Alcohol Use Disorder (AUD; Everitt & Robbins, 2016).
- These behaviors are supported by distinct corticostriatal circuits involving the nucleus accumbens (NAcc), caudate, and putamen (Balleine & O'Doherty, 2010).
  - These regions have been implicated in the initiation and maintenance of alcohol use behaviors (Koob & Volkow, 2010).
- Corticostriatal circuits undergo significant maturational changes from adolescence to adulthood (Parr et al., 2021).
  - Adolescent alcohol use has been linked to alterations in developmental trajectories (Dawson et al., 2008).
    - It remains unclear whether alterations reflect preexisting vulnerabilities or consequences of alcohol exposure.
- Despite these findings, the relationship between the maturation of these overlapping circuits and alcohol use during development remains unclear.

We used the National Consortium on Alcohol and Neurodevelopment in Adolescence – Adulthood (NCANDA-A) sample to assess the relationship between developmental trajectories of corticostriatal circuitry and longitudinal patterns of alcohol use.

Methods

Participants

- NCANDA-A study integrates neuroimaging with substance use assessments using an accelerated longitudinal design (*n* = 822, ages 12–21 at baseline, 1-9 visits per participant; Brown et al., 2015).

Alcohol Use

- Participants completed the Customary Drinking and Drug Use Record (CDDR; Brown et al., 1998).
  - CDDR #21 ("*During past year, how many days did you drink alcohol")*
  - CDDR #30 ("*During past year, how many times have you consumed 4+ [females]/ 5+ [males] drinks within an occasion")*

Resting-state functional connectivity (FC)

- Whole-brain networks for regions of interest (ROIs) including the NAcc, caudate, and putamen were generated by extracting seed-based time series from resting-state scans and computing voxel-wise correlations.
- Correlation maps were averaged within Gordon parcels (Gordon et al., 2016) to create network measures for each ROI.
- We then fitted generalized additive mixed models (GAMMs) to each seed-parcel pair to test for age-related change in connectivity, adjusting for multiple comparisons using Bonferroni correction.
  - Only significant age effects were retained.
- For these significant models, we extracted predicted trajectories of age-related change and used k-means clustering to group similar developmental patterns within each seed network.

Statistical analyses

- GAMMs were used to capture non-linear trends in the data, examining developmental trajectories of past-year alcohol use, past-year binge episodes and corticostriatal FC. Additional analyses examined age-varying effects of corticostriatal FC and past-year alcohol use, and whether FC was associated with drinking initiation.

Conclusions

Our findings show that individual differences in striatal FC are uniquely linked to alcohol use across development. Increases in NAcc/caudate FC followed drinking onset, while higher putamen FC was linked to more drinking days after age 23, suggesting that maturation of reward processes in NAcc/caudate FC may be associated with initiation, whereas habitual processes in putamen FC may reflect (habitual) maintenance behaviors in adulthood. Using repeated measures of striatal connectivity with detailed drinking histories, we identified distinct brain profiles associated with adolescent and young adult alcohol use.

