A Multi-Modal Neuroimaging Study on the Prediction of Alcohol Sipping Patterns in Children: Results from the ABCD Study

Ana Ferariu (af682@drexel.edu)
Department of Psychology, Drexel University, 3201 Chestnut Street
Philadelphia, PA 19104 USA

Hansoo Chang (hc842@drexel.edu)
Department of Psychology, Drexel University, 3201 Chestnut Street
Philadelphia, PA 19104 USA

Alexei Taylor (at3334@drexel.edu)
Department of Psychology, Drexel University, 3201 Chestnut Street
Philadelphia, PA 19104 USA

Fengqing Zhang (fz53@drexel.edu)
Department of Psychology, Drexel University, 3201 Chestnut Street
Philadelphia, PA 19104 USA

Abstract:

As individuals transition from childhood to adolescence, alcohol sipping and drug initiation increases. Early alcohol exposure can lead to risky alcohol consumption and alcohol dependence later in life. We previously used data from the Adolescent Brain and Cognitive Development Study (ABCD) to detect latent alcohol sipping trajectories over time. In the current study we examined brain imaging data measured at baseline as a potential biomarker in predicting alcohol sipping patterns. We used several popular machine learning methods on structural (sMRI) and resting-state functional magnetic resonance imaging data (rs-fMRI) separately and then combined to detect important features that can predict alcohol sipping in children aged between 9 and 14. Ridge regression showed the best performance and results show that the latent alcohol sipping groups can be better predicted by rs-fMRI data than by sMRI data at baseline.

Keywords: multi-modal brain imaging; alcohol sipping; machine learning; longitudinal analysis

Introduction

Adolescence is a critical period for brain and body development, and early structural and functional brain changes can influence future risky behaviors, including alcohol and drug use (Honarvar et al., 2023; May et al., 2022; Squeglia et al., 2017). Brain development in adolescence involves a peak in gray matter volume followed by a decline into adulthood, while white matter volume steadily increases until mid-to-late adolescence before slowing (Lebel et al., 2012). Neuroanatomical predictors of adolescent alcohol consumption include thinner cortices, lower gray matter volume, and decreased surface area in regions linked to reward and executive function, although findings are inconsistent (Honarvar et al., 2023). Functional connectivity, particularly in networks like the default-mode, salience, frontoparietal, and dorsal attentional networks, has also been studied as a predictor of transitioning from minimal to heavy drinking in adolescents (Fede et al., 2019; Ramage et al., 2015).While much research has focused on brain alterations in adolescents who use alcohol, there is a gap in understanding abnormalities that precede alcohol initiation, especially in longitudinal studies (Feldstein Ewing et al., 2014). Our study aims to use machine learning techniques to identify potential risk factors for adolescent drinking patterns over time by analyzing multimodal neuroimaging data.

Methods

Alcohol sipping

We used three previously identified latent classes representing alcohol sipping trajectories over time in the Adolescent Brain and Cognitive Development (ABCD) study, categorized as no-sip group (84.22%, N=9700), low-sip group (5.34%, N=615) and high-sip group (10.44%, N=1202) (Ferariu et al., under revision). Figure 1. shows the average curve of the three latent classes representative of alcohol sipping behavior over time in the ABCD cohort.

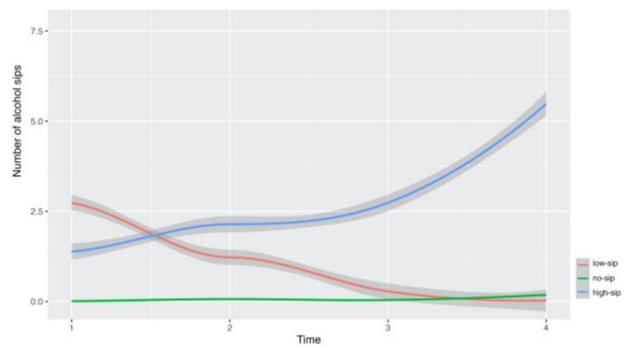

Figure 1: The average curve for the latent classes representing the sipping behavior over time in the ABCD cohort and the corresponding standard error.

Brain imaging data

We obtained multimodal brain imaging data including T1-wighted structural brain imaging (sMRI) of 34 regions of interest (ROIs) in each hemisphere based on the Desikan atlas and resting state functional brain imaging (rs-fMRI) for average pairwise ROIs correlations between and within 13 cortical networks parcellated based on the Gordon atlas (auditory network, audN; cingulo-opercular network, CON; cingulo-parietal network, CPN; default-mode network, DMN; dorsal attention network, DAN; fronto-parietal network, FPN; retrosplenial temporal network, RTN; salience network, SN; sensorimotor hand network, SMNh; sensorimotor mouth network, SMNm; ventral attention network, VAN; visual network, visN). The neuroimaging data was pre-processed by the ABCD study using FreeSurfer software (Fischl, 2012), while the pipeline can be found elsewhere (Hagler et al., 2019). We selected the participants with complete baseline sMRI data (N=10741) and rs-fMRI data (N=10096), as well as latent class data (N=11517). We excluded participants with poor or incomplete Freesurfer deconstruction and subjects who should consider clinical referral.

