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ABSTRACT

Individuals who engage in binge drinking behaviors may show evidence of impaired cognitive function and emotional dysregulation. Impaired empathy, characterized by a reduced ability to understand and respond appropriately to feelings of others, is increasingly recognized for its role in Alcohol Use Disorders (AUD). The present study examined a population of young adult social drinkers to compare individuals who show binge drinking behavior to those who do not on measures of empathic processing and associated neural responses. A secondary aim explored similarities and differences between binge drinkers living in the UK and France. Alcohol drinking history and impulsivity ratings were recorded from seventy-one participants [[37 UK (Binge drinkers N = 19); 34 France (Binge drinkers N = 17)], who then underwent a neuroimaging study. During functional magnetic resonance imaging, participants viewed images of bodily pain (vs. no-pain), while adopting the perspective of self (pain recipient) or other (observer of someone else experiencing pain). Anterior midcingulate cortex (aMCC) and insula activation distinguished pain from no-pain conditions. Binge drinkers showed stronger regional neural activation than non-binge drinkers within a cluster spanning fusiform gyrus and inferior temporal gyrus, encompassing the Fusiform Body Area. Binge drinkers compared to non-binge drinkers also took longer to respond when viewing pictures depicting pain, in particular when adopting the perspective of self. Relationships between changes in brain activation and behavioural responses in pain versus no pain conditions (self or other perspective) indicated that whereas non-binge drinkers engage areas supporting self to other distinction, binge drinkers do not. Our findings suggest that alcohol binge drinking is associated with different empathy-related behavioral and brain responses, consistent with the proposed importance of empathy in the development of AUD.

1. Introduction

Binge drinking is a widespread social problem and is particularly prevalent in the young adult population. Binge drinking (heavy episodic drinking) can be defined as consuming > 60 g of pure alcohol in at least one occasion in the past 30 days. About 30% of all adults (> 15 years of age) who drink alcohol in UK and France meet this criterion (World Health Organisation, 2019).

High levels of binge drinking may be particularly damaging to the brains of young adults, as the prefrontal cortex and hippocampus are not fully developed until early twenties (Casey et al., 2000; De Bellis et al., 1999). A common pattern of binge drinking is characterized by repeated bouts of drinking, leading to high levels of alcohol in the brain, followed by periods in which brain alcohol levels return to zero. The withdrawal kindling hypothesis (Stephens and Duka, 2008), proposes that such repeated cycles induce structural and functional brain changes that are associated with observable cognitive and affective deficits (De Bellis et al., 1999; Duka et al., 2004; Glenn et al., 1988; McQueeny et al., 2009; Smith et al., 2017).

Importantly, emotional dysregulation is identified as an important

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contributor to alcohol use in young adults. For instance, childhood deficits in emotional and interpersonal skills are related to risky alcohol consumption and drug use in adolescence (Hessler and Katz, 2010). Decreased trait empathy is shown to contribute to a reduced resistance to peer pressure to drink among binge drinking adolescents (Laghi et al., 2019). There is also evidence that difficulties in the recognition of emotions of fear and sadness are associated with a pattern of binge drinking behavior in young individuals (Lannoy et al., 2019), while decreased empathy is associated with increased alcohol consumption in 13–20 years old youths (Lannoy et al., 2020). Thus deficits in emotional reactivity and empathy are present in the context of binge drinking behavior among young individuals.

Empathy is the capacity to appreciate and simulate at a subjective level a different affective state, usually the emotions of another person. Previous research into empathy has highlighted the utility of experimental paradigms involving the appraisal of actual or implied experiences of pain, perceived from the perspectives of self or other (Jackson et al., 2006a; Singer et al., 2004). Our aim here was to extend the literature on maladaptive empathy in binge drinkers by investigating its neural underpinnings in healthy young adult social drinkers who pursue a pattern of binge drinking.

By identifying differential self/other responses, at the neural level, to stimuli that normally engage empathy can provide valuable insight into mechanisms underlying maladaptive drinking behavior during a drinking session (binge drinking). It is proposed that empathic sensitivity, if reduced, can blunt the perception of suffering of self or others during a drinking session and lead to repeated binges. That is how deficits in empathy may contribute to heavy alcohol drinking and eventually to Alcohol Use disorders

Empathy can be elicited using images depicting pain, and further probed by instructing the participant to respond from the distinct perspectives of self and other. Neural activations within the pain matrix can objectively index empathic processing. This objectivity is useful as questionnaires measures often rely paradoxically on subjective insight into one's deficits in empathy. Empathic neural responses include the engagement of somatosensory cortices bilaterally and of regions processing affective aspects of pain, including anterior insula cortex (AIC), dorsal mid and anterior cingulate cortex (MCC and ACC) and inferior frontal gyrus (Jackson et al., 2006a; Lamm et al., 2011; Lamm et al., 2007; Lamm et al., 2019). Additionally, attending to and mentalizing depictions of pain engages regions of premotor, parietal and temporal cortices (including the fusiform gyrus) linked to representations of action and perceived body image (Lamm et al., 2007; Xiang et al., 2018). The distinction self/other perspective enables insight into the specific neural underpinnings of sharing and understanding another person's affective state. Responses attributable to simulating the experience of pain from the self-perspective link 'empathy for self' to activation in the supramarginal gyrus, whereas 'empathy for other' is associated with activation in left middle temporal gyrus, left inferior frontal gyrus, and supplementary motor area (Lamm et al., 2019; Silani et al., 2013). Commonly also, the right temporo-parietal junction (rTPJ) is highlighted as a neural substrate for self–other distinctions (e.g., Jackson et al., 2006a; Lamm et al., 2019).

In the literature on brain substrates of empathy for pain, there are no previous studies, to our knowledge, that examine differences between binge drinkers and non-binge drinkers in empathy for pain. Thus, the aim of the present study was to investigate neural mechanisms underlying binge drinking, utilizing functional magnetic resonance imaging (fMRI) to compare brain responses to the depiction of pain between bingeing and non-bingeing groups of young alcohol users. Empathy was tracked at the neural level by acquiring and analyzing functional brain images while participants viewed images of pain and no pain, from perspectives of self and other, using an established procedure (Jackson et al., 2005). Individuals were scored for binge drinking, calculated from metrics encompassing speed of drinking and occurrence of drunkenness (Townshend and Duka, 2002). Grams of

alcohol drunk per week and AUDIT (Alcohol Use Disorders Identification Test) scores were also obtained to test for differences in the amount of alcohol drunk per week and the risk of alcohol dependence between the groups. There is a large body of research showing a positive association between trait impulsivity and binge drinking in young adults (Caswell et al., 2016; King et al., 2011; Lannoy et al., 2017; Sanchez-Roige et al., 2014). Recently, it has also been suggested that impulsive traits associated with antisocial behavior compromise the development of empathy (see Massey et al., 2018); this suggestion has yet to be confirmed. A recent review highlights the interrelationship between emotional processing, affective states and impulsivity (Herman and Duka 2018). These ideas further motivated us to include measurements of impulsivity within the current study; trait impulsivity ratings were taken to test the relationship between predicted changes in brain activation related to empathy in binge drinkers and their impulsivity ratings.

Based on the evidence presented above linking empathy deficits in young binge drinking adults, we predicted firstly, that the 'empathy for pain' task would give rise to a smaller increase in brain activation in binge drinkers compared to non-binge drinkers within AIC and ACC (areas involved in emotional processing and feelings, including affective aspects of pain). Similar differences would also be expected in areas involved in sensorimotor processing (parietal and temporal cortices including the fusiform gyrus). Secondly, we predicted that binge drinkers, on exposure to implicit pain to self would not show higher brain activation vs. pain to other, when compared to non-binge drinkers; most particularly in the rTPJ, but also in sensorimotor areas. Finally, we predicted that binge-drinkers, compared to non-binge drinkers, would show attenuated empathy for others. We tested the role of impulsivity as a contributing factor in the empathic responses of binge drinkers in an exploratory manner.

