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Alcohol related brain damage. State of the art and a call for action

Daño cerebral relacionado con el alcohol. Situación actual y llamada a la acción

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Concerns about the harmful health effects of alcohol and calls for moderate drinking are found in mankind's earliest written records. Babylonian and Egyptian laws aimed to regulate alcohol consumption, and Homer's *Odysseus* is full of references to the toxic effects of wine. Many Roman writers, like Pliny and Seneca, anticipated modern observations about the effects of alcohol abuse emphasising associations with loss of memory, antisocial behaviour, and early death. Our current ambivalent relationship with alcohol is foreseen by the fact that whereas most Greek philosophers highlighted the virtues of temperance, others were devoted to the Greek God of Wine, Dionysius (Hornblower & Spaworth, 2012).

Alcohol is the world's third largest risk factor for disease burden (WHO, 2011). Much of the burden is due to the persistent effects of alcohol in the central nervous system. It is well established that excessive alcohol use can lead to permanent brain damage. However, there is little consensus on the characteristics of the associated cognitive impairment.

There is also much debate as to whether acquired cognitive impairment is due to a direct neurotoxic effect of alcohol or if it is more attributable to secondary causes like thiamine deficiency. In this context the use of the label "alcohol related brain damage" (ARBD) to group a wide etiologic and clinical range of pathologies seems very appropriate (Ridley, Draper & Withall, 2013). What is clear is that Wernicke's Encephalopathy (WE) is still misdiagnosed and mistreated (Isenberg-Grezda, Kutberg & Nicolson, 2012, Isenberg-Grezda; Chabon & Nicolson, 2014).

There is a need for translational research in this field to connect "bench to bedside" in order to find the best ways to help patients with ARBD. Public health managers should take responsibility of such a relevant issue, as many of these patients are at the boundaries of different medical specialities, with the consequence that their needs are poorly met.

Alcohol-related brain damage. From categories to dimensions

Established, long-term neurocognitive symptoms are frequently reported in alcohol-dependent patients. These have been traditionally divided in two categories (Ridley et al., 2013):

1. Alcoholic Dementia (AD), a term introduced in the early 1970's (Boeke, 1970, Mallinson & Hoffbrand, 1974). There have been several attempts to establish operative diagnostic criteria (Oslin & Cary, 2003). However, the existence of a specific dementia directly related to ethanol toxicity has been debated for a long time (Victor, 1994). The psychopathologic characterisation of AD is inaccurate, although some authors distinguish two different patterns: frontal and sub-cortical.
2. Secondary forms. The most important is the Korsakoff's Syndrome (KS), the continuum of thiamine deficiency-related WE. Classically described as

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a combination of diencephalic amnesia, confabulation, false recognisances and space-temporal disorientation, with typically preserved instrumental functions. Other important syndromes would be Marchiafava-Bignami, pellagrous encephalopathy and acquired hepatocerebral degeneration, all of them with a reasonably well-established pathogenesis (Victor, 1994).

However, the picture is not so clear in daily practice. Many factors may act synergistically with ethanol toxicity and its related consequences to cause cognitive deterioration (e.g., brain vascular pathology, traumatic brain injury, psychiatric comorbidity). The classical syndromes rarely appear isolated, but often overlapping, incompletely or atypically.

Human behaviour and cognition are not linear products of independent "brain modules". They emerge from a complex net of variables that often interact in a modulation/moderation way (Bates, Buckman & Nguyen, 2013). Therefore, their alterations might not fit into categorical taxonomies. We now see addiction as a brain disorder caused by intricated interactions between predisposing traits, environmental factors and neural impairments due to sustained drug abuse (Jupp & Dalley, 2014). Due to this complexity, a big knowledge gap still exists. Deep comprehension that leads to solid theoretical models is probably still out of reach.

Many cognitive and behavioural disturbances have been shown to precede the onset of alcohol consumption and have been detected in non-affected relatives (Ersche et al., 2012). Some have been pointed out as addiction biomarkers or endophenotypes: working memory, behavioral inhibition (Iacono, Malone & McGue, 2008), error processing (Euser, Evans, Greaves-Lord, Huizink & Franken, 2013), anxiety-impulsivity traits like delayed reward discounting (MacKillop, 2013) and even subjective responses to alcohol (Setiawan et al., 2014). Neuroanatomical correlates of these predisposing factors have been described (Wetherhill et al., 2012; Seigneurie, Guérin Langlois & Limosin, 2013). A dimensional approach provides promising insights on how their interaction could predispose to addiction (Grégoire, Rivalan, Le Moine & Dellu-Hagedorn, 2012). The way these primary "addiction-related" impairments overlap with acquired ARBD warrants further research.

In this sense, fronto-cerebellar connexions are worth to mention. The cerebellum seems to have an important role in cognition and affect regulation. It also seems to be particularly sensitive to thiamine deficiency and alcohol neurotoxicity and is considered one of their initial "targets" (Wijnia & Goossensen, 2010; Fitzpatrick & Crowe, 2013). Moreover, altered fronto-cerebellar connectivity is a candidate amongst addiction biomarkers, as it has been found in alcohol-naïve youngsters with a family history of alcohol use disorders (AUD) (Herting, Fair & Nagel, 2011).

Even at a population level, many authors have defended the need for introducing drinking patterns into alcohol economic studies in order to better reflect alcohol impact over time (Barbosa et al., 2010). It is well known that distinct drinking patterns can cause different brain alterations in the long term. Binge drinking and the number of "heavy drinking occasions" have received much attention (Hunt, 1993, Ward, Lallemand & de Witte, 2009; Maurage et al., 2012), with results suggesting they could be particularly harmful. It is worth to mention that the raise of these patterns in adolescent and young populations, with their vulnerable, developing brains, has called the attention of specialists and authorities.

Epidemiological findings reflect the abovementioned complexity. Several reviews reported a high prevalence of alcohol abuse in patients with dementia (9-22%) and high rates of dementia in alcohol abusers (up to 24%). Variability may be partially explained by differences in sampling, alcohol use quantification and age limits (Ritchie & Villebrun, 2008). The latter is very relevant. In an Australian analysis of hospital admissions of more than 20.000 dementia patients, AD was found in 1,4% of them, but in 22% of dementia patients under 65 (Draper, Karmel, Gibson, Peut & Anderson, 2011). Similarly, rates of around 10% were found in an English epidemiological study of young-onset dementia (less than 65 years) (Harvey, Skelton-Robinson & Rossor, 2003). Such a prevalence in a relatively young population and on an acquired disease calls for proper interventions.

Apart from the most severe forms, a sizeable proportion (50-70%) of persons with AUD display some degree of neurocognitive deficit (Martin, Adinoff, Weingartner, Mukherjee & Eckardt, 1986; Fein, Bachman, Fisher & Davenport, 1990). Literature remains inconclusive with respect to which cognitive domains are more vulnerable. Some authors claim for a more specific affectation and others defend that impairment is diffuse, the latter perhaps with a little more evidence on their side (Stavro, Pelletier & Potvin, 2012). Anyway, most information is from treatment samples, so numbers could change in general population (Fein & Greenstein, 2012). Some recent approaches have studied community samples (Houston et al., 2014) and detected a positive correlation between executive dysfunction and alcohol consumption.

In the light of this complexity, as mentioned before, the term ARBD has been used for quite a long time (Harper & Kril 1984, Butterworth, 1995). Similarly, DSM V (APA, 2013) uses the categories of major and minor "neurocognitive disorder due to substance abuse".

Wernicke-Korsakoff syndrome: unforgivably forgotten

Concern has been raised on the persistent mismanagement of WE (Rinblad, Blomström, Anevret, Palmstierna, 2012; Day & Del Campo, 2013; Oisezagha et al., 2013; Tartara et al., 2013; Soler-González, Balcells-Oliveró, Sánchez-Peñataro & Gual-Solé, 2013; Wijnia & Oudman, 2013).

Against what is usually thought, WE is frequent and often presents atypically (Donnino, Vega, Miller & Walsh, 2007). Post-mortem studies found WE lesions in 2% of the general population, and up to 12% in alcoholics. The classical triad (ophtalmoparesia, ataxia and confusion) appears complete in less than ¼ of the patients and is absent in up to 1/5. This adds to the low clinician's suspicion rate and the lack of sensitive diagnostic tools to favour the accumulation of undetected WE episodes (Isenberg-Grzeda, Kutner & Nicolson, 2012) that contribute substantially to the ARBD burden, including progression to the KS (Thomson, Guerrini & Marshall, 2012). This is shocking, considering that WE is long-known and has a cheap and safe treatment (Thomson, Cook & Guerrini, 2008).

WE should be diagnosed with broad operational criteria to raise clinical suspicion, and treated as an emergency (Sechi & Serra, 2007). AUD are associated with an impairment of thiamine absorption, storage, transport and utilisation (Thomson et al., 2012). Accordingly, the latest reviews and guidelines recommend treatment with high and frequent doses of parenteral thiamine (up to 500 mg/8h) (Galvin et al.2010; NICE, 2010; Thomson et al., 2012).

Despite this, a recent Cochrane review (Day, Bentham, Callaghan, Kuruvilla & George, 2013) remarked the lack of evidence about optimal thiamine dosage. Only two randomised trials were identified, both with major caveats. Thus, it is mandatory to conduct well-designed trials to determine optimal regimes, also for prophylaxis. Afterwards, clinical guidelines should be properly implemented, as that their mere existence is not enough to change clinician's attitudes (Ward, Murch, Agarwal & Bell, 2009).

Why is neurocognitive evaluation in alcohol use disorders so important? Measuring for change

In alcoholic patients, greater cognitive impairment has been associated with less treatment compliance and fewer days of abstinence (Bates, Pawlak, Tonigan & Buckman, 2006). This redounds in huge socioeconomic costs. Although the interference of cognitive impairment with treatment outcome appears self-evident, this interaction is not simple.

Executive and amnestic problems, including prospective memory, have received particular attention, as they are linked to treatment outcomes and maintenance of abstinence (Le Berre et al., 2010; Fish, Wilson & Manly, 2010, Montgomery, Ashmore & Jansari, 2011; Griffiths et al., 2012; Lyu & Lee, 2012). Despite this, literature remains inconclusive on their extent and clinical relevance. Great individual variability and confounding factors have complicated study designs and replication (Bates, Labouvie & Voelbel, 2002; Hedden et al., 2002).

Most of previous studies focused on the direct effect of cognitive impairment on drinking outcomes, without accounting for other possible ways of influence. Literature about other sources of brain injury suggests that the effects of cognitive impairment are often mediated by some factors and may moderate the influence of others. For instance, cognitive deficits may affect psychosocial outcomes by changing the person's emotional and motivational responses. This is important for AUD treatment, because therapeutic alliance, self-efficacy, readiness to change behaviour, and the use of social support to reinforce treatment goals are key therapeutic processes (Gizewski et al., 2012; Le Berre et al., 2012). Therefore, a mediator-moderator variable distinction in the context of alternative models of brain-behaviour relations may be useful for understanding how cognitive impairment disrupts outcomes in AUD and then for tailoring therapeutic interventions.

Considering its impact, cognitive screening should be generalised and those impaired must be treated. eHealth solutions, which have been suggested to be cost-effective for AUD management (Smit et al., 2011; Stoner & Hendershot, 2012; Brendryen, Johansen, Nesvåg, Kok & Duckert, 2013), could ease the implementation of cognitive testing and rehabilitation.

Neurocognitive evaluation in alcohol use disorders: challenges

There are many good bedside screening tools for cognitive deficits (e.g. MOCA or Addenbrookes') (Copersino et al., 2009; Rojo-Mota, Pedrero-Perez, Ruiz-Sanchez de Leon, Llanero-Luque & Puerta-Garcia, 2013), and there is a great amount of evidence on screening for cognitive impairment in acquired brain damage (stroke, traumatic brain injury, HIV). But there is a shortage of literature about cognitive screening in alcoholism. It is stunning that, despite the growing evidence about ARBD, a significant proportion of alcoholic patients are not systematically screened for cognitive deficits, particularly those with mild and moderate impairments. Several factors may contribute to this situation:

1. The difficulty in distinguishing apparent impairment due to intoxication or withdrawal states from that attributable to more persistent ARBD. Other confounders also challenge the quest for specificity (e.g. psychiatric and somatic comorbidity).
2. The lack of specifically validated screening tests for ARBD. Furthermore, we know from other domains that tests that perform well to screen severe cognitive deficits do not always work for milder conditions. In addition, the results of cognitive tests do not always correlate with everyday functioning, thus failing to provide clinically relevant information.
3. Standard comprehensive neurocognitive tests are high resource-consuming.
4. The shortage of structured services for cognitive rehabilitation.

Neurocognitive rehabilitation: time to act

Is abstinence enough to recover functionality? Many cross-sectional studies have captured some spontaneous cognitive recovery in abstinent alcoholics. A few limited longitudinal designs have compared the same alcohol dependent sample tested twice: early after detoxification and later in treatment or soon after the end of it. Only a few studies have used a longitudinal, prospective design with several assessment points to study within-person changes in cognitive function over time (Bates et al., 2004; Bates, Voelbel, Buckman, Labouvie & Barry, 2005; Bartels et al., 2007). A recent review (Fernandez-Serrano, Perez-Garcia & Verdejo-Garcia, 2011) and a metaanalysis (Stavro, Pelletier & Potvin, 2012) found a similar cognitive performance in multiple domains when comparing 1 month of abstinence versus 1 year, which suggests a stabilisation during the first year of sobriety. Analyses on a longer run revealed less severe cognitive impairment among long-term abstinent patients, which would support previous findings from longitudinal studies (Parsons, 1998; Rourke & Grant, 1999). A strong limitation is the evaluation of long-term abstinent alcoholics, with potential confounding factors like selection bias and differential survivorship rates (Fein & McGillivray, 2007). Effect size estimates could be underestimated, because of relapsing and most severe patients (KS, AD) being excluded from the analyses. Thus, long-term abstinence samples may be overrepresented by former dependent patients that were more cognitively fit at the beginning and therefore, better able to respond to therapy. It could also mean that they are less vulnerable to ARBD.

