Neuroscience and Biobehavioral Reviews 137 (2022) 104637

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

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

Review article

Effects of binge drinking during adolescence and emerging adulthood on the brain: A systematic review of neuroimaging studies

Jose Manuel Pérez-García [*,1], Samuel Suárez-Suárez [1], Sonia Doallo, Fernando Cadaveira

Department of Clinical Psychology and Psychobiology, Universidade de Santiago de Compostela, Santiago de Compostela, Galicia, Spain

ARTICLE INFO

Keywords:
Alcohol
Adolescence
Binge drinking
Brain structure
Brain function

ABSTRACT

Binge drinking (BD) is a common pattern of alcohol consumption which is generating great concern because of its deleterious consequences. We selected 33 neuroimaging studies of healthy young binge drinkers (BDs) by following PRISMA guidelines. This review provides a comprehensive overview of the relationship between BD and neurocognitive anomalies reported across magnetic resonance studies. Moreover, this work is the first in which results of relatively new imaging techniques, such as resting-state functional connectivity (RS-FC) and neurite orientation dispersion and density imaging (NODDI), have been reviewed using a systematic procedure. We established strict inclusion criteria in order to isolate the various potential effects of BD on the adolescent brain. Two authors independently evaluated the methodological quality, assessing different aspects related to sample size, and statistical correction methods, which are of particular importance in neuroimaging studies. BD is associated with structural and functional anomalies in several cortical and subcortical brain regions intimately involved in the control and regulation of impulsive or risky behaviours, as well as in the processing of reinforcing stimuli.

1. Introduction

Different international epidemiological studies (European School Survey Project on Alcohol and other Drugs [ESPAD, 2020]; Substance Abuse and Mental Health Services Administration [SAMSHA, 2021]) have shown that alcohol is one of the most widely available and commonly used drugs among teenagers and young adults worldwide. Among the various patterns of alcohol consumption, one in particular is generating strong concern in both the scientific community and society because of its deleterious consequences. Binge drinking (BD) is a common pattern of alcohol intake among adolescents and is defined as the consumption of 5 or more standard drinks per drinking session for males (4 or more for females), over the course of 2 h, leading to a blood alcohol concentration (BAC) of 0.08 g/dL, according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA, 2004). This hazardous pattern of drinking usually starts at very early ages and is firmly established among young adults because of its recreational character, the low perception of risk and the positive alcohol expectancies (Borsari et al., 2007; Patrick and Schulenberg, 2010; Petit et al., 2014).

According to the latest results reported by SAMSHA (2021), 31.4% of people aged 18–25 in the United States (US) had practiced BD in the previous 30 days, corresponding to approximately 10.5 million young adults. Similar results were found in the major European survey (ESPAD, 2020), in which 34% of students between 15 and 16 years of age reported to have engaged in BD during the previous month. These alarmingly high rates of BD are of great concern because they occur during a period in which the brain is still developing and may be especially vulnerable to the neurotoxic effects of alcohol (for a review see Crews et al., 2007; Jacobus and Tapert, 2013).

Adolescence is a critical neurodevelopmental period characterized by a series of significant changes in brain morphology and function. Several magnetic resonance imaging (MRI) studies have demonstrated structural changes, usually reflected in an overall reduction in grey matter and a general increase in white matter (Gogtay et al., 2004; Raznahan et al., 2011; Tamnes et al., 2010; Wierenga et al., 2014). In addition, important changes take place in the patterns of functional and structural connectivity in the brain during this period, leading to increased efficiency of the interactions between brain regions (Grayson

* Correspondence to: Dpto. de Psicoloxía Clínica e Psicobioloxía, Facultade de Psicoloxía, Universidade de Santiago de Compostela, Campus Universitario Sur, s/n, Santiago de Compostela, 15782 Galicia, Spain.

E-mail addresses: jmanuel.perez.garcia@usc.es (J.M. Pérez-García), samuel.suarez@usc.es (S. Suárez-Suárez), sonia.doallo@usc.es (S. Doallo), fernando.cadaveira@usc.es (F. Cadaveira).

[1] These authors contributed equally.

https://doi.org/10.1016/j.neubiorev.2022.104637
Received 14 June 2021; Received in revised form 19 January 2022; Accepted 21 March 2022
Available online 24 March 2022

and Fair, 2017; Vogel et al., 2010). These changes in the brain lead to significant improvements in the efficiency of the most complex cognitive processing, such as cognitive control and self-regulation processes (Casey et al., 2005, 2008; Crone and Steinbeis, 2017; Luna et al., 2010).

During this life-changing period, brain regions associated with motivational processes (reward sensitivity, emotions, pleasure…), such as the amygdala and the nucleus accumbens (NAcc), reach their maximum development, while other regions intimately involved in executive processes (i.e. decision-making, planning and inhibitory control), such as the prefrontal cortex (PFC), are less well developed (Van Duijvenvoorde et al., 2016). In this regard, neuroscientific models of addiction have indicated that an imbalance between self-regulatory and motivational processes may lead to the development of addictive behaviours (Goldstein and Volkow, 2011, 2002; Wiers et al., 2007), highlighting the key role of the PFC in this process (Goldstein and Volkow, 2011). Consequently, the asynchrony in brain maturation processes makes adolescents particularly susceptible to becoming involved in risky behaviours such as illicit drug use and BD (Bjork and Pardini, 2015). Interestingly, brain structures with protracted development (e.g. PFC) and greater plasticity (e.g. hippocampus) seem to be particularly sensitive to the deleterious effects of alcohol, as shown in both human and animal models (Crews et al., 2007, 2000; Guerri and Pascual, 2010; Oscar-Berman and Marinković, 2007; Spear, 2018). Specifically regarding the potentially negative effects of BD during adolescence and emerging adulthood, a recent review and a meta-analysis (Carbia et al., 2018; Lees et al., 2019) have both reported that this consumption pattern affects executive control and verbal memory processes, which are subserved precisely by these brain regions that tend to take longer to mature (e.g. PFC) (Carbia et al., 2017; Goudriaan et al., 2007; Parada et al., 2011; Scaife and Duka, 2009). Moreover, BD has also been related to other important negative outcomes, including behavioural problems such as drink-driving (Hingson, 2010), fighting (Swahn et al., 2004) and unsafe sexual practices (Moure-Rodríguez et al., 2016), as well as decline in academic performance (Miller et al., 2007) and also an increased risk of developing alcohol use disorder (AUD) during adulthood (Addolorato et al., 2018; Olsson et al., 2016; Wechsler et al., 1994).

Considering that BD is the most prevalent pattern of alcohol consumption among adolescents and taking into account the aforementioned deleterious effects, it is not surprising that the impact of BD on the still developing brain during this important stage of life is a field of growing interest, as reflected by more than 30 neuroimaging studies published on this topic in the last decade.

Collectively, BD research has revealed several structural and functional anomalies; however, some of these studies have reported widely varying, if not contradictory, results. These apparently inconsistent neurocognitive findings between studies may be due to the following: (i) heterogeneity in the alcohol consumption criteria used to classify study subjects as binge drinkers (BDs) (studies focused on investigating the effects of alcohol consumption on the adolescent brain have traditionally included individuals with a diagnosis of AUD); and (ii) the presence of confounding factors that may bias the results (e.g. psychiatric comorbidity, concomitant substance use or gender-related differences).

In this respect, although numerous neuroimaging narrative reviews have evaluated how BD consumption specifically affects the architecture and functionality of the human brain (e.g. Cservenka and Brumback, 2017; Hermens et al., 2013; Jones et al., 2018; Petit et al., 2014), only one study has compiled the most relevant results from the literature considering the above-mentioned aspects and using a systematic procedure (Lees et al., 2019). However, to date, no systematic review has integrated the results obtained using relatively new imaging techniques such as neurite orientation dispersion and density imaging (NODDI) and resting-state functional connectivity (RS-FC). The findings of such studies may provide relevant information that will help to clarify the relationship between BD and neurocognitive anomalies.

We, therefore, propose carrying out an exhaustive systematic review of neuroimaging studies in order to better understand the specific effects of BD in adolescents and young adults. Specifically, we aim to consider the previously mentioned possible confounding factors in order to fill the gaps that remain to be resolved regarding the integration of findings related to this pattern of alcohol consumption. More concretely, the current review attempts to address the following aspects: (i) the neurostructural and functional (in terms of blood oxygen level dependent [BOLD] activity) anomalies associated with BD during adolescence and emerging adulthood; (ii) possible evidence of anomalies in the basal brain activity associated with BD; (iii) possible differences in the structural or functional brain connectivity between adolescents and young adult BDs relative to non-BDs; (iv) the potential increase in any anomalies observed due to the medium/long term maintenance of BD; (v) any gender differences in BD-related effects on the brain.

Finally, in order to achieve the proposed objectives, we consulted a systematic review carried out by Ewing et al. (2014) as a reference article regarding structure and methodology. The aforementioned review is an extensive compilation of the effects of different alcohol consumption patterns on the brain of young and adolescents and it thus seems to us a very valuable starting point from which to dig deeper into the specific effects of the BD pattern of alcohol consumption.

2. Methods

2.1. Search strategy and article selection

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2015). An advanced document protocol was registered in the PROSPERO database (registration number CRD42018086114; https://www.crd.york.ac.uk/prospero/). An exhaustive search of the Pubmed and Web of Science databases was completed on manuscripts published between 1 January 2000 and 31 December 2020 by using keywords covering the three domains of the review (i.e. binge drinking, adolescence and neuroimaging). The full search strategy can be found at PROSPERO.

Given the considerable number of confounding factors that can influence neuroimaging results, we established strict inclusion criteria in order to better isolate the effects of a BD pattern of consumption on the developing brain. Hence, we only included studies in which the drinking group comprised participants who engaged in BD, defined as the consumption of five (or more) drinks for male and four (or more) drinks for female in about 2 h according NIAAA's criteria (NIAAA, 2004). We also only included articles that evaluated the consequences of BD on a healthy young population that had not experienced any current or

Table 1
Inclusion criteria.

1. English language.
2. Peer-reviewed and journals indexed in journal citations reports (JCR).
3. Published between 1 st January 2000 and 31 st December 2020.
4. Empirical studies.
5. Age range of 13–30 years
6. N $\geq$ 10 BD participants.
7. Healthy adolescents or young adults without any psychiatric diagnosis.
8. Participants must have experienced BD episodes (see definition provided by NIAAA, 2004).
9. Studies must explore the relationships between BD pattern and brain structure and/or function through neuroimaging techniques; dMRI, fMRI and MRI.
10. Studies must examine mainly the effects of BD on the brain; articles with other substance use groups only will be included when the experimental design allows to isolate the specific effects of BD.
11. Excluded if aimed to evaluate psychiatric disorders, to determine the effects of other conditions (such as acute ethanol effects), to explore the effects of polysubstance use, or to identify cognitive functions that may play a role as risk factors for BD.

Note. BD: Binge Drinking; dMRI: diffusion magnetic resonance imaging; fMRI: functional magnetic resonance imaging; MRI: magnetic resonance imaging.

lifetime history of AUD or other substance use disorder. For a more detailed description of the inclusion criteria, see Table 1. Furthermore, although it is worth noting the efforts made by different multisite longitudinal studies to characterize the normative development and the association between adolescent brain and alcohol use (e.g. NCANDA, IMAGEN), we decided not to include the articles arising from those projects (except Whelan et al., 2014), because they do not allow the effects of BD to be isolated from those of other patterns of consumption. Finally, we considered as single studies the research led by Whelan et al. (2014) and Sousa et al. (2019), although we split the results into different sections in order to report separately on each of the neuroimaging techniques used (i.e. structural and functional MRI).

Two authors (JMP and SS) independently reviewed the articles retrieved through the search strategy, as recommended by the PRISMA guidelines. Selection of the articles at each stage of the review process was conducted using Covidence (Babineau, 2014), an online systematic review platform which facilitates the process of screening and data extraction. Any discrepancies in the articles selected by the review authors were resolved by consensus, when necessary with the assistance of other authors (SD, FC).

According to the PRISMA guidelines, data from each study were extracted by two authors (JMP and SS) and summarized in tables including the following categories: Study & design, Sample characteristics, BD criteria, non-BD criteria, Exclusion criteria, Imaging modality, Region of interest (ROI), Group by gender interactions.

Even though meta-analyses provide robust evidence and address significant issues as the effect sizes of findings and publication bias, we considered that the reviewed results are no suitable for that kind of approach because the selected neuroimaging data did not meet two important aspects to perform robust analysis (Müller et al., 2018): (i) same original search coverage across studies (e.g. MRI metrics and functional tasks, brain coverage or statistical correction methods); and (ii) sufficient number of studies/experiments. Therefore, our results will be reported through a narrative synthesis.

2.2. Quality assessment

Methodological quality assessment of all included studies was performed by JMP and SS using adapted version of the National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (National Heart, Lung, and Blood Institute, 2014). In order to better explore any potential bias in neuroimaging studies, we adapted questions 5 and 14 of the questionnaire. These modifications were specifically chosen to assess aspects related to the sample size and statistical correction methods, which are of particular importance in neuroimaging studies (Brown and Behrmann, 2017; David et al., 2018; Eklund et al., 2016; Poldrack et al., 2017) (see supplementary Table S1 and S2 for further details). Total agreement (Good/Fair/Poor) between assessors was high (29/33 = 88%). Inter-rater reliability, measured using Cohen's Kappa coefficient, was high to moderate (K= 0.79) (McHugh, 2012).

3. Results

3.1. Selected studies and summary characteristics

The search strategy generated a total of 1915 studies. After removing duplicates (n = 1034) and adding articles retrieved from other sources (n = 3), 1037 studies were identified. Screening based on titles and abstracts yielded 214 articles, which were assessed by reading the full text. Of these, 181 studies were excluded following the inclusion and exclusion criteria outlined above. Finally, 33 papers were included in the data analysis (see Fig. 1).

The results of these 33 selected studies were classified according to their image modality, as follows: 16 structural studies (9 volumetric and cortical thickness [MRI] studies and 7 diffusion MRI [dMRI] studies) and 18 functional imaging (fMRI) studies. Among the fMRI studies included in the review, 15 measured brain activity during the performance of different experimental tasks, while the remaining 3 studies examined

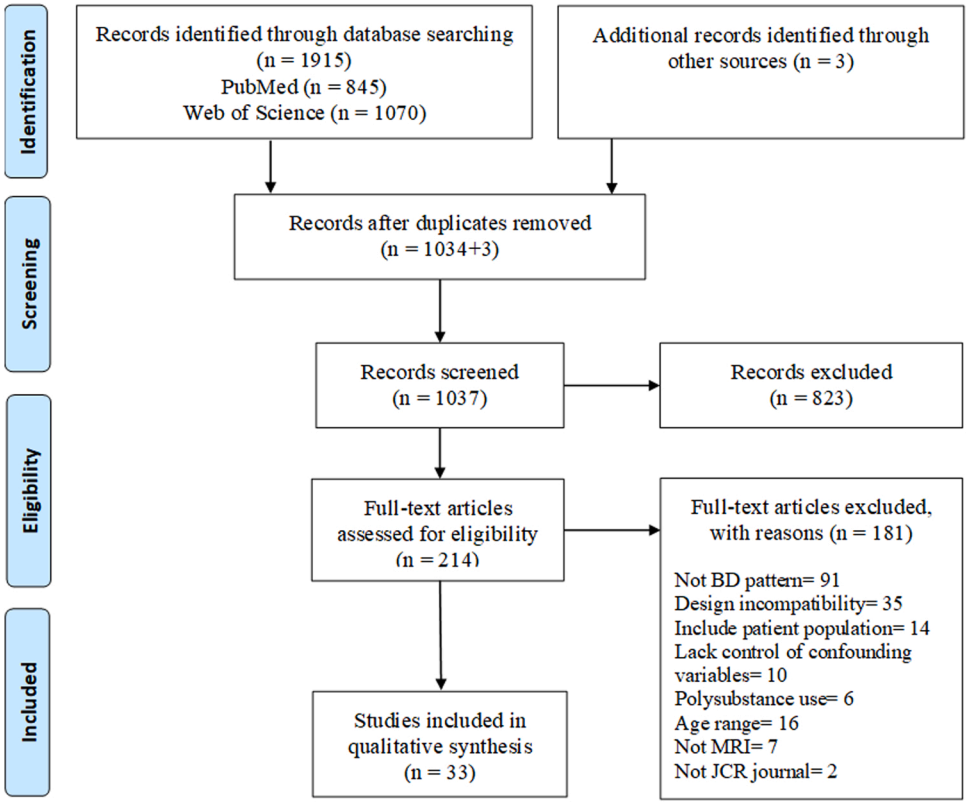

Fig. 1. PRISMA flow chart of literature search.

resting-state functional connectivity (RS-FC) between brain regions. The main characteristics of each study are summarized in Table 2 and Table 3.

Given the heterogeneity of the results summarized in the following sections, we illustrate, in Fig. 2, the number of publications and anatomical locations where significant differences have been reported in BDs relative to non-BDs. We then plotted brain regions that showed structural or functional significant alterations in, at least, two independent studies, highlighting in bold those in which the anomalies followed a common direction (see Fig. 3).

3.2. Quality assessment results

Most of the studies were of intermediate quality (61%), 30% were of high quality and 9% of poor quality (see Table 4). One of the main limitations of the studies was that potential confounding factors that could influence the results were overlooked, either because of a lack of relevant and clearly specified exclusion criteria or because of a lack of statistical control over confounders. The use of other drugs (including cannabis) as well as family history of alcoholism were the most frequent unspecified confounders. Specifically, a total of 14/33 studies did not record past and, in some cases, current use of illicit drugs while only 10/33 studies explicitly reported on the family history of alcoholism in their sample. It should also be taken into consideration that none of the selected studies informed whether the assessors were blinded to the exposure status of the participants (Q12, Table 4). Another factor that should be considered is the implementation of the neuroimaging technique selected and the adjustment of the specific potential confounders for this type of measurement. Thus, although most studies (27/33) reported the use of correction methods for multiple comparisons (e.g. FWE, FDR, etc.), 4 studies did not use formally statistical methods with this purpose, while 2 studies, in the absence of significant group differences, did not report whether these results were corrected for multiple comparisons. Furthermore, in most of the studies the sample size was relatively small (20/33), which can lead to modest effect sizes. In this respect, only 11/33 studies provided effect size estimates. Finally, only 9/33 studies specifically evaluated the presence of any potential gender differences. Among the common strengths for all the studies, it is worth noting the precise descriptions of both the objectives as well as the independent and dependent variables.

3.3. Structural findings in BDs

We then summarized 16 structural studies that characterized anatomical organization of brain tissues (Table 2) and provided quantitative information about structural differences between young BDs and non-BDs.

3.3.1. Volumetric and cortical thickness (MRI) studies

Nine studies analyzed the macrostructure of grey matter using different morphometric methods, such as voxel-based morphometry (VBM) and surface-based morphometry (SBM). VBM is the most common approach used to quantify morphological features such as volume and tissue concentration (Whitwell, 2009). SBM, on the other hand, enables estimation of more specific metrics (e.g. cortical thickness, surface area, cortical curvature) and exploration of how each of these measures contributes individually to the variability in cortical anatomy (Greve, 2011).

Squeglia et al. (2012) examined the impact of BD history on frontal lobe cortical thickness in adolescent male and females. The sample was formed by 29 BDs and 30 non-BDs. Imaging analysis did not reveal any main effect, either of group or gender on cortical thickness; however, group by gender interactions were observed in four frontal regions in the left hemisphere: frontal pole, pars orbitalis, medial orbital frontal gyrus (mOFG) and rostral anterior cingulate cortex (ACC). Thus, in male BDs the cortex was thinner in the left pars orbitalis, left mOFG and left rostral ACC than in male non-BDs, while in female BDs the frontal pole cortex was thicker than in female non-BDs. Moreover, these anomalies were associated with different levels of performance in a series of neuropsychological tests. Specifically, thicker left pars orbitalis areas were correlated with worse visuospatial construction, and the thicker left frontal poles were correlated with worse inhibition and attention in female BDs, while in male BDs, thicker rostral ACC was correlated with worse performance in an attention test. The authors suggested that these neuroimaging findings may reflect greater vulnerability to deleterious effects of alcohol use on neuromaturation in females than in males.

Howell et al. (2013) characterized the volume of grey matter in cortical and subcortical regions among university students with and without a BD pattern of consumption, focusing on the ventral striatum (VS), hippocampus and amygdala. The participants were classified as BDs (n = 19) and non-BDs (n = 19). ROI analysis, targeting previously identified regions, reported larger grey matter volume in the VS in the BDs than in non-BDs. Furthermore, whole-brain exploratory analysis also revealed higher grey matter volume in the left thalamus and the right lingual gyrus as well as lower volume in the right precuneus in BDs relative to non-BDs. Across all participants (i.e. BDs and non-BDs combined), grey matter volume in the left VS, amygdala and left hippocampus was negatively correlated with Alcohol Use Disorders Identification Test (AUDIT) scores. The increase in volume in the VS was interpreted as an indicator of a possible neuromaturational delay related to the intermittent use of alcohol.

Doallo et al. (2014) examined the effects of a persistent (at least 3 years) BD pattern on grey matter volume in various frontal regions. The sample comprised university students, who were classified as BDs (n = 11) or non-BDs (n = 21) according to their consumption trajectory. The ROI analysis showed that the BDs had larger grey matter volume in the left mid-dorsolateral prefrontal cortex (DLPFC) and ACC than non-BDs. Correlation analysis in the BDs showed a positive association between the left mid-DLPFC volume and the Self-Ordered Pointing Test (SOPT) total error scores. Across both BDs and non-BDs, the left mid-DLPFC volume was positively correlated with the quantity and speed of alcohol intake. These results may indicate that persistent BD throughout young adulthood is associated with structural anomalies in a region critically involved in high-level executive aspects of working memory.

A study conducted by Mashhoon et al. (2014) evaluated the impact of alcohol consumption on cortical thickness in young adults with and without a BD pattern. The groups were formed by 23 BDs and 31 non-BDs. ROI analysis showed lower cortical thickness in the right middle ACC and left dorsal posterior cingulate cortex (PCC) in BDs than in non-BDs peers. The results also revealed that middle ACC cortical thickness in the BDs was negatively correlated with the number of drinks consumed per occasion and per week in the previous 3 months. For both groups (BDs/non-BDs), the right middle ACC cortical thickness was negatively correlated with (i) number of hours spent consuming alcohol and number of drinks consumed during the most recent use, and (ii) quantity of drinks consumed per occasion and per week over the previous 3 months; the same measure was also positively correlated with the number of days elapsed since the last BD episode. These findings, according to the authors, suggest that BD may interfere with neuromaturational processes, leading to increased synaptic pruning and resulting thinning of the microarchitecture in the frontal lobe.

Whelan et al. (2014). This longitudinal paper, whose authors are involved in the IMAGEN project, was the first study to apply machine learning techniques to predict the consumption trajectories of adolescents with different levels of alcohol consumption. Among the different measures included in the machine learning model, neuroimaging evaluations were carried out to obtain grey matter volume of a sample composed of current BDs (n = 115) and non-BDs (n = 150). MRI analysis revealed smaller grey matter volume in ventromedial prefrontal cortex (vmPFC), right inferior frontal gyrus (IFG) and left middle frontal gyrus (MFG), as well as a larger grey matter volume in right putamen in

Table 2
Summary of neurostructural studies of BDs young adults.

