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# Emotional memory bias in binge drinking women

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Keywords:
Binge drinking
Alcohol
Bias
Emotion
Emotional memory

#### ABSTRACT

Background: Heightened emotionality and overrepresentation of memories are typical features of adolescence. Binge drinking (BD) during emerging adulthood has been linked to cognitive difficulties such as deficits in episodic memory. Despite that impairments in emotional functioning have been associated with the development of alcohol use disorders, particularly in females, the emotional sphere has been relatively unexplored in BDs. Therefore, the purpose of this study is to examine the effects of BD in emotional episodic memory from a gender perspective.

*Methods*: One hundred and eighty (96 females) university students were followed during two years (18–20 years old) and their alcohol use was recorded. In the last assessment, participants completed an emotional list-learning task. Generalized linear mixed models were applied separately for males and females, in accordance with sex differences in the development of emotion circuitry.

Results: In females, BD was associated with an emotional memory bias in favour of negative information and lower recall of positive and neutral words. In addition, females BDs showed more false alarms for negative distractors. Whereas in males, no alcohol-related effects were found.

Conclusions: Female BDs present a negative memory bias, poor learning and delayed episodic recall linked to the interference of negative content, which suggests difficulties in disengaging attention to salient negative stimuli and a reduction of inhibitory capacities. This might result in greater vulnerability to alcohol-related emotional disturbances among women. Further research is needed to understand the role of emotional regulation in the escalation of alcohol abuse from a gender perspective.

# 1. Introduction

Adolescence and young adulthood represent "the roller-coaster years": a tumultuous period characterized by risky behaviour and heightened emotional reactivity (Ahmed et al., 2015). These stereotypical behaviours are accompanied by significant emotional and cognitive development driven by asynchronous neuromaturational trajectories (Blakemore, 2008). Indeed, the imbalance between cortical and subcortical circuitry (e.g. subcortical regions such as the amygdala reach maturity much earlier than the prefrontal cortex) contributes to the emergence of mood disorders and substance abuse during adolescence (Fuhrmann et al., 2015). At the same time, this relative immaturity seems to involve greater vulnerability- in comparison to adulthood- to disruptive events in the brain such as binge drinking (BD) (Silveri et al., 2016). This pattern of repeated intoxications is usually defined as the consumption of a large amount of alcohol within a short

period of time, leading to a blood alcohol concentration of at least 0.8 g/l (National Institute of Alcohol Abuse, Alcoholism, 2004). BD peaks during late adolescence (Merrill and Carey, 2016), considering adolescence as the period ranging from age 10–24 years (Sawyer et al., 2018). It is particularly prevalent among young people –one in three young Europeans and North Americans engage in frequent BD (Kraus et al., 2016; Substance Abuse and Mental Health Services Administration (SAMHSA), 2020).

Over the last decade, an increasing number of studies have shown that BD is associated with neuroanatomical alterations (e.g. lower volume in prefrontal and hippocampal regions) accompanied by neuropsychological deficits such as difficulties in inhibitory control and verbal episodic memory, particularly in consolidation processes (Carbia et al., 2018; Silveri et al., 2016). Although the effects of BD in cold cognition have been thoroughly investigated, emotional functioning –on the contrary- has been relatively unexplored. This gap is somewhat

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surprising since emotional and social disturbances play a crucial role in the escalation of alcohol use (Hardee et al., 2017a; Koob and Volkow, 2016; Zhang and Volkow, 2019). Patients with alcohol use disorders (AUDs) display deficits in the interpretation of emotional intonations, the attribution of mental states to others (theory of mind) and the recognition of emotions from facial expressions (e.g. decoding and overestimation of negative emotions) (Bora and Zorlu, 2017; Oscar-Berman and Bowirrat, 2005). Such deficits have been linked to interpersonal difficulties, emotional dysregulation and increased alcohol consumption and may be an underlying factor leading to the development and maintenance of AUD (Sawyer et al., 2019). Preliminary findings in BDs, suggest difficulties in decoding emotions and -more specifically- in processing negative stimuli (Connell et al., 2015; Lannoy et al., 2018, 2019; Maurage et al., 2013).

Despite marked sex differences in brain growth trajectories during adolescence (Hardee et al., 2017b), sex-related differences are another poorly studied aspect. In fact, more than one third of the neuropsychological studies in BDs have not analyzed sex-dependent effects (e.g. no mention of sex as a covariable; Carbia et al., 2018). In addition, there is substantial evidence for sex differences in the vulnerability to alcohol addiction, with internalizing factors such as emotional disturbances (i.e. negative reinforcement; Koob and Volkow, 2016) contributing more to female risk (Hardee et al., 2017a, b). Thus, the effects of BD in emotional functioning, from a gender perspective, deserve further attention.

