Psicothema

Psicothema 2019, Vol. 31, No. 4, 393-399
doi: 10.7334/psicothema2019.10

ISSN 0214 - 9915 CODEN PSOTEG

www.psicothema.com

Reinforcer pathology among cigarette smokers with and without history of alcohol use disorder

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Abstract

Background: Delay discounting (DD) and cigarette demand contribute to an understanding of nicotine reward and dependence. However, no prior attempt has been made to examine the effect of a history of Alcohol Use Disorder (AUD) on DD and tobacco demand in current smokers. This study sought to compare DD and cigarette demand in smokers with and without a history of AUD. **Methods:** The sample comprised 43 smokers with a history of AUD and 49 with no history of drug use. Participants completed the DD task and the 19-item version of the Cigarette Purchase Task. Mazur's equation and the Koffarnus et al. model were used to derive the discounting rates and elasticity of demand, respectively. **Results:** Smokers with a history of AUD discounted delayed rewards more steeply (Mlogk= -1.77, SD=1.46) than those without such a history (Mlogk= -2.32, SD=1.04). No statistically significant differences in cigarette demand emerged between groups. **Conclusions:** The excessive preference for immediate rewards in smokers with a history of AUD suggests that impulsive choice persists even after alcohol abstinence. As DD constitutes an important marker of poor treatment outcomes, targeting this specific facet of impulsivity in broader clinical interventions might be helpful.

Keywords: Delay discounting, alcoholism, cigarette demand, nicotine dependence.

Resumen

Patología del refuerzo en fumadores con y sin trastorno por uso de alcohol. **Antecedentes:** el descuento por demora (DD) y la demanda de cigarrillos facilitan la comprensión de los efectos reforzantes de la nicotina y la dependencia. Sin embargo, no se ha evaluado el efecto de la historia de trastorno por uso de alcohol (TUA) en la demanda de cigarrillos y el DD en fumadores. El objetivo de este estudio fue comparar estas variables en fumadores con y sin historia de TUA. **Método:** la muestra incluyó 43 fumadores con historia de TUA y 49 sin historia de uso de drogas. Se utilizó la tarea de DD y la Tarea de Compra de Cigarrillos de 19 ítems. Las ecuaciones de Mazur y de Koffarnus et al. se utilizaron para derivar las tasas de descuento y la elasticidad de la demanda. **Resultados:** los fumadores con historia de TUA mostraron unas tasas de descuento superiores (Mlogk=-1,77, DT=1,46) a aquellos sin dicha historia (Mlogk= -2,32, DT=1,04). Ambos grupos no difirieron en la demanda de cigarrillos. **Conclusiones:** la preferencia excesiva por las recompensas inmediatas entre los fumadores con historia de TUA sugiere una persistente toma de decisiones impulsiva incluso tras la abstinencia del alcohol. Abordar esta faceta de impulsividad en intervenciones clínicas más amplias puede ser beneficioso.

Palabras clave: descuento por demora, alcoholismo, demanda de cigarrillos, dependencia de la nicotina.

Nicotine dependence (ND) and alcohol use disorders (AUD) commonly co-occur, with approximately 65%-80% of alcohol users also being smokers (Daeppen et al., 2000; Hufnagel, Frick, Ridinger, & Wodarz, 2017). This comorbidity causes significant impairments in the physical and mental health of these individuals and has exponential negative effects when compared to the use of each drug in isolation (MacLean, Sofuoglu, & Rosenheck, 2018; Míguez et al., 2018). Relative to non-polydrug users, smokers with AUD or recovery from AUD are more heavily dependent on nicotine and alcohol, and present higher carbon monoxide readings (Hughes & Kalman, 2006; McKee & Weinberger, 2013; Rohsenow et al., 2014).

Received: January 18, 2019 • Accepted: June 15, 2019
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Contemporary conceptualizations of drug addiction include the biopsychosocial perspective (Becoña, 2018) and the behavioral economics framework (Bickel, Moody, & Higgins, 2016). The latter conceptualizes drug misuse as an impaired decision-making process that leads individuals to engage in drug-related behaviors instead of healthy ones (Bickel, Yi, Mueller, Jones, & Christensen, 2010; Mishra & Lalumière, 2017). From this perspective, the reinforcer pathology results from the interaction between two processes, measured by the Delay Discounting task (DD) and the Cigarette Purchase Task (CPT) (Koffarnus & Kaplan, 2018). The DD supplies a measure of impulsive choice that refers to the depreciation of a particular reinforcer as the time to its receipt increases (Odum, 2011), while the CPT provides an operative measure of the relative reinforcing efficacy of nicotine when constraints to its receipt (i.e., raising costs) are set (MacKillop et al., 2008).

