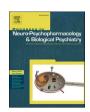


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# Risky alcohol use during youth: Impact on emotion, cognitive networks, and resting-state EEG activity

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#### ABSTRACT

The identification of the risk factors of alcohol consumption in youths is crucial for early interventions focused on reducing harmful alcohol use. In our study, 82 college students (40 healthy control (CO group) and 42 with risky alcohol use (RAU group) determined by AUDIT questionnaire) between the ages of 18 and 25 years underwent a comprehensive neuropsychological assessment covering emotional and cognitive functioning. Their resting-state activity was also recorded with an EEG for 10 min with their eyes open (EO) and 10 min with their eyes closed (EC) and analyzed using the Fitting Oscillations & One-Over-F (FOOOF) paradigm. After adjusting for sex, those in the RAU group had higher emotional dysregulation and impulsivity traits. The RAU girls presented more emotional regulation problems, such as dysregulation and negative urgency compared with the RAU boys. The RAU youths had significantly worse functioning in several cognitive domains, such as sustained attention, verbal memory, and executive functions. Cognitive network analysis revealed a different pattern of connections in each group showing that in the RAU group, the verbal memory domain had the highest connection with other cognitive functions. The EEG analyses did not reveal any significant differences between the CO and the RAU groups. However, we observed only in the EO condition that boys the from the RAU group displayed a higher theta/beta ratio than the RAU girls, whereas these differences were not observed within the CO group. Our findings highlight the need to explore more deeply the emotional, cognitive and brain changes underlying the RAU in young people.

### 1. Introduction

The engagement in substance use during youth has been a long-standing health concern in terms of its predictive link with future drug abuse in adulthood (Gray and Squeglia, 2018). Specifically, in Western countries, alcohol is one of the most available and used drug at this age together with the gradual increase in cannabis consumption (Messina et al., 2021; Thomasius et al., 2022). In recent years, it appears that among the motives leading young people to engage in risky alcohol use (RAU) are not only those related to social pressure, or the disinhibiting effects of alcohol, but also those associated with alleviating psychological distress, such as anxiety, especially in young people with emotional regulation difficulties (Bravo and Pearson, 2017; Goldsmith et al.,

2012). The relationship between starting drinking early and experiencing anxiety or depressive symptoms tends to be more pronounced in girls than in boys (Johannessen et al., 2017). Early signs of depression in girls during adolescence are also linked to later problematic alcohol consumption (Edwards et al., 2014). These findings were also found in animal research studies, indicating that female adolescent rodents displaying higher levels of social anxiety-like behaviour tend to consume more alcohol than their male counterparts (Varlinskaya and Spear, 2015). Some authors have also proposed that compared to men who drink for positive reinforcement, women are more likely to drink to regulate negative affect and stress reactivity (Stoica et al., 2021). In addition to these factors, some other reasons that lead young people to consume alcohol include the substance's own reinforcement effects,

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positive expectations towards it, together with the craving or desire generated by its continued consumption (Cronin, 1997; Kuntsche et al., 2005). Related to this, the Motivational Model of Alcohol Use (Cooper et al., 2016) proposes that drinking or not drinking alcohol is based on a decision, in most of cases unconscious, that arises from considering both the emotional and rational aspects about the affective change (related to the biochemical effect of the drug or indirect, such as peer acceptance) that drinking alcohol will produce when compared to not drinking. Thereby, the motives or reasons for drinking among young people are varied and they represent a personally derived framework for alcohol use, shaped by individual experiences, circumstances, and expectations (Carey and Correia, 1997). Regardless of the motives behind the alcohol intake, from a biological point of view, substance use during this critical period of brain development is usually associated with persistent alterations in brain structure and function which may be different, and more severe, than in adulthood (Lees et al., 2019; Sousa et al., 2019).

Regarding cognitive performance, young people with RAU (6 or more points for girls and 8 or more for boys in the Alcohol Use Disorder Identification test (AUDIT), Encuesta sobre alcohol y drogas en España (EDADES) 1995-2022, 2022) appear to have a poorer performance in attention, executive functioning, impulsivity, psychomotor speed, and learning. Particularly in the learning domain, they perform worse in tasks of short and long-term verbal memory (Lees et al., 2020; Squeglia and Cservenka, 2017). In addition, executive functioning performance may make young people more vulnerable to engage in substance use because inhibitory control is one of the most predictive variables (Antón-Toro et al., 2021; Heitzeg et al., 2014; Quach et al., 2020). Poorer performance in spatial planning and problem-solving tasks (Squeglia et al., 2017), as well as deficits in working memory (Khurana et al., 2013) have also been linked to an escalation in drinking during youth. Nevertheless, there are also studies in which no deficits have been found, and this is probably due to methodological differences in the sample characteristics, the tests administered, the pattern of alcohol intake, or even, sex-related differences (Carbia et al., 2018). A relevant question regarding the relationship between cognition and RAU is whether the cognitive profile observed in young people is induced by drug intake or it precedes drug exposure, entailing a vulnerability factor to engage in chronic drug use and/or addiction (Sampedro-Piquero et al., 2019). In this respect, neuropsychological data could be helpful in identifying those teens at risk of initiating problematic substance use. In this field of research, translating the concept of connectome from the neuroimaging field to cognitive data is expected to provide relevant new insights into how human cognition is organized (Fonseca-Pedrero, 2017). Multiple studies on young individuals have identified changes in their brain connectivity associated with binge drinking (BD) behaviour (Almeida-Antunes et al., 2022; Arienzo et al., 2020; Correas et al., 2016; Crane et al., 2018; Morales et al., 2020; Tong et al., 2021). For example, some research has found increased connectivity in the brain's reward system but decreased connectivity in networks related to decisionmaking and self-control (Arienzo et al., 2020). Other findings suggest that certain brain differences may predispose adolescents to start BD earlier. Thus, adolescents with a lower medial orbital gyrus functional Fractional anisotropy have greater nucleus accumbens activation during decision-making involving risk and reward and began BD sooner (Morales et al., 2020). Together with this finding, increased brain connectivity of the default mode network (DMN) was also described in young BD which contrasts with the lower activation that occurs during the normal development resulting in a more efficient neural network (Correas et al., 2016). Additionally, BD also exhibited altered brain connectivity patterns when exposed to alcohol-related stimuli (increased beta band functional connectivity particularly in the fronto-parietal, fronto-temporal and fronto-occipital networks) compared with the non-alcoholic cues (reduced theta-band in the fronto-occipital network) (Almeida-Antunes et al., 2022). Overall, these studies indicate that both before and during the development of BD habits, significant alterations occur in the brain networks of young people.

Thus, despite the extensive evidence into how RAU induces changes in the brain connectivity in young people, or even in some of them prior to the onset of consumption, few data exist on the connectivity of cognitive functions in these developing brains. A network analysis approach would allow us to determine which cognitive areas are dominant in the network, in order to use the most central domains for prevention, diagnosis, and planning treatment. Nonetheless, despite the potential of network analysis (Garcia-Cabello et al., 2021), to our knowledge, no study has applied this promising methodology on cognitive data in a study of RAU in young people. Some approaches to this methodology in the field of substance use disorder were performed with the aim of identifying core symptoms of abuse and dependence that could contribute to the chronicity of the disorder during adulthood (Gharahi et al., 2023; Rhemtulla et al., 2016; Rutten et al., 2021). With regard to young people, a recent study using network analysis has observed few connections between depressive symptoms and substance use (Wasil et al., 2020).

The resting-state EEG may also act as a potential biomarker of the neurotoxic effects of substance use (Liu et al., 2022). The effects of alcohol consumption in young people on resting brain activity are still poorly understood, but the limited studies seem to indicate that they share the same alterations as those described in adults, i.e. an increased theta (4-8 Hz) and/or beta (13-21 Hz) power, (Herrera-Díaz et al., 2016; López-Caneda et al., 2017; Mumtaz et al., 2017). Recently, a growing number of studies have suggested that the EEG theta/beta ratio (TBR) is inversely related to executive cognitive control, representing a measurement of cognitive processing capacity (Clarke et al., 2019; van Son et al., 2019a). Interestingly, previous research has suggested that the impact of the anxiety trait on attentional function can be detected by resting TBR acting as a potential biomarker for cognitive control and resilience (Putman et al., 2014; Sari et al., 2016). Consequently, it seems that the assessment of this biomarker could shed light on the detection of cognitive deficits in both clinical and risk populations.

