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Article

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Neural Responses to the Implicit Processing of Emotional Facial Expressions in Binge Drinking

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Abstract

Aims: Emotional processing is a crucial ability in human and impairments in the processing of emotions are considered as transdiagnostic processes in psychopathology. In alcohol use disorder, numerous studies have investigated emotional processing and showed emotional deficits related to the perpetuation of alcohol use. Recent studies have also explored this topic in binge drinking, but few studies are available. In this paper, we explored whether emotional difficulties in binge drinking may be extended to implicit emotion processing.

Methods: We compared 39 binge drinkers (BD) and 40 non-binge drinkers who performed a gender categorization task while faces represented emotional expressions of anger, fear, happiness and sadness. Emotional brain responses were assessed thanks to functional magnetic resonance imaging. Emotional versus non-emotional conditions were first contrasted in the whole sample and groups were then compared.

Results: Emotional condition led to differential activations than non-emotional condition, supporting the validity of the paradigm. Regarding group comparisons, BD exhibited higher activations in the left posterior cerebellum (anger processing) and the right anterior cingulate (fear processing) as well as lower activations in the left insula (happiness), the right post-central gyrus, the right cingulate gyrus and the right medial frontal gyrus (sadness processing).

Conclusions: Beyond emotional identification, BD presented differential brain responses following the implicit processing of emotions. Emotional difficulties in binge drinking might be related to a more automatic/unconscious processing of emotions.

INTRODUCTION

Human beings are unconditionally social beings, they are defined by their relationships with others and the world. Social cognition processes (i.e. allowing the building of representations from interactions with others; Adolphs, 2001) are thus essential to promote social integration and well-being. Among social cognition, emotional processing plays a major role in the initiation and maintenance of healthy social relationships. Emotional processing encompasses identification, response and regulation of emotions (Phillips *et al.*, 2003), and is considered an important transdiagnostic process in psychopathology (Sloan *et al.*, 2017). In addiction, the role of emotional processing is critical and may explain the maintenance of substance abuse (Koob, 2015). This proposal has been supported in severe alcohol use disorder (AUD). Especially, it has been advanced that (a) AUD patients exhibit emotional deficits resulting from the neurotoxic alcohol's effects (Bora and Zorlu, 2017), (b), emotional deficits are key factors in the explanation of relapse in AUD (Le Berre, 2019).

Whereas emotional research has been flourishing in AUD, few insights are available in other alcohol consumption patterns. In particular, binge drinking currently constitutes an important research topic and may be considered a first step towards AUD (Lannoy *et al.*, 2019a). Binge drinking is defined by occasional but high alcohol intoxications—often described as the consumption of more than six alcohol doses (60 g of pure ethanol) on one occasion in Europe (Maurage *et al.*, 2020). Beyond this alcohol quantity measure, which varies a lot among countries, binge drinking can be evaluated by a binge drinking score, taking into account drunkenness frequency and consumption speed to capture heavy use in a 6-month timeframe (Townshend and Duka, 2005).

Binge drinking has been related to cognitive dysfunctions (i.e. memory and executive functions; see Carbia *et al.*, 2018 for a systematic review) and to widespread alterations in brain structures and functions (Cservenka and Brumback, 2017). It has been proposed that this drinking pattern would induce brain alterations in amygdala and prefrontal cortex, leading to comparable cognitive and affective impairments than AUD (Stephens and Duka, 2008). Neuroimaging studies support the existence of alterations in brain regions involved in affective processing in binge drinkers (BD; Cservenka and Brumback, 2017), but these studies did not assess emotional processing *per se*. When the processing of emotional contents is evaluated, BD have lower brain activations in prefrontal, frontal and cingulate cortices (Cohen-Gilbert *et al.*, 2017; Herman *et al.*, 2019). In particular, findings underline lower activations in the dorsolateral prefrontal cortex, the dorsomedial prefrontal cortex and the anterior cingulate cortex when viewing negative emotional backgrounds before inhibition trials (Cohen-Gilbert *et al.*, 2017). Also, lower frontal and parietal brain activations are observed during successful inhibition of fear (Herman *et al.*, 2019). When BD have to identify affective bursts, results highlight lower activations in the bilateral superior temporal gyrus together with increased activations of the right middle frontal gyrus (Maurage *et al.*, 2013).

During the identification of emotions, modifications of electrophysiological activities are also observed in BD (Ehlers *et al.*, 2007; Maurage *et al.*, 2009; Lannoy *et al.*, 2018a). Moreover, electrophysiological changes are found after the view of negative emotional scenes (Connell *et al.*, 2015; Huang *et al.*, 2018). These difficulties to process emotional contents are also supported at the behavioral level, studies showing that BD have poorer performance for the identification of anger and fear affective bursts (Maurage *et al.*, 2013) and for the recognition of fear and sadness facial expressions (Lannoy *et al.*, 2018b, 2019b). One may wonder if these difficulties would result from an impaired cognitive ability to identify emotional contents or would be related to the basic processing of emotion (e.g. implicit processing, referring to an unconscious processing or a processing without a high level of awareness). Preliminary studies suggest that the simple view of emotional images already leads to the modification of brain activity (Connell *et al.*, 2015; Huang *et al.*, 2018) but to our knowledge, no studies explored the neural responses after the view of socio-emotional stimuli (e.g. emotional facial expressions).

The aim of this study is to explore whether BD may exhibit impaired emotional responses after the view of emotional facial expressions. In particular, we investigated the nature of emotional difficulties in binge drinking by targeting implicit emotion processing (view of emotional faces) while another explicit non-emotional processing (gender categorization) was required. We compared BD to non-binge drinkers (NBD) and collected functional magnetic resonance imaging (fMRI) data during a gender categorization task presenting emotional facial expressions of anger, fear, happiness and sadness. According to previous studies (Maurage *et al.*, 2013; Cohen-Gilbert *et al.*, 2017; Herman *et al.*, 2019), we hypothesized modifications of brain activations in BD in brain regions involved in emotional processing (frontal and limbic brain regions).