This investigation was part of a larger study examining factors associated with binge drinking in young adults in the UK and in France, with the aim to identify cultural, behavioral and/or brain activation differences under cognitive and emotional challenges in these two culturally different cohorts. In the current investigation, our aim was to study young adults in both the UK and France with respect to empathic responses to implied pain in self and others.

2. Materials and methods

2.1. Participants

Eighty-three social alcohol drinkers (42 male and 41 female) were recruited across two sites in France and the UK. Participants were university students from the University of Sussex, UK, and l'Université de Reims Champagne-Ardenne, France. During recruitment, they were assigned to one of two groups: binge drinkers (22 male, 21 female, age ranges 18–23) or non-binge drinkers (20 male, 20 females, age range 18–26). Binge group classification depended on binge scores derived from the Alcohol Use Questionnaire (AUQ; (Mehrabian and Russell, 1978) as in previous research (Townshend and Duka, 2002). Binge drinkers had a binge score of 30 or above, while non-binge drinkers scored below 16.

Inclusion to the study required being over 18 years old, drinking 8 units (64 g) or more of alcohol per week, being right-handed (determined by handedness questionnaire (Porac and Coren, 1981), and having normal BMI. Exclusion criteria were a history of psychiatric or neurological problems, and being on any medication for any psychological or physical condition at the time of the study (including paracetamol and antibiotics, but excluding the contraceptive pill; assessed using questions from the Nuffield Hospitals Medical History Questionnaire, which covers past and present physical and psychiatric health status, including any current medication). Additional exclusion criteria were pregnancy, trying to conceive or breastfeeding, and MRI contraindications (i.e. having any metal implants, teeth braces or bridges,

tattoos above the shoulder, or a cardiac pacemaker etc.). Participants were asked to refrain from drinking alcohol for at least 12 h before the session, and from taking illicit drugs for one week. Participants were allowed to smoke as they would normally before the session, but smoking was not permitted during testing.

In accordance with the Declaration of Helsinki, all participants provided written informed consent at the start of the study, and the study was approved by the Brighton and Sussex Medical School Research Governance & Ethics Committee in the UK and by the French national regulatory authority (ethics committee CCP Nord Ouest-II: ID-RCB: 2011-A01071-40). Participants were compensated in cash for their participation.

Due to a technical fault, data from one participant from the UK and eight participants from France were not included in any analyses. Data from one UK participant who fell asleep during scanning were also excluded. Following preprocessing of the fMRI data, an additional two participants (one from the UK sample and one from the French cohort) were excluded from subsequent analyses due to excessive head movements (see below for details). The final sample used in all analyses described here consisted of 71 participants (37 UK [Binge drinkers N = 19]; 34 France [Binge drinkers N = 17]). Of the 71 participants, 35 were males (18 UK & 17 France) and 36 were females (19 UK & 17 France). Mean age was 20.24 years (UK cohort) and 20.91 years (French cohort).

2.2. Design/Procedure

Each participant completed a single testing session. Breath alcohol concentration (BrAC) was measured at the start of the session using a standard breathalyzer (Lion Alcolmeter SD-400, Lion Laboratories Ltd, Barry, UK; Dräger 6810 med, Dräger Safety Company, Strasbourg, France) with a detection-limit equivalent to 0.01 g/l alcohol in the bloodstream. Participants were only allowed to continue with testing if BrAC was 0.

Each participant then provided demographic information (age, gender, mother tongue; age of drinking onset) and completed the Alcohol Use Disorders Identification Test (AUDIT; Saunders et al., 1993), the Barratt Impulsiveness Scale (BIS; Patton et al., 1995), the Spielberger State-Trait Anxiety Inventory (STAI; Spielberger et al., 1970), and the National Adult Reading Test (NART; Nelson, 1982) among other questionnaires that will not be presented here. The participant was then placed in a 1.5 Tesla Siemens Avanto Magnetic Resonance Imaging (MRI) scanner, in which the Empathy task (alongside additional tasks) was completed during the acquisition of functional (fMRI) datasets (T2*-weighted images). The same model of scanner was used in UK and France.

2.3. Materials

2.3.1. Alcohol use questionnaire (AUQ; Mehrabian and Russell, 1978)

The AUQ gives an estimate of the average number of weekly alcohol-units consumed over the previous 6 months (a glass of wine is measured as 1.5 units; a pint of beer/cider as 2.4 units; a shot of spirit as 1 unit; and a bottle of alcopops as 1.7 units). We calculated the sum of weekly alcohol-unit consumption. This score was converted to average weekly grams for generalizability across sites. Townshend and Duka (2002) have previously demonstrated that the AUQ is a reliable measure of drinking quantity. High scores indicate increased average weekly alcohol use. A binge score was also calculated based on the speed of drinking (number of drinks per hour), the number of episodes of alcohol intoxication in the past 6 months, and the percentage of alcohol intoxications out of the total number of times of going out drinking episodes (Scaife and Duka, 2009).

2.3.2. Alcohol use Disorders Identification test (AUDIT; Saunders et al., 1993)

The AUDIT is designed to identify individuals with harmful or hazardous alcohol consumption. It consists of 10 questions measuring alcohol use, and an individual's assessment of others' feelings towards the individual's alcohol consumption. The present study used the total AUDIT score, with high scores reflecting greater severity of alcohol use.

2.3.3. Barratt Impulsiveness scale (BIS; Patton et al., 1995); French version: (Bayle et al., 2000)

The BIS is a 30-item questionnaire designed to measure three aspects of impulsivity: (a) non-planning impulsivity or the inability to plan and think carefully; (b) motor impulsivity or acting on the spur of the moment; and (c) attentional impulsivity or the inability to focus on the task at hand. Items are rated on a 4 point Likert-type scale ranging from "rarely/never" to "almost always". Higher scores on each factor loading represent greater levels of impulsive behavior.

2.3.4. Spielberger State-Trait anxiety Inventory (STAI; Spielberger et al., 1970); French version: (Bruchon-Schweitzer and Paulhan, 1993)

The STAI is a measure of trait and state anxiety. It consists of 20 items for assessing trait anxiety and 20 for state anxiety. All items are rated on a 4-point scale ("Almost Never" - "Almost Always"). Higher scores indicate greater anxiety.

2.3.5. The national adult Reading test (NART; Nelson, 1982); French version: (Mackinnon and Mulligan, 2005)

The NART is an estimate of premorbid intellectual ability. It consists of 50 short, irregular words of increasing complexity which subjects are required to read aloud. The number of errors made on the NART were processed to estimate premorbid WAIS-R Full Scale IQ (Wechsler, 1981).

2.3.6. Empathy task ((Jackson et al., 2005)

The empathy task (see Fig. 1) was an adaptation of an established task (Jackson et al., 2005), using the same series of 128 images (image size 400 × 300 pixels; we acknowledge the contribution of Professor Harold Mouras, Université de Picardie Jules Verne (UPJV), Amiens France, in obtaining permission for use). Stimuli depicted right hands and right feet (64 each). Half of the images portrayed an injury to the body part (Pain condition; P), while the other half consisted of a matched non-injury control image (No-Pain condition; NP). Injury-depicting pictures included situations that arise in daily life: cutting, burning and pinching. Different types of injury were presented in the pictures: mechanical, heat and pressure.

