

Sex Differences in Comorbidity Between Substance Use and Mental Health in Adolescents: Two Sides of the Same Coin

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Abstract

Background: This study aims to evaluate sex differences in alcohol and cannabis use and mental health disorders (MHD) in adolescents, and to evaluate the predictive role of mental health disorders for alcohol and cannabis use disorders (AUD and CUD respectively). **Method:** A sample of 863 adolescents from the general population (53.7% girls, Mage = 16.62, SD = 0.85) completed a computerized battery including questions on substance use frequency, the Brief Symptom Inventory, the Cannabis Problems Questionnaire for Adolescents – Short version, the Rutgers Alcohol Problem Index and the DSM-IV-TR criteria for AUD and CUD. Bivariate analyses and binary logistic regressions were performed. **Results:** Girls presented significantly more mental health problems and a higher prevalence of comorbidity between SUD and MHD. Obsessive-compulsive symptoms and phobic anxiety indicated a higher risk of AUD, whereas depression and interaction between hostility and obsessive-compulsive disorder indicated a higher risk of CUD. **Conclusions:** Comorbidity between SUD and MHD is high among adolescents, and significantly higher among girls.

Keywords: Alcohol, cannabis, mental health, gender differences, adolescents.

Resumen

Diferencias de Sexo en Comorbilidad entre Consumo de Sustancias y Salud Mental en Adolescentes: Dos Caras de la Misma Moneda.

Antecedentes: el objetivo de esta investigación es evaluar las diferencias de sexo en el uso de cannabis y alcohol y en trastornos de salud mental TSM en adolescentes, y el rol predictivo de los TSM sobre los trastornos por uso de alcohol y cannabis (TUA y TUC, respectivamente). **Método:** una muestra de 863 adolescentes de la población general (53,7% chicas, edad media = 16.62, DT = 0,85) completaron una batería informatizada sobre la frecuencia de uso de sustancias, el Inventario Breve de Síntomas, el Cuestionario de Problemas por Consumo de Cannabis - versión breve, el Índice de Rutgers de Problemas con el Alcohol y los criterios DSM-IV-TR para el TUA y TUC. Se realizaron análisis bivariados y de regresión logística binaria. **Resultados:** las chicas presentaron significativamente más problemas de salud mental y mayor prevalencia de comorbilidad entre TUS y TSM. El trastorno obsesivo-compulsivo (TOC) y la ansiedad fóbica indicaron un mayor riesgo de TUA, mientras que la depresión y la interacción entre hostilidad y TOC indicaron mayor riesgo de TUC. **Conclusiones:** la comorbilidad entre TUS y TSM es alta entre los adolescentes, y significativamente mayor entre las chicas.

Palabras clave: alcohol, cannabis, salud mental, diferencias de género, adolescentes.

Despite the substantial functional impairment associated with the coexistence of SUD and MHD in adolescents (Roberts et al., 2007), and recent recommendations to integrate their care (Brewer et al., 2017), research on adolescent comorbidity is still scarce and inconclusive (Skogen et al., 2014). Among the substances used by adolescents, alcohol and cannabis present some of the highest prevalences (Plan Nacional Sobre Drogas, 2019), raising concern given the increased risk of further alcohol and cannabis use disorders (Duncan et al., 2015). It is estimated that 20% of adolescents may experience a mental health problem during their adolescence (World Health Organization, 2003). Data indicates that 7.4% of children between 3 and 17 have a behavioral disorder, 7.1% have

a diagnosis of anxiety, and up to 3.2% have depression (Ghandour et al., 2018). In Spain, 3.2% of boys and 4.8% of girls between 15 and 24 years of age have a mental disorder. Particularly, 1.1% of boys and 1.4% of girls have a depressive disorder, and 1.1% of boys and 3.0% of girls have an anxiety disorder (Ministerio de Sanidad, Consumo y Bienestar Social, 2017).

The association between adolescent drinking and externalizing problems has been widely reported (Bousoño Serrano et al., 2019; Colder et al., 2013; Colder et al., 2017; Strandheim et al., 2011; Pedersen et al., 2018). Different studies also indicate that a significant association exists in adolescents between drinking (González et al., 2020), problem drinking (Chhoa et al., 2019), high-risk drinking (Ritcher et al., 2016) and depression; and between alcohol use (Ritcher et al., 2016), high-risk drinking (Villarosa et al., 2014), alcohol abuse (Low et al., 2008) and anxiety. Also, higher prevalence of alcohol use disorders (AUD) has been reported among adults with obsessive-compulsive disorder (Gentil et al., 2009). Although a clear and consistent association between internalizing symptoms and alcohol use problems is still not

evident (Homman et al., 2016), it has been associated with self-medication purposes (Foster et al., 2018). This is not surprising since the risk of addiction in adolescents has been linked to poor emotional regulation (Cornellà-Font et al., 2020). Other studies have failed to detect significant associations between alcohol and internalizing problems (Pedersen et al., 2018).

Cannabis use has been consistently associated to externalizing problems (e.g., Griffith-Lendering et al., 2011; Pedersen et al., 2018). It has been also repeatedly associated with internalizing problems in adolescents, such as depression (Rasic et al., 2013) and anxiety (Kedzior & Laeber, 2014). Other studies have failed to detect significant associations between cannabis use and internalizing symptoms (Griffith-Lendering et al., 2011), or cannabis abuse and anxiety (Low et al., 2008). Comorbidity between cannabis use and obsessive-compulsive disorders in young adults (Spradin et al., 2017) has also been reported. Finally, while abundant research has linked cannabis use in adolescents with an increased risk of psychosis later on (Marconi et al., 2016), this association in adolescents might disappear when accounting for confounding variables (Fonseca-Pedrero et al., 2020).

Furthermore, research with adult populations has consistently shown that sex differences exist in the prevalence and features of the comorbidity between MHD and SUD (e.g., Frem et al., 2017; Khan et al., 2013). However, not many studies have evaluated sex differences in the association between mental health and substance use problems in adolescents, and inconsistent results have been reported. Data has shown that girls with SUD often present with higher rates of comorbidity (Robert et al., 2007), and girls in SUD treatment present with higher levels of mental health problems. Other studies failed to find significant sex differences in the associations between mental health symptoms and alcohol and other drugs use (Heradsveit et al., 2018).