Study & design	Sample characteristics	BD criteria	non-BD criteria	Exclusion criteria: Control of confounding variables (neurological or psychiatric comorbidity, AUD, etc.)	Imaging modality / Measure	Regions of interest (ROI)	Group-by-gender interactions
Volumetric and cortical thickness (MRI) studies							
Squeglia et al. (2012) CS	Age range: 16–19 29 BDs (14 F) M: 18.59 ± 0.56 F: 17.81 ± 1.01 30 non-BDs (15 F) M: 17.89 ± 1.15 F: 18.02 ± 1.08	> 1 BDE[a] in past 3 months.	< 3 drinks total for the last 3 months and no lifetime BDE.	Parental history of psychotic, bipolar, or antisocial personality disorder; premature birth or prenatal exposure to drugs or alcohol; serious medical problem; left-handedness; lifetime use of psychotropic medications; current or past DSM-IV Axis I diagnosis (except conduct disorder, oppositional defiant disorder, simple phobia, or AUD); marijuana use > 3 × /month in the past 3 months; > 25 lifetime total uses of other illicit substances; positive alcohol or substance use test on the day of scanning.	MRI-SBM **Thickness**	13 frontal lobe regions were selected by automated parcellation method based on Desikan-Killiany cortical atlas.	Males: BDs < non-BDs CT in the left pars orbitalis, left medial OFG, and left rostral ACC. Females: BDs > non-BDs CT in the frontal pole.
Howell et al. (2013) CS	Age range: NR 19 BDs (12 F) 22.95 ± 3.41 19 non-BDs (12 F) 24.63 ± 4.40	BDE at least once a week for the last 3 months.	NR	History of regular or current use of other substances; major psychiatric disorders according to Mini International Neuropsychiatric Inventory; major neurological illness, or head injury; positive alcohol or substance use test on the day of scanning.	MRI-VBM **Volume**	- VS - AMYG - HIPP	NA
Doallo et al. (2014) CS	Age range: 20–24 11 BDs (4 F) 22.18 ± 1.08 21 non-BDs (11 F) 22.43 ± 1.03	≥ 6 standard drinks on same occasion (≈ BDE), at least once a week, or (ii) ≥ 6 standard drinks on same occasion (≈ BDE), at least once a month with a consumption speed ≥ 2 drinks per hour. All participants maintained this pattern during ≥ 3 years.	≤ 6 standard drinks on same occasion, less than once a month with a consumption speed ≤ 2 drinks per hour.	Score > 90 GSI of the SCL-90-R or in at least two of the symptomatic dimensions; history of neurological disorders; regular (i.e. on a weekly basis) consumption of cannabis or other drugs (legal or illegal) with psychoactive effects; alcohol abuse/dependence according to the DSM-III-R criteria; personal and/or family history of major mental disorder and history of alcoholism in first-degree relatives.	MRI-VBM **Volume**	- DLPFC - VLPFC - OFG - ACC - DLPMC	NA
Mashhoon et al. (2014) CS	Age range: 18–24 23 BDs (11 F) 22.0 ± 1.2 31 non-BDs (15 F) 21.5 ± 1.6	≥ 3 BDE per month for the last 3 months.	1–2 drinks per week and no BDE in past 3.5 years.	Past or present mental health disorders (DSM-IV, Axis I disorders); neurological illness; current psychoactive substance use and/or dependence (including nicotine); current psychoactive medication use; any severe medical problems (including prior episodes of loss of consciousness); positive substance use test on the day of scanning.	MRI-SBM **Thickness**	- ACC - PCC - POS	NA
Whelan et al. (2014) CS	Age range: 14 115 BDs (66 F) 14.62 ± 0.39 150 non-BDs (79 F) 14.53 ± 0.43	≥ 3 lifetime drinking episodes[b] leading to drunkenness.	≤ 2 lifetime drinking episodes leading to drunkenness.	Pregnancy and birth concerns (e.g. prenatal alcohol exposure); medical history (e.g. diabetes); neurological or developmental conditions (e.g. major neuro-developmental disorders); mental health and abilities (i.e. treatment for	MRI-VBM **Volume**		NA

(*continued on next page*)

Table 2 (*continued*)

Study & design	Sample characteristics	BD criteria	non-BD criteria	Exclusion criteria: Control of confounding variables (neurological or psychiatric comorbidity, AUD, etc.)	Imaging modality / Measure	Regions of interest (ROI)	Group-by-gender interactions
				schizophrenia, bipolar disorder or IQ < 70).			
Banca et al. (2016) CS	Age range: NR 30 BDs (13 F) 22.22 ± 3.35 30 non-BDs (13 F) 21.85 ± 3.26 29 subjects completed MRI session (BD = 14; non-BDs = 15)	BDE at least once a week for the last 3 months.	NR	Any substance-use disorders; neurological concerns (e.g. head injury); medical or psychiatric disorders; positive alcohol or substance use test on the day of scanning.	MRI - VBM **Volume**	- Cerebellum - DLPFC - IPC - Thalamus	NA
Kvamme et al. (2016) CS	Age range: NR 30 BDs (12 F) M: 21.38 ± 2.83 F: 21.08 ± 1.78 46 non-BDs (23 F) M: 22.30 ± 2.05 F: 20.26 ± 1.28	BDE at least once a week for the last 6 months.	NR	History of regular or current use of other substances; major psychiatric disorders assessed with the Mini International Neuropsychiatric Inventory; major neurological illness, or head injury; positive alcohol or substance use test on the day of scanning.	MRI-VBM **Volume**	- VS	Males: BDs < Non-BDs GM in IFG, right medial SFG, left caudate, VS, right fusiform gyrus, right SMA, right postcentral gyrus, left MTG and left precuneus. Females: BDs > non-BDs GM in the same regions informed for males.
Sousa et al. (2017) CS	Age range: 18–23 20 BDs (10 F) 20.45 ± 1.60 16 AACs (10 F) 21.00 ± 1.71	≥ 1 BDE per month for the last 10 months (minimum).	No alcohol use experience.	Scores ≥ 20 in the AUDIT; GSI ≥ 90 or scoring in at least 2 symptomatic dimensions of the SCL-90-R; uncorrected sensory deficits; left-handedness; personal history of traumatic brain injury or neurologic disorder; regular (i.e. on a weekly basis) consumption of cannabis, personal history of regular or occasional use of other drugs (illegal or medically prescribed psychoactive substances); personal and/or family history of any neurological or DSM-IV axis I disorder in first-degree relatives (including AUD).	MRI-VBM **Density**	A mask including regions associated with inhibitory control and self-regulatory processes (i.e. SFG, MFG, IFG, FSOG, CC, Caudate, NAcc) was generated.	Males: BDs > AACs GM in the left MFG Females: BDs > AACs GM in the left MFG.
Sousa et al. (2020) CS	Age range: 18–23 20 BDs (10 F) 20.45 ± 1.60 16 AACs (10 F) 21.00 ± 1.71	≥ 1 BDE per month for the last 10 months (minimum).	No alcohol use experience.	Scores ≥ 20 in the AUDIT; GSI ≥ 90 or scoring in at least 2 symptomatic dimensions of the SCL-90-R; uncorrected sensory deficits; left-handedness; personal history of traumatic brain injury or neurologic disorder; regular (i.e. on a weekly basis) consumption of cannabis, personal history of regular or occasional use of other drugs (illegal or medically prescribed psychoactive substances); personal and/or family history of any neurological or DSM-IV axis I disorder in first-degree relatives (including AUD).	MRI-VBM **Volume**	- Caudate - NAcc	None
Diffusion MRI (dMRI) studies							
McQueeny et al. (2009) CS	Age range: 16–19 14 BDs (2 F) 18.09 ± 0.69 14 non-BDs (2 F) 17.95 ± 0.88	≥ 1 BDE in past 3 months.	No lifetime BDE.	History of neurological concerns (e.g. learning disorder; head trauma with loss of consciousness >2 min, migraine) or psychiatric disorders; history of alcohol or other drug use disorder (abuse or dependence); left-	dMRI-DTI **FA**		NA

(*continued on next page*)

Table 2 (*continued*)

Study & design	Sample characteristics	BD criteria	non-BD criteria	Exclusion criteria: Control of confounding variables (neurological or psychiatric comorbidity, AUD, etc.)	Imaging modality / Measure	Regions of interest (ROI)	Group-by-gender interactions
				handedness; prenatal exposure to alcohol or drugs; use of psychotropic medication; substance use in the 72 h previous to MRI scanning.			
Jacobus et al. (2009) CS	Age range: 16–19 14 BDs (2 F)[c] 18.1 ± 0.7 14 non-BDs (2 F) 17.3 ± 0.8	History of at least one BDE.	Very limited if any substance use history.	History of: DSM-IV Axis I disorder other than alcohol or cannabis use disorder; use of psychoactive medications; chronic medical illness; history of neurological concerns (e.g. learning disorder; head trauma with loss of consciousness >2 min); premature birth or prenatal alcohol or drug exposure; left handedness; uncorrected sensory deficits; parental history of bipolar I or psychotic disorder; non-fluency in English; positive alcohol or substance use test on the day of scanning.	dMRI-DTI **FA, MD**		NA
Correas et al. (2016) LNG	Age range baseline/follow-up: 18–19/20–21 17 BDs (8 F) 22 non-BDs (12 F)	BAC[d] of 0.08% or above (≈ BDE), at least once during the last month.	No lifetime BDE.	Personal history DSM-IV-TR disorders; family history of major psychopathological disorders in first degree relatives; family history of alcoholism or substance abuse in first or second-degree relatives; use of illegal drugs (except occasional cannabis consumption); regular use of psychoactive medications; uncorrected sensory deficits; AUDIT scores ≥ 20; positive alcohol test on the day of scanning.	dMRI-DTI **FA, MD, RD, AD**		NA
Smith et al. (2017) LNG	Age range: 18–25 Session 1 20 BDs (10 F) M: 20.3 ± 1.06 F: 19.6 ± 0.97 20 non-BDs (10 F) M: 20.5 ± 2.46 F: 20.8 ± 2.15 Session 2 (8–12 months later) 19 BDs (9 F) 18 non-BDs (9 F)	Binge score higher than 30.[e]	Binge score > 4 and < 16 (non-binge range for the employed scale).	Past or present medical, neurological or psychiatric disorder; any medication use.	dMRI-DTI **FA**	Five segments of the CC: - (i) prefrontal - (ii) premotor/ SMA - (iii) motor - (iv) sensory - (v) parietal, temporal and occipital	Males: BDs < non-BDs FA in different areas of the CC. Females: BDs > non-BDs FA in the same regions as those informed for males.
Kashfi et al. (2017) CS	Age range: 21–26 12 BDs (6 F) 22.08 ± 1.38 12 MoDs (6 F) 23.42 ± 1.51	≥ 3 BDE for the last 3 months.	≤ 5 drinks at same occasion, with ≤ 9 drinks per week for females and ≤ 12–14 drinks per week for males.	Positive alcohol or substance use test on the day of scanning.	dMRI-DTI **FA, MD, AD, RD**	- ACR - Genu and body of the CC -Cingulum - Anterior/posterior limbs of the IC and EC	NA
Morris et al. (2018) CS	Age range: NR 28 BDs (11 F) 22.03 ± 4.47 38 non-BDs (24 F) 23.69 ± 3.85	> 8 drinks for males and > 6 drinks for females (≈ BDE), at least once a week for the last 6 months.	No BDE in past 6 months.	Major psychiatric disorder; substance addiction (including alcohol dependence and excluding nicotine); history of regular or current use of other substances; medical illness or use of psychotropic medications; left-handedness.	dMRI-NODDI **NDI, ODI**	- VS	NA NA

(*continued on next page*)

Table 2 (*continued*)

Study & design	Sample characteristics	BD criteria	non-BD criteria	Exclusion criteria: Control of confounding variables (neurological or psychiatric comorbidity, AUD, etc.)	Imaging modality / Measure	Regions of interest (ROI)	Group-by-gender interactions
Sousa et al. (2019) CS	Age range: 18–23 20 BDs (10 F) 20.45 ± 1.60 14 AACs (8 F) 20.86 ± 1.75	≥ 1 BDE per month for the last 10 months (minimum).	No alcohol use experience.	Scores ≥ 20 in the AUDIT; GSI ≥ 90 or scoring in at least 2 symptomatic dimensions of the SCL-90-R; uncorrected sensory deficits; left-handedness; history of traumatic brain injury; regular (i.e. on a weekly basis) consumption of cannabis, personal history of regular or occasional use of other drugs (illegal or medically prescribed psychoactive substances); personal and/or family history of any neurological or DSM-IV axis I disorder in first-degree relatives (including AUD).	dMRI-DTI **FA, AD, RD, MD**	- Left ECN - Right ECN - MFG of the left ECN	

Note. **AACs**, alcohol abstinent controls; **ACC**, anterior cingulate cortex; **ACR**, anterior corona radiata; **AD**, axial diffusivity**; AMYG**, amygdala; **AUD**, alcohol use disorder; **AUDIT**, alcohol use disorders identification test; **BAC**, blood alcohol content; **BD**, Binge drinking (pattern); **BDs**, binge drinkers; **CC**, corpus callosum; **CS**, cross-sectional; **CT**, cortical thickness; **DLPFC**, dorsolateral prefrontal cortex; **DLPMC**, dorsolateral premotor cortex; **DTI,** diffusion tensor imaging; **dMRI**, diffusion MRI; **EC**, external capsule; **ECN**, Executive Control Network; **F**, females; **FA**, fractional anisotropy; **FSOG**, frontal superior orbital gyrus; **GM**, grey matter; **GSI**, Global Severity Index; **HIPP**, hippocampus; **IC**, internal capsule; **IFG**, inferior frontal gyrus; **IPC**, inferior parietal cortex; **LNG**, longitudinal; **M**, males; **MD**, mean diffusivity; **MFG**, middle frontal gyrus; **MJ**, marijuana; **MoDs**, moderate drinkers; **MRI**, magnetic resonance imaging**; MTG**, middle temporal gyrus; **NA**, non-assessed; **NAcc**, nucleus accumbens; **NDI**, neurite density index; **NODDI**, Neurite Orientation Dispersion and Density Imaging; **non-BDs**, Non-binge drinkers; **NR**, non-reported; **LNG**, longitudinal; **ODI**, orientation dispersion index; **OFG**, orbital frontal gyrus; **PCC**, posterior cingulate cortex; **POS**, parietal occipital sulcus; **RD**, radial diffusivity; **ROI**, region of interest; **SBM**, surface-based morphometry; **SCL-90-R**, Symptom Checklist-90-Revised; **SFC**, superior frontal cortex; **SFG**, superior frontal gyrus; **SLF**, superior longitudinal fasciculus; **SMA**, supplementary motor area; **VBM**, voxel-based morphometry; **VLPFC**, ventrolateral prefrontal cortex; **VS**, ventral striatum.
a: BDE; binge drinking episode, defined by NIAAA as consuming five or more drinks (male), or four or more drinks (female), in about two hours.
b: Following the European School Survey Project on Alcohol and Drugs (ESPAD).
c: Only results of this article which assessed specifically BD effects were included in the current summary.
d: BAC was assessed in every participant according to the following algorithm: [BAC= g of alcohol consumed/weight in Kg x r (where r is a constant with value 0.68 for male and 0.55 for female)] – mr (where mr is the metabolization rate with value 0.15 for male and 0.18 for female) x hours, based on the number of standard drinks consumed in one single occasion.
e: Binge score was calculated from ítems 10 ('average drinks per hour'), 11 ('number of times being drunk in the previous 6 months') and 12 ('percentage of times getting drunk when drinking (average)') from the Alcohol Use Questionnaire (AUQ) (Townshend and Duka, 2002).

current BDs than in non-BDs. These authors also reported functional anomalies in the three different cognitive tasks explored (i.e. inhibition, reward and emotional processing), which will be described extensively in the corresponding sections of this review.

Banca et al. (2016). The main objective of this study was to evaluate decisional impulsivity in BDs and its relationship with potential brain volume differences. More specifically, 60 volunteers (30 BDs and 30 non-BDs) completed two tasks assessing reflection impulsivity (the beads task and the information sampling task [IST]) and a delay discounting task (DDT). Twenty-nine of the participants (14 BDs and 15 non-BDs) were examined by MRI. At the behavioural level, BDs performed less well in the beads task than non-BDs; however, regarding neuroimaging analysis, no volumetric differences between groups were observed in the ROIs examined (i.e. cerebellum, DLPFC, inferior parietal cortex and thalamus).

Kvamme et al. (2016) explored brain volumetric differences between genders in college-aged BDs (n = 30) and non-BDs (n = 46). Although the data analysis did not reveal a main effect of group, significant group by gender interactions were observed in several areas, including the prefrontal (IFG; right medial superior frontal gyrus [SFG]), striatal (left caudate, putamen and VS), right fusiform gyrus, motor preparatory regions (right supplementary motor area [SMA]), somatosensory cortex (right postcentral gyrus), left middle temporal gyrus (MTG) and left precuneus. Specifically, the results showed that male BDs had smaller grey matter volumes in these regions than male non-BDs and, in turn, female BDs had a greater volume than the counterpart non-BDs. In addition, for the BDs, the AUDIT scores were negatively correlated with volume in the right SFG and left paracentral lobule. These results indicate that cortical volume abnormalities among young people partaking in BD vary depending gender and suggest differences in vulnerability to the neurotoxic effects of alcohol between males and females.

Sousa et al. (2017) examined the grey matter density in 20 BDs and 16 alcohol abstinent controls (AACs) within the core brain regions associated with self-regulatory processes. ROI analysis showed increased grey matter densities in the left MFG in the BDs than in AACs. Additionally, a group by gender interaction effect was observed in the left MFG. Post hoc analysis revealed that male BDs had greater grey matter density in this region than male AACs; the same pattern was also reported for female BDs and female AACs. Furthermore, correlation analysis showed a positive correlation between the grey matter density in left MFG and the self-control subscale of the Barratt Impulsiveness Scale (BIS) in young BDs. This study suggests grey matter abnormalities associated with a BD pattern in the left MFG, a key region in self-regulatory processes.

Another recent study conducted by Sousa et al. (2020) explored the potential morphological anomalies of 20 college BDs and 16 AACs by using manually segmented protocol to delineate the anatomical ROIs (i.e. NAcc and caudate). MRI analysis revealed larger grey matter volume in the NAcc in BDs than in their AAC peers. The authors suggest that these results may indicate that the BD pattern is associated with neuroanatomical immaturity in a region of the brain (i.e. NAcc) that appears to play a key role in the cycle of addiction (Koob and Volkow, 2010).

Table 3
Summary of functional MRI studies of BDs young adults.

Study & design	Sample characteristics	BD criteria	non-BD criteria	Exclusion criteria: Control of Confounding Variables (neurological or psychiatric comorbidity, AUD, etc.)	Imaging modality/ fMRI task	Regions of interest (ROI)	Group-by-gender interactions
Working memory							
Squeglia et al. (2011) CS	Age range: NR 40 BD (13 F) M: 18.1 ± 0.7 F:17.8 ± 1.0 55 non-BDs (24 F) M: 17.7 ± 1.0 F: 18.1 ± 0.92	≥ 1 BDE[a] in past 3 months.	< 3 drinks in the past 3 months.	Parental history of bipolar, psychotic, or antisocial disorder; prenatal exposure to alcohol or illicit drugs; premature birth; history of neurological or serious medical illness; lifetime use of psychotropic medications; current or past DSM-IV Axis I diagnosis other than conduct disorder, oppositional defiant disorder, phobia, or alcohol abuse; left-handedness; sensory problems; marijuana use > 3x/month in past three months; > 25 lifetime uses of other illicit substances; positive alcohol or substance use test on the day of scanning.	Spatial Working Memory task	- SFG - Right IFG - ACC - Right SPL	Males: BDs > non-BDs activation during SWM vs. vigilance trials. Females: BDs < non-BDs activation during SWM vs. vigilance trials.
Campanella et al. (2013) CS	Age range: NR 16 BD (9 F) 20.9 ± 1.8 16 non-BDs (9 F) 21.6 ± 2.6	≥ 6 drinks (10 g of alcohol) on the same occasion at a speed of 2 drinks per hour, at most 2–3 times per week.	Drank 1–30 days/month, ≤ 5 standard alcoholic drinks/occasion and ≤ 2 drinks/hour.	Major medical problems; conditions of the central nervous system (e.g. epilepsy or history of brain injury); sensory problems, past or current drug use (other than cannabis and tobacco); positive alcohol or substance use test on the day of scanning.	N-back		NA
Inhibitory control							
Ames et al. (2014b) CS	Age range: 18–22 21 BDs (11 F) 20.2 ± 1.4 20 non-BDs (13 F) 20.7 ± 1.1	BDE at least twice weekly. Males: ≥ 15 drinks/week. Females: ≥ 8 drinks/week.	Expected to drink < 3 times/week and consume ≤ 2 drinks/occasion, with no reported binging behavior.	History of psychiatric or neurological disorders; use of medications that affect the central nervous system; left-handedness.	Alcohol-specific Go/ NoGo task		NA
Whelan et al. (2014) CS	Age range: NR 115 BDs (66 F) 14.62 ± 0.39 150 non-BDs (79 F) 14.53 ± 0.43	≥ 3 lifetime drinking episodes[b] leading to drunkenness.	≤ 2 lifetime drinking episodes leading to drunkenness.	Pregnancy and birth concerns (e.g. prenatal alcohol exposure); medical neurological or developmental conditions (e.g. major neuro-developmental disorders); mental health and abilities (i.e. treatment for schizophrenia, bipolar disorder or IQ < 70).	Stop Signal Task		NA
Molnar et al. (2018) CS	Age range: NR 14 BDs (9 F) 23.8 ± 3.4 17 non-BDs (9 F) 25.5 ± 4.1	≥ 5 binge episodes in the last 6 months. A binge episode was defined as consuming 5 + /6 + drinks for females/males within a 2 h-period.	≤ 2 binge episodes in the last 6 months.	History of seizures or traumatic brain injury; neurological or neuropsychiatric disorders; visions or hearing non-corrected impairments; left-handedness; positive substance use test on the day of scanning. Participants were medication-free, and they reported no use of drugs or tobacco at least one month prior to the study, and none had been enrolled in alcohol abuse treatment.	Stroop task	- VLPFC - Thalamus - PreSMA - PreCent - Parietal - Insula - Motor	At the behavioural level there were no differences between males and females. Gender differences on fMRI data were not assessed.
Suárez-Suárez et al. (2020) CS	Age range: 18–19 32 BDs (20 F) 18.22 ± 0.42 35 non-BDs (16 F) 18.08 ± 0.28	At least 1 binge episode once a month for the last 6 months. A binge episode was defined as consuming 5 + /7 + drinks for females/males in one drinking occasion.	Less than 1 binge episode once a month for the last 6 months.	Scores > 20 in the AUDIT; GSI ≥ 90 or scoring in at least 2 symptomatic dimensions of the SCL-90-R; uncorrected sensory deficits; left-handedness; personal history of neurological disorder or traumatic brain injury; history of regular use of other drugs (except occasional use of cannabis); personal history of chronic medical conditions that affect neurocognitive functioning (i.e. hypothyroidism); personal and/or family history of DSM-IV axis I or II disorder in first-degree relatives; family history of alcoholism in first-degree relatives.	Alcohol-specific Go/ NoGo task	- Right IPL - Right IFG - Left IFG - Right MFG - Right SFG	NA
Decision making and reward-related decision making							
Xiao et al. (2013) CS	Age range: NR 14 BDs (6 F) 17.3 ± 0.5	≥ 5 drinks/occasion, ≥ 1 occasion in the past month.	Alcohol naïve.	History of neurological or psychiatric disorder; left-handedness; sensory problems.	Iowa Gambling Task (IGT)		NA