Alcohol sipping patterns prediction with multivariate pattern analysis

We ran multivariate pattern analysis (MVPA) by training several popular machine learning methods, such as support vector machines (SVM) with radial kernel, LASSO, Elastic net and Ridge regression. We conducted binary classification for 3 different contrasts: no-vs-high sip, no-vs-low sip and low-vs-high sip. For each contrast, data were split into a training set (75% of the data) and test set (the remaining 25%). We used a 10-fold cross validation on the training set, extracting the parameter of regularization that provided the minimum mean cross-validation error and then we evaluated the performance on the test set. We assessed model performance from accuracy, sensitivity, specificity and the area under the receiving operating characteristic (ROC) curve (AUC). Since the data was imbalanced, we over- and under-sampled the data during the training stage. The models were run with sMRI data and rs-fMRI data separately and with both modalities combined.

Results

Results show that the latent alcohol sipping groups can be better predicted by rs-fMRI data than by sMRI data at baseline. Additionally, combining both modalities did not yield significant improvement in prediction accuracy. The model with ridge regression performed best on all three contrasts. Table 1. shows the prediction performance for the three contrasts using ridge regression. The prediction accuracy was significantly better than random guessing for all three contrasts ($p < 0.001$). Moreover, the 95% confidence interval for the AUC of all three contrasts was above 0.5.

Table 1: Prediction accuracy of ridge regression

	No-vs-high sip	No-vs-low sip	Low-vs-high sip
Accuracy	0.57	0.60	0.57
Sensitivity	0.51	0.50	0.59
Specificity	0.58	0.60	0.53
AUC	0.55	0.55	0.56

Figure 1. shows the top 15 predictive brain imaging features for each of the three contrasts and their corresponding coefficients with 95% confidence intervals. For positive coefficients, a larger functional network correlation would increase the likelihood of belonging to the group with more alcohol sipping over time. Negative coefficients imply that a larger functional network correlation would decrease the likelihood of belonging to the group with more alcohol sipping over time or in other words it would increase the likelihood of belonging to the group with less alcohol sipping over time.

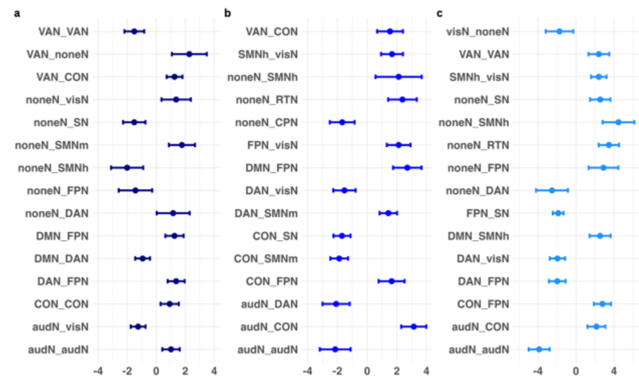

Figure 1: Top 15 features based on the magnitude of the coefficients for the (a) no-vs-high sip, (b) no-vs-low sip and (c) low-vs-high sip contrasts with corresponding 95% confidence intervals.

Positive correlations at baseline between the DMN, SN and FPN were indicative of participants belonging to the high-sip group rather than no-sip group. Additionally, participants exhibiting positive DMN-DAN, SN-DAN and CON-FPN correlations at baseline were more likely to belong to a group that sips more on average over time. Conversely, those with SN-DAN anticorrelations at baseline were more likely to be in the group that sips less or not at all over time. There were some inconsistencies in the coefficients for the DMN - SN correlation and DAN - FPN correlation across the three contrasts, which might arise from the small difference in the average number of alcohol sips between the low-sip and high-sip groups.

Conclusion

Resting-state functional connectivity can serve as a biomarker for predicting alcohol sipping patterns as individuals transition from childhood to adolescence. Previous research has focused on single modalities or older adolescents, but our study examines multimodal brain imaging features in participants as young as 9-10 years old to predict sipping behavior (Honarvar et al., 2023). However, a limitation is the young age of the participants, which may affect data quality due to participants' difficulty in staying still. Moreover, incorporating demographics, family characteristics, personality traits, and psychopathology could enhance prediction.

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