Drug and Alcohol Dependence 265 (2024) 112489

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Neurostructural features predict binge drinking in emerging adulthood: Evidence from a 5-year follow-up study

Jose Manuel Pérez-García [c], Samuel Suárez-Suárez [a,d,*], María Soledad Rodríguez González [b,d], Socorro Rodríguez Holguín [a,d], Fernando Cadaveira [a,d], Sonia Doallo [a,d]

[a] Department of Clinical Psychology and Psychobiology, Faculty of Psychology, Universidade de Santiago de Compostela, Galicia, Spain
[b] Department of Social, Basic Psychology and Methodology, Faculty of Psychology, Universidade de Santiago de Compostela, Galicia, Spain
[c] Department of Educational Psychology and Psychobiology, Faculty of Education, Universidad Internacional de La Rioja, Logroño, Spain
[d] Instituto de Psicoloxía (IPsiUS), Universidade de Santiago de Compostela, Spain

ARTICLE INFO

Keywords:
Adolescence
Emerging adulthood
Binge drinking
Prospective longitudinal study
Follow-up
Brain structure

ABSTRACT

Background: Binge drinking (BD) involves consuming large amounts of alcohol within a short timeframe, leading to a blood alcohol concentration of 0.08 g/dL or above. This pattern of alcohol consumption is prevalent among young adults and has significant implications for brain structure and subsequent drinking behaviors.
Methods: In this prospective longitudinal study, we employed zero-inflated negative binomial regression models to examine whether various neurostructural features (i.e., volume, surface area, cortical thickness) of brain regions involved in executive and emotional/motivational processes at the age of 18–19 could predict number of BD episodes five years later, at ages 23–24, once participants were expected to complete their university degree. Specifically, we recorded magnetic resonance imaging (MRI) data from 68 students who completed both the baseline MRI and follow-up alcohol use assessment, with the aim of analyzing the predictive value of these neurostructural characteristics five years later.
Results: The analysis revealed that a larger surface area in the caudal division of the right middle frontal gyrus was significantly associated with a higher incidence rate of BD episodes (IRR = 2.24, 95 % CI = 1.28–3.91, p = 0.005). Conversely, a smaller surface area in the right caudal anterior cingulate cortex was associated with a higher incidence rate of BD episodes (IRR = 0.61, 95 % CI = 0.44–0.85, p = 0.004).
Conclusions: These findings suggest that specific neurostructural characteristics during adolescence can predict BD behaviors in young adulthood. This highlights the potential of neuroimaging to identify individuals at risk for developing problematic alcohol use.

1. Introduction

The term "adolescence" encompasses a developmental stage between childhood and adulthood, marked by profound multidimensional transformations across behavioral, emotional, and physiological domains. This period is further characterized by an upswing in risk-taking behaviors, a pursuit of novel sensations, and inherent challenges in emotional regulation (Crone and Dahl, 2012; Telzer, 2016). Neurobiological theories of adolescent development propose that the elevated prevalence of risk behaviors among adolescents, compared to other age groups, fundamentally arises from an asynchrony in brain maturation processes. In this sense, subcortical areas linked to affective and motivational processes, such as the amygdala and nucleus accumbens (NAcc), mature earlier than regions intimately involved in executive functions (i.e., decision-making, planning, and inhibitory control), such as the prefrontal cortex (Duijvenvoorde et al., 2016; Shulman et al., 2016; Wojciechowski, 2021). Thus, these theoretical proposals indicate that the imbalance between the developmental trajectories of motivational systems and cognitive control systems places adolescents in a particularly sensitive window for engaging in risky behaviors. A similar model has been suggested in the context of addiction, indicating that the imbalance between self-regulation and motivation processes makes the

* Correspondence to: Department of Clinical Psychology and Psychobiology, Faculty of Psychology, Universidade de Santiago de Compostela, Campus Universitario Sur, s/n, Santiago de Compostela, Galicia 15782, Spain.
E-mail addresses: josemanuel.perezgarcia@unir.net (J.M. Pérez-García), samuel.suarez@usc.es (S. Suárez-Suárez), msoledad.rodriguez@usc.es (M.S. Rodríguez González), rodriguez.holguin@usc.es (S. Rodríguez Holguín), fernando.cadaveira@usc.es (F. Cadaveira), sonia.doallo@usc.es (S. Doallo).

https://doi.org/10.1016/j.drugalcdep.2024.112489
Received 17 June 2024; Received in revised form 23 October 2024; Accepted 25 October 2024
Available online 30 October 2024

adolescent population particularly prone to involvement in risky behaviors, such as the use of alcohol or illicit drugs (Bjork and Pardini, 2015; Gladwin et al., 2011).

Within this neurodevelopmental phase, alcohol consumption raises significant concerns due to potential long-term health and well-being consequences (Lees et al., 2020; Squeglia and Gray, 2016). A substantial number of adolescents partake in risky and excessive alcohol consumption, particularly in European and North American countries (ESPAD, 2020; SAMSHA, 2023). Among the different patterns of alcohol consumption, one has primarily become widespread, known as binge drinking (BD). This pattern involves the consumption of large quantities of alcohol in one single occasion (Courtney and Polich, 2009; Kuntsche et al., 2017; Lannoy et al., 2021a; Maurage et al., 2020). The National Institute on Alcohol Abuse and Alcoholism (NIAAA, 2004) defines BD as the intake of high amounts of alcohol, resulting in a blood alcohol concentration of 0.08 g/dL or higher. This concentration is typically reached with the consumption of 70 g for men or 50 g for women of alcohol within an approximately 2–3-hour interval. According to the latest prevalence data from the leading international epidemiological reports, this pattern is most common in youth (ESPAD, 2020; SAMSHA, 2023). In the United States, for instance, 29.5 % of individuals aged 18–25 admit to having engaged in at least one episode of BD in the last 30 days, equating to approximately 10.3 million young people (SAMSHA, 2023). Likewise, findings from the primary European survey indicate that 34 % of students aged 15–16 reported engaging BD during the previous month (ESPAD, 2020). Importantly, BD has been associated to structural and functional brain abnormalities (Almeida-Antunes et al., 2021; Carbia et al., 2018; Lees et al., 2019; Pérez-García et al., 2022b), impairments in emotional processing (Lannoy et al., 2021b), and it can be considered a risk factor as well as an initial step for developing alcohol use disorders (AUD) (Addolorato et al., 2018; Bonomo et al., 2004; Crabbe et al., 2011; Olsson et al., 2016; Wechsler et al., 1994). Furthermore, this pattern of alcohol consumption has also been linked to the display of risky behaviors, such as participating in fights, driving under the influence, engaging in unsafe sexual practices, as well as having poorer academic performance (Hingson, 2010; Miller et al., 2007; Moure-Rodríguez et al., 2016; Páramo et al., 2023; Swahn et al., 2004; Wechsler et al., 1994).