Each participant was asked to indicate via button presses whether the image depicted a painful scene or a non-painful scene. Four blocks were given consisting of 16 P and 16 NP trials, randomly presented. At the start of each block, the participant was instructed by a 30-second written cue to adopt the perspective that the images depicted events occurring either to themselves (Self condition; S) or to another, unfamiliar, person (Other condition; O). The task therefore consisted of four conditions: Pain Self (PS); Pain Other (PO); No-Pain Self (NPS); No-Pain Other (NPO).

Perspective-block presentation order was counterbalanced across participants, with four possible orders: OSSO, SOOS, OSOS, or SOSO. In addition, 50% of the participants were instructed to use the index finger of their right hand to indicate that a scene depicted a painful event, and the middle finger of their right hand to indicate the presence of a non-painful event. The other 50% of participants used the middle finger of their right hand to press for painful events and the index finger for non-painful events.

Each trial began with the presentation of an image for 2000 ms and was followed by a fixation cross for 2000 ms. Eight null events (a fixation cross presented for 2000 ms) were included in each block to ensure asynchrony between trial type (P and NP) and scan acquisition

Fig. 1. Examples of images in the Pain and the matched No-pain conditions. In each trial in the task, an image was presented for 2000 ms and participants were required to press a key to indicate whether the image depicted a painful scene or a non-painful scene. The image was followed by a fixation cross for 2000 ms. In each block of trials, fixation crosses representing null events (8 per block of 16 P and 16 NP trials) were presented for 2000 ms to ensure asynchrony of trial type with scan acquisition.

across the experiment.

We recorded correct responses (i.e. the proportion of times participants correctly identified that an image depicted a painful or a non-painful event) at each level of perspective (i.e. Self vs. Other), and reaction time to correct responses (i.e. latencies) under each condition. The reaction time to each NPO and NPS stimulus was subtracted from reaction time to the corresponding PO and PS stimulus to give a difference score, used as a covariate in fMRI analyses (see '**fMRI Analyses**' below).

Outside the scanner, participants provided post-scan ratings, trial by trial, of pain intensity, on a 9-point scale (using the keyboard, where 1 indicated no pain and 9 indicated extreme pain), for each image seen during scanning, again adopting the perspective of self and other in blocks, in the same counterbalanced order as that implemented in the scanner. Rating values were converted to the range 0–8, so that 0 would indicate 'no pain'. Average rating scores were created for each participant under each condition (i.e. PO, NPO, PS, NPS). The rating of each NPO and NPS stimulus was subtracted from the rating of the corresponding PO and PS stimulus to give a difference score, used as a covariate in fMRI analyses (see '**fMRI** Analyses' below). Furthermore, in half of the sample (UK) participants were also asked to rate their subjective sense of how successful they had been in adopting the perspectives of self and other respectively during the in-scanner task, on a scale from 0 (no success) to 10 (complete success).

2.4. MRI methods

fMRI data at both UK and French sites were acquired on a Siemens Avanto 1.5 T (32 channel head coil, T2*-weighted echo planar images, repetition time = 3300 ms, echo time = 50 ms, 36 interleaved 3 mm slices, 0.75 mm slice gap, in-plane resolution 3x3 mm, 255 volumes total). The first six volumes were discarded for steady-state magnetization. A T1 was acquired for co-registration in fMRI preprocessing (repetition time = 1160 ms, echo time = 4.24 ms, 0.9x0.9x0.9 mm resolution).

2.5. Analyses of behavioral data

Univariate Analyses of Variance (ANOVAs) with site (UK vs. France) and binge-group (binge drinkers vs. non-binge drinkers) as between subjects factors, were used to assess differences between binge groups and Sites in age, age of drinking onset, average weekly alcohol consumption in grams and total AUDIT scores. In addition, chi-square was used to check binge-group distribution differences between the two sites, and to check gender distribution differences between the Binge-groups, one for the UK and another for the French cohort.

Latencies and proportion of correct responses in each condition of the task in the scanner as well as post-scanning average ratings, were compared between binge-groups using two $2 \times 2 \times 2 \times 2$ repeated measures ANOVAs, with Site (UK vs. France), and binge-group (binge drinkers vs. non-binge drinkers) as between subjects factors. Perspective (self vs. other) and pain (pain vs. no-pain) were included as within subject factors.

Post-hoc analyses of significant interactions were all corrected for multiple comparisons using Bonferroni correction.

Participants' subjective sense of how successful they had been in adopting the perspectives of self and other during the in-scanner task were analyzed using a repeated measures ANOVA with binge group as a between-, and perspective condition as within-, participant factor.

2.6. fMRI analyses

2.6.1. fMRI preprocessing

fMRI data were preprocessed and analyzed using SPM12 (v6225, www.fil.ion.ucl.ac.uk/spm), including realignment to the mean image, slice-time correction to the (anatomically) middle slice number 18, co-registration with T1 structural and MNI normalization, and 8 mm smoothing, with default settings applied for all options.

2.6.2. fMRI first-level models

A general linear model represented task events, with regressors for 1) pain self (PS), 2) no-pain self (NPS), 3) pain other (PO), 4) no pain other (NPO), 5) null events, and 6) response period. If participants

neglected to make a button press during the response period, these failed response periods were added in an additional regressor. The regressors were stick functions, with onset time given at the start of each event, and durations of 0.

For all participants, head movements were modelled using six regressors of the preprocessing realignment parameters. The realignment parameters of each participant were inspected to identify any volumes showing movement close to the voxel size of 3 mm (Poldrack et al., 2011). Two participants made more than one head movement > 3 mm, and were excluded from analysis (see 'Participants' section above). The realignment parameters were also inspected for any volumes showing movement between 2 and 3 mm, as translational displacements of more than ½ the voxel size may be cause for concern (Poldrack et al., 2011). Four participants showed head movements (translation at a single volume) of a magnitude between 2 and 3 mm (two participants showed 2 and two participants showed 1 movement of this nature); one of the participants with 2 such head movements, made also one single head movement > 3 mm. We therefore used spike regression to remove the influence of these volumes, by adding a binary regressor to the participant's general linear model, indexing the time points where motion between 2 and 3 mm occurred (Poldrack et al., 2011; Satterthwaite et al., 2019). For the four participants with an additional head movement regressor, the duration of the head movement 'events' was a boxcar 3 TRs in duration (9900 ms), spanning the volume showing the large translation, and the volume preceding and following this.

Single regressor t-contrasts were generated for 1) pain self (PS), 2) no pain self (NPS), 3) pain other (PO), and 4) no pain other (NPO), with a contrast weight of [1] for each respectively. These were entered to a full factorial second-level analysis.

2.6.3. fMRI second-level models: Task and group effects

The full factorial second-level analysis contained group (binge, non-binge) and site (UK, France) as independent (between-participant) factors, and task condition (PS, NPS, PO, NPO) as a non-independent (within-participant) factor.

F-contrasts were generated for all effects ('eye (16)' matrix 16x16 factors; giving an overview of task activations in general), pain effects (PS & PO versus NPS & NPO) and self/other effects (PS & NPS versus PO & NPO). Post-hoc t-tests identified the direction of significant effects.

F-contrasts examining group effects (binge versus non-binge) were generated for pain (binge PS & PO versus non-binge PS & PO), no pain (binge NPS & NPO versus non-binge NPS & NPO), self (binge PS & NPS versus non-binge PS & NPS), and other (binge PO & NPO versus non-binge PO & NPO). Group effects for each condition were also examined using F-contrasts (binge versus non-binge) for PS, NPS, PO, and NPO, with post-hoc t-tests identifying the direction of significant effects. Finally, an F-contrast tested for an interaction between binge status and pain conditions.