References & Support

References

NIH National Institute on Alcohol Abuse and Alcoholism

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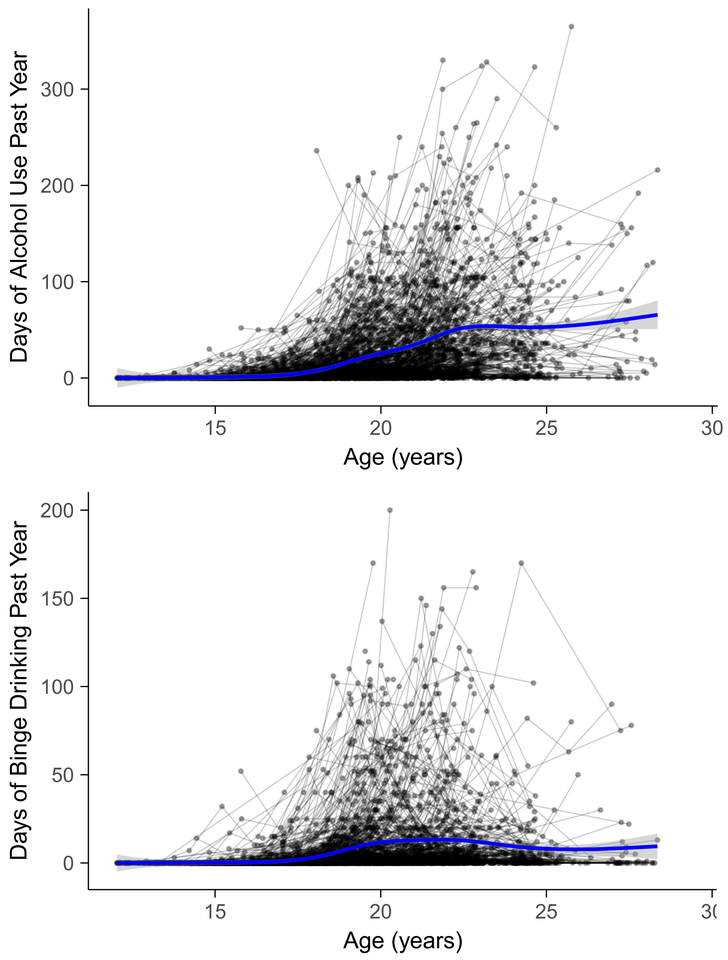
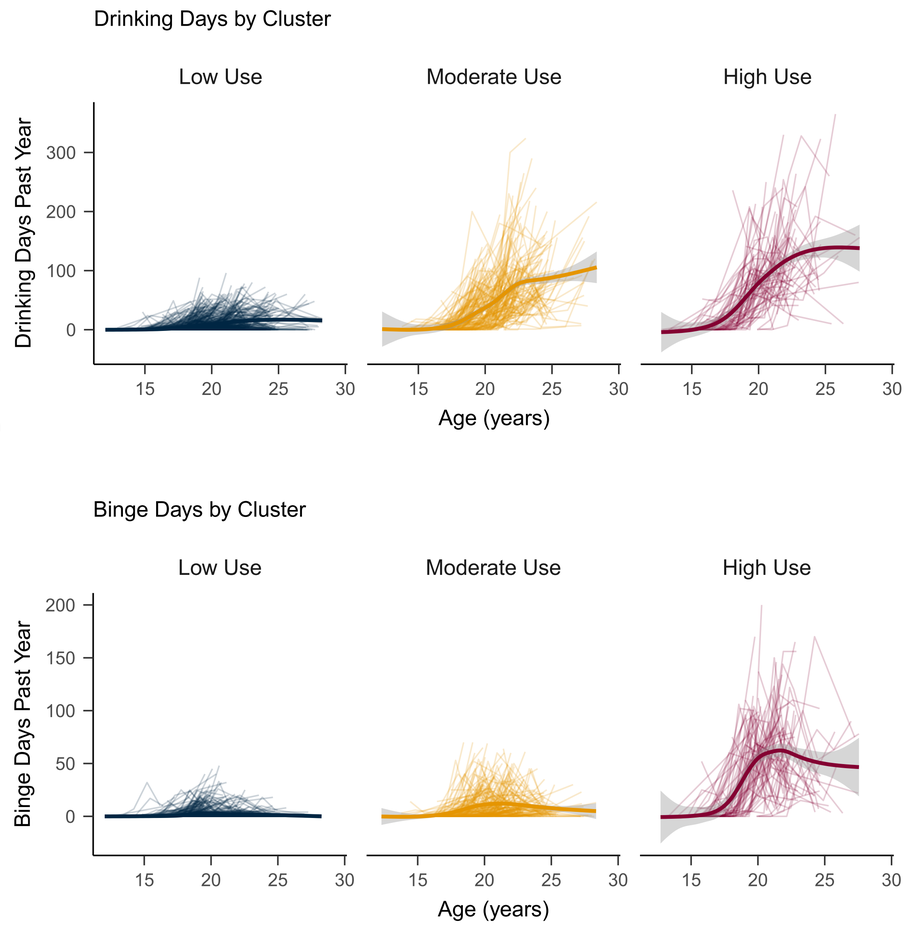
NCANDA-A Adolescence-Adulthood