Evidence-based interventions taking into account both SUD and MHD in adolescents are currently underdeveloped (Brewer et al., 2017). In order to design tailored treatment strategies, clarifying this specific association between SUD and MHD seems crucial. Moreover, more research is needed to be able to identify specific treatment approaches that address sex differences in comorbidity, particularly among adolescents (Dir et al., 2017). The purpose of this study is two-fold: 1) to evaluate sex differences in alcohol and cannabis use patterns and mental health symptoms, and 2) to evaluate the predictive role of MHD with regards to alcohol and cannabis use disorders. With this aim, secondary analyses have been carried out with data from a research study conducted between 2010 and 2012 (Fernández-Artamendi et al., 2013).

Method

Participants

The initial sample was made up of 863 adolescents from nine high schools offering academic and technical courses from the Principality of Asturias (Spain). The exclusion criteria for this study were: 1) Not providing a valid questionnaire according to the criteria established by the Infrequency Scale, as indicated below and 2) being 18 years of age or older. A total of 772 participants provided a valid questionnaire (89.5%) and 684 were 18 years or younger (79.26% of the initial sample). These 684 participants (53.7% girls; mean age = 16.62 years; SD = 0.852) made up the final sample. The descriptive characteristics of participants are shown in Table 1.

Instruments

Sociodemographic information. Participants were requested to provide information on their age and sex.

Frequency and patterns of alcohol and cannabis use in the last month were evaluated through the items of the European School Survey Project on Alcohol and Other Drugs Student Questionnaire (European Monitoring Centre for Drugs and Drug Addiction [EMCDDA], 2007). These questions measured the frequency of substance use using a Likert scale (1-7) corresponding to 7 alternatives (namely: never/1-2 times/3-5/6-9/10-19/20-39/more than 40 times).

Alcohol-related problems. To detect the presence of alcohol-related problems, the Spanish version (López-Núñez et al., 2012) of the Rutgers Alcohol Problem Index (RAPI; White & Labouvie, 1989), validated in this study, was used. Only those adolescents reporting any alcohol use were presented the RAPI. This version has shown excellent reliability (Cronbach's $\alpha = .91$) with adolescents (López-Núñez et al., 2012). The self-report includes 23 questions with Likert-type responses (where 0 = never; 1 = 1 to 2 times; 2 = 3 to 5 times; 3 = more than 5 times) on the frequency of alcohol-related events that occurred in the previous year. A cut-off level of 7 points in the RAPI showed a high reliability (Cronbach's Alpha = .87) and a sensitivity and specificity of 81.9% and 71.3% respectively for alcohol dependence.

Cannabis-related problems. To evaluate problems associated to cannabis use, the Spanish version (Fernández-Artamendi et al., 2012) of the Cannabis Problems Questionnaire for Adolescents – Short Form (CPQ-A-S; Proudfoot et al., 2010), validated as part of this study, was used. Only adolescents reporting any cannabis use were presented the CPQ-A-S. This questionnaire includes 12 dichotomous items on the presence of different problems commonly associated to cannabis use. Reliability of CPQ-A-S is moderate (Cronbach's Alpha = .70). A score of 3 points presents a sensitivity and specificity of 83% and 77.5% respectively for cannabis dependence (Fernández-Artamendi et al., 2012).

Presence of a DSM-IV-TR diagnosis of abuse or dependence of alcohol and cannabis was evaluated by means of self-reported dichotomous questions on the corresponding criteria. According to DSM-IV-TR (American Psychological Association [APA], 2000) presence of one or more symptoms of abuse was considered a diagnosis of alcohol/cannabis abuse, and presence of three or more criteria of dependence, was considered a diagnosis of alcohol/cannabis dependence (clustered within a year). For analytic purposes, diagnoses were merged into alcohol use disorder (AUD) in case alcohol abuse or alcohol dependence was detected; and cannabis use disorder (CUD) in case cannabis abuse or cannabis dependence was detected.

Psychopathological problems were assessed by means of the Brief Symptom Inventory (BSI) by Derogatis and Melisaratos (1983). This instrument yields scores on nine dimensions and one global index: somatization, obsessive-compulsive (OCD), interpersonal sensitivity (IS), depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, and Global Severity Index (GSI). Reliability of each dimension of the BSI ranges between .72 and .95 (Pereda et al., 2007). Following the administration manual of the BSI (Derogatis & Melisaratos, 1983), positive diagnoses for each dimension were calculated following normative scores.

An infrequency scale was included in the assessment battery in order to detect questionnaires that had been filled up in a random

or erratic manner. The instrument was the Oviedo Infrequency Scale (INF-OV; Fonseca-Pedrero et al., 2009) which evaluates the participants' agreement or disagreement with 12 items such as the following: 'Have you ever seen a film on television?'. Following the rules established by the authors, questionnaires with more than three wrong answers were excluded from statistical analyses.

Procedure

All the data was collected through self-administered questionnaires that were included as part of a computerized survey that permits the design and application of an adaptive test with all the instruments. The software was set up to alert respondents if they gave an incongruent answer and to warn them if they left any blank item. All students in courses aimed at adolescents with ages ranging from 14 to 18 years (from the third year of secondary education up to technical training and baccalaureate courses), from nine randomly selected high schools in the region, participated in the study. The study was approved by the Ethics Committee of the Ministry of Science and Innovation, and the Department of Education of the regional government. Individual and family consent was obtained through the schools following their regular protocols. All participants filled up the questionnaires in their own classrooms, with no teaching staff present. Trained researchers supervised the application of the survey, guaranteeing that students respected the privacy of their classmates