Overall, the aim of the current study was to describe the behavioural, cognitive, and electrophysiological profile of substance abuse vulnerability in a sample of young people with RAU. New methodological approaches, such as network analysis on neuropsychological measurements or Fitting Oscillations & One-Over-F (FOOOF) algorithm in the case of EEG data, were carried out in this study. FOOOF algorithm parametrizes the EEG signal into two different components: a rhythmic, oscillatory component, and a non-rhythmic, aperiodic component (Donoghue et al., 2020). This separation is critical, as previous reports have shown that the aperiodic component of the EEG signal can easily camouflage -or exacerbate- the actual relationship between TBRs and other cognitive measures (Azami et al., 2023; Finley et al., 2022). As a hypothesis, it is possible that the set of tests administered in this study will allow us to observe greater difficulties in emotional regulation, especially in young girls, and impulsivity in the group of young individuals with RAU, as well as a poorer performance in certain cognitive tests related to executive functioning and declarative memory. This pattern of impulsive behaviour and poor executive control may be reflected in a higher TBR in the resting state. Finally, our cognitive network analysis may also shed light on the cognitive domains most connected with other functions and may lay the foundation for neuropsychological intervention.

# 2. Materials and methods

#### 2.1.1. Participants

College students aged between 18 and 25 years were recruited through verbal disclosure, e-mails, and notice boards at the Autonomous University of Madrid and Drug Dependency Treatment Center of Hortaleza (Madrid) (Caucasian, 22 male and 60 female, age  $18.9 \pm 0.12$  and

matched for education level). All the volunteers included in the study signed the informed consent, accompanied by an informative note, and they created an alphanumeric code based on the first letter of their first name, the last letter of their first surname followed by their date of birth (e.g., RO2410) to guarantee privacy during the data processing and analysis phases. Firstly, information was collected regarding their substance use, anxiety trait, emotional regulation, impulsivity and prefrontal symptoms, using several on-line standardized questionnaires were administered: the Alcohol Use Disorder Identification Test (AUDIT, Spanish adaptation: Contel Guillamon et al., 1999); the Cannabis Abuse Screening Test (CAST, Legleye et al., 2007); State-Trait Anxiety Inventory (STAI-t, Spielberger et al., 1970); the Difficulties in Emotion Regulation Scale (DERS, Spanish adaptation: Hervas and Jódar, 2008); the Impulsive Behaviour Scale (UPPS-P, Spanish adaptation: Cándido et al., 2012); the Prefrontal Symptoms Inventory (PSI-20, Pedrero-Perez et al., 2016). RAU was determined using the AUDIT questionnaire (girls  $\geq$ 6; boys  $\geq$ 8 points) (Encuesta sobre alcohol y drogas en España (EDADES) 1995–2022, 2022). All volunteers with an AUDIT score above 19 points were excluded. In our study, we were interested in young people with RAU who did not meet the criteria for addiction, and according to the AUDIT questionnaire, a score higher than 19, i.e. from 20 to 40 points, is indicative of probable alcohol addiction. Based on this score, we divided the sample into 2 groups: the control group (CO, n = 40 (12 boys)) and the risky alcohol use group (RAU, n = 42 (10 boys)). The inclusion criteria were: 1) aged 18-25 years; 2) an absence of diagnosis of substance use disorder; 3) an absence of comorbid disease, such as anxietyrelated disorders, depression, psychotic disorder or (Attention-deficit/ hyperactivity disorder) ADHD; 4) alcohol as the predominant substance of consumption and non-problematic consumption of other drugs, specifically cannabis. Problematic cannabis use was determined by the CAST questionnaire, where a score above 4 points is considered to be indicative of problematic use. Additionally, we conducted an interview with the participants, in which we included questions about the consumption of other drugs, and whether participants reported consuming other drugs, e.g. cocaine, methamphetamine, etc., all these subjects who responded positively to these questions were excluded from the study regardless of the frequency or quantity. Moreover, healthy controls were excluded if they had a history of drug use, including nicotine and alcohol. All volunteers were excluded if they exhibited severe difficulties in understanding the test instructions, exhibited altered consciousness or agitation and if they consumed prescription drugs affecting the central nervous system (mainly anxiolytics and antidepressants).

The study received approval from the Ethics Committee of the Autonomous University of Madrid (code: CEI-122-2490) in accordance with the Ethical Principles for Medical Research Involving Human Subjects adopted in the Declaration of Helsinki by the World Medical Association (64th WMA General Assembly, Fortaleza, Brazil, October 2013), Recommendation No. R (97) 5 of the Committee of Ministers to Member States on the Protection of Medical Data (1997), and the Spanish Data Protection Act (Ley Orgánica 15/1999 de Protección de Datos, LOPD). All the participants were informed about the study prior to their inclusion in the study and had provided their written informed consent.

### 2.1.2. Assessment protocol

After completing the online questionnaires via the Qualtrics® survey platform, we contacted the participants via the email they had provided. We arranged a testing session in our laboratory to perform a resting-state EEG recording (approximately 30 min) and a neuropsychological assessment (approximately 90 min).

2.1.2.1. Resting-state EEG. EEG data were collected using Bitbrain's Versatile 32 cap (model E32.A1), which comprises of 32 electrodes (plus ground and reference) set in the international 10–10 system (Bitbrain Technologies 2018, Zaragoza, Spain). After informing them about what

the task entailed the participants were seated in a comfortable chair during the EEG set-up, where the experimenter placed the EEG cap on and ensured that all electrode impedances were kept below 5 k $\Omega$ . Afterwards, the lights in the room were dimmed, and the participants sat still while the EEG recording was ongoing. The participants alternated twice between sitting with their eyes closed for five minutes (Eyes Closed/EC condition) and sitting with their eyes open for five minutes while staring at a fixation dot painted on the wall 90 cm away from them (Eyes Open/EO condition). This resulted in a total of ten minutes of resting-EEG recording per condition per participant. The conditions were counterbalanced so that half of the participants started with the EC condition and the other half started with the EO condition. The EEG signals were preprocessed using a combination of manual and automated procedures. Firstly, all EEG recordings were examined visually by one of the authors in order to reject the most notable portions of noisy data. Then, the EEGlab (Delorme and Makeig, 2004) pipeline provided by Hatlestad-Hall et al. (2022) was used to automatically reject the more subtle instances of noise in the data. This pipeline started by iteratively referencing the data, searching for noisy channels, and excluding them from the computation of the average reference, which increased the robustness of the referenced data. Afterwards, a 1 Hz high-pass filter was applied, together with the removal of the power line noise using the nt\_zapline function from the NoiseTools toolbox (de Cheveigné, 2020). Then, muscle and eye artifacts were identified using the SOBI algorithm (Belouchrani et al., 1993) and subsequently removed using the IClabel function (Pion-Tonachini et al., 2019). Next, a total of 3.23  $\pm$  0.004 of bad channels were interpolated, and a 40 Hz low-pass filter was applied. Finally, the continuous data was segmented into non-overlapping 4 s epochs for posterior analysis, and the two runs of the EO and EC conditions respectively were appended. All the specific parameters can be consulted in the 'code' folder provided with the data.

The frequency decomposition of the EEG signal was performed by using the FOOOF paradigm (Donoghue et al., 2020) through the Field-Trip toolbox (Oostenveld et al., 2011). This paradigm separates the oscillatory (rhythmic activity within a frequency band) and aperiodic (non-rhythmic activity with no characteristic frequency) components of the frequency signals, enabling us to obtain a more accurate representation of the synchronized neuronal activity within the brain. Then, we calculated the Individual TBR of the Cz and Fz electrodes respectively by computing the average of the oscillatory power in the theta band (4-8 Hz) and dividing it by the average of the oscillatory power in the beta band (12-30 Hz). Alpha/Beta Peak Frequencies (APF/BPF) and Amplitudes (APA/BPA) were also obtained by extracting the frequency and amplitude of the largest peak between 7 and 14 Hz (alpha) and 15-30 Hz (beta) in each electrode and averaging them. In addition, we have included the classical analysis of power spectra without using FOOOF in the Supplementary Material to facilitate the identification of any potential differences between the analytical approaches.