In this sense, we were interested in investigating -for the first timethe association between BD and emotional memory. During adolescence and young adulthood, individuals tend to form strong longlasting memories, and this is especially true for emotional memories. Events that occurred throughout this period of life are remarkably overrepresented in memory (i.e. reminiscence bump), suggesting a sensitive period for mnemonic capacity (Fuhrmann et al., 2015). Emotional episodic memory involves the ability to learn, store, and retrieve information about events or experiences with emotional significance (LaBar and Cabeza, 2006). The formation of new emotional memories has been consistently linked to brain regions undergoing profound neuromaturational changes during adolescence including the bilateral amygdala, anterior hippocampus and prefrontal cortex (PFC) (Murty et al., 2010). In particular, the amygdala and the hippocampus follow sexually dimorphic developmental trajectories (Fish et al., 2019). Considering both that excessive alcohol use has been found to disrupt these structures (Ewing et al., 2014; Oscar-Berman and Bowirrat, 2005) and that emotional memory plays a critical role in life (biased recollection guiding future thinking, self-referential processing, etc.), the aim of this study was to explore potential emotional memory biases in BDs. In order to ensure the stability of alcohol use patterns, we followed university students during two years (18-20 years old) and, at the end of the follow-up, we assessed their performance in an emotional listlearning paradigm. Given that this is the first study to examine emotional memory in alcohol use, our a priori hypothesis is based on both the (I) results from emotional deficits (across different paradigms; Bora and Zorlu, 2017) found in alcoholics and BDs and the (II) expected performance in this type of task in other populations (Durand et al., 2019). We hypothesize that BDs -especially females- will display an emotional memory bias for salient negative stimuli. As emotional memory biases tend to increase with time (after post-encoding process), we predict greater negative bias in delayed recall due to an amplification effect in the consolidation process.

# 2. Material and methods

### 2.1. Participants

A total of 180 (84 males and 96 females) healthy college students (part of a larger cohort) were followed during two years (18–20 years old) and their alcohol consumption and other drug use was recorded.

The individuals gave their written informed consent and received monetary compensation for participation. This study was approved by the Bioethics Committee of the Universidade de Santiago de Compostela, according to the principles expressed in the Declaration of Helsinki.

#### 2.2. General procedure

In this prospective study we recruited first-year university students through an anonymous questionnaire administered in the classroom, including the Alcohol Use Disorders Identification Test (AUDIT) (Babor et al., 2001) and other questions about substance use and health-related behaviours. All participants who were 18 years old, did not report having consumed any illegal drug in the last 6 months and showed their interest in collaborating by providing a contact method (phone or email) were invited to participate in the study. In order to select a sample of healthy college students, students who accepted to participate underwent a screening interview and the following exclusion criteria were applied: history of neurological disorders or severe conditions that affect neurocognitive functioning; history of major psychiatric disorders including alcohol use disorders; current psychopathological symptoms as assessed by the Symptom Checklist-90-R (SCL-90-R) (Degoratis, 1983; Spanish version González de Rivera et al., 1989). Participants were excluded if they had scores above 90th in the Global Severity Index (GSI); presented motor or sensory deficits; reported regular consumption of psychoactive medications; had family history of alcoholism (two or more first degree relatives or three or more first/second degree relatives); or family history of psychopathology (i.e. major psychopathological disorder such as depression, anxiety or schizophrenia diagnoses in first degree relatives).

One hundred and eighty participants completed the two years follow-up. More details regarding sample attrition can be found in supplementary material. First, they underwent a baseline evaluation in which information regarding their alcohol consumption patterns was recorded. In particular, we administered the AUDIT and an alcohol consumption calendar comprising 180 days prior to the evaluation (Alcohol Timeline Followback [TLFB], Sobell and Sobell, 1995). A binge drinking episode was defined as 4/6 standard drinks (or more) for females and males respectively (National Institute on Alcohol Abuse and Alcoholism (NIAAA), 2004: in Spain a standard drink contains 10 g of alcohol). In addition, participants also completed a cannabis consumption calendar (TLFB) comprising 90 days prior to the evaluation. Two years later, the same participants underwent a follow-up in which a neuropsychological assessment was performed and again their alcohol consumption and drug use as well as psychopathological symptoms were recorded (Global Severity Index [GSI], Brief Symptom Inventory [BSI-18], Derogatis, 2001; Spanish version, Andreu et al., 2008).