(*continued on next page*)

Table 3 (*continued*)

Study & design	Sample characteristics	BD criteria	non-BD criteria	Exclusion criteria: Control of Confounding Variables (neurological or psychiatric comorbidity, AUD, etc.)	Imaging modality/ fMRI task	Regions of interest (ROI)	Group-by-gender interactions
	14 non-BDs (11 F) 17.1 ± 0.7						
Whelan et al. (2014) CS	Age range: NR 115 BDs (66 F) 14.62 ± 0.39 150 non-BDs (79 F) 14.53 ± 0.43	≥ 3 lifetime drinking episodes[b] leading to drunkenness.	≤ 2 lifetime drinking episodes leading to drunkenness.	Pregnancy and birth concerns (e.g. prenatal alcohol exposure); medical neurological or developmental conditions (e.g. major neuro-developmental disorders); mental health and abilities (i.e. treatment for schizophrenia, bipolar disorder or IQ < 70).	Monetary Incentive Delay task		NA
Worbe et al. (2014) CS	Age range: NR 19 BD (11 F) 23.2 ± 3.5 21 non-BDs (12 F) 24.1 ± 3.1	> 8 alcohol units/occasion (> 6 alcohol units/occasion for females) in a 2-hour period, ≥ 1 occasion/week, over a period of 3 months.	NR	History of neurological or psychiatric disorders; regular use of drugs (except nicotine); < 18 years old; positive substance use test on the day of scanning.	Anticipatory risk-taking task with and without feedback	- SPC - DLPFC - DMPFC - Anterior insula - Lateral OFC	NA
Cservenka et al. (2015) LNG	Age range baseline: 12–16 17 BDs (9 F) Baseline: 14.9 ± 1.0 Follow-up: 16.9 ± 1.3 17 non-BDs (9 F) Baseline: 14.8 ± 0.8 Follow-up: 16.7 ± 1.2	≥ 1 BDE in past 3 months and, ≥ 2 occasions of ≥ 4 drinks/ occasion in the same 90-days period.	Alcohol and substance-naïve.	At baseline: > 10 lifetime alcoholic beverages, > 2 drinks/occasion, > 5 lifetime uses of marijuana, or > 4 cigarettes/day. Both baseline and follow-up: DSM-IV Axis I disorder; psychotic disorders in first-degree biological parents; prenatal alcohol exposure; head injury with loss of consciousness; use of psychotropic medication; left-handedness; serious medical/ neurological conditions; alcohol consumption on the day of scanning.	Wheel of Fortune (Reward-based decision-making task)	-VS	None
Jones et al. (2016) LNG	Age range baseline: 13–16 13 BDs (5 F) Baseline: 14.9 ± 1.2 Follow-up: 17.7 ± 1.2 13 non-BDs (5 F) Baseline: 14.9 ± 1.1 Follow-up: 17.0 ± 1.1	≥ 1 BDE in past 3 months and, ≥ 3 occasions of ≥ 4 drinks/ occasion in the same 3-month period.	Alcohol and substance naïve.	At baseline: > 10 lifetime alcoholic beverages, > 2 drinks/occasion, > 5 lifetime uses of marijuana, or > 4 cigarettes/day. Both baseline and follow-up: Any other drug use; DSM-IV psychiatric disorder; serious medical/ neurological problems; learning disorder; psychotic disorder in a biological parent; prenatal drug or alcohol exposure; left-handedness; alcohol consumption on the day of scanning.	Wheel of Fortune (Reward-based decision-making task)	- DS - DC - DLPFC	NA
Garbusow et al. (2019) CS	Age: 18 years old 94 high-risk drinkers (all of them male) 97 low-risk drinkers (all of them male)	An average intake > 60 g of ethanol per drinking occasion.	An average intake < 60 g of ethanol per drinking occasion.	History of major neurological or major mental disorders, including substance abuse (except for nicotine dependence and alcohol abuse); current alcohol abstinence; left-handedness.	Pavlovian-to-instrumental transfer (PIT)	- NAcc - Amygdala	NA
Chen et al. (2020) CS	Age: 18 years old 94 high-risk drinkers (all of them male) 97 low-risk drinkers (all of them male)	An average intake > 60 g of ethanol per drinking occasion.	An average intake < 60 g of ethanol per drinking occasion.	History of major neurological or major mental disorders, including substance abuse (except for nicotine dependence and alcohol abuse); current alcohol abstinence; left-handedness.	Pavlovian-to-instrumental transfer (PIT)		NA
Alcohol cue reactivity							

(*continued on next page*)

Table 3 (*continued*)

Study & design	Sample characteristics	BD criteria	non-BD criteria	Exclusion criteria: Control of Confounding Variables (neurological or psychiatric comorbidity, AUD, etc.)	Imaging modality/ fMRI task	Regions of interest (ROI)	Group-by-gender interactions
Ames et al. (2014a) CS	Age range: 18–22 17 BDs (8 F) 20.2 ± 1.2 19 non-BDs (14 F) 20.8 ± 1.1	BDE at least twice weekly. Males: ≥ 15 drinks/week Females: ≥ 8 drinks/week.	Drink < 3 times/week and consume ≤ 2 drinks/ occasion, with no reported binging behavior.	History of psychiatric or neurological disorders; use of medications that affect the central nervous system; left-handedness; alcohol consumption on the day of scanning.	Alcohol-IAT		NA
Brumback et al. (2015) LNG	Age range: 16–19 22 BDs (12 F) 17.9 ± 0.7 16 non-BDs (7 F) 17.4 ± 0.7	≥ 3 BDE in past month. ≥ 100 lifetime drinking episodes.	< 5 lifetime drinking episodes. No history of heavy drinking (i.e. > 4/5 standard alcoholic drinks/ occasion for females/males).	History of psychiatric disorder; head trauma; learning disorder; neurological medical illness; family history of bipolar I or psychotic disorder; prenatal alcohol exposure; sensory problems; use of psychoactive medications; extensive marijuana (>50 lifetimes) or other drug use (>15 times); and alcohol or substance use during the abstinence protocol.	Alcohol-specific cue reactivity task	- DS/GP - NAcc - OFC - ACC - DLPFC	NA
Socio-emotional processing							
Maurage et al. (2013) CS	Age range: NR 12 BD (5 F) 24.2 ± 4.5 12 non-BDs (5 F) 23.4 ± 4.2	> 5 doses (10 g of ethanol)/ occasion, > 3 occasions/week, > 2 doses/hour in the last 6 months.	< 2 doses (10 g of ethanol)/ occasion; < 1 occasion/week; < 1 dose/hour in the last 6 months.	Positive personal or family history of alcohol-dependence; past or present drug or psychotropic medication consumption (including tobacco); major medical or central nervous system disorder; auditory impairment; high depression (BDI) and anxiety scores (STAI A–B); left-handedness.	Emotional categorization task (taken from Montreal Affective Voices Battery)		NA
Whelan et al. (2014) CS	Age range: NR 115 BDs (66 F) 14.62 ± 0.39 150 non-BDs (79 F) 14.53 ± 0.43	≥ 3 lifetime drinking episodes leading to drunkenness.	≤ 2 lifetime drinking episodes leading to drunkenness.	Pregnancy and birth concerns (e.g. prenatal alcohol exposure); medical neurological or developmental conditions (e.g. major neuro-developmental disorders); mental health and abilities (i.e. treatment for schizophrenia, bipolar disorder or IQ < 70).	Face Task		NA
Rae et al. (2020) CS	Age range: 18–26 36 BDs (19 F) 20.17 ± 1.13 35 non-BDs (17 F) 20.97 ± 2.4	Binge score higher than 30.[d]	Binge score < 16	History of psychiatric or neurological problems; current medication at the time of the study (including paracetamol and antibiotics); left-handedness; below or above normal BMI; alcohol consumption 12 h before the MRI session.	Empathy task		NA
Resting-state							
Morris et al. (2016) CS	Age range: NR Study 3[c] 32 BDs (14 F) 22.1 ± 3.3 32 non-BDs (16 F) 24.1 ± 3.4	> 8 alcohol units/occasion (> 6 alcohol units/occasion for females) in a 2-hour period, ≥ 1 occasion/week, over a period of 3 months.	NR	Current major depression or another major psychiatric disorder; any substance addiction; major medical illness; or use of psychotropic medication.	fMRI resting-state seed-to-voxel	- STN - VS - SGC - Putamen	NA
Arienzo et al. (2020) CS	Age range: 18–30 18 BDs (11 F) 23.3 ± 3.1 17 LDs (8 F) 25.6 ± 4.2	≥ 5 BDE in past 6 months.	≤ 1 BDE in past 6 months.	History of neurological or psychiatric disorder; History of seizures or traumatic brain injury; non-corrected vision or hearing problems; learning difficulties; medication use; tobacco or drug illicit use in the past month; positive alcohol or substance use test on the day of scanning.	fMRI resting-state seed-to-voxel	- Caudate - NAcc - ACC - IFC	None
Sousa et al. (2019) CS	Age range: 18–23 20 BDs (10 F) 20.45 ± 1.6 14 AACs (8 F) 20.86 ± 1.7	≥ 1 BDE per month for the past 10 months.	No alcohol use experience.	Scores ≥ 20 in the AUDIT; GSI ≥ 90 or scoring in at least 2 symptomatic dimensions of the SCL-90-R; uncorrected sensory deficits; left-handedness; personal history of traumatic brain injury; regular (i.e. on a weekly basis) consumption of cannabis, personal history of regular or occasional use of other drugs (illegal or medically prescribed psychoactive substances); personal and/or family history of any neurological or DSM-IV axis I disorder in first-degree relatives; family history of alcoholism in first-degree relatives; AUD.	fMRI resting-state Independent Component Analysis (ICA)		None

Note. **AACs**, alcohol-abstinent controls; **ACC**, anterior cingulate cortex**; AUD**, alcohol use disorder; **AUDIT**, alcohol use disorders identification test; **BA**, Brodmann's Area; **BAC**, blood alcohol content; **BD**; Binge drinking (pattern); **BDs**, binge drinkers; **BDI**, beck depression inventory; **BMI**, body mass index; **BOLD**, blood oxygen level-dependent; **CS**, cross-sectional; **DC**, dorsal caudate; **DLPFC**, dorsolateral prefrontal cortex; **DMPFC**, dorsomedial prefrontal cortex; **DS**, dorsal striatum; **DSGP**, dorsal striatum/globus pallidus; **GSI**, global severity index; **IAT**, implicit association test; **IFC**, inferior frontal cortex; **IFG**, inferior frontal gyrus; **IPL**, inferior parietal lobule; **ILF**: inferior longitudinal fasciculus; **LNG**, longitudinal; **MFG**, middle frontal gyrus; **MJ,** marijuana; **mOFG**, medial orbital frontal gyrus; **MOG**, middle occipital gyrus; **MRI**, magnetic resonance imaging; **MTG**, middle temporal gyrus; **NA**, non-assessed; **NAcc**, nucleus accumbens; **non-BDs**, non-binge drinkers; **NR**, non-reported; **LDs**, light episodic drinkers; **OFC**, orbitofrontal cortex; **PPI**, psychophysiological interaction; **ROI**, region of interest; **SFG**, superior frontal gyrus; **SGC**, subgenual cingulate cortex; **SMA**, supplementary motor area; **SPC**, superior parietal cortex; **SPL**, superior parietal lobule; **STAI A-B**, state and trait anxiety inventory; **STN**, subthalamic nucleus; **SWM**, spatial working memory; **VLPFC**: ventrolateral prefrontal cortex; **VS**, ventral striatum.
a: BDE; binge drinking episode, defined by NIAAA as consuming five or more drinks (male), or four or more drinks (female), in about two hours.
b: Following the European School Survey Project on Alcohol and Drugs (ESPAD).
c: Only results of this article which assessed specifically BD effects were included in the current summary.
d: Binge score was calculated from ítems 10 ('average drinks per hour'), 11 ('number of times being drunk in the previous 6 months') and 12 ('percentage of times getting drunk when drinking (average)') from the Alcohol Use Questionnaire (AUQ) (Townshend and Duka, 2002).

3.3.1.1. Overview of MRI studies. Structural imaging studies that evaluated grey matter in BDs relative to non-BDs have largely indicated morphological brain abnormalities in adolescents who report a BD pattern of consumption. Most of the studies that have examined volume and cortical thickness measures found widespread alterations (both increases and decreases) in cortical and subcortical regions (Doallo et al., 2014; Howell et al., 2013; Kvamme et al., 2016; Mashhoon et al., 2014; Sousa et al., 2020, 2017; Squeglia et al., 2012; Whelan et al., 2014), although not all of the studies reviewed reported differences between groups (Banca et al., 2016). Among the different structures where anomalies were found, the prefrontal cortex was the most commonly identified region (n = 5) followed by different subcortical (n = 4) and cingulum areas (n = 3, Fig. 2).

Among studies that reported structural changes in prefrontal regions (Doallo et al., 2014; Kvamme et al., 2016; Mashhoon et al., 2014; Sousa et al., 2017; Squeglia et al., 2012; Whelan et al., 2014), some revealed higher ACC (Doallo et al., 2014) and left MFG/DLPFC grey matter volume in BDs than in non-BDs (Doallo et al., 2014; Sousa et al., 2017). By contrast, other studies reported lower vmPFC, right IFG, and left MFG volume (Whelan et al., 2014) as well as a reduced thickness in the right middle ACC (Mashhoon et al., 2014).

Regarding the possible gender differences associated with BD and including, but not limited to, prefrontal frontal regions, various studies reported group by gender interactions (Kvamme et al., 2016; Squeglia et al., 2012), showing that, in comparison their control peers, male BDs tend to show lower thickness or volume in the left frontal pole, left pars orbitalis, left mOFG, left rostral ACC (Squeglia et al., 2012), IFG and right medial SFG (Kvamme et al., 2016), while female BDs showed the opposite pattern. These findings, according to the authors, may indicate a differential effect of episodic BD between males and females, reflecting differences in neuromaturation trajectories and neurotoxic sensitivities depending on gender.

Other cortical regions where structural differences between BDs and non-BDs have been identified (Howell et al., 2013; Kvamme et al., 2016; Mashhoon et al., 2014) showed increased right lingual gyrus and right precuneus grey matter volume (Howell et al., 2013) as well as decreased left dorsal PCC cortical thickness (Mashhoon et al., 2014); group by gender interactions were observed in right fusiform gyrus, right SMA, right postcentral gyrus and left MTG volume (Kvamme et al., 2016).

Studies that have focused on how BD impacts subcortical areas (Howell et al., 2013; Kvamme et al., 2016; Sousa et al., 2020; Whelan et al., 2014) have also observed different alterations in BDs relative to non-BDs, showing larger volume in the VS/NAcc (Howell et al., 2013; Kvamme et al., 2016; Sousa et al., 2020), right putamen (Whelan et al., 2014) and left thalamus (Howell et al., 2013). Regarding VS/NAcc findings, the results reported by Kvamme et al. (2016) may suggest partial replication, as although these authors did not observe any significant main effect, they did observe a group by gender interaction, in which female BDs had a larger VS volume than female non-BDs, while male BDs showed the opposite pattern.

At this point it is important to note that, although it has been proposed that these structural variations may reflect the deleterious effects of alcohol on typical brain development, the significance of alterations in grey matter measures has not yet been clarified. Some researchers have suggested that greater grey matter volume or cortical thickness may represent alteration of synaptic pruning processes, probably caused by the neurotoxic effects of alcohol. On the other hand, it has been suggested that a decrease in grey matter may indicate an atypical trajectory in cortical development, reflected by loss or decreased volume or cortical thickness also associated with neurotoxic effects.

Exploration of the relationship between structural changes and differences at the neurocognitive level revealed various associations (Doallo et al., 2014; Sousa et al., 2017; Squeglia et al., 2012). Specifically, alterations in prefrontal grey matter were correlated with worse performance in neuropsychological tests involving response inhibition, attention, visuospatial skills (Squeglia et al., 2012) and executive aspects of working memory (Doallo et al., 2014), as well as with higher scores on an impulsiveness scale (Sousa et al., 2017).

Furthermore, some studies have also shown that grey matter measures are correlated with consumption variables, such as AUDIT scores (Howell et al., 2013; Kvamme et al., 2016) and quantity of alcohol intake (Doallo et al., 2014; Mashhoon et al., 2014).

Finally, one of the objectives of the present review was to explore the possible differences between BDs and non-BDs observed in longitudinal studies (i.e. whether the observed abnormalities increased by the medium/long-term maintenance of the BD pattern). However, as all the MRI studies included in this review were cross-sectional (i.e. only one MRI scan was performed), we cannot address this aspect in this section.

3.3.2. Diffusion MRI (dMRI) studies

Seven studies used diffusion MRI techniques to investigate how BD can affect the white matter tracts that connect different brain structures, as well as grey and white matter microstructure. While most of the studies used diffusion tensor imaging (DTI; n = 6), one study, conducted by Morris et al. (2018), used neurite orientation dispersion and density imaging (NODDI) model. DTI is a conventional variant of dMRI that is sensitive to directional displacement of molecular water and provides some insight into properties of brain microstructure, including fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD) and radial diffusivity (RD) (Qiu et al., 2015). Collectively, these parameters are indicators of the microstructure of white matter, with FA and MD being the most widely used indices (Lebel et al., 2012). In healthy individuals, high values of FA have been associated with enhanced neural connectivity, greater fibre integrity and white matter myelination. By contrast, increased MD values seem to be associated with decreased myelination. Thus, a reduction in FA and an increase in MD may reflect damaged or disordered neuronal fibre tracts caused by tissue loss or potential demyelination (Chanraud et al., 2010; Madden et al., 2012). NODDI is a more recent and advanced dMRI model that estimates the microstructural complexity of dendrite and axon morphology in the form of the neurite density index (NDI) and the orientation dispersion

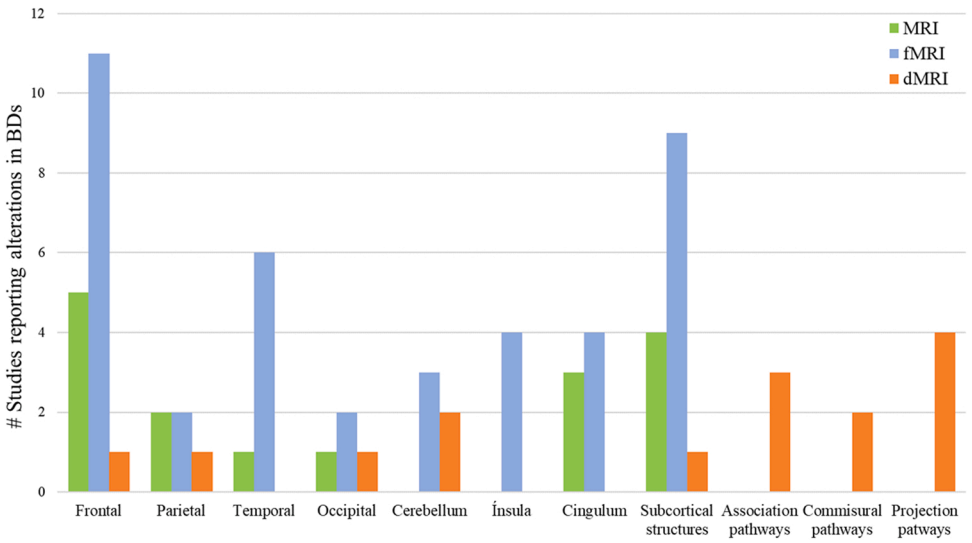

Fig. 2. Anatomical regions where significant differences have been reported in BDs compared to non-BDs.

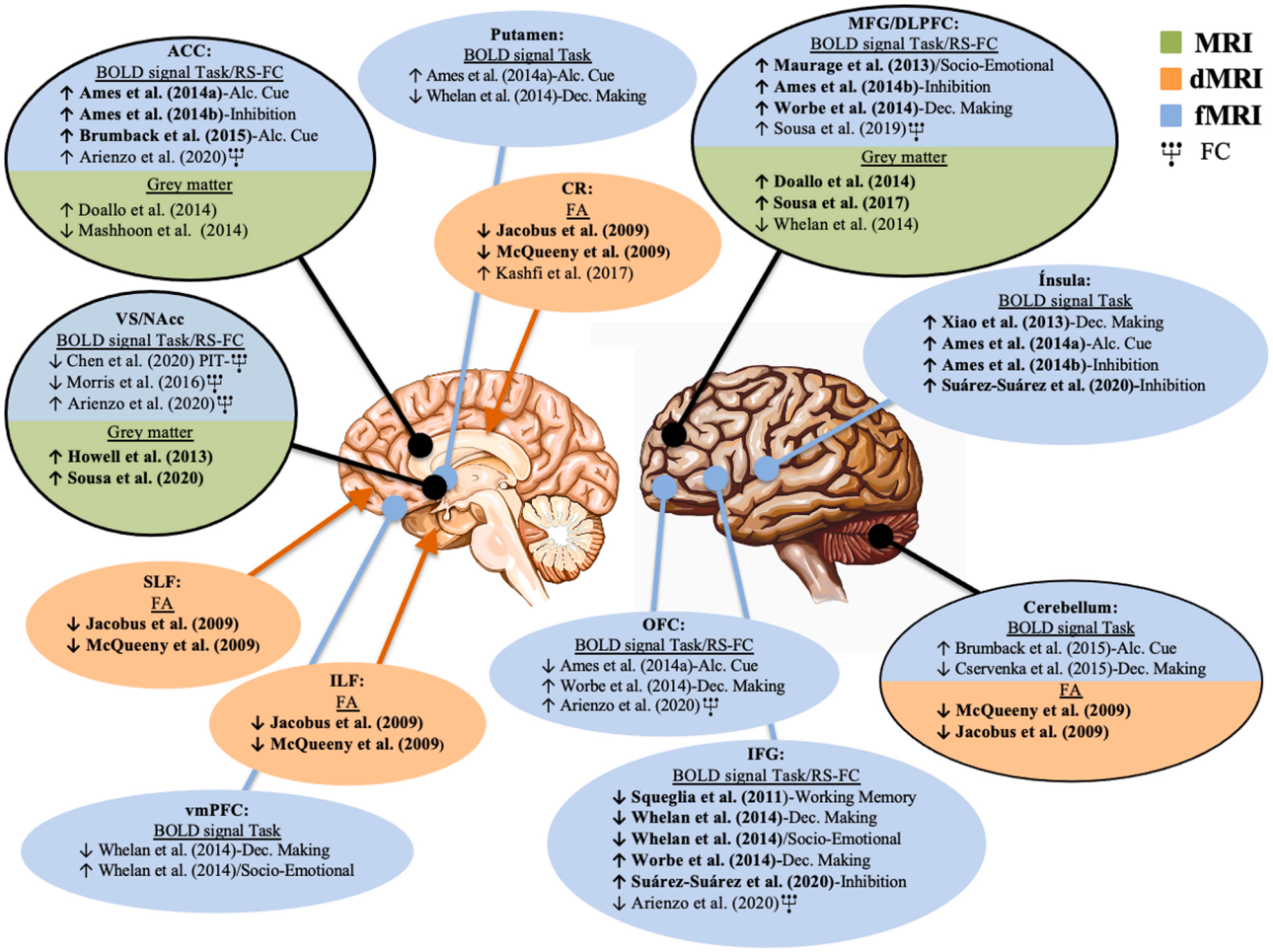

Fig. 3. Replicated findings. Brain regions that showed significant structural or functional alterations in at least two independent studies. Those areas with common anomalies direction are indicated in bold. Acronyms: ACC, anterior cingulate cortex; CR, corona radiata; DLPFC, dorsolateral prefrontal cortex; FA, fractional anisotropy; FC: Functional Connectivity: IFG, inferior frontal gyrus; ILF, inferior longitudinal fasciculus; MFG, middle frontal gyrus; NAcc, nucleus accumbens; OFC, orbitofrontal cortex; PIT, pavlovian-to-instrumental transfer; RS-FC, resting-state functional connectivity; SLF, superior longitudinal fasciculus; vmPFC, ventromedial prefrontal cortex, VS, ventral striatum; ↓, less or decreased; ↑, higher or increased.