2.1.2.2. Neuropsychological assessment. After obtaining the informed consent, trained psychologists conducted a structured interview to obtain data about the sociodemographic variables: alcohol abuse, e.g. age of onset, drugs consumed, years of abuse, last consumption, etc., scale of cognitively stimulating activities (León-Estrada et al., 2017), and the Parent-Adolescent Communication Scale ((PACS) Barnes and Olson, 1982). Subsequently, the participants underwent a comprehensive single-session neuropsychological assessment as described below (approximately 90 min). The participants were allowed to take a break, and they could revoke their consent at any time. Table 1 shows the mean  $\pm$  standard error of the mean (SEM) for each experimental condition (CO and RAU) taking into consideration the sex of the participants.

Attentional functioning, psychomotor speed, and visual searching were assessed with the *d*2 Test (Brickenkamp and Cubero, 2002) and the Test de los Senderos, parts A and B (TESEN) which is Spanish version of the Trail Making Test (TMT) (Portellano and Martínez Arias, 2014).

**Table 1**Emotional and behavioural results for each group.

	CO		RAU	RAU		$\eta p2$	
	BOYS	GIRLS	BOYS	GIRLS	values		
Age	18.67	18.82	19.70	18.81	p =	_	
	$\pm \ 0.40$	$\pm$ 0.27	$\pm~0.82$	$\pm~0.26$	0.32		
Years of study	12.02	12.07	12.13	12.06	p =	-	
	$\pm \ 0.10$	$\pm~0.04$	$\pm~0.13$	$\pm~0.06$	0.67		
Onset age	16.9 $\pm$	16.09	15.2 $\pm$	$15.9~\pm$	p =	0.3	
(alcohol)	1.3	$\pm \ 1.02$	0.9	1.1	0.03		
AUDIT	$3 \pm$	2.92 $\pm$	10 $\pm$	11.19	*p <	0.52	
	0.66	0.34	0.71	$\pm~0.81$	0.001		
CAST	$0.33 \pm$	0.18 $\pm$	3.8 $\pm$	2.33 $\pm$	p =	0.1	
	0.19	0.12	1.1	1.82	0.001		
STAI trait	20.17	25.93	21.30	32.36	#p <	0.1	
	$\pm 2.20$	$\pm~1.81$	$\pm$ 3.21	$\pm~1.68$	0.001		
DERS	57.58	62.18	59.40	75.81	*p =	0.0	
	± 3.89	± 3.53	± 4.06	± 3.15	0.05;	0.0	
	_ 0.00	_ 0.00		_ 0.10	#p =	0.0	
					0.01		
Emotional	12.17	10.79	12.50	12.15	p =	_	
neglect	± 1.04	± 0.67	$\pm 1.06$	± 0.69	0.36		
Emotional	6.5 ±	7.07 ±	7.1 ±	7.33 ±	p =		
confusion	0.93	0.50	0.75	7.33 ± 0.48	р — 0.77	_	
Emotional	8.92 ±	10.61	10.90	13.10		0.0	
interference	0.79			$\pm 0.62$	#p = 0.04	0.0	
,		$\pm~0.78$ $17.68$	$\pm 1.22$ $14.90$	± 0.62 24 ±		0.0	
Emotional	17.17				dp =	0.0	
dysregulation	± 1.39	± 1.28	$\pm 1.29$	1.46	0.02		
Emotional	12.83	16.04	14 ±	19.27	#p =	0.0	
rejection	$\pm 1.81$	$\pm 1.43$	2.10	± 1.25	0.02		
UPPS-P	42.42	44.14	47.70	47.67	p =	0.1	
	$\pm 2.20$	$\pm 1.30$	$\pm 2.69$	$\pm 1.40$	0.01		
Negative	8.58 $\pm$	8.82 $\pm$	7.80 $\pm$	9.61 $\pm$	&p =	0.1	
urgency	0.74	0.43	0.53	0.40	0.03		
Lack of	6.58 $\pm$	7.39 $\pm$	8.5 $\pm$	8.36 $\pm$	p =	0.0	
perseverance	0.73	0.46	1.10	0.51	0.04		
Lack of	7.25 $\pm$	7.25 $\pm$	8 ±	7.61 $\pm$	p =	-	
premeditation	0.73	0.41	0.71	0.41	0.78		
Sensation	10.58	10.71	12.30	11.45	p =	0.0	
seeking	$\pm 0.86$	$\pm 0.36$	$\pm~0.75$	$\pm 0.53$	0.04		
Positive	9.42 $\pm$	$9.96 \pm$	11.10	10.64	p =	0.0	
urgency	0.78	0.35	$\pm~0.66$	$\pm~0.41$	0.02		
PSI-20	24.33	30.25	26.40	32.30	#p =	0.0	
	$\pm 3$	$\pm$ 2.04	$\pm$ 3.62	$\pm 1.61$	0.02		
Emotional	4.33 $\pm$	7.43 $\pm$	4.20 $\pm$	8.61 $\pm$	#p <	0.2	
behaviour	0.96	0.56	0.57	0.62	0.001		
Social	4.33 $\pm$	$3.89~\pm$	3.4 $\pm$	4.58 $\pm$	p =	_	
behaviour	0.91	0.62	1.11	0.57	0.67		
Behavioural	15.67	18.93	18.80	19.12	p =	_	
control	± 1.99	± 1.51	$\pm$ 2.48	$\pm 1.25$	0.53		
CSAs	82.42	86.46	84.10	81.88	p =	_	
	$\pm 1.88$	± 1.46	± 3.68	± 1.59	0.25		
PACS	139.33	143.21	127.60	133.27	p =	_	
	+ 6.18	± 4.94	$\pm 8.02$	± 3.84	<i>p</i> – 0.24	_	

Values are means  $\pm$  SEM or percentages. CSAs: cognitively stimulating activities scale. PACS: Parent-Adolescent Communication Scale.

Verbal and nonverbal declarative memory were measured with the Spain-Complutense Verbal Learning Test (TAVEC) which consists of a Spanish version of the California Verbal Learning Test (CVLT) with the advantage that the TAVEC test also includes several recall trials facilitated by semantic cues in contrast to the CVLT (Benedet and Alejandre, 2014) and the Rey-Osterrieth Complex Figure Test (Osterrieth, 1944), respectively. The copying part of the latter test allowed us to eliminate possible visuoperceptive and visuospatial problems. Executive functioning was tested with different tests such as the CAMBIOS test for mental flexibility (Seisdedos, 1997), the TESEN, part C and D for working memory, mental flexibility and alternation increasing the level

of difficulty between version C and version D (Portellano and Martínez Arias, 2014), the forward and backwards digit span task of the Wechsler Memory Scale for assessing working memory (WAIS-IV; Wechsler, 2008), a verbal semantic and phonological fluency test (Portellano Pérez and Martínez-Arias, 2020), part of the Stroop Test relating to word/ colour, and for assessing inhibitory control (Golden, 1999). In order to evaluate the prospective memory, at the beginning of the evaluation, we told the participants to remember that at the end of the evaluation they would have to remind us to tell them something and that if they remembered they would be given a sweet as a gift. In addition, for emotional perception, we used the Reading the Mind in the Eyes Test (RMET) (Baron-Cohen et al., 2001). The administration order of the tests was controlled to avoid any possible interference from verbal material with the recall of the word list. All the neuropsychological assessments were carried out using pencil and paper, except for the images from the RMET, which were presented using a Samsung Galaxy 10.1" tablet. The specific cognitive domains measured with the different tests, together with the mean  $\pm$  SEM for each group, are displayed in Table 2. Further details about the tests employed are shown in the Supplementary Material.

#### 2.1.3. Statistical analysis

All statistical analyses were performed using SPSS 25 (IBM SPSS Statistics, Corporate headquarters, New Orchard Road, Armonk, New York 10,504–1722, USA). All p values were two-tailed, and the level of significance was taken as  $p \leq 0.05$ . Descriptive analyses (mean  $\pm$  SEM) were performed on the demographic variables; information related to drug use, online questionnaires, and neuropsychological tests results (more details are displayed in Table 1 and Table 2). GROUP (CO / RAU) and SEX (boys/girls) were considered between-factors with two levels each and then, two-way MANOVA was performed for all the measures taken throughout the study, i.e. the behavioural, emotional, cognitive and EEG variables). Appropriate post hoc comparisons were conducted when significant differences were found using the Bonferroni's test.