In recent years, several prospective longitudinal studies have suggested that brain morphology may serve as an indicator of preexisting vulnerabilities preceding and predicting the initiation and escalation of alcohol use (for a comprehensive review, see Boer et al., 2022; Spear, 2018). Also, prior investigations have indicated that early alcohol consumption during adolescence constitutes the major risk factor for alcohol dependence in adulthood (Kranzler and Soyka, 2018). In this regard, some of the neurocognitive abnormalities associated with BD pattern may precede its onset and could predict it, while others emerge with it and worsen or increase its effects with persistent use of alcohol (Lees et al., 2019). Exploring which of these abnormalities can serve as early indicators of vulnerability to AUD would contribute to the identification of risk profiles on which to focus preventive strategies in healthcare, education, and family settings.

Taking into account the previous considerations, we employed a prospective design to examine whether the structural features (i.e., volume, surface area, and cortical thickness) of brain regions associated with cognitive control and emotional-motivational processing at the age of 18–19 (at baseline) predict BD consumption upon completing their university stage (ages 23–24). Our focus was primarily on those regions that, in a recent previous systematic review, have consistently shown anomalies related to BD in adolescents and emerging adults (i.e., cingulate anterior, middle frontal gyrus, nucleus accumbens) (Pérez-García et al., 2022b). We hypothesized that structural characteristics in these regions at baseline will predict more episodes of BD five years later.

2. Material and methods

2.1. Participants and procedure

A sample of undergraduate students was enrolled in a prospective longitudinal study focusing on alcohol consumption. Evaluations were conducted at two distinct time points: initially through neuroimaging assessment when participants were between the ages of 18 and 19 years old (baseline), and subsequently, five years later, to assess their alcohol consumption (follow-up).

At baseline, 112 first-year university students underwent structural brain magnetic resonance imaging (MRI) scanning within the framework of a broader research project (for structural MRI results, see Pérez-García et al., 2022a; for task-related fMRI results, see Suárez-Suárez et al., 2020; for ERPs results, see Blanco-Ramos et al., 2019, 2022). These 112 volunteers completed a classroom questionnaire assessing alcohol and substance consumption, including the adapted version of the Alcohol Use Disorders Identification Test (AUDIT; Saunders et al., 1993) as well as sociodemographic information. Participants also completed a semi-structured interview in which quantity and frequency of alcohol use over the past 180 days were assessed via the Timeline Follow-Back calendar (TLFB; Sobell and Sobell, 1992), as well as personal and family history of psychopathological disorders (Symptom Checklist-90-Revised, SCL-90-R; González de Rivera et al., 1989).

BD was defined as the consumption of $\geq$ 70 g (for males) or $\geq$ 50 g (for females) of alcohol on a single occasion, leading to a blood alcohol concentration exceeding 0.08 g/dL. This measurement aligns with the criteria of 4/5 standard drinks as outlined in the NIAAA's definition of BD. Exclusion criteria for all participants at baseline included: chronic medical conditions that could affect neurocognitive functioning (diabetes, hypothyroidism, liver diseases, etc.), history of neurological disorders or brain injury, personal history of DSM-IV-TR Axis I and/or II diagnosed disorders, a score above 90th percentile in the Global Severity Index (GSI) or in two or more symptoms dimensions of the SCL- 90-R, family history of major psychopathological disorders in first- degree relatives (clinically diagnosed by a professional), family history of alcoholism or substance use disorders (at least two first- degree relatives or three or more first- or second-degree relatives), AUDIT scores > 20, use of psychoactive medications, use of illegal drugs in the last 6 months (except occasional consumption of cannabis; subjects who consumed >12 units of cannabis over the last 90 days were not included), non-corrected sensory deficits and MRI contraindications. All participants provided written informed consent and were compensated with 40 euros for their participation, which included interviews and the MRI baseline assessment. The study was approved by the Bioethics Committee of the University of Santiago de Compostela (Spain).

The sample size decreased over the course of the study, with 68 out of 112 subjects participating in both the baseline MRI scan and the follow-up assessment regarding alcohol use habits. Our focus was on the alcohol use information collected 5 years post-baseline assessment, specifically when participants were aged 23–24 years, serving as the primary outcome of interest. Remarkably, no statistically significant differences were observed between participants included in the final follow-up (n = 68) and those who discontinued the study (n = 44) concerning key parameters, including sociodemographic variables (gender, educational level, and socioeconomic status), related consumption variables (age of onset of alcohol use, AUDIT scores, and number of BD episodes) and neurostructural characteristics (volume, surface area, and cortical thickness) for any neuroimaging predictors evaluated (i.e., all p-values > 0.05).

2.2. Alcohol use variable (at follow-up)

The analysis in the present study was mainly interested in investigating one alcohol-related variable, associated with quantity and frequency of alcohol consumption. Specifically, the count variable "number of days of BD in the past six months" was extracted from the retrospective (covering a 180-day period) TLFB calendar used during the follow-up assessment.

2.3. Imaging data acquisition

MRI evaluation was performed at baseline using a Philips Achieva 3 T system (Philips Medical Systems, Best, NL) equipped with a 32-channel SENSE-HEAD coil (located at the University Hospital Complex of Santiago de Compostela). High-resolution anatomical images were acquired using a T1W/3D TFE (Turbo Field Echo) sequence with the following parameters: TR/TE = 7.7/3.4 ms, rotation angle = 8°, field of view (FOV) = 240 mm, voxel size = 0.8 mm^3, 200 transverse slices, acquisition time = 7 min. All images were stored in DICOM (Digital Imaging and Communications in Medicine) format and then converted to NIfTI (Neuroimaging Informatics Technology Initiative) format.

2.4. Image processing

Neuroanatomy is commonly evaluated through three key components: cortical thickness, surface area, and volume. Each component follows a distinct developmental trajectory (Vijayakumar et al., 2016; Wierenga et al., 2014). It has been suggested that cortical thickness and surface area are heritable but genetically and phenotypically independent (Panizzon et al., 2009; Winkler et al., 2010), and they are regulated by different processes (Panizzon et al., 2009; Rimol et al., 2012). Given the potential uniqueness of each component and to ensure all potential sensitivities are captured, this study considers and analyzes each measurement individually. All images were manually inspected to assess any potential artifacts or abnormal structural features prior to preprocessing steps.

The cortical surfaces and subcortical volumes were reconstructed and segmented using the FreeSurfer 7.2 image analysis suite (Dale et al., 1999; Fischl et al., 1999). The processing steps included the removal of non-brain tissue (Fischl et al., 2004), automated Talairach transformation, segmentation, intensity normalization (Sled et al., 1998), tessellation of the gray/white matter boundary (Fischl et al., 2001; Segonne et al., 2007), topology correction, and surface deformation. Anatomical gray matter parcellations were labeled with reference to the Desikan-Killiany atlas (Desikan et al., 2006), while subcortical segmentation was derived from Fischl et al. (2002). After completing all reconstructions, the resulting surfaces were used to calculate cortical thickness and surface area vertex-wise representations. Thickness is defined as the shortest distance between the gray-white matter and pial surfaces, while surface area was calculated as the sum of the area within a given region on the white surface (Mills et al., 2014; Raznahan et al., 2011; Winkler et al., 2010).