Whether DD is state or trait in nature is still a matter of debate (Madden & Bickel, 2010). Consistent with a trait interpretation, test-retest studies in both clinical (Levy, Katz, Das, Stevens, &

Tolin, 2019) and non-clinical populations (Martínez-Loredo, Fernández-Hermida, Carballo, & Fernández-Artamendi, 2017) showed similar DD rates up to two years later. However, more recent research suggests that DD is malleable through framing effects, and neuropsychological and psychological interventions (Rung & Madden, 2018; Verdejo-García, Alcázar-Córcoles, & Albein-Urios, 2019). Both smokers and alcohol abusers discount future rewards more (i.e., show greater DD) than former dependents or controls (i.e., never users) (MacKillop et al., 2011; Weidberg, González-Roz, & Secades-Villa, 2017). Similarly, lower DD is obtained in both former smokers (Weidberg et al., 2015) and previously alcohol dependent individuals (Petry, 2001), thereby yielding further proof of the modifiable nature of DD in response to abstinence. Length of abstinence seems to impact DD differentially (Gowin, Sloan, Ramchandani, Paulus, & Lane, 2018). Whereas prior evidence found no differences in DD between active alcohol drinkers and those abstinent for at least 14 days (Kirby & Petry, 2004), lower DD has been obtained when a 30-day period of sobriety is attained (Petry, 2001). So far, no prior research on this issue has been conducted among cigarette users with a history of AUD, thereby representing a gap in our understanding of ND in this portion of the population.

Cumulative research has been published on drug demand in the population of users of alcohol (Yurasek, Murphy, Clawson, Dennhardt, & MacKillop, 2013), tobacco (Secades-Villa, Weidberg, González-Roz, Reed, & Fernández-Hermida, 2018), and other illicit drugs (Aston, Metrik, & MacKillop, 2015) with most of this research being focused on mono-substance drug users or dependents. No previous study has examined tobacco demand in the population of individuals that report a history of using drugs other than nicotine. This, however, represents a relevant unsolved issue that might contribute to better characterizing ND and, furthermore, the reinforcing pathology, in this vulnerable group of smokers.

Against this background, the primary aim of this study was to compare reinforcer pathology (i.e., DD rates and cigarette demand) between treatment-seeking smokers with and without a history of AUD.

Method

Participants

The study sample comprised 92 treatment-seeking individuals (43 smokers with a history of AUD and 49 smokers without such a history) recruited from two clinical trials related to the effects of cognitive-behavioral treatments for ND (see for further details, NCT03551704; López-Núñez, Martínez-Loredo, Weidberg, Pericot-Valverde, & Secades-Villa, 2016). Smokers with AUD history were receiving a psychosocial treatment for alcohol dishabituation at the intake assessment. Treatment components addressed emotional and family-related problems. Table 1 shows the descriptive characteristics by study group.

Individuals were deemed eligible for this study if they met the following inclusion criteria: 1) being aged 18 or over; and 2) smoking 10 or more cigarettes per day for the last year. Additionally, individuals who met lifetime AUD criteria were required to report no alcohol/other drug use apart from nicotine within the last 30 days. They were also asked to provide breath alcohol concentrations of 0.00. Participants were excluded from this study if they self-reported current substance use disorders (e.g., cannabis, cocaine) other than nicotine.

The study protocols were approved by the Ethics Committee of Investigation of the Principality of Asturias (Spain) (nº 114/16) and all participants provided informed consent prior to study initiation.

Instruments

Participants filled out a battery of questions which gathered information on sociodemographic (e.g. sex, income, and educational level) and smoking/alcohol use characteristics. Data on the following variables were collected: cigarettes per day and years of regular alcohol/tobacco use. Alcohol abstinence (months) and prior alcohol abstinence attempts were reported as well.