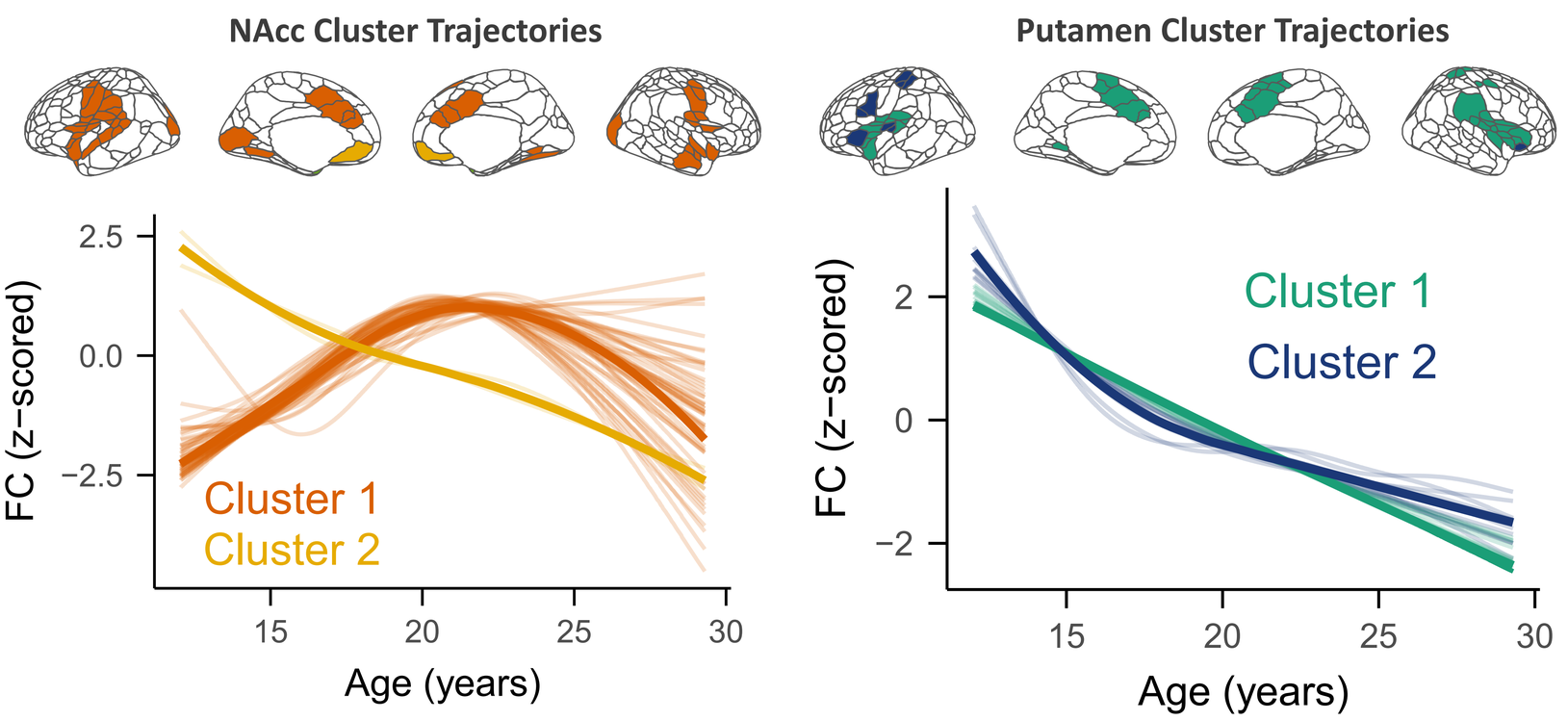
Alcohol use rises in adolescence; clustering identifies high-risk subgroup





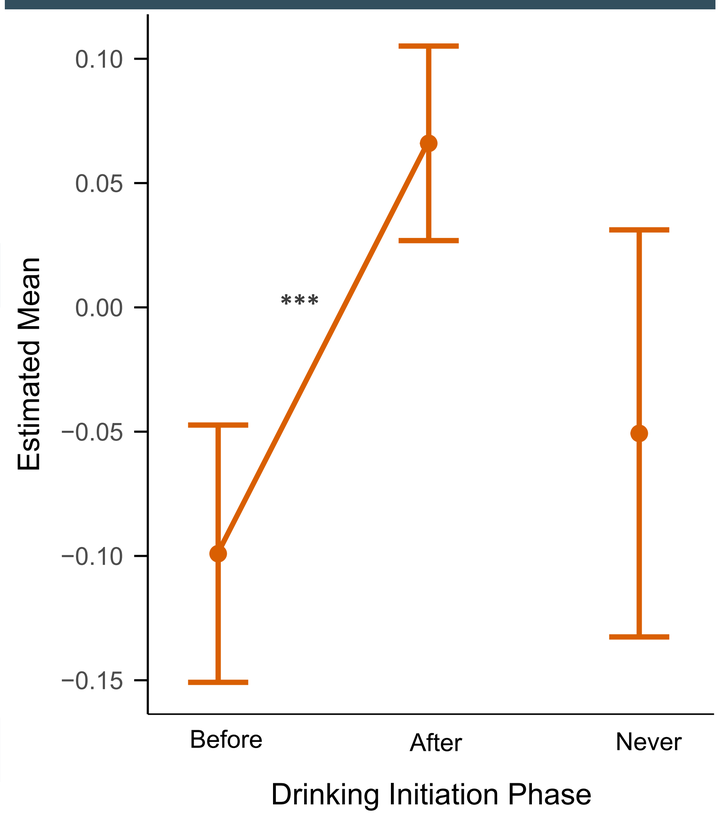
Left: Average developmental trajectories of past-year alcohol use (edf = 3.90, $F = 252.10$, $p < 0.001$) and past year binge drinking (edf = 3.91, F = 123.90, p < 0.001) **Right:** To explore alcohol use patterns, we applied k-means clustering to features of drinking behavior (e.g., average, peak, and variability in drinking days and binge episodes) from CDDR responses across visits.