Table 4
Quality assessment scores according to the NHLBI Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.

Study	Q1	Q2	Q3	Q4	Q5a/Q5b	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14a/Q14b	Quality Rating
Ames et al. (2014a)	Yes	Yes	NR	Yes	No/No	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Fair**
Ames et al. (2014b)	Yes	Yes	NR	Yes	Yes/No	No	No	No	Yes	No	Yes	NR	NA	No/No	**Poor**
Arienzo et al. (2020)	Yes	Yes	NR	Yes	No/No	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Fair**
Banca et al. (2016)[a]	Yes	Yes	NR	Yes	No/Yes	No	No	No	Yes	No	Yes	NR	NA	No/Yes	**Fair**
Brumback et al. (2015)	Yes	Yes	NR	Yes	No[b]/Yes	No	No? (4 weeks)[c]	No	Yes	Yes	Yes	NR	Yes	No/Yes	**Good**
Campanella et al. (2013)	Yes	Yes	NR	Yes	No/No	No	No	No	Yes	No	Yes	NR	NA	Yes/No	**Fair**
Chen et al. (2020)	Yes	Yes	NR	Yes	Yes/No	No	No	No	Yes	No	Yes	NR	NA	No/Yes	**Fair**
Correas et al. (2016)[a]	Yes	Yes	NR	Yes	No/No	No	Yes	No	Yes	Yes	Yes	NR	Yes	Yes/CD	**Good**
Cservenka et al. (2015)	Yes	Yes	NR	Yes	No/Yes	Yes	Yes	No	Yes	Yes	Yes	NR	Yes	No/Yes	**Fair**
Doallo et al. (2014)	Yes	Yes	NR	Yes	No/No	Yes	Yes	No	Yes	No	Yes	NR	NA	Yes/Yes	**Fair**
Garbusow et al. (2019)	Yes	Yes	NR	Yes	Yes/No	No	No	No	Yes	No	Yes	NR	NA	No/Yes	**Fair**
Howell et al. (2013)	Yes	Yes	NR	Yes	No/No	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Fair**
Jacobus et al. (2009)	Yes	Yes	NR	Yes	No/Yes	No	No	No	Yes	No	Yes	NR	NA	No/Yes	**Fair**
Jones et al. (2016)	Yes	Yes	NR	Yes	No/Yes	Yes	Yes	No	Yes	Yes	Yes	NR	Yes	No/Yes	**Fair**
Kashfi et al. (2017)	Yes	Yes	NR	Yes	No/Yes	No	No	No	Yes	No	Yes	NR	NA	No/No	**Poor**
Kvamme et al. (2016)	Yes	Yes	NR	Yes	Yes/No	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Good**
Mashhoon et al. (2014)	Yes	Yes	NR	Yes	Yes/No	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Good**
Maurage et al. (2013)	Yes	Yes	NR	Yes	No/No	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Fair**
McQueeny et al. (2009)	Yes	Yes	NR	Yes	No/Yes	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Fair**
Molnar et al. (2018)	Yes	Yes	NR	Yes	No/No	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Fair**
Morris et al. (2016)[a]	Yes	Yes	NR	CD	Yes/No	No	No	No	Yes	No	Yes	NR	NA	No/Yes	**Fair**
Morris et al. (2018)	Yes	Yes	NR	Yes	Yes/No	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Good**
Rae et al. (2020)	Yes	Yes	Yes	Yes	Yes/Yes	No	No	No	Yes	No	Yes	NR	NA	No/Yes	**Fair**
Smith et al. (2017)	Yes	Yes	Yes	Yes	Yes/Yes	No	Yes	No	Yes	Yes	Yes	NR	Yes	No/Yes	**Good**
Sousa et al. (2017)	Yes	Yes	NR	Yes	No[b]/No	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Good**
Sousa et al. (2019)	Yes	Yes	NR	Yes	No[b]/No	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Good**
Sousa et al. (2020)	Yes	Yes	NR	Yes	No[b]/No	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Good**
Squeglia et al. (2011)	Yes	Yes	NR	Yes	Yes/Yes	No	No	No	Yes	No	Yes	NR	NA	No/Yes	**Fair**
Squeglia et al. (2012)	Yes	Yes	NR	Yes	Yes/Yes	No	No	No	Yes	No	Yes	NR	NA	No/No	**Poor**
Suárez-Suárez et al. (2020)	Yes	Yes	NR	Yes	Yes/No	No	No	No	Yes	No	Yes	NR	NA	Yes/Yes	**Good**
Whelan et al. (2014)[a]	No[d]	Yes	NR	Yes	Yes/No	No	No	No	Yes	No	Yes	NR	NA	Yes/CD	**Fair**
Worbe et al. (2014)	Yes	Yes	NR	Yes	No/No	No	No	No	Yes	No	Yes	NR	NA	No/Yes	**Fair**
Xiao et al. (2013)	Yes	Yes	NR	Yes	No/No	No	No	No	Yes	No	Yes	NR	NA	No/Yes	**Fair**

Note.
[a] = The quality assessment scores are referred exclusively to the experiment(s) in which neuroimaging measures (MRI, dMRI, fMRI) explored differences between BDs and controls.
[b] = Sample size ≥ 20 in BD group.
[c] = It is not clear which is the minimum duration required to observe changes after an abstinence period.
[d] = The focus is on machine learning; CD = cannot be determined; NA = not applicable; NR = not reported.

index (ODI) (Zhang et al., 2012).

McQueeny et al. (2009) assessed microstructural white matter integrity among adolescent BDs. The sample was composed by a group of 14 participants who met BD criteria and another 14 who were classified as non-BDs. The FA index was lower in BDs than in non-BDs across the 18 brain regions examined, which included the inferior longitudinal fasciculus (ILF), superior longitudinal fasciculus (SLF), corona radiata (CR), internal and external capsule (IC, EC), corpus callosum (CC), cerebellum and limbic projection fibres. Moreover, in the BDs, exploratory bivariate correlations between FA values and alcohol use measures revealed negative correlations between the following: (i) more lifetime alcohol hangover experiences and lower FA in CC; (ii) peak estimated BAC in the 3 months prior to scanning and lower FA in the body of CC, left IC, right EC and left posterior CR. According to the authors, these findings suggest that BD could lead to microscopic disruption of white matter fibres.

Jacobus et al. (2009) evaluated the integrity of white matter in adolescents with a BD pattern. In this study, participants were classified according to a three-group design, as follows: 14 BDs, 14 non-BDs and 14 BD + MJs (marijuana users). Thus, diffusion findings showed that the BDs had lower FA than the non-BDs in all the regions studied (including the right ILF, left inferior fronto-occipital fasciculus [IFOF], left middle cerebellar peduncle, left SLF, and four clusters in the left superior CR). No significant between-group differences were observed in the MD index. These results indicate the possible neurocognitive consequences of BD in adolescents, regardless of the use of marijuana.

Correas et al. (2016). This study explored the evolution of the white matter connectivity in 17 BDs and 22 non-BDs throughout a two-year-long period. DTI analysis did not reveal any significant differences associated with a BD pattern of consumption in any of the indices explored (i.e. FA, MD, AD, RD), or at baseline or in the follow-up evaluation; however, it is worth noting that the authors reported a differential functional connectivity pattern in the default mode network using magnetoencephalography (MEG). Nevertheless, interpretation of these results is beyond the scope of this review.

Smith et al. (2017). This longitudinal study explored the effects of a BD pattern consumption on the integrity of white matter at a whole-brain level and also in five segments of the CC (prefrontal, premotor/SMA, motor, sensory and parietal/temporal/occipital [PTO]). The sample included 20 BDs and 20 non-BDs, who were given MRI scans in two different sessions separated by an interval of one year. Despite the absence of a main effect of group or gender in any of the sessions, significant group by gender interactions were observed, both at a whole-brain and CC ROI level. Whole brain analysis showed lower FA in male BDs than in male non-BDs and higher FA in female BDs than in female non-BDs in forceps minor/major, IFOF, left corticospinal tract and body and splenium of CC in both sessions. Regarding ROI analysis, the results showed the same pattern of significant group by gender interactions as in the whole-brain analysis for prefrontal, sensory and PTO segments of the CC in session 1, and for the sensory and PTO regions in session 2. However, the differences in mean FA from Session 1 to Session 2 did not reveal significant group by gender interaction, or any significant main effect associated with the temporal factor. Furthermore, correlation analysis (session 1) also showed several negative relationships between mean FA and the following: (i) binge scores for the prefrontal and PTO segments, only in male BDs; (ii) types of drugs used, in

the premotor/SMA and motor segment, in both groups combined; (iii) quantity of drug used, in all segments of CC in male participants; (iv) performance deficits in a spatial working memory (SWM) test and prefrontal, PTO, motor and sensory segments of the CC across all participants. Neuroimaging findings revealed that the BD pattern of consumption in adolescents may be associated with white matter alterations in several brain areas during a developmental period of particular cognitive vulnerability.

Kashfi et al. (2017) examined microstructural white matter integrity in young college-age adults. The sample was formed by a group of 12 BDs and 12 moderate drinkers (MoDs). Whole-brain analysis revealed higher FA in the right anterior CR in BDs than in MoDs, while the AD, MD, and RD measures revealed no significant differences between the groups. On the other hand, ROI analysis showed higher AD of the right EC and cingulum in BDs than in MoDs. In addition, the following correlations between connectivity metrics (i.e. FA, AD) and drinking behaviour were observed at the ROI level: (i) for the BD group, FA values of the right anterior CR were negatively correlated with total number of drinks consumed and with the average number of drinks per episode, while AD values of the left and right cingulum correlated negatively with the total number of drinks consumed and the frequency of BD episodes; (ii) for both groups combined, AD values of the right EC were positively correlated with the total number of drinks and number of BD episodes, as well as with the number of drinks per drinking episode.

Morris et al. (2018) used the NODDI model to evaluate possible differences between young BDs (n = 28) and non-BDs (n = 38) in both grey matter ODI and white matter NDI. This study reported that BDs had higher ODI in regions throughout the parietal cortex (i.e. right angular gyrus, right supramarginal gyrus, left superior parietal lobule [SPL] and left inferior parietal lobule IPL)) as well as reduced ODI in several regions, including the right IPL, right SFG (DLPFC), right postcentral gyrus, left middle occipital gyrus (MOG) and left SPL, than in non-BDs. On the other hand, BDs showed increased white matter NDI in right SFG, right supramarginal gyrus, left MFG and bilateral IPL, as well as lower NDI in right angular gyrus, right postcentral gyrus and left MOG than in non-BDs. In addition, ROI analysis showed that BDs had greater VS ODI than non-BDs. Correlation analysis examining the relationship between microstructural features and drinking severity indicated that VS ODI values were positively correlated with binge score in the BDs. These findings suggest that BD may lead to anomalies in the cortical microstructure of prefrontal and parietal regions implicated in higher-order attentional and executive functioning, as well as in the VS, an important region in reward-related processes.

Sousa et al. (2019) explored the functional and structural connectivity of frontoparietal regions associated with executive control processes (executive control network [ECN]) in young college-age adults. Regarding structural measures, this study used DTI in a sample formed by 20 BDs and 14 AACs. No main group effect was found for the FA, AD, RD, and MD indices in the frontoparietal regions previously identified as part of the ECN by the FIND lab atlas (Shirer et al., 2012) (i.e. left ECN, right ECN and the MFG node of the left ECN). However, and similarly to the study conducted by Correas et al. (2016), significant between-group differences in functional connectivity were observed (see Resting-state for details).

3.3.2.1. Overview of dMRI studies. Few studies have examined the possible relationship between white matter integrity and BD pattern (Correas et al., 2016; Jacobus et al., 2009; Kashfi et al., 2017; McQueeny et al., 2009; Morris et al., 2018; Smith et al., 2017; Sousa et al., 2019). Four of these studies reported FA alterations in adolescent BDs relative to their non-BD counterparts (Jacobus et al., 2009; Kashfi et al., 2017; McQueeny et al., 2009; Smith et al., 2017) while two studies did not reveal differences between BDs and non-BDs in the FA index (Correas et al., 2016; Sousa et al., 2019). Specifically, the studies led by Jacobus et al. (2009) and McQueeny et al. (2009) showed decreased FA values in the major white matter pathways explored, with some of these regions (i.e. ILF, SLF, CR, and cerebellar tracts) replicated in both studies (see Fig. 3), while a single study revealed higher FA values in young college students categorized as BDs (Kashfi et al., 2017). Likewise, Smith et al. (2017) reported group by gender interactions for various white matter tracts, with male BDs having lower FA values than their control peers, while the inverse pattern was observed in female BDs. Furthermore, as observed in MRI studies (Kvamme et al., 2016; Squeglia et al., 2012), these findings suggest that a BD pattern of consumption has different impacts on the white matter integrity in males than in females. On the other hand, regarding other DTI indices (i.e. MD, AD, RD), only one study revealed differences between BDs and non-BDs in the AD index (Kashfi et al., 2017).

Overall, research that has examined the white matter microstructure tends to show inconsistencies. However, the results of studies that observed significant differences between groups suggest that BD during adolescence may be associated with poor white matter integrity in projection fibers (e.g. CR), tracts considered important for connecting the two hemispheres (e.g. CC) and tracts connecting sensory structures to higher-order frontal cortices (e.g. ILF, SLF), as well as on the grey matter dendritic features (i.e. ODI) in VS, a region previously associated with reward/motivation processes.

Only one of the dMRI studies evaluated the relationship between white matter metrics and performance in cognitive domain (Smith et al., 2017). More specifically, the authors observed that performance deficits in a SWM task were negatively correlated with FA. Thus, the findings of this study support previous reports mentioned in the section on MRI, which showed an association between poorer neurocognitive functioning in various cognitive domains and structural anomalies in young people who reported a BD pattern of alcohol consumption (Doallo et al., 2014; Squeglia et al., 2012).

Four dMRI studies have also related microstructural indexes and alcohol use/severity variables (Kashfi et al., 2017; McQueeny et al., 2009; Morris et al., 2018; Smith et al., 2017). Two of these studies associated diffusion indexes with binge score in the BDs (Morris et al., 2018; Smith et al., 2017).

Unlike in the MRI section, various longitudinal dMRI studies examined whether white matter integrity would change across time differently in BDs and non-BDs participants (Correas et al., 2016; Smith et al., 2017), implications of the findings will be discussed in the overall discussion section.

3.4. Functional findings in BDs

A large body of research has investigated the effects of BD on brain function using fMRI (Table 3), which depicts changes in blood oxygen level-dependent (BOLD) signal across time. We identified 19 studies that used this technique to compare brain activity in BDs and non-BDs in relation to different cognitive functions. Most of the studies (16/19) were designed to evaluate task-related cognitive and affective processes. The most widely studied cognitive processes were executive functions (working memory [2/16] and inhibitory control [4/16]), as well as decision-making and reward-related decision-making (7/16). In addition, two studies focused on the brain activity of young BDs during an alcohol cue reactivity task and another three studies examined the brain correlates of socio-emotional processing in young adults with and without a BD pattern. The remaining three studies (3/19) aimed to assess potential differences in the resting-state functional connectivity of different brain regions between BDs and non-BDs.

3.4.1. Working memory

Working memory (WM) is considered a core element of executive functioning, in which information is temporarily analyzed, held and manipulated in order to perform a specific mental process (Baddeley and Hitch, 1994). Typically, WM has been classified into different subcomponents according to content (verbal WM and visual-spatial WM).

Brain areas supporting this function predominantly include prefrontal structures (both ventrolateral and dorsolateral cortices), as well as the premotor cortex, the posterior parietal cortex (Owen et al., 2005). The present review identified two studies that investigated underlying brain activity in BDs while they performed spatial and verbal working memory tasks, respectively.

Squeglia et al. (2011) characterized the gender-specific influences of BD on brain activity related to working memory in young people (40 BDs and 55 non-BDs). During the fMRI session, participants completed a spatial working memory (SWM) task, which considered two conditions: an experimental condition, in which subjects had to respond when a design (drawing) reappeared in a previously occupied location during that block (SWM condition), and a vigilance (baseline) condition, in which the same stimulus was presented in identical locations, but participants only had to respond when a dot appeared above the stimulus. There were no significant differences between groups in terms of task accuracy or reaction time (RT). ROI analysis findings showed less activation in right SFG and right IFG during SWM vs. vigilance trials in BDs than in non-BDs, as well as group by gender interactions in three of the ROIs analyzed: ACC, right IFG and right SFG. In addition, significant group by gender interactions were also found in exploratory whole-brain analysis, despite the absence of main effects of group and gender. On this occasion, interactions were observed in the left medial frontal gyrus, right MTG, left superior temporal gyrus (STG) and left cerebellar declive. In all regions with group by gender interactions (both ROI and whole-brain analysis), female BDs showed lower activation during SWM vs. vigilance trials than female non-BDs, while male BDs showed the opposite pattern to male non-BDs. Moreover, correlation analysis in BDs during SWM vs. vigilance trials showed the following: (i) greater right IFG activity was positively correlated with better spatial performance in males and (ii) lower right dorsal SFG and left cerebellar declive activation was associated with worse attention and working memory performance in females. The authors reported that the significant gender-specific differences in frontal, temporal and cerebellar regions seem to suggest that female BDs may be more vulnerable to the effects of this consumption pattern. On the other hand, the greater BOLD activity observed in male drinkers may reflect some capacity to recruit compensatory systems.

Campanella et al. (2013). This study explored the potentially different neural regions recruited during a WM n-back task in 16 BDs and 16 non-BDs. In this task, subjects were asked to detect when the number presented was identical to the number displayed two trials before (two-back condition; N2) or whenever the number “2” was presented (control zero-back condition; N0). The fMRI analysis revealed greater activation in pre-SMA during N2 vs. N0 trials in young BDs than in non-BDs in the absence of behavioural differences. In addition, relative to BDs, BOLD activity during N2 vs. N0 trials was positively correlated with the following: (i) the number of alcohol doses consumed on each occasion (higher activity in the dorsomedial prefrontal cortex); and (ii) the number of drinking occasions per week (higher activity in cerebellum, right thalamus and right insula). The authors interpreted these findings as a greater use of attentional resources by BDs, which may reflect "compensatory strategies" to reach equivalent behavioural performance to that in non-BDs.

3.4.1.1. Summary of working memory studies. In the revised studies, young BDs presented neural anomalies relative to non-BDs in both spatial and verbal WM in the absence of performance differences. These anomalies included the engagement of both more and fewer neural resources in different task-related brain structures as well as a group by gender interaction in some non-hypothesized areas during an SWM task. Furthermore, the findings of the study of Squeglia et al. (2011) seem to indicate that the relationship between BD and neural abnormalities is modulated by gender, at least for the visuospatial component. These gender-modulated differences were interpreted as female vulnerability to the potential neurotoxic effects of alcohol consumption.

In an effort to deal with the observed mixed pattern of results (higher and lower levels of neural activation), the authors of each of the studies proposed different hypotheses. Thus, greater BOLD activity was interpreted as a need to mobilize more neural resources to achieve equivalent performance in participants and controls (Campanella et al., 2013; Squeglia et al., 2011). On the other hand, Squeglia et al. (2011) proposed that the lower activation in female BDs may reflect some kind of difficulty in engaging task-relevant areas. Nevertheless, these different results and interpretations are not limited to working memory studies but apply generally to the literature on adolescent alcohol use, as mentioned in a previous study (Ewing et al., 2014).

3.4.2. Inhibitory control

Successful human behaviour requires the ability to suppress automatic actions or thoughts that are contextually inappropriate. This executive function is generally defined as inhibitory control (Aron, 2007) and is critical for goal-oriented behaviour. As identified in several meta-analyses, this executive function is supported by a fronto-parietal network, including the IPL, IFG, MFG and anterior insula, among other structures (Cai et al., 2014; Swick et al., 2011; Zhang et al., 2017). We identified three studies which evaluated inhibitory control using experimental paradigms from motor response inhibition (Go/NoGo and Stop Signal tasks) and interference control (Stroop task) approaches.

Ames et al. (2014b). This study explored the potential modulating effect of alcohol-related stimuli on response inhibition processes in a sample of college students with and without a BD pattern of alcohol consumption. The participants (21 BDs and 20 non-BDs) completed an alcohol-cue Go/NoGo task in which they had to respond to pictures corresponding to the category designated as “Go” signals (i.e. non-alcoholic drinks such as cola and water) and suppressing their response when stimuli of the NoGo category (alcoholic drinks) were presented (i.e. a bottle of beer). fMRI findings revealed greater BOLD activity in right DLPFC, anterior/mid cingulate and right anterior insula during correct NoGo trials in BDs relative to non-BDs in the absence of behavioural differences in the number of false alarms. The authors suggest that these results may be explained by greater task difficulty for the BDs, given the salience of the NoGo cues, which may demand increased activation of neural regions implicated in working memory and inhibitory control.