Neuroimaging has shown some anatomical and functional correlates of spontaneous brain recovery after alcohol cessation (Bartsch et al., 2007; Gazdzinski, Durazzo, Mon, Yeh & Meyerhoff, 2010; Monnig, Tonigan, Yeo, Thoma & McCrady, 2012) and has linked this recovery to several genetic and neurochemical factors, like BDNF (Mon et al., 2013). Despite this, we are still far from depicting at an individual level how the brain recovers from ARBD. More research is warranted, as the prediction of individual recovery trajectories would be useful for developing and tailoring cognitive interventions.

Back to the opening question: within one year, data suggests abstinence *per se* could stop the progression of cognitive impairment. Existing evidence indirectly suggests that this could be a necessary but insufficient condition. Cognitive impairment can affect treatment outcomes and relapse rates are high among alcoholics (Moos & Moos 2006). Moreover, alcoholics who relapse following a prolonged period of abstinence experience a further decline in cognitive function (Loeber et al. 2009; Pitel et al. 2009). Thus, an existing challenge is to help addicted patients to maintain abstinence long enough to benefit from cognitive recovery-potential.

In short, we are facing a harmful loop: heavy alcohol use over time impairs cognition, which affects self-control and can lower the efficacy of standard therapies and subsequently, increases relapsing probability. This should be untangled in two non-excluding ways: researching how to adapt or develop therapies to help cognitively impaired alcoholic patients to control their drinking and also looking for the best cognitive rehabilitation strategies for them (which, in turn, would be expected to impact on treatment outcomes).

Tailoring psychological therapies to the cognitive impaired

Motivational Interviewing (MI) has been adapted for brief interventions in traumatic brain injured patients (Ponsford, Tweedly, Lee & Taffe, 2012) and also for schizophrenic patients with AUD (Carey, Leontieva, Dimmock, Maisto & Batki, 2007). Improving executive function, like working memory, has shown some effectiveness (Houben, Wiers & Jansen, 2011). Attention bias (the automatic distraction towards stimuli related to an addictive substance) modification is also promising, as the attention training techniques are inexpensive, flexible and have shown some effectiveness (Cox, Fadardi, Intriligator & Klinger, 2014). We should also ensure that all who could benefit get pharmacological treatment.

From a global perspective, reduction strategies are getting more attention as an alternative to abstinence as the only therapeutic goal in AUD (Gastfriend, Garbutt, Pettinati & Forman, 2007). Measurement of continuous variables, such as the quantity and frequency of alcohol consumption, has enriched our understanding of alcoholism. In this sense, measurements like heavy drinking days or risk-stratified alcohol consumption are acquiring relevance as treatment outcomes (Falk et al., 2010; Aubin & Daeppen, 2013). A reduction in these has been proven beneficial in many important aspects (Kline-Simon et al., 2013), so it would be interesting to dig in their relationship with cognitive dysfunction and recovery.

Neurocognitive rehabilitation in alcohol use disorders

There is a shortage of evidence about neurocognitive rehabilitation for alcoholic patients (Bates, Buckman & Nguyen, 2013). Three decades ago some reviews associated altered brain function and its significance to the treatment of alcoholism (Parsons et al., 1987). There was evidence for an at least partial recovery of function with cessation or substantial reduction of drinking, and that cognitive rehabilitation could facilitate it.

Fifteen years later, the topic was revisited (Bates et al., 2002). It was reported a substantial progress in the knowledge about the nature and course of alcohol-related cognitive disorders, but a significant lag in the development of effective treatments. Strong scientific data supported this kind of treatment for other types of acquired brain damage (e.g., stroke or traumatic brain injury), but innovations were not being applied in the addictions field. The lack of conceptual models of alcohol-related cognitive disorders as moderators and modulators of treatment outcomes also contributed to the discordance.

The trend seems to have reverted over the past decade, with an increasing research interest that has unveiled some of the relation between cognition and treatment outcomes, and has generated new conceptual models (Wiers et al., 2011; Bates & Buckman, 2013) and intervention programmes (Alfonso, Caracuel, Delgado-Pastor & Verdejo-García, 2011; Houben et al., 2011; Rupp, Kemmler, Kurz, Hinterhuber & Fleischhacker, 2012).

The integration of current knowledge on time-dependent recovery on the neural and cognitive levels is a major challenge for translational research. For instance, when compared to controls in task performance, alcoholic patients have shown spontaneous, compensatory recruitment of additional brain networks like fronto-cerebellar and others (Chanraud, Pitel, Rohlfing, Pfefferbaum & Sullivan, 2010; Chanraud, Pitel, Pfefferbaum & Sullivan, 2011; Parks et al., 2012; Camchong, Stenger & Fein 2012; Chanraud, Pitel, Muller-Ohering, Pfefferbaum & Sullivan, 2013). Some of these compensatory strategies have been linked to the ability to sustain abstinence (Camchong et al., 2013).

Anyhow, work in the cognitive rehabilitation field is still in its early stages. We should keep an eye on other acquired causes of brain damage and on dementia. In these domains, evidence to support the use of cognitive interventions is cumulating (Hopper et al., 2013) with strategies like goal management training and errorless learning (Bertens, Fasotti, Boelen & Kessels, 2013). But replication of results in large clinical trials is needed and there is not enough evidence to decide if the aim should be restoring cognitive function or enhancing compensatory strategies (van Heughten, 2012, Chung, 2013, Kim & Kim, 2014). The latter have been reported successful in TBI or Schizophrenia (Twamley, Vella, Burton, Heaton & Jeste, 2012), so they deserve further study.

More studies with multiple time point assessments are needed to elucidate the length of abstinence necessary to start rehabilitation, and to rule out other factors that can impact on recovery trajectories. This way we will better understand recovery at the individual level, and so use this knowledge for clinical decisions. The question of whether cognitive rehabilitation also improves treatment efficacy should be addressed. In this sense, studies involving active cognitive interventions are needed, accounting for their ecological validity. It would be of great interest to explore a broad range of approaches to cognitive rehabilitation, from training impaired domains to strengthening and developing compensatory strategies. Future research should be carefully designed and consider several questions, like how cognitive rehabilitation would fit into current AUD treatments that have proven success and whether this rehabilitation should be offered universally or only to those patients with some level of impairment. Moreover, only a limited number of studies have evaluated if neurocognitive training can also improve alcohol outcomes in both non-treatment seeking and treatment seeking populations.

Conclusions

Neurocognitive impairment is common in alcohol use disorders and has a deep negative impact. It is the product of complex interactions between predisposing traits, environmental factors and neural impairments due to the heavy use over time. The synergistic effects of multiple insults, from direct ethanol neurotoxicity to thiamine deficiency, lead to a wide range of dysfunctions, much broader than the classical picture, and are often named under the umbrella term "alcohol-related brain damage" to reflect their etiological and clinical heterogeneity.

Cognitive screening in patients with alcohol-use disorders is crucial in order to early identify and manage those who are impaired. But this is a challenging issue, as it is difficult to distinguish the cognitive impact of intoxication/withdrawal from persistent impairment and to separate them from other sources of brain damage. There are many good bedside tools for cognitive screening, but they need specific validation and, perhaps, some fine tuning for their application in AUD patients.

More research is needed to determine the impact of cognitive impairment on treatment outcomes and how best to improve functional ability in this population. Some approaches, like modified MI, compensatory strategies or errorless learning, have been suggested.

Thiamine deficiency is an important and potentially preventable source of ARBD. Alcoholic patients should be systematically screened for WE risk and receive prophylaxis or treatment if necessary. Randomised clinical trials are needed in order to find the optimal dose regimes.

There is large room for improvement, and we think that it is time for action. To overcome this challenge, we should join our resources and skills in order to offer alcoholic patients the most appropriate evaluation and treatment, keeping an eye on its cost/effectiveness. In the XXI century addictions have been defined as brain diseases (Volkow, 2005). Maybe it is time to look also at brain damage more carefully than we have done in the past.

Conflict of interest

Carlos Soler-González has received travel grants from Lundbeck and Janssen. Antoni Gual-Solé has received honoraria and travel grants from Lundbeck, Janssen and Servier. Mercè Balcells-Oliveró declares no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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Sexual risk behaviors in non-injecting substance-dependent Brazilian patients

Comportamientos sexuales de riesgo en pacientes brasileños dependientes de drogas no inyectables

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Resumen

Este estudio pretende evaluar los comportamientos sexuales de riesgo en pacientes dependientes de sustancias no inyectables admitidos en hospitalización especializada brasileña. Se realizó un estudio transversal con información sociodemográfica, información sobre el comportamiento sexual, droga de elección y se les aplicó el Short Alcohol Dependence Data, Drug Abuse Screening, Test for Nicotine Dependence. La muestra fueron 299 sujetos con distintos niveles de vulnerabilidad sexual medida combinando el número de parejas sexuales con la frecuencia de uso del condón en sus relaciones sexuales durante el último año. Los resultados muestran que entre los sujetos del grupo de alto riesgo aproximadamente un 39% tuvieron también una mayor prevalencia de otros comportamientos sexuales de riesgo, como sexo con prostitutas (RR1.96), experiencias homosexuales y experiencias homosexuales a cambio de drogas, historia de infecciones de transmisión sexual (RR1.39), realización de la prueba del VIH, uso de la píldora del día después (RR1.78) y aborto inducido. La probabilidad de que los usuarios de alcohol o cocaína tuvieran un comportamiento sexual de alto riesgo fue 2.47 y 1.66 veces respectivamente más alta que los consumidores de crack. Además, los usuarios con niveles sustanciales o graves de problemas de drogas tenían 3.64 veces mayor probabilidad de comportamiento sexual de alto riesgo. Identificar, prevenir y gestionar las conductas sexuales relacionadas con el consumo de alcohol y otras de drogas es una excelente oportunidad para fortalecer su tratamiento.

Palabras Clave: comportamiento sexual, trastornos relacionados con sustancias, preservativos, parejas sexuales, crack / cocaína.

Abstract

This study seeks to evaluate sexual risk behaviors in non-injecting substance-dependent patients admitted for specialized inpatient Brazilian care. A cross-sectional study using socio-demographic and sexual behavior information, drug of choice, Short Alcohol Dependence Data, Drug Abuse Screening, and Test for Nicotine Dependence was used in 299 subjects with different levels of sexual vulnerability as measured by the number of sexual partners in the last year and the frequency of condom use with intercourse/penetration. The findings showed that approximately 39% the subjects of the high risk sexual behavior group exhibited a higher prevalence of others sexual risk behaviors, including having sex with sex workers (RP=1.96), homosexual experiences, and homosexual experiences in exchange for drugs, history of STIs (RP=1.39), HIV testing, use of the morning–after pill (RP=1.78) and induced abortion. The probability of alcohol and cocaine snorted user having high risk sexual behaviors is 2.47 and 1.66 times respectively higher than crack users. In addition, users with substantial or severe levels of problems with drugs had a probability of 3.64 times greater of high risk sexual behaviors. Identifying, preventing, and managing these high risk sexual behaviors related to alcohol and other drugs are an excellent opportunity to bolster their treatment.

Key Words: sexual behavior, substance-related disorders, condoms, sexual partners, crack/cocaine

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Substance-dependent patients are a particularly complex population with regard to sexual risk behaviors. Within this population, sexual risks vary with the type of drug used, route of administration, social context, gender, sexual orientation, and type of sexual interaction (Celentano, Latimore, & Mehta, 2008). Many clinical reports, including a few Brazilian studies, have reported elevated rates of unprotected sex in this population (Malta et al., 2010; Nappo, Sanchez, & De Oliveira, 2011; Remy et al., 2013). Twenty-nine studies targeting substance-dependent patients were identified in a systematic review and meta-analysis conducted by Malta et al. (2010) with 13 063 participants in Brazil from 1999 to 2009. Those studies consistently recognized injecting drug user (IDUs) and needle sharing as key predictors of HIV-infection as well as engagement in sex work and male-to-male sex. The findings showed that the combined HIV prevalence across the studies aimed at drug users was 23.1% (95% confidence interval (CI): 16.7-30.2), and 38.3% of subjects with occasional partners never or almost never used condoms (Malta et al., 2010).

Programmes to prevent HIV transmission among drug users have focused primarily on IDUs. These programmes have produced measurable reductions in HIV incidence and prevalence (Booth et al., 2009; Do et al., 2012). However, the majority of substances abusers worldwide are non-injecting drug users (non-IDUs), and there has been a scarcity of HIV prevention interventions strategies targeting non-IDUs (Shoptaw et al., 2013).

This reality has become a new focus of research due to the role unprotected sex plays in the transmission of HIV and other sexually transmitted infections (STIs) in non-IDUs. With the advent of crack smoking in the early 1990s, this changed the technology of use of cocaine administration among users worldwide (Dickson-Gomez, McAuliffe, Rivas de Mendoza, Glasman, & Gaborit, 2012; Dunn & Laranjeira, 1999; Nappo et al., 2011). Among female Brazilian crack users, for example, the growing number of recorded cases of HIV infection may be associated with the development of sexual risk behaviors involving the exchange of sexual favors for drugs or money (Nappo et al., 2011). These users generally exchange sex when craving for drugs and leave the use of protection up to the client, engaging in several sexual activities per day in unsafe locations, and with multiple partners (Nappo et al., 2011).