METHODS

Participants and procedure

Eighty social drinkers (40 females, mean age = 21.60, SD = 1.72) were recruited from the University of Reims Champagne-Ardenne (France) according to their alcohol consumption pattern: 40 BD and 40 non-binge drinkers (NBD). Group classification was based on the binge-drinking score (Binge-drinking score = (4 × Consumption speed) + drunkenness frequency + (0.2 × percentage of drunkenness)) (Townshend and Duka, 2005): BD had a binge-drinking score of 24 or above, whereas NBD scored below 16. This group categorization has been supported by other alcohol variables (Table 1). To be included in the study, participants had to be 18 years old or older, right-handed (the Edinburgh Handedness Inventory; Oldfield, 1971), have no current or past psychopathological or neurological problems (Mini-International Neuropsychiatric Interview; Sheehan, 1998), and take no psychotropic medication. Participants had no MRI contraindications: being pregnant or breastfeeding, trying to conceive, having any metal implants, teeth braces or bridges, tattoos above the shoulder or a cardiac pacemaker. Participants were asked to refrain from drinking alcohol and consuming cannabis and other drugs for at least 12 h before the experiment (tobacco was allowed for current smokers). To ensure the alcohol-related compliance, breath alcohol concentration was measured at the beginning of the experiment (Dräger 6810 med, Dräger Safety Company, Strasbourg, France). Participants were included in the study if the breath alcohol concentration was 0. The absence of drug use was evaluated by self-reported dichotomous items.

Participants first answered self-reported questionnaires assessing age, sex, native language, family history of AUD (yes/no), tobacco use, cannabis use (yes/no and the frequency of use; i.e. at least once a week), other drugs use (yes/no), alcohol use, depression, anxiety and intellectual abilities. Breath alcohol concentration was then measured and participants were placed in the scanner. They performed the gender categorization task, while the fMRI data were collected (T2*-weighted images). This study is part of a larger research project (https://clinicaltrials.gov/ct2/show/NCT02794311),

Table 1. Demographic, psychopathological and substances use measures for BD and NBD

Variables	Binge drinkers ($n = 39$)	Non-binge drinkers ($n = 40$)
Age[ns]	21.82 (1.52)	21.45 (1.87)
Gender ratio (M/F)[ns]	19/20	20/20
Family history of AUD (n)[ns]	7	3
Cannabis users (n)[ns]	4	2
Current tobacco users (n)[ns]	16	13
FTND score[ns]	0.38 (0.96)	0.33 (0.83)
Depressive symptoms (BDI)[ns]	2.69 (3.33)	2.70 (2.97)
State anxiety (STAI)[ns]	28.95 (8.75)	27.10 (6.69)
Trait anxiety (STAI)[ns]	37.21 (9.26)	38.82 (9.53)
UPPS-P negative urgency[ns]	8.28 (2.74)	7.95 (2.40)
UPPS-P positive urgency[ns]	10.08 (2.32)	9.85 (1.88)
UPPS-P lack of premeditation[ns]	7.21 (1.67)	6.93 (1.72)
UPPS-P lack of perseverance[ns]	6.56 (2.30)	6.53 (1.95)
UPPS-P sensation seeking[ns]	10.26 (2.38)	10.10 (2.33)
Estimated IQ (NART)[ns]	111.94 (5.00)	110.06 (6.97)
Binge drinking score*	46.77 (24.02)	8.96 (3.66)
Alcohol use (AUDIT)*	11.55 (5.63)	4.50 (2.56)
Weekly alcohol use*	19.50 (2.99)	2.76 (2.45)

Data are mean (SD), unless otherwise specified; ns = non-significant. AUD = Alcohol Use Disorder; FTND = Fagerström Test for Nicotine Dependence; BDI = Beck Depression Inventory; STAI = State–Trait Anxiety Inventory; NART = National Adult Reading Test; AUDIT = Alcohol Use Disorder Identification Test.
*$P < 0.001$.

but the data used in this study have not been related to other publications. This study was approved by the French national regulatory authority (ethics committee CCP Est-I: ID-RCB: 2013-A01436-39 and CNIL: DR2015-118). All participants provided written informed consent. They were compensated for their participation (30€ for the clinical assessment and 30€ for the fMRI).

MATERIALS AND MEASURES

Self-reported questionnaires

The Alcohol Use Questionnaire (AUQ; Mehrabian and Russell, 1978) is a 12-item measure assessing alcohol consumption over the previous 6 months: the mean number of weekly alcohol units (an alcohol unit in France corresponding to 10 g of pure ethanol) and specific binge drinking variables, i.e. consumption speed and drunkenness frequency.

The Alcohol Use Disorders Identification Test (AUDIT; Gache *et al.*, 2005) is a 10-item measure assessing alcohol consumption over the past year: alcohol use and alcohol-related impairments. This test allows the identification of hazardous drinking and AUD.

The Fagerström Test for Nicotine Dependence (FTND; Heatherton *et al.*, 1991) is a 6-item measure evaluating cigarette consumption and dependence. Scores between 4 and 5 reflect low dependence and scores equal or higher than 6 (moderate) or 7 (high) reflect dependence.

The Beck Depression Inventory (BDI; Beck *et al.*, 1996) is a 13-item measure evaluating the intensity of depressive symptoms.

The Spielberger State–Trait Anxiety Inventory (STAI; Spielberger *et al.*, 1983) is a 40-item measure of trait and state anxiety by frequency estimates of anxiety-related statements.

The National Adult Reading Test (NART; Mackinnon *et al.*, 1999) is a 40-item measure estimating premorbid intellectual abilities. Participants have to read aloud short and irregular words of increasing complexity. The number of errors made are processed to estimate IQ.

The UPPS Impulsive Behavior Scale (UPPS; Billieux *et al.*, 2012) is a 20-item measure evaluating impulsivity with four facets: urgency (acting rashly in emotional contexts), lack of premeditation (difficulty to consider long-term consequences), lack of perseverance (difficulty to focus on demanding tasks) and sensation seeking (seeking for new experiences). Greater scores reflect higher impulsivity.

Experimental task

To evaluate implicit emotion processing, we used an experimental paradigm that required participants to perform an explicit non-emotional processing, namely a gender categorization (i.e. determining if the face displayed is a male or a female face). The use of gender categorization tasks to assess brain activations following implicit emotion processing has a good test–retest reliability (Haller *et al.*, 2018) and has been supported in previous binge drinking studies (Herman *et al.*, 2019). The gender categorization task used in this study is validated in subclinical populations (Carré *et al.*, 2014) and demonstrates enough sensitivity for adaptation in MRI. Stimuli consisted of emotional facial expressions produced by male and female actors (all details around the face were removed) as emotional condition and color circles (blue and pink) as non-emotional condition. The task initially presented five emotional categories, namely anger, contempt, fear, happiness and sadness. In the current study, we explored the response to implicit emotion processing based on the four fundamental emotions (anger, fear, happiness, sadness). We thus excluded trials in which contempt faces were presented.