Data analysis

First of all, descriptive analyses of demographic variables, substance use, substance use problems and mental health symptoms

were calculated, for the full sample and by sex. Analysis of variance (ANOVA) and chi-square statistic with Yates correction for continuity were carried out to evaluate sex differences in continuous variables evaluating substance use, substance use problems and mental health symptoms. Secondly, chi-square statistics with Yates correction for continuity, and the Fisher exact test were carried out to evaluate sex differences in the prevalence of MHD, according to thresholds established by the BSI, among participants with AUD and CUD. Effect sizes were calculated using Phi coefficient (Φ) and eta-squared for all the aforementioned chi-square and ANOVA calculations, respectively. Confidence level was set at 95%. Thirdly, two logistic regressions were carried out to evaluate the predictive role of a positive diagnosis in each mental health dimension with regards to the presence of AUD or CUD. With this purpose, firstly, chi square odd ratios for each mental health diagnosis and AUD/CUD were calculated. Those variables reporting significant odd ratios were included in the model. Secondly, possible interactions between mental health diagnoses and sex, and between every two mental health diagnoses were calculated with the Breslow-Day test. Significant interactions were also included in the models. Finally, two independent logistic regression models (one for AUD, and one for CUD) were carried out with backwards stepwise elimination conditional model. Confidence level was 95%. The statistical package SPSS Version 26.0 was used for all analyses.

Results

Descriptive results (Table 1) indicate that frequent (monthly) use of alcohol is considerably prevalent in this sample (77.5%), and that 29.8% of adolescents report having intoxicated with alcohol at least once in this period; with no significant sex

Table 1
Descriptive analyses and gender differences in substance use prevalence, substance use problems and mental health scores

	Total (n = 684) [M (SD)]	Boys (n = 367) [M (SD)]	Girls (n = 317) [M (SD)]	Statistic (p-value)	Effect size
Age	16.62 (0.85)	16.76 (0.87)	16.45 (0.80)	23.60 ($\leq .001$) ¹	.033
Alcohol last month (%)	77.5%	79.0%	75.7%	0.886 (.346) ²	-.040
Drunk last month (%)	29.8%	32.7%	26.5%	2.834 (.092) ²	-.068
Cannabis last month (%)	17.7%	22.3%	12.3%	11.097 (.003) ²	-.131
RAPI (among drinkers)	6.12 (7.55)	6.66 (7.92)	5.49 (7.05)	4.121 (.043) ¹	.006
CPQ-A-S (among users)	.57 (1.45)	.74 (1.69)	.36 (1.08)	4.604 (.033) ¹	.017
AUD (%)	27.2%	33.0%	20.5%	12.727 ($\leq .001$) ²	-.140
CUD (%)	9.6%	14.4%	4.1%	19.691 ($\leq .001$) ²	-.175
Somatization	0.99 (0.85)	0.92 (0.89)	1.06 (0.79)	5.004 (.026) ¹	.007
OC	0.89 (0.86)	0.82 (0.85)	0.96 (0.86)	4.590 (.033) ¹	.007
IS	0.79 (0.84)	0.77 (0.85)	0.81 (0.83)	.363 (.547) ¹	.001
Depression	1.08 (0.75)	1.02 (0.78)	1.14 (0.71)	3.983 (.046) ¹	.006
Anxiety	1.06 (0.84)	1.04 (0.86)	1.09 (0.82)	.724 (.395) ¹	.001
Hostility	0.96 (0.92)	0.91 (0.95)	1.01 (0.87)	1.970 (.161) ¹	.003
Phobic Anxiety	0.92 (0.86)	0.89 (0.88)	0.95 (0.84)	.804 (.370) ¹	.001
Paranoid ideation	0.96 (0.89)	0.83 (0.88)	1.11 (0.88)	16.894 ($\leq .001$) ¹	.024
Psychoticism	0.93 (0.82)	0.90 (0.83)	0.98 (0.81)	1.665 (.197) ¹	.002
GSI	0.42 (0.46)	0.38 (0.45)	0.46 (0.46)	4.877 (.028) ¹	.007

Notes: RAPI: Rutgers Alcohol Problem Index; CPQ-A-S: the Cannabis Problems Questionnaire for Adolescents – Short Form; AUD: Alcohol Use Disorder; CUD: Cannabis Use Disorder; OCD: Obsessive-Compulsive Disorder; IS: Interpersonal Sensitivity; GSI: Global Severity Index
¹ANOVA; ²Chi-square

differences. However, among drinkers, boys presented with a significantly higher severity of alcohol-related problems according to the RAPI. As of cannabis, significantly more boys (22.3%) than girls (12.3%) had used it in the last month. Among cannabis users, boys presented also with significantly more cannabis-related problems. The prevalence of AUD and CUD was also significantly higher among boys. Regarding mental health, girls presented with significantly more symptoms of somatization, paranoid ideation, OC and depression. Results of the GSI also show significantly higher scores among girls. For all mental health dimensions, the effect sizes were small, except for paranoid ideation, which was between medium and large.

As reported in Table 2, among adolescents with AUD, a significantly higher number of girls resulted positive for somatization, paranoid ideation and hostility. Among adolescents with CUD, girls were more likely to be positive for OCD, hostility and interpersonal sensitivity. Also, girls with CUD presented with a higher prevalence of positive cases than boys according to the GSI.

Finally, two logistic regression models were calculated. Regarding the AUD model, preliminary analyses indicated that anxiety, obsessive-compulsive, hostility, depression, phobic anxiety and the interaction between depression and paranoid ideation were significant predictors of AUD ($p < .05$), and consequently were included in the model. As of the CUD model, preliminary analyses indicated that anxiety, psychoticism, paranoid ideation, obsessive-compulsive, hostility, depression, interpersonal sensitivity, phobic anxiety and the interaction between obsessive-compulsive and sex, hostility and sex, interpersonal sensitivity and sex, and hostility

and obsessive-compulsive were significant predictors ($p < .05$). Consequently, they were all included in the CUD model.

Results from logistic regression model for AUD (Nagelkerke $R^2 = .044$) indicate that a positive diagnosis of obsessive-compulsive disorder and phobic anxiety were significant predictors of AUD.

As of the CUD model (Nagelkerke $R^2 = .078$), depression and the interaction between hostility and obsessive-compulsive were significant predictors of CUD.