While cocaine and heroin have been reported to both increase and depress sexual arousal in men and women, methamphetamine has been reported to increase libido and the number of sexual partners, particularly in men who have sex with men (Kopetz et al., 2010; Benotsch et al., 2012). Methamphetamine use among non-IDUs has been associated with a number of HIV risk behaviors, including sex with multiple partners and decreased condom use due to the loss of inhibitory control (Frohmader, Bateman, Lehman & Coolen, 2010; Wechsberg et al., 2010).

Drug users, in the context of the Club scene, are another population that has dramatically increased over the last two decades according to the latest World Drug Reports (UNODC, 2013). Some studies have documented a higher prevalence of inconsistent condom use and multiple sexual partners among club drug users compared with the general population (Ibanez, Kurtz, Surrat, & Inciardi, 2010; Zuckerman & Boyer, 2012). In a Brazilian study conducted by Remy et al. (2013) with 240 club drug users, 80% reported having used alcohol/drugs to make sex last longer, 52.5% reported having had unprotected sex, 63% reported having more than two sex partners, 40% reported having had anal sex, and 15% had exchanged money for sex or sex for money (sex trading) in the 12 months prior to the interview. Finally, 84% reported having had sex with a man who most likely had had sex with another man in the 12 months prior to the interview (Remy et al., 2013).

High levels of marijuana dependence and sexual risk behaviors have been reported among youths. Recent evidence suggests an association between marijuana use and erectile dysfunction in men and risky sexual behaviors such as premature sexual intercourse, non-condom use, and an increased number of sexual partners in men and women (Aversa et al., 2008; Eloi-Stiven, Channaveeraiah, Christos, Finkel, & Reddy, 2007; Hendershot, Magnan, & Bryan, 2010; Saso, 2002).

All of the above psychoactive substances cause impaired cognitive functioning, poor decision-making capacity, and diminished judgment and perception, which increase the susceptibility of engaging in sexual risk behaviors (Kopetz, Reynolds, Hart, Kruglanski, & Lejuez, 2010). Among drug users, greater perceived risk of HIV/STI and positive attitudes regarding the effects of condoms on sexual pleasure have been shown to be associated (Mitchell & Latimer, 2009; Weinstock, Lindan, Bolan, Kegeles, & Hearts, 1993) with an increased probability of reporting condom use. Common reasons for not using condoms include lower perceived risk of contracting HIV/STI, negative attitudes regarding the effects of condoms on pleasure, cravings, high sexual arousal, being under the influence of drugs, difficulty convincing partners to use condoms, and lack of condom availability (Mitchell & Latimer, 2009; Weinstock et al., 1993).

Despite the abundant of the literature on sexual behaviors and drug abuse, few studies in Brazil have explored the prevalence of unprotected sexual intercourse in non-IDUs and their associated sexual behaviors with respect to gender in a clinical setting (Barbosa Júnior, Szwarcwald, Pascom, & Souza Júnior, 2009; Bassols, Boni, & Pechansky, 2010; Cortez, Boer, & Baltieri, 2011; de Souza, Diaz, Sutmoller, & Bastos, 2002; Malta et al., 2010; Nunes, Andrade, Galvão-Castro, Bastos, & Reingold, 2007). This lack of information justifies expanding the available national evidence because such studies are necessary due to the unique characteristics and risky sexual practices among men and women with substance-related disorders (Dickson-Gomez et al., 2012; Nappo et

al., 2011; Wechsberg et al., 2010). There are also significant gender differences in substance-related epidemiology, social factors, characteristics, biological responses, progression and level of dependence, clinical consequences, co-occurring psychiatric disorders, and barriers to treatment entry, retention, and completion (Tuchman, 2010).

Our hypothesis is that the prevalence of high-risk sexual behaviors is high among psychoactive substance-dependent individuals and that such high-risk sexual behaviors correlate with the severity of dependence. The objective of this study was to evaluate high-risk sexual behaviors in a sample of substance-disorder patients admitted in an inpatient addiction unit.

Method

This study involved a cross-sectional design and was conducted at an inpatient addiction treatment unit in Sao Paulo, Brazil. The sample comprised consecutive admissions of 616 users of psychoactive substance aged 18 years of age or older with a confirmed clinical dependence diagnosis according to the DSM-IV-TR diagnosis criteria (American Psychiatric Association, 2000). Subjects were selected on the basis of having different levels of sexual vulnerability as measured by the number of sexual partners (up to 2 and 3 or more) in the last year and the frequency (always use or use sporadically / never uses) of condom use with intercourse/penetration (vaginal, anal, and/or oral). Analyses were conducted on the interviews provided by 299 participants. The remaining subjects were excluded due to risk behaviors sexual intermediary avoiding such extensive sample stratification.

A two-step cluster analysis was performed first, but it proved to be a poor indicator for real-world patients because it established a cutoff point of 25 sexual partners. Therefore, the groups were divided by assuming a cut-off point of two sexual partners, which corresponded to the sample's second tertile and 67% of the participants.

The subjects were separated into two groups, classified as low sexually vulnerable, composed by subjects who had up to two sexual partners and reported using condoms during every sexual encounter in the past year ($N = 181$), denominate GR1. And the other, classified as highly sexually vulnerable subjects who had three or more sexual partners in the past year and reported either never using condoms or using them sporadically ($N = 118$) the GR2.

The patients were interviewed up to two weeks after admission. Data collection was conducted by four members of the staff who were previously trained to apply the questionnaire of this study. No refusals were recorded. This study was approved by the Federal University of Sao Paulo (UNIFESP) Ethics Committee (protocol number 1193/09), and all the subjects signed an informed consent form. The patients did not receive any refunds or compensation for participating in this study.

A structured questionnaire containing socio-demographic information, sexual behavior information, Drug of choice (DOC), Short Alcohol Dependence Data (SADD), Drug Abuse Screening Test (DAST-20) and The Fagerström Test for Nicotine Dependence (FTND) was used. The socio-demographic data included age, educational level, ethnicity, marital status, monthly income, employment status, and religious affiliation.

Sexual behavior information. These questions assessed patients' sexual activity in the past 12 months; frequency of condom use (always, sometimes, never) with penetration (oral, vaginal and/or anal) in the past 12 months; number of lifetime sexual partners; lifetime history of sex with sex workers; sexual orientation (hetero, homo and bisexual); homosexual experiences in exchange for drugs in the past 12 months; history of STIs; HIV testing; induced abortion (in female patients; in male patients, induced abortion in a corresponding sexual partner); sexual intercourse per week; use of the morning-after pill in the lifetime (only for female gender); and age at the time of first intercourse with penetration. The formulated questions were based on two Brazilian research studies (Abdo, 2004; Berquó & Barbosa, 2008).

Drug of choice (DOC) refers to the misuser's preferred drug. This information was elicited directly by the question: "What is your drug of choice?" Although substance users often meet the diagnostic criteria for dependence on multiple drugs, DOC is usually included in the clinical status of the patient because it helps to identify user profiles for the provision of appropriate case management (Clark et al., 2012). Considered poly drug user the individual who failed to set his/her drug of choice and has more than three drugs (licit and illicit) abuse as their preference is considered as a poly drug user.

Characteristics related to the treatment of the substance-related disorder. The duration of substance abuse and the number of previous treatments excluding the present one were elicited.

Short Alcohol Dependence Data (SADD). The Short Alcohol Dependence Data (SADD) consisted of 15 questions related to severity of alcohol dependence. The severity was classified on a scale from 0 to 20 and was scored as follows: mild (0-9), moderate (10-19), and severe alcohol dependence (≥ 20). The Brazilian version of the SADD and the original English version are highly correlated, and the coefficient of internal consistency is 0.79 (Rosa-Oliveira et al., 2011).

Drug Abuse Screening Test (DAST-20). The Drug Abuse Screening Test (DAST) consisted of 20 questions related to drug use within the last year. The problem severity was classified on a scale from 0 to 20 and was scored as follows: 0 =

no problem; from 1 to 5 = mild; 6 to 10 = moderate; 11 to 15 = substantial; and 16 to 20 = severe. The severity scale has been used in several studies, and measures of reliability and validity have been reported to be satisfactory in all the versions for utilization as a clinical and/or research tools (Yudko, Lozhkina & Fouts, 2007). In the latter study, the Cronbach's alpha of DAST was 0.92, which indicates excellent internal consistency (Diehl, Silva, & Laranjeira, 2013).

The Fagerström Test for Nicotine Dependence (FTND). This test consists of six items. The scores obtained on the test permit the classification of nicotine dependence into five levels: very low (0-2 points); low (3-4 points); moderate (5 points); high (6-7 points); and very high (8-10 points). The reliability index is excellent (0.87), and Cronbach's alpha coefficient ranges from 0.55 to 0.74 (Meneses-Gaya et al., 2009).

A descriptive data analysis was initially performed. For the categorical variables, the absolute and relative frequencies are presented, and for the numerical variables, the frequency measurements (mean, minimum, maximum, and standard deviation) are presented. Statistical analyses include chi-square test or Student's t-test for independent samples and logistic regression. Due to the dichotomous nature of the dependent variable and to facilitate the interpretation of the results, Prevalence ratio (PR) was used (Poisson regression model with robust estimation for the standard error). A significance level of 5% was used for al statistical tests. The Statistical Package for Social Science (SPSS Inc., Chicago, USA), version 17.0 was used for the analysis of the data.

Results

Socio-demographic Data

The socio-demographic characteristics of both groups are displayed in Table 1. The sample (N = 299) was divided in two groups of subjects classified as, low sexually vulnerable (GR1) 181 (60.5%) and highly sexually vulnerable (GR2) 118 (39.5%). The total sample was characterized predominantly by adults, Caucasian, unmarried, and Catholic, unemployed, and earned a minimum wage of less than $330 dollars. However, there were associations between group of risk sexual behaviour and education level ($p < 0.001$), race ($p < 0.001$), religion ($p < 0.001$), occupational status ($p = 0.007$) and salary range ($p < 0.001$).

There has been a predominance of individual with secondary school 53.4%, white 51.7%, Evangelical 58.6%, non-registered employee/liberal profession 58.8%, income (2 a 3 MW) 56.6% more than 7 MW 68.2%, among the group of highly vulnerable sexual behaviour (GR2). In contrast, the group with low vulnerable sexual behaviour (GR1) showed the highest percentage of illiterate 95.4%, Catholic 71.6%, totally unemployed 66.5%, and earned approximately USD 330 at the time of the study 76.4%.

Characteristics of substance use

The characteristics of substance use of the 299 participants are shown in Table 2. In the total sample the DOC the most frequent were 56.2% crack, 18.7% alcohol, and 16.4% cocaine. There were no reports of previous or current use of injectable drugs in this sample, although this was not an exclusion criterion. The tests for the evaluation of severity of dependence indicated that 31.8% of subjects exhibited high/very high FTND scores, 25.1% scored severe on the SADD, and 49.2% scored substantial on the DAST.

Associations were identified between the groups of sexual risk behavior and all variables related to the use of psychoactive substances. As show in Table 2, heterogeneous distributions were observed in both groups. In the GR2, the findings showed a higher percentage in the use of snorted cocaine (DOC) (69.4%), poly-drug user (70%), tobacco - very low/low/moderate (FTND) (56.2%), mild dependence (66.7%), severe dependence of alcohol (58.7%) (SAAD), and substantial /severe dependence of drug (DAST) (64.6%).

In contrast, the group with low sexually vulnerable (GR1) presented higher percentages of individuals the use of crack (DOC) (72.6%), non-smoker (FTND) (81.7%), does not use alcohol (SAAD) and (74.8%) no problem/low/moderate (91.5%) (DAST). The findings also showed that there were no significant differences between the two groups (data not displayed in table) in relation to the average time of use of psychoactive substances (GR1 15±9.8 versus GR2 14.7±9.4, $p = 0.793$) and the number of previous treatment for drug addiction (GR1 2.7±4.1 versus GR2 2.8±2.7, $p = 0.915$).

Characteristics of sexual behavior

The characteristics of sexual behaviour of the sample are shown in Table 3. Fifth-seven percent had sexual activity in the past 12 months. The distribution of sexual orientation in the sample was (94%) heterosexual, (4%) homosexual, and (2%) of bisexual.

The average age in the total sample at the time of first intercourse was (mean 14.6; *SD* 3.4) years old, and in the comparison between the groups, (GR1 15.2±3.2, versus GR2 14.2±3.4), no statistically significant difference was identified. The average number of sexual partners in the past year was 2.9. However, there was significant statistical difference between the two groups (GR1 0.4±0.7 versus GR2 6.7±5.1; $p < 0.001$).

Accordingly, the average number of sexual encounters per week was (Mean 4.5; *SD 4.9*), and when comparing the groups (GR1 3.2±2.5 versus GR2 5.4±5.9) a significant statistical difference ($p < 0.001$) was observed.

However, there were association between high risk sexual behaviour (GR2) and sexual activity in the last 12 months ($p < 0.001$), homosexual experience ($p < 0.001$), homosexual experiences in exchange sex for drugs ($p < 0.001$), history of STIs ($p < 0.001$), HIV testing ($p < 0.001$), induced abortion ($p < 0.001$) and, sex with sex worker ($p < 0.001$).