Based on a recent systematic review focusing on the specific brain correlates associated with BD in adolescence (Pérez-García et al., 2022b) we targeted the following bilateral regions of interest (ROIs): the

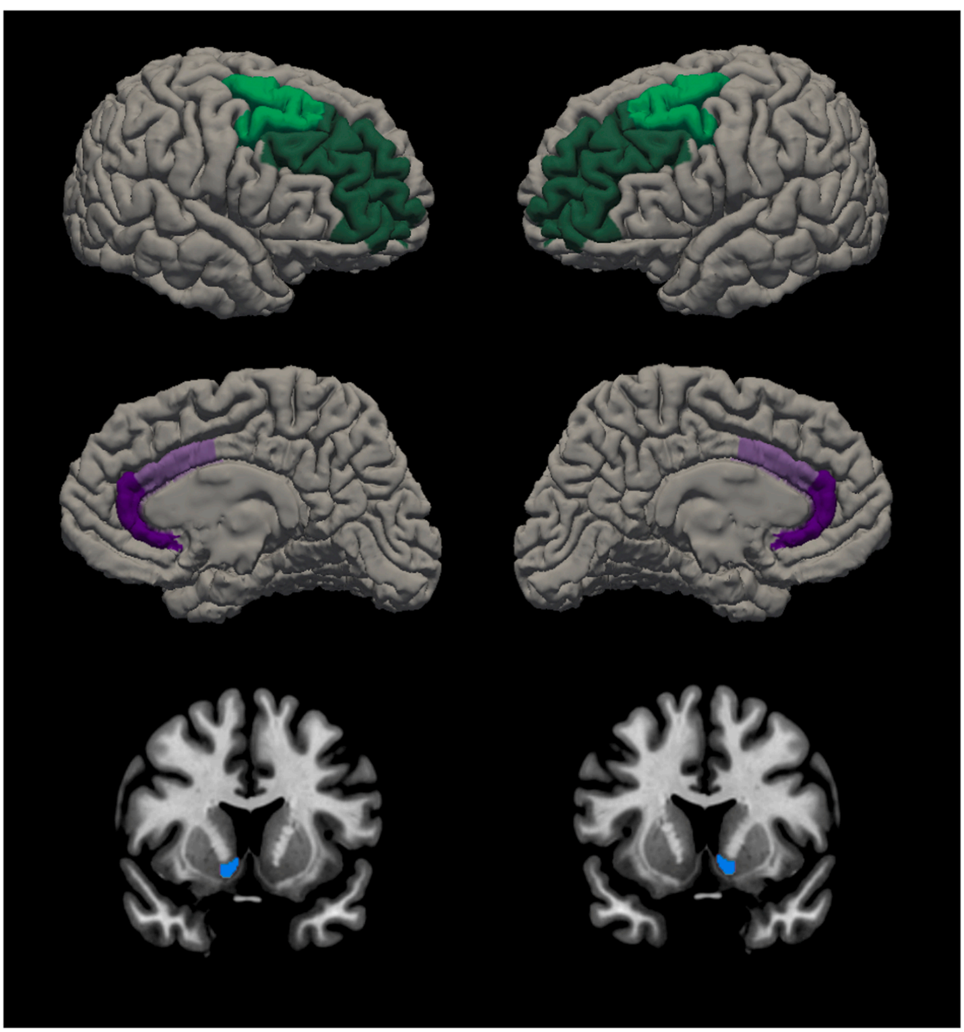

Fig. 1. Regions of interest (ROIs) for predictive models: Areas in green illustrate caudal (light) and rostral (dark) division of the MFG, areas in violet illustrate caudal (light) and rostral (dark) division of the ACC, while areas in blue show NAcc (displayed in radiological convention [i.e., left is right]).

anterior cingulate cortex (ACC) and middle frontal gyrus (MFG), defined according to the Desikan-Killiany atlas (Desikan et al., 2006), as well as the NAcc, delineated using the Aseg atlas (Fischl et al., 2002) (see Fig. 1). Cortical and subcortical structural values were computed in Freesurfer for each ROI, such as mean thickness (in mm), surface area (in mm^2), and subcortical volume (in mm^3), extracting this information from the statistical files. Subsequently, these data were exported to Stata for comprehensive statistical analysis. To ensure precision, the outputs at each stage underwent scrutiny based on the validation protocol established by the ENIGMA consortium (http://enigma.ini.usc.edu/protocols/imaging- protocols/).

2.5. Data analytic plan

Descriptive statistics, including demographic data and alcohol consumption, were computed. To model the number of BD episodes, several count data models were evaluated, considering both overdispersion and potential zero inflation (28 out of 68 participants; 41.2 %) in the primary outcome variable. The models considered included the zero-inflated Poisson, the zero-inflated negative binomial, and the negative binomial. A comparative analysis of model fit was conducted using the Akaike Information Criterion (AIC) and the Bayesian Information Criterion (BIC). The model fit analysis showed that the zero-inflated negative binomial had the lowest AIC (289.3808) and BIC (320.4539) compared to the zero-inflated Poisson (AIC = 492.611, BIC = 521.4646) and the negative binomial (AIC = 363.8617, BIC = 390.4958), indicating that the zero-inflated negative binomial model provided the best fit and was the most appropriate model for our data. This approach was selected because it effectively addresses both the overdispersion in the data and the high proportion of zero responses, which could not be adequately modeled using traditional Poisson or negative binomial models. Thus, the zero-inflated negative binomial regression model was employed to predict the number of BD episodes from neurostructural features (surface area, cortical thickness, volume) of brain regions involved in executive and emotional/motivational processes. For count models, the most common statistic is the incidence rate ratios (IRRs), which involves the number of events predicted to occur per unit time, in this case, the IRRs of BD episodes over the past 6 months. The goal of the zero-inflated negative binomial regression model was to determine if structural neuroimaging variables in the baseline assessment were significant predictors, five years later, of the number of BD days. Robust standard errors were applied to account for variability in the data. Covariates for all models included sex, and continuous measure of BD episodes at baseline. Additionally, the structural variables were standardized using z-score transformation before conducting the analyses.

To control for multiple comparisons, Bonferroni correction was applied for each measure (surface area, cortical thickness, volume) by adjusting the significance level based on the number of ROIs examined. As a result, only p-values < 0.00625 ($\alpha = 0.05/8$) for cortical regions (i.e., rostral and caudal divisions of the ACC and MFG) and p-values < 0.025 ($\alpha = 0.05/2$) for subcortical regions (i.e., NAcc) were considered significant. All statistical analyses were performed using Stata software, version 16.

3. Results

3.1. Sample characteristics

A total of 68 participants (39 females) had valid MRI data paired with follow-up assessment. Table 1 presents the sociodemographic characteristics and alcohol consumption habits of the study sample. The mean age at the follow-up assessment was 23.59 ± 0.31 years, with a mean total study duration of 59.58 ± 2.25 months. On average, participants in the follow-up experienced 7.32 ± 13.28 BD episodes in the past six months.

Table 1
Demographic and alcohol use characteristics of the final sample (mean ± SD).

N (females)	68 (39)
Age baseline MRI	18.62 (± 0.33)
Age follow-up assessment	23.59 (± 0.31)
Mean time (months) between baseline and follow-up	59.58 (± 2.25)
Number of BD episodes at baseline [a], past 6 months[b]	11.06 (± 13.98)
Number of BD episodes at follow-up [a], past 6 months[b]	7.32 (± 13.28)

[a] BD episode: consumption of ≥ 5 (female) or ≥ 7 (male) Spanish standard drinks (10 g of alcohol) on one occasion.
[b] In the six prior months to evaluation according to the alcohol Timeline Follow Back (TLFB).