To perform the task, participants had to categorize gender/color with a two-response button (right hand, the index for male/blue and the middle finger for female/pink). Participants thus completed the task by categorizing gender (explicit processing) and were not required to directly process emotional facial expressions (implicit processing). We used an event-related design. Each trial began by

a fixation cross presented at the center of the screen for a variable duration between 200 and 900 ms and was followed, in some trials, by a blank screen. Blank screens were introduced randomly to maximize attention and to minimize inter-event correlation ("jittering"). Then, the emotional face/color circle was displayed for 1000 ms and followed by a mask representing a degraded face (sex and emotion were unidentifiable) for 150 ms (Esteves and Öhman, 1993). The stimuli consisted of 40 emotional facial expressions, 40 shape stimuli, 40 color circles and 40 blank screens. The occurrence of emotional facial expressions versus color circles was pseudo-randomly distributed. Stimuli were projected on a screen and were viewed through a prismatic mirror mounted on the head coil. To ensure the understanding of the task and the adaptation with the MRI environment, participants performed a training block at the beginning of the experiment.

Imaging acquisition parameters

MRI data were acquired using a 1.5 T scanner (Avanto, Siemens Healthineers, Erlangen, Germany) with a 32-channel phased array head coil. Functional MR images were collected using repeated single-shot echo-planar imaging (TE = 40 ms, FA = 90°, resolution = 3.75*3.75 mm^2, 26 slices, ascending interleaved order, thickness = 4.5 mm, TR = 2000 ms, 302 volumes). A 3D heavily T1-weighted images was also acquired (TR/TE/flip angle = 9.1 ms/4.6 ms/8°, 150 slices, thickness = 1 mm, resolution = 0.81 × 0.95 mm^2 (acquisition) reconstructed in 0.75 × 0.75 mm^2).

Data analytic approach

Due to a technical issue, behavioral data (gender categorization) were not available in the current study, but the validity of brain data (emotional processing) was ensured by: (a) the careful inspection of participants first-level activation maps; (b) previous research, showing reliable brain responses following implicit emotion processing (Carré *et al.*, 2014; Haller *et al.*, 2018). We excluded data of one participant who was falling asleep in the scanner, resulting in a final sample of 40 NBD and 39 BD.

The fMRI data were analyzed using BrainVoyager (Version 3.6, Brain Innovation, Maastricht, The Netherlands). Preprocessing of the data consisted of a correction for time differences in the acquisition of the different slices, a correction for head movements using a rigid body algorithm for rotating and translating each functional volume in a 3D space, a linear trend removal for excluding scanner-related signal drift, and finally a temporal high-pass filter to remove frequencies below 0.008 Hz. The functional data of each subject were then co-registered to their corresponding 3D T1-weighted anatomical scan, normalized in MNI space and smoothed in the spatial domain (Gaussian filter: full width at half maximum = 5 mm). All co-registrations were manually corrected, if needed, and movement corrections were optimized using a sinc interpolation. Analyses for emotion and group comparisons were conducted with random-effects analysis to control for individual variabilities and increase inferences of the results.

Statistical analysis

Descriptive statistics were performed for BD and NBD. To ensure the correct group matching, between group comparisons (independent sample *t*-tests and chi-square independent test) were performed on demographic, psychopathological and alcohol consumption characteristics.

Neuroimaging data (implicit emotion processing) were investigated with two main analyses. First, to explore activations related to the presentation of emotional faces, a general comparison between emotional (i.e. anger, fear, happiness, sadness) and non-emotional (i.e. pink or blue circles) conditions was performed. A within-group comparison was computed among the whole sample using whole-brain one-sample *t*-test corrected for multiple comparisons (i.e. uncorrected threshold of 0.01 corrected by the cluster size). Second, as we were particularly interested in differences between BD and NBD, we performed group comparisons for each emotional category separately. Between-group contrast-based comparisons were computed using whole-brain two-sample *t*-tests corrected for multiple comparisons (i.e. uncorrected threshold of 0.01 corrected by the cluster size). Corrections were performed in two stages for both analyses: (a) a pre-determined voxel-level primary threshold defined clusters by retaining groups of suprathreshold voxels (here fixed at 0.01); (b) a cluster-level extent threshold, measured in units of contiguous voxels, is determined based on the estimated distribution of cluster sizes under the null hypothesis (no activation in any voxel in that cluster). We adjusted the threshold based on a Monte Carlo simulation procedure (1000 iterations) to estimate cluster level false-positive rates. This approach resulted in a minimum cluster size of 567 mm^3 for the one-sample *t*-test and 726 mm^3 for the two-sample *t*-tests performed. The statistical maps were overlaid on the subject's 3D T1-weighted averaged scans in MNI space. Finally, correlational analyses were performed for each corrected brain activation map, among contrast-based beta weights of the activated voxel-clusters, alcohol consumption variables (binge-drinking score, AUDIT score) and impulsivity facets (positive and negative urgency, lack of premeditation, lack of perseverance, sensation seeking). These complementary analyses aimed to explore the relationships between brain responses, alcohol use and impulsive behaviors. Correlations were adjusted for multiple comparisons thanks to the Bonferroni procedure (i.e. the threshold considered for significance [0.05] divided by the number of comparisons performed [6], resulting in an adjusted threshold of 0.0083).

RESULTS

Descriptive statistics and general comparison

As shown in Table 1, there was no significant group difference for gender [$\chi^2(79) = 0.01$, $P = 0.909$], the number of participants having a family history of AUD [$\chi^2(79) = 1.95$, $P = 0.163$], or being cannabis users [$\chi^2(79) = 0.78$, $P = 0.378$]. Moreover, BD did not differ from NBD for age [$t(77) = 0.97$, $P = 0.337$], depressive symptoms [$t(77) = 0.01$, $P = 0.99$], state anxiety [$t(77) = 1.06$, $P = 0.294$], trait anxiety [$t(77) = 0.77$, $P = 0.446$], estimated IQ [$t(77) = 1.38$, $P = 0.172$] or tobacco use [$t(77) = 0.30$, $P = 0.769$]. Regarding tobacco use, results showed that all FTND scores were below 5, the cutoff indicating nicotine dependence. Groups did not differ either regarding impulsivity facets (all $t < 0.74$, all $P > 0.465$) Significant differences were, however, observed regarding alcohol consumption: BD had higher binge-drinking [$t(77) = 9.84$, $P < 0.001$] but also AUDIT [$t(77) = 7.19$, $P < 0.001$] scores than NBD.

fMRI data

Results showed a significant effect of emotional versus non-emotional conditions in the whole sample (Table 2, first part; Fig. 1), supporting the validity of the paradigm.