Table 1
Socio-demographic Characteristics of Sexual Risk Groups (N = 299)

	Total		Sexual risk group				p value
			Up to 2 sexual partners in the last year and always uses condoms (n = 181) GR1		Three or more sexual partner in the last year and uses condoms sporadically or never uses condoms (n = 118) GR2		
	N	%	N	%	N	%	
Gender							
Male	260	87.0	155	59.6	105	40.4	0.401
Female	39	13.0	26	66.7	13	33.3	
Marital status							
Single	180	60.2	116	64.4	64	35.6	
Married/stable union	68	22.7	35	51.5	33	48.5	0.169
Widowed/Divorced/Separated	51	17.1	30	58.8	21	41.2	
Educational level							
Illiterate	65	21.7	62	95.4	3	4.6	
Elementary school	130	43.5	72	55.4	58	44.6	**<0.001**
Secondary school	88	29.4	41	46.6	47	53.4	
Higher education/graduate education	16	5.4	6	37.5	10	62.5	
Ethnicity/skin color/race							
Non-white	148	49.5	108	73.0	40	27.0	**<0.001**
White	151	50.5	73	48.3	78	51.7	
Religion							
Catholic	176	58.9	126	71.6	50	28.4	
Evangelical	58	19.4	24	41.4	34	58.6	**<0.001**
Spiritist/Umbanda/Candomblé/ Other	38	12.7	18	47.4	20	52.6	
Firm atheist/without religion	27	9.0	13	48.1	14	51.9	
Occupational status							
Retired	2	0.7	1	50.0	1	50.0	
Registered employee	36	12.0	19	52.8	17	47.2	**0.007[a]**
Non-registered employee/liberal profession	51	17,1	21	41.2	30	58.8	
Fully unemployed	206	68.9	137	66.5	69	33.5	
Homemaker	4	1.3	3	75.0	1	25.0	
Salary range							
Up to 1 MW	144	48.2	110	76.4	34	23.6	
2 to 3 MW	76	25.4	33	43.4	43	56.6	**<0.001**
4 to 5 MW	41	13.7	22	53.7	19	46.3	
6 to 7 MW	16	5.4	9	56.3	7	43.8	
More than 7 MW	22	7.4	7	31.8	15	68.2	

[p] Descriptive level of the chi-squared test [a] Descriptive level of the Fisher's exact test.

Table 2
Characteristics of substance use and dependence and Sexual risk groups (N = 299)

	Total		Sexual risk group				p
			Up to 2 sexual partners in the last year and always uses condoms (n = 181) GR1		Three or more sexual partner in the last year and uses condoms sporadically or never uses condoms (n = 118) GR2		
	N	%	N	%	N	%	
DOC							
Alcohol	56	18,7	31	55.4	25	44.6	
Marijuana	15	5.0	9	60.0	6	40.0	
Snorted cocaine	49	16.4	15	30.6	34	69.4	<0.001[a]
Crack	168	56.2	122	72.6	46	27.4	
Poly Drug user	10	3.3	3	30.0	7	70.0	
Oral Opiates	1	0.3	1	100	-	-	
FTND							
Very low /Low/Moderate	73	24.4	32	43.8	41	56.2	
High/very high	95	31.8	42	44.2	53	55.8	<0.001
Non smoker	131	43.8	107	81.7	24	18.3	
SAAD							
Mild dependence	27	9.0	9	33.3	18	66.7	
Moderate dependence	42	14.0	25	59.5	17	40.5	<0.001
Severe dependence	75	25.1	31	41.3	44	58.7	
Does not use alcohol	155	51.8	116	74.8	39	25.2	
DAST							
No problem/low /Moderate level	118	39.5	108	91.5	10	8.5	<0.001
Substantial /severe level	147	49.2	52	35.4	95	64.6	
Does not use drugs	34	11.4	21	61.8	13	38.2	

[p] Descriptive level of the chi-squared test (test statistics; degrees of freedom). [a] Descriptive level of the Fisher's exact test.
Note. DOC=Drug of Choice; FTND= The Fagerström Test for Nicotine Dependence; SADD= Short Alcohol Dependence Data; DAST= Drug Abuse Screening Test

There was a high percentage of individuals without sexual intercourse in the last 12 months (99.2%), without homosexual experience (66.9%), without homosexual experiences in exchange sex for drugs (64.8%), without history of STIs 67.8%, without HIV testing (81.1%), without induced abortion (67.8%), without sex with sex worker (81%), predominantly in the group with low vulnerable sexual behaviour (GR1).

It is the higher percentage of individuals with some homosexual experience (92.9 %), in the group that showed sexual behavior vulnerability (GR2).

Highly Vulnerable Sexual Behaviour

According to the Poisson regression model (Figure 1), the variables that remaining significant were DOC, SAAD, DAST, history of STIs, sex with sex workers and use of the morning–after pill. Thus, it was observed that the likelihood of users of alcohol and cocaine snorted, it have high-risk sexual behavior is 2.47 and 1.66 times to users of crack/opiate/poly-drug respectively.

In relation to scores of DAST, note that those who did not present any risk or low and moderate level presented probabilities of having high-risk sexual behavior similar to those of who do not use drugs. On the other hand, those who have substantial or severe level presented likelihood 3.64 times greater. It was also noted that those who have sex with sex workers (males only), which made use of the morning-after pill and have a history of Sexual Transmitted Infection (STI) presented probabilities respectively of (96 %), (78%) and (39%) higher than those belonging to the group of high risky sexual behavior.

Table 3
Characteristics of Sexual Behavior and Sexual Risk Groups (N = 299)

	Total		Sexual risk group				p. value
			Up to 2 sexual partners in the last year and always uses condoms (n = 181) GR1		Three or more sexual partner in the last year and uses condoms sporadically or never uses condoms (n = 118) GR2		
	N	**%**	N	%	N	%	
Sexual activity in the past 12 months							
Yes	172	57.5	55	32.0	117	68.0	<0.001
No	127	42.5	126	99.2	1	0.8	
Sexual orientation							
Heterosexual	281	94.0	170	60.5	111	39.5	
Homosexual	12	4.0	7	58.3	5	41.7	1.000[b]
Bisexual	6	2.0	4	66.7	2	33.3	
Homosexual experience							
Never	239	79.9	160	66.9	79	33.1	
At least once	14	4.7	1	7.1	13	92.9	<0.001
More than once	46	15.4	20	43.5	26	56.5	
Homosexual experience in exchange for drugs							
Yes	32	10.7	8	25.0	24	75.0	<0.001
No	267	89.3	173	64.8	94	35.2	
History of STIs							
Yes	66	22.1	23	34.8	43	65.2	<0.001
No	233	77.9	158	67.8	75	32.2	
HIV testing							
Yes	167	55,9	74	44.3	93	55.7	<0.001
N**o**	132	44,1	107	81.1	25	18.9	
Use of the morning-after pill							
Yes	12	4.0	4	33.3	8	66.7	0.069[a]
No	287	96.0	177	61.7	110	38.3	
Induced abortion							
Yes	66	22.1	23	34.8	43	65.2	<0.001
No	233	77.9	158	67.8	75	32.2	
Sex with sex workers							
Yes	136	45.5	49	36.0	87	64.0	<0.001
No	163	54.5	132	81.0	31	19.0	

[p] Descriptive level of the chi-squared test (test statistics; degrees of freedom). [a] Descriptive level of the Fisher's exact test. [b]

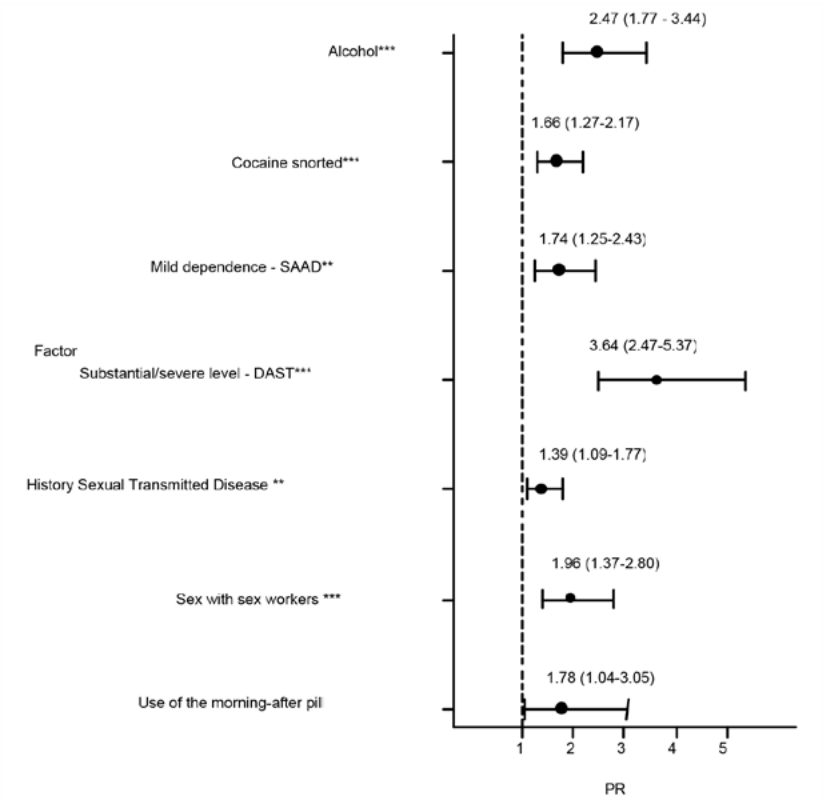

Figure 1. Factors associated to sexual risky behavior prevalence ratios and 95% Confidence Intervals obtained from a Poisson regression model with robust variance

Discussion

The purpose of this investigation was to evaluate high-risk sexual behaviors in a sample of substance-disorder patients admitted in an inpatient addiction unit. Socio-demographics characteristics of this sample are peculiar according to different levels of sexual risk behaviors. Evidence suggests that drug addicts are characterised in particular by a complex population because of the diversity of sexual risk behaviors that those users engage (social context, sexual orientation, and type of sexual interaction) (Celentano, Latimore, & Mehta, 2008).

Thirty-nine percent the subjects of the high risk sexual behavior group also exhibited a higher prevalence of risky behaviors including having sex with sex workers, homosexual experiences and homosexual experiences in exchange for drugs, history of STIs, HIV testing, use of the morning–after pill, induced abortion. These findings are similar to those presented in the literature (Harzke, Williams, & Bowen, 2009; Pallonen, Timpson, Williams, & Ross, 2009). Evidences show that high level of dependence on alcohol and illegal drugs increased the probability of belonging to the group with the highest sexual risk, independent of gender (Celentano et al., 2008; Dickson-Gomez et al., 2012; Mitchell et al., 2009).

The finding of the present study also indicated that this sample exhibited high rates of vulnerable sexual behavior: non-use or inconsistent use of condoms; a high number of sexual partners over the course of a year, earlier onset of sexual activity; and multiple sexual encounters per week. Furthermore, other sexual behavior traits, such as homosexual experiences in exchange for drugs, earlier onset of sexual activity, and a larger number of sexual partners, were more frequent. Individual characteristics and treatment approaches can differentially affect outcomes (for example: safe sex, less use of drugs, reduces sex under the influence of drugs), and these differences have important clinical and treatment implications (Tuchman, 2012).

Many studies have identified high levels of sexual risk behaviors among crack users (Atkinson et al., 2010; de Souza et al., 2002; Dickson-Gomez et al., 2012), including sex with multiple partners, inconsistent or non-use of condoms, and high rates of exchanging sex for drugs (Dickson-Gomez et al., 2012; Pallonen et al., 2009; Schönnesson et al., 2008). In our sample, however, the high sexual risk group was observed in individual who snorted cocaine and the use of opiate and alcohol as their DOC. One reason for the difference may be that, although crack was statistically the most frequent DOC, this variable was associated with high-risk behavior group. (GR2). In addition, most individuals reported crack as their drug of choice

Data on frequency and patterns of psychoactive drug use were not collected in this study, since the authors were interes-

ted in assessing the associations with the DOC. However, the absence of this information may be considered one of limitations of this study since frequency and pattern of consumption tend to be less subjective measures that DOC.The increase in sexual behavior while intoxicated with snorted cocaine may be due to the direct pharmacological effects of the drug, which increase sexual desire. Alternatively, especially among long-term cocaine users, it may be due to the increased opportunities for sex that exist in the context of cocaine use (For example, opportunities for sexual behavior, expectations about the effects of the drug, social norms) (Kopetz et al., 2010; Wright, 2012). One of the damaging effects of cocaine use is compromised judgment capacity, which leads to hazardous sexual behaviors and increases the chances of contracting HIV (Dunn & Laranjeira, 1999; Kumar, 2011). Crack also has deleterious effects on perceived sexual desire and erectile function, though sexual behavior in crack users seems to be more frequently linked to "sex for crack" exchanges than sexual desire per se (Nappo et al., 2011).

Previous research has also linked alcohol dependence with an increased number of sexual partners, inconsistent condom use, and an increased incidence of STIs (Berbesí-Fernández, Montoya-Vélez, & Segura-Cardona, 2013; Espada, Morales, Orgilés, Piqueras, & Carballo, 2013). The effects of alcohol on the appraisal of sexual potential differed by partner risk condition. Some results have suggested that wives of alcoholic men are unknowingly placed at risk for indirect exposure to STIs as a result of their husbands' sexual risk behaviors (Hall, Fals-Stewart, & Fincham, 2008; Osborne & Cottler, 2012; Varma, Chandra, Callahan, Reich, & Cottler, 2010).