Contrast estimate effect size plots for the four trial types, in binge and non-binge groups, were generated for the left and right anterior insula, and anterior midcingulate cortex (aMCC), at each region's peak co-ordinate in the PAIN > NO PAIN t-contrast (Fig. 2, Supplementary Fig. 1 also plots the contrast estimate effect sizes for the four trial types, in binge and non-binge groups, at the UK and France sites separately). A contrast estimate effect size plot was generated for the fusiform body area (FBA) at this region's peak co-ordinate in the binge PO > non-binge PO t-contrast (Fig. 3, with UK and France sites plotted separately in Supplementary Fig. 2).

2.6.4. fMRI second-level models: Correlations between task effects and BIS

To explore further a potential association of trait impulsivity (BIS) with task effects, we generated a series of four second-level models, examining the correlation of BIS scores with activation on 1) PS, 2) NPS, 3) PO and 4) NPO trials. First-level contrasts for each trial type were entered to four second-level multiple regressions, with (mean centered) BIS scores as a covariate of interest, and site (0/1 UK/France)

as a nuisance covariate. Two t-contrasts per model tested for positive and negative correlations of BIS scores with task effects.

2.6.5. fMRI second-level model: Correlations between task effects and age of alcohol drinking onset

It is plausible that drinking at an earlier age is associated with greater abnormalities in processing the pain of others. Therefore, for the binge group only, a second-level model examined the correlation of age of alcohol drinking onset with activation on PO trials (which showed a significant binge group difference; see Results). First-level contrasts for PO trials were entered to a second-level multiple regression, with (mean centred) age of alcohol drinking onset as a covariate of interest, and site (0/1 UK/France) as a nuisance covariate. Two t-contrasts tested for positive and negative correlations of age of alcohol drinking onset with PO trials.

2.6.6. fMRI second-level models: Behavioural and brain differences in reaction time and pain intensity

Following Jackson and colleagues (Jackson et al., 2005), we also explored the relationships between behavioral indices of pain perception and brain activations in the two groups with different alcohol drinking behavior (BD and non-BD). Jackson et al. (2005) reported that differences in pain intensity scores between NPO and PO correlated with change in activity in the ACC between NPO and PO conditions. We conducted eight second-level models to examine correlations between behavioural and brain effects.

Two first-level t-contrasts for 1) PS > NPS [1–1], and 2) PO > NPO [1–1], were generated for each participant. These were entered respectively to two sets of four second-level multiple regressions, with the following mean centered measures as covariates of interest: 1) PS reaction time – NPS reaction time; 2) PS pain intensity rating – NPS pain intensity rating; 3) PO reaction time – NPO reaction time; 4) PO pain intensity rating – NPO pain intensity rating; in the binge group and non-binge groups separately.

In all regressions, site (0/1 UK/France) was entered as a nuisance covariate. The reaction times were taken in-scanner during the task, while the pain intensity ratings were taken out-of-scanner in a post-scan rating session. For each model, two t-contrasts tested for positive and negative correlations of behavioural measures with the change in activity between PS and NPS or PO and NPO trials.

2.6.7. Statistic image thresholding

Statistic images were thresholded at cluster-forming threshold $p < 0.001$ for cluster-wise false discovery rate (FDR) correction for multiple comparisons at $p < 0.05$ (Chumbley et al., 2010; Eklund et al., 2016). Significant clusters were localized using the Anatomy toolbox (v2.2b, Eickhoff et al., 2007)).

2.7. Data availability

Anonymized demographic, alcohol use, BIS, STAI, NART and empathy task behavioral data are available at https://osf.io/rg9am/. fMRI statistic images are in Neurovault (Gorgolewski et al., 2015) at https://nam03.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.neurovault.org%2Fcollections%2F8400%2F&data=02%7C01%7CC.Corrections%40elsevier.com%7C1cce7a2afae545b70b2508d82f1d20be%7C9274ee3f94254109a27f9fb15c10675d%7C0%7C0%7C637311149445740069&sdata=WJndjiCOZipoPqXXQTwz%2BIGmqd3hhdlDwoiYuQxISJc%3D&reserved=0.

3. Results

3.1. Behavioral results

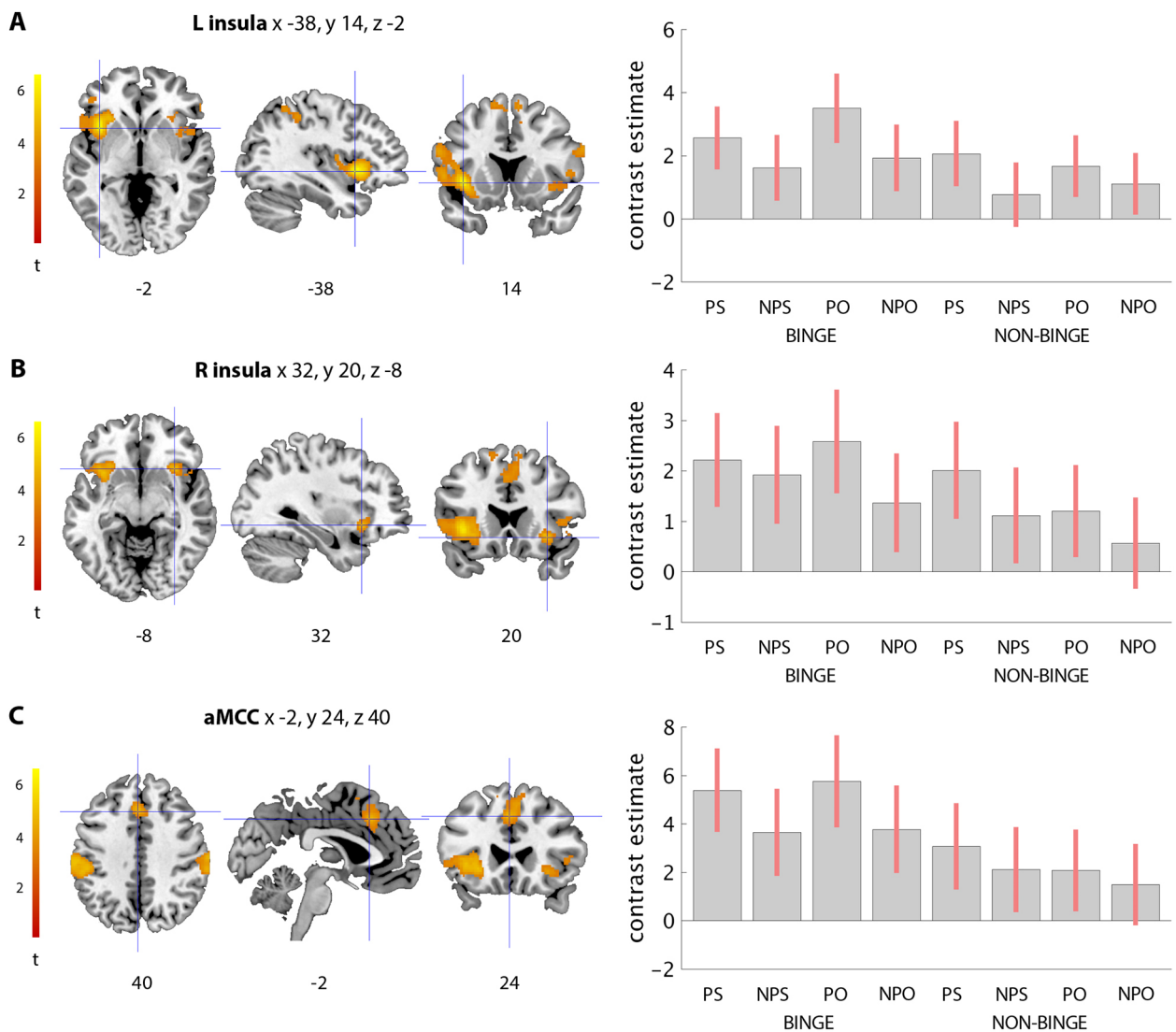Table 1 summarizes demographic details, information about