Table 2. Brain regions showing significant activations to the emotion effect (anger, fear, happiness, sadness versus color circles; first part) and to the group effect (BD versus NBD; second part)

Contrast	Brain areas	*X*	*Y*	*Z*	Cluster size (mm^3)	Brodmann areas	Right/left
Emotion effect							
Emotional > non-emotional	Fusiform Gyrus	33.70	-71.37	-4.05	55,064	BA 19	Right
	Inferior Frontal Gyrus	40.55	18.23	13.72	13,209	BA 9	Right
	Superior Frontal Gyrus	4.32	12.79	51.54	2393	BA 6	Right
	Amygdala	24.97	-4.70	-19.58	4331	/	Right
	Precuneus	26.04	-56.97	52.72	714	BA 7	Right
	Thalamus	22.74	-28.92	-2.63	2143	/	Right
	Lingual Gyrus	-29.69	-75.43	-6.60	39,053	BA 18	Left
	Anterior Cingulate	0.32	47.54	-15.71	3669	BA 32	Left
	Amygdala	-25.37	-3.09	-18.58	3324	/	Left
	Insula	-35.83	24.16	2.68	1123	BA 13	Left
	Thalamus	-20.38	-30.73	-2.03	844	/	Left
Non-emotional > emotional	Precuneus	3.00	-62.00	56.65	577	BA 7	Right
	Middle Frontal Gyrus	25.38	22.57	53.78	618	BA 6	Right
	Middle Frontal Gyrus	-26.75	19.69	54.19	4023	BA 6	Left
	Inferior Parietal Gyrus	-39.41	-64.01	46.41	1558	BA 39	Left
	Inferior Temporal Gyrus	-57.69	-33.85	-13.37	1580	BA 20	Left
	Cuneus	-3.13	-80.22	32.75	891	BA 18	Left
Group effect							
Anger—BD > NBD	Cerebellum	-34.99	-58.52	-38.11	791	/	Left
Fear—BD > NBD	Anterior Cingulate	4.81	16.00	-7.24	1155	BA 25	Right
Happiness—BD < NBD	Insula	-34.24	10.05	-5.17	1063	BA 13	Left
Sadness—BD < NBD	Postcentral Gyrus	52.13	-30.18	56.52	833	BA 2	Right
	Cingulate Gyrus	20.98	-1.89	35.41	783	BA 24	Right
	Medial Frontal Gyrus	7.76	25.27	42.79	726	BA 8	Right

X, *Y* and *Z* are the peak MNI coordinates. BA = Brodmann's area.

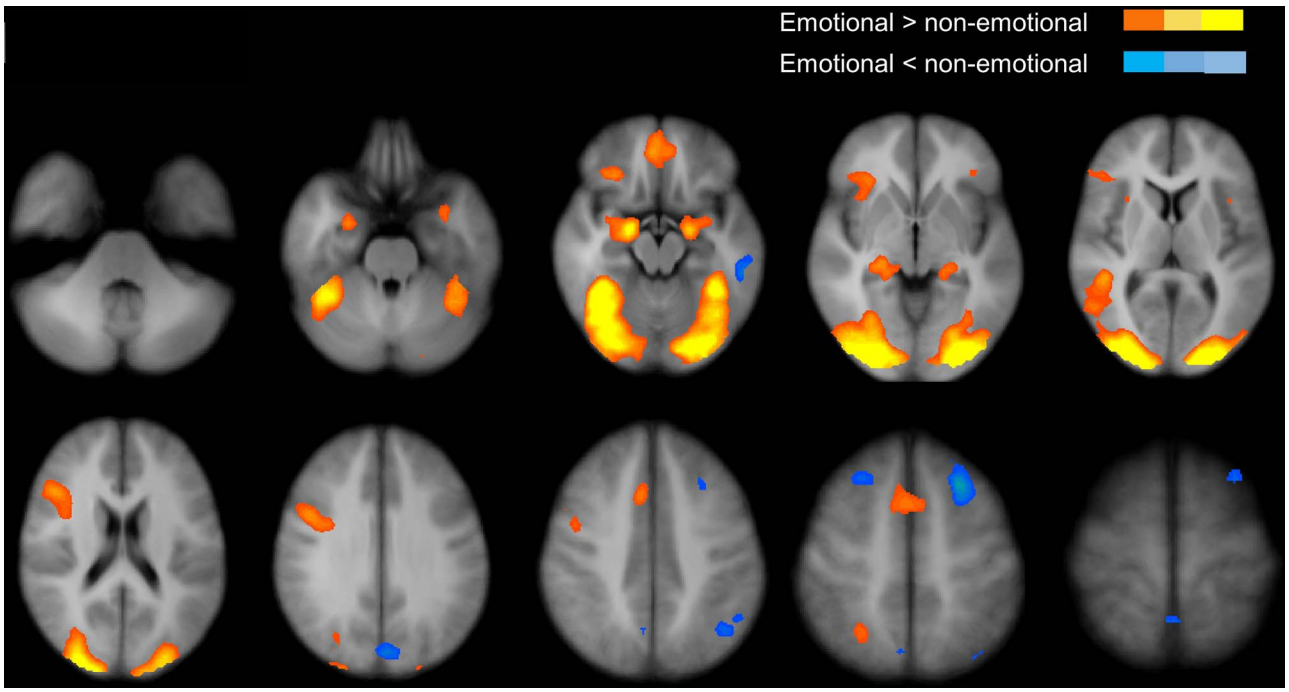

Fig. 1. Emotional-related activations. Emotional in contrast to non-emotional conditions (emotional > non-emotional; in red to yellow) activated in cortical frontal (right inferior and superior frontal gyrus), parietal (right precuneus), occipital (right fusiform gyrus and left lingual gyrus) and limbic (anterior cingulate and amygdala bilaterally) brain regions, and in sub-cortical (insula and thalamus bilaterally) regions. Non-emotional in contrast to emotional conditions (emotional < non-emotional; in blue) activated in cortical frontal (middle frontal gyrus bilaterally), parietal (right precuneus, left inferior parietal gyrus), temporal (left inferior temporal gyrus) and occipital (left cuneus) brain regions.