Breath carbon monoxide (CO) was assessed using a piCO Smokerlyzer (Bedfont Scientific Ltd., Harrietsham, Kent) to confirm smoking status. The Fagerström test for nicotine dependence (FTND; Becoña & Vázquez, 1998) was used to evaluate nicotine dependence severity. Scores range between 0 and 10 and are interpreted according to the guidelines of Fagerström, Heatheron, and Kozlowski (1990): very low dependence (0-2), low (3-4), medium (5), high (6-7), and very high (8-10).

Given the interest in examining the effects of psychopathology on behavioral economic indicators (Farris, Aston, Zvolensky, Abrantes, & Metric, 2017), we used the Beck Depression Inventory-II to assess depressive symptomatology (BDI-II; Sanz, Perdigón, & Vázquez, 2003). Scores vary between 0 and 63. Total

Table 1
Descriptive statistics by study group

	History of AUD (n = 43)	No history of AUD (n = 49)	p
Sex (% males)	37 (86)	15 (30.6)	< .001
Age[a]	50.14 (7.75)	44.37 (12.26)	.009
Income (%)	–	–	.019
<600€[US$670]	24 (55.8)	15 (32.8)	–
601-1200€[US$671-1,340]	13 (30.3)	15 (32.8)	–
>1201€[US$1,341]	6 (14)	16 (34.4)	–
Educational level (%)	-	-	.013
< High School	16 (37.2)	13 (26.5)	–
High School	25 (58.1)	19 (38.8)	–
University	2 (4.7)	17 (34.7)	–
Cigarettes/day[a]	16.37 (6.39)	18.02 (7.66)	.270
Years of regular tobacco use[a]	32.77 (7.73)	25.08 (11.24)	<.001
FTND[a]	5.09 (1.54)	5.10 (1.82)	.980
Alcohol abstinence (months)[a]	9.72 (9.30)	–	–
Alcohol abstinence attempts[a]	5 (6.03)	–	–
Years of regular alcohol use[a]	23.59 (11.44)	–	–
BDI-II[a]	12.53 (7.85)	7.45 (8.37)	.004
STAI-S[a]	36.51 (28.30)	31.77 (28.62)	.556
STAI-T[b]	69.14 (29.73)	26.13 (23.85)	< .001

Note: [a]Mean±SD; AUD: Alcohol Use Disorder; FTND: Fagerström Test for Nicotine Dependence; BDI-II: Beck Depression Inventory II; STAI-S: State Anxiety Inventory-state; STAI-T: State Anxiety Inventory-trait

scores between 0-13 are indicative of minimal depression, scores between 14 and 19 denote mild depression, scores between 20 and 28 suggest moderate depression, and scores ≥ 29 consider individuals to be severely depressed. The BDI-II has demonstrated high internal consistency in both comorbid and non-comorbid populations (.73-.96) (Wang & Gorenstein, 2013), supporting its adequacy for assessing depression in this study sample.

The Spielberger State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970) was used to evaluate anxiety symptoms. The STAI is a 40-item self-reported questionnaire comprising two 20-item subsections: state anxiety and trait anxiety. Scores range between 0 and 60; with higher scores indicating greater anxiety symptomatology. Reliability analyses have demonstrated good internal consistency in this population (Cronbach's α .88-.90) (Del Río Olvera, Cabello Santamaría, Cabello García, & Aragón Vela, 2018). Considering both the high prevalence of anxiety in substance use dependents (Kingston, Marel, & Mills, 2017) and its relationship with impulsive decision making (Xia, Gu, Zhang, & Luo, 2017), using the STAI is expected to accurately characterize AUD smokers.

Participants completed the 19 item version of the CPT (MacKillop et al., 2008). This task allows the generation of a demand curve while providing an operational measure of the relative reinforcing efficacy of nicotine through five demand indices: breakpoint (i.e., the first price at which consumption ceases), O_{max} (i.e., maximum expenditure), P_{max} (i.e., the price related to maximum consumption), elasticity (i.e., sensitivity to rises in costs), and intensity of demand (i.e., demand at no cost). Participants were asked to indicate how many cigarettes they would smoke if each cigarette cost a range of prices from zero (free) to €1,000 ($1,226). The prices were presented in escalating order.

All participants completed the hypothetical DD task on a laptop (García-Rodríguez, Secades-Villa, Weidberg, & Yoon, 2013). Participants were presented with a choice between €1,000 (US$1,226) after a fixed delay versus several amounts of money ranging from €5 (US$6.13) to €955 (US$1,170.97) available immediately. The adjusting-amount procedure was applied (Holt, Green, & Myerson, 2012). This method generates an indifference point, at which the amount of the immediate reward and the delayed €1,000 (US$1,226) reward are estimated equal. The following delays were used: one day, one week, one month, six months, one year, five years, and twenty-five years.