Corticostriatal FC trajectories cluster into different developmental patterns



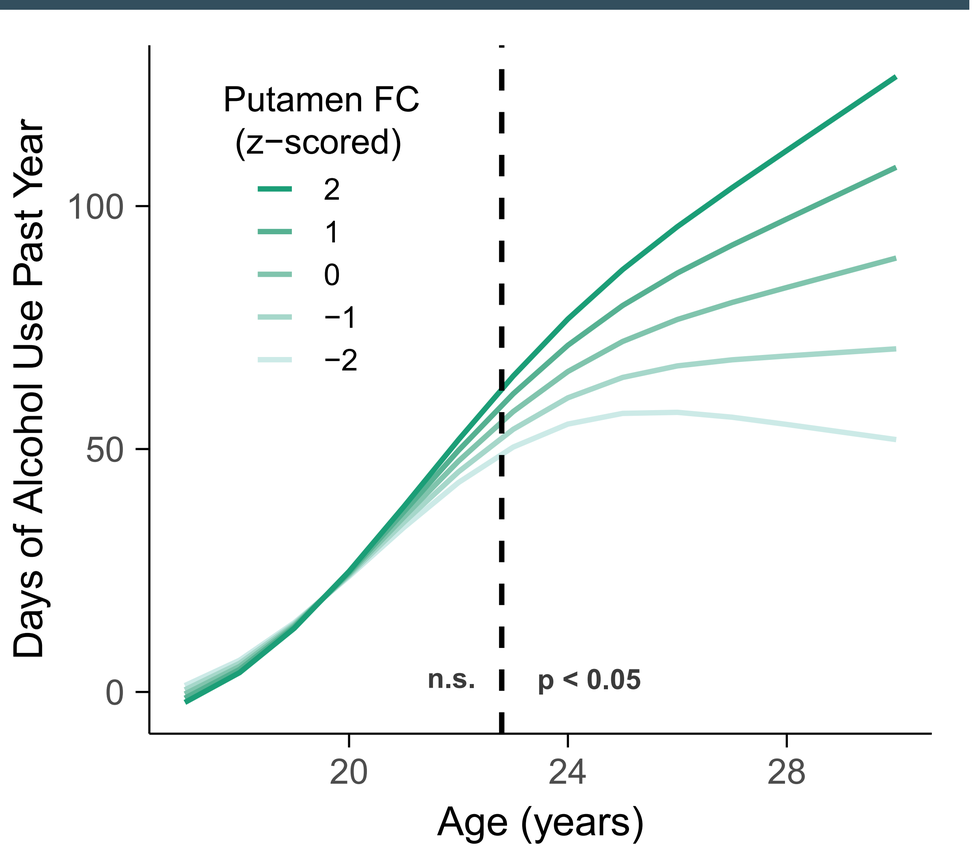
At the population level, 142 out of 999 parcels derived from the three striatal seeds showed significant age-related effects after Bonferroni correction. K-means clustering within each striatal network (NAcc, caudate, putamen) identified two clusters per network with distinct developmental trajectories. In the NAcc, cluster 1 showed an inverted-U trajectory, while cluster 2 exhibited a steady decline. Both putamen clusters demonstrated decreasing connectivity, with differences in slope suggesting varying rates of developmental change.

Drinking onset liked to higher NAcc FC



We tested FC differences by drinking onset using a GAMM with seed-cluster, drinking phase, and their interaction (controlling for non-linear age). NAcc Cluster 1 connectivity increased after drinking onset.

Greater putamen FC linked to more drinking days



Differences in putamen FC to cortical regions were associated with variation in alcohol use after approximately 23 years (edf = 3.37, F = 4.42, p < 0.001), with higher FC linked to more drinking days.