Interestingly, the present study found an association between FTND scores and the sexually vulnerable groups. As a rule, studies tend to focus on the relationship between smoking and sexual dysfunction, while the association of the former with high-risk sexual behavior has scarcely been addressed (Diehl et al., 2013; Zaazaa, Bella, & Shamloul, 2013). That scarcity notwithstanding, there are reports in the literature on the correlation between the exposure of oral mucosa to tobacco, which causes abrasions and makes it susceptible to human papilloma virus (HPV), and impaired reproductive health (Kazemi et al., 2013; Zil-A-Rubab et al., 2013). Furthermore, many studies have reported tobacco use by adolescents and young adults as a predictor of early sexual intercourse, unwanted pregnancy, infrequent condom use, receiving money for sexual services, and lifetime risk of contracting an STI (Hanna, Yi, Dufour, & Whitmore, 2001; Wu, Witkiewitz, McMahon, Dodge, & Conduct Problems Prevention Research Group, 2010).

This study was limited by its recruitment, which took place at only one tertiary service. Therefore, this convenience sample of patients may not be representative of the population of substance abusers because it is expected that only the most serious or highly motivated patients seek treatment. In this sample, there were no injecting drug users, which is not surprising for a Brazilian population of drug abusers because this country does not have a prevalent "injecting culture". This trend has been especially prevalent since crack became available in the 1990s, which corresponded to the period during which the present sample initiated drug abuse (Dias et al., 2011). In addition, opioids, which are also known to be mainly used intravenously, are more expensive and less available in Brazil. Consequently, these factors may limit the external validity of these findings.

Nevertheless, the present sample could be considered similar to others that have been previously studied in the clinical setting in Brazil with respect to the prevalence of various drugs of choice and the sample profile. Among the illicit drugs, treatment demand for crack abuse has perhaps increased the most in recent years. Crack addiction is the most frequent cause of cocaine-related hospitalization. A national review study indicated that the profile of crack users included young, unemployed, unschooled, and poor individuals from broken families with many sexual vulnerability behaviors (Duailibi et al., 2008). This review study also demonstrated that the most frequent risk behaviors associated with crack/cocaine users are a high number of partners, unprotected sex, and trading sex for crack or for money to purchase the drug of choice (Duailibi et al., 2008).

Another limitation is that we did not investigate sex under the influence of substances; doing so is difficult, partly due to the ethical issues, the research methods used and also to the complexity of studying these dynamic associations. It is unknown whether hazardous sex is antecedent to or a result of drug use or if both behaviors are concurrently associated with other factors. In addition, the presence of psychiatric comorbidities (in either axis I or II) associated with substance dependence was not investigated by means of standardized instruments, for example, the Composite International Diagnostic Interview (CIDI) (Kessler et al., 1998). Although countless studies have indicated that the presence of psychiatric comorbidities in drug users is associated with a higher frequency of high-risk sexual behaviors (Meade & Sikkema, 2005; Newville & Haller, 2012). Even though investigating the presence of psychiatric comorbidities would have increased the relevance of the results of the present study, we decided not to include such efforts in the study protocol for practical reasons. We acknowledge that the selection of the DAST might represent another limitation in the present study. However, it is worth emphasizing that the Cronbach's alpha of this tool was 0.92 in a previous study conducted by our group (Diehl et al., 2013), which indicates excellent internal consistency. Additionally, in the present study, none of the scales data were represented as continuous variables. Instead, all of the scale data were represented as categorical variables only, which hindered any analysis of the internal consistency of the scales used. Finally, we recognize that issues related to HIV infection may strongly condition the sexual risk behavior in the study population. However, current informa-

tion on HIV status sample are not included. This can be considered another limitation of this study.

The clinical implication is that substance abuse is one of the strongest predictors of sexual risk behavior. Thus, treating substance abuse should focus on harm-reduction in reducing sexual risk behaviors. As such, the focus should be on identifying individuals for medical and/or behavioral treatments for substance abuse to reduce or eliminate substance-related sexual transmission behaviors in combination with HIV-prevention strategies in substance users to reduce sexual risk behaviors and related outcomes (e.g., HIV, STI) (Shoptaw et al., 2013). In addition, sexual health should be a part of the recovery process and should not be subject to discrimination. Because sexual health and its correlates, including responsibility, self-efficacy, the intentional use of condoms, and condom-use behaviors, are not directly addressed in alcohol and drug treatment centers, poor sexual health may contribute to treatment failure, leading to relapse and the consequent substantial risk of HIV exposure, STIs, and unplanned pregnancies. This relationship occurs because drugs affect the ability to make assertive decisions relative to the use of condoms, and casual sexual encounters may be related to increased opportunities for drug abuse (Harvey, 2009; Williams et al., 2008; Zule, Costenbader, Coomes, & Wechsberg, 2009).

Brief group interventions, such as positive choice interventions, educational interventions, and motivational interventions, have been found to increase condom use and the intention to use condoms and also to alter condom-use attitudes and beliefs in substance-related disorder patients (Harvey,2009). Some evidence for sexual risk reduction interventions for alcohol and drug addiction patients suggests that substance-dependent patients are diverse in terms of HIV status and substance of choice; as a result, interventions that can be tailored to meet the recipients' individual needs with respect to gender and sexual orientation are required. It is also important that such interventions be deliverable in a variety of venues and by different staff members (For example: social workers, counselors, nurses, outreach workers) who may not possess advanced clinical or psychological training (Harvey, 2009; Wright, 2012).

Although the literature is quite informative with respect to risk behaviors and infection rates for different blood-borne and sexually transmitted infections, this knowledge alone does not seem to be sufficient to change sexual behavior (Williams et al., 2008). Many patients come to treatment with feelings of guilt and shame related to their sexual behavior prior to recovery; if these feelings are not resolved, they can be a factor in relapse and non-compliance rates. Therefore, identifying, preventing, and managing these issues in alcohol and other drugs users are an excellent opportunity to bolster their treatment (Kopetz et al., 2010; Williams et al., 2008). Although this subject has been addressed as an overlying topic, this study had several strengths once that included a large clinical sample of Brazilians with substance use disorders, one group of the population that is particularly underrepresented in the body of literature.

One of the possible implications of the present study concerns attempts to improve our understanding of high-risk sexual behaviors in drug users who are not undergoing treatment by accessing the use of other methods, such as community-based outreach methods, including establishing contacts with the local leadership in areas of poverty or areas that are difficult to access, e.g., as a function of their high risk of violence (Schwartz, Kelly, O'Grady, Mitchell, & Brown, 2011). These topics should be addressed in future research according to the number of drug users who seek treatment is still low, and many of users are marginalized as a result of untreated sexually transmitted diseases, such as hepatitis B and C, for which they seldom seek healthcare services (Malta et al., 2011).

The present sample exhibited traits related to the level of dependence, drug of choice and sexual behaviors that increased prevalence ratios of high-risk sexual behaviors.

Conflict of interest

None.

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Desempeño neuropsicológico y características sociodemográficas en pacientes alcohólicos en tratamiento

Neuropsychological performance and demographic characteristics in alcoholic patients in treatment

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Resumen

Este estudio comparó el desempeño cognitivo de sujetos alcohólicos (GA) y de participantes de la población general (GC) sin la dependencia del alcohol. La muestra estuvo compuesta por 141 hombres, con edad entre 18 y 59 años. Divididos en dos grupos, 101 pacientes alcohólicos sin comorbilidades, internados para el tratamiento de la dependencia química, y 40 sujetos de la población general sin dependencia, emparejados por edad y nivel socioeconómico. Los instrumentos utilizados evaluarán los datos socio-demográficos y la clasificación económica, la dependencia del alcohol, las comorbilidades psiquiátricas, el desempeño cognitivo, las funciones ejecutivas, la memoria y la percepción. Los resultados mostraron que el grupo dos GA denota dependencia grave en relación al alcohol y el 92,1% indican tener algún familiar con problemas asociados al alcohol; para el GC, el 41,5% afirmaron este dato. En el GA 59,4% estaban abstinentes entre 8 y 15 días, en la evaluación, y en el GC el 43,9%, lo estaban más de 60 días. En el desempeño neuropsicológico, fue verificado que había una disminución de las funciones cognitivas en los participantes alcohólicos, siendo que el GA sugiere un enlentecimiento psicomotor. Así, se puede inferir que el alcohol afecta en gran medida las funciones cognitivas de las personas que dependen de esta sustancia. Además, hubo un mayor número de historias familiares con prevalencia de síntomas de ansiedad y depresión y de adicción a la nicotina en pacientes alcohólicos en comparación con la población general.

Palabras Clave: desempeño cognitivo, dependencia del alcohol, estudio cuantitativo.

Abstract

This study compared the cognitive performance of alcoholics (AG) and participants from the general population (CG) without alcohol dependence. The sample consisted of 141 men, aged 18 and 59. Divided into two groups, 101 alcoholic patients without comorbidities, hospitalized for drug abuse treatment, and 40 healthy individuals from the general population, matched for age and socioeconomic status. The instruments assessed the sociodemographics data and economic classification, alcohol dependence, psychiatric comorbidities, cognitive performance, executive functions, memory and perception. The results showed that the AG group presented severe dependence on alcohol and 92.1% indicated having a family with problems associated with alcohol for only 41.5 % of the CG. At the moment of the evaluation, 59.4 % of the participants of the AG group were abstinent between 8 and 15 days, and the in CG, 43.9%, were more than 60 days alcohol free. The neuropsychological performance verified that there was a decline in cognitive functions in alcoholics' participants, whereas the AG suggests psychomotor retardation. Thus, it can be inferred that alcohol greatly affects cognitive functions of people who depend on this substance. In addition, there was a greater number of family stories with prevalence of symptoms of anxiety and depression and nicotine addiction in alcoholic patients compared with the general population.

Key Words: cognitive performance, alcohol dependence, quantitative study.

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El alcohol es una droga depresora del Sistema Nervioso Central que puede afectar a todas las funciones cerebrales, como comportamiento, cognición, razonamiento, respiración, coordinación psicomotora y la sexualidad (Washton y Zweben, 2009). La dependencia del alcohol se caracteriza por la preocupación en obtener y consumir la substancia, con falta de capacidad de controlar el consumo de manera responsable, así como la diminución de la función psicosocial y el uso continuado a pesar de las consecuencias negativas (American Psychiatric Association, 2002).

Conforme Monteiro (2013), el consumo de alcohol es un problema de salud pública en toda América Latina, ocasionando muertes y enfermedades cau¬sadas por su consumo. Se estima que el 9% de la población brasileña es dependiente del alcohol y presenta problemas relacionados con el uso excesivo de esta substancia (Laranjeira, Pinsky, Zaleski y Caetano, 2007).Una investigación con 7.939 personas brasileñas reveló que el 74,6% de los participantes que contestaron a la encuesta ya habían tomado bebidas alcohólicas alguna vez a lo largo de su vida, siendo ese un porcentaje inferior a la de otros países (Chile con 86,5% y EUA, 82,4%). La estimativa de dependientes del alcohol fue de 12,3% siendo mayor para el sexo masculino (19,5%) que para el sexo femenino (6,9%) (Galduróz, Noto, Fonseca y Carlini, 2007).

Un estudio español (Fernández-Serrano, Pérez-García, Río-Valle, y Verdejo-Garcia, , 2009) examinó la asociación entre el alcohol comparado con la cocaína, heroína y marihuana en el desempeño de funciones ejecutivas en una muestra de personas que utilizan diversas sustancias. En este estudio, las personas dependientes de sustancias mostraron un rendimiento significativamente inferior en comparación con el grupo control en todos los ámbitos ejecutivos evaluados. Además, los resultados indicaron que el abuso de alcohol aparece asociado negativamente con deficiencias en la fluidez verbal y la toma de decisiones.

Las alteraciones en las funciones cognitivas, como déficits de aprendizaje y memoria, capacidad visuoespacial, habilidades perceptivo-motrices, abstracción y funciones ejecutivas asociadas a las regiones frontales, de los alcohólicos son bastante mencionadas en la literatura especializada (Arias, Santin, y Rubio, 2000; Langlais y Ciccia, 2000; Pfefferbaum, Sullivan y Rosenbloon, 2000; Oliveira, Laranjeira y Jaeger, 2002; Cunha y Novaes, 2004; Uekermann, Crannon, Winkel, Schlebusch y Daum, 2007). Conforme Uekermann et al. (2007) los cambios en las funciones ejecutivas y en la memoria son interpretados como una vulnerabilidad específica de los lóbulos frontales a los efectos tóxicos del alcohol.

Aunque, se encuentra crecientes problemas relacionados con el consumo de drogas, no hay consenso sobre los cambios cognitivos resultantes de la dependencia del alcohol, en especial los efectos en las funciones ejecutivas (Goldstein y Volkow, 2002; Lubman et al., 2004). Por otra parte, en el contexto brasileño hay una falta de estudios que abordan este tema. Por lo tanto, el objetivo de este estudio es comparar el desempeño neuropsicológico de pacientes alcohólicos en tratamiento de desintoxicación con la población general. Además, se buscó identificar si existe asociación entre factores sociodemográficos y alcoholismo.

Método

Participantes

Este estudio de caso-control tuvo 141 sujetos, del sexo masculino, en el rango de edad de 18 a 59 años, con por lo menos de cinco años de estudio. Se decidió trabajar exclusivamente con una muestra de hombres debido a que en las instituciones donde se obtuvo autorización contaban exclusivamente con internos varones. La muestra fue dividida en dos grupos: 101 sujetos alcohólicos sin comorbilidades (Grupo de Alcohólicos), internados en tres unidades de tratamiento para la dependencia química en la ciudad de Porto Alegre-RS, siendo dos de ellas públicas y una privada, y 40 sujetos de la población general sin dependencia del alcohol (Grupo Control), emparejados por: edad y nivel socioeconómico. El Grupo Control fue reclutado por la red de contactos de los investigadores.