3.2. Zero-inflated negative binomial regression analysis

Zero-inflated negative binomial regression analyses were conducted to predict the number of BD episodes using neurostructural features such as surface area, cortical thickness, and volume. The results, presented in Table 2, revealed significant associations between neurostructural characteristics and BD episodes.

Results on surface area revealed associations statistically significant in the MFG and ACC. Specifically, a greater surface area in the caudal division of the right MFG was associated with a higher incidence rate of BD episodes (IRR = 2.24, 95 % CI = 1.28–3.91, p = 0.005), indicating a positive relationship. Conversely, a smaller surface area in the right caudal ACC was linked with a higher incidence rate of BD episodes (IRR = 0.61, 95 % CI = 0.44–0.85, p = 0.004).

No significant associations were observed for cortical thickness or subcortical volume in any of the other ROIs examined.

4. Discussion

The findings of this prospective longitudinal study provide valuable insights into potential neurobiological predictors of BD episodes in young adults, specifically focusing on brain structural features identified during adolescence. Our results shed light on the complex interplay between neuroanatomical characteristics and subsequent alcohol consumption behaviors, offering implications for preventive interventions targeting at-risk populations. The use of zero-inflated negative binomial

Table 2
Zero-inflated negative binomial model predicting number of BD episodes from surface area, cortical thickness, and subcortical volume in each individual ROI.

ROI	Coefficient	Std. Error	IRR	95 % CI	Sig.
Surface Area					
Left caudal MFG	0.08	0.22	1.08	0.69–1.68	0.736
Right caudal MFG	0.81	0.28	2.24	1.28–3.91	**0.005***
Left rostral MFG	−0.30	0.40	0.74	0.34–1.63	0.455
Right rostral MFG	−0.05	0.26	0.95	0.57–1.59	0.841
Left caudal ACC	−0.17	0.16	0.85	0.61–1.17	0.311
Right caudal ACC	−0.49	0.17	0.61	0.44–0.85	**0.004***
Left rostral ACC	−0.07	0.33	0.93	0.49–1.77	0.832
Right rostral ACC	0.31	0.31	1.36	0.74–2.50	0.320
Cortical Thickness					
Left caudal MFG	−0.12	0.32	1.13	0.60–2.11	0.712
Right caudal MFG	−0.29	0.37	0.75	0.37–1.54	0.432
Left rostral MFG	−0.27	0.40	0.77	0.35–1.67	0.505
Right rostral MFG	0.23	0.23	1.26	0.81–1.95	0.310
Left caudal ACC	−0.01	0.21	0.98	0.66–1.48	0.950
Right caudal ACC	−0.09	0.29	0.92	0.52–1.63	0.768
Left rostral ACC	−0.12	0.19	0.89	0.61–1.23	0.534
Right rostral ACC	0.15	0.17	1.16	0.84–1.60	0.381
Subcortical Volume					
Left NAcc	−0.46	0.40	0.63	0.29–1.38	0.247
Right NAcc	0.48	0.32	1.62	0.86–3.06	0.139

Note: Asterisk (*) indicates statistically significant p-values then corrected for multiple comparisons with Bonferroni procedure. IRR = incidence rate ratio.

regression allowed us to account for both overdispersion and the high frequency of zero values in BD episodes variable, enhancing the robustness of our findings.

The present work revealed that specific structural features of MFG and ACC at baseline (when they were aged 18–19 years) are significantly associated with the number of BD episodes five years later. These findings suggest that individual differences in brain morphology may confer vulnerability to problematic alcohol use trajectories. Consistent with neurodevelopmental theories, our study emphasizes the significance of specific brain regions implicated in cognitive control and emotional regulation in the context of alcohol consumption during emerging adulthood.

Previous studies have highlighted the role of the MFG and ACC, demonstrating that differences in brain structural characteristics and functional activation in these regions are indicative of a higher risk of initiating alcohol and other substance use during adolescence (Boer et al., 2022; Heitzeg et al., 2015; Squeglia and Cservenka, 2017). Similarly, in line with our findings, several studies have revealed that structural alterations in the MFG and ACC are associated with future alcohol use as well as more episodes of BD (Baranger et al., 2020; Brumback et al., 2016; Cheetham et al., 2014; Squeglia et al., 2014). Our study extends these findings and provides additional insights into the relationship between these structures and alcohol consumption behaviors.

It is important to note that although some studies suggest that structural variations in the brain may reflect the harmful effects of alcohol on typical brain development, the exact meaning of the direction of these changes in gray matter measurements remain unclear. Some researchers propose that greater gray matter could indicate alterations in synaptic pruning processes, potentially caused by the neurotoxic effects of alcohol. Conversely, lower gray matter may reflect an atypical developmental trajectory, characterized by the loss or thinning of cortical structures, which is also associated with alcohol-related neurotoxicity.

Our findings revealed distinct patterns of association across different ROIs, with both positive and negative relationships observed between surface area in the MFG and ACC and future BD frequency. Specifically, a greater surface area in the caudal division of the right MFG was significantly associated with a higher incidence rate of BD episodes, indicating a positive relationship between cortical surface area in the MFG and BD behavior. Conversely, a smaller surface area in the caudal division of the right ACC was associated with a higher incidence rate of BD episodes, suggesting that a reduced surface area in the ACC may predispose individuals to more frequent drinking episodes.

The MFG is crucial for executive functions such as working memory, inhibitory control, and decision-making processes (Hofmann et al., 2012). On the other hand, the ACC is involved in a variety of functions, including emotional regulation, cognitive control, or conflict monitoring (Brockett and Roesch, 2021). Structural and functional anomalies in both the MFG and ACC have been implicated in the development of addiction (Koob and Volkow, 2016; Voon et al., 2020; Zakiniaeiz et al., 2017; Zhao et al., 2021). In this context, the positive link between surface area in the MFG and BD aligns with earlier cross-sectional studies, which found larger gray matter in individuals with BD compared to healthy controls (Doallo et al., 2014; Sousa et al., 2017). However, prospective research has pointed in the opposite direction, with findings showing that a lower surface area (Brumback et al., 2016) and reduced gray matter volume (Baranger et al., 2020) in the dorsolateral prefrontal cortex were associated with increased alcohol use. Regarding the ACC, results from cross-sectional studies on BD have been more mixed, reporting both larger (Doallo et al., 2014) and smaller gray matter volume (Mashhoon et al., 2014) in this region. In contrast, prospective studies are more consistent with our findings, showing a negative relationship between ACC structural measures and future alcohol use (Boer et al., 2022; Cheetham et al., 2014; Squeglia et al., 2014). However, the interpretation of the directionality of these alterations remains unclear, with conflicting findings regarding increased or decreased gray matter metrics in both the MFG and ACC frequently reported in the BD literature (see Pérez-García et al., 2022b for a review). Several factors have been proposed to explain these inconsistencies, including sex-related differences in neurodevelopmental trajectories, the neurotoxic effects of alcohol on the brain, the individuals' history of alcohol consumption, and the design of the study itself.