Procedure

Controls (i.e., non-comorbid smokers) were recruited by means of flyers and advertisements distributed around the local community. Smokers with lifetime AUD were recruited from a therapeutic community for alcohol dishabituation. Interested participants were required to contact the clinic to request an appointment for a pre-treatment baseline session.

Data analysis

Non-systematic data was checked using the three-criterion algorithm (i.e., bounce, trend, reversal from zero) based on Stein, Koffarnus, Snider, Quisenberry, and Bickel (2015). CPT data were then manually checked to detect outliers. Six outliers (i.e., Z = ± 3.29) were identified. We corrected outliers as follows: breakpoint, O_{max}, $P_{max,}$ and intensity were replaced by their nearest non-outlying value plus one unit (i.e. + 1), whereas elasticity of demand was replaced by its nearest non-outlying value plus one decimal (i.e. +.1).

A demand curve reflecting the relationship between cigarette demand and rises in costs was generated for each study group. Four CPT observed indices were calculated (breakpoint, O_{max}, $P_{max,}$ and intensity). Elasticity was derived using the exponentiated equation proposed by Koffarnus, Franck, Stein, and Bickel (2015): $Q = Q^0 \times 10^{k(e-\alpha Q_0 C-1)}$, where Q = consumption at a certain price; Q_0 = consumption at no cost, k = range of the dependent variable (cigarettes), C = price, and α = elasticity. A value of k = 1.28 was fixed. Indices of demand were log transformed to improve skewness and kurtosis, except intensity which was square root transformed.

CPT-AUC values were calculated for each participant following the method described in Myerson, Green, and Warusawitharana (2001). The area of each trapezoid was calculated using the following formula:

$(x_2 - x_1)\ [(y_1 + y_2/2]$, where x_1 and x_2 represent the consumption for each price and y_2 and y_1 are subsequent prices. The AUC is equal to the sum of the areas of these trapezoids. Higher CPT-AUC values mean greater tobacco demand.

DD was assessed by fitting individuals' indifference points to the hyperbolic equation of Mazur (1987): $V = A/(1 + kD)$, where: V = the value of the reward at a certain amount (A) that is discounted by the delay (D) to receiving it. The parameter k describes the rate of discounting; greater k values mean higher discounting, and thus, more impulsive behavior. K values were log transformed to reduce skewness.

The student t test and a one-way analysis of covariance (ANCOVA) were performed to analyze differences between groups in impulsive choice and cigarette demand. Variables that showed statistical significance ($p < .05$) in the bivariate analyses were entered as covariates: 1) sex ($p = < .001$); 2) age ($p = .009$); 3) income level ($p = .019$); 4) educational level ($p = .013$); 5) years of regular smoking ($p < .001$); 6) depression ($p = .004$); 7) trait anxiety ($p < .001$). Given the significance of educational level, this variable was assessed as a potential moderator in the relationship between membership group (i.e. smokers with a history of AUD vs. those with no history of AUD) and impulsive choice (i.e., DD). For this purpose, Model 1 was implemented using the PROCESS macro for SPSS. A total of 5,000 bootstrap samples for bias-corrected confidence intervals were specified.

All analyses were carried out using the SPSS version 24 (Inc., Chicago, IL, USA) and the GraphPad Prism 7.0 (La Jolla, California). Moderation analysis was conducted using the PROCESS macro, version 2.16 (Hayes, 2013). A 95% confidence level was set. G*Power 3.1.9.2 was also used to conduct *a priori* power analyses.

Results

Delay Discounting (DD)

According to the criterion of $R^2 \geq .30$ posed by Reynolds and Shiffbauer (2004), Mazur's equation yielded a good fit to the DD data of all participants (*Mdn* R^2 = .89) and to each of the study groups: smokers with a history of AUD (*Mdn* R^2 = .88) and smokers without a history of AUD (*Mdn* R^2 = .91).