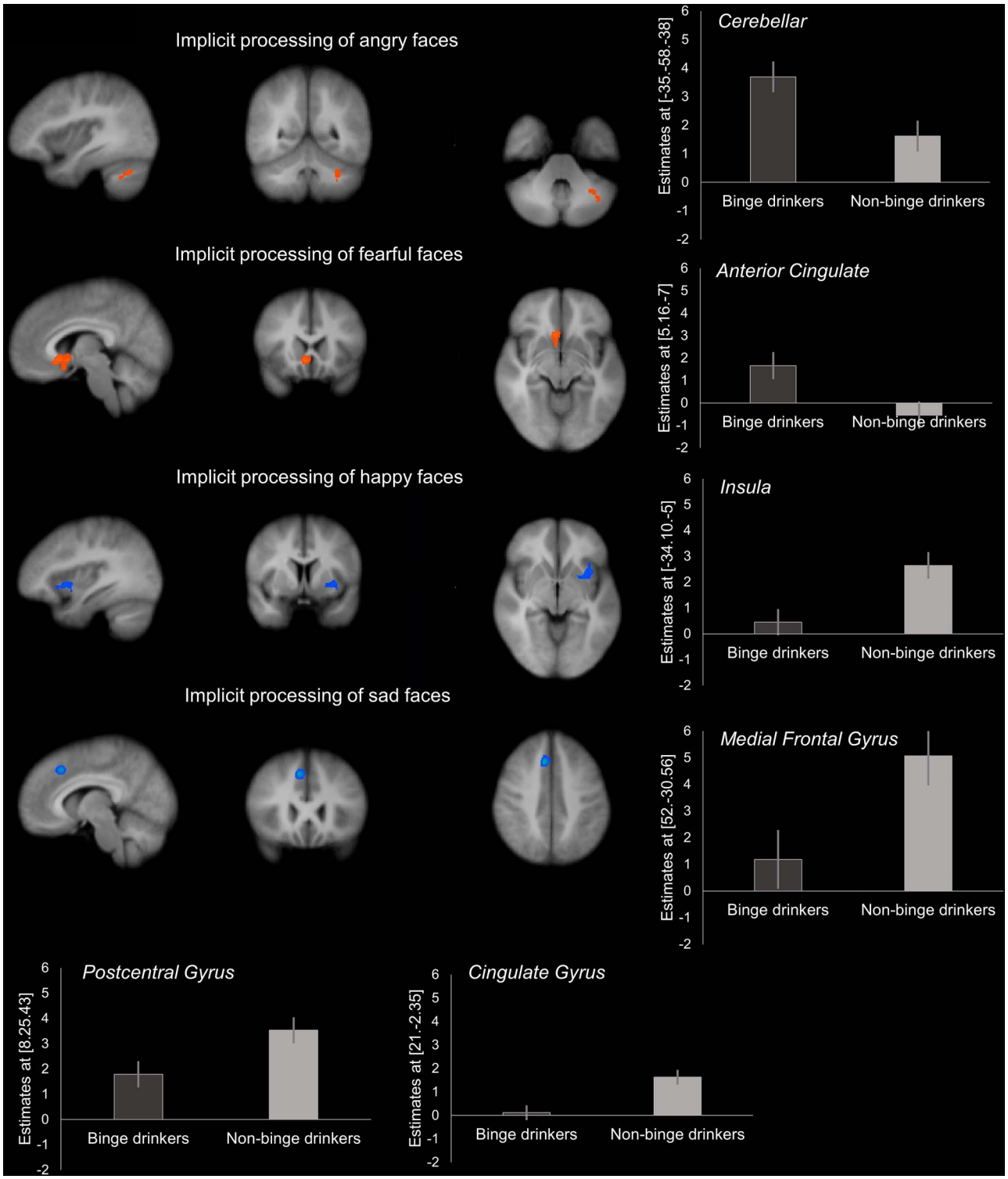

Fig. 2. Group-related activations. BD in contrast to control participants for each emotional content, from upper to lower: BD exhibited greater brain activation in cerebellar (left side, anger processing) and cortical (right anterior cingulate, fear processing) brain regions. They also showed reduced activations in sub-cortical (left insula, happiness processing) and in cortical frontal (right medial frontal gyrus), parietal (right postcentral gyrus) and limbic (right cingulate gyrus) brain regions (sadness in blue).

Regarding group comparisons (Table 2, second part; Fig. 2), the brain response of BD differed from NBD for all emotional conditions (Note: These comparisons were performed with sex as between subject factor, but no significant main effect or interaction was found; these comparisons were performed without cannabis users, and results remained significant). During anger and fear implicit processing, BD exhibited greater activations than NBD, respectively in the left posterior cerebellum [$t(77) = 4.07$, $P < 0.01$] and in the

right anterior cingulate [$t(77) = 3.88$, $P < 0.01$]. During happiness and sadness processing, BD showed lower activations than NBD: when processing happiness, BD showed lower activations in the left insula [$t(77) = 3.89$, $P < 0.01$]; when processing sadness, BD had lower brain activations in the right post-central gyrus [$t(77) = 4.21$, $P < 0.01$], the right cingulate gyrus [$t(77) = 4.36$, $P < 0.01$] and the right medial frontal gyrus [$t(77) = 5.65$, $P < 0.01$].

Correlation analyses

Correlations were performed between alcohol use variables (binge-drinking and AUDIT scores) and the brain areas that differed between groups. Significance thresholds were corrected for multiple comparisons by the Bonferroni procedure. Results indicated that the binge-drinking score was positively related to the activation in the left cerebellum ($r = 0.38$, $P = 0.001$) and negatively related to the activations in the right cingulate gyrus ($r = -0.46$, $P < 0.001$) and the right medial frontal gyrus ($r = -0.35$, $P = 0.002$). The AUDIT score was positively related to the activation in the left cerebellum ($r = 0.37$, $P = 0.001$) and negatively related to the activations in the left insula ($r = -0.32$, $P = 0.004$), right cingulate gyrus ($r = -0.53$, $P < 0.001$), and the right medial frontal gyrus ($r = -0.38$, $P = 0.002$).

Correlations were also performed between impulsivity facets and brain areas, while corrected for multiple comparisons. Results showed that the lack of premeditation impulsivity facet was positively correlated with the left cerebellum activation ($r = 0.30$, $P = 0.008$).

DISCUSSION

This study evaluates the brain responses to the implicit processing of emotional facial expressions in binge drinking. Results showed that, although participants did not have to explicitly process emotional contents (e.g. recognition), BD presented a modification of brain responses compared to NBD. The current findings showed that BD differed from NBD in response to all emotional expressions. For anger and fear, emotions usually related to threat processing (Haller *et al.*, 2018), BD had greater brain activations whereas for happiness and sadness, BD had lower brain activations.