Interestingly, our analyses did not reveal significant associations between cortical thickness and BD episodes. This could indicate that surface area may be a more sensitive predictor of BD behaviors compared to cortical thickness. These contrasting patterns highlight the complexity of characterizing neurobiological predictors of alcohol use behaviors and emphasize the need for a more detailed understanding of brain-behavior relationships in substance use contexts. Consistent with Vijayakumar et al. (2016), who found that surface area increases non-linearly while cortical thickness decreases during adolescence, our results suggest that these neurostructural characteristics can independently and complementarily indicate risk for future alcohol use.

Contrary to our hypothesis, we did not observe a significant association between NAcc volume and BD episodes five years later. This contrasts with previous studies, which have shown structural alterations in the NAcc in young individuals with BD consumption (Pérez-García et al., 2022b) and associations between NAcc morphology during adolescence and future alcohol use (Morales et al., 2019). This suggests that further research is needed to better understand the role of the NAcc as a potential predictor of drinking behavior.

Notably, our study contributes to the growing body of literature on neurobiological predictors of alcohol use by employing a prospective longitudinal design, allowing for the examination of temporal relationships between brain structural features and successive alcohol consumption. By prospectively assessing participants from late adolescence to emerging adulthood, we were able to elucidate the predictive utility of baseline neuroanatomical characteristics in identifying individuals at risk for problematic alcohol use trajectories. As noted by Heitzeg et al. (2015) such designs enable researchers to track changes in brain structure and function over time, providing insights into how early neurobiological differences may influence later substance use outcomes. Our study extends this approach by demonstrating that baseline structural features in the MFG and ACC are significant predictors of BD frequency five years later. These structural findings are aligned with other prospective studies that have examined brain function and predicted BD in youth. Both task-based functional activity and connectivity studies highlight the involvement of the MFG and ACC in predicting future BD episodes (Gorka et al., 2023; Lesnewich et al., 2022; Whelan et al., 2014). Taken together, these findings suggest that both structural and functional features can serve as important markers of vulnerability to developing harmful drinking patterns.

In terms of public health relevance, considering neurobiological markers associated with an increased frequency of BD has important implications. Understanding the neurobiological underpinnings of substance use could guide the development of more effective prevention strategies that mitigate the likelihood of developing problematic alcohol use behaviors.

Despite the novel insights provided by our study, several limitations should be acknowledged. First, a key consideration is that our study's exclusion criteria removed individuals with high levels of alcohol consumption or a family history of substance use. While we recognize that these individuals may be at higher risk for future substance use issues, our goal was to investigate neurobiological vulnerabilities in a university student population, without the confounding effects of prior conditions. This allowed us to identify structural brain features that may predispose individuals to BD use during young adulthood, independent of pre-existing conditions. Additionally, it is important to note that while our findings suggest that individual differences in brain structure may predict risky alcohol use after 5 years, they may also reflect compensatory neural mechanisms in response to environmental factors, such as the neurotoxic effects of the adolescent BD pattern.

Second, and partially due to the aforementioned limitation, the sample size was relatively modest, potentially limiting the generalizability of our findings. Future studies with larger, more diverse samples are warranted to validate our results and explore potential moderating factors influencing the observed associations.

Third, multimodal imaging approaches that integrate structural and functional data could offer deeper insights into the complex interplay between brain structure and function in predicting alcohol use. Potential research should consider these factors to provide a more comprehensive understanding of the neurobiological underpinnings of BD.

In conclusion, our study provides compelling evidence for the predictive utility of baseline brain structural features in identifying individuals at risk for future BD during young adulthood.

Contributors

F.C., S.R.H., and S.D. designed the study. S.S.-S. and J.M.P.-G. participated in the data collection & curation for MRI analysis. S.R.H. and S.D. were responsible for sample selection. J.M.P.-G., M.S.R.G., and S.D. analyzed and interpreted the data. J.M.P.-G. wrote the article. All authors reviewed the final version of the manuscript and approved it for publication.

Funding

This work was supported by grants from the Spanish Ministerio de Ciencia, Innovación y Universidades (PID2020-113487RB-100) and Xunta de Galicia (GRC ED431C 2021/08). SS-S was supported by a postdoctoral fellowship from the Universidade de Santiago de Compostela co-funded with European Funds (Margarita Salas 2022-2024).

CRediT authorship contribution statement

Fernando Cadaveira: Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **Sonia Doallo:** Writing – review & editing, Supervision, Project administration, Methodology, Funding acquisition, Conceptualization. **María Soledad Rodríguez González:** Writing – review & editing, Validation, Methodology, Formal analysis. **Socorro Rodríguez Holguín:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization. **Jose Manuel Pérez-García:** Writing – original draft, Visualization, Methodology, Investigation, Data curation. **Samuel Suarez-Suarez:** Writing – review & editing, Resources, Investigation, Data curation.

Declaration of Competing Interest

All authors declare no potential conflict of interest.

Data availability

The MRI and behavioral data supporting the conclusions of this article have been deposited at Open Science Framework repository (https://osf.io/utcqk/?view_only=f0d255083d25477d980a692b06cc1655).

References

Addolorato, G., Vassallo, G.A., Antonelli, G., Antonelli, M., Tarli, C., Mirijello, A., Agyei-Nkansah, A., Mentella, M.C., Ferrarese, D., Mora, V., Barbàra, M., Maida, M., Cammà, C., Gasbarrini, A., 2018. Binge drinking among adolescents is related to the development of alcohol use disorders: results from a cross-sectional study. Sci. Rep. 8, 12624. https://doi.org/10.1038/s41598-018-29311-y.

Almeida-Antunes, N., Crego, A., Carbia, C., Sousa, S.S., Rodrigues, R., Sampaio, A., López-Caneda, E., 2021. Electroencephalographic signatures of the binge drinking pattern during adolescence and young adulthood: a PRISMA-driven systematic review. Neuroimage Clin. 29, 102537. https://doi.org/10.1016/j.nicl.2020.102537.

Baranger, D.A.A., Demers, C.H., Elsayed, N.M., Knodt, A.R., Radtke, S.R., Desmarais, A., Few, L.R., Agrawal, A., Heath, A.C., Barch, D.M., Squeglia, L.M., Williamson, D.E., Hariri, A.R., Bogdan, R., 2020. Convergent evidence for predispositional effects of brain gray matter volume on alcohol consumption. Biol. Psychiatry 87, 645–655. https://doi.org/10.1016/j.biopsych.2019.08.029.

Bjork, J.M., Pardini, D.A., 2015. Developmental cognitive neuroscience who are those "risk-taking adolescents"? individual differences in developmental neuroimaging research. Accid. Anal. Prev. 11, 56–64. https://doi.org/10.1016/j.dcn.2014.07.008.

Blanco-Ramos, J., Antón-Toro, L.F., Cadaveira, F., Doallo, S., Suárez-Suárez, S., Rodríguez Holguín, S., 2022. Alcohol-related stimuli modulate functional connectivity during response inhibition in young binge drinkers. Addict. Biol. 27, e13141. https://doi.org/10.1111/adb.13141.