To investigate how cognitive domains were organized and interrelated with each other constituting a cognitive connectome, we performed Pearson's correlations coefficients on each group (CO and RAU), together with the multiple comparison method of False Discovery Rate (FDR) in order to ensure statistical significance following the Benjamini-Hochberg procedure to avoid false positives and to control alpha inflation (Storey et al., 2023; Storey, 2002). This analysis was performed in the R package qualue through its GUI version. On the other hand, a network analysis was carried out to explore the relationships between neuropsychological variables. Weighted networks were estimated using JASP 17.2.1 (University of Amsterdam), which graphically represent a model in which statistically significant relationships between variables are displayed. Weights under 0.4 were excluded which indicated that the variables had a low correlation (Akoglu, 2018; Dancey and Reidy, 2007)). By default, JASP 17.2.1 runs the sampler for 10.000 iterations following the instructions in the manual (Han and Dawson, 2020). To identify the most salient variables, standard centrality measures were evaluated: strength: which is the sum of absolute partial correlation coefficients between a node and all other nodes, betweenness: how many of the shortest paths between two nodes go through the node in question, closeness: how strongly a node is indirectly connected to other nodes in the network, and expected influence: which takes into account negative associations between the nodes (Costantini et al., 2015; Epskamp et al., 2017). Matlab R2022a was used to create the matrix plots with the aim of providing further insights into the role and influence of the specific cognitive nodes (Zuo et al., 2012).

 $<sup>^{*}</sup>$  Asterisk represents significant differences between the CO and the RAU groups ( $p \le 0.05$ ).

<sup>\*</sup> Represents significant differences between the boys and the girls regardless of the experimental condition.

<sup>&</sup>amp; Represents significant differences between the boys and the girls within the RAU group.

Total Colours/Words

Interference index

Prospective memory Recall instruction (%)  $54.25\pm3.10$ 

 $9.10\pm3.21$ 

50%

Table 2

Attention, psychomotor spe	eed and visual searching						
	CO		RAU			p values	ηр2
	Boys	Girls	Boys	Gi	rls		
d2							
Correct answers	$196.67\pm7.55$	$188.04 \pm 4.90$	$172.40 \pm 10.75$	5 19	$0.39 \pm 5.63$	p = 0.08	_
Omissions	$12.92\pm3.63$	$12.54\pm2.25$	$14.50\pm4.72$	14	$0.64 \pm 1.62$	p = 0.93	_
Commissions	$0.58 \pm 0.19$	$0.39 \pm 0.14$	$0.80\pm0.29$	0.3	$33 \pm 0.14$	p = 0.48	_
TOT index	$483.42 \pm 14.88$	$462.04 \pm 9.23$	$446.30 \pm 20.02$	2 47	$1.21 \pm 11.44$	p = 0.12	_
CON index	$196.08 \pm 7.48$	$187.64 \pm 4.85$	$171.60 \pm 10.66$	6 18	$9.10 \pm 5.88$	p = 0.09	_
VAR index	$14.67 \pm 2.39$	$11.54\pm0.63$	$10.60\pm0.81$	10	$0.94 \pm 0.54$	p = 0.03	0.06
TESEN						-	
Time part A (s)	$77.22 \pm 8.47$	$85.52 \pm 3.79$	$99.25 \pm 9.36$	85	$0.24 \pm 3.24$	&p = 0.05	0.05
Time part B (s)	$97.65 \pm 12.71$	$86.08 \pm 3.38$	$94.64 \pm 9.93$	88	$3.88 \pm 3.42$	p = 0.65	_
Errors part A	$0.08\pm0.08$	$0.07\pm0.05$	$0.001 \pm 0.001$	0.	$12\pm0.06$	p = 0.35	_
Errors part B	$0.17\pm0.18$	$0.25\pm0.10$	$0.001 \pm 0.001$		$24\pm0.17$	p = 0.89	-
Declarative memory							
		CO		RAU		p values	ηр2
		Boys	Girls	Boys	Girls		
TAVEC		T.00   0.10	F F1 + 0.61	T + 0.60	6.10 : 0.00	"	
Trial 1		$7.33 \pm 0.48$	$7.71 \pm 0.34$	$7 \pm 0.68$	$6.13 \pm 0.30$	#p = 0.009	0.08
Trial 5		$13.67 \pm 0.51$	$14.18 \pm 0.24$	$12.10 \pm 0.43$	$13.18 \pm 0.31$	p = 0.002	0.12
Trial B		$6.25\pm0.70$	$7.39 \pm 0.32$	$5.7\pm0.87$	$6.55 \pm 0.34$	p = 0.77	-
Free STM		$13\pm0.64$	$12.68\pm0.35$	$11.30\pm0.67$	$11.55\pm0.43$	p = 0.01	0.08
STM with semantic cues		$12.58\pm0.56$	$13.18\pm0.35$	$12.30\pm0.67$	$11.85\pm0.43$	p = 0.34	-
Free LTM		$13.42\pm0.68$	$13.11\pm0.33$	$11.60\pm0.97$	$12\pm0.38$	p = 0.009	0.08
LTM with semantic cues		$12.83\pm0.65$	$13.43\pm0.37$	$12.10\pm0.91$	$12.18\pm0.39$	p = 0.65	-
Semantic strategy use du	= =	$13.08\pm1.91$	$16.75\pm1.34$	$13.60\pm1.99$	$14.85\pm1.60$	p = 0.54	-
Semantic strategy use du	=	$4.5\pm0.70$	$5.43 \pm 0.61$	$4.1\pm0.84$	$5.18\pm0.51$	p = 0.92	-
Semantic strategy use du	ring LTM	$5.08\pm1.03$	$6.14\pm0.64$	$4.7\pm0.84$	$5.79 \pm 0.64$	p = 0.98	-
Serial strategy use during	g the list acquisition	$9.67\pm2.07$	$8.43\pm1.20$	$10.10\pm2.12$	$6.70\pm0.81$	p = 0.46	-
Serial strategy use during	g free STM	$1.83\pm0.55$	$1.36\pm0.36$	$1.3\pm0.50$	$0.76\pm0.18$	p = 0.93	-
Serial strategy use during	g free LTM	$1.75\pm0.65$	$1.14\pm0.35$	$1.70\pm0.60$	$0.79\pm0.25$	p = 0.73	-
Total intrusions		$1.75\pm0.99$	$0.96\pm0.26$	$3.70\pm1.21$	$2.12\pm0.50$	p = 0.04	-
Total perseverations		$3.17\pm1.18$	$4.57 \pm 0.76$	$5\pm1.11$	$3.94\pm0.56$	p = 0.18	-
Recognition		$15.17\pm0.21$	$15.18\pm0.19$	$15.10\pm0.35$	$14.97\pm0.20$	p = 0.79	-
Rey Complex Figure							
Copy score		$35.17\pm0.67$	$35.75\pm0.14$	$35.70\pm0.30$	$35.85\pm0.09$	p = 0.42	-
Delayed score		$28.42\pm1.68$	$27.93\pm1.04$	$25.50\pm2.19$	$25.30\pm1.13$	p = 0.92	-
Time copy (s)		$125.44 \pm 11.57$	$116.51 \pm 8.89$	$142.77 \pm 14.81$	$113.35\pm5.93$	p = 0.32	-
Time delayed recall (s)		$109.61 \pm 12.14$	$97.73 \pm 6.16$	$120.02 \pm 12.09$	$103.83 \pm 5.42$	p = 0.80	-
Executive functions							
	CO		RAU			p values	$\eta p2$
	Boys	Girls	Boys	-	Girls		
CAMBIOS							
Correct items TESEN	$24.50\pm0.43$	$21.75\pm0.45$	$20.80\pm1.8$	31	$21.85 \pm 0.42$	&p = 0.01	0.08
Time part C (s)	$95.27 \pm 8.58$	$90.83 \pm 2.88$	$121.05\pm16$	6.55	$97.77 \pm 4.07$	p = 0.02	0.07
Time part D (s)	$109.30 \pm 6.07$	$114.76 \pm 4.27$	$143.89 \pm 19$		$120.97 \pm 4.41$	p = 0.04	0.05
Errors part C	$0.33 \pm 0.18$	$0.21 \pm 0.09$	$0.60 \pm 0.50$		$0.42 \pm 0.14$	p = 0.89	-
Errors part D	$0.17\pm0.11$	$0.10 \pm 0.05$	$0.60 \pm 0.60$		$0.27 \pm 0.13$	p = 0.58	_
Total time (s)	$379.48 \pm 24.53$	$377.20 \pm 11.35$			$392.86 \pm 12.36$	p = 0.02	0.07
Total errors	$0.75 \pm 0.30$	$0.57 \pm 0.16$	$1.20 \pm 0.73$		$0.97 \pm 0.34$	p = 0.95	_
Digit span						-	
Forward	$6.42 \pm 0.23$	$6.07 \pm 0.18$	$6.1 \pm 0.18$		$5.9 \pm 0.12$	p = 0.70	_
Backward	$5.42 \pm 0.36$	$4.75 \pm 0.18$	$4.40 \pm 0.16$		$4.85 \pm 0.12$	p = 0.70 p = 0.01	0.0
Verbal Fluency Test	22 ± 0.00	0 ± 0.10	10 1 0.10			-r	0.0
FAS total	$36.25\pm1.81$	$37.43\pm1.54$	$37.50 \pm 3.5$	53	$36.39 \pm 1.17$	p = 0.56	_
Animals	$32.17 \pm 8.72$	$23.61 \pm 0.85$	$21.10 \pm 1.5$		$22.46 \pm 0.66$	p = 0.30 * $p = 0.04$	0.0
Stroop test	32.17 ± 0.72	20.01 ± 0.00	21.10 ± 1.0	•	= 3.00	r 0.0.	5.5
Words	$110.33\pm5.12$	$107.36\pm3.22$	$102 \pm 6.02$		$106.67 \pm 3.59$	p = 0.42	_
Colours	$77.75 \pm 4.90$	$76.29 \pm 1.72$	$71.10 \pm 3.3$		$74.36 \pm 1.80$	p = 0.42 p = 0.40	_
	77.70 ± 1.50		71.10 ± 5.5	-		P 00	