Regarding anger processing, higher activations are found in BD in the left posterior cerebellum. The cerebellum is engaged in motor coordination, cognitive processing, and sensory discrimination (Sullivan, 2010). The role of the cerebellum is widely acknowledged in AUD while recent findings have highlighted a disrupted cerebellar growing in adolescent drinkers (Sullivan *et al.*, 2020), supporting the neurotoxic alcohol's effects in youth who did not meet AUD criteria. Moreover, the cerebellum is involved in the processing of negative emotional stimuli (Schraa-Tam *et al.*, 2012; Lange *et al.*, 2015; Adamaszek *et al.*, 2017). In particular, previous studies showed that specific regions of the cerebellum are related to negative emotions processing (Schraa-Tam *et al.*, 2012). The current region activated in response to angry faces corresponds to the cerebellum crus 1 and has been related to disinhibition (Schraa-Tam *et al.*, 2012). This proposal is in accordance with the specific correlation observed between lack of premeditation and cerebellar activation. It suggests that this greater brain response in BD may lead, at the behavioral level, to impulsive reactions. This result is in line with the interpersonal difficulties related to anger processing impairments described in AUD (Maurage *et al.*, 2008) and previously hypothesized in binge drinking (e.g. Lannoy *et al.*, 2018a). Another interesting point is that this increased activation in the cerebellum is related with both alcohol use scores, supporting a specific association with excessive drinking.

For fear processing, BD had greater brain activations in the right anterior cingulate, associated with the emotion system and particularly with regulatory functions (Stevens, 2011). The anterior cingulate cortex is widely identified as impaired in substance use disorders (Wilcox *et al.*, 2016), and is also altered in binge drinking (see Cservenka and Brumback, 2017 for a review). This study indicates that these impairments could be extended in response to fear processing. Indeed, previous studies evaluating implicit emotion processing (Haller *et al.*, 2018) showed that fear is related to indirect threat processing and activates the anterior cingulate cortex. Compared to NBD, BD thus exhibit an increased regulatory response to environmental threats. This observation aligns with a recent study assessing brain empathic responses to visual pain perception in BD (Rae *et al.*, 2020). Nevertheless, in contrast with previous proposals (Stephens and Duka, 2008), these results show that amygdala responses do not allow distinguishing BD from NBD. This appears in line with previous binge drinking studies (e.g. Cohen-Gilbert *et al.*, 2017) but should be further supported.

Beyond these greater brain activations, BD also exhibited lower responses following the view of happy and sad faces. Regarding happiness processing, decreased activations is found in the insula, generally described in emotional processing and mainly related to the identification of emotionally salient pictures (Wilcox *et al.*, 2016). Very few studies have been interested in the processing of positive emotional expressions in binge drinking, except those comparing positive and negative emotional contents in emotion identification (Lannoy *et al.*, 2017; Lannoy *et al.*, 2018a). To our knowledge, this is the first result showing that BD would have a specific emotional response to happiness. This poor emotional response to arousing and social images has to be deeply investigated, as it could be related to the individual and interpersonal issues described among BD (Swahn *et al.*, 2013).

Finally, findings showed that BD depicted lower brain activations in several brain regions in response to sad faces: the right post-central gyrus, medial frontal gyrus, and cingulate gyrus. These results thus support a disrupted involvement of the fronto-striatal network during emotional processing in binge drinking (Maurage *et al.*, 2013; Cohen-Gilbert *et al.*, 2017). Especially, the lower activation in the cingulate gyrus is in line with results found in AUD (Salloum *et al.*, 2007), showing that the processing of sadness elicited brain activations in the anterior cingulate in controls but not in AUD patients. In the current research, we did not find an absence of activation in BD but rather a reduction. This observation is in accordance with the proposal that BD and AUD patients would exhibit similar qualitative impairments with quantitative differences (Lannoy *et al.*, 2019a). Importantly, the cingulate gyrus is associated with sadness processing (Stevens, 2011) while disrupted sadness processing is indexed in BD (Lannoy *et al.*, 2019b). Eventually, it is worth noting that these group differences are supported by specific correlations showing a relationship between alcohol use on the one hand and cingulate and frontal activations during emotional processing on the other hand.

This study shows that BD differ from NBD in the brain responses to implicit emotional processing. These differences could explain emotional difficulties and might contribute to poor emotional responses in social context (e.g. a poor ability to detect sadness in others may lead to inappropriate responses and reject from others) and be a risk factor for subsequent excessive alcohol use. Nevertheless, we have to acknowledge some limitations to offer further perspectives. First, the absence of behavioral data has to be discussed. In such a way, it is worth noting that behavioral

data relied on explicit gender categorization whereas neural data relied on implicit emotion processing. Emotional processing is thus not related to behavioral data. However, future studies have to support our results, as this absence may hamper to precisely determine the appropriate task processing. Possible relationships between brain and behavior should also be established, especially the association between reaction times and cerebellar activations (e.g. emotion regulation can be explained through motor behavioral processing; Adamaszek *et al.*, 2017). Second, whereas we consider group comparisons as the main control in the current study, it would be interesting to support the existence of emotional difficulties in binge drinking by comparing BD to NBD in emotional and non-emotional matched conditions (e.g. the processing of neutral faces, although the question of neutrality is debated: Lee *et al.*, 2008). Indeed, amygdala activation supports the existence of emotional response in this study, but the nature of emotional and non-emotional conditions may lead to non-emotional differences (e.g. related to face complexity). Similarly, it could be interesting to investigate whether gender in the picture may influence implicit processing in neutral and emotional conditions. Here, we offer a first exploration of brain response following the implicit processing of emotional facial expressions, but future works should also design experiments to bring insights related to specific emotion processing (e.g. sadness). Third, consistently with previous studies (e.g. Maurage *et al.*, 2013; Connell *et al.*, 2015; Herman *et al.*, 2019), we did not observe sex differences in brain responses to implicit emotion processing. However, it has been shown that women might be more vulnerable to alcohol's effects (Erol and Karpyak, 2015) or emotional difficulties, future studies should thus further explore this question by targeting high-level cognitive processing (Carbia *et al.*, 2020). In the same vein, our results support the absence of cannabis influence, but subsequent works have to explore the respective and joint effects of binge drinking and cannabis use with validated measures (Tavolacci *et al.*, 2016). Finally, it should be emphasized that the current study has been conducted with a 1.5 T MRI system, which has lower signal-to-noise ratio than high or ultra-high field magnets (van der Zwaag *et al.*, 2009). Future studies could thus consider increasing image quality by using a high or ultra-high field scanner.