# 2.3. Material

During the follow-up assessment, participants completed a list-learning task based on the Emotional Verbal Learning Test (EVLT) (Strauss and Allen, 2013). Apart from yielding traditional memory scores, this task allows for an evaluation of the preferential processing of specific emotional content. The task consists of remembering a list of 18 words (List A), composed by six emotional words from three emotional categories (neutral, positive and negative). These words are read out loud in three consecutive trials. After each trial the subject is asked to recall as many of the words as possible. An interference list (List B) was then presented and free-recall tested (18 new words neutral, positive and negative). The subject was then again asked to recall the words on list A without these words having been presented a second

<sup>&</sup>lt;sup>1</sup> Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi...

time (Trial IV). After 30 min, subjects were asked for their free recall of list A (Trial V) and list B and were then given a recognition task, consisting of a list of 60 words formed by the words from List A, the words from List B and phonologically or semantically similar words (distractors). Participants had to indicate if a word was from list A, list B or none of them (recognition memory trial). The characteristics of the task (long-term recall of both lists, increased numbers of words in comparison with the RAVLT [Rey, 1964], etc.) make it particularly suitable -in terms of avoiding ceiling effects- for episodic memory characterization in preclinical and normal populations (Hale et al., 2017).

Several variables were recorded: the number of words in learning trials (I-III), the immediate recall of list A (IV, immediate recall); the number of words recalled after a 30 min delay (V), as well as immediate and delayed free recall of list B. In addition, the number of words by emotion category was registered separately for each variable. An emotional bias score was calculated (negative minus neutral; positive minus neutral and negative minus positive). Total intrusions (words that are not part of the list that is being considered at that moment) were recorded. In the recognition trial, number of correct responses and false alarms for list A and B were recorded.

Words were drawn from the Spanish adaptation of Affective Norms for English Words (Redondo et al., 2007). Statistical analysis were performed to control for the three basic underlying dimensions of emotion (valence, arousal, dominance) and ensure equal values for objective, subjective and psycholinguistic indexes: number of letters, number of syllables, frequency, number of orthographic neighbours, familiarity and imageability. More details about the task can be found in the supplementary material<sup>2</sup>.

#### 2.4. Statistical analysis

The data were analyzed using generalized linear mixed models (GLMMs) implemented in SPSS Statistics Base 22.0 Software - with confidence intervals (CI) of 95 %. These models enable analysis of repeated measurements while controlling for correlated errors of measurement and individual heterogeneity, and they provide greater statistical power than ordinary regression models (Gibbons et al., 2010). The main independent variable was number of BD episodes from the TLFB (past 180 days) over time (baseline and follow-up). The dependent variables were the neuropsychological scores in the emotional memory task. The neuropsychological analyses were carried out separately for males and females, in accordance with sex differences in the development of emotion circuitry in adolescents. The models were fitted with the negative binomial distribution for the variable intrusions to obtain standard errors corrected for the overdispersion parameter. The models were adjusted by cannabis use (TLFB baseline and followup), tobacco use and psychopathology (GSI index of the BSI-18). We first performed a bivariate analysis with these covariates. We then carried out a multivariate analysis in which we included all those independent variables which had yielded a statistical significance lower than 0.2. The nonsignificant independent variables were eliminated from this maximum model when the coefficients of the main exposure variables did not vary by more than 10 % and the value of Akaike Information Criterion (AIC) decreased. Graphs were created using GraphPad Prism software.

# 3. Results

# 3.1. Sample characteristics

Sociodemographic and clinical variables for the first and second evaluation can be found in Table 1. Males and females did not show

statistical differences in any of the sociodemographical and clinical variables in the two evaluations, with the exception of tobacco use at baseline,  $X^2$  (1) = 5.99, p = .014; and follow-up,  $X^2$  (1) = 4.11, p = .043 and GSI score (BSI-18) at follow-up, t(174) = 2.38, p = .018. In particular, females showed higher scores in the GSI index and greater tobacco use. Fig. 1 and Fig. 2 depict the number of binge drinking episodes and general alcohol consumption (AUDIT-C) for both sexes at baseline and follow-up.