Los criterios de exclusión de la investigación para el GA fueron: presencia del síndrome de privación grave, con síntomas de abstinencia del alcohol (delirios, alucinaciones) que cambiasen el desempeño en los tests neuropsicológicos, trastornos orgánicos cerebrales y trastornos psiquiátricos graves de acuerdo con la entrevista estructurada basada en los criterios del DSM – IV – TR (American Psychiatric Association, 2002) y en el ASR (*Adult Self Report- ASR* - Achenbach y Rescorla, 2001), además de que los individuos presentasen un potencial intelectual verbal pre-mórbido inferior a la media (*Screening* Cognitivo del WAIS-III - Wechsler, 1997). De acuerdo con estos criterios fueron excluidos tres participantes, uno de ellos por indicar la presencia de un trastorno cerebral orgánico y dos por presentar un nivel intelectual pre-mórbido inferior a la media estimada para el rango de edad.

Los criterios de exclusión de la investigación para el GC fueron: presencia de algún trastorno orgánico cerebral y trastornos psiquiátricos graves de acuerdo con el ASR (*Adult Self Report- ASR* - Achenbach y Rescorla, 2001), así como los individuos con un potencial intelectual pre-mórbido verbal por debajo de la media (*Screening* Cognitivo do WAIS-III - Wechsler, 1997). En este sentido, dos participantes fueron excluidos por presentar un potencial intelectual pre-mórbido por debajo de la edad media estimada.

Instrumentos

Entrevista estructurada: Basada en los criterios del DSM – IV- TR (American Psychiatric Association, 2002), con el objetivo de recoger los datos socio-demográficos y evaluar los criterios diagnósticos para la dependencia del alcohol.

Criterio de Clasificación Económico Brasil (2007): Sistema de clasificación de precios para el pueblo brasileño (ABEP, 2007).

Cuestionario SADD (Short Alcohol Dependence Data) (Raistrick, Dunbor y Davidson, 1983): Fue adaptado para el uso en Brasil por Jorge y Masur (1986). Es una escala de auto-informe, constituida por 15 ítems relacionados al consumo del alcohol, que evalúa el grado de dependencia de esta substancia.

***Adult Self Report*- ASR** (Achenbach y Rescorla, 2001) – Este cuestionario es de auto-informe, para el rango de edad de los 18 a los 59 años, y analiza diversos aspectos del funcionamiento adaptativo de los adultos.

BAI – Inventario de Ansiedad de Beck (Beck y Steer, 1990; Cunha, 2001), fue aplicado para evaluar la presencia de síntomas de ansiedad.

BDI-II – Inventario de Depresión de Beck (Beck, Steer y Brown, 1996)[1] compuesto por 21 ítems, fue aplicado para evaluar la presencia de síntomas de depresión. La validación de la versión brasileña está en curso, por lo que se utilizó un punto de corte de validación americana.

Screening **Cognitivo del WAIS-III**[2] (Wechsler, 1997): incluye los subtests Vocabulario, Cubos y Códigos.

Test de clasificación de tarjetas de Wisconsin[3] (Heaton et al., 1993): el Test de Clasificación de Tarjetas de Wisconsin es un test de evaluación cognitiva que mide la flexibilidad del pensamiento del sujeto para generar estrategias de solución de problemas (Heaton et al., 1993).

Test de la Figura Compleja de Rey – forma A[4] (Rey, 1959): Su objetivo es identificar prejuicios en la percepción visual y en la memoria inmediata.

Procedimientos para la recogida de datos. Este estudio fue evaluado y aprobado por el Comité de Ética de la PUCRS, tiene el protocolo de investigación nº 07/03979. Todos aquellos que aceptaron participar en el estudio firmaron un Consentimiento Informado, respetando la declaración de Helsinki. Las evaluaciones fueron realizadas individualmente. El grupo de participantes alcohólicos realizó la evaluación después de los siete días de desintoxicación.

Análisis Estadístico. Los datos fueron compilados y analizados mediante el SPSS 17.0 y sometidos a la estadística descriptiva (media, desviación típica, frecuencia), la normalidad de la muestra se evaluó mediante la prueba de Kolmogorov-Smirnov (p> 0,05). Se utilizó la prueba no paramétrica de Mann-Whitney para comparar las variables sin distribución normal y la prueba de "t" para las variables con distribución normal. La prueba de Chi-cuadrado de Pearson se determinó para las variables categóricas. El nivel de significación fue de 0,05.

Resultados

Características socio-demográficas y Riesgo Familiar

Cuanto al estado civil el GA indicó que el 20,8% (n= 21) están solteros, el 50,5% (n= 51) están casados y el 28,7% (n= 29) están separados/ divorciados o viudos. En el GC el 26,8% (n= 11) están solteros, el 61,0% (n= 25) están casados y el 12,2% (n= 5) están separados/ divorciados o viudos, y de acuerdo con la prueba Chi-Cuadrado de Pearson demuestra que no hay dependencia entre los grupos (c^2= 0,367, p= 0,887). Los datos sobre la edad y los años de estudio de los participantes se describen en la Tabla 1.

Tabla 1
Distribución de la muestra por edad y años de estudio

	Grupo de Alcohólicos (n= 101)			Grupo Control (n= 41)			Mann-Whitney z (p*)
	Mediana	Mín.	Máx.	Mediana	Mín.	Máx.	
Edad	43,00	24	60	42,00	18	60	-1,300 (p= 0,194)
Años de estudio	10,00	5	22	12,00	5	18	-3,729 (p≤ 0,001)

* Los resultados fueron significativos al nivel de 5%.
Nota. Mín. (mínimo); Máx.(máximo); n (número da la muestra); z (estadística test); p (nivel mínimo de significancia).

La Tabla 2 muestra la estratificación de la muestra por nivel socioeconómico, de acuerdo con el Criterio de Clasificación Económica Brasil (2007), los datos sobre ocupación que no demuestran una diferencia significativa entre los grupos, y la evaluación del riesgo familiar.

Análisis de la gravedad de la dependencia, edad de inicio de uso del alcohol y edad de la primera embriaguez

De acuerdo con el SADD, el GA sugiere un grado de dependencia del alcohol considerado grave, pues la mediana de puntos fue de 22 (mín.=5 y máx.= 40), mientras el GC demostró una mediana de 0 (mín.= 0 y máx.= 6) puntos, lo que comprende un grado de dependencia leve, es decir, caracteriza el uso esporádico y no una dependencia propiamente dicha, de acuerdo con la prueba Mann-Whitney que demuestra una diferencia estadística entre los grupos (z= -9,350; p<0,001). La mediana de la edad de inicio del consumo de bebidas alcohólicas en el GA fue de 15 años (mín.=5 y máx.= 28), siendo para el GC de 16 (mín.= 3 y máx.= 20), según el Mann-Whitney no hay una diferencia estadística significativa (z= -0,381, p=0,703). En relación a la edad de la primera embriaguez, se observa que la mediana relata-

1 La adaptación y estandarización brasileña de las Escalas Beck de Depresión – II está siendo realizada por la Drª Irani Argimon y por la Casa do Psicólogo® en 2009.

2 La adaptación y estandarización brasileña de la Escala de Inteligencia Wechsler para Adultos fue realizada por Elizabeth Nascimento en 2004 por la Casa do Psicólogo® .

3 La versión brasileña del Test de Clasificación de Tarjetas de Wisconsin fue adaptada y estandarizada por Jurema Alcides Cunha y cols. en 2005 por la Casa do Psicólogo®.

4 La adaptación brasileña fue realizada por Margareth da Silva Oliveira en 1999 por la Casa do Psicólogo®.

Tabla 2
Clasificación Socioeconómica, Ocupación y Riesgo Familiar en relación al consumo de alcohol

	GA (n= 101)		GC (n= 41)		Chi-cuadrado (p)
	n	%	n	%	
Clase					
A1 y A2	7	6,9	1	2,4	
B1 y B2	32	31,7	22	53,6	χ^2= 11,786 (p=0,067)
C	40	39,6	17	41,5	
D y E	22	21,8	1	2,4	
Ocupación					
Trabajan	65	64,4	35	85,4	χ^2= 6,180 (p=0,013)
No trabajan	36	35,6	6	14,6	
Estudiantes					
Estudian	3	3,0	9	22,0	χ^2= 13,580 (p<0,001)
No estudian	98	97,0	32	78,0	
Riesgo Familiar					
Familiar con problemas con el consumo del alcohol	93	92,0	17	41,5	χ^2= 42,798 (p<0,001)
Padre	49	48,5	3	7,3	χ^2= 2,325 p<0,001)
Hermanos	35	34,7	2	4,9	χ^2= 13,419 (p<0,001)
Abuelos	29	28,7	6	14,6	χ^2= 3,112 (p=0,089)
Madre	13	12,9	2	4,9	χ^2= 1,926 (p=0,231)
Otro Familiar	55	54,5	8	19,5	χ^2= 14,426 (p<0,001)

Nota. n (número de la muestra); % (porcentaje); p (nivel mínimo de significancia); c^2(Chi-cuadrado de Pearson).

Tabla 3
Frecuencia del consumo de bebidas alcohólicas y Período de días sin beber

	GA (n=101)		GC (n=41)		Test Exacto de Fisher
	n	%	n	%	
Frecuencia de consumo					
Diariamente	92	91,1	-	-	
Días Alternos	7	6,9	1	2,4	
Fin de Semana	2	2,0	8	19,5	c^2=143,203 - p<0,001
Esporádicamente	-	-	14	34,1	
No beben	-	-	18	43,9	
Período de Abstinencia					
Hasta 7 días	39	38,6	14	34,1	
De 8 a 15 días	60	59,4	6	14,6	
16 a 30	2	2,0	1	2,4	c^2=60,703 - p<0,001
31 a 60	-	-	2	4,9	
Mas de 60	-	-	18	43,9	

Nota. GA (Grupo de sujetos Alcohólicos); GC (grupo Control); n (número de la muestra); % (porcentaje); p (nivel mínimo de significancia); c^2(Test Exacto de Fisher).

da por el GA fue de 17 años (mín.=5 y máx.=52), siendo la misma para el GC (mín.=12 e máx.30), y de acuerdo con el test Mann-Whitney no demuestra una diferencia estadísticamente significativa entre los dos grupos (z=-0,084; p=0,933).

Análisis de los hábitos de bebida y Período de abstinencia

La frecuencia de uso de las bebidas alcohólicas relatada por los grupos y el tiempo de abstinencia evaluado por días sin consumir bebida alcohólica se muestran en la tabla 3.

El patrón medio de consumo de alcohol diario en mililitros indicado por el grupo de pacientes alcohólicos fue de 25,01 ml (mín.=3.38 y máx.=111,58), mientras que el grupo control consume una media de 0 mililitros (mín.=0 y máx.=7.81) de alcohol, que de acuerdo con la prueba Mann-Whitney (z=-8,920 y p<0,001) indicó una diferencia estadística significativa entre los grupos. En el grupo de alcohólicos 78 (77,2%) de los participantes suelen beber solos, mientras que en el grupo control un participante mencionó beber solo (c^2=66,084 - p<0,001). Los participantes del grupo de alcohólicos que beben con amigos fueron 54 (53,5%) y del grupo control fueran 13(31,7%) (c^2=5,540 – p=0,026). Todos los que relataron beber con desconocidos eran del grupo de sujetos alcohólicos (c^2=4,840 – p=0,034). Con respecto a beber con la familia, 8 (7,9%) del grupo de participantes alcohólicos y 13 (31,7%) del grupo control (c^2=13,093 – p=0,001).

Los síntomas físicos de abstinencia del alcohol verbalizados por los grupos fueron temblores para 58 (57,4%) de los participantes del GA y para uno del GC (2,4%), (c^2=36,306 - p<0,001). En el GA 15 (14,9%) de los participantes relataron ya haber tenido sudoración y 1 (2,4%) del GC indicó ya haber tenido este síntoma (c^2=4,494 – p=0,040). Ningún participante del GC presentó otro tipo de síntoma de abstinencia, mientras que en el GA 29 (28,7%) presentaron insomnio (c^2=14,793- p<0,001), 25 (24,8%) ya habían presentado alucinaciones (c^2=12,317 - p<0,001), y 18 (17,8%) relataron haber experimentado ya la irritabilidad como síntoma de abstinencia (c^2=8,368 – p=0,004).

Consumo de otras drogas

Actualmente ninguno de los participantes de la muestra consume cualquier droga legal o ilegal, excepto tabaco, 77 (76,2%) de los participantes del grupo de alcohólicos y 4 (9,8%) del grupo control consumen esta substancia (c^2=52,599 - p<0,001). Con respecto al consumo a lo largo de la vida de alguna droga legal o ilegal, 82(81,2%) personas del grupo de sujetos alcohólicos comentaron haber tomado droga alguna vez en su vida y 4 (9,8%) del grupo control afirmaron haber tomado alguna vez drogas (c^2=62,301 - p<0,001). En el grupo de participantes alcohólicos 19 (18,8%) habían consumido cannabis y, en cambio, nadie del grupo control había experimentado esta substancia (c^2=8,904 – p=0,005). En relación al consumo de cocaína, 13 (12,9%) del grupo de sujetos alcohólicos ya habían experimentado esta sustancia anteriormente, sin embargo, ninguno de los participantes del grupo control la había probado antes, (c^2=5,809 – p=0,020). En cuanto a la inhalación de disolventes, 3 (3,0%) pacientes del grupo de alcohólicos ya la habían consumido con anterioridad, en cambio, ningún participante del grupo control lo había hecho antes (c^2=1,244 – p=0,557).