As implications, our results support that BD exhibit a differential processing of emotional contents and these difficulties exist during the implicit processing of emotional facial expressions. This suggests that the primary automatic/unconscious steps of emotional processing are already disrupted in BD, which may explain that the identification and recognition of emotions are impaired (Lannoy *et al.*, 2019b). It reinforces the similarities observed between binge drinking and AUD (Maurage *et al.*, 2013) by underlining emotional processes as a potential target to prevent the appearance of problematic alcohol use. Overall, this study supports the relevance to open and develop emotion research in binge drinking.

DATA AVAILABILITY STATEMENT

We will be pleased to provide any information about the data upon request addressed to the corresponding author.

CONFLICT OF INTEREST STATEMENT

Dr. Lannoy is funded by the Belgian American Educational Foundation and Dr. Benzerouk reports personal fees from Eutherapie and Lundbeck, but these funds are not related to the submitted work and have exercised no influence on the current study. The other authors declare no conflict of interest to disclose.

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CONTRIBUTIONS

F.G., V.Q., A.K. and M.N. designed the study, wrote the protocol, and obtained the financial support. F.G., F.B., C.P. and S.B. collected the data. S.L., L.D. and F.G. conducted the statistical analyses and wrote the first draft of the manuscript. All authors contributed to the interpretation of the data, reviewed, and approved the final manuscript.

REFERENCES

Adamaszek M, D'Agata F, Ferrucci R, *et al.* (2017) Consensus paper: cerebellum and emotion. *Cerebellum* **16**:552–76. doi: 10.1007/s12311-016-0815-8.

Adolphs R. (2001) The neurobiology of social cognition. *Curr Opin Neurobiol* **11**:231–9. doi: 10.1016/S0959-4388(00)00202-6.

Beck AT, Steer RA, Brown GK. (1996) *Beck Depression Inventory Manual*, 2nd edn. San Antonio, TXPsychological Corporation.

Billieux J, Rochat L, Ceschi G, *et al.* (2012) Validation of a short French version of the UPPS-P impulsive behavior scale. *Compr Psychiatry* **53**:609–15. doi: 10.1016/j.comppsych.2011.09.001.

Bora E, Zorlu N. (2017) Social cognition in alcohol use disorder: a meta-analysis: social cognition in AUD. *Addiction* **112**:40–8. doi: 10.1111/add.13486.

Carbia C, López-Caneda E, Corral M, *et al.* (2018) A systematic review of neuropsychological studies involving young binge drinkers. *Neurosci Biobehav Rev* **90**:332–49. doi: 10.1016/j.neubiorev.2018.04.013.

Carbia C, Corral M, Caamaño-Isorna F, *et al.* (2020) Emotional memory bias in binge drinking women. *Drug Alcohol Depend* **209**:107888. doi: 10.1016/j.drugalcdep.2020.107888.

Carré A, Gierski F, Lemogne C, *et al.* (2014) Linear association between social anxiety symptoms and neural activations to angry faces: from subclinical to clinical levels. *Soc Cogn Affect Neurosci* **9**:880–6. doi: 10.1093/scan/nst061.

Cohen-Gilbert JE, Nickerson LD, Sneider JT, *et al.* (2017) College binge drinking associated with decreased frontal activation to negative emotional distractors during inhibitory control. *Front Psychol* **8**:1650. doi: 10.3389/fpsyg.2017.01650.

Connell AM, Patton E, McKillop H. (2015) Binge drinking, depression, and electrocortical responses to emotional images. *Psychol Addict Behav* **29**:673–82. doi: 10.1037/adb0000071.

Cservenka A, Brumback T. (2017) The burden of binge and heavy drinking on the brain: effects on adolescent and young adult neural structure and function. *Front Psychol* **8**:1111. doi: 10.3389/fpsyg.2017.01111.

Ehlers CL, Phillips E, Finnerman G, *et al.* (2007) P 3 components and adolescent binge drinking in Southwest California Indians. *Neurotoxicol Teratol* **29**:153–63. doi: 10.1016/j.ntt.2006.11.013.

Erol A, Karpyak VM. (2015) Sex and gender-related differences in alcohol use and its consequences: contemporary knowledge and future research considerations. *Drug Alcohol Depend* **156**:1–13. doi: 10.1016/j.drugalcdep.2015.08.023.

Esteves F, Öhman A. (1993) Masking the face: Recognition of emotional facial expressions as a function of the parameters of backward masking. *Scand J Psychol* **34**:1–18. doi: 10.1111/j.1467-9450.1993.tb01096.x.

Gache P, Michaud P, Landry U, *et al.* (2005) The alcohol use disorders identification test (AUDIT) as a screening tool for excessive drinking in primary care: reliability and validity of a French version. *Alcohol Clin Exp Res* **29**:2001–7. doi: 10.1097/01.alc.0000187034.58955.64.

Haller SP, Kircanski K, Stoddard J, *et al.* (2018) Reliability of neural activation and connectivity during implicit face emotion processing in youth. *Dev Cogn Neurosci* **31**:67–73. doi: 10.1016/j.dcn.2018.03.010.

Heatherton TD, Kozlowski LT, Frecker RC, *et al.* (1991) The fagerström test for nicotine dependence: a revision of the Fagerström Tolerance Questionnaire. *Br J Addict* **86**:1119–27.

Herman AM, Critchley HD, Duka T. (2019) Binge drinking is associated with attenuated frontal and parietal activation during successful response inhibition in fearful context. *Eur J Neurosci* **50**:2297–310. doi: 10.1111/ejn.14108.

Huang S, Holcomb LA, Cruz SM, *et al.* (2018) Altered oscillatory brain dynamics of emotional processing in young binge drinkers. *Cogn Affect Behav Neurosci* **18**:43–57. doi: 10.3758/s13415-017-0551-7.

Koob GF. (2015) The dark side of emotion: the addiction perspective. *Eur J Pharmacol* **753**:73–87. doi: 10.1016/j.ejphar.2014.11.044.

Lange I, Kasanova Z, Goossens L, *et al.* (2015) The anatomy of fear learning in the cerebellum: a systematic meta-analysis. *Neurosci Biobehav Rev* **59**:83–91. doi: 10.1016/j.neubiorev.2015.09.019.

Lannoy S, Benzerouk F, Maurage P, *et al.* (2019b) Disrupted fear and sadness recognition in binge drinking: a combined group and individual analysis. *Alcohol Clin Exp Res* **43**:1978–85. doi: 10.1111/acer.14151.