# 3.2. Emotional episodic memory

Means and standard deviations for neuropsychological performance by sex are shown in Table 2. In females, a higher number of BD episodes was associated with lower recall of neutral, b = -0.02, SE = 0.01, p =.022, 95 % CI [-0.03, -0.003] and positive words, b = -0.02, SE = 0.01, p = .030, 95 % CI [-0.04, -0.002] in learning trials (I-III). The maincoefficient (relative risk [RR]) represents the increase that occurs in the dependent variable in relation to any increase in the independent variable. In this case, there is a decrease of 0.33 % in total recall by each new episode of BD. Considering the mean of BD episodes in the TLFB at follow-up (17.13 [SD = 16.89] for females), there was an average risk of 6 % that goes up to 25 % of learning difficulties. There were no alcohol-related effects for total list B and immediate recall of list A (IV). However, in delayed recall female BDs showed lower recall of delayed list A (V) for neutral words b = -0.01, SE = 0.00, p = .028, 95 % CI [-0.010, -0.001]. It represents an increase of 0.16 % in the risk of presenting deficits by each new episode of BD and a maximum risk up to 12 %. With regard to recognition, females with higher number of BD episodes showed more total false alarms for negative distractors b =0.03, SE = 0.004, p = .048, 95 % CI [0.000, 0.016]. The other covariables in the models were not significantly associated with performance.

Regarding the emotional bias, female BDs showed a greater recall of negative words (versus neutral) in trials I-III, b=0.02, SE = 0.01, p=0.01, 95 % CI [0.004, 0.044]. The increase of this negative bias (i.e. remembering more negative information) by each new episode of BD was 0.18 %, with an average risk of 3 % that range up to 14 %. In addition, female BDs recalled more negative (versus positive) words in learning trials (I-III), b=0.03, SE = 0.01, p=0.021, 95 % CI [0.004, 0.050], a risk of bias up to 21 %. The effects in delayed recall were similar. Female BDs presented a greater recall of negative words (versus neutral) in delayed recall of List A (V), b=0.01, SE = 0.01, p=0.03, 95 % CI [0.001, 0.022], which represents an average risk of bias up to 7% in the present sample.

In males, there were no effects on task performance associated with alcohol consumption. However, males with a higher consumption of cannabis showed greater number of intrusions in the task, b=0.12, SE = 0.01, p<0.01, 95 % CI [0.096, 0.150].

Finally, we also performed Pearson's correlations to further analyse the relationship between emotional memory and binge drinking; specifically we used maximum drinks per occasion as an index of losing control over drinking episodes. In females, a higher number of drinks per occasion showed a positive association with false alarms for negative distractors (words from list A or B that were incorrectly identified as distractors), (r = 335, p < .001). Regarding males, no associations were found.

# 4. Discussion

This is the first study to examine the relationship between emotional memory and BD trajectory during adolescence. One-hundred eighty university students (53 % females) –with no other risk factors- were followed during two years (18–20 years old) to better capture the stability of drinking patterns. At the end of the follow-up, participants completed an emotional memory task. Results revealed an augmented negative bias and difficulties in episodic memory linked to the

<sup>&</sup>lt;sup>2</sup> Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi...

Table 1
Mean values (and standard deviations) for demographical and clinical data at baseline and follow-up.

	Baseline		Follow-up	
	Males (N = 84)	Females (N = 96)	Males $(N = 84)$	Females (N = 96)
Age	18.02 (0.18)	18.00 (0.00)	19.89 (0.32)	19.93 (0.25)
AUDIT Total	6.33 (5.10)	6.45 (5.70)	6.36 (4.81)	6.15 (5.31)
AUDIT-C	3.87 (2.70)	3.74 (2.67)	3.95 (2.64)	3.63 (2.45)
Age of drinking onset	15.70 (1.26)	15.71 (1.23)		
Maximum drinks <sup>a,b</sup>	12.17 (8.37)	10.17 (7.38)	10.32 (6.59)	8.98 (6.74)
Number of BD episodes <sup>a</sup>	13.14 (13.90)	16.96 (17.10)	14.52 (14.72)	17.13 (16.89)
Number of cannabis days <sup>c</sup>	3.90 (11.55)	12.39 (18.19)	5.65 (15.20)	18.51 (21.69)
Tobacco smokers*	6	19	15	31
GSI (SCL90-R)	51.73 (24.82)	53.02 (25.78)		
GSI (BSI-18)*			0.40 (0.31)	0.53 (0.39)

<sup>&</sup>lt;sup>a</sup> Timeline Follow Back (TLFB) alcohol 180 days.