Discussion

To our knowledge, no previous study has evaluated sex differences in comorbidity of SUD and MHD among Spanish adolescents. Our results indicate that boys present with significantly more substance use problems and disorders, whereas girls reported significantly more mental health problems. Comorbidity between MHD and SUD was also significantly higher among girls.

In our study, no significant sex differences were found in the frequency of alcohol drinking or intoxication, in line with previous research with Spanish adolescents (Prieto-Ursúa et al., 2020). Only a significantly higher number of boys reported using cannabis in the last month compared to girls. These trends are in line with current national data (Plan Nacional Sobre Drogas, 2019). However, the prevalence of AUD and CUD was significantly higher in boys than in girls, in line with previous studies (Duncan et al., 2015; Goldstein et al., 2012). Moreover, and among users, alcohol and cannabis-related problems were significantly higher in boys than in girls. Previous studies have indicated that men are more likely to be hazardous drinkers (Erol & Karpayak, 2015), and that early

Table 2
Prevalence (%) of positive cases by sex in the Brief Symptom Inventory dimensions among adolescents with AUD and CUD

	Alcohol Use Disorder (AUD)					Cannabis Use Disorder (CUD)				
	Boys (%) n = 121	Girls (%) n = 65	χ^2	p	Effect size	Boys (%) n = 53	Girls (%) n = 13	χ^2	p	Effect size
Anxiety	28.1	34.4	0.499	.480	.065	30.2	50.0**	*	.310	.162
Somatization	21.5	43.1	8.547	.003	.227	24.5	53.8	*	.050	.254
Psychoticism	19.0	24.6	0.500	.480	.066	26.4	46.2	*	.190	.171
Paranoid	5.8	16.9	4.795	.029	.163	9.4	30.8	*	.067	.247
OCD	19.0	29.2	1.977	.160	.117	24.5	69.2	*	.006	.377
Hostility	10.7	33.8	13.300	≤.001	.282	13.2	61.5	*	.001	.459
Depression	20.7	20.0	0.000	1.000	-.008	30.2	38.5	*	.741	.071
Interpersonal Sensitivity	5.0	10.8	*	.226	.109	7.5	46.2	*	.003	.428
Phobic Anxiety	30.6	43.1	2.382	.123	.125	35.8	61.5	1.886	.170	.208
GSI	4.1	7.7	0.470	.323	.075	5.7	38.5	*	.006	.400

Note: OCD: Obsessive-Compulsive Disorder; GSI: Global Severity Index
*Fisher exact test
** n = 12 due to missing values

Table 3
Logistic regression model showing mental health dimensions significantly predicting the presence of Alcohol Use Disorders among adolescents

	B	Df	p	OR	CI 95%
Depression	.968	1	.004	2.631	1.374 5.040
Hostility * OCD	1.179	1	.004	3.252	1.450 7.292

Table 4
Logistic regression model showing mental health dimensions significantly predicting the presence of Cannabis Use Disorders among adolescents

	B	Df	p	OR	CI 95%
OCD	.671	1	.007	1.957	1.202 3.186
Phobic Anxiety	.517	1	.013	1.677	1.116 2.520

drinking is more associated with problem drinking in males (Tedor et al., 2018), for whom drinking is more closely associated with negative consequences such as aggression (Gussler-Burkhardt & Giancola, 2005). On the other hand, women have shown to be less likely to engage in problem drinking (Erol & Karpyak, 2015). Similar results have been reported on cannabis use, since girls present with more protective factors than men that prevent them from escalating their cannabis use (Butters, 2004). Finally, and regarding mental health, world reports from the World Health Organization (WHO, n.d.) concludes that rates of depression, anxiety and somatic complaints are higher among women. Our results show a similar trend since girls reported significantly higher scores in somatization, obsessive-compulsive symptomatology and depression, and also in paranoid ideation and overall global severity.

Among adolescents with AUD, girls presented with higher rates of comorbidity than boys in all areas, in line with previous studies (Goldstein et al., 2012; Robert et al., 2007). However, according to our results, only the prevalence of somatization, hostility and paranoid ideation was significantly higher among girls with AUD than among boys with AUD. Higher rates of somatization among young female heavy drinkers have already been reported (Laukkanen et al., 2001; Milani et al., 2004). Also, drinking among women has been linked to masculinity and aggression (Patr6-Hernández et al., 2019), which could be ultimately related to the high levels of hostility found in our study. Moreover, girls have shown higher sensitivity (Erol & Karpyak, 2015; Salvatore et al., 2017) and vulnerability to alcohol effects and their interpersonal consequences (Chandley et al., 2014; Presley & Pimentel, 2006). Drinking among women goes against traditional gender norms (Fernández-Rodríguez et al., 2019), making it is less socially acceptable for them (Harrison & Esqueda, 2000). Consequently, alcohol use among women is associated with increased social and personal stigma (da Silveira et al., 2018) and might be linked to additional mental health problems. As of paranoid ideation, previous studies have also reported high levels of paranoid ideation among women with SUD (Newland et al., 2015), which the authors link to possible symptoms of anxiety and untreated withdrawal symptoms. However, further studies are required that confirm this hypothesis.

As of CUD, rates of comorbidity are also higher among girls in all areas. However, only the prevalence of obsessive-compulsive disorder, hostility, interpersonal sensitivity and global severity resulted significantly higher among girls. Effect sizes indicate a moderate effect, which might reflect a considerable clinical relevance of these sex differences, with a more severe profile of mental health problems among girls than among boys with CUD. Our results are in line with previous research indicating that cannabis use is more strongly linked to aggressiveness and conduct problems in girls than in boys (Pedersen et al., 2001). Again, cannabis use has been commonly associated with male typicality and traditional male gender norms, whereas it goes against traditional female roles (Hemsing & Greaves, 2020). Moreover, these authors conclude that cannabis use is associated with aggressive masculinity among girls. These results might explain the higher levels of hostility and interpersonal sensitivity found in our sample of girls with CUD. Finally, the association between OCD and CUD had already been reported (Spradin et al., 2017), and CUD might emerge as a consequence of an excessive use of cannabis as a coping mechanism against intruding thoughts.

In our study, the high rates of comorbidity between OCD and CUD among girls suggests that young female adolescents might be more vulnerable to this association. However, these hypotheses still require further research.