En cuanto al tabaquismo, 68 (67,3%) de los participantes que componen el grupo de alcohólicos fuma diariamente y 2 (4,9%) del grupo control lo hacen con esta esta frecuencia (c^2 Exacto de Fisher= 10,822 – p=0,082). En cuanto al patrón de consumo de tabaco se identifica que 35 (34,7%) del grupo de pacientes alcohólicos fuman entre 11 y 20 cigarrillos, seguido por el patrón de fumar más de 20 cigarrillos (n= 25- 24,8%) y por el de consumir entre 1 y 10 cigarrillos (n=7 – 6,9 %). En el grupo control 1 (2,4%) participante fuma entre 1 y 10 cigarrillos al día y 1 (2,4%) fuma entre 11 y 20 cigarrillos al día (c^2=Exacto de Fisher= 3,012 – p=0,220).

Síntomas de ansiedad y depresión

En relación a los síntomas de ansiedad la mediana del grupo de alcohólicos fue de 11 (mín.= 0 y máx.= 53) y en el grupo control fue de 5 (mín.=0 y máx.=30), siendo que de acuerdo con la prueba no-paramétrico Mann-Whitney hay una diferencia estadísticamente significativa entre los grupos z=-4,482 ($p \leq 0,001$).

Cuanto a los síntomas de depresión la mediana fue de 16 (mín.=0 y máx.=43) en el grupo de alcohólicos y de 9 (mín.=0 e máx.=31) en el grupo control, indicando de acuerdo con la prueba Mann-Whitney una diferencia estadísticamente significativa entre os los dos grupos z=-4,898 ($p \leq 0,001$).

Análisis del desempeño neuropsicológico

En la tabla siguiente se verifica el desempeño de los grupos en las variables: Vocabulario, Códigos, Copia del Test de la Figura Compleja de Rey y las categorías del WCST, número de Categorías Completadas, Errores No-Perseverativos, Errores Perseverativos, Ensayos para Completar a la 1ª Categoría y Fracaso en Mantener el Contexto.

Tabla 4
Comparación del desempeño neuropsicológico entre los grupos

Instrumentos	Grupo de alcohólicos (n=101)			Grupo control (n=41)			Mann-Whitney (p)
	Mediana	Mín.	Máx.	Mediana	Mín.	Máx.	
WAIS-III							
Vocabulario	10,0	3	18	9,00	5	14	0 (p=1,000)
Códigos	6,00	2	14	10,00	4	16	-4,622 (p≤ 0,001)
Fig. Comp. de Rey							
Copia	31,00	7	36	34,00	27	36	-4,582 (p≤ 0,001)
WCST							
Nº de Categorías Completadas	2,00	0	6	6,00	0	6	-4,470 (p≤ 0,001)
Errores no-perseverativos	22,0	1	83	12,00	4	38	-3,020 (p= 0,003)
Errores perseverativos	25,0	3	94	15,00	4	92	-2,887 (p= 0,004)
Ensayos para completar a la 1ª categoría	23,0	10	129	12,00	10	129	-3,464 (p= 0,001)
Fracaso en mantener el contexto	1,00	0	6	0,00	0	3	-1,168 (p=0,243)

Nota. WAIS-III (Wechsler Adult Intelligence Scale); Fig. Compl. (Figura Compleja); WCST (Test de Clasificación de Tarjetas de Wisconsin); Nº (Número); Mín. (Mínimo); Máx. (Máximo); n (número de la muestra); p (nivel mínimo de significancia).

Tabla 5
Desempeño neuropsicológico de alcohólicos y controles

Instrumentos	Grupo de alcohólicos (n=101)		Grupo control (n=41)		Test t (p)
	Media	DT	Media	DT	
WAIS-III					
Cubos	8,32	3,21	11,76	2,62	-6,07 (p≤ 0,001)
Fig. Compl. de Rey					
Memoria	13,38	7,55	17,84	6,66	-3,30 (p= 0,001)
WCST					
Nº Total de Errores	56,07	26,36	35,78	23,83	4,27 (p≤ 0,001)
% de Respuesta de Nivel Conceptual	40,02	25,06	59,83	22,22	-4,41 (p≤ 0,001)

Nota. WAIS-III (Wechsler Adult Intelligence Scale); Fig. Compl. (Figura Compleja); WCST (Test de Clasificación de Tarjetas de Wisconsin); Nº (Número); % (Porcentual); Mín. (Mínimo); Máx. (Máximo); n (número de la muestra); DP (Desviación Típica); t (estadística test); p (nivel mínimo de significancia).

En la tabla 5 se puede ver que la comparación entre los grupos en las variables Cubos del WAIS-III, Memoria del Test de la Figura Compleja de Rey, y las variables del WCST Numero Total de Errores y Porcentaje de Respuesta del Nivel Conceptual obedecen a una distribución normal.

Discusión

El objetivo principal de este estudio fue comparar el desempeño neuropsicológico de pacientes en tratamiento de desintoxicación de alcohol con la población general. Los resultados mostraron que hay un déficit en el desempeño de las funciones cognitivas de los pacientes dependientes de alcohol cuando se compara con no dependientes, principalmente respecto de la coordinación viso motora, memoria, inhibición de las respuestas, y dificultad de usar informaciones previamente aprendidas para delinear estrategias futuras, observadas en los resultados del WCST referentes a las categorías número total de errores, errores perseverativos, errores no-perseverativos, porcentaje de respuesta de nivel conceptual y ensayos para completar a la 1ª Categoría.

El grupo de sujetos alcohólicos evidencio un enlentecimiento psicomotor, lo que corrobora los datos facilitados por Cunha y Novaes (2004), Arias et al. (2000), Langlais y Ciccia (2000), Pfefferbaum et al. (2000) y los estudios de Fein, Torres, Price y Di Sclafani (2006) y Meyerhoff et al. (2004), que encontraron déficit en la velocidad psicomotora en sujetos alcohólicos. Esta muestra también revela un descenso en la capacidad de percepción visual y un déficit en la memoria inmediata, lo que es coherente con los hallazgos de Rigoni y Oliveira (2009), que al aplicar el Test de la Figura Compleja de Rey en una población de pacientes alcohólicos, detectaron déficits en la capacidad visual y memoria inmediata.

En el Test de Clasificación de Tarjetas de Wisconsin (WCST), los resultados mostraron que los sujetos alcohólicos completan menos categorías, cometen más errores, errores perseverativos, más errores no perseverativos, presentan menos respuestas de nivel conceptual y gastan más ensayos para completar a la 1ª categoría, posiblemente porque no han conseguido aprovechar el *feedback* realizado por el examinador. Esto puede estar asociado a la dificultad en adoptar estrategias eficientes para resolver problemas, como destaca Bachara et al. (2001), lo que refuerza la cuestión de que los prejuicios en el proceso de toma de decisión pueden influenciar el paciente a tomar decisiones inadecuadas sin medir futuras consecuencias.

En el alcoholismo, los errores perseverativos del WCST pueden resultar de un fallo para recordar las respuestas anteriores, falta de atención o déficit en la inhibición de la respuesta, lo que puede sugerir un comportamiento impulsivo, incapacidad de interrumpir un comportamiento negativo, incluso cuando las nuevas informaciones así lo surgieren, evitando el logro de los posibles objetivos a largo plazo (Bardenhagen y Bowden, 1998; Nigg, 2006; Oscar-Berman y Marinkovic, 2007). La disminución en la capacidad de flexibilidad mental de esta muestra de sujetos alcohólicos corrobora los hallazgos de Zin, Stein y Swartzwelder (2004) que también verificaron un prejuicio en la capacidad de flexibilidad mental en alcohólicos. Además, otro estudio encontró que los estudiantes que abusan del tabaco y el alcohol presentan un rendimiento académico más pobre (Inglés et al., 2013).

La mayoría de los pacientes alcohólicos (59,4%) se encontraban en un período de 8 a 15 días de abstinencia. Muchos de los problemas neuropsicológicos asociados a la gravedad del alcoholismo crónico pueden persistir en la abstinencia (Nigg et al., 2006) y algunos estudios han comprobado que los sujetos alcohólicos abstinentes durante 2 o 3 semanas sufren una variedad de deficiencias cognitivas que pueden persistir después de algunas semanas de abstinencia. Estos pacientes presentan severos déficits en las funciones ejecutivas, incluyendo la inhibición de la respuesta, razonamiento abstracto, toma de decisión y resolución de problemas, que se han relacionado con anomalías estructurales y funcionales en los lóbulos frontales (Noel et al., 2005).

El grupo de sujetos alcohólicos estudiado denota un grado de dependencia considerado grave, reforzando la opinión de Myrick y Wright (2008) que sugiere que los pacientes con síntomas graves de dependencia del alcohol presentan, posiblemente, un pronóstico reservado. Este dato también corrobora los hallazgos de Edwards, Marshall y Cook (2005), destacando que el grado de dependencia es un predictor del éxito para obtener niveles de moderación versus abstinencia.

Pudo constatarse que más de la mitad de los pacientes alcohólicos presentaban antecedentes familiares de alcoholismo (que podían tener relación con el padre en casi la mitad, con un hermano en uno de cada 3, y con un abuelo en 1 de cada 4); y que esta proporción es significativamente mayor en los pacientes alcohólicos que en la población general. Así mismo, los síntomas de ansiedade, depresión y la dependencia de nicotina tienen una prevalencia significativamente más elevada en los pacientes alcohólicos que en la población general. Por tanto, estas tres características diferenciales, entre los pacientes alcohólicos y la población general, podrían llegar a convertirse en rasgos específicos asociados al alcoholismo, que pueden resultar orientativos, tanto para la detección del alcoholismo, como de la mencionada comorbilidad psiquiátrica y adictiva. además, las dos últimas tal vez deberían ser tenidas en cuenta en el tratamiento de los pacientes alcohólicos. La mayoría de los individuos que componen el grupo de pacientes alcohólicos tienen o han tenido algún familiar con problemas relacionados con el consumo de alcohol, siendo el más citado el padre, lo que hace pensar que puedan presentar una pre-disposición al alcoholismo. Esto corrobora otros estudios que indican que factores hereditarios y de aprendizaje por modelo influencian en la vulnerabilidad al alcoholismo (Messas y Vallada Filho, 2004; Dick y Foroud, 2003; Schukit, Smith y Kalmijn, 2004; Whitfield et al., 2004). El consumo de alcohol por parte de familiares es un factor de riesgo que contribuye al inicio y al mantenimiento de los problemas relacionados con el consumo de alcohol en adolescentes, siendo un predictor de la severidad de la sintomatología en la etapa adulta (Nigg et al., 2006). Estos datos pueden explicar el hecho de que la muestra de alcohólicos presente dificultad para utilizar las informaciones previamente aprendidas para delinear estrategias futuras, observadas en los resultados del WCST. Lo anterior debido a que nos enfrentamos a la vez a una predisposición genética y a un modelo presente desde la infancia.

El grupo de sujetos alcohólicos indicó beber diariamente, lo que refuerza la cuestión del Síndrome de la Dependencia del Alcohol (SDA), en la que mismo sufriendo algún tipo de consecuencia negativa, que en el caso de la muestra de alcohólicos es la internación, el individuo sigue el consumo de la substancia. La SDA se caracterizada por una relación considerado patológico entre la persona y el alcohol (Edwards, Marshall y Cook, 2005), en que la persona sigue el consumo de la substancia a pesar de tener consciencia de problemas físicos o psicológicos recidivantes o persistentes que parecen causados o exacerbados por el consumo de la substancia (American Psychiatric Association, 2002). Estos resultados también pueden estar asociados con los aspectos de la impulsividad, lo que corrobora el estudio realizado por Pedrero Pérez, Ruiz Sánchez de León, Rojo Mota, Llanero Luque y Puerta García (2012), que evaluaran 52 adictos en tratamiento, y hallaron correlaciones moderadas entre la impulsividad funcional y los indicadores de éxito en tareas neuropsicológicas. Además, han identificado que la impulsividad disfuncional aparece como una disposición que dificulta la realización de tareas a nivel global, lo que implica directamente en el tratamiento de las adicciones.

En la muestra estudiada se puede destacar una diferencia estadísticamente significativa entre los síntomas de ansiedad y depresión indicados por los dos grupos. Los sujetos alcohólicos presentan síntomas leves de ansiedad y depresión y el grupo control presenta síntomas mínimos. A pesar de que los pacientes alcohólicos no presentan síntomas suficientes para diagnosticar un trastorno, sí se observa una mayor posibilidad de asociación entre estos síntomas y el alcoholismo, los cual esta corroborado en la literatura sobre el tema (Alves, Kessler y Ratto, 2004; Brower, 2003; Pulcherio y Bicca, 2002).

Es interesante observar que más de la mitad (n= 68) del grupo de pacientes alcohólicos fuma tabaco a diario, mientras que en el grupo control sólo dos participantes lo consumen con esta frecuencia, lo que está en consonancia con la revisión hecha por Malbergier y Oliveira Júnior (2005), que verifican que la dependencia de nicotina está relacionada al aumento en el consumo de alcohol, así como el consumo de alcohol puede favorecer el consumo de tabaco, revelando una relación bidireccional.

Se concluyó a partir de estos hallazgos y el deterioro cognitivo, que la persona dependiente del alcohol puede tener dificultades para adherirse al tratamiento y para mantener la abstinencia, ya que delante de un problema, es probable que persevere sus respuestas y acciones. Se destaca la vulnerabilidad del lóbulo frontal hacia el uso del alcohol, lo que puede interferir negativamente en la adhesión del dependiente en relación con el tratamiento y puede estar asociada con la perseveración de su comportamiento y dificultad en la toma de decisiones. Esta asociación entre el consumo de alcohol y el consecuente deterioro cognitivo, también se encontró en el estudio realizado por Aguiar Navarro, Reyes Guerrero y Borges (2007), que investigaron mexicanos con más de 65 años de edad, consumidores de alcohol y que presentaban deterioro cognitivo.