Blanco-Ramos, J., Cadaveira, F., Folgueira-Ares, R., Corral, M., Rodríguez Holguín, S., 2019. Electrophysiological correlates of an alcohol-cued go/nogo task: a dual-process approach to binge drinking in university students. Int J. Environ. Res Public Health 16, 4550. https://doi.org/10.3390/ijerph16224550.

Boer, O.D., El Marroun, H., Franken, I.H.A., 2022. Brain morphology predictors of alcohol, tobacco, and cannabis use in adolescence: a systematic review. Brain Res 1795, 148020. https://doi.org/10.1016/j.brainres.2022.148020.

Bonomo, Y.A., Bowes, G., Coffey, C., Carlin, J.B., Patton, G.C., 2004. Teenage drinking and the onset of alcohol dependence: a cohort study over seven years. Addiction 99, 1520–1528. https://doi.org/10.1111/j.1360-0443.2004.00846.x.

Brockett, A.T., Roesch, M.R., 2021. Anterior cingulate cortex and adaptive control of brain and behavior, in: Brockett, A.T., Amarante, L.M., Laubach, M., Roesch, M.R.B. T.-I.R. of N. (Eds.), What does medial frontal cortex signal during behavior? insights from behavioral neurophysiology. Academic Press, pp. 283–309. https://doi.org/10.1016/bs.irn.2020.11.013

Brumback, T., Worley, M., Nguyen-Louie, T.T., Squeglia, L.M., Jacobus, J., Tapert, S.F., 2016. Neural predictors of alcohol use and psychopathology symptoms in adolescents. Dev. Psychopathol. 28, 1209–1216. https://doi.org/10.1017/S0954579416000766.

Carbia, C., López-Caneda, E., Corral, M., Cadaveira, F., 2018. A systematic review of neuropsychological studies involving young binge drinkers. Neurosci. Biobehav Rev. 90, 332–349. https://doi.org/10.1016/j.neubiorev.2018.04.013.

Cheetham, A., Allen, N.B., Whittle, S., Simmons, J., Yuecel, M., Lubman, D.I., 2014. Volumetric differences in the anterior cingulate cortex prospectively predict alcohol-related problems in adolescence. Psychopharmacol. (Berl.) 231, 1731–1742. https://doi.org/10.1007/s00213-014-3483-8.

Courtney, K.E., Polich, J., 2009. Binge drinking in young adults: data, definitions, and determinants. Psychol. Bull. 135, 142–156. https://doi.org/10.1037/a0014414.

Crabbe, J.C., Harris, R.A., Koob, G.F., 2011. Preclinical studies of alcohol binge drinking. Ann. N. Y Acad. Sci. 1216, 24–40. https://doi.org/10.1111/j.1749-6632.2010.05895.x.

Crone, E.A., Dahl, R.E., 2012. Understanding adolescence as a period of social–affective engagement and goal flexibility. Nat. Rev. Neurosci. 13, 636–650. https://doi.org/10.1038/nrn3313.

Dale, A.M., Fischl, B., Sereno, M.I., 1999. Cortical surface-based analysis: I. segmentation and surface reconstruction. Neuroimage 9, 179–194. https://doi.org/10.1006/nimg.1998.0395.

Desikan, R.S., Ségonne, F., Fischl, B., Quinn, B.T., Dickerson, B.C., Blacker, D., Buckner, R.L., Dale, A.M., Maguire, R.P., Hyman, B.T., Albert, M.S., Killiany, R.J., 2006. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. Neuroimage 31, 968–980. https://doi.org/10.1016/j.neuroimage.2006.01.021.

Doallo, S., Cadaveira, F., Corral, M., Mota, N., López-Caneda, E., Holguín, S.R., 2014. Larger mid-dorsolateral prefrontal gray matter volume in young binge drinkers revealed by voxel-based morphometry. PLoS One 9, e96380. https://doi.org/10.1371/journal.pone.0096380.

Duijvenvoorde, A.C.K., Van, Peters, S., Braams, B.R., Crone, E.A., 2016. Neuroscience and biobehavioral reviews what motivates adolescents? neural responses to rewards and their influence on adolescents' risk taking, learning, and cognitive control. Neurosci. Biobehav Rev. 70, 135–147. https://doi.org/10.1016/j.neubiorev.2016.06.037.

ESPAD, 2020. ESPAD Report 2019: Results from the European School Survey Project on Alcohol and Other Drugs. Publications Office of the European Union, Luxembourg.

Fischl, B., Liu, A., Dale, A.M., 2001. Automated manifold surgery: constructing geometrically accurate and topologically correct models of the human cerebral cortex. IEEE Trans. Med Imaging 20, 70–80. https://doi.org/10.1109/42.906426.

Fischl, B., Salat, D.H., Busa, E., Albert, M., Dieterich, M., Haselgrove, C., van der Kouwe, A., Killiany, R., Kennedy, D., Klaveness, S., Montillo, A., Makris, N., Rosen, B., Dale, A.M., 2002. Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. Neuron 33, 341–355. https://doi.org/10.1016/S0896-6273(02)00569-X.

Fischl, B., Salat, D.H., van der Kouwe, A.J.W., Makris, N., Ségonne, F., Quinn, B.T., Dale, A.M., 2004. Sequence-independent segmentation of magnetic resonance images. Neuroimage 23, S69–S84. https://doi.org/10.1016/j.neuroimage.2004.07.016.

Fischl, B., Sereno, M.I., Dale, A.M., 1999. Cortical surface-based analysis: II: inflation, flattening, and a surface-based coordinate system. Neuroimage 9, 195–207. https://doi.org/10.1006/nimg.1998.0396.

Gladwin, T.E., Figner, B., Crone, E.A., Wiers, R.W., 2011. Addiction, adolescence, and the integration of control and motivation. Dev. Cogn. Neurosci. 1, 364–376. https://doi.org/10.1016/j.dcn.2011.06.008.

González de Rivera, J.L., Derogatis, L.R., De las Cuevas, C., Gracia Marco, R., Rodríguez-Pulido, F., Henry-Benítez, M., Monterrey, A.L., 1989. The spanish version of the SCL-