Finally, and according to logistic regression models, depression and the interaction between obsessive-compulsive disorder and hostility increased three-fold the likelihood of presenting an AUD. These results would confirm previous associations reported between high-risk drinking patterns, alcohol abuse and depression (Chhoa et al., 2019; Low et al., 2008; Ritcher et al., 2016). Previous studies have also reported a significant association between externalizing problems and drinking (Colder et al., 2013; Colder et al., 2017; Strandheim et al., 2011). Interestingly, according to our results, externalizing problems represented by hostility (which includes irritability, urges to break things, arguments and outburst of temper) would be a risk factor only when interacting with internalizing problems such as intrusive thoughts of OCD. It could be that alcohol use can become problematic when drinking is used to deal with intrusive thoughts in an impulsive manner among these adolescents. This is of great clinical relevance given that comorbidity between AUD and OCD has shown specific associated risks such as suicidal thoughts (Gentil et al., 2009).

Regarding CUD, logistic regression indicates that obsessive-compulsive disorder and phobic anxiety increased nearly two-fold the likelihood of presenting a CUD. These results corroborate the results by Spradlin et al. (2017), who find a specific association between OCD and cannabis misuse. Additionally, our results are in line with the results from the meta-analyses by Kedzior and Laeber (2014), linking anxiety and cannabis use disorder. However, in our study, this association was specific only to phobic anxiety, which includes fear of crowds, public spaces and transports. It has been reported that cannabis users have difficulties and present with evasive styles when coping with anxiety (Wilcockson & Sanal, 2016), and that social anxiety and avoidance are closely related with coping motives for cannabis use (Buckner & Zvolensky, 2014), which is in turn linked to cannabis dependence (Johnson et al., 2010). Further studies should corroborate these associations. Surprisingly, and despite the sex differences found in the bivariate analyses, no significant interactions between sex and mental health problems have resulted significant in the logistic regression models. This suggests that additional variables, not included here, might be mediating the sex differences detected in the association between MHD and SUD.

The present study has several limitations. Firstly, this is a secondary analysis of a previous research, and epidemiological data might not be up to date with most current trends. Also, no data could be collected regarding additional sociodemographic variables that could influence the evaluated relationships. However, and given the considerable necessity of evaluating comorbidity between substance use and mental health, particularly among Spanish adolescents, as well as of improving our knowledge on sex differences in this regard, the present results are of great interest. Secondly, only alcohol and cannabis use patterns, problems and disorders have been thoroughly evaluated in our study. Further research should address comorbidity of additional substances and SUD, such as tobacco, the second most used substance by this population. The use of these substances could have additional impacts on the results of the relationships analyzed in this study. Besides, our study did not analyze the effect of possible comorbidities in mental health dimensions, neither comorbidities in substance use disorders.

Further studies are necessary that address these issues. Thirdly, screening tests have been used to evaluate MHD. Although this has allowed us to carry out a comprehensive evaluation of multiple MHD, conclusions on the rates of comorbidity for the reported diagnoses have to be interpreted with caution. Finally, the cross-sectional nature of our study prevents us from discussing possible causality in the reported associations.

Despite boys presenting more alcohol and cannabis-related problems, as well as higher prevalence of AUD and CUD, girls reported significantly more mental health problems and higher comorbidity between MHD and SUD. In particular, depression and the interaction between hostility and obsessive-compulsive symptoms indicated a higher risk of AUD, whereas obsessive-compulsive symptoms and phobic anxiety increased the risk of presenting CUD. Further studies should continue evaluating the associations between SUD and MHD and symptoms in adolescents, focusing on sex differences.

Our study stresses the importance of addressing mental health problems among adolescents presenting with substance use problems and disorders, in order to provide a comprehensive psychological assistance. Particularly, special attention needs to be placed on adolescent girls, who present with significantly more comorbid mental health problems. Finally, our results indicate that providing appropriate mental health care services and prevention programs to adolescents could contribute to reduce substance use problems in this population.