 $46.30\pm2.84$ 

 $\textbf{3.44} \pm \textbf{1.87}$ 

20%

 $53.18\pm1.94$ 

 $9.15\pm1.74$ 

18.2%

p = 0.05

p = 0.002

p=0.11

0.04

0.12

 $51.57\pm1.57$ 

 $\textbf{7.78} \pm \textbf{1.26}$ 

60.7%

Emotional Recognition									
	CO	СО		RAU		ηр2			
	Boys	Girls	Boys	Girls					
Correct answers	$24.17 \pm 0.94$	$24.39 \pm 0.63$	$22.90 \pm 1.04$	$22.85\pm0.66$	p = 0.88	-			

Values are means  $\pm$  SEM or percentages.

- \* Asterisk represents significant differences between the CO and the RAU groups ( $p \leq 0.05$ ).
- $^{\&}$  Represents significant differences between the CO boys and the RAU boys ( $p \leq 0.05$ ).
- $^{\#}$  Represents significant differences between the CO girls and the RAU girls ( $p \leq 0.05$ ).

#### 3. Results

#### 3.1.1. Online psychological questionnaires

The RAU group, regardless of the sex, showed higher AUDIT and CAST scores ( $F_{(1,\ 82)}=85.49,\ p<0.001;\ F_{(1,\ 82)}=14.67,\ p<0.001,$  respectively) and an earlier age of alcohol use ( $F_{(1,\ 82)}=13.89,\ p=0.001$ ) by comparison with the CO group. The DERS total score ( $F_{(1,\ 82)}=3.80,\ p=0.048$ ), in the subscale of the emotional interference ( $F_{(1,\ 82)}=5.67,\ p=0.02$ ) and UPPS-P ( $F_{(1,\ 82)}=6.81,\ p=0.008$ ) scale scores, specifically in the subscales scores for a lack of perseverance ( $F_{(1,\ 82)}=4.56,\ p=0.04$ ), sensation seeking ( $F_{(1,\ 82)}=4.41,\ p=0.04$ ) and positive urgency ( $F_{(1,\ 82)}=5.55,\ p=0.02$ ) were also higher in the RAU group with respect to the CO condition. Sex-related differences showed that, regardless of group condition (RAU or CO), the girls displayed a higher STAI trait score ( $F_{(1,\ 82)}=13.61,\ p=0.001$ ), more emotional regulation problems assessed by DERS ( $F_{(1,\ 82)}=6.79,\ p=0.007$ ), specifically in the

subscales for emotional interference ( $F_{(1, 82)} = 4.27$ , p = 0.04) and emotional rejection ( $F_{(1, 82)} = 6.03$ , p = 0.02), and higher prefrontal symptoms ( $F_{(1, 82)} = 6.12$ , p = 0.006), above all those related to emotional behaviour ( $F_{(1, 82)} = 25.24$ , p < 0.001) assessed by PSI-20. Finally, the GROUP x SEX interaction was significant in the DERS subscale for emotional dysregulation ( $F_{(1, 82)} = 6.99$ , p = 0.009). Post hoc analysis showed that the RAU girls presented a higher result in these scales when compared to the RAU boys, but these sex-related differences were not found in the CO group (for more details see Table 1).

#### 3.1.2. Resting-state EEG

In the EC condition, the two-way MANOVA did not show any significant differences with respect to the GROUP factor. Sex-related differences were found, regardless of the GROUP condition (CO or RAU), showing that boys presented higher TBR CZ (F(1, 82) = 3.91, p = 0.046) compared with the girls, whereas the APF was higher in the girls (F(1, 82) = 4.02, p = 0.048). The interaction between GROUP x SEX was not significant in any of the variables registered in this condition (Fig. 1). In the EO condition, our results showed a significant GROUP x SEX

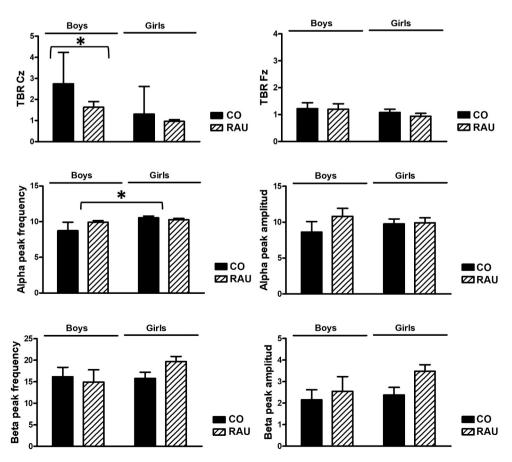


Fig. 1. TBR Cz, TBR Fz, APF, AFA, BPF and BPA under EC condition. Graphs represent comparisons between the CO and the RAU groups considering sex-related differences. Regardless of alcohol use, the boys presented a higher TBR CZ (p = 0.046) when compared to the girls, whereas the Alpha peak frequency was higher in the girls (p = 0.048). All data are the mean  $\pm$  SEM and statistically significant differences were considered when  $p \le 0.05$  (\*).

interaction in the TBR Cz (F(1, 82) = 6.62, p = 0.009) and TBR Fz variables (F(1, 82) = 6.48, p = 0.007), revealing that the boys from the RAU group displayed a higher TBR than the RAU girls, whereas these differences were not observed in the CO group (Fig. 2). Fig. 3 represents group differences, i.e. the CO and the RAU, in the resting state spectral power (decibels (dB)) under the eyes closed condition (3a) and the eyes open condition (3b). Finally, to identify the relationship between the cognitive variables and the APF, a Pearson's bivariate correlation analysis was performed (only correlations >0.4 are displayed). Additionally, the False Discovery Rate (FDR) was determined for multiple comparisons (51 cognitive variables), and the q values were extracted (only q < 0.05 were considered statistically significant). In the CO group, we observed significant positive Pearson's correlations between the APF and the correct answers and the TOT index of the d2 test (r =0.46, p = 0.003, q = 0.01, r = 0.50, p = 0.001, q = 0.01, respectively). In the RAU group, we found negative Pearson's correlations between the APF and the CON and TOT indexes of the d2 test (r = -0.47, p = 0.002, q= 0.034, r = -0.51, p = 0.001, q = 0.017, respectively), as well as with the copy time of the Rey Complex Figure (r = -0.54, p = 0.001, q = 0. 017).