Figure 1 displays DD curves by study group. There were statistically significant differences in DD by study group (t (75) = -2.04, p = .045, d = .43). Smokers with a history of AUD presented greater DD rates (M_{logk} = -1.77, SD = 1.46) relative to those without such a history (M_{logk} = -2.32, SD = 1.04). Group differences dissipated after adjusting for relevant variables, [F (1, 67), p = .81, $\eta^2_{partial}$ = .001]. Of the covariates, the educational level was significantly related to the dependent variable (p = .009). However, no moderating effect was found of this variable on the relationship between group membership (smokers with a history of AUD vs. smokers without a history of AUD) and impulsive choice (b = -.63, 95% CI [-1.44, .17], p = .12).

Cigarette demand

The exponentiated equation performed excellently in fitting the data of all participants (*Mdn* R^2 = .97) and those pertaining to each of the study groups: smokers with a history of AUD (*Mdn* R^2 = .97) and smokers without a history of AUD (*Mdn* R^2 =.97).

Table 2 shows cigarette demand by group. There were no significant differences in the CPT demand indices across groups. At the actual market price (€0.25/US$0.31), smokers with and without a history of AUD reported a similar number of daily purchased cigarettes (M = 16.51; SD = 9.01; M = 16.59, SD = 7.12). About half of the smokers with (58.1%) and without (59.2%) a history of AUD reported zero consumption at a price of €5 (US$6.17), and no significant difference was found at the remaining prices either.

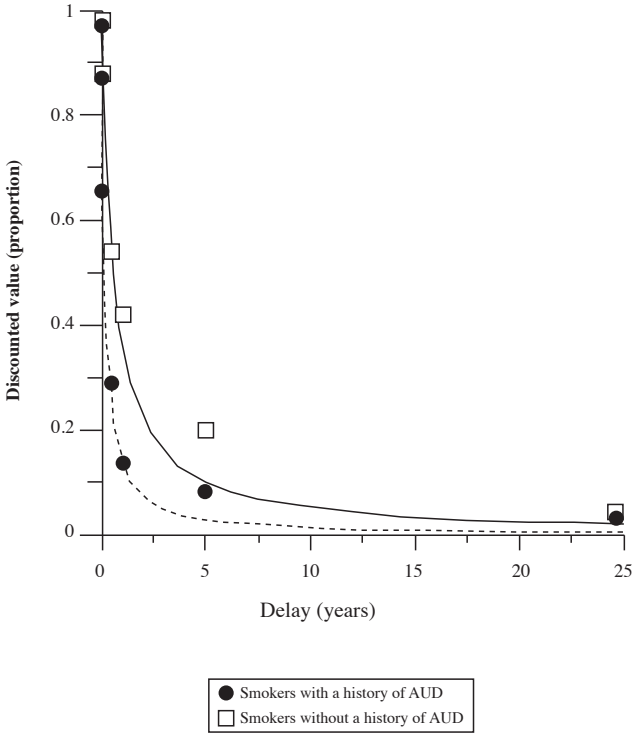

Figure 1. Comparison of delay discounting among smokers with and without a history of AUD. The two curves depict Mazur's hyperbolic function fitted to each study group. Symbols represent the median indifference points for each delay in each of the groups. Black triangles are used for smokers with a history of AUD and white inverted triangles for smokers without a history of AUD

Table 2
Cigarette demand by study group

	History of AUD (n = 43)		No history of AUD (n = 49)			
Index	**Mean**	**SEM**	**Mean**	**SEM**	**t**	**p**
Breakpoint[a]	.83	.08	.80	.08	-.28	.78
O_{max}[a]	1.01	.06	.96	.05	-.58	.56
P_{max}[a]	.40	.08	.31	.08	-.82	.41
Intensity[b]	4.29	.13	4.23	.12	-.37	.71
Elasticity[a]	-1.73	.05	-1.70	.05	.44	.66

Note: [a] indicates a log transformation was used; [b] indicates a root square transformation was used. AUD: Alcohol use disorder; SEM: Standard error of the mean

Discussion

The results herein build on new evidence about DD and cigarette demand in smokers with a history of AUD. We highlight two main findings: 1) smokers with a history of AUD showed greater DD than smokers without a history of AUD, and educational level did not moderate this association; and 2) study groups did not differ in terms of tobacco demand.