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References

- American Psychological Association (2000). *Diagnostic Statistical Manual of Mental Disorders - IV Edition Revised*. American Psychological Association.
- Bousoño Serrano, M., Al-Halabí, S., Burón, P., Garrido, M., Díaz-Mesa, E., Galván, G., García-Álvarez, L., Velasco, A., Wasserman, C., Carli, V., Hoven, C., Sarchiapone, M., Wasserman, D., Bousoño, M., García-Portilla, M. P., Iglesias, C., Sáiz, P. A., & Bobes, J. (2019). Predictive factors of alcohol consumption in adolescents: Data from 1-year follow-up prospective study. *Adicciones*, *31*(1), 52-63. <http://dx.doi.org/10.20882/adicciones.998>
- Brewer, S., Godley, M., & Hulveshorn, L. A. (2017). Treating mental health and substance use disorders in adolescents. *Current Psychiatric Reports*, *19*(1), 5. <https://doi.org/10.1007/s11920-017-0755-0>
- Buckner, J. D., & Zvolensky, M. J. (2014). Cannabis and related impairment: The unique roles of cannabis use to cope with social anxiety and social avoidance. *The American Journal on Addictions*, *23*(6), 598-603. <https://doi.org/10.1111/j.1521-0391.2014.12150.x>
- Butters, J. E. (2004). The impact of peers and social disapproval on high-risk cannabis use: Gender differences and implications for drug education. *Drugs: Education, Prevention and Policy*, *11*(5), 381-390. <https://doi.org/10.1080/09687630410001704437>
- Chandley, R. B., Luebke, A. M., Messman-Moore, T. L., & Rose, M. W. (2014). Anxiety sensitivity, coping motives, emotion dysregulation, and alcohol-related outcomes in college women: A moderated-mediation model. *Journal of Studies on Alcohol and Drugs*, *75*(1), 83-92. <https://doi.org/10.15288/jsad.2014.75.83>
- Chhoa, K. H., Zakaria, H., & Rahman, F-N-A. (2019). Problematic alcohol use and depression in secondary school students in Miri, Malaysia. *Pediatrics International*, *61*(3), 284-292. <https://doi.org/10.1111/ped.13789>
- Colder, C. R., Frndak, S., Lengua, L. J., Read, J. P., Hawk Jr., L. W., & Wieczorek, W. F. (2017). Internalizing and externalizing problem behavior: A test of a latent variable interaction predicting a two-part growth model of adolescent substance use. *Journal of Abnormal Child Psychology*, *46*(2), 319-339. <https://doi.org/10.1007/s10802-017-0277-6>
- Colder, C. R., Scalco, M., Trucco, E. M., Read, J. P., Lengua, L. J., Wieczorek, W. F., & Hawk Jr., L. W. (2013). Prospective associations of internalizing and externalizing problems and their co-occurrence with early adolescent substance use. *Journal of Abnormal Child Psychology*, *41*(4), 667-677. <https://doi.org/10.1007/s10802-012-9701-0>
- Cornellà-Font, M. G., Viñas-Poch, F., Juárez-López, J. R., & Malo-Cerrato, S. (2020). Risk of addiction: Its prevalence in adolescence and its relationship with security of attachment and self-concept. *Clínica y Salud*, *31*(1), 21-25. <https://doi.org/10.5093/clysa2020a1>
- da Silveira, P. S., Casela, A. L. M., Monteiro, É. P., Ferreira, G. C. L., de Freitas, J. V. T., Machado, N. M., Noto, A. R., & Ronzani, T. M. (2018). Psychosocial understanding of self-stigma among people who seek treatment for drug addiction. *Stigma and Health*, *3*(1), 42-52. <https://doi.org/10.1037/sah0000069>
- Derogatis, L. R., & Melisaratos, N. (1983). The Brief Symptom Inventory: An introductory report. *Psychological Medicine*, *13*(3), 595-605. <https://doi.org/10.1017/S0033291700048017>
- Dir, A. L., Bell, R. L., Adams, Z. W., & Hulveshorn, L. A. (2017). Gender differences in risk factors for adolescent binge drinking and implications for intervention and prevention. *Frontiers in Psychiatry*, *8*, 289. <https://doi.org/10.3389/fpsy.2017.00289>
- Duncan, S. C., Gau, J. M., Farmer, R. F., Seeley, J. R., Kosty, D. B., & Lewinshon, P. M. (2015). Comorbidity and temporal relations of alcohol and cannabis use disorders from youth through adulthood. *Drug and Alcohol Dependence*, *149*, 80-86. <https://doi.org/10.1016/j.drugalcdep.2015.01.025>
- European Monitoring Centre for Drugs and Drug Addiction (2007). *The 2007 ESPAD Report. Substance Use Among Students in 35 European Countries*. European Monitoring Centre for Drugs and Drug Addiction. http://www.espad.org/sites/espad.org/files/The_2007_ESPAD_Report-FULL_091006.pdf
- Erol, A., & Karpyak, V. M. (2015). Sex and gender-related differences in alcohol use and its consequences: Contemporary knowledge and future research considerations. *Drug and Alcohol Dependence*, *156*, 1-13. <https://doi.org/10.1016/j.drugalcdep.2015.08.023>
- Fernández-Artamendi, S., Fernández-Hermida, J.R., Muñoz-Fernández, J., Secades-Villa, R., & García-Fernández, G. (2012). Screening of cannabis-related problems among youth: The CPQ-A-S and CAST questionnaires. *Substance Abuse, Treatment, Prevention and Policy*, *7*(13), 1-9.
- Fernández-Artamendi, S., Fernández-Hermida, J.R., García-Fernández, G., Secades-Villa, R., & García-Rodríguez, O. (2013). Motivation to change and barriers to treatment among young cannabis users. *European Addiction Research*, *19*, 29-41.
- Fernández-Rodríguez, M. A., Dema Moreno, S., & Fontanil-Gómez, Y. (2019). The influence of gender roles in alcohol consumption: A qualitative study of adolescents and young adults in Asturias. *Adicciones*, *31*(4), 260-273. <http://dx.doi.org/10.20882/adicciones.1003>
- Fonseca-Pedrero, E., Lucas-Molina, B., Pérez-Albéniz, A., Inchausti, F., & Ortuño-Sierra, J. (2020). Psychotic-like experiences and cannabis use in adolescents from the general population. *Adicciones*, *32*(1), 41-51. <http://dx.doi.org/10.20882/adicciones.1149>
- Fonseca-Pedrero, E., Paño-Piñero, M., Lemos-Giráldez, S., Villazón-García, U., & Muñoz, J. (2009). Validation of the Schizotypal Personality