#### 3.1.3. Neuropsychological assessment and cognitive network analysis

The RAU group, regardless of the sex, showed a higher VAR index of d2 test (F(1, 82) = 4.85, p = 0.03), a poorer recall in trial 5 (F(1, 82) = 10.59, p = 0.002), as well as in the free short and long-term memory recall trials of the TAVEC test (F(1, 82) = 6.65, p = 0.01; F(1, 82) = 7.13, p = 0.009, respectively) together with a higher number of total intrusions

(F(1, 82) = 4.38, p = 0.036) compared to the CO group. In addition, a higher total time in TESEN and total time of trail C (F(1, 82) = 5.76, p = 0.02; F(1, 82) = 5.83, p = 0.02, respectively), poorer semantic fluency (F(1, 82) = 4.13, p = 0.045) and prospective memory (F(1, 82) = 10.30, p = 0.002) was also found in the RAU condition with respect to the CO group. The SEX factor did not show ANY significant differences, whereas THE interaction between GROUP x SEX revealed that the boys in the RAU group performed worse than boys in the CO group in total time of trail A and D (F(1, 82) = 4.01, p = 0.049; F(1, 82) = 4.27, p = 0.042, respectively), the CAMBIOS test (F(1, 82) = 6.95, p = 0.01), the Backwards digit span (F(1, 82) = 6.70, p = 0.01), and the Total Colours/Words (F(1, 82) = 3.85, p = 0.048). Concerning the girls, we observed that risky alcohol use impaired the performance of the first trial of TAVEC test (F(1, 82) = 7.23, p = 0.009). More details and comparisons between the groups are displayed in Table 2.

Regarding the cognitive network analysis, we observed very similar patterns in the absolute weighted matrices of both groups, as can be seen in the boxes of speed processing and attention (SPA), and declarative memory (DM; Fig. 4). However, slight differences can be found in the most relevant nodes of each group (Fig. 5). For instance, the highest value of betweenness in the RAU group is short-term memory in the TAVEC task, which could mean that it acts as an important bridge or link between the nodes of the group, or the increase scores of TESEN time in betweenness, closeness, and strengths, only in RAU group, whereas in the d2 measures the centrality seems to be higher in the CO group. This is particularly relevant because, as we stated in the previous paragraph, the RAU group performed significantly worse than the others in this

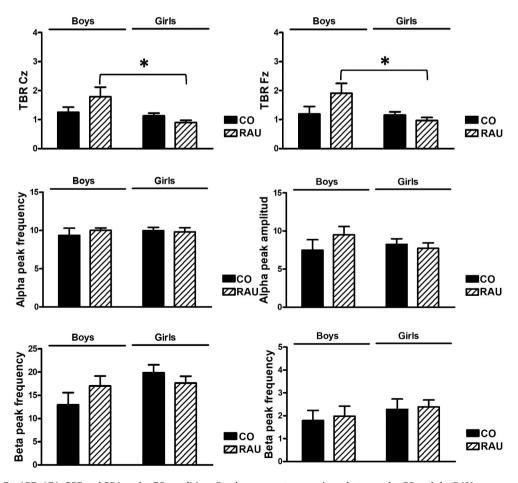


Fig. 2. TBR Cz, TBR Fz, APF, AFA, BPF and BPA under EO condition. Graphs represent comparisons between the CO and the RAU groups considering sex-related differences. Significant GROUP x SEX interaction was found in the TBR Cz (p = 0.009) and TBR Fz variables (p = 0.007), revealing that the boys from the RAU group displayed a higher TBR than the RAU girls, whereas these differences were not observed in the CO group. All data are the mean  $\pm$  SEM and statistically significant differences were considered when  $p \le 0.05$  (\*).

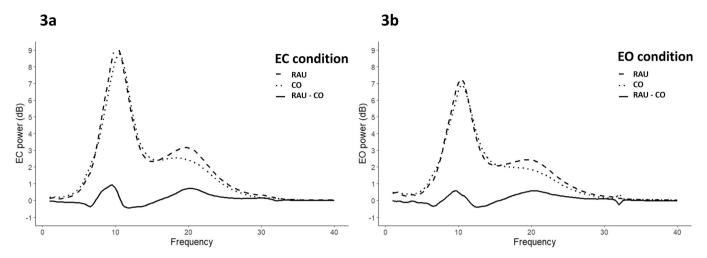
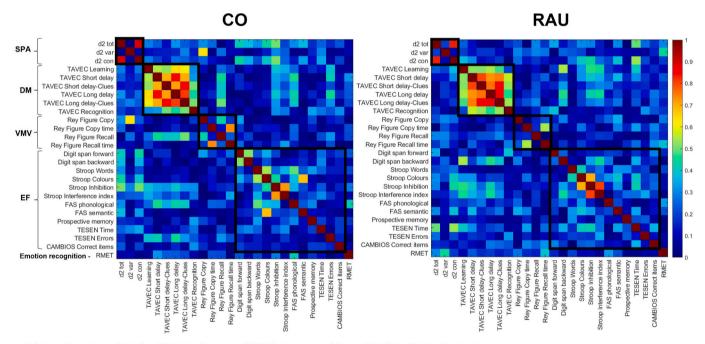


Fig. 3. The EEG power spectral density in the RAU and the CO groups, as well as the difference in activity between both (RAU - CO). The x-axis represents the frequency in Hz and the y-axis represents the power spectral density in dB under EC (3a) and EO (3b) conditions. The frequency range analyzed corresponds to the following frequency bands: delta (1 to 4 Hz), theta (4 to 8 Hz), alpha (8 to 12 Hz), beta (12 to 30 Hz) and gamma (30 to 45 Hz).



SPA: Speed Processing and Attention; DM: Declarative memory; VMV: Visual memory and visuospatial abilities; EF: Executive functions

Fig. 4. Cognitive connectome in the CO and the RAU groups. Pearson's correlation coefficients were used to build the matrix. The colour bar indicates the strength of the Pearson's correlation coefficients: the colder colours represent the weaker correlations, and the warmer colours represent the stronger correlations. Neuropsychological variables are grouped in cognitive modules: SPA (speed processing and attention); DM (declarative memory); VMV (visual memory and visuospatial abilities); EF (executive functions).

task. In addition, the patterns of strong weights (> |0.4|) were different as can be seen in the circle representation in Fig. 6. Finally, the number of connections from the SPA variables was higher in the CO group than in the RAU group, suggesting a possible greater involvement of attentional and speed processing functions in the performance of the other cognitive domains (Fig. 6).

#### 4. Discussion

In this study, we have investigated the psychological profile (emotional, behavioural, cognitive, and psychophysiological) of young individuals with RAU. Our results showed that young people with RAU presented greater difficulties in emotional regulation and impulsivity

compared with the CO group, with the emotional-related problems particularly relevant in the girls. With regard to cognition, a poorer performance in sustained attention, verbal memory, and certain executive functions related to cognitive flexibility, verbal fluency, and prospective memory was observed in the RAU group when compared with the young people in the CO group. Interestingly, our cognitive network analysis showed that in the RAU group, the verbal memory domain had the highest connection with other functions thereby facilitating and mediating fast activation among other cognitive variables. This result could indicate the relevance of this cognitive domain when treatment programmes are designed. Finally, our EEG analysis did not reveal significant differences in the TBR between the CO and the RAU groups. The interaction GROUP x SEX reached statistical significance showing that

# **Centrality Plot**

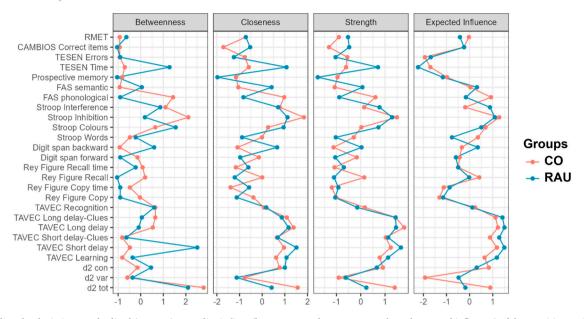
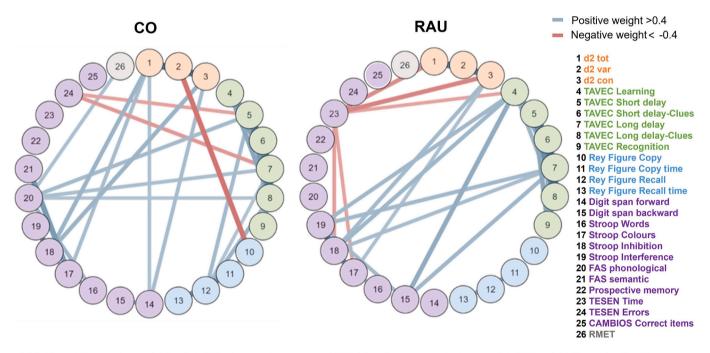


Fig. 5. Centrality plot depicting standardized (z-scores) centrality indices (betweenness, closeness, strength, and expected influence) of the cognitive variables in the CO and the RAU groups.