Our results document that smokers with a history of AUD discounted the future more than smokers without a history of AUD. This finding aligns with studies indicating that impulsive choice persists in abstinent alcohol dependent individuals (Naim-Feil, Fitzgerald, Bradshaw, Lubman, & Sheppard, 2014). As alcohol misuse hinders the executive functions, poor performance is displayed in DD tasks (Crews & Boettiger, 2009; Day, Kahler, Ahern, & Clark, 2015). The fact that the executive functions rarely recover before one year of abstinence (Camchong, Endres, & Fein, 2014) arguably accounts for such unexpectedly high DD rates.

Smokers with a history of AUD did not show higher tobacco demand relative to those without such a history. These findings contrast with a piece of laboratory research (Hughes, Rose, & Callas, 2000) aimed at comparing the nicotine reinforcing effects in smokers with and without a history of AUD. The fact that it included individuals with a recent history of alcohol consumption (i.e., 2 months previously), and used a nicotine self-administration test rather than the CPT, might account for such a divergent result. In addition to the above, other mechanisms are raised. As the co-use of nicotine and alcohol has interactive effects that increase motivation to use either drug (Dermody & Hendershot, 2017), it might be that abstaining from alcohol led patients to experience less pleasure from nicotine and consequently lowered their motivation to smoke cigarettes (Aubin, Laureaux, Tilikete, & Barrucand, 1999; Hintz & Mann, 2007; Kalman, Kahler, Garvey, & Monti, 2006; Kalman et al., 2004). Furthermore, use of alcohol and nicotine is prompted by similar cues (Burton, Hoek, Nesbit, & Khan, 2015), so alcohol abstinence may have led the patients to reduce their exposure to alcohol-related cues paired with smoking and thereby the reward obtained by nicotine.

Several clinical implications are noted. Impulsive decision-making characterizes smokers with a history of AUD, even when nine months of alcohol abstinence is achieved. Consequently, efforts to promote smoking abstinence in this population might benefit from incorporating specific components for reducing DD that have shown promising results in the alcohol and tobacco

cigarette population, such as contingency management (García-Rodríguez et al., 2007) and episodic future thinking (Stein, Tegge, Turner, & Bickel, 2017). Akin to alcohol abusers (Snider, LaConte, & Bickel, 2016), it seems that smokers with a history of AUD present difficulties in planning the future and thus will benefit from training in self-controlled decision-making. From the neuropsychological field, goal management training and working memory training show promise in treating substance use and executive difficulties such as planning or problem-solving (Bickel, Yi, Landes, Hill, & Baxter, 2011; Stamenova & Levine, 2018). It is important to note that there is also evidence that finds no effects of these interventions on substance use or impulsivity (Khemiri, Brynte, Stunkel, Klingberg, & Jayaram-Lindström, 2019). Neuropsychological approaches have shown increased effects when delivered alongside other cognitive-behavioral therapies (Wiers, Boffo, & Field, 2018), and the extent to which they enhance cessation outcomes, when delivered as part of broader smoking cessation treatments, merits consideration.

This study is subject to at least four limitations. First, as a cross-sectional design, we cannot draw clear conclusions on higher DD as a determinant or consequence of a history of AUD. Second, given the specific sample characteristics, caution should be adopted when interpreting the results. Also, although we assessed the presence of lifetime AUD, past substance use disorders other than nicotine and alcohol were not evaluated and might have potentially influenced the study results. Similarly, we did not gather information on comorbid personality disorders, so we cannot exclude the possibility that psychopathological variables such as the one noted may have acted as confounding variables. Finally, behavioral measures used herein are hypothetical and not real, thus arguably not reflecting real decisions. However, research has shown that using either DD or CPT to predict outcomes among drug-dependent users does lead to similar results to real outcomes (Wilson, Franck, Koffarnus, & Bickel, 2016).

Even with these limitations, our study indicates that smokers with a history of AUD showed greater DD than smokers without a history of AUD, and that these study groups did not differ in terms of tobacco demand. Given the paucity of studies assessing these two behavioral economics constructs in smokers with a history of AUD, more studies will be needed to confirm the present results.

Acknowledgements

This research was supported by the Spanish National Plan on Drugs (PNSD: Ref. MSSSI-17-2017I036), grants from the National Agency of Research of the Spanish Ministry of Science, Innovation and Universities (BES-2016-076663: FPU17/00659: FPU15/04327), and a predoctoral grant from the Ministry of Education and Culture of the Principality of Asturias (BP17-78). These institutions were not involved in the study design, collection, analysis, or interpretation of the data, writing the manuscript, or the decision to submit the paper for publication.

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