El enfoque de este estudio no se ocupa de los tipos de tratamientos de rehabilitación, a partir de los datos que se encuentran en esta muestra podrían centrarse más investigaciones sobre el tema. Desde el punto de vista científico, el estudio es relevante porque necesitamos detectar el perfil de los pacientes alcohólicos y sus vulnerabilidades, para que las nuevas formas de evaluación y acompañamiento puedan ser implementadas. Rehm, Rehm, Shield, Gmel y Gual (2013) sugieren la incrementacion de las tasas de tratamiento para reducir los costes para la salud y la mortalidad atribuibles al alcohol. Tales como la normalización de las evaluaciones neuropsicológicas

en clínicas para pacientes hospitalizados, lo que no ocurre en la práctica brasileña, excepto por la petición de algún profesional o cuando alguna investigación se centra en esta área.

Conflicto de intereses

Ninguno.

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Craving and nicotine withdrawal in a Spanish smoking cessation sample

Craving y abstinencia de la nicotina en fumadores españoles en un tratamiento para dejar de fumar

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Resumen

El craving y el síndrome de abstinencia de la nicotina (SAN) forman parte del trastorno por consumo del tabaco en el DSM-5. Ambos aparecen tras dejar de fumar o tras una reducción brusca del consumo de tabaco, y están relacionados con los resultados de dejar de fumar a corto y largo plazo. El objetivo del presente estudio fue analizar la relación del craving y del síndrome de abstinencia con dejar de fumar al final del tratamiento y con la recaída a los 3 meses de seguimiento en una muestra de fumadores españoles. La muestra estaba formada por 342 fumadores (37,7% hombres; 62,3% mujeres) que recibieron tratamiento cognitivo-conductual para dejar de fumar. La evaluación del craving y del síndrome de abstinencia se realizó a través de la escala Minnesota Nicotine Withdrawal Scale. Los abstinentes al final del tratamiento, comparados con los no abstinentes, mostraron un síndrome de abstinencia y un craving significativamente menor al finalizar el tratamiento. Además, los abstinentes tenían puntuaciones menores en dependencia de la nicotina antes del tratamiento. Entre los abstinentes, el craving descendió significativamente desde los valores presentados antes de dejar de fumar, mientras que en los participantes que no dejaron de fumar los valores de craving permanecieron en los mismos niveles. La dependencia de la nicotina elevada fue el predictor de fumar al final del tratamiento, mientras que el síndrome de abstinencia de la nicotina elevado fue predictor de la recaída a los 3 meses. Los resultados apoyan el papel robusto del craving y del SAN en dejar de fumar y en la recaída, aunque difieren en sus patrones de cambio a lo largo del tiempo.

Palabras Clave: craving, abstinencia, recaída, España, dejar de fumar.

Abstract

Craving and nicotine withdrawal syndrome (NWS) are components of the tobacco use disorder in DSM-5. They both appear after smoking cessation or an abrupt reduction in tobacco use, and they are associated with both short and long-term smoking-cessation outcomes. The aim of the present study was to examine the association of craving and withdrawal with smoking cessation at the end of the treatment and relapse at 3 months follow-up in a Spanish sample of smokers. The sample comprised 342 smokers (37.7% men; 62.3% women) receiving a cognitive-behavioral treatment for smoking cessation. The assessments of craving and withdrawal were conducted using the Minnesota Nicotine Withdrawal Scale. Abstainers at the end of the treatment, compared to non abstainers, showed significantly lower post-treatment withdrawal, and post-treatment craving. Furthermore, they had lower scores in pre-treatment nicotine dependence. Among abstainers, craving decreased significantly from pre-cessation levels, while in those participants who did not quit smoking it remained on the same levels. High nicotine dependence was a predictor of smoking at the end of the treatment, whereas high nicotine withdrawal predicted relapse at 3 months. Findings support the robust role of craving and NWS in smoking cessation and relapse, although they differ in their specific patterns of change over time.

Key Words: craving, withdrawal, relapse, Spain, smoking cessation.

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Nicotine withdrawal syndrome (NWS) is considered an important component of tobacco dependence (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Hughes, Higgins, & Hatsukami, 1990). It includes subjective, cognitive, and physiological symptoms that appear when giving up smoking, which make it more difficult to maintain abstinence (Shiffman, West, & Gilbert, 2004) and it plays an important role in relapse (Piasecki, Jorenby, Smith, Fiore, & Baker, 2003b). In the recent published DSM-5 (American Psychiatric Association [APA], 2013), the signs or symptoms of NWS are irritability, frustration or anger, anxiety, difficulty concentrating, increased appetite, restlessness, depressed mood, and insomnia.

Craving is considered a criterion for the diagnostic of tobacco use disorder in DSM-5 (APA, 2013). However, previously, craving was not consider as a formal criterion of nicotine dependence or NWS in DSM-IV (APA, 1994), nevertheless it was included by different researchers in the scales that assess this syndrome (Etter & Hughes, 2006; West & Hajek, 2004). Craving was not included in the DSM-IV as a symptom of withdrawal because of its inconsistent association with tobacco abstinence (Hughes, Higgins, & Bickel, 1994). Compared to other withdrawal features, craving seems to have a distinctive time course (Gilbert et al., 1998; Hughes, 1992; Shiffman et al., 1997).

Accordingly, it has been considered craving as a subjective experience of a desire or intense need for substance use (APA, 2013), as an important symptom of tobacco dependence (Baker, Breslau, Covey, & Shiffman, 2012; Tiffany, Warthen, & Goedeker, 2009), and there is evidence that it plays a causal role in smoking relapse (Baker et al., 2004; Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996).

The inability to cope with NWS and craving when quitting smoking appears to account for the failure of many cessation attempts (Ferguson, Shiffman, & Gwaltney, 2006).
In addition, several studies indicate that the pattern, duration, and severity of NWS and craving experienced by smokers who are abstinent during the first day or the first weeks after quitting are significant predictors of relapse in smokers (Allen, Bade, Hatsukami, & Center, 2008; Hughes, 2007; Piasecki et al., 2003b; Shiffman et al., 1997). For example, Allen et al. (2008) found that higher levels of NWS and craving were associated with relapse. Piasecki et al. (2003b) reported that subjects who relapse reported more severe NWS during smoking abstinence than did non relapsers.

The purpose of the current study was to assess the generalizability of these constructs by analyzing the relationship of craving and NWS with smoking cessation at the end of the treatment, and with relapse at 3 months follow-up, in a sample of Spanish smokers who received a cognitive behavioral smoking cessation intervention. Compared to the United States, where much of the previous research occurred, Spain has a higher prevalence of smoking (24% vs 19%; CDC, 2012; Ministerio de Sanidad, 2013), and Spanish smokers, on average, are less nicotine-dependent (de Leon, Becoña, Gurpegui, Gonzalez-Pinto, & Diaz, 2002). Given these differences, along with more general cultural differences, confirmation of the role of nicotine dependence and NWS upon smoking cessation in this population would strengthen the construct validity of addiction models that emphasize these factors, including DSM-5.

Methods

Participants

The study sample consisted of male and female Spanish smokers (N = 342) who requested smoking cessation treatment at the Smoking Cessation Unit of the Faculty of Psychology at the University of Santiago de Compostela (Spain). Recruitment of the smokers was carried out by advertisements in the media (radio, press and local television), through other smokers who had previously sought treatment, or through referral from general practitioners. Selection of participants used the following inclusion criteria: at least 18 years of age; desire to participate in the treatment program; smoking ≥ 10 cigarettes per day; and having completed the questionnaires in the pretreatment assessment. Exclusion criteria were: a diagnosis of a severe mental illness (bipolar disorder and/or psychotic disorder); concurrent dependence on other substances (cocaine, cannabis, and/or heroin); having participated in the same or similar treatment over the previous year; having received another type of effective smoking cessation treatment (nicotine replacement therapy, bupropion, varenicline) in the past year; suffering from a severe physical pathology that would require immediate medical intervention (e.g., recent myocardial infarction, pneumothorax); smoking tobacco other than cigarettes (e.g., cigars); refusing to be video-recorded during the sessions; and failing to attend the first treatment session.

From an initial sample of 412 smokers, 70 were excluded based on exclusion criteria, with the final sample comprising 342 smokers (37.7% men and 62.3% women) with a mean age of 41.58 years (SD = 10.87).

Measures

All participants completed the Smoking Habit questionnaire (Becoña, 1994), which obtains information on sociodemographic variables (e.g., gender, age) and aspects related to smoking and smoking history (e.g., number of cigarettes smoked per day, number of years smoking).

For the assessment of nicotine dependence (ND) we used the *Fagerström Test for Nicotine Dependence* (FTND, Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991; Spanish version by Becoña & Vázquez, 1998).

To assess nicotine withdrawal, the Spanish version of the *Minnesota Nicotine Withdrawal Scale* (Hughes & Hatsukami, 1998) was used (see Table 1). This scale consists of eight

Table 1
Spanish version of the 'Minnesota Nicotine Withdrawal Scale'

Por favor, indique si en las últimas 24 horas, ha sentido usted alguno de estos síntomas					
	Nada	Escaso	Leve	Moderado	Severo
	0	1	2	3	4
1. Enfado/Irritabilidad/Frustración					
2. Ansiedad/Nerviosismo					
3. Dificultad de concentración					
4. Impaciencia/Intranquilidad					
5. Incremento del apetito, hambre, ganancia de peso					
6. Insomnio, problemas con el sueño, despertar a media noche					
7. Ánimo deprimido, tristeza					
8. Deseo o necesidad de fumar					

items (irritability, angry or frustrated; anxiety or tension; difficulty concentrating; restlessness or impatience; increased appetite, hungry or weight gain; depressed mood or sad; insomnia, sleep problems or awakening at night; and, desire or craving to smoke) measured with a Likert scale ranging from 0 (no symptoms) to 4 (severe symptoms). The sum of the items, minus the craving score which is assessed separately, was used to assess overall NWS. This scale has been found to have fair to good internal consistency with alpha ranging from .80 to .83 (Toll, O'Malley, McKee, Salovey, & Krishnan-Sarin, 2007). Craving was assessed as a single item on the scale, due to evidence suggesting that craving patterns are distinct from other symptoms of withdrawal (Hughes & Hatsukami, 1998), and scores were analyzed separately.

We used the Micro^{+} Smokerlyzer® (Bedfont Scientific Ltd, Sittingbourne, UK) to measure carbon monoxide (CO) in expired air, to corroborate self-reported abstinence at the end of the treatment and at 3-month follow-up (cut-off point of < 10 ppm to be considered a non-smoker) (West, Hajek, Stead, & Stapleton, 2005).

Procedure

At the initial assessment, we administered the measurements described above. *Minnesota Nicotine Withdrawal Scale* was administered again for the assessment of craving and NWS at the end of the treatment and at 3 months follow-up. All smokers gave their informed consent to participate in the research, and the Bioethics Committee of the University of Santiago de Compostela authorized the study.

The psychological treatment administered was the *Smoking Cessation Program* by Becoña (2007), a manualized cognitive-behavioral treatment that comprises 6 group-format sessions over six weeks (one session per week). The treatment was administered by psychologists trained in its application.

We considered that a participant relapsed when he or she had been abstinent for at least 24 hours at the end of the treatment, but reported any smoking during the 7 days prior to the date of the 3-month follow-up (Velicer, Prochaska, Rossi, & Snow, 1992).

Data analysis

Analyses were conducted using SPSS 20. Descriptive statistics were used to describe demographic and smoking history characteristics of the participants. Comparisons of clinical characteristics pre- and post-treatment and at 3-months follow-up were conducted using t-test. The effect size (ES) of significant results is reported in the tables (d = 0.20-0.49 small ES, d = 0.50-0.79 medium ES, and d = 0.80 and above large ES, Cohen, 1988).

For testing the change in craving and NWS over the three times points (pre, post-treatment and 3 months follow-up), among abstainers and relapsers at 3 months follow-up, mixed factor analyses of variance (ANOVAs) were conducted, with time as the repeated factor and smoking status at 3 months follow-up (abstainer-relapser) as the between-subjects factor. We used Bonferroni's post-hoc tests for verifying the existence of significant differences in the pairwise comparison.

Additionally, the role of craving and NWS in predicting smoking at the end of the treatment and smoking relapse at 3 months follow-up was analyzed using stepwise logistic regression (forward conditional). According to this method, variables are selected in the order in which they maximize the statistically significant contribution to the model. The significance level for all analyses was set at 0.05.

Results

Sample characteristics

Participants in this study (N = 342) smoked a mean of 21.62 cigarettes per day (*SD* = 8.16, range: 10-40). FTND

mean as 5.28 (*SD* = 2.12), NWS mean was 7.18 (*SD* = 6.21), and craving mean was 2.92 (*SD* = 1.02).

Smoking status at the end of the treatment and its relationship with NWS and craving

We had data at the end of the treatment from 312 participants (91.23% of the initial sample). Of them, 201 (64.42%) were abstinent and 111 (35.58%) continued smoking. Among those who continued smoking a significant reduction in the number of cigarettes at the end of the treatment was produced (*M* = 24.85, *SD* = 9.37 pre-treatment, and *M* = 7.93, *SD* = 6.74, post-treatment; *t* = 18.34, *p* < .001).

Regarding variables assessed pre-treatment (ND, NWS and craving) significant differences were found at the end of the treatment for only ND; abstainers had lower ND than participants who continued smoking (*M* = 4.84, *SD