Whelan et al. (2014). In this study, already described in the section on MRI studies, the authors also evaluated the brain activity in 115 current BDs and 150 non-BDs with different fMRI tasks. The neural activity in response inhibition was assessed in participants during performance of a Stop Signal task. In this task, participants were asked to respond when go stimuli were presented (arrows pointing left or right) but refrain from responding when the go stimulus was followed by a stop-signal (an arrow pointing upwards). The fMRI analysis showed greater activation in right precentral and left postcentral gyrus when failing to inhibit a response, as well as higher activation in the precuneus during correct response inhibition in BDs than in non-BDs.

Molnar et al. (2018) characterized the neural correlates of interference control, usually defined as the ability to inhibit prepotent mental representations, in a sample of 14 young BDs and 17 non-BDs. In this study, participants completed a Stroop task in which they had to identify the colour of the font from different words under two conditions: (i) congruent, the colour of the font matched the meaning of the colour word; (ii) incongruent, the colour of the font was different from the colour word, inducing interference. At performance level, there were no differences between groups on accuracy, although RT was significantly longer in BDs than in non-BDs during incongruent trials. Regarding the neural response, ROI analysis revealed higher BOLD activity in the ventrolateral prefrontal cortex (VLPFC) and the left thalamus during the incongruent trials in BDs compared to non-BDs. Moreover, correlations across groups during both congruent and incongruent conditions revealed that the right VLPFC activity was positively correlated with

Stroop difficulty. Furthermore, correlation analysis during the incongruent condition showed positive associations between the following: (i) the left thalamus peak activity with BD episodes and (ii) the VLPFC peak activity with BD episodes, blackouts and the Short Michigan Alcoholism Screening Test (SMAST) and AUDIT measures. On the other hand, in correlation analysis of separate groups, a positive correlation between the right VLPFC with non-planning impulsivity scores was observed in BDs during incongruent trials. The prolonged RT and the stronger activation pattern were interpreted as a possible compensatory mechanism to meet the higher cognitive demands of the incongruent trials.

The final article included in the category of inhibitory control is a recent publication by Suárez-Suárez et al. (2020). This study attempted to explore the potential the impact of BD on the neural activity evoked by a Go/NoGo task and its modulation by motivational salience of stimuli (alcohol-related content). In a similar manner to the task used by Ames et al. (2014b), the participants (32 BDs and 35 non-BDs) completed a Go/NoGo task in which pictures of alcoholic and non-alcoholic beverages were used as stimuli. However, in this case, there were two different blocks in which both alcohol and non-alcohol related pictures acted as Go and NoGo stimuli, depending on the instructions received at the start of each block. fMRI results revealed greater activity in BDs than in non-BDs in the bilateral IFG, extending to the anterior insula, during successful inhibition trials (irrespective of the alcoholic content of stimuli), in the absence of behavioural differences. Moreover, BDs displayed greater BOLD activity than non-BDs in the IFG/insula of the right hemisphere when inhibiting a prepotent response to alcohol-related stimuli. These findings suggest that the motivational salience of stimuli modulates the inhibition-related activity in the right IFG/insula, highlighting the role of this brain region in suppressing responses to substance-associated cues.

3.4.2.1. Summary of inhibitory control studies. Response inhibition and interference control studies have reported the presence of increased activity in prefrontal regions (e.g. DLPFC, VLPFC and IFG), anterior insula and precuneus during successful inhibition in BDs assessed with three different tasks (i.e. Go/NoGo, Stop Signal and Stroop), as well as increased response in precentral and postcentral gyrus during inhibition errors. This consistent hyperactivation pattern of task-relevant areas may differentiate inhibitory control anomalies from other cognitive processes in which the pattern of results is less clear and reinforces the notion that BDs present anomalies related to inhibitory control functioning. Moreover, the prolonged RT observed in BDs during the Stroop task (Molnar et al., 2018) seems to support the hypothesis proposed in some of the studies reviewed (Ames et al., 2014b; Molnar et al., 2018), i.e. increased difficulty associated with the performance of inhibitory control tasks that would be solved by the recruitment of more neural resources (i.e. hyperactivation of task-relevant areas). Interestingly, this neurocompensation hypothesis has also been proposed in event related-potential (ERP) studies, in which one of the most robust findings in tasks involving response inhibition is an augmented P3 amplitude. Similar to the interpretation proposed in the aforementioned fMRI studies, this finding has been suggested to indicate brain overactivation in BDs, allowing them to perform tasks with a normal level of performance (for a review see Almeida-Antunes et al., 2021).

3.4.3. Decision-making and reward-related decision-making processing

The adequate functioning of affective decision-making and reward processing is essential for selection of advantageous alternatives according to the possible future consequences and coping successfully with everyday life (Ruff and Fehr, 2014; Van den Bos et al., 2013). Seven neuroimaging studies investigated neural activity elicited by a set of behavioural paradigms related to the anticipation and receipt of rewards as well as their impact on risky decision-making.

Xiao et al. (2013) investigated the neural correlates of affective decision-making, measured by the Iowa Gambling Test (IGT), during an fMRI session. The sample was divided in two groups according to their consumption profile, with 14 BDs and 14 non-BDs. In the IGT task, participants must make a series of choices (through 4 decks of cards) that can lead to monetary gains or losses without the probabilities of each condition being known. Behavioural data revealed that BDs made more selections from the disadvantageous packs of cards while non-BDs switched to advantageous packs as the task progressed, leading to significantly worse performance in BDs than in non-BDs. The neural findings reported a greater BOLD signal in the left amygdala and insula in adolescent BDs than in non-BDs during the active versus control conditions. Furthermore, in the BDs, drinking-related problems were negatively correlated with BOLD activity in the right orbitofrontal cortex (OFC) and positively correlated with the activity in the right insula. Correlation analysis across groups yielded higher urgency scores associated with the following: (i) lower activity in the right OFC; and (ii) higher activity in the right insula. These findings were interpreted as an increase in incentive-related behaviours in young BDs that may have implications regarding the risk of and susceptibility to developing potential substance abuse disorders.

Whelan et al. (2014). In this study, adolescents completed a Monetary Incentive Delay task to assess the neural activity in response to reward processing. The participants had to respond to a briefly presented target by pressing a button to indicate that the target appeared on a particular side of the screen. The position of the target as well as the points that could be earned with each successful response were indicated by a signal that preceded the start of each trial. The fMRI analysis reported that current BDs showed lower neural activation than non-BDs in different brain areas. More specifically, less activity was observed in the left putamen and left hippocampus when a reward was anticipated, in the right hippocampus when it was received and in the vmPFC and left IFG both during anticipation and reception of reward.

Worbe et al. (2014) investigated the differences in affective decision-making associated with a risky situation in adolescent BDs. The sample comprised 19 BDs and 21 non-BDs who performed an anticipatory risk-taking task in which they had to choose between two options (low-risk or a high-risk probability) during two sessions with reward and loss conditions. In the baseline session, volunteers did not have any explicit information about the probability and magnitude of loss (feedback presentation), while in a second session feedback was presented in high-risk situations. Behavioural results indicated that in the baseline session BDs took more risky choices in the high-loss (HL) condition than non-BDs. However, when feedback was included, BDs made significantly fewer risky choices in HL conditions than at baseline. The reduction in the number of risky choices matched the performance of both groups. The ROI analysis showed higher BOLD activity in superior parietal cortex (SPC), lateral OFC and DLPFC during HL and low-loss conditions in BDs than in non-BDs. In addition, when feedback was included, whole-brain analysis for the HL condition showed that BDs had greater BOLD activity in the left IFG, which was positively associated with the decrease in risky choices. These results indicate that when anticipating large unlikely losses, BDs took greater risks than their counterpart non-BDs. However, this higher risk-attitude disappeared with feedback presentation, which was associated with greater IFG activity. According to the authors, these findings in the BD group may indicate deterioration in the anticipation of negative results associated with risky choices.

Cservenka et al. (2015) examined, in a longitudinal study, the neural basis of a reward processing task and its possible relationship to alcohol consumption during adolescence. The baseline assessment only included adolescents without regular alcohol consumption. For follow-up, conducted two years later, the sample was classified as BDs ($n = 17$) or non-BDs ($n = 17$) depending on how their alcohol consumption had changed. Participants were required to complete an adapted version of the "Wheel of Fortune" (WOF) test during the fMRI scanning. This task consisted of the presentation of several options of monetary gain (staged in the form of portions of a wheel) with different risk probabilities. The

trials were classified as "Wins" or "No Wins" depending on pre-defined probabilities of winning for each portion of the wheel. There were no significant behavioural differences in task performance between BDs and non-BDs in any of the evaluations. The ROI analysis did not detect significant effects between groups in the VS in any of the assessments; however, whole-brain analysis showed that BDs had lower BOLD response during Win vs. No Wins trials in the left cerebellum (lobe VII) at follow-up. The analysis also revealed significant effects of gender during Wins vs. No Wins responses at follow-up, showing lower brain response in males than females in the left cerebellum. Furthermore, in BDs, No Wins vs. baseline BOLD response in the left cerebellum was negatively correlated with average drinks consumed in the past 90 days. The observed findings highlight the deleterious effects of BD on brain activity during reward reception in a sample of adolescent drinkers.

The objective of the 3-year longitudinal study conducted by Jones et al. (2016) was to compare the differences in neural activation between young BDs and non-BDs in the decision-making process during a reward-based decision-making task similar to that used by Cservenka et al. (2015). The sample was evaluated at two different times; at baseline, the participants had not started on alcohol consumption, while at the follow-up assessment, the participants were classified as BDs (n = 13) and non-BDs (n = 13) according to their consumption pattern. No behavioural differences between groups were observed, in either the number of risky choice selections in the baseline or at follow-up. On the other hand, the ROI analysis revealed reduced activation during risky vs. safe selections in the left dorsal caudate in BDs relative to non-BDs during follow-up. In addition, whole-brain data analysis revealed pre-existing differences at the baseline between future BDs and non-BDs, showing a reduced risky vs. safe selection brain response in the left IPL, left IFG, MTG and STG, which persisted over time. These findings suggest two different types of anomalies associated with BD, represented by reduced BOLD activity in fronto-parietal regions in future BDs, as well as decreased brain activation in the dorsal caudate revealed once the BD pattern has been established.

More recently, two studies using the same sample data set (191 healthy 18-year-old males) (Chen et al., 2020; Garbusow et al., 2019) explored the potential influence of contextual task-irrelevant cues (Pavlovian stimuli) ongoing reward-oriented behaviour. More precisely, the studies examined whether the susceptibility to interference between conditioned stimuli (CS) and instrumental control (Pavlovian-to-Instrumental Transfer [PIT]) was enhanced in 94 high-risk drinkers relative to 97 low-risk drinkers. The experimental procedure was similar in both studies, with participants having to complete four tasks including a monetary-rewarded instrumental approach-avoidance learning task in which they had to learn to collect (approach to) “good shells” and leave “bad shells”. The second task was a Pavlovian conditioning programme associating five fractal images to different monetary outcomes (−2€, −1€, 0€, +1€, +2€). Once the instrumental and Pavlovian conditioning programmes were completed, participants performed the PIT task inside an MRI scanner. In the task they had to decide whether or not to collect the shells presented to try to earn the maximum amount of money while ignoring background images (CS). Finally, once outside the scanner volunteers also completed a forced choice task where they had to decide which of two CS presented was better.

In the investigation published by Garbusow et al. (2019), behavioural results indicated a higher response rate in the PIT task associated with the valence of the contextual CS presented in the whole sample, with CS associated with the receipt of a positive monetary outcome during the Pavlovian conditioning eliciting higher response rates in the decision to collect shells. Moreover, high-risk drinkers showed a higher PIT effect than low-risk drinkers. However, no differences between groups were observed in the fMRI analysis. In addition, higher alcohol consumption was associated with higher behavioural PIT effect and alcohol-related polygenic risk. The authors conclude that behavioural PIT can be considered a potential marker for a subclinical phenotype of risky alcohol consumption.

On the other hand, the paper published by Chen et al. (2020) focused on the PIT effect for congruent and incongruent conditions (e.g. positive CS + collect shell and negative CS + collect shell). Similarly to the results of the previous study, volunteers showed a significant PIT effect, measured in this case as an increased error rate when Pavlovian contextual cues (CS) conflicted with the instrumental behaviour (collect or leave). Moreover, participants in the high-risk group again showed a higher PIT effect than the participants in the low-risk drinking group. In addition, between-group differences in neural activity were observed. More specifically, high-risk drinkers showed a decreased lateral PFC response as well as a weaker connectivity between the VS and lateral PFC during incongruent trials. These results were interpreted as a potential alteration in high-risk drinkers between their bottom-up and top-down resources, which may explain the greater impact that CS have on the ability to choose the appropriate response in the presence of motivational stimuli.

3.4.3.1. Summary of decision-making and reward-related decision-making processing studies. Reward-related decision-making is the category with the greatest number of selected studies in this review, with 5 cross-sectional and 2 longitudinal studies. When the studies are considered together, some patterns emerge. First of all, behavioural differences arose in some of the experimental paradigms examined (Chen et al., 2020; Garbusow et al., 2019; Worbe et al., 2014; Xiao et al., 2013), showing that some aspects of decision-making, especially in high-risk and reward-associated contexts, may be compromised. Furthermore, in gambling paradigms (i.e. IGT and anticipatory risk-taking task) BDs showed a greater neural response than controls in the amygdala, the insula, the OFC and other fronto-parietal regions (Worbe et al., 2014; Xiao et al., 2013), as well as more risky choices. However, presentation of feedback about the consequences of risk taking enhanced the behavioural performance (Worbe et al., 2014), suggesting a potential target for prevention programmes. On the other hand, four different studies focusing on the anticipation and reception of a reward have observed a reduced neural response in BDs in subcortical regions such as the putamen, dorsal caudate, hippocampus and cerebellum, as well as cortical regions related to executive control (e.g. IFG, lateral PFC), among others (Chen et al., 2020; Cservenka et al., 2015; Jones et al., 2016; Whelan et al., 2014).

3.4.4. Alcohol cue reactivity

Neuroscientific models of addictive behaviours have proposed that the transition from recreational to pathological consumption patterns is partly characterized by increased salience attribution towards drug-related stimuli (Goldstein and Volkow, 2011, 2002; Koob and Volkow, 2016). Moreover, as shown by a previous meta-analysis, alcohol cue reactivity tasks elicited greater neural activity in brain regions implicated in incentive salience, reward processing and habit circuitry (e.g. dorsal striatum, prefrontal areas, ACC and insula) in alcohol-dependent patients (Schacht et al., 2013). However, the effects of BD on alcohol cue reactivity tasks seem to have been less well explored, with only two selected studies in this review.

Ames et al. (2014a). This study assessed neural correlates of alcohol-related associative processes during compatible and incompatible Implicit Association Test (IAT) focused on positive outcomes of alcohol use. This task, defined as a concept categorization task, provides a measure of automatic associations used to assess unconscious bias (Greenwald et al., 1998). Participants had to categorize randomly presented words into four possible categories (Alcohol positive, Mammal neutral, Alcohol neutral, Mammal positive). The set of words used comprised target words (e.g. whisky, rabbit) and attribute words (e.g. happy, stationary), which could be presented as compatible (Alcohol + Positive vs. Mammal + Neutral word combinations) or incompatible trials (Mammal + Positive vs. Alcohol + Neutral). Behavioural findings showed stronger positive implicit associations towards alcohol use,

reflected as shorter response latencies in BDs than in non-BDs. fMRI analysis revealed that BDs showed lower activation in the left OFC during both compatible and incompatible association trials than non-BDs. In addition, a significant group by condition interaction was observed. Thus, BDs showed greater activation in the left putamen and the right insula during the compatible trials (relative to incompatible trials), while non-BDs did not show differences in the neural response as a function of trial type. Finally, t-test comparisons between groups revealed that for compatible trials BDs (vs. non-BDs) showed higher activity in bilateral insula and ACC. These results indicated that BD is associated with differences in the neural response of different brain regions related to habit formation as well as with higher level of implicit associations towards alcohol cues.

Brumback et al. (2015) identified the neural substrates associated with alcohol cue reactivity and examined the potential effects of monitored abstinence from alcohol by using fMRI. The study participants (22 BDs compared to 16 non-BDs) had to complete an alcohol-specific cue reactivity task, in which images of alcoholic and non-alcoholic beverages presented had to be classified according to three possible categories: appetizing (like), unappetizing (dislike) or neutral. The behavioural results at baseline indicated that young BDs liked a significantly higher proportion of alcohol-content images than non-BDs (55% vs. 24%). ROI analysis revealed that BDs showed greater BOLD response to alcohol vs. non-alcohol cues in dorsal striatum and globus pallidus (DSGP) and left ACC at baseline than non-BDs. In addition, exploratory whole-brain analysis also revealed higher cerebellum and left parahippocampal gyrus activity in BDs than in non-BDs. However, these differences decreased to non-significant levels after one month of abstinence from alcohol. In BDs, greater activation in left ACC was positively correlated with: (i) higher positive alcohol expectancies at baseline (disappearing after one month); and (ii) higher alcohol craving at follow-up. Moreover, two different correlations emerged across groups: the percentage of alcohol pictures rated as "like" was positively correlated with left ACC BOLD response, and the percentage of alcohol pictures rated as "dislike" was negatively correlated with left ACC and left DSGP BOLD response at baseline (without any significant correlation in the follow-up).

3.4.4.1. Summary of alcohol cue reactivity studies. Both of the studies included in this category show differences in behavioural and neural responses in young BDs relative to non-BDs. More specifically, these studies showed higher neural activity in BDs in several incentive salience- and reward-related areas including, but not limited to, the ACC, insula and dorsal striatum, suggesting an enhanced salience attribution towards alcohol-related stimuli. These results may represent a form of habit (associative) learning that can lead to a transition in which implicit associative processes override control processes perpetuating hazardous behaviour (Ames et al., 2014a). However, unlike observations in studies with AUD patients, the greater salience of alcohol-related stimuli seems to be associated with the maintenance of the consumption pattern, as indicated by the fact that the differences observed disappeared after a period of abstinence (Brumback et al., 2015), which, without a doubt, should be considered in future prevention policies.

3.4.5. Socio-emotional processing

Despite the importance of social interaction and emotional processing in everyday life, studies focused on these dimensions in young BDs remain scarce; we found only three such studies.

Maurage et al. (2013) explored the effects of BD on the neural substrates of emotional processing. The sample comprised 24 adolescents (12 BD and 12 non-BDs). Participants had to complete an adapted task from the Montreal Affective Voices Battery during the fMRI scan, in which they had to classify different vocal stimuli as angry or fearful. The behavioural results showed lower correct response rates in BDs than in non-BDs. Regarding the neural response during the voice recognition, BDs showed lower activity in the STG, as well as a greater activity in the right MFG, than in non-BDs. Additional correlation analysis across groups showed a positive association between activation in STG and behavioural accuracy. The authors suggested that the greater activation of the MFG may reflect the involvement of alternative areas to compensate for the reduced temporal activity during emotional categorization.

Whelan et al. (2014). In this study, participants completed an emotional reactivity task (Faces task) during an fMRI session. In the task, volunteers had to pay attention to short videoclips displaying ambiguous expressions (emotionally "neutral"), angry face expressions or control stimuli (non-biological motion). The fMRI analysis showed higher activation in vmPFC in current BDs, relative to non-BDs, but reduced activation in the left IFG, right temporal pole and right cuneus during processing of angry faces.

Rae et al. (2020) examined the neural responses associated with empathic processing of pain-related pictures on young adult social drinkers with (n = 36) and without (n = 35) a BD consumption pattern. Participants were required to complete an empathy task (adapted from Jackson et al., 2005) in which they viewed images of bodily pain (vs. no-pain), while adopting the perspective of self (pain recipient) or other (observer of someone else experiencing pain) to categorize the image as painful or non-painful scene. At a behavioural level, BDs showed longer RTs, especially when categorizing pain-related images adopting the perspective of self. On the other hand, fMRI analysis revealed differences in the neural activity of the fusiform gyrus and inferior temporal gyrus. In particular, BDs showed stronger activation of the fusiform body area (FBA) than non-BDs while viewing pain-related images from the perspective of another person. These results have been interpreted as a potentially increased demand in BDs associated with the processing of pain perceived in others. The authors suggest that this hyperactivity of the FBA represents a compensatory mechanism to overcome potential deficits in the processing of emotional stimuli.

3.4.5.1. Summary of socio-emotional processing studies. Two of the three studies included in this category (Maurage et al., 2013; Whelan et al., 2014) highlighted the presence of lower neural activity in BDs in some task-relevant areas (i.e. STG, IFG or cuneus) than in non-BDs, as well as the recruitment of additional brain structures such as the MFG or the FBA (Maurage et al., 2013; Rae et al., 2020). In addition, Whelan et al. (2014) reported greater activation of the vmPFC, a region that has been linked to emotion and negative affect regulation (Diekhof et al., 2011; Morawetz et al., 2016), suggesting that young BDs may need additional resources to deal with negative-related stimuli. This hypothesis is consistent with the interpretation of the results by Rae and colleagues (2020), who proposed that the higher neural activity observed corresponds to a compensatory mechanism dealing with the increased demands of processing pain-related stimuli. Moreover, the behavioural results seem to suggest the existence of impairments in the perception of emotional stimuli as indicated by lower correct response rates (Maurage et al., 2013) and longer RTs (Rae et al., 2020). These results indicate the need to obtain further information about the relationship between BD and socio-emotional processing difficulties.

3.4.5.2. Overview of fMRI task studies. In summary, the main findings derived from studies based on fMRI during the execution of different cognitive tasks indicate that BD is linked to anomalies in the neuronal response associated with all the evaluated processes, with most of the studies reporting abnormalities in frontal regions, as well as in specific subcortical regions, especially in studies focused on motivational processes (e.g. VS, dorsal caudate, putamen or amygdala; see Fig. 2). However, the direction of the observed anomalies is not clear. Although the most common pattern has been the hyperactivation of brain areas such as the insula, DLPFC and the ACC (see Fig. 3), or the recruitment of

a greater number of brain areas during task performance, in BDs relative to non-BDs (Ames et al., 2014a, 2014b; Brumback et al., 2015; Campanella et al., 2013; Maurage et al., 2013; Molnar et al., 2018; Suárez-Suárez et al., 2020; Whelan et al., 2014; Worbe et al., 2014; Xiao et al., 2013; 10/16 studies), some articles have reported a decrease in neuronal response associated with the alcohol consumption pattern (Cservenka et al., 2015; Jones et al., 2016; Maurage et al., 2013; Squeglia et al., 2011; Whelan et al., 2014). It is also possible that instead of a general relationship between BD and brain activation (hyper or hypo), the direction of the anomalies may vary specifically according to the regions and tasks evaluated. In some studies, greater and lower BOLD activity have been observed simultaneously in BDs, relative to the control group, in different brain structures (Ames et al., 2014a; Maurage et al., 2013; Whelan et al., 2014).

Regarding behavioural results, most studies have reported the absence of significant differences in task performance. However, some studies observed performance deficits in BDs relative to the respective controls, especially in gambling (Worbe et al., 2014; Xiao et al., 2013), alcohol cue reactivity (Ames et al., 2014a; Brumback et al., 2015) and socio-emotional paradigms (Maurage et al., 2013; Rae et al., 2020). This absence of behavioural differences, together with the aforementioned neural anomalies, has been interpreted in some studies as a compensatory mechanism in which the greater BOLD activity reflects the greater cognitive demands of the task faced by BDs.