90-R. Normative data in the general population. Towson, MD: Clinical Psychometric Research.
Gorka, S.M., Radoman, M., Jimmy, J., Kreutzer, K.A., Manzler, C., Culp, S., 2023. Behavioral and brain reactivity to uncertain stress prospectively predicts binge drinking in youth. Neuropsychopharmacology 48, 1194–1200. https://doi.org/10.1038/s41386-023-01571-x.
Heitzeg, M.M., Cope, L.M., Martz, M.E., Hardee, J.E., 2015. Neuroimaging risk markers for substance abuse: recent findings on inhibitory control and reward system functioning. Curr. Addict. Rep. 2, 91–103. https://doi.org/10.1007/s40429-015-0048-9.
Hingson, R.W., 2010. Focus on: college drinking and related problems magnitude and prevention. Alcohol Res Health 33, 45–54.
Hofmann, W., Schmeichel, B.J., Baddeley, A.D., 2012. Executive functions and self-regulation. Trends Cogn. Sci. 16, 174–180. https://doi.org/10.1016/j.tics.2012.01.006.
Koob, G.F., Volkow, N.D., 2016. Neurobiology of addiction: a neurocircuitry analysis. Lancet Psychiatry 3, 760–773. https://doi.org/10.1016/S2215-0366(16)00104-8.
Kranzler, H.R., Soyka, M., 2018. Diagnosis and pharmacotherapy of alcohol use disorder: a review. JAMA 320, 815–824. https://doi.org/10.1001/jama.2018.11406.
Kuntsche, E., Kuntsche, S., Thrul, J., Gmel, G., 2017. Binge drinking: health impact, prevalence, correlates and interventions. Psychol. Health 32, 976–1017. https://doi.org/10.1080/08870446.2017.1325889.
Lannoy, S., Baggio, S., Heeren, A., Dormal, V., Maurage, P., Billieux, J., 2021a. What is binge drinking? Insights from a network perspective. Addict. Behav. 117, 106848. https://doi.org/10.1016/j.addbeh.2021.106848.
Lannoy, S., Duka, T., Carbia, C., Billieux, J., Fontesse, S., Dormal, V., Gierski, F., López-Caneda, E., Sullivan, E.V., Maurage, P., 2021b. Emotional processes in binge drinking: a systematic review and perspective. Clin. Psychol. Rev. 84, 101971. https://doi.org/10.1016/j.cpr.2021.101971.
Lees, B., Meredith, L.R., Kirkland, A.E., Bryant, B.E., Squeglia, L.M., 2020. Effect of alcohol use on the adolescent brain and behavior. Pharm. Biochem Behav. 192, 172906. https://doi.org/10.1016/j.pbb.2020.172906.
Lees, B., Mewton, L., Stapinski, L.A., Squeglia, L.M., Rae, C.D., Teesson, M., 2019. Neurobiological and cognitive profile of young binge drinkers: a systematic review and meta-analysis. Neuropsychol. Rev. 29, 357–385. https://doi.org/10.1007/s11065-019-09411-w.
Lesnewich, L.M., Pawlak, A.P., Gohel, S., Bates, M.E., 2022. Functional connectivity in the central executive network predicts changes in binge drinking behavior during emerging adulthood: an observational prospective study. Addiction 117, 1899–1907. https://doi.org/10.1111/add.15828.
Mashhoon, Y., Czerkawski, C., Crowley, D.J., Cohen-Gilbert, J.E., Sneider, J.T., Silveri, M.M., 2014. Binge alcohol consumption in emerging adults: anterior cingulate cortical "Thinness" is associated with alcohol use Patterns. Alcohol Clin. Exp. Res 38, 1955–1964. https://doi.org/10.1111/acer.12475.
Maurage, P., Lannoy, S., Mange, J., Grynberg, D., Beaunieux, H., Banovic, I., Gierski, F., Naassila, M., 2020. What we talk about when we talk about binge drinking: towards an integrated conceptualization and evaluation. Alcohol Alcohol 55, 468–479. https://doi.org/10.1093/alcalc/agaa041.
Miller, J.W., Naimi, T.S., Brewer, R.D., Jones, S.E., 2007. Binge drinking and associated health risk behaviors among high school students. Pediatrics 119, 76–85. https://doi.org/10.1542/peds.2006-1517.
Mills, K.L., Lalonde, F., Clasen, L.S., Giedd, J.N., Blakemore, S.-J., 2014. Developmental changes in the structure of the social brain in late childhood and adolescence. Soc. Cogn. Affect Neurosci. 9, 123–131. https://doi.org/10.1093/scan/nss113.
Morales, A.M., Boyd, S.J., Mackiewicz Seghete, K.L., Johnson, A.J., De Bellis, M.D., Nagel, B.J., 2019. Sex differences in the effect of nucleus accumbens volume on adolescent drinking: the mediating role of sensation seeking in the NCANDA sample. J. Stud. Alcohol Drugs 80, 594–601. https://doi.org/10.15288/jsad.2019.80.594.
Moure-Rodríguez, L., Doallo, S., Juan-Salvadores, P., Corral, M., Cadaveira, F., Caamaño-Isorna, F., 2016. Consumo intensivo de alcohol y cannabis, y prácticas sexuales de riesgo en estudiantes universitarios. Gac. Sanit. 30, 438–443. https://doi.org/10.1016/j.gaceta.2016.03.007.
NIAAA, 2004. NIAAA council approves definition of binge drinking. NIAAA Newsl. 3, 3.
Olsson, C.A., Romaniuk, H., Salinger, J., Staiger, P.K., Bonomo, Y., Hulbert, C., Patton, G.C., 2016. Drinking patterns of adolescents who develop alcohol use disorders: results from the Victorian Adolescent Health Cohort Study. BMJ Open 6, e010455. https://doi.org/10.1136/bmjopen-2015-010455.
Panizzon, M.S., Fennema-Notestine, C., Eyler, L.T., Jernigan, T.L., Prom-Wormley, E., Neale, M., Jacobson, K., Lyons, M.J., Grant, M.D., Franz, C.E., Xian, H., Tsuang, M., Fischl, B., Seidman, L., Dale, A., Kremen, W.S., 2009. distinct genetic influences on cortical surface area and cortical thickness. Cereb. Cortex 19, 2728–2735. https://doi.org/10.1093/cercor/bhp026.
Páramo, M.F., Cadaveira, F., Rodríguez, M.S., 2023. A 2-year follow-up of the effects of combined binge drinking and cannabis consumption on academic performance and adjustment in Spanish third-year university students. Front Psychol. 14, 1223597. https://doi.org/10.3389/fpsyg.2023.1223597.
Pérez-García, J.M., Cadaveira, F., Canales-Rodríguez, E.J., Suárez-Suárez, S., Rodríguez Holguín, S., Corral, M., Blanco-Ramos, J., Doallo, S., 2022a. Effects of persistent binge drinking on brain structure in emerging adults: a longitudinal study. Front Psychiatry 13, 935043. https://doi.org/10.3389/fpsyt.2022.935043.
Pérez-García, J.M., Suárez-Suárez, S., Doallo, S., Cadaveira, F., 2022b. Effects of binge drinking during adolescence and emerging adulthood on the brain: a systematic review of neuroimaging studies. Neurosci. Biobehav Rev. 137, 104637. https://doi.org/10.1016/j.neubiorev.2022.104637.
Raznahan, A., Shaw, P., Lalonde, F., Stockman, M., Wallace, G.L., Greenstein, D., Clasen, L., Gogtay, N., Giedd, J.N., 2011. How does your cortex grow?, 7174 LP – 7177 J. Neurosci. 31. https://doi.org/10.1523/JNEUROSCI.0054-11.2011.