- Questionnaire - Brief Form in adolescents. *Schizophrenia Research*, 111(1-3), 53-60. <http://dx.doi.org/10.1016/j.schres.2009.03.006>
- Foster, K. T., Hicks, B. M., & Zucker, R. A. (2018). Positive and negative effects of internalizing on alcohol use problems from childhood to young adulthood: The mediating and suppressing role of externalizing. *Journal of Abnormal Psychology*, 127(4), 394-403. <https://doi.org/10.1037/abn0000337>
- Frem, Y., Torrens, M., Domingo-Salvany, A., & Gilchrist, G. (2017). Gender differences in lifetime psychiatric and substance use disorders among people who use substances in Barcelona, Spain. *Advances in Dual Diagnosis*, 10(2), 45-56. <https://doi.org/10.1108/ADD-01-2017-0002>
- Ghandour, R.M., Sherman, L.J., Vladutiu, C.J. Ali, M.M., Lynch, S.E., Bitsko, R.H., & Blumberg, S.J. (2018). Prevalence and treatment of depression, anxiety, and conduct problems in U.S. children. *The Journal of Pediatrics*, 206, 256-267.
- Gentil, A. F., de Mathis, M. A., Torresan, R. C., Diniz, J. B., Alvarenga, P., do Rosário, M. C., Cordoli, A. V., Torres, A. R., & Miguel, E. C. (2009). Alcohol use disorders in patients with obsessive-compulsive disorder: The importance of appropriate dual-diagnosis. *Drug and Alcohol Dependence*, 100(1-2), 173-177. <https://doi.org/10.1016/j.drugalcdep.2008.09.010>
- Goldstein, R. B., Dawson, D. A., Chou, S. P., & Grant, B. F. (2012). Sex differences in prevalence and comorbidity of alcohol and drug use disorders: Results from wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. *Journal of Studies on Alcohol and Drugs*, 73(6), 938-950. doi: <https://doi.org/10.15288/jsad.2012.73.938>
- González, M. T., Espada, J. P., Fernández-Martínez, I., Orgilés, M., & Sussman, S. (2020). Group self-identification, drug use and psychosocial correlates among Spanish Adolescents. *Revista de Psicología Clínica con Niños y Adolescentes*, 7(1), 59-64. <https://doi.org/10.21134/rpcna.2020.07.1.8>
- Griffith-Lending, M. F. H., Huijbregts, S. C. J., Mooijaart, A., Vollebergh, W. A. M., & Swaab, H. (2011). Cannabis use and development of externalizing and internalizing behavior problems in early adolescence: A TRAILS study. *Drug and Alcohol Dependence*, 116(1-3), 11-17. <https://doi.org/10.1016/j.drugalcdep.2010.11.024>
- Gussler-Burkhardt, N. L., & Giancola, P. R. (2005). A further examination of gender differences in alcohol-related aggression. *Journal of Studies on Alcohol*, 66(3), 413-422. <https://doi.org/10.15288/jsa.2005.66.413>
- Harrison, L. A., & Esqueda, C. W. (2000). Effects of race and victim drinking on domestic violence attributions. *Sex Roles*, 42(11-12), 1043-1057. <https://doi.org/10.1023/A:1007040701889>
- Hemsing, N., & Greaves, L. (2020). Gender norms, roles and relations and cannabis-use patterns: A scoping review. *International Journal of Environmental Research and Public Health*, 17(3), 947. <https://doi.org/10.3390/ijerph17030947>
- Heradsveit, O., Skogen, J. C., Bøe, T., Hetland, J., Pedersen, M. U., & Hysing, M. (2018). Prospective associations between childhood externalizing and internalising problems and adolescent alcohol and drug use: The Bergen Child Study. *Nordic Studies on Alcohol and Drugs*, 35(1), 11-15. <https://doi.org/10.1177/1455072518789852>
- Homman, L. E., Edwards, A. C., Cho, S. B., Dick, D. M., & Kendler, K. S. (2016). Gender and direction of effect of alcohol problems and internalizing symptoms in a longitudinal sample of college students. *Substance Use & Misuse*, 52(4), 429-438. <https://doi.org/10.1080/10826084.2016.1233983>
- Johnson, K., Mullin, J. L., Marshall, E. C., Bonn-Miller, M. O., & Zvolensky, M. (2010). Exploring the mediational role of coping motives for marijuana use in terms of the relation between anxiety sensitivity and marijuana dependence. *The American Journal on Addictions*, 19(3), 277-282. <https://doi.org/10.1111/j.1521-0391.2010.00041.x>
- Kedzior, K. K., & Laeber, L. T. (2014). A positive association between anxiety disorders and cannabis use or cannabis use disorders in the general population- a meta-analysis of 31 studies. *BMC Psychiatry*, 14, 136. <https://doi.org/10.1186/1471-244X-14-136>
- Khan, S., Okuda, M., Hasin, D. H., Secades-Villa, R., Keyes, K., Lin, K.-H., Grant, B., & Blanco, C. (2013). Gender differences in lifetime alcohol dependence: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Alcoholism: Clinical and Experimental Research*, 37(10), 1696-1705. <https://doi.org/10.1111/acer.12158>
- Laukkanen, E. R., Shemeikka, S. L., Viinamäki, H. T., Pölkki, P. L., & Lehtonen, J. O. (2001). Heavy drinking is associated with more severe psychosocial dysfunction among girls than boys in Finland. *Journal of Adolescent Health*, 28(4), 270-277. [https://doi.org/10.1016/S1054-139X\(00\)00183-X](https://doi.org/10.1016/S1054-139X(00)00183-X)
- López-Núñez, C., Fernández-Artamendi, S., Fernández-Hermida, J.R., Campillo-Álvarez, A., & Secades-Villa, R. (2012). Spanish adaptation and validation of the Rutgers Alcohol Problems Index (RAPI). *International Journal of Clinical and Health Psychology*, 12(2), 251-264
- Low, N. C., Lee, S. S., Johnson, J. G., Williams, J. B., & Harris, E. S. (2008). The association between anxiety and alcohol versus cannabis abuse disorders among adolescents in primary care settings. *Family Practice*, 25(5), 321-327. <https://doi.org/10.1093/fampra/cmn049>
- Marconi, A., Di Forti, M., Lewis, C. M., Murray, R. M., & Vassos, E. (2016). Meta-analysis of the association between the level of cannabis use and risk of psychosis. *Schizophrenia Bulletin*, 42(5), 1262-1269. <https://doi.org/10.1093/schbul/sbw003>
- Milani, R. M., Parrott, A. C., Turner, J. J. D., & Fox, H. C. (2004). Gender differences in self-reported anxiety, depression, and somatization among ecstasy/MDMA polydrug users, alcohol/tobacco users, and nondrug users. *Addictive Behaviors*, 29(5), 965-971. <https://doi.org/10.1016/j.addbeh.2004.02.044>
- Ministerio de Sanidad, Consumo y Bienestar Social (2017). Encuesta nacional de salud ENSE, España 2017 [ENSE National survey on health, Spain 2017]. Ministerio de Sanidad, Consumo y Bienestar Social.
- Newland, P., Meshberg-Cohen, S., Flick, L., Beatty, K., & Smith, J. M. (2015). Comorbid alcohol disorder intensifies patterns of psychological symptoms among women. *The Journal of Nurse Practitioners*, 11(6), 618-625. <https://doi.org/10.1016/j.nurpra.2015.03.016>
- Plan Nacional Sobre Drogas (2019). *Encuesta sobre Uso de Drogas en Enseñanzas Secundarias en España (ESTUDES) 1994-2018* [Survey on Drug Use among Secondary School Students in Spain 1994-2018]. Plan Nacional Sobre Drogas. https://pnsd.sanidad.gob.es/profesionales/sistemasInformacion/sistemaInformacion/pdf/ESTUDES_2018-19_Informe.pdf
- Patró-Hernández, R. M., Nieto Robles, Y., & Limiñana-Gras, R. M. (2020). The relationship between gender norms and alcohol consumption: A systematic review. *Adicciones*, 32(2), 145-158. <https://doi.org/10.20882/adicciones.1195>
- Pedersen, W., Mastekaasa, A., & Wichstrøm, L. (2001). Conduct problems and early cannabis initiation: A longitudinal study of gender differences. *Addiction*, 96(3), 415-431. <https://doi.org/10.1046/j.1360-0443.2001.9634156.x>
- Pedersen, M. U., Thomsen, K. R., Heradstveit, O., Skogen, J. C., Hesse, M., & Jones, S. (2018). Externalizing behavior problems are related to substance use in adolescents across six samples from Nordic countries. *European Child & Adolescent Psychiatry*, 27(12), 1551-1561. <https://doi.org/10.1007/s00787-018-1148-6>
- Pereda, N., Forn, M., & Peró, M. (2007). Dimensional structure of the Brief Symptom Inventory with Spanish college students. *Psicothema*, 19(4), 634-639.
- Presley, C. A., & Pimentel, E. R. (2006). The introduction of the heavy and frequent drinker: A proposed classification to increase accuracy of alcohol assessments in postsecondary educational settings. *Journal of Studies on Alcohol*, 67(2), 324-331. <https://doi.org/10.15288/jsa.2006.67.324>
- Prieto-Ursúa, M., Charro-Baena, B., Caperos, J. M., Meneses Falcón, C., & Uroz Olivares, J. (2020). Alcohol consumption in adolescents: The predictive role of drinking motives. *Psicothema*, 32(2), 189-196. <https://doi.org/10.7334/psicothema2019.263>
- Proudfoot, H., Vogl, L., Swift, W., Martin, G., & Copeland, J. (2010). Development of a short cannabis problems questionnaire for adolescents in the community. *Addictive Behaviors*, 35(7), 734-737. <https://doi.org/10.1016/j.addbeh.2010.03.012>
- Rasic, D., Weerasinghe, S., Asbridge, M., & Langille, D. B. (2013). Longitudinal associations of cannabis and illicit drug use with depression, suicidal ideation and suicidal attempts among Nova Scotia high school students. *Drug and Alcohol Dependence*, 129(1-2), 49-53. <https://doi.org/10.1016/j.drugalcdep.2012.09.009>
- Ritcher, L., Pugh, B. S., Peters, E. A., Vaughan, R. D., & Foster, S. E. (2016). Underage drinking: Prevalence and correlates of risky drinking measures