Finally, many of the cognitive domains explored by fMRI investigations were addressed only by a few studies. In addition to the reduced number of works included in some of these cognitive domains, we identified considerable heterogeneity in the design of experimental tasks. For instance, among the categories reviewed, only in the decision-making/reward processing category, more than one study (n = 2) used the same task. This fact makes it challenging to find consistent results between independent studies, which is, without a doubt, another drawback to the possibility of replicating findings. Thus, we believe that carrying out new studies using well-established experimental paradigms is essential to confirm the findings observed to date.

3.4.6. Resting state

Examination of resting-state functional connectivity (RS-FC) by fMRI involves analysis of spontaneous BOLD signal fluctuations in order to identify correlations between brain regions. This methodological approach has revealed that these apparent spontaneous fluctuations are highly organized and tend to resemble the patterns of activity observed in participants while performing different behavioural tasks (Biswal et al., 1995; Fox and Raichle, 2007). In recent years, study of the RS-FC has undergone a great advance both in healthy and in clinical populations. Nevertheless, the potential anomalies in the RS-FC associated with a BD pattern of consumption remain relatively unexplored, and we identified only three studies that used this methodological approach and that matched our inclusion criteria.

The first study that assessed the potential differences in RS-FC between young adults with and without a BD pattern was that conducted by Morris et al. (2016). The main objective of this study was to explore the neural correlates of waiting impulsivity through RS-FC measures in different experimental groups (healthy volunteers, AUD patients and young BDs). Of the three experiments carried out in this study, only one explored the association between BD and the RS-FC of the subthalamic nucleus (STN), an important region of a frontostriatal network involved in inhibitory control. The comparison revealed that relative to non-BDs (n = 32), BDs (n = 32) had reduced STN connectivity with subgenual cingulate cortex (SGC) and VS. In addition, correlation analysis across the sample revealed that the functional connectivity between the STN and the SGC was negatively associated with AUDIT scores.

Arienzo et al. (2020) examined RS-FC in a group of young people, classified as BDs (n = 18) or LDs (n = 17), in a number of ROIs defined from research on AUD patients. Comparisons revealed that BDs had greater connectivity between regions involved in reward processing (NAcc and caudate) and ACC and OFC, as well as lower connectivity of the IFC, a key region in cognitive control processes, with the left hippocampus. In addition, correlation analysis showed that the connectivity of NAcc and caudate with the ACC and OFC was positively related to drinking variables (e.g. number of BD episodes in the last 6 months and AUDIT scores), while the IFC connectivity to the hippocampus was negatively associated with these consumption variables. These results were interpreted as potential dysregulation of the reward circuit that would place young BDs in a vulnerable position regarding transition from recreational to pathological consumption. The reduced connectivity between the IFC and the hippocampus was interpreted as greater difficulty in inhibiting unwanted or alcohol-associated thoughts and memories.

Finally, based on the frontal anomalies found in previous studies, Sousa et al. (2019) explored the functional connectivity of frontoparietal regions associated with executive control processes (executive control network) in a group of 34 college students (20 BDs and 14 AACs). The authors reported increased RS-FC of the left MFG in BDs (vs. non-BDs), as well as a positive correlation between the functional connectivity of this region and the frequency of BD episodes in the previous month. These findings reinforce previous evidence about the presence of alterations in the MFG in young BDs, both at a structural level (Doallo et al., 2014; Sousa et al., 2017) and during the performance of inhibitory control tasks (e.g. Ames et al., 2014b); the results thus highlight the possible vulnerability of prefrontal regions, still under development, to the effects of an intensive consumption pattern.

3.4.6.1. Overview of resting-state studies. The RS-FC studies selected for this review used different analytical methods to explore the relationship between BD and the functional connectivity of different brain regions and networks. It is difficult to draw firm conclusions, owing to relatively small number of studies in this field, together with the heterogeneity of the regions explored. Although it seems clear that young BDs present anomalies in RS-FC compared to non-BDs, as observed in studies focused on evaluating task-evoked activity, the direction of these anomalies is not yet clear, with findings indicating both greater and lower connectivity, depending on the region explored. Thus, greater connectivity has been observed in regions associated with reward processing (Arienzo et al., 2020), and greater (Sousa et al., 2019) and lower (Arienzo et al., 2020; Morris et al., 2016) connectivity have been observed in regions associated with inhibitory control processes. In this regard, further fMRI studies are needed to continue to elucidate the anomalies present in the RS-FC of young BDs in other relevant networks such as the default mode network (for MEG results in this topic, see Correas et al., 2016).

4. Discussion

4.1. Integration of observed evidence

Among the studies included in the present review, some patterns seem to emerge that relate binge drinking to brain anomalies (see Fig. 3). Next, we will present the most notable and common findings across studies.

Collectively, the results collected using this systematic review approach reported structural and functional brain abnormalities in adolescents who engaged BD pattern. By integrating the anomalies in common regions observed by different techniques, some structures have been highlighted as being a target of the observed differences between groups, including MFG/DLPFC (Ames et al., 2014b; Doallo et al., 2014; Maurage et al., 2013; Morris et al., 2018; Sousa et al., 2019, 2017; Whelan et al., 2014; Worbe et al., 2014), ACC (Ames et al., 2014a, 2014b; Arienzo et al., 2020; Brumback et al., 2015; Doallo et al., 2014; Mashhoon et al., 2014), VS/NAcc (Arienzo et al., 2020; Chen et al., 2020; Howell et al., 2013; Morris et al., 2018, 2016; Sousa et al., 2020) and cerebellum (Brumback et al., 2015; Cservenka et al., 2015; Jacobus

et al., 2009; McQueeny et al., 2009).

Notably, the recurrent abnormalities observed across multimodal imaging coincide in indicating prefrontal areas that are strongly involved in executive control processes (i.e. MFG/DLPFC and ACC) as being especially sensitive to the impact of the BD pattern. Specifically, in accordance with the direction of MRI and dMRI (NODDI) findings (Doallo et al., 2014; Morris et al., 2018; Sousa et al., 2017; however see Whelan et al., 2014), functional studies have also reported neural anomalies in MFG/DLPFC (Ames et al., 2014b; Maurage et al., 2013; Sousa et al., 2019; Worbe et al., 2014). Three of these fMRI studies revealed greater BOLD activity during performing of tasks which evaluated processes, such as inhibition (Ames et al., 2014b), decision-making (Worbe et al., 2014) and socio-emotional processing (Maurage et al., 2013), while the remainder showed greater RS-FC (Sousa et al., 2019). Regarding the ACC findings, two structural studies revealed grey matter anomalies that were not consistent with each other (Doallo et al., 2014; Mashhoon et al., 2014). Likewise, both task-related (i.e. inhibition and alcohol cue reactivity) and resting-state studies have revealed greater BOLD response (Ames et al., 2014a, 2014b; Brumback et al., 2015) and higher RS-FC (Arienzo et al., 2020) in BDs than in non-BDs.

Another region that we consider important to highlight is the VS/NAcc, in which replicated anomalies have been detected in MRI studies (Howell et al., 2013; Sousa et al., 2020), fMRI studies (Arienzo et al., 2020; Chen et al., 2020; Morris et al., 2016) and in one NODDI study (Morris et al., 2018). In this regard, structural studies have reported an increased volume (Howell et al., 2013; Sousa et al., 2020) and greater ODI (Morris et al., 2018) in BDs (vs. non-BDs), while fMRI research has detected anomalies in the functional connectivity of this region with frontal structures involved in executive and attentional processes (e.g. PFC, STN, ACC) both at resting-state (Arienzo et al., 2020; Morris et al., 2016) and during the performance of an experimental task (Chen et al., 2020).

The last region identified in which converge structural and functional alterations is the cerebellum. The findings regarding this structure revealed differences between groups in brain activity (Brumback et al., 2015; Cservenka et al., 2015) and white matter microstructure (Jacobus et al., 2009; McQueeny et al., 2009). These aforementioned abnormalities in white matter studies (i.e. decreased FA values) were also consistent in other association and projection fibres (e.g. CR, ILF, SLF) (see Fig. 3).

Beyond the regions where differences between groups were observed through various neuroimaging techniques, it is also important to note two additional structures that we think deserve special mention because of both the large number of studies reporting alterations (i.e. IFG; n = 6) and the degree of consistency of the observed findings (i.e. insula). Importantly, these two regions are strongly associated with cognitive control, interoceptive and socio-emotional processes (Cai et al., 2014; Chung and Clark, 2014; Uddin et al., 2017; Zhang et al., 2017).

Finally, significant functional differences in three motivation-related regions (i.e. vmPFC, OFC and putamen) have been reported in at least two independent studies. Although the findings have been less consistent, young BDs showed differences in task-related BOLD response in vmPFC, putamen and OFC (Ames et al., 2014a; Whelan et al., 2014; Worbe et al., 2014) and greater RS-FC connectivity in OFC (Arienzo et al., 2020) relative to non-BDs.

4.2. *Differences and similarities between BD and other consumption patterns*

One of the great efforts in elaborating this systematic review was to use a strict inclusion criterion (see Table 1), which enabled us to distinguish the specific impact of a BD pattern on a developing brain from other types of drinking behaviour (i.e. heavy alcohol use and AUD). This approach contrasts with that used in previous reviews (Ewing et al., 2014; Jones et al., 2018; Lees et al., 2020; Silveri et al., 2016; Spear, 2018), which have compared and integrated results of studies that included samples ranging across youth BDs and participants with different severities of consumption.

In this respect, the BD studies examined here and those reported in above-mentioned alcohol use literature agree in pointing out that alcohol consumption during adolescence and early adulthood is associated with structural and functional anomalies. These neurocognitive changes have been observed in several cortical (especially in the prefrontal cortex) and subcortical brain regions intimately involved in the control and regulation of impulsive or risky behaviours, as well as in the processing of reinforcing stimuli.

However, relative to our main consistent results (shown in bold, Fig. 3), these studies appear to differ, at least partially, suggesting that the BD pattern could lead to distinctive neurocognitive abnormalities compared to both heavy alcohol use and AUD.

For instance, most of the studies included in the current review that examined structural features across prefrontal regions revealed increased grey matter in the MFG/DLPFC in youth BDs relative to non-BDs (Doallo et al., 2014; Sousa et al., 2017), in contrast with prefrontal morphological reductions reported in both heavy drinkers (Heikkinen et al., 2017; Luciana et al., 2013; Meda et al., 2017; Pfefferbaum et al., 2017; Squeglia et al., 2015) and young people with AUD (De Bellis et al., 2005) relative to controls.

Another particularly noteworthy finding was observed in VS/NAcc (Howell et al., 2013; Sousa et al., 2020), showing larger grey matter volumes in youth BDs compared to non-BDs. Curiously, although this region has been associated with the rewarding effect of alcohol consumption (Mitchell et al., 2012), structural changes in the VS/NAcc have not been reported in adolescents with heavy alcohol use or AUD diagnosis (for review see Silveri et al., 2016).

Moreover, none of the studies considered in the current review, even those including ROI analysis (Howell et al., 2013), found significant differences between BDs and non-BDs in the hippocampus. This may indicate that, despite the vulnerability of the hippocampus to the neurotoxic effects of alcohol reported in several studies with both heavy drinking (Meda et al., 2018) and AUD samples (De Bellis, 2000; Medina et al., 2007; Nagel et al., 2005), there might be no differences in the early stages of alcohol consumption associated with a BD pattern.

Taken together, these differences in grey matter characteristics would indicate that the BD pattern is associated with morphological changes that differ to those observed in other types of alcohol consumption. Nevertheless, this proposition requires further research, specifically with structural studies comparing BDs, heavy drinkers and AUD population.

Among the dMRI studies that found anomalies in the white matter integrity of the main brain tracts in BDs, the most replicated findings were reduced FA in the CR, ILF, SLF and cerebellum relative to controls (Jacobus et al., 2009; McQueeny et al., 2009). Also, significant differences in FA were observed in different segments of the CC (McQueeny et al., 2009; Smith et al., 2017). Although one of these studies only reported a significant gender by group interaction (Smith et al., 2017; see Section 4.4 Gender effects related to BD pattern). Remarkably, other studies that explored white matter microstructure in adolescent heavy drinkers (Thayer et al., 2013; Shen et al., 2019) and young adults with AUD (De Bellis et al., 2008; Chumin et al., 2019) have found abnormalities in the same brain tracts (among others) as targets for alcohol effects, despite some differences in the direction of the FA effects. Specifically, these studies revealed both decreased FA in the anterior CR of male heavy drinkers (Shen et al., 2019), in the SLF, posterior CR (Thayer et al., 2013) and cerebellum (Chumin et al., 2019) as well as increased FA in ILF, SLF (Chumin et al., 2019), eight regions of the CC (De Bellis et al., 2008) and anterior portion of CR (Thayer et al., 2013). The inconsistencies observed regarding the FA of the anterior CR (Thayer et al., 2013 vs. Jacobus et al., 2009; McQueeny et al., 2009; and Shen et al., 2019) may be explained by the concomitant use of marijuana and the shorter lifetime use of alcohol in the paper by Thayer and colleagues

(2013). Regarding studies with AUD (Chumin et al., 2019; De Bellis et al., 2008), the increased FA observed may suggest a distinct effect (at least within the discussed regions) to what has been observed with young BDs.

Regarding fMRI findings in the highlighted regions (i.e. the ACC, MFG/DLPFC, insula, IFG), there are both differences and similarities between specific findings on BD and those provided in heavy drinking and AUD research with young adults. For example, in terms of response inhibition, although hyperactivity was observed in key regions of inhibitory control (e.g. ACC, MFG/DLPFC, IFG, insula) in BDs (Ames et al., 2014b; Suárez-Suárez et al., 2020) and adolescent heavy drinkers (Wetherill et al., 2013), less activity was observed in similar regions in a study involving college students with AUD (Ahmadi et al., 2013). Similarly, the anomalies observed in the RS-FC of the MFG as part of the executive control network seem to differ according to the alcohol consumption pattern. Thus, while young BDs showed greater RS-FC in the MFG (Sousa et al., 2019), a study combining individuals with different severities of consumption showed lower connectivity strength than in controls in this same network (Weiland et al., 2014).

On the other hand, both young BDs (Ames et al., 2014a; Brumback et al., 2015) and emerging adults with heavy drinking (Dager et al., 2014) and AUD (Tapert et al., 2003) showed a high activation pattern in ACC and insula during the performance of tasks exploring alcohol cue reactivity. A similar pattern of results was found in decision-making tasks where significant hyperactivity in the MFG/DLPFC and insula was observed in young BDs (Worbe et al., 2014; Xiao et al., 2013) and in clinical samples (Amlung et al., 2014). Finally, alcohol consumption seems to be related to higher RS-FC within regions of the salience and reward networks (i.e. ACC, OFC) as observed in young BDs (Arienzo et al., 2020) and young adults with AUD (Zhu et al., 2017).

4.3. Longitudinal studies

Engaging in a BD pattern of consumption during adolescence appears to affect brain maturation trajectory. Consequently, although longitudinal studies remain scarce in BD research, they are of considerable value, especially when they include pre-BD measures, as they help elucidate the difference between the neurotoxic effects of the consumption pattern from pre-existing brain differences that may make some adolescents more vulnerable to alcohol use. In the current review, we identified five longitudinal studies, including both diffusion (Correas et al., 2016; Smith et al., 2017) and functional studies (Brumback et al., 2015; Cservenka et al., 2015; Jones et al., 2016). In relation to the review question of whether the maintenance of the BD pattern may potentially increase the anomalies associated with alcohol consumption (see Introduction), the included longitudinal studies do not seem to provide a clear answer yet. First, Correas et al. (2016) did not find any differences between groups in any of the assessments, while Smith et al. (2017) informed about significant gender by group interactions in both assessments but with no significant differences associated with the time factor. On the other hand, the results by Jones et al. (2016) provide valuable information more about the effects of short-term abstinence than about the maintenance of the consumption pattern.

Importantly, the remaining two longitudinal studies (Cservenka et al., 2015; Jones et al., 2016) explored differences in brain function prior to the onset of the BD pattern. One of these studies indicated the presence of abnormalities prior to alcohol consumption (Jones et al., 2016), characterized by a lower neuronal response in fronto-parietal regions during risky decision-making in those adolescents who went on to develop a BD pattern of consumption, relative to adolescents who maintained low levels of alcohol use. Similar to the findings of other longitudinal studies including more severe alcohol consumption patterns (e.g. Wetherill et al., 2013), these differences prior to the onset of BD may act as a risk factor for some adolescents to engage in high-risk consumption patterns and should be taken in consideration when interpreting the results of cross-sectional studies. However, the parent study published by Cservenka et al. (2015) did not reveal any significant differences prior to the start of BD, reporting reduced neural activation in the cerebellum only after initiation of the BD pattern. These results are particularly interesting because they highlight that although prior-to-BD differences may exist, this pattern of alcohol consumption may affect the structure and function of the adolescent brain.

4.4. Gender effects related to BD pattern

Previous studies have reported the presence of gender-related differences in the effects of BD (for a review see Wilsnack et al., 2018). However, possible differences at the neurostructural and/or functional level are still far from being understood. For this reason, one of the objectives of this review was to explore gender differences related to the BD pattern in brain structure and function.

All of the studies reviewed were formed by samples of males and females; however, only nine studies assessed the influence of gender in the neuroimaging results (Arienzo et al., 2020; Cservenka et al., 2015; Kvamme et al., 2016; Smith et al., 2017; Sousa et al., 2020, 2019, 2017; Squeglia et al., 2012, 2011).

Five of these studies revealed gender differences in brain function and morphometry related to BD in adolescence; three MRI studies (Kvamme et al., 2016; Sousa et al., 2017; Squeglia et al., 2012), one dMRI study (Smith et al., 2017) and one fMRI study (Squeglia et al., 2011).

Two of the MRI studies reported both lower volume and less cortical thickness in frontal, striatal, middle temporal, and parietal regions in male BDs than their control peers, whereas the opposite pattern was observed in females (Kvamme et al., 2016; Squeglia et al., 2012). Regarding dMRI studies, similar to previously observed findings in grey matter, Smith et al. (2017) reported that male BDs showed lower FA index in various white matter fibre tracts (including various segments of the CC) relative to male non-BDs, while females with a history of BD demonstrated higher FA values relative to their non-BD peers. Interestingly, these structural results suggest a pattern of gender-specific effects in young BDs. However, interpretation regarding the direction of these differences between males and females remains unclear; they may be related to the different rhythm in neuromaturation processes in males and females (Gennatas et al., 2017; Giedd et al., 2012) which may modulate the effects of BD in adolescence.

At the functional level, five studies explored the potential differences between female and male drinkers. Among these studies, only Squeglia et al. (2011) revealed significant gender by drinking status in all regions examined (both ROI and whole-brain analysis). Thus, activation during SWM vs. vigilance trials was lower in female BDs than in female non-BDs, while the opposite pattern was observed in male BDs.

Overall, although gender differences have been observed in BD research across multiple imaging modalities, future studies replicating these results will be critical to the understanding of gender differences related to BD.

5. Methodological considerations and future directions

This systematic review attempted to synthesize the research findings and draw conclusions about the relationship between the BD pattern of consumption and adolescent brain structure and function. Nevertheless, some methodological points must be considered when interpreting the previously discussed findings.

First of all, the weak control (or absence of control) over potential confounders should be noted, such as use of illicit drugs and family history of alcoholism (Quality assessment results) or even personal psychiatric comorbidities in some of the studies reviewed. Second, the relatively small sample size, together with the small number of studies that aimed to explore gender-related differences, and also the scarcity of longitudinal studies, prevent us from drawing strong conclusions concerning some of the objectives of this review (i.e. whether the

(potentially) observed anomalies are increased by the medium/long term maintenance of the BD pattern and the possible gender differences in BD-related effects on the brain). Furthermore, and similar to observations made in other analytical approaches (neuropsychological, electroencephalography [EEG] and magnetoencephalography), there remain a relatively small number of studies for each of the different cognitive processes evaluated. This is not only reflected by the fact that in most of the cognitive domains reviewed only two or three studies have been conducted, but also by the fact that only two of the experimental tasks used have been implemented in more than one study (from the same research group), which may account for some of the observed inconsistencies (see Overview of task-related fMRI studies).

We selected only studies that follow the NIAAA definition of BD for this review. However, during the screening and selection phases, we observed an important lack of consistency in the conceptualization of this alcohol consumption pattern, as recently pointed out by Maurage and colleagues (2020). Moreover, although the selected works fulfilled the NIAAA criteria, they differed significantly in some alcohol consumption characteristics of the experimental groups: the intensity of the BD sessions (e.g. absence of an upper-threshold for the number of drinks per occasion); the frequency of consumption criterion for classifying BDs (e.g. from at least once a week for the last six months to one lifetime BD episode); and alcohol consumption in the control group (ranging from alcohol abstinent controls to samples partaking two BDE in the last 6 months).

On the other hand, some aspects related to the techniques evaluated (MRI, dMRI and fMRI) should be taken into account when interpreting the results. Thus, as previously mentioned in methodological reviews in the neuroimaging field (e.g. Poldrack et al., 2017), the data treatment (quality checks, pre-processing steps and statistical analysis) varied significantly across studies with different implementation of similar steps. Such differences in approaches can undermine the consistency of the results in neuroimaging experiments (Botvinik-Nezer et al., 2020).

In addition, it must be noted that there are more neuroimaging studies focused on the BD pattern than those included in the present review. However, in order to adhere to the proposed objectives (see Introduction), we finally decided to exclude prospective, machine learning and other methodological approaches that did not allow us to clearly isolate the potential effects of BD on the adolescent brain (e.g. Cohen-Gilbert et al., 2017; Kühn et al., 2019; Morales et al., 2018; Ruan et al., 2019; Squeglia et al., 2017; Stacey et al., 2016).

Lastly, although the aim of applying the strict selection criterion was to overcome the inconsistencies observed (see Introduction) to extract a number of common patterns in the articles reviewed, this proposal has both strengths and important limitations. In this regard, the selection of studies in the present review focusing on healthy young BDs has allowed us to identify consistent results (Fig. 3, Section 4.1) and to draw conclusions about structural and functional anomalies based on the more solid findings of BD studies conducted to date. However, some inconsistencies remain that should be systematically addressed together with heavy drinking and AUD studies to better characterize the common and differential effects of these consumption patterns. Future works exploring all these types of drinking behaviours, and taking into account the potential effects of confounding variables, such as poly-consumption or psychiatric comorbidity, would be of great interest in this regard. Another worth-noting limitation derived from the strict selection criteria was the small number of studies selected for each imaging modality, which prevented us from using a meta-analytic approach in this review.

6. Conclusions

Overall, the findings of the literature examined in this systematic review suggest that adolescents and young adults who report engaging in a BD pattern show both structural and functional anomalies, relative to the respective controls.

This evidence, although still scarce, provides important information about the relationship between the adolescent brain and the BD pattern. In addition, it enables some conclusions to be reached that seem to emerge more consistently when different neuroimaging techniques are integrated (for a summary of most common abnormalities reported in BDs, see Fig. 3).