Rimol, L.M., Nesvåg, R., Hagler, D.J., Bergmann, Ø., Fennema-Notestine, C., Hartberg, C. B., Haukvik, U.K., Lange, E., Pung, C.J., Server, A., Melle, I., Andreassen, O.A., Agartz, I., Dale, A.M., 2012. Cortical volume, surface area, and thickness in schizophrenia and bipolar disorder. Biol. Psychiatry 71, 552–560. https://doi.org/10.1016/j.biopsych.2011.11.026.
SAMSHA, 2023. Key substance use and mental health indicators in the United States: Results from the 2022 National Survey on Drug Use and Health (HHS Publication No. PEP23-07-01-006, NSDUH Series H-58). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/report/2022-nsduh-annual-national-report
Saunders, J.B., Aasland, O.G., Babor, T.F., de la Fuente, J.R., Grant, M., 1993. Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. Addiction 88, 791–804. https://doi.org/10.1111/j.1360-0443.1993.tb02093.x.
Segonne, F., Pacheco, J., Fischl, B., 2007. Geometrically accurate topology-correction of cortical surfaces using nonseparating loops. IEEE Trans. Med Imaging 26, 518–529. https://doi.org/10.1109/TMI.2006.887364.
Shulman, E.P., Smith, A.R., Silva, K., Icenogle, G., Duell, N., Chein, J., Steinberg, L., 2016. The dual systems model: review, reappraisal, and reaffirmation. Dev. Cogn. Neurosci. 17, 103–117. https://doi.org/10.1016/j.dcn.2015.12.010.
Sled, J.G., Zijdenbos, A.P., Evans, A.C., 1998. A nonparametric method for automatic correction of intensity nonuniformity in MRI data. IEEE Trans. Med Imaging 17, 87–97. https://doi.org/10.1109/42.668698.
Sobell, L.C., Sobell, M.B., 1992. Timeline Follow-Back. In: Litten, R.Z., Allen, J.P. (Eds.), Measuring alcohol consumption: psychosocial and biochemical methods. Humana Press, Totowa, NJ, pp. 41–72. https://doi.org/10.1007/978-1-4612-0357-5_3.
Sousa, S.S., Sampaio, A., Marques, P., Gonçalves, Ó.F., Crego, A., 2017. Gray Matter Abnormalities in the Inhibitory Circuitry of Young Binge Drinkers: A Voxel-Based Morphometry Study. Front Psychol. 8, 1567. https://doi.org/10.3389/fpsyg.2017.01567.
Spear, L.P., 2018. Effects of adolescent alcohol consumption on the brain and behaviour. Nat. Rev. Neurosci. 19, 197–214. https://doi.org/10.1038/nrn.2018.10.
Squeglia, L.M., Cservenka, A., 2017. Adolescence and drug use vulnerability: findings from neuroimaging. Curr. Opin. Behav. Sci. 13, 164–170. https://doi.org/10.1016/j.cobeha.2016.12.005.
Squeglia, L.M., Gray, K.M., 2016. Alcohol and drug use and the developing brain. Curr. Psychiatry Rep. 18, 1–10. https://doi.org/10.1007/s11920-016-0689-y.
Squeglia, L.M., Rinker, D.A., Bartsch, H., Castro, N., Chung, Y., Dale, A.M., Jernigan, T.L., Tapert, S.F., 2014. Brain volume reductions in adolescent heavy drinkers. Dev. Cogn. Neurosci. 9, 117–125. https://doi.org/10.1016/j.dcn.2014.02.005.
Suárez-Suárez, S., Doallo, S., Pérez-García, J.M., Corral, M., Rodríguez Holguín, S., Cadaveira, F., 2020. Response inhibition and binge drinking during transition to university: an fMRI study. Front Psychiatry 11, 535. https://doi.org/10.3389/fpsyt.2020.00535.
Swahn, M.H., Simon, T.R., Hammig, B.J., Guerrero, J.L., 2004. Alcohol-consumption behaviors and risk for physical fighting and injuries among adolescent drinkers. Addict. Behav. 29, 959–963. https://doi.org/10.1016/j.addbeh.2004.02.043.
Telzer, E.H., 2016. Dopaminergic reward sensitivity can promote adolescent health: A new perspective on the mechanism of ventral striatum activation. Dev. Cogn. Neurosci. 17, 57–67. https://doi.org/10.1016/j.dcn.2015.10.010.
Vijayakumar, N., Allen, N.B., Youssef, G., Dennison, M., Yücel, M., Simmons, J.G., Whittle, S., 2016. Brain development during adolescence: a mixed-longitudinal investigation of cortical thickness, surface area, and volume. Hum. Brain Mapp. 37, 2027–2038. https://doi.org/10.1002/hbm.23154.
Voon, V., Grodin, E., Mandali, A., Morris, L., Doñamayor, N., Weidacker, K., Kwako, L., Goldman, D., Koob, G.F., Momenan, R., 2020. Addictions neuroimaging assessment (ANIA): towards an integrative framework for alcohol use disorder. Neurosci. Biobehav Rev. 113, 492–506.
Wechsler, H., Davenport, A., Dowdall, G., Moeykens, B., Castillo, S., 1994. Health and behavioral consequences of binge drinking in college: a national survey of students at 140 campuses. JAMA 272, 1672–1677. https://doi.org/10.1001/jama.1994.03520210056032.
Whelan, R., Watts, R., Orr, C.A., Althoff, R.R., Artiges, E., Banaschewski, T., Barker, G.J., Bokde, A.L.W., Büchel, C., Carvalho, F.M., Conrod, P.J., Flor, H., Fauth-Bühler, M., Frouin, V., Gallinat, J., Gan, G., Gowland, P., Heinz, A., Ittermann, B., Lawrence, C., Mann, K., Martinot, J.L., Nees, F., Ortiz, N., Paillère-Martinot, M.L., Paus, T., Pausova, Z., Rietschel, M., Robbins, T.W., Smolka, M.N., Ströhle, A., Schumann, G., Garavan, H., 2014. Neuropsychosocial profiles of current and future adolescent alcohol misusers. Nature 512, 185–189. https://doi.org/10.1038/nature13402.
Wierenga, L.M., Langen, M., Oranje, B., Durston, S., 2014. Unique developmental trajectories of cortical thickness and surface area. Neuroimage 87, 120–126. https://doi.org/10.1016/j.neuroimage.2013.11.010.
Winkler, A.M., Kochunov, P., Blangero, J., Almasy, L., Zilles, K., Fox, P.T., Duggirala, R., Glahn, D.C., 2010. Cortical thickness or grey matter volume? The importance of selecting the phenotype for imaging genetics studies. Neuroimage 53, 1135–1146. https://doi.org/10.1016/j.neuroimage.2009.12.028.
Wojciechowski, T., 2021. Relevance of the dual systems model for predicting drug/alcohol dependence in early adulthood among previously adjudicated young adults.

Drug Alcohol Depend. 226, 108876. https://doi.org/10.1016/j.drugalcdep.2021.108876.

Zakiniaeiz, Y., Scheinost, D., Seo, D., Sinha, R., Constable, R.T., 2017. Cingulate cortex functional connectivity predicts future relapse in alcohol dependent individuals. Neuroimage Clin. 13, 181–187. https://doi.org/10.1016/j.nicl.2016.10.019.

Zhao, Y., Sallie, S.N., Cui, H., Zeng, N., Du, J., Yuan, T., Li, D., De Ridder, D., Zhang, C., 2021. Anterior cingulate cortex in addiction: new insights for neuromodulation. Neuromodulation 24, 187–196. https://doi.org/10.1111/ner.13291.