Fig. 2. Neural activity associated with viewing of stimuli representing pain, versus stimuli representing no pain (PAIN > NO PAIN), and contrast estimate effect size plots of activity during the four trial types, in binge and non-binge groups, for (A) left anterior insula, (B) right anterior insula, and (C) anterior midcingulate cortex (aMCC). Plotted are contrast estimates at each region's peak co-ordinate in PAIN > NO PAIN for (left-to-right), binge drinkers (PS, NPS, PO, NPO) and non-binge drinkers (as for BINGE). Error bars represent 90% confidence interval. PS: Pain Self; NPS: No Pain Self; PO: Pain Other; NPO: No Pain Other. See Supplementary Fig. 3 for additional illustration of regions showing higher activity for (PAIN > NO PAIN). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
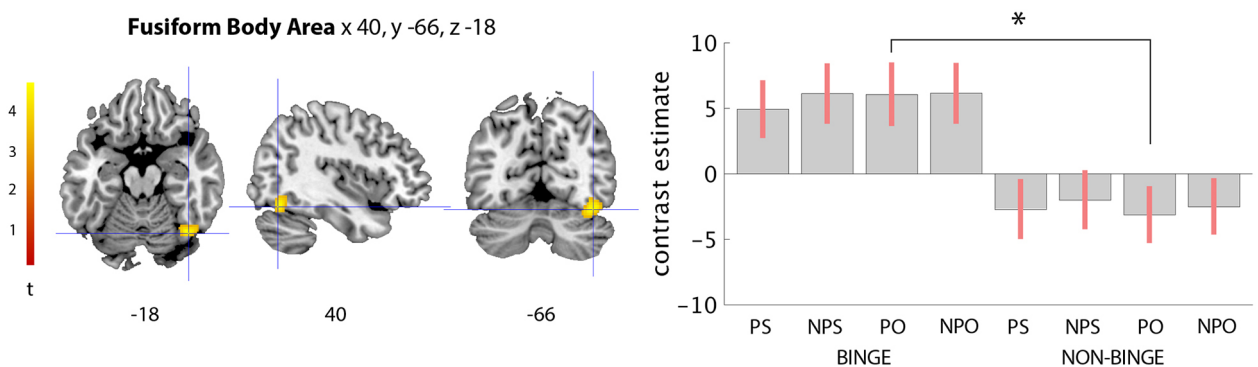

Fig. 3. Neural activity associated with viewing of stimuli representing pain in other (PO), in binge drinkers versus non-binge drinkers (BINGE PO > NON-BINGE PO). Contrast estimate effect size plot shows activity in the Fusiform Body Area (FBA) at the peak co-ordinate in Binge PO > Non-binge PO, for (left-to-right) binge drinkers (PS, NPS, PO, NPO) and non-binge drinkers (as for BINGE). Error bars represent 90% confidence interval. The peak co-ordinate of the cluster was on the fusiform gyrus, and encompassing FBA, although the cluster extended from part of the fusiform gyrus to part of the inferior temporal gyrus. PS: Pain Self; NPS: Non Pain Self; PO: Pain Other; NPO: Non Pain Other. The asterisk indicates the significant difference between groups in the PO condition.

Table 1

Demographic details, participants' characteristics, and behavioral performance on the empathy task in the scanner and outside the scanner. Data are presented as means (SD). Group difference *p*-values refer to two-tailed *t*-tests or chi-square for number of males/females. Due to Site not interacting with any effect of interest, the data are presented for the binge/non-binge drinker groups collapsed across sites; AUDIT: Alcohol Use Disorder Identification Test; BIS: Barratt Impulsiveness Scale; NART: Full scale IQ; Accuracy: % correct responses; RT: reaction time in ms. PS: Pain Self; NPS: Non Pain Self; PO: Pain Other; NPO: Non Pain Other.

Features/measures	Binge (n = 36)	Non-binge (n = 35)	Group difference
Number of males/females	17/19	18/17	$x^2 < 1$, p > 0.1
Age	20.17 (1.13)	20.97 (2.40)	t(48.2) = 1.8; p = 0.08
Age of alcohol drinking onset	14.97 (1.39)	15.34 (1.89)	t(62.2) = 0.94; p > 0.1
Weekly alcohol use in grams	236.77 (147.32)	128.16 (85.36)	t(56.4) = 3.81; p < 0.001
AUDIT total score	15.86 (7.51)	7.20 (4.10)	t(54.5) = 6.06; p < 0.001
Binge score	48.84 (15.82)	10.96 (2.69)	t(37.1) = 14.15; p < 0.001
BIS	68.06 (11.62)	58.83 (10.65)	t(69) = 3.49; p = 0.001
NART	111.56 (3.96)	112.57 (5.55)	t(69) = 0.89; p > 0.1
Empathy Accuracy and RT of responses in the scanner			
Empathy – Accuracy – PS	84.20 (11.74)	84.82 (13.28)	t(69) = 0.21; p > 0.1
Empathy – Accuracy – NPS	94.18 (8.29)	93.39 (6.64)	t(69) = 0.44; p > 0.1
Empathy – Accuracy – PO	83.16 (14.22)	85.71 (13.75)	t(69) = 0.77; p > 0.1
Empathy – Accuracy – NPO	95.75 (4.03)	94.11 (5.51)	t(69) = 1.43; p > 0.1
Empathy – RT – PS	2434.87 (787.34)	1998.39 (777.6)	t(69) = 2.35; p = 0.022
Empathy – RT – NPS	2365.34 (789.89)	1994.18 (814.71)	t(69) = 1.95; p = 0.055
Empathy – RT – PO	2432.73 (761.03)	2070.43 (844.45)	t(69) = 1.90; p = 0.062
Empathy – RT – NPO	2399.31 (770.36)	2030.97 (852.45)	t(69) = 1.91; p = 0.060
Ratings of empathy outside the scanner			
Empathy – Ratings – PS	4.88 (1.18)	4.82 (1.35)	t(68) = 0.19; p > 0.1
Empathy – Ratings – NPS	0.28 (0.79)	0.17 (0.20)	t(68) = 0.82; p > 0.1
Empathy – Ratings – PO	4.81 (1.21)	4.79 (1.21)	t(68) = 0.07; p > 0.1
Empathy – Ratings – NPO	0.17 (0.34)	0.13 (0.14)	t(68) = 0.57; p > 0.1

fMRI task and group effects.

participants' drinking as well as data on IQ and anxiety and a summary of behavioral performance on the task.

3.1.1. Demographics; drinking variables; BIS

There was a trend for a main effect of Site with respect to the age of drinking onset, with participants in France starting to drink alcohol at an earlier age than those in the UK [$F(1, 67) = 3.77$, $p = 0.057$]. The French and UK cohorts did not differ on any other baseline index (i.e. Age, Alcohol grams per week, binge score, AUDIT total and BIS; $F < 2.51$, ns, in all cases)

Regarding binge group characteristics (Table 1), the binge drinkers drank significantly more grams of alcohol per week [$F(1, 67) = 14.32$, $p < 0.001$], had a higher binge score [$F(1, 67) = 188.91$, $p < 0.001$] and a higher AUDIT score than non-binge drinkers [$F(1, 67) = 34.96$, $p < 0.001$]. Audit scores of the binge drinking group confirmed a harmful pattern of alcohol drinking among binge drinkers. There was a general trend for binge drinkers to be younger than non-binge drinkers, but it was not statistically significant [$F(1, 67) = 3.31$, $p = 0.073$].