<sup>\*</sup> P ≤ 0.05 GSI = Global Severity Index.

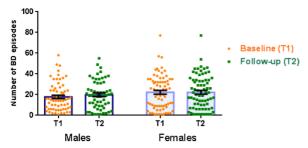


Fig. 1. Number of BD episodes in 180 days prior to the evaluation using the Alcohol Timeline Followback (TLFB).

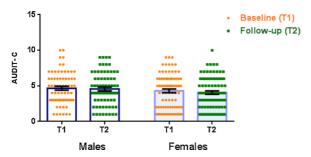


Fig. 2. The AUDIT-C comprises the first 3 questions of the AUDIT.

**Table 2**Means (and standard deviations) for emotional memory performance.

	Males $(n = 84)$	Females $(n = 96)$
Total list A (I-III)	36.20 (5.47)	38.80 (4.54)
Neutral	12.18 (2.70)	13.13 (1.91)
Positive	11.37 (2.30)	12.41 (2.32)
Negative	12.65 (2.35)	13.26 (2.15)
Total List B	8.25 (2.34)	8.88 (2.26)
Immediate List A (IV)	12.24 (2.59)	13.24 (2.59)
Neutral	4.53 (1.30)	4.80 (1.11)
Positive	3.81 (1.20)	4.39 (1.24)
Negative	3.90 (1.32)	4.04 (1.18)
Delayed List A (V)	12.40 (2.60)	13.57 (2.52)
Neutral	4.57 (1.23)	4.85 (0.98)
Positive	3.84 (1.20)	4.43 (1.18)
Negative	3.99 (1.32)	4.29 (1.17)
Delayed list B	4.47 (2.60)	5.45 (2.58)
Recognition list A	15.51 (2.17)	16.14 (1.67)
Intrusions	2.58 (2.72)	2.42 (2.48)
False alarms	12.58 (5.40)	10.56 (4.68)

interference of negative content in female BDs -but not in males. In learning trials, females with more BD episodes showed a negative bias, that is, a greater recall of negative words (versus positive and neutral). As expected, female BDs recalled more negative words (than neutral) in delayed trials, reflecting a time-dependent effect as the gradual process of consolidation proceed. This bias in favour of negative information comes at the cost of difficulties in encoding and consolidation of information of positive and, especially, of neutral items. Interestingly, BD in females was also associated with more false alarms for negative distractors, which positively correlated with increased loss of control over drinking (i.e. a greater number of drinks per episode). Errors in source attribution for negative items might occur due to activation of mood-congruent schemas that interfere and affect source memory decisions, reinforcing negative biases (Besken and Gülgöz, 2008; Bogie et al., 2019).

Studies of episodic emotional memory show that the PFC and mediotemporal lobe (MTL) memory system and the amygdala- through activation of neurohormonal systems- act conjointly to promote the retention and retrieval of emotionally arousing events (LaBar and Cabeza, 2006). The observed results parallel findings in emotional memory bias in other populations (post-traumatic stress [Durand et al., 2019] and depression [Bogie et al., 2019]). This bias could be interpreted as difficulties in disengaging attention to salient negative stimuli and a reduction of inhibition capacities (Durand et al., 2019). In this vein, neuroimaging studies have shown that AUD severity in adolescents is related to hyper-responsiveness of the amygdala to negative stimuli that partially stems from decreased inhibitory control by prefrontal regions (Aloi et al., 2018). Similarly, Cohen-Gilbert et al. (2017) observed an interference of negative emotional content in cognitive control in young BDs. Alcohol-related impairments in executive functions seem to contribute to the dysregulation of the extended amygdala (Hu et al., 2018; Zhang and Volkow, 2019) and this may promote a negative emotional state (or allostatic state) difficult to be inhibited at later stages of the addiction cycle (Koob and Volkow, 2016). Previous studies have found that alcoholics overestimated the intensity of emotional facial expressions, especially for fear (Townshend and Duka, 2003), showing a tendency to exaggerate emotions that may be related to a disinhibitory effect of long-term alcohol use (Oscar-Berman and Bowirrat, 2005). Although inconsistencies in the literature exists, several studies in young BDs have also suggested a specific difficulty for the processing of negative stimuli (Connell et al., 2015; Lannoy et al., 2018, 2019; Maurage et al., 2013). For example, Lannoy et al., 2019 administered an emotional recognition task and observed a reduced performance in the recognition of fear and sadness in young BDs, in line with amygdala dysfunctions observed in this population (Stephens and Duka, 2008).