- among youth aged 12-20. *The Journal of Drug and Alcohol Abuse*, 42(4), 385-394. <https://doi.org/10.1016/j.drugalcdep.2012.09.009>
- Roberts, R. E., Roberts, C. R., & Xing, J. (2007). Comorbidity of substance use disorders and other psychiatric disorders among adolescents: Evidence from an epidemiologic survey. *Drug and Alcohol Dependence*, 88(Suppl. 1), S4-13. <https://doi.org/10.1016/j.drugalcdep.2006.12.010>
- Salvatore, J. E., Cho, S. B., & Dick, D. M. (2017). Environments, and sex differences in alcohol research. *Journal of Studies on Alcohol and Drugs*, 78(4), 494-501. <https://doi.org/10.15288/jsad.2017.78.494>
- Skogen, J. C., Siversten, B., Lundervold, A. J., Stormark, K. M., Jakobsen, R., & Hysing, M. (2014). Alcohol and drug use among adolescents: And the co-occurrence of mental health problems. Ung@hordaland, a population-based study. *British Medical Journal Open*, 4(9), e005357. <http://dx.doi.org/10.1136/bmjopen-2014-005357>
- Spradin, A., Mauzay, D., & Cuttler, C. (2017). Symptoms of obsessive-compulsive disorder predict cannabis misuse. *Addictive Behaviors*, 72, 159-164. <https://doi.org/10.1016/j.addbeh.2017.03.023>
- Strandheim, A., Bratberg, G. H., Holmen, T. L., Coombes, L., & Bentzen, N. (2011). The influence of behavioural and health problems on alcohol and drug use in late adolescence - a follow up study of 2 399 young Norwegians. *Child and Adolescent Psychiatry and Mental Health*, 5(1), 17. <https://doi.org/10.1186/1753-2000-5-17>
- Tedor, M. F., Quinn, L. M., Wilsnack, S. C., Wilsnack, R. W., & Greenfield, T. K. (2018). The gender difference in the association between early onset of drinking and problem drinking between the U.S. and Japan. *Deviant Behavior*, 39(12), 1578-1599. <https://doi.org/10.1080/01639625.2017.1410622>
- Villarosa, M. C., Madson, M. B., Zeigler-Hill, V., Noble, J. J., & Mohn, R. S. (2014). Social anxiety symptoms and drinking behaviors among college students: The mediating effects of drinking motives. *Psychology of Addictive Behaviors*, 28(3), 710-718. <https://doi.org/10.1037/a0036501>
- White, H. R., & Labouvie, E. W. (1989). Towards the assessment of adolescent problem drinking. *Journal of Studies on Alcohol*, 50(1), 30-37. <https://doi.org/10.15288/jsa.1989.50.30>
- Wilcockson, T. D. W., & Sanal, N. E. M. (2016). Heavy cannabis use and attentional avoidance of anxiety-related stimuli. *Addictive Behaviors Reports*, 3, 38-42. <https://doi.org/10.1016/j.abrep.2016.02.004>
- World Health Organization (2003). Caring for children and adolescents with mental disorders: Setting WHO directions. World Health Organization. http://www.who.int/mental_health/media/en/785.pdf
- World Health Organization (n.a.). *Gender disparities in mental health*. Department of Mental Health and Substance Dependence, World Health Organization. https://www.who.int/mental_health/media/en/242.pdf?ua=1