Finally, binge drinkers had significantly higher scores on all three BIS impulsivity factors compared to the non-binge drinkers [BIS attention: $F(1, 67) = 8.13$, $p < 0.05$; BIS non-planning: $F(1, 67) = 7.51$, $p < 0.05$; BIS motor: $F(1, 67) = 10.67$, $p < 0.05$]. The two binge groups did not differ on any other baseline index (i.e. Age of drinking onset, STAI and NART; $F < 1$, ns, in all cases).

Importantly, there were no differences on any baseline measure between sites and binge groups; all binge-group × site interactions were non-significant ($F < 3.66$, ns, in all cases).

Finally, all groups were well matched in terms of gender and binge/non-binge drinker distributions ($\chi^2 < 1$, ns, in all cases). For additional details on demographics for UK and France separately, see Supplementary Table 1.

3.1.2. Empathy task

Data on the empathy-task behavioral responses are given in Table 1. Analysis of the accuracy data during scanning showed no main effect for Site, and Site did not interact with any effect of theoretical interest ($F < 2.61$, ns, in all cases). In addition, there were no main effects of

perspective or binge-group ($F < 1$, ns, in both cases), nor any pain × perspective, binge × pain, binge × perspective, or binge × pain × perspective interactions ($F < 1$, ns, in all cases). These results suggest that all groups performed equally accurately in all conditions. However, we did find a main effect for pain [$F(1, 67) = 41.37$, $p < 0.001$], with all participants being generally less accurate in the pain compared to the no-pain condition.

Analysis of the in-scanner latency data showed a main effect for Site [$F(1, 67) = 18.38$, $p < 0.001$], with participants in France responding overall faster than those in the UK. Site however, did not interact with any effect of theoretical interest ($F < 3.38$, ns, in all cases). Participants were also overall faster in the no-pain than the pain condition, and in the self than the other condition [Main effects pain $F(1, 67) = 4.64$, $p < 0.05$, and perspective $F(1, 67) = 4.26$, $p < 0.05$]. Furthermore, binge drinkers were generally slower than non-binge drinkers [Main effect binge-group $F(1, 67) = 4.89$, $p < 0.05$]. There were no pain × perspective, binge × pain, or binge × perspective interactions ($F < 1.15$, ns, in all cases). However, we did find a binge × pain × perspective interaction [$F(1, 67) = 6.24$, $p < 0.05$]. Post hoc analyses showed that the non-binge drinkers did not respond differently between levels of pain and perspective [pain × perspective interaction in the non-binger group $F(1, 33) = 2.29$, $p > 0.05$]. By contrast, we found a significant pain × perspective interaction in binge drinkers [$F(1, 34) = 4.72$, $p < 0.05$]. Examination of the mean response time suggests overall slower responses of binge drinkers in the no-pain-other condition compared to the no-pain-self condition [$t(35 = 2.51$, $p = 0.017$]. However, no post-hoc *t*-test survived Bonferroni correction [pain self vs no pain self t = 2.19, p = 0.035; pain other vs no pain other t = 1.34, p = 0.19; pain self vs pain other t < 1, ns].

Finally, as expected, all participants gave a higher perceived-pain rating to pain than to no-pain images [Main effect for pain $F(1, 66) = 995.69$, $p < 0.001$]. No other effect of interest met criterion significance ($F < 1.24$, ns, in all cases). However, we did find a main effect of site [$F(1, 66) = 5.69$, $p < 0.05$], as participants in France gave overall higher ratings to the pictures, than did participants in the UK. Site did not interact with any effect of theoretical interest.

In the UK sample who gave post-scan subjective ratings of how successful they had been in adopting the perspectives of self and other during the in-scanner task, participants were significantly more likely to report being successful at adopting the perspective of self (mean rating: 7.83/10) than other [mean rating: 6.27/10] (t(29) = 4.379, p < 0.001]. There was a main effect of perspective [F (1, 28) = 18.79, p < 0.001)] but no effect of group [F (1, 28) = 2.48, p = 1.30], or a group by perspective interaction [F (1, 28) = 0.42, p = 0.52].

3.2. fMRI results

3.2.1. fMRI tasks and group effects

The F-contrast for all effects ('eye') identified canonical pain processing regions, including bilateral anterior insula, anterior midcingulate cortex (aMCC; extending superiorly to preSMA), and secondary somatosensory cortices (Supplementary Table 2A). This 'all effects' F-contrast also revealed task engagement of early visual cortices, fusiform gyrus, superior temporal sulcus, posterior insula, and premotor cortex.

The F-contrast for pain effects (PS & PO versus NPS & NPO) was significant. Post-hoc t-tests revealed effects for both PAIN > NO PAIN and NO PAIN > PAIN (Supplementary Table 2B–D). The PAIN > NO PAIN contrast revealed canonical pain processing regions, including bilateral anterior insula, aMCC (extending superiorly to preSMA), and secondary somatosensory cortices, as well as premotor cortex and inferior frontal gyrus (Fig. 2, Supplementary Fig. 3). The contrast estimate plots at the peak anterior insula and aMCC co-ordinates of PAIN > NO PAIN generally reflect the elevated activity evoked when viewing stimuli representing pain, versus stimuli representing no pain. The NO PAIN > PAIN contrast revealed early visual cortices, posterior parietal cortex, posterior cingulate cortex, superior temporal sulcus, posterior insula, and premotor cortex.

The F-contrast for self/other effects (PS & NPS versus PO & NPO) was not significant.

Among group effects, the binge versus non-binge F-contrast for other (binge PO & NPO versus non-binge PO & NPO) was significant, revealing engagement of a temporal cortical region implicated in body representation; the fusiform body area (FBA), which is associated with the visual perception of body parts [(Ewbank et al., 2011); Supplementary Table 2E]. However, t-tests to determine the direction of the effect did not meet criterion significance.

Within the specific conditions, there were significant group effects in the PO trials (binge PO versus non-binge PO), with post-hoc t-tests confirming greater activity in the FBA in the binge group (binge PO > non-binge PO) (Fig. 3, Supplementary Table 2F–G). The reverse contrast of non-binge PO > binge PO was not significant.

Appraisal of Fig. 3 indicates a general elevation of activity in this region across all task conditions within the binge drinkers; however, this only reaches threshold significance versus non-binge drinkers (p < 0.05 FDRc) in the PO condition.

The interaction between binge status and pain was not significant.

3.2.2. Trait impulsivity (BIS score)

None of the t-contrasts testing for positive and negative correlations of BIS scores with task effects (PS, NPS, PO, NPO) was significant.

3.2.3. Age of alcohol drinking onset

Neither of the t-contrasts testing for positive and negative correlations of age of alcohol drinking onset with PO trials in the binge group were significant.

3.2.4. Behavioural and brain differences in reaction time and pain intensity

In the statistical model testing for a correlation of PS > NPS and

reaction time in the binge group, the higher the difference in neural activation between the two trial types in aMCC, inferior frontal gyrus, and premotor cortex, the greater the difference in reaction time (Fig. 4a, Supplementary Table 2). Furthermore, in the model testing for a correlation of PS > NPS and pain intensity rating in the non-binge group, the higher the difference in neural activation between the two trial types in posterior superior parietal lobule, the greater the difference in pain intensity rating (Fig. 4b, Supplementary Table 2). Finally, in the model testing for a correlation of PO > NPO and reaction time in the non-binge group, the higher the difference in neural activation between the two trial types in a number of visual areas, including the FBA, the greater the difference in reaction time (Fig. 4c, Supplementary Table 2).