Considering that maturational changes during early adolescence are

<sup>&</sup>lt;sup>b</sup> Measure as maximum number of standard drink units on a drinking occasion.

<sup>&</sup>lt;sup>c</sup> TLFB cannabis 90 days.

regionally-, age-, and sex-dependent, alcohol misuse may have sexspecific effects (Spear, 2015). However, sex-related effects in the neurocognitive consequences of alcohol use has been largely overlooked (Carbia et al., 2018). In the present study, an enhancement of memory for negative content at the cost of positive and neutral information in female BDs- but not in males- might be indicating a greater vulnerability to alcohol-related emotional disturbances among women. One possible explanation for these differences may be the sexually dimorphic maturation of the amygdalo-hippocampal region, which constitutes a key anatomical underpinning of emotional memory also implicated in sex-biased and developmentally-emergent psychopathology (Fish et al., 2019). The amygdala assigns emotional salience to internal and external stimuli- especially negative stimuli- and it is a critical structure related to arousal and negative reinforcement. The amygdala is therefore a region where alcohol effects and emotional disturbances converge and a likely underlying neuroanatomical basis for comorbid alcohol abuse and internalizing disorders, which affect much more women than men (Peltier et al., 2019). In fact, women with AUDs are 3 times more likely to be diagnosed with comorbid internalizing disorders (Sawyer et al., 2019). While emotional dysregulation is strongly associated with all phases of addiction; it plays a critical role for women, who tend to increase -in a vicious circle- their alcohol use as a coping mechanism (Koob and Volkow, 2016; Zachry et al., 2019).

The effects of emotion on memory increase with time, facilitating consolidation processes which are thought to continue for an extended period (Dolcos et al., 2017; Hamann, 2001). Thus, it is likely that after longer time intervals (e.g. recall trials after one day) the alcohol-related effects on emotional bias would be enhanced, reflecting a strengthening of the memory trace that is disproportional to memory importance (Hamann, 2001).

One potential limitation of this study is the assessment of long-term recall only after a 30 min delay (typical delay in list-learning paradigms), which could be reducing the intensity of the observed bias. Another potential limitation is the lack of a neuropsychological assessment of participants before they first engaged in BD, which prevents us from discounting the possibility of pre-existing memory biases. Finally, the use of a retrospective estimate of drinking episodes (past 180 days), might introduce some inaccuracies in the recording of drinking behaviour. However, the TLFB has been proved to be a reliable measure to collect psychometrically sound information about substance use (Sobell and Sobell, 1995). We believe that the potential loss of accuracy has a minimal impact in the results as we were interested in capturing general drinking patterns (frequent bingers versus low drinkers) maintained over time (two years).

Emotional memory biases can negatively influence future thinking and self-referential processing (e.g. rumination; Nandrino et al., 2017), especially memories formed during the sensitive period of adolescence (for example, due to the phenomena known as reminiscence bump [Fuhrmann et al., 2015]). Thus, future studies should further investigate the effects of BD on emotional memory (e.g. by increasing the length of time for recall; by examining the effects under alcohol intoxication or by exploring the mediating role of stress hormones), as well as focus on specific types of memory such as autobiographical memory or source memory (Morgan et al., 2004; Nandrino et al., 2017).

#### 5. Conclusion

This study provides novel information indicating that female BDs -but not males- display an alcohol-related mnemonic increase of negative information in episodic memory, at the expenses of less memorization of neutral information. The results highlight early sex-dependent alterations in BDs regarding emotional memory bias. A malfunction in this -otherwise adaptive process- could offer new insights into the theory that females may be more vulnerable to addiction risk through an emotion-mediated pathway.

#### **Declaration of Competing Interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

#### **Funding**

This work was supported by grants from Plan Nacional Sobre Drogas (PNSD 2015/034) and Ministerio de Economía, Industria y Competitividad together with European Regional Development Fund (PSI2015-70525-P) and Xunta de Galicia (ED431C 2917/06).Carina Carbia has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No. 754535.

# CRediT authorship contribution statement

C. Carbia, M. Corral and F. Cadaveira have designed the study. All authors participated in the data collection. C. Carbia, Caamaño-Isorna, F. and M. Corral have analyzed and interpreted the data. C. Carbia and M. Corral have written the article. All authors revised and made significant contributions to the final manuscript. All authors have approved the final version of the manuscript.

#### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugalcdep.2020. 107888.

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