Regarding grey matter features, changes in both volume and thickness of cortical (especially in the prefrontal cortex) and subcortical structures have been reported (see Fig. 2). With respect to white matter studies, although observation of differences is usual, the results tend to be variable (see Overview of dMRI studies for more details).

At the functional level, the results seem to indicate that the BD pattern of consumption is related to abnormalities in the neuronal response associated with all the processes evaluated across a variety of tasks, with most anomalies observed in frontal regions (see Fig. 2). Likewise, although the direction of the findings is not clear, the most common patterns observed were the hyperactivation of brain areas such as the insula, DLPFC and the ACC (see Fig. 3), as well as recruitment of additional areas.

Regarding RS-FC studies, the findings seem to suggest that young people who report engaging in BD during adolescence present anomalies in the connectivity in regions associated with reward processing and inhibitory control processes, although the direction of these anomalies is not yet clear.

Notably, the results of this review seem to indicate that the BD pattern is associated with a series of anomalies different from those previously observed in samples with more severe patterns of consumption (e.g. AUD, polydrug use), such as the increase in grey matter in the MFG/DLPFC and VS/NAcc or the hyperactivity observed during the performance of inhibitory control tasks. However, our findings also highlight the existence of similarities with these more severe types of consumption, such as the hyperactivity observed in alcohol cue paradigms, both in young BDs and young people with a more problematic alcohol consumption; a pattern of brain activity similar to that observed by studies using EEG (Almeida-Antunes et al., 2021).

Finally, we believe it is necessary to emphasize the need to carry out more longitudinal studies that allow to determine whether the observed differences will change throughout the long-term maintenance (or abandonment) of the BD pattern, as well as allow measurements to be obtained prior to initiation of this pattern of consumption to further understand the risk factors that may contribute to alcohol use.

Fundings

This work was supported by grants from the Spanish Ministerio de Sanidad, Servicios Sociales e Igualdad, Plan Nacional sobre Drogas (PNSD 2015/034), Ministerio de Economía y Competitividad (PSI2015-70525-P) co-funded for European Regional Development Fund, Ministerio de Ciencia e Innovación (PID2020-113487RB-100) and Xunta de Galicia (GRC ED431C 2017/06; ED431C 2021/08). Jose Manuel Pérez-García was supported by the FPU program from the Spanish Ministerio de Educación, Cultura y Deporte (FPU16/01573). Samuel Suárez-Suárez was supported by a predoctoral fellowship from the Spanish Ministerio de Economía y Competitividad (BES-2016-076298).

Acknowledgments

The authors thank illustrator Estefanía Moreno for her contribution in the design of Fig. 3. We also want to thank Dr. Carina Carbia for her contribution in everything related to the PRISMA methodology.

Conflict of interest statement

The authors declare that the research was carried out in the absence of commercial or financial relationships that could be interpreted as possible conflicts of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.neubiorev.2022.104637.

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.

Ahmadi, A., Pearlson, G.D., Meda, S.A., Dager, A., Potenza, M.N., Rosen, R., Austad, C.S., Raskin, S.A., Fallahi, C.R., Tennen, H., Wood, R.M., Stevens, M.C., 2013. Influence of alcohol use on neural response to go/no-go task in college drinkers. Neuropsychopharmacology 38, 2197–2208. https://doi.org/10.1038/npp.2013.119.

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.

Ames, S.L., Grenard, J.L., He, Q., Stacy, A.W., Wong, S.W., Xiao, L., Xue, G., Bechara, A., 2014a. Functional imaging of an alcohol-implicit association test (IAT). Addict. Biol. 19, 467–481. https://doi.org/10.1111/adb.12071.

Ames, S.L., Wong, S.W., Bechara, A., Cappelli, C., Dust, M., Grenard, J.L., Stacy, A.W., 2014b. Neural correlates of a Go/NoGo task with alcohol stimuli in light and heavy young drinkers. Behav. Brain Res. 274, 382–389. https://doi.org/10.1016/j.bbr.2014.08.039.

Amlung, M., Sweet, L.H., Acker, J., Brown, C.L., MacKillop, J., 2014. Dissociable brain signatures of choice conflict and immediate reward preferences in alcohol use disorders. Addict. Biol. 19, 743–753. https://doi.org/10.1111/adb.12017.

Arienzo, D., Happer, J.P., Molnar, S.M., Alderson-Myers, A., Marinkovic, K., 2020. Binge drinking is associated with altered resting state functional connectivity of reward-salience and top down control networks. Brain Imaging Behav. 14, 1731–1746. https://doi.org/10.1007/s11682-019-00107-6.

Aron, A.R., 2007. The neural basis of inhibition in cognitive control. Neuroscience 13, 214–228. https://doi.org/10.1177/1073858407299288.

Babineau, J., 2014. Product review: covidence (systematic review software). J. Can. Heal. Libr. Assoc. 35, 68. https://doi.org/10.5596/c14-016.

Baddeley, A.D., Hitch, G.J., 1994. Developments in the concept of working memory. Neuropsychology 8, 485–493. https://doi.org/10.1037/0894-4105.8.4.485.

Banca, P., Lange, I., Worbe, Y., Howell, N.A., Irvine, M., Harrison, N.A., Moutoussis, M., Voon, V., 2016. Reflection impulsivity in binge drinking: behavioural and volumetric correlates. Addict. Biol. 21, 504–515. https://doi.org/10.1111/adb.12227.

Biswal, B., Zerrin Yetkin, F., Haughton, V.M., Hyde, J.S., 1995. Functional connectivity in the motor cortex of resting human brain using echo-planar mri. Magn. Reson. Med. 34, 537–541. https://doi.org/10.1002/mrm.1910340409.

Bjork, J.M., Pardini, D.A., 2015. Who are those "risk-taking adolescents"? Individual differences in developmental neuroimaging research. Dev. Cogn. Neurosci. 11, 56–64. https://doi.org/10.1016/j.dcn.2014.07.008.

Borsari, B., Murphy, J.G., Barnett, N.P., 2007. Predictors of alcohol use during the first year of college:implications for prevention. Addict. Behav. 32, 2062–2086. https://doi.org/10.1016/j.addbeh.2007.01.017.

Botvinik-Nezer, R., Holzmeister, F., Camerer, C.F., Dreber, A., Huber, J., Johannesson, M., Kirchler, M., Iwanir, R., Mumford, J.A., Adcock, R.A., Avesani, P., Baczkowski, B.M., Bajracharya, A., Bakst, L., Ball, S., Barilari, M., Bault, N., Beaton, D., Beitner, J., Benoit, R.G., Berkers, R.M.W.J., Bhanji, J.P., Biswal, B.B., Bobadilla-Suarez, S., Bortolini, T., Bottenhorn, K.L., Bowring, A., Braem, S., Brooks, H.R., Brudner, E.G., Calderon, C.B., Camilleri, J.A., Castrellon, J.J., Cecchetti, L., Cieslik, E.C., Cole, Z.J., Collignon, O., Cox, R.W., Cunningham, W.A., Czoschke, S., Dadi, K., Davis, C.P., Luca, A., De, Delgado, M.R., Demetriou, L., Dennison, J.B., Di, X., Dickie, E.W., Dobryakova, E., Donnat, C.L., Dukart, J., Duncan, N.W., Durnez, J., Eed, A., Eickhoff, S.B., Erhart, A., Fontanesi, L., Fricke, G.M., Fu, S., Galván, A., Gau, R., Genon, S., Glatard, T., Glerean, E., Goeman, J.J., Golowin, S.A.E., González-García, C., Gorgolewski, K.J., Grady, C.L., Green, M.A., Guassi Moreira, J.F., Guest, O., Hakimi, S., Hamilton, J.P., Hancock, R., Handjaras, G., Harry, B.B., Hawco, C., Herholz, P., Herman, G., Heunis, S., Hoffstaedter, F., Hogeveen, J., Holmes, S., Hu, C.-P., Huettel, S.A., Hughes, M.E., Iacovella, V., Iordan, A.D., Isager, P.M., Isik, A.I., Jahn, A., Johnson, M.R., Johnstone, T., Joseph, M.J.E., Juliano, A.C., Kable, J.W., Kassinopoulos, M., Koba, C., Kong, X.-Z., Koscik, T.R., Kucukboyaci, N.E., Kuhl, B.A., Kupek, S., Laird, A.R., Lamm, C., Langner, R., Lauharatanahirun, N., Lee, H., Lee, S., Leemans, A., Leo, A., Lesage, E., Li, F., Li, M.Y.C., Lim, P.C., Lintz, E.N., Liphardt, S.W., Losecaat Vermeer, A.B., Love, B.C., Mack, M.L., Malpica, N., Marins, T., Maumet, C., McDonald, K., McGuire, J.T., Melero, H., Méndez Leal, A.S., Meyer, B., Meyer, K.N., Mihai, G., Mitsis, G.D., Moll, J., Nielson, D.M., Nilsonne, G., Notter, M.P., Olivetti, E., Onicas, A.I., Papale, P., Patil, K.R., Peelle, J.E., Pérez, A., Pischedda, D., Poline, J.-B., Prystauka, Y., Ray, S., Reuter-Lorenz, P.A., Reynolds, R.C., Ricciardi, E., Rieck, J.R., Rodriguez-Thompson, A.M., Romyn, A., Salo, T., Samanez-Larkin, G.R., Sanz-Morales, E., Schlichting, M.L., Schultz, D.H., Shen, Q., Sheridan, M.A., Silvers, J.A., Skagerlund, K., Smith, A., Smith, D.V., Sokol-Hessner, P., Steinkamp, S.R., Tashjian, S.M., Thirion, B., Thorp, J.N., Tinghög, G., Tisdall, L., Tompson, S.H., Toro-Serey, C., Torre Tresols, J.J., Tozzi, L., Truong, V., Turella, L., van 't Veer, A.E., Verguts, T., Vettel, J.M., Vijayarajah, S., Vo, K., Wall, M.B., Weeda, W.D., Weis, S., White, D.J., Wisniewski, D., Xifra-Porxas, A., Yearling, E.A., Yoon, S., Yuan, R., Yuen, K.S.L., Zhang, L., Zhang, X., Zosky, J.E., Nichols, T.E., Poldrack, R.A., Schonberg, T., 2020. Variability in the analysis of a single neuroimaging dataset by many teams. Nature 582, 84–88. https://doi.org/10.1038/s41586-020-2314-9.

Brown, E.N., Behrmann, M., 2017. Controversy in statistical analysis of functional magnetic resonance imaging data. Proc. Natl. Acad. Sci. U.S.A. 114, E3368–E3369. https://doi.org/10.1073/pnas.1705513114.

Brumback, T., Squeglia, L.M., Jacobus, J., Pulido, C., Tapert, S.F., Brown, S.A., 2015. Adolescent heavy drinkers' amplified brain responses to alcohol cues decrease over one month of abstinence. Addict. Behav. 46, 45–52. https://doi.org/10.1016/j.addbeh.2015.03.001.

Cai, W., Ryali, S., Chen, T., Li, C.-S.R., Menon, V., 2014. Dissociable roles of right inferior frontal cortex and anterior insula in inhibitory control: evidence from intrinsic and task-related functional parcellation, connectivity, and response profile analyses across multiple datasets. J. Neurosci. 34, 14652–14667. https://doi.org/10.1523/JNEUROSCI.3048-14.2014.

Campanella, S., Peigneux, P., Petit, G., Lallemand, F., Saeremans, M., Noël, X., Metens, T., Nouali, M., De Tiège, X., De Witte, P., Ward, R., Verbanck, P., 2013. Increased cortical activity in binge drinkers during working memory task: a preliminary assessment through a functional magnetic resonance imaging study. PLoS One 8, e62260. https://doi.org/10.1371/journal.pone.0062260.

Carbia, C., Cadaveira, F., López-Caneda, E., Caamaño-Isorna, F., Rodríguez Holguín, S., Corral, M., 2017. Working memory over a six-year period in young binge drinkers. Alcohol 61, 17–23. https://doi.org/10.1016/j.alcohol.2017.01.013.

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.

Casey, B., Galvan, A., Hare, T.A., 2005. Changes in cerebral functional organization during cognitive development. Curr. Opin. Neurobiol. 15, 239–244. https://doi.org/10.1016/j.conb.2005.03.012.

Casey, B.J., Jones, R.M., Hare, T.A., 2008. The adolescent brain. Ann. N. Y. Acad. Sci. 1124, 111–126. https://doi.org/10.1196/annals.1440.010.

Chanraud, S., Zahr, N., Sullivan, E.V., Pfefferbaum, A., 2010. MR diffusion tensor imaging: a window into white matter integrity of the working brain. Neuropsychol. Rev. 20, 209–225. https://doi.org/10.1007/s11065-010-9129-7.

Chen, H., Nebe, S., Mojtahedzadeh, N., Kuitunen-Paul, S., Garbusow, M., Schad, D.J., Rapp, M.A., Huys, Q.J.M., Heinz, A., Smolka, M.N., 2020. Susceptibility to interference between Pavlovian and instrumental control is associated with early hazardous alcohol use (n/a). Addict. Biol., e12983. https://doi.org/10.1111/adb.12983.

Chumin, E.J., Grecco, G.G., Dzemidzic, M., Cheng, H., Finn, P., Sporns, O., Newman, S.D., Yoder, K.K., 2019. Alterations in white matter microstructure and connectivity in young adults with alcohol use disorder. Alcohol. Clin. Exp. Res 43, 1170–1179. https://doi.org/10.1111/acer.14048.

Chung, T., Clark, D.B., 2014. Insula white matter volume linked to binge drinking frequency through enhancement motives in treated adolescents. Alcohol. Exp. Res. 38, 1932–1940. https://doi.org/10.1111/acer.12461.

Cohen-Gilbert, J.E., Nickerson, L.D., Sneider, J.T., Oot, E.N., Seraikas, A.M., Rohan, M.L., Silveri, M.M., 2017. College binge drinking associated with decreased frontal activation to negative emotional distractors during inhibitory control. Front. Psychol. 8, 1650. https://doi.org/10.3389/fpsyg.2017.01650.

Correas, A., Cuesta, P., López-Caneda, E., Rodríguez Holguín, S., García-Moreno, L.M., Pineda-Pardo, J.A., Cadaveira, F., Maestú, F., 2016. Functional and structural brain connectivity of young binge drinkers: a follow-up study. Sci. Rep. 6. https://doi.org/10.1038/srep31293.

Crews, F., He, J., Hodge, C., 2007. Adolescent cortical development: a critical period of vulnerability for addiction. Pharmacol. Biochem. Behav. 86, 189–199. https://doi.org/10.1016/j.pbb.2006.12.001.

Crews, F.T., Braun, C.J., Hoplight, B., Switzer, R.C., Knapp, D.J., 2000. Binge ethanol consumption causes differential brain damage in young adolescent rats compared with adult rats. Alcohol. Clin. Exp. Res. 24, 1712–1723. https://doi.org/10.1111/j.1530-0277.2000.tb01973.x.

Crone, E.A., Steinbeis, N., 2017. Neural perspectives on cognitive control development during childhood and adolescence. Trends Cogn. Sci. 21, 205–215. https://doi.org/10.1016/j.tics.2017.01.003.

Cservenka, A., Brumback, T., 2017. The burden of binge and heavy drinking on the brain: effects on adolescent and young adult neural structural and function. Front. Psychol. 8 https://doi.org/10.3389/fpsyg.2017.01111.

Cservenka, A., Jones, S.A., Nagel, B.J., 2015. Reduced cerebellar brain activity during reward processing in adolescent binge drinkers. Dev. Cogn. Neurosci. 16, 110–120. https://doi.org/10.1016/j.dcn.2015.06.004.

Dager, A.D., Anderson, B.M., Rosen, R., Khadka, S., Sawyer, B., Jiantonio-Kelly, R.E., Austad, C.S., Raskin, S.A., Tennen, H., Wood, R.M., Fallahi, C.R., Pearlson, G.D., 2014. Functional magnetic resonance imaging (fMRI) response to alcohol pictures predicts subsequent transition to heavy drinking in college students. Addiction 109, 585–595. https://doi.org/10.1111/add.12437.

David, S.P., Naudet, F., Laude, J., Radua, J., Fusar-Poli, P., Chu, I., Stefanick, M.L., Ioannidis, J.P.A., 2018. Potential reporting bias in neuroimaging studies of sex differences. Sci. Rep. 8 https://doi.org/10.1038/s41598-018-23976-1.

De Bellis, M.D., 2000. Hippocampal volume in adolescent-onset alcohol use disorders. Am. J. Psychiatry 157, 737–744. https://doi.org/10.1176/appi.ajp.157.5.737.

De Bellis, M.D., Narasimhan, A., Thatcher, D.L., Keshavan, M.S., Soloff, P., Clark, D.B., 2005. Prefrontal cortex, thalamus, and cerebellar volumes in adolescents and young adults with adolescent-onset alcohol use disorders and comorbid mental disorders. Alcohol. Clin. Exp. Res 29, 1590–1600. https://doi.org/10.1097/01.alc.0000179368.87886.76.

De Bellis, M.D., Voorhees, E., Van, Hooper, S.R., Gibler, N., Nelson, L., Hege, S.G., Payne, M.E., MacFall, J., 2008. Diffusion tensor measures of the corpus callosum in adolescents with adolescent onset alcohol use disorders. Alcohol. Exp. Res. 32, 395–404. https://doi.org/10.1111/j.1530-0277.2007.00603.x.

Diekhof, E.K., Geier, K., Falkai, P., Gruber, O., 2011. Fear is only as deep as the mind allows. Neuroimage 58, 275–285. https://doi.org/10.1016/j.neuroimage.2011.05.073.

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.

Eklund, A., Nichols, T.E., Knutsson, H., 2016. Cluster failure: why fMRI inferences for spatial extent have inflated false-positive rates. Proc. Natl. Acad. Sci. U.S.A. 113, 7900–7905. https://doi.org/10.1073/pnas.1602413113.

ESPAD, 2020. ESPAD Report 2019: Results from the European School Survey Project on Alcohol and Other Drugs.

Ewing, S.W., Sakhardande, A., Blakemore, S.-J., 2014. The effect of alcohol consumption on the adolescent brain: a systematic review of MRI and fMRI studies of alcohol-using youth. NeuroImage Clin. 5, 420–437. https://doi.org/10.1016/j.nicl.2014.06.011.

Fox, M.D., Raichle, M.E., 2007. Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. Nat. Rev. Neurosci. 8, 700–711. https://doi.org/10.1038/nrn2201.

Garbusow, M., Nebe, S., Sommer, C., Kuitunen-Paul, S., Sebold, M., Schad, D.J., Friedel, E., Veer, I.M., Wittchen, H.-U., Rapp, M.A., Ripke, S., Walter, H., Huys, Q.J. M., Schlagenhauf, F., Smolka, M.N., Heinz, A., 2019. Pavlovian-to-instrumental transfer and alcohol consumption in young male social drinkers: behavioral, neural and polygenic correlates. J. Clin. Med. https://doi.org/10.3390/jcm8081188.

Gennatas, E.D., Avants, B.B., Wolf, D.H., Satterthwaite, T.D., Ruparel, K., Ciric, R., Hakonarson, H., Gur, R.E., Gur, R.C., 2017. Age-related effects and sex differences in gray matter density, volume, mass, and cortical thickness from childhood to young adulthood. J. Neurosci. 37, 5065. https://doi.org/10.1523/JNEUROSCI.3550-16.2017.

Giedd, J.N., Raznahan, A., Mills, K.L., Lenroot, R.K., 2012. Review: magnetic resonance imaging of male/female differences in human adolescent brain anatomy. Biol. Sex. Differ. 3, 19. https://doi.org/10.1186/2042-6410-3-19.

Gogtay, N., Giedd, J.N., Lusk, L., Hayashi, K.M., Greenstein, D., Vaituzis, A.C., Nugent, T. F., Herman, D.H., Clasen, L.S., Toga, A.W., Rapoport, J.L., Thompson, P.M., 2004. Dynamic mapping of human cortical development during childhood through early adulthood. Proc. Natl. Acad. Sci. U.S.A. 101, 8174–8179. https://doi.org/10.1073/pnas.0402680101.

Goldstein, R.Z., Volkow, N.D., 2011. Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications. Nat. Rev. Neurosci. 12, 652–669. https://doi.org/10.1038/nrn3119.

Goldstein, R.Z., Volkow, N.D., 2002. Drug addiction and Its underlying neurobiological basis: neuroimaging evidence for the involvement of the frontal cortex. Am. J. Psychiatry 159, 1642–1652. https://doi.org/10.1176/appi.ajp.159.10.1642.

Goudriaan, A.E., Grekin, E.R., Sher, K.J., 2007. Decision making and binge drinking: a longitudinal study. Alcohol. Clin. Exp. Res. 31, 928–938. https://doi.org/10.1111/j.1530-0277.2007.00378.x.

Grayson, D.S., Fair, D.A., 2017. Development of large-scale functional networks from birth to adulthood:a guide to the neuroimaging literature. Neuroimage 160, 15–31. https://doi.org/10.1016/j.neuroimage.2017.01.079.

Greenwald, A.G., McGhee, D.E., Schwartz, J.L., 1998. Measuring individual differences in implicit cognition: the implicit association test. J. Pers. Soc. Psychol. 74, 1464–1480. https://doi.org/10.1037//0022-3514.74.6.1464.

Greve, D.N., 2011. An absolute beginner's guide to surface- and voxel-based morphometric analysis. Proc. Int. Soc. Mag. Reson. Med. 1–7.

Guerri, C., Pascual, M., 2010. Mechanisms involved in the neurotoxic, cognitive, and neurobehavioral effects of alcohol consumption during adolescence. Alcohol 44, 15–26. https://doi.org/10.1016/j.alcohol.2009.10.003.

Heikkinen, N., Niskanen, E., Kononen, M., Tolmunen, T., Kekkonen, V., Kivimaki, P., Tanila, H., Laukkanen, E., Vanninen, R., 2017. Alcohol consumption during adolescence is associated with reduced grey matter volumes. Addiction 112, 604–613. https://doi.org/10.1111/add.13697.

Hermens, D.F., Lagopoulos, J., Tobias-Webb, J., De Regt, T., Dore, G., Juckes, L., Latt, N., Hickie, I.B., 2013. Pathways to alcohol-induced brain impairment in young people: a review. Cortex 49, 3–17. https://doi.org/10.1016/j.cortex.2012.05.021.

Hingson, R.W., 2010. Focus on: college drinking and related problems: magnitude and prevention of college drinking and related problems. Alcohol Res. Health 33, 45–54.

Howell, N.A., Worbe, Y., Lange, I., Tait, R., Irvine, M., Banca, P., Harrison, N.A., Bullmore, E.T., Hutchison, W.D., Voon, V., 2013. Increased ventral striatal volume in college-aged binge drinkers. PLoS One 8, e74164. https://doi.org/10.1371/journal.pone.0074164.

Jackson, P.L., Meltzoff, A.N., Decety, J., 2005. How do we perceive the pain of others? A window into the neural processes involved in empathy. Neuroimage 24, 771–779. https://doi.org/10.1016/j.neuroimage.2004.09.006.