None of the remaining t-contrasts testing for positive and negative correlations of reaction time and pain intensity rating with PS > NPS or PO > NPO were significant.

4. Discussion

This study aimed to evoke empathic reactions through presentation of images depicting pain and no pain scenes, in order to compare empathy-related behavioral and neural responses between binge and non-binge drinkers. The viewing of painful images successfully activated pain-related areas, without any actual physical pain being administered. Activated regions included somatosensory cortex, aMCC (extending superiorly to preSMA) and insula, areas identified in previous research as components of a 'pain matrix', supporting the perception and the affective experience of pain (Jackson et al., 2006a; Lamm et al., 2011; Ogino et al., 2007).

Activation of somatosensory cortex when observing stimuli depicting the delivery of pain to different body area is suggested to represent the brain substrate of pain perception and its location on the body (Xiang et al., 2018). In parallel, anterior insula and aMCC are implicated in mediating the affective-motivational components of pain processing as reported by Jackson et al. (2006a) and subsequently confirmed in a *meta*-analysis report of 32 such studies (Lamm et al., 2011). This view is further supported by the findings of the present study of a greater activation in the pain vs. no pain condition in aMCC, spreading superiorly into preSMA. This finding is coherent with the view that one function of this region is to support motivated imagery action, such as withdrawal of limbs from a nociceptive stimulus (e.g., Nachev et al., 2007; Qiu et al., 2006).

The central aim of the present study was to identify differences in empathic behavioral and brain responses between binge drinkers and non-binge drinkers among young adult social drinkers. As expected, the condition that produced a significant difference between groups was perception of pain from the perspective of another person ('pain other' contrast). In this condition, activations were higher in binge drinkers compared to non-binge drinkers within fusiform gyrus (notably in a specific sub-region, the Fusiform Body Area; FBA). The cluster that showed a higher activation in binge drinkers spanned the fusiform and inferior temporal gyri. Confirmation that this cluster encompassed the FBA was possible through direct reference to Ewbank and colleagues study (Ewbank et al., 2011). In that seminal study, peak FBA co-ordinates were x44, y-46 and z-18, while in our study peak cluster co-orindates were x40, y-66 and z-18, indicating that the cluster we identified overlapped topographically, yet was marginally posterior in position in the sagittal and axial planes.

Activation of the fusiform gyrus was previously identified when pain is both directly experienced, and when observing another experiencing pain (Singer et al., 2004). Fusiform activation also occurs when viewing painful facial expressions (Botvinick et al., 2005) and images depicting fear (Hadjikhani and de Gelder, 2003). Although neuroimaging activation in fusiform gyrus is perhaps most commonly identified within the proposed 'Fusiform Face Area' (FFA), the apparent modular organization also extends to visual representations across adjacent
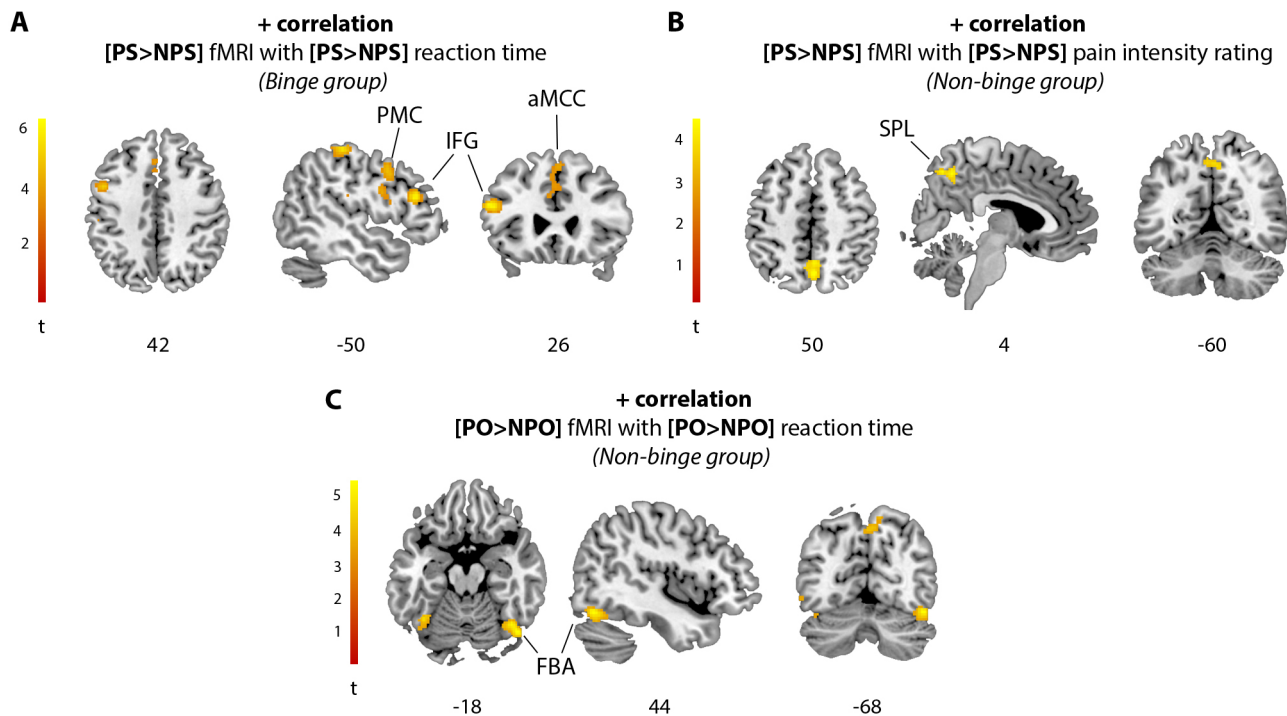
Fig. 4. Correlations with task-related neural activity A) Positive correlation between PS > NPS and reaction time in binge group, (B) Positive correlation between PS > NPS and pain intensity rating in non-binge group, (C) Positive correlation between PO > NPO and reaction time in non-binge group. PMC = premotor cortex, IFG = inferior frontal gyrus, aMCC = anterior midcingulate cortex, SPL = superior parietal lobule, FBA = fusiform body area.

fusiform areas, including a region seeming specific to body areas only (Schwarzlose et al., 2005). This Fusiform Body Area (FBA) overlaps with, but is separated from, the FFA (Peelen et al., 2006). Interestingly, binge drinkers compared to non-binge drinkers showed higher activation in this region during only the 'pain other' condition, suggesting that the processing of pain perceived in others requires more energy demanding computation for binge drinkers than it does for non-binge drinkers; this computation involves integrating pain perception, somatic location and body ownership with relevance to social emotional behaviors.

The neural areas, aMCC and insula, which support the affective experience of pain (e.g., Jackson et al., 2006b; Xiang et al., 2018), did not in fact show a supra-threshold difference in activation between groups. Moreover, aMCC and insula were not hyper-reactive to perceived pain in others relative to self, contrary to previous research, (Jackson et al., 2006a; Lamm et al., 2007; Singer et al., 2004). Methodological differences in testing empathy may perhaps have played a role. Singer et al.'s (2004) research design tested participants who actually observed cues indicating the real-time delivery of inflicted pain upon the visible hand of their partner. In contrast, the study by Jackson et al. (2006a,b) and our current study asked participants to adopt the perspective of another person experiencing the pain while viewing static images. It could be that in our case the perspective self versus other may not have been reliably or successfully adopted by the participants. However, no difference was found between the two groups regarding their ratings of how successfully they adopted the self versus the other perspectives; all participants tested reported that they were more successful in adopting the perspective of self than that of other. Note, however, that these data were obtained only from the UK subgroup. Nevertheless, binge drinkers showed, increased activation during the 'pain for other' condition when compared to non-binge drinkers, albeit in an area within the fusiform gyrus and not in more classic affective pain regions (aMCC and insula). It is also worth noting, that inspection of the distribution of activations in both the insula and, in particular, aMCC (extending superiorly to preSMA) indicated overall higher activations in binge drinkers compared to non-binge drinkers.