Lannoy S, Billieux J, Dormal V, *et al.* (2019a) Behavioral and cerebral impairments associated with binge drinking in youth: a critical review. *Psychol Belg* **59**:116–55. doi: 10.5334/pb.476.

Lannoy S, D'Hondt F, Dormal V, *et al.* (2018a) Electrophysiological correlates of emotional crossmodal processing in binge drinking. *Cogn Affect Behav Neurosci* **18**:1076–88. doi: 10.3758/s13415-018-0623-3.

Lannoy S, Dormal V, Brion M, *et al.* (2017) Preserved crossmodal integration of emotional signals in binge drinking. *Front Psychol* **8**:984. doi: 10.3389/fpsyg.2017.00984.

Lannoy S, Dormal V, Brion M, *et al.* (2018b) Affective impairments in binge drinking: investigation through emotional facial expression decoding. *Compr Psychiatry* **83**:59–63. doi: 10.1016/j.comppsych.2018.03.004.

Le Berre A-P. (2019) Emotional processing and social cognition in alcohol use disorder. *Neuropsychology* **33**:808–21. doi: 10.1037/neu0000572.

Lee E, Kang JI, Park IH, *et al.* (2008) Is a neutral face really evaluated as being emotionally neutral. *Psychiatry Res* **157**:77–85. doi: 10.1016/j.psychres.2007.02.005.

Mackinnon A, Ritchie K, Mulligan R. (1999) The measurement properties of a French language adaptation of the National Adult Reading Test. *Int J Methods Psychiatr Res* **8**:27–38. doi: 10.1002/mpr.54.

Maurage P, Bestelmeyer PEG, Rouger J, *et al.* (2013) Binge drinking influences the cerebral processing of vocal affective bursts in young adults. *NeuroImage Clin* **3**:218–25. doi: 10.1016/j.nicl.2013.08.010.

Maurage P, Campanella S, Philippot P, *et al.* (2008) Electrophysiological correlates of the disrupted processing of anger in alcoholism. *Int J Psychophysiol* **70**:50–62. doi: 10.1016/j.ijpsycho.2008.05.572.

Maurage P, Lannoy S, Mange J, *et al.* (2020) What we talk about when we talk about binge drinking: towards an integrated conceptualization and evaluation. *Alcohol Alcohol*. **55**:468–479. doi: 10.1093/alcalc/agaa041.

Maurage P, Pesenti M, Philippot P, *et al.* (2009) Latent deleterious effects of binge drinking over a short period of time revealed only by electrophysiological measures. *J Psychiatry Neurosci* **34**:111–8.

Mehrabian A, Russell JA. (1978) A questionnaire measure of habitual alcohol use. *Psychol Rep* **43**:803–6. doi: 10.2466/pr0.1978.43.3.803.

Oldfield RC. (1971) The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* **9**:97–113. doi: 10.1016/0028-3932(71)90067-4.

Phillips ML, Drevets WC, Rauch SL, *et al.* (2003) Neurobiology of emotion perception I: the neural basis of normal emotion perception. *Biol Psychiatry* **54**:504–14. doi: 10.1016/S0006-3223(03)00168-9.

Rae CL, Gierski F, Smith KW, *et al.* (2020) Differential brain responses for perception of pain during empathic response in binge drinkers compared to non-binge drinkers. *NeuroImage Clin* **27**:102322. doi: 10.1016/j.nicl.2020.102322.

Salloum JB, Ramchandani VA, Bodurka J, *et al.* (2007) Blunted rostral anterior cingulate response during a simplified decoding task of negative emotional facial expressions in alcoholic patients. *Alcohol Clin Exp Res* **31**:1490–504. doi: 10.1111/j.1530-0277.2007.00447.x.

Schraa-Tam CKL, Rietdijk WJR, Verbeke WJMI, *et al.* (2012) fMRI activities in the emotional cerebellum: a preference for negative stimuli and goal-directed behavior. *Cerebellum* **11**:233–45. doi: 10.1007/s12311-011-0301-2.

Sheehan DV. (1998) The mini-international neuropsychiatric interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* **59**:20–33.

Sloan E, Hall K, Moulding R, *et al.* (2017) Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: a systematic review. *Clin Psychol Rev* **57**:141–63. doi: 10.1016/j.cpr.2017.09.002.

Spielberger DC, Gorsuch RL, Lushene R, *et al.* (1983) *Manual for the State-trait Anxiety Inventory*. Palo AltoConsulting Psychology Press.

Stephens DN, Duka T. (2008) Cognitive and emotional consequences of binge drinking: role of amygdala and prefrontal cortex. *Philos Trans R Soc B Biol Sci* **363**:3169–79. doi: 10.1098/rstb.2008.0097.

Stevens FL. (2011) Anterior cingulate cortex: unique role in cognition and emotion. *J Neuropsychiatry Clin Neurosci* **23**:120–5.

Sullivan EV. (2010) Cognitive functions of the cerebellum. *Neuropsychol Rev* **20**:227–8. doi: 10.1007/s11065-010-9144-8.

Sullivan EV, Brumback T, Tapert SF, *et al.* (2020) Disturbed cerebellar growth trajectories in adolescents who initiate alcohol drinking. *Biol Psychiatry* **87**:632–44. doi: 10.1016/j.biopsych.2019.08.026.

Swahn MH, Bossarte RM, Palmier JB, *et al.* (2013) Co-occurring physical fighting and suicide attempts among U.S. high school students: examining patterns of early alcohol use initiation and current binge drinking. *West J Emerg Med* **14**:341–6. doi: 10.5811/westjem.2013.3.15705.

Tavolacci M-P, Boerg E, Richard L, *et al.* (2016) Prevalence of binge drinking and associated behaviours among 3286 college students in France. *BMC Public Health* **16**:178. doi: 10.1186/s12889-016-2863-x.

Townshend JM, Duka T. (2005) Binge drinking, cognitive performance and mood in a population of young social drinkers. *Alcohol Clin Exp Res* **29**:317–25. doi: 10.1097/01.ALC.0000156453.05028.F5.

Van der Zwaag W, Francis S, Head K, Peters A, Gowland P, Morris P, Bowtell R. (2009) fMRI at 1.5, 3 and 7 T: characterising BOLD signal changes. *NeuroImage* **47**(4): 1425–1434. doi:10.1016/j.neuroimage.2009.05.015

Wilcox CE, Pommy JM, Adinoff B. (2016) Neural circuitry of impaired emotion regulation in substance use disorders. *Am J Psychiatry* **173**:344–61. doi: 10.1176/appi.ajp.2015.15060710.