Jacobus, J., McQueeny, T., Bava, S., Schweinsburg, B.C., Frank, L.R., Yang, T.T., Tapert, S.F., 2009. White matter integrity in adolescents with histories of marijuana use and binge drinking. Neurotoxicol. Teratol. 31, 349–355. https://doi.org/10.1016/j.ntt.2009.07.006.

Jacobus, J., Tapert, S.F., 2013. Neurotoxic effects of alcohol in adolescence. Annu. Rev. Clin. Psychol. 9, 703–721. https://doi.org/10.1146/annurev-clinpsy-050212-185610.

Jones, S.A., Cservenka, A., Nagel, B.J., 2016. Binge drinking impacts dorsal striatal response during decision making in adolescents. Neuroimage 129, 378–388. https://doi.org/10.1016/j.neuroimage.2016.01.044.

Jones, S.A., Lueras, J.M., Nagel, B.J., 2018. Effects of binge drinking on the developing brain. Alcohol Res. 39, 87–96.

Kashfi, K., Al-Khalil, K., Hou, J., Fang, D., Anderson, R., Rajmohan, R., Syapin, P., O'Boyle, M.W., 2017. Hyper-brain connectivity in binge drinking college students: a diffusion tensor imaging study. Neurocase 23, 179–186. https://doi.org/10.1080/13554794.2017.1347264.

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.

Koob, G.F., Volkow, N.D., 2010. Neurocircuitry of addiction. Neuropsychopharmacology 35, 217–238. https://doi.org/10.1038/npp.2009.110.

Kühn, S., Mascharek, A., Banaschewski, T., Bodke, A., Bromberg, U., Büchel, C., Quinlan, E.B., Desrivieres, S., Flor, H., Grigis, A., Garavan, H., Gowland, P.A., Heinz, A., Ittermann, B., Martinot, J.-L., Nees, F., Papadopoulos Orfanos, D., Paus, T., Poustka, L., Millenet, S., Fröhner, J.H., Smolka, M.N., Walter, H., Whelan, R., Schumann, G., Lindenberger, U., Gallinat, J., Consortium, I., 2019. Predicting development of adolescent drinking behaviour from whole brain structure at 14 years of age. Elife 8, e44056. https://doi.org/10.7554/eLife.44056.

Kvamme, T.L., Schmidt, C., Strelchuk, D., Chang-Webb, Y.C., Baek, K., Voon, V., 2016. Sexually dimorphic brain volume interaction in college-aged binge drinkers. NeuroImage Clin. 10, 310–317. https://doi.org/10.1016/j.nicl.2015.12.004.

Lebel, C., Gee, M., Camicioli, R., Wieler, M., Martin, W., Beaulieu, C., 2012. Diffusion tensor imaging of white matter tract evolution over the lifespan. Neuroimage 60, 340–352. https://doi.org/10.1016/j.neuroimage.2011.11.094.

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. Pharmacol. 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.

Luciana, M., Collins, P.F., Muetzel, R.L., Lim, K.O., 2013. Effects of alcohol use initiation on brain structure in typically developing adolescents. Am. J. Drug Alcohol Abus. 39, 345–355. https://doi.org/10.3109/00952990.2013.837057.

Luna, B., Padmanabhan, A., O'Hearn, K., 2010. What has fMRI told us about the development of cognitive control through adolescence? Brain Cogn. 72, 101–113. https://doi.org/10.1016/j.bandc.2009.08.005.

Madden, D.J., Bennett, I.J., Burzynska, A., Potter, G.G., Chen, N., Song, A.W., 2012. Diffusion tensor imaging of cerebral white matter integrity in cognitive aging. Biochim. Biophys. Acta - Mol. Basis Dis. 1822, 386–400. https://doi.org/10.1016/j.bbadis.2011.08.003.

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., Bestelmeyer, P.E.G., Rouger, J., Charest, I., Belin, P., 2013. Binge drinking influences the cerebral processing of vocal affective bursts in young adults. NeuroImage Clin. 3, 218–225. https://doi.org/10.1016/j.nicl.2013.08.010.

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.

McHugh, M.L., 2012. Interrater reliability: the kappa statistic. Biochem. Med. 22, 276–282.

McQueeny, T., Schweinsburg, B.C., Schweinsburg, A.D., Jacobus, J., Bava, S., Frank, L.R., Tapert, S.F., 2009. Altered white matter integrity in adolescent binge drinkers. Alcohol. Clin. Exp. Res. 33, 1278–1285. https://doi.org/10.1111/j.1530-0277.2009.00953.x.

Meda, S.A., Dager, A.D., Hawkins, K.A., Tennen, H., Raskin, S., Wood, R.M., Austad, C.S., Fallahi, C.R., Pearlson, G.D., 2017. Heavy drinking in college students is associated with accelerated gray matter volumetric decline over a 2 year. Front. Behav. Neurosci. 11, 176. https://doi.org/10.3389/fnbeh.2017.00176.

Meda, S.A., Hawkins, K.A., Dager, A.D., Tennen, H., Khadka, S., Austad, C.S., Wood, R. M., Raskin, S., Fallahi, C.R., Pearlson, G.D., 2018. Longitudinal effects of alcohol consumption on the hippocampus and parahippocampus in college students. Biol. Psychiatry Cogn. Neurosci. Neuroimaging 3, 610–617. https://doi.org/10.1016/j.bpsc.2018.02.006.

Medina, K.L., Schweinsburg, A.D., Cohen-Zion, M., Nagel, B.J., Tapert, S.F., 2007. Effects of alcohol and combined marijuana and alcohol use during adolescence on hippocampal volume and asymmetry. Neurotoxicol. Teratol. 29, 141–152. https://doi.org/10.1016/j.ntt.2006.10.010.

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.

Mitchell, J.M., O'Neil, J.P., Janabi, M., Marks, S.M., Jagust, W.J., Fields, H.L., 2012. Alcohol consumption induces endogenous opioid release in the human orbitofrontal cortex and nucleus accumbens, 116ra6 LP-116ra6 Sci. Transl. Med. 4. https://doi.org/10.1126/scitranslmed.3002902.

Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P., Stewart, L.A., Group, P.-P., 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst. Rev. 4, 1. https://doi.org/10.1186/2046-4053-4-1.

Molnar, S., Beaton, L., Happer, J., Holcomb, L., Huang, S., Arienzo, D., Marinkovic, K., 2018. Behavioral and brain activity indices of cognitive control deficits in binge drinkers. Brain Sci. 8, 9. https://doi.org/10.3390/brainsci8010009.

Morales, A.M., Jones, S.A., Ehlers, A., Lavine, J.B., Nagel, B.J., 2018. Ventral striatal response during decision making involving risk and reward is associated with future binge drinking in adolescents. Neuropsychopharmacology 43, 1884–1890. https://doi.org/10.1038/s41386-018-0087-8.

Morawetz, C., Bode, S., Baudewig, J., Kirilina, E., Heekeren, H.R., 2016. Changes in effective connectivity between dorsal and ventral prefrontal regions moderate emotion regulation. Cereb. Cortex 26, 1923–1937. https://doi.org/10.1093/cercor/bhv005.

Morris, L.S., Dowell, N.G., Cercignani, M., Harrison, N.A., Voon, V., 2018. Binge drinking differentially affects cortical and subcortical microstructure. Addict. Biol. 23, 403–411. https://doi.org/10.1111/adb.12493.

Morris, L.S., Kundu, P., Baek, K., Irvine, M.A., Mechelmans, D.J., Wood, J., Harrison, N. A., Robbins, T.W., Bullmore, E.T., Voon, V., 2016. Jumping the gun: mapping neural correlates of waiting impulsivity and relevance across alcohol misuse. Biol. Psychiatry 79, 499–507. https://doi.org/10.1016/j.biopsych.2015.06.009.

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.

Müller, V.I., Cieslik, E.C., Laird, A.R., Fox, P.T., Radua, J., Mataix-Cols, D., Tench, C.R., Yarkoni, T., Nichols, T.E., Turkeltaub, P.E., Wager, T.D., Eickhoff, S.B., 2018. Ten simple rules for neuroimaging meta-analysis. Neurosci. Biobehav. Rev. 84, 151–161. https://doi.org/10.1016/j.neubiorev.2017.11.012.

Nagel, B.J., Schweinsburg, A.D., Phan, V., Tapert, S.F., 2005. Reduced hippocampal volume among adolescents with alcohol use disorders without psychiatric comorbidity. Psychiatry Res. 139, 181–190. https://doi.org/10.1016/j.pscychresns.2005.05.008.

National Heart, Lung, and Blood Institute (NHLBI), 2014. Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. Available at: National Heart, Lung, and Blood Institute, Bethesda, MD.

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.

Oscar-Berman, M., Marinković, K., 2007. Alcohol: effects on neurobehavioral functions and the brain. Neuropsychol. Rev. 17, 239–257. https://doi.org/10.1007/s11065-007-9038-6.

Owen, A.M., McMillan, K.M., Laird, A.R., Bullmore, E., 2005. N-back working memory paradigm: a meta-analysis of normative functional neuroimaging studies. Hum. Brain Mapp. 25, 46–59. https://doi.org/10.1002/hbm.20131.

Parada, M., Corral, M., Caamaño-Isorna, F., Mota, N., Crego, A., Holguín, S.R., Cadaveira, F., 2011. Binge drinking and declarative memory in university students (no-no). Alcohol. Clin. Exp. Res. 35. https://doi.org/10.1111/j.1530-0277.2011.01484.x.

Patrick, M.E., Schulenberg, J.E., 2010. Alcohol use and heavy episodic drinking prevalence and predictors among national samples of american eighth-and tenth-grade students. J. Stud. Alcohol Drugs 71, 41–45. https://doi.org/10.15288/jsad.2010.71.41.

Petit, G., Maurage, P., Kornreich, C., Verbanck, P., Campanella, S., 2014. Binge drinking in adolescents: a review of neurophysiological and neuroimaging research. Alcohol Alcohol. 49, 198–206. https://doi.org/10.1093/alcalc/agt172.

Pfefferbaum, A., Kwon, D., Brumback, T., Thompson, W.K., Cummins, K., Tapert, S.F., Brown, S.A., Colrain, I.M., Baker, F.C., Prouty, D., De Bellis, M.D., Clark, D.B., Nagel, B.J., Chu, W., Park, S.H., Pohl, K.M., Sullivan, E.V., 2017. Altered brain developmental trajectories in adolescents after initiating drinking. Am. J. Psychiatry 175, 370–380. https://doi.org/10.1176/appi.ajp.2017.17040469.

Poldrack, R.A., Baker, C.I., Durnez, J., Gorgolewski, K.J., Matthews, P.M., Munafò, M.R., Nichols, T.E., Poline, J.-B., Vul, E., Yarkoni, T., 2017. Scanning the horizon: towards transparent and reproducible neuroimaging research. Nat. Rev. Neurosci. 18, 115–126. https://doi.org/10.1038/nrn.2016.167.

Qiu, A., Mori, S., Miller, M.I., 2015. Diffusion tensor imaging for understanding brain development in early life. Annu. Rev. Psychol. 66, 853–876. https://doi.org/10.1146/annurev-psych-010814-015340.

Rae, C.L., Gierski, F., Smith, K.W., Nikolaou, K., Davies, A., Critchley, H.D., Naassila, M., Duka, T., 2020. Differential brain responses for perception of pain during empathic response in binge drinkers compared to non-binge drinkers. NeuroImage Clin. 27, 102322 https://doi.org/10.1016/j.nicl.2020.102322.

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.

Ruan, H., Zhou, Y., Luo, Q., Robert, G.H., Desrivières, S., Quinlan, E.B., Liu, Z., Banaschewski, T., Bokde, A.L.W., Bromberg, U., Büchel, C., Flor, H., Frouin, V., Garavan, H., Gowland, P., Heinz, A., Ittermann, B., Martinot, J.-L., Martinot, M.-L.P., Nees, F., Orfanos, D.P., Poustka, L., Hohmann, S., Fröhner, J.H., Smolka, M.N., Walter, H., Whelan, R., Li, F., Schumann, G., Feng, J., 2019. Adolescent binge drinking disrupts normal trajectories of brain functional organization and personality maturation. NeuroImage Clin. 22, 101804 https://doi.org/10.1016/j.nicl.2019.101804.

Ruff, C.C., Fehr, E., 2014. The neurobiology of rewards and values in social decision making. Nat. Rev. Neurosci. 15, 549–562. https://doi.org/10.1038/nrn3776.

SAMSHA, 2021. Key substance use and mental health indicators in the United States: Results from the 2020 National Survey on Drug Use and Health, HHS Publication No. PEP21–07-01–003, NSDUH Series H-56.

Scaife, J.C., Duka, T., 2009. Behavioural measures of frontal lobe function in a population of young social drinkers with binge drinking pattern. Pharmacol. Biochem. Behav. 93, 354–362. https://doi.org/10.1016/j.pbb.2009.05.015.

Schacht, J.P., Anton, R.F., Myrick, H., 2013. Functional neuroimaging studies of alcohol cue reactivity: a quantitative meta-analysis and systematic review. Addict. Biol. 18, 121–133. https://doi.org/10.1111/j.1369-1600.2012.00464.x.

Shen, Q., Heikkinen, N., Karkkainen, O., Grohn, H., Kononen, M., Liu, Y., Kaarre, O., Zhang, Z., Tan, C., Tolmunen, T., Vanninen, R., 2019. Effects of long-term adolescent alcohol consumption on white matter integrity and their correlations with metabolic alterations. Psychiatry Res. 294, 111003 https://doi.org/S0925-4927(19)30133-7 [pii].

Shirer, W.R., Ryali, S., Rykhlevskaia, E., Menon, V., Greicius, M.D., 2012. Decoding Subject-Driven Cognitive States with Whole-Brain Connectivity Patterns. Cereb. Cortex 22, 158–165. https://doi.org/10.1093/cercor/bhr099.

Silveri, M.M., Dager, A.D., Cohen-Gilbert, J.E., Sneider, J.T., 2016. Neurobiological signatures associated with alcohol and drug use in the human adolescent brain. Neurosci. Biobehav. Rev. 70, 244–259. https://doi.org/10.1016/j.neubiorev.2016.06.042.

Smith, K.W., Gierski, F., Andre, J., Dowell, N.G., Cercignani, M., Naassila, M., Duka, T., 2017. Altered white matter integrity in whole brain and segments of corpus callosum, in young social drinkers with binge drinking pattern: alcohol and white matter. Addict. Biol. 22, 490–501. https://doi.org/10.1111/adb.12332.

Sousa, S.S., Sampaio, A., López-Caneda, E., Bec, C., Gonçalves, Ó.F., Crego, A., 2020. Increased nucleus accumbens volume in college binge drinkers - preliminary evidence from manually segmented MRI analysis. Front. Psychiatry. https://doi.org/10.3389/fpsyt.2019.01005.

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 https://doi.org/10.3389/fpsyg.2017.01567.

Sousa, S.S., Sampaio, A., Marques, P., López-Caneda, E., Gonçalves, Ó.F., Crego, A., 2019. Functional and structural connectivity of the executive control network in college binge drinkers. Addict. Behav. 99, 106009 https://doi.org/10.1016/j.addbeh.2019.05.033.

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., Ball, T.M., Jacobus, J., Brumback, T., McKenna, B.S., Nguyen-Louie, T.T., Sorg, S.F., Paulus, M.P., Tapert, S.F., 2017. Neural predictors of initiating alcohol use during adolescence. Am. J. Psychiatry 174, 172–185. https://doi.org/10.1176/appi.ajp.2016.15121587.

Squeglia, L.M., Schweinsburg, A.D., Pulido, C., Tapert, S.F., 2011. Adolescent binge drinking linked to abnormal spatial working memory brain activation: differential gender effects. Alcohol. Clin. Exp. Res. 35, 1831–1841. https://doi.org/10.1111/j.1530-0277.2011.01527.x.

Squeglia, L.M., Sorg, S.F., Schweinsburg, A.D., Wetherill, R.R., Pulido, C., Tapert, S.F., 2012. Binge drinking differentially affects adolescent male and female brain morphometry. Psychopharmacology 220, 529–539. https://doi.org/10.1007/s00213-011-2500-4.

Squeglia, L.M., Tapert, S.F., Sullivan, E.V., Jacobus, J., Meloy, M.J., Rohlfing, T., Pfefferbaum, A., 2015. Brain development in heavy-drinking adolescents. Am. J. Psychiatry 172, 531–542. https://doi.org/10.1176/appi.ajp.2015.14101249.

Stacey, D., Lourdusamy, A., Ruggeri, B., Maroteaux, M., Jia, T., Cattrell, A., Nymberg, C., Banaschewski, T., Bhattacharyya, S., Band, H., Barker, G., Bokde, A., Buchel, C., Carvalho, F., Conrod, P., Desrivieres, S., Easton, A., Fauth-Buehler, M., Fernandez-Medarde, A., Flor, H., Frouin, V., Gallinat, J., Garavanh, H., Heinz, A., Ittermann, B., Lathrop, M., Lawrence, C., Loth, E., Mann, K., Martinot, J.-L., Nees, F., Paus, T., Pausova, Z., Rietschel, M., Rotter, A., Santos, E., Smolka, M., Sommer, W., Mameli, M., Spanagel, R., Girault, J.-A., Mueller, C., Schumann, G., Consortium, I., 2016. A translational systems biology approach in both animals and humans identifies a functionally related module of accumbal genes involved in the regulation of reward processing and binge drinking in males. J. Psychiatry Neurosci. 41, 192–202. https://doi.org/10.1503/jpn.150138.

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.

Swick, D., Ashley, V., Turken, U., 2011. Are the neural correlates of stopping and not going identical? Quantitative meta-analysis of two response inhibition tasks. Neuroimage 56, 1655–1665. https://doi.org/10.1016/j.neuroimage.2011.02.070.

Tamnes, C.K., Østby, Y., Fjell, A.M., Westlye, L.T., Due-Tønnessen, P., Walhovd, K.B., 2010. Brain maturation in adolescence and young adulthood: regional age-related changes in cortical thickness and white matter volume and microstructure. Cereb. Cortex 20, 534–548. https://doi.org/10.1093/cercor/bhp118.

Tapert, S.F., Cheung, E.H., Brown, G.G., Frank, L.R., Paulus, M.P., Schweinsburg, A.D., Meloy, M.J., Brown, S.A., 2003. Neural response to alcohol stimuli in adolescents with alcohol use disorder. Arch. Gen. Psychiatry 60, 727–735. https://doi.org/10.1001/archpsyc.60.7.727.

Thayer, R.E., Callahan, T.J., Weiland, B.J., Hutchison, K.E., Bryan, A.D., 2013. Associations between fractional anisotropy and problematic alcohol use in juvenile justice-involved adolescents. Am. J. Drug Alcohol Abus. 39, 365–371. https://doi.org/10.3109/00952990.2013.834909.

Townshend, J.M., Duka, T., 2002. Patterns of alcohol drinking in a population of young social drinkers: a comparison of questionnaire and diary measures. Alcohol Alcohol 37, 187–192. https://doi.org/10.1093/alcalc/37.2.187.

Uddin, L.Q., Nomi, J.S., Hébert-Seropian, B., Ghaziri, J., Boucher, O., 2017. Structure and Function of the Human Insula. J. Clin. Neurophysiol. 34, 300–306. https://doi.org/10.1097/WNP.0000000000000377.

Van den Bos, R., Homberg, J., de Visser, L., 2013. A critical review of sex differences in decision-making tasks: Focus on the Iowa Gambling Task. Behav. Brain Res. 238, 95–108. https://doi.org/10.1016/j.bbr.2012.10.002.

Van Duijvenvoorde, A.C.K., Peters, S., Braams, B.R., Crone, E.A., 2016. 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.

Vogel, A.C., Power, J.D., Petersen, S.E., Schlaggar, B.L., 2010. Development of the brain's functional network architecture. Neuropsychol. Rev. 20, 362–375. https://doi.org/10.1007/s11065-010-9145-7.

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.

Weiland, B.J., Sabbineni, A., Calhoun, V.D., Welsh, R.C., Bryan, A.D., Jung, R.E., Mayer, A.R., Hutchison, K.E., 2014. Reduced left executive control network functional connectivity is associated with alcohol use disorders. Alcohol. Exp. Res. 38, 2445–2453. https://doi.org/10.1111/acer.12505.

Wetherill, R.R., Squeglia, L.M., Yang, T.T., Tapert, S.F., 2013. A longitudinal examination of adolescent response inhibition: neural differences before and after the initiation of heavy drinking. Psychopharmacology 230, 663–671. https://doi.org/10.1007/s00213-013-3198-2.

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.

Whitwell, J.L., 2009. Voxel-based morphometry: an automated technique for assessing structural changes in the brain. J. Neurosci. 29, 9661–9664. https://doi.org/10.1523/JNEUROSCI.2160-09.2009.

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.

Wiers, R.W., Bartholow, B.D., van den Wildenberg, E., Thush, C., Engels, R.C.M.E., Sher, K.J., Grenard, J., Ames, S.L., Stacy, A.W., 2007. Automatic and controlled processes and the development of addictive behaviors in adolescents: a review and a model. Pharmacol. Biochem. Behav. 86, 263–283. https://doi.org/10.1016/j.pbb.2006.09.021.

Wilsnack, R.W., Wilsnack, S.C., Gmel, G., Kantor, L.W., 2018. Gender differences in binge drinking: prevalence, predictors, and consequences. Alcohol Res. Curr. Rev.

Worbe, Y., Irvine, M., Lange, I., Kundu, P., Howell, N.A., Harrison, N.A., Bullmore, E.T., Robbins, T.W., Voon, V., 2014. Neuronal correlates of risk-seeking attitudes to anticipated losses in binge drinkers. Biol. Psychiatry 76, 717–724. https://doi.org/10.1016/j.biopsych.2013.11.028.

Xiao, L., Bechara, A., Gong, Q., Huang, X., Li, X., Xue, G., Wong, S., Lu, Z.-L., Palmer, P., Wei, Y., Jia, Y., Johnson, C.A., 2013. Abnormal affective decision making revealed in adolescent binge drinkers using a functional magnetic resonance imaging study. Psychol. Addict. Behav. 27, 443–454. https://doi.org/10.1037/a0027892.

Zhang, H., Schneider, T., Wheeler-Kingshott, C.A., Alexander, D.C., 2012. NODDI: practical in vivo neurite orientation dispersion and density imaging of the human brain. Neuroimage 61, 1000–1016. https://doi.org/10.1016/j.neuroimage.2012.03.072.

Zhang, R., Geng, X., Lee, T.M.C., 2017. Large-scale functional neural network correlates of response inhibition: an fMRI meta-analysis. Brain Struct. Funct. 222, 3973–3990. https://doi.org/10.1007/s00429-017-1443-x.

Zhu, X., Cortes, C.R., Mathur, K., Tomasi, D., Momenan, R., 2017. Model-free functional connectivity and impulsivity correlates of alcohol dependence: a resting-state study. Addict. Biol. 22, 206–217. https://doi.org/10.1111/adb.12272.