Future studies would benefit from use of experimental procedures that might include stronger challenges to empathic responses than we included here. Such an approach may reveal significant differences in reactivity of affective pain regions between binge drinkers and non-binge drinkers.

The greater activations seen in the FBA in binge drinkers (compared to non-binge drinkers) in the pain other condition is intriguing. We argue that it may represent a compensatory mechanism for impairments in the processing of emotional stimuli that have previously been described in AUD and binge drinkers. For instance, Philippot and colleagues proposed a visuospatial cognitive deficit as a cause of the impaired decoding and judgement of emotional information (facial emotion recognition) in AUD. Stephens and colleagues (1995) reported that binge drinkers show difficulties in discriminating a stimulus that predicts fear from a stimulus that is safe. Both reports indicate a deficit in perception / attention related decoding within an emotional context that is related to alcohol use. Patients with AUD show also greater activity in temporal cortices, including the fusiform gyrus, compared to controls, in response to negative images (Gilman and Hommer, 2008). Interestingly, higher activation is also found in the FBA in response to viewing body images of one's own body compared to viewing images of another person's body (although emotional challenge was not involved) (Vocks et al., 2010), indicating that these perspectives (self vs other) demand different degrees of engagement of this region.

We hypothesize that the level of recruitment demand may be even greater for binge drinkers, compared to non-binge drinkers. Activations of the FBA in binge drinkers compared to non-binge drinkers, during the 'pain other' condition, therefore could suggests hyper-responsiveness of the cortical visual representation of the body, in the context of a representation of negative valence event experienced by others. This suggestion is further supported by the fact that all participants were overall faster (responding to whether a picture depicts pain or no pain), in the self than the other condition, probably due to higher demand in processing the other than the self perspective generally. Furthermore binge drinkers who were generally slower than non-binge drinkers, presented also with slower responses (p = 0.062) in the Pain-Other

condition, supporting the higher demand for that response in binge drinkers. In addition, we were motivated to propose the existence of such a compensatory mechanism in view of recent findings: The severity of binge drinking predicts enhanced activation of brain areas including the lateral occipital cortex and angular gyrus during successful response inhibition in a Stop Signal Task within a negative emotional context (Herman et al., 2018). These data were interpreted as revealing a compensatory mechanism engaged by the extra cognitive and emotional requirements associated with processing challenging aspects of the task, which further increase as level of binge drinking increases in severity.

Previous research showed that binge drinking is associated with reduced subjective ratings of empathy (e.g. Laghi et al., 2019; Lannoy et al., 2020). To our knowledge, there are no previous studies addressing such empathy responses in binge drinking using behavioral measures. Interestingly, and despite their higher impulsiveness, binge drinkers compared to non-binge drinkers showed a tendency to take longer to respond if the picture portrayed pain, in self and other conditions, suggesting a general difference in processing perceived pain. It is a limitation of the current study that subjective ratings of empathy were not taken to replicate the findings from the previous studies in which empathy characteristics in subjective ratings were compared between bingers and non-bingers. In the present study, we aimed to further support these findings by examining differences between binge drinkers and non-binge drinkers using objective behavioral measures of empathy and examining their brain substrates.

Our study tested for a possible role of impulsivity in such empathic responses, yet we revealed no significant relationship between impulsivity ratings and brain activations under any of the empathic conditions. Furthermore, we tested for a possible role of age of alcohol drinking onset and activity on PO trials, since drinking at an earlier age might predict greater dysfunction in processing the pain of others, and thereby the degree of FBA activation. However, there were no significant relationships identified.

Regarding correlations between brain activity and behavioral indices, binge drinkers showed positive correlations between changes in neural activity in MCC, Inferior frontal gyrus and premotor cortex and reaction time taken to process the stimulus (in self pain versus no pain conditions). These data suggest that the processing of pain versus no pain in binge drinkers concurrently activates parts of the pain matrix and substrates for emotional processing as well as areas supporting motor action. These relationships were only seen in the self and not the other perspective, which may indicate that binge drinkers find it easier to adopt the self perspective. On the other hand, non-binge drinkers showed positive associations between changes in pain intensity ratings during the self pain versus no pain condition and changes in activation in parietal cortex. an area putatively contributing to self vs. other distinction; such a relationship was not seen in the binge drinkers.

Interestingly, in non-binge drinkers, reaction time changes when perceiving pain versus no pain during the other perspective condition correlated positively with changes in FBA activation. This finding indicates that efficient social empathic responses in non-binge drinkers are coupled to the engagement of a neural substrate for body representation that participates in processes requiring between self versus other distinction.

The present study across both European countries studied (UK and France) identified differences between binge and non-binge drinkers in brain activation within areas associated with pain perception and its location on the body. These differences were most pronounced in a condition that requires empathic response (pain experienced by other), indicating a greater failure in this type of pain processing in binge drinkers. Importantly, relevant differences were not observed between the cohorts from the UK and France. Binge drinkers compared to non-binge drinkers also showed prolonged responses in identifying a picture depicting pain or no-pain; prolonged responses in binge drinkers were found also between other and self condition, which, in conjunction with

the brain activation seen in pain processing areas in binge drinkers, allow us to infer the presence of compensatory mechanisms required by binge drinkers to process pain of other people, indicating a specific failure in empathy. This is the first study, to our knowledge, that compared brain and behavioral responses between young adult social drinkers that binge drink with those that do not. Also, to our knowledge this is the first study to test for differences in empathy between binge drinkers and non-binge drinkers from two countries with different cultures. With the assumption that empathy is important for optimal social functioning, not least to understand and respond to the needs of others (Eisenberg, 2000; Mitchell, 2009) it follows logically that interventions to improve empathic responses and increase sensitivity to the perception of negative experiences of both self and others may improve self control during a drinking session and mitigate to repeated binges. It is of particular interest to the current study that the recent findings by Laghi and colleagues (Laghi et al., 2019) show that high ratings of empathic concerns are negative predictors of binge drinking in adolescents. Thus, the targetted strengthening of empathic skills could be proved to be beneficial as a prevention strategy for binge drinking and other expression of alcohol abuse.

Thus, in summary, our findings partly support and refine previous observations that binge drinkers, compared to non-binge drinkers, exhibit differential behavioral responses to empathy for pain. Furthermore, our findings demonstrate, for the first time, differential brain responses to empathy for pain between these two groups of social drinkers. The current findings highlight the importance of empathic responses in the control of binge drinking. Importantly these findings may inform prevention and treatment strategies for AUD.

CRediT authorship contribution statement

TD, MN, and HDC conceptualized, designed and supervised the study. KWS and FG contributed significantly to the design of the study, carried out the investigation and, collected and analysed the UK and France data respectively. FG also contributed to the formal analysis. CR and KN analyzed the combined data set and provided a detailed summary of the findings. TD, CR and KN interpreted the findings and drafted the manuscript. All remaining authors provided critical revisions of the manuscript for important intellectual content.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nicl.2020.102322.

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