SPA: Speed Processing and Attention; DM: Declarative memory; VMV: Visual memory and visuospatial abilities; EF: Executive functions

Fig. 6. Connectograms showing those connections with a significant association (>0.4 (indicates that variables are moderately correlated (Akoglu, 2018; Dancey and Reidy, 2007)). The positive significant connections between two cognitive variables are displayed by red lines, and the negative significant connections by the blue lines. The neuropsychological variables are grouped in cognitive modules: SPA (speed processing and attention); DM (declarative memory); VMV (visual memory and visuospatial abilities); EF (executive functions). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

only the boys with RAU exhibited a higher TBR compared to the RAU girls, which could be used a psychophysiological index of impulsivity and poor cognitive control.

4.1.1. RAU was related to higher impulsiveness and emotional regulation difficulties

Despite the heterogeneity of the studies and the substances under

investigation, several studies have found a positive association between high impulsivity and drug abuse in adolescents (Chuang et al., 2017; Nawi et al., 2021). Thus, university students with higher levels of impulsivity reported starting to use cigarettes, alcohol, and cannabis at a younger age when compared to their less impulsive counterparts (Kollins, 2003). Furthermore, an increased impulsivity during youth seems to be a predictor of higher alcohol consumption in the future (Fernie et al., 2013). Research also suggests that different facets of impulsivity may predict different aspects of alcohol use. In our study, we found that the UPPS-P subscales of lack of perseverance, sensation seeking, and positive urgency showed significant differences between the CO and the RAU groups. Studies related to this topic have also found that sensation seeking was associated with alcohol use frequency and intake (Fischer and Smith, 2004; Whiteside and Lynam, 2003), whereas mixed results have been found regarding its relationship with alcohol-related problems (Shin et al., 2012). There are also mixed results in relation to lack of perserverance, with most research reporting that there is no link (Cyders et al., 2009), while a meta-analysis has revealed a link to alcohol intake, but not to alcohol related problems (Coskunpinar et al., 2013). Positive urgency was associated with alcohol-related problems suggesting the need to develop interventions to help young people avoid RAU when experiencing positive emotional states (Tran et al., 2018).

Conversely, it is plausible that engaging in such impulsive-related behaviours could lead to a heightened sense of positive emotion and feelings of well-being. This issue constitutes an important point on which to focus preventive interventions, e.g. aerobic exercise, mindfulness, psychoeducation, etc. because as our results have also shown, adolescents, particularly girls, usually have difficulties in self-regulating their emotions. The onset of adolescent alcohol abuse in women has been associated with more substance use and abuse/dependence, antisocial behaviour, behavioural disinhibition, mental health problems, as well as academic problems during adulthood (Foster et al., 2014). Interestingly, and regarding our observed differences between the groups (Table 1), a previous study applying DERS in a similar sample observed that the subscales of emotional rejection, emotional dysregulation, emotional confusion, and emotional interference were all positively associated with alcohol consequences, e.g. social interpersonal problems, self-perception and self-care, risky behaviours, academic/occupational consequences, or physiological dependence, among others. Moreover, emotional interference was also positively associated with the likelihood of experiencing any alcohol-related consequences in the future (Dvorak et al., 2014). In general, the evidence suggests a broad association between impulsivity traits and difficulties in emotional regulation with alcohol-related consequences, which were the specific aspects of these constructs that were associated with the most problematic outcomes. According to the motivational model discussed in the introduction, the higher impulsivity traits and emotional alterations observed in the RAU group, together with factors such as genetic predisposition to alcohol reactions, the socio-cultural environment, and past experiences with drinking, could contribute to their decision to drink alcohol. In this sense, these personality traits, categorized as historical factors in the motivational model, play a crucial role because they are the initial factors in this complex process (Cooper, 1994; Cooper et al., 2016; Cox and Klinger, 1988, 1990). In addition, although we did not investigate the reasons for alcohol consumption by our sample of young people, it appears that drinking alcohol to improve mood or regulate emotions is highly associated with potential long-term alcohol consumption problems (Kassel et al., 2000; Simons et al., 2000).

# 4.1.2. RAU increased TBR in boys, whereas APF was higher in CO girls

On the one hand, the TBR did not show significant differences between the CO and the RAU groups. This EEG measurement has scarcely been studied in problematic alcohol use among young populations, but possible explanations for this result include that our RAU group, despite scoring high on the AUDIT, averaged around moderate risk, indicating it is not a highly severe consumption profile (Contel Guillamon et al.,

1999). Furthermore, some of the studies conducted on the TBR in youth focused on BD, an alcohol consumption pattern which was not present in most of our RAU group (Holcomb et al., 2019; López-Caneda et al., 2017). On the other hand, our results showed that, in the EO condition, the TBRs at both of the Fz and Cz electrodes were larger for boys than for girls within the RAU group but remained the same across the sexes in the CO group (significant interaction GROUP x SEX). The TBR is considered to be a stable electrophysiological marker of executive control, wherein the faster beta waves are believed to represent an increased top-down inhibitory control, while the slower theta waves represent a lack of such control (Angelidis et al., 2018; Clarke et al., 2019; van Son et al., 2019a; van Son et al., 2019b). Indeed, several studies have found that TBRs are negatively correlated with performance in executive control tasks (Howells et al., 2010; Sari et al., 2016; Schutte et al., 2017; van Son et al., 2019a; van Son et al., 2019b), as well as negatively influencing other electrophysiological indicators of cognitive performance, such P300 latency (Clarke et al., 2019) and connectivity within the executive control network (van Son et al., 2019b). Several studies have also found that TBRs inversely correlate with measures of stress and anxiety (Kobayashi et al., 2020; Putman et al., 2010, 2014; Sari et al., 2016; Wei et al., 2020), suggesting that the top-down inhibitory mechanism reflected by the TBR influences both cognitive and emotional processes. However, our results seem to contradict this notion, as the girls tended to score higher than the boys in emotional dysregulation scales, while also displaying lower TBRs than the boys within the RAU group, but not the CO group. These paradoxical results might reflect the possibility that the lower TBR displayed by RAU girls compared to RAU boys is a compensatory mechanism through which they attempt to offset their higher stress and anxiety indices, even if unsuccessfully. This would indicate that, while the RAU boys seemed to be more vulnerable to executive functioning impairment related to cognitive performance, the RAU girls would be more vulnerable to impairments related to emotional regulation, thereby unable to reduce their stress/anxiety levels even despite a lower TBR. Indeed, Carbia et al. (2020) have also found that women tend to be more vulnerable to alcohol-related emotional impairments, while Stoica et al. (2021) showed that women tend to rely more on frontal top-down systems to regulate emotion than men, providing support for this notion. Finally, and regarding our observed differences in the condition of EO versus EC, it has been observed that opening and closing the eyes strongly modulates the electro- and magnetoencephalography (EEG and MEG) signals acquired during wakeful rest (Barry et al., 2007; Petro et al., 2022). With regard to the differences that we observed in the condition of EO versus EC, it has been suggested that frontal TBR is usually higher during mind wandering (MW) than during controlled thought. MW is typically studied with EO, focusing on a fixation cross during the resting state, as was carried out in our study (Krasich et al., 2020). An increased TBR was observed during MW, which is associated with decreased connectivity in the executive control network and increased connectivity in the default mode network (DMN) (van Son et al., 2019a, 2019b). As mentioned in the Introduction, heightened DMN connectivity has been reported in young individuals with BD (Correas et al., 2016). In addition to this finding, other research has indicated that high levels of MW were correlated with elevated AUDIT scores (Liu et al., 2023). Additionally, an increased MW has been linked to traits of impulsivity (Arabacı and Parris, 2018) and the reduced ability to inhibit habitual responses (Hawkins et al., 2022), factors that contribute to the high risk of alcohol consumption (Bernard et al., 2021; Dick et al., 2010). Longitudinal studies may be helpful to understand the relationship between these processes.

We also found that the girls, regardless of their alcohol consumption, displayed higher APFs when compared with the boys in the EC condition. Higher APFs have been reported to correlate positively with cognitive performance in working memory in healthy participants (Bertaccini et al., 2022; Clark et al., 2004) as well as being a protecting factor against cognitive impairment related to both normal and

pathological ageing (Garcés et al., 2013; Puttaert et al., 2021; Stacey et al., 2021). Furthermore, Affan et al. (2018) also report a slowing APF in BD young adults, as well as a positive correlation with theta power. The combination of these findings, together with the sex differences observed in the present study, suggests that the APF might also act as a factor modulating the negative impact that alcohol consumption has on cognitive performance. In this study some cognitive variables related to attention and speed processing were negatively correlated with APF in the RAU group (more details can be found in the Supplementary Material). According to this theory, the lower APF displayed by the boys would make them more susceptible to the cognitive-impairing effects of alcohol, possibly leading to the observed increased in TBRs in the RAU boys compared to the RAU girls. Nonetheless, we must also consider that it is necessary to conduct further studies with larger samples in which the ratio of boys and girls is similar, as well as longitudinal studies in order to understand the progression of these electrophysiological differences.

# 4.1.3. RAU was associated with cognitive deficits and a different cognitive network

In our study, RAU had a negative impact on several cognitive domains, such as sustained attention, verbal memory, and executive functions such as cognitive flexibility, verbal fluency, and prospective memory. According to this, there is evidence that adolescent alcohol users have a poorer performance in working memory, verbal learning and memory, visuospatial functioning, and motor speed tasks, and poorer performance has been observed with higher doses and an earlier age of onset (Nguyen-Louie et al., 2015). Unfortunately, there have been few longitudinal studies regarding the association between alcohol use and cognitive functioning in young people, but some evidence indicates that deficits in learning and memory following adolescent alcohol use endure into adulthood, even though the exposure has subsided (Mahedy et al., 2021; Mooney-Leber and Gould, 2018). Moreover, when alcohol is co-used with cannabis, additional attentional deficits appeared (Randolph et al., 2013). In our sample, we cannot exclude the effect of cannabis, although the consumption of our sample cannot be to be considered problematic, as indicated by the CAST questionnaire (< 4 points, Table 1). Previous research has also demonstrated that high-level cognition, such as prefrontal dependent functions, predicts the initiation of substance use in adolescence, lifetime drug use and abuse, and addiction treatment outcomes. The multimodal model of AUD, described by Rawls et al., 2021, proposes a causal role of cognition as a primary resilience factor and potential treatment target in AUD. On the other hand, studies about sex-specific trajectories of alcohol use are scarce, and much more in early ages. In our study, we wanted to analyze sexrelated differences in cognitive performance, but in general, we did not observe a different profile in deficits. Other studies, carried out on adult women with alcohol use disorder, revealed that chronic excessive drinking was associated with a myriad of cognitive deficits overlapping, but not identical to the pattern of deficits observed in men (Fama et al., 2020; Foster et al., 2014). In addition, although some evidence indicates that women develop cognitive deficits earlier or at lower lifetime consumption rates than men, its generalizability has not been clearly established (Fama et al., 2020).

Concerning cognitive network analysis, some differences were observed between groups in the modular organization, the strength of correlations between cognitive variables, and the characteristics of the networks. Our correlation matrixes did not reveal any significant differences in the relationships between the different cognitive variables in either group (CO and RAU). However, it is worth noting that the attentional domain, assessed through the d2 test, was more strongly associated with other neuropsychological variables in the CO group compared with the RAU group. This association was particularly evident in the performance of working memory and inhibitory control tasks (Digit span and Stroop tests, respectively) (Fig. 3). On the other hand, our centrality analysis revealed that the nodes with a higher association

with others (strength), as well as those with a greater predictive capacity of others (closeness) or with more ability to establish intermediate links between several nodes (betweenness), differed according to our experimental condition (Figs. 4 and 5). In the CO group, we observed that the total effectiveness variable of the d2 (TOT) was one of the nodes with the highest relevance in this group across the different indices evaluated. On the other hand, in the RAU group, the nodes with the highest relevance belonged to the variables from the TAVEC test (mainly short-term recall). In both groups, it appeared that the node corresponding to inhibitory capacity from the Stroop test was also relevant. With regard to TAVEC performance in the RAU group, Fig. 6 shows that this test was also associated with executive functions, such as working memory and inhibitory control, which may be a reflection of the greater effort made by this group during the performance of the verbal recall test. A recent study which also carried out the TAVEC test on BD young people revealed that the use of semantic strategies during the verbal recall was an executive function that could determinate the performance of the subjects (Porras Truque et al., 2023). Thus, different studies suggest that there is a relationship between the executive components of memory performance and global memory performance (Carbia et al., 2018; Gierski et al., 2020). According to network theory, cognition is not simply the summation of discrete abilities but is a dynamic network in which training in one cognitive domain augments skills in a different domain (Borsboom and Cramer, 2013; Jaeggi et al., 2011), our findings suggest that declarative verbal memory training could be a relevant cognitive area on which to focus preventive programmes. A recent study in a similar sample of young people also found poorer verbal memory performance associated with BD using the TAVEC test (Rodríguez Holguín et al., 2023). In our research, the impairments would not be associated with executive deficits, such as poor semantic clustering because no differences between the groups were observed in these trials (Table 2). However, they could be explained in part, by deficits in the storage and recollection processes of verbal episodic memory. On the other hand, we must also take into account potentially confounding factors, such as anxiety or impulsivity symptoms in our sample, which can impact cognitive performance. For instance, the higher number of intrusions committed by the RAU group (Table 2) could partly be due to the impulsivity traits observed in this condition (Table 1), although other factors such as poorer cognitive control to cope with distractions should be also considered. Finally, some studies have related these memory deficits to a higher rate of academic failure among these young people, as well as difficulties integrating the negative consequences of alcohol use constituting a risk factor in the subsequent development of an alcohol use disorder (Gierski et al., 2020). Thereby, the influence of cognitive deficits on a prognosis highlights the importance of detecting these deficits at an early stage, so that personalized treatment can be implemented. With regard to this, The Research Domain Criteria (RDoC: Insel et al., 2010) provides an evidence-based framework to standardize existing results offering a comprehensive and evolving list of neurocognitive constructs that have neurobiological correlates, as well as experimental protocols to assess these constructs. Nevertheless, the effectiveness of cognitive training as a preventative strategy has not been thoroughly investigated, despite the evidence suggesting that cognitive impairments frequently precede the onset of mental disease and may represent a non-specific prodromal phase for a broad range of psychological disorders (Mewton et al., 2017).

Finally, we would like to mention several limitations in our study. With regard to our sample, although it is not very small, testing more participants would have increased the statistical power needed to draw stronger conclusions from our results. In addition, the ratio of men and women was not homogenous in each group and therefore, the results of this study could be attributed to differential sex ratios in the different groups. Furthermore, our sample was primarily comprised of women and young white college students; consequently, it may not be possible to extrapolate our results to more diverse groups of college students or to young adults who do not attend college. Finally, as we performed a

cross-sectional study, we cannot determine the causal relationship between the variables registered, and additionally, data from self-reported questionnaires may have been overestimated or biased.

#### 5. Conclusions

In summary, the present research aimed to analyze the psychological profile (emotional, behavioural, cognitive, and psychophysiological) of college students with RAU by promising methodological approaches (cognitive networks or the FOOOF applied to the EEG resting-state data) to understand the features of this vulnerable population. Our results have revealed the presence of certain emotional and behavioural alterations, i.e. impulsivity, as well as cognitive deficits in different neuropsychological domains. Conversely, the analysis of their resting brain activity showed a significant GROUP x SEX interaction in the TBR Cz, revealing that boys from the RAU group displayed a higher TBR than the RAU girls, whereas these differences were not observed in the CO group. This result could be associated with a poorer cognitive control in the boys when compared to the girls from RAU condition. Moreover, the study of the cognitive networks suggests the key role of declarative verbal memory to improve other cognitive areas in the RAU group. It would be very interesting to develop longitudinal studies to understand the progression of these psychological alterations or the impact of prevention strategies. Furthermore, it is exceedingly challenging to ascertain whether some of these observed alterations were already present before alcohol consumption, constituting other risk factors. Finally, it is important to note that this study was observational, which means that it did not enable us to establish causal relationships between the variables investigated.

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#### CRediT authorship contribution statement

P. Sampedro-Piquero: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. F. Buades-Sitjar: Writing – original draft, Methodology, Formal analysis. A. Capilla: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis. C. Zancada-Menéndez: Writing – review & editing, Writing – original draft, Methodology, Formal analysis. A. González-Baeza: Writing – original draft, Methodology, Investigation. R.D. Moreno-Fernández: Writing review & editing, Writing - original draft, Methodology, Investigation

## Declaration of competing interest

The authors declare that there are no conflicts of interest.

#### Data availability statement

The data that support the findings of this study are available on request from the corresponding author.

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#### Appendix A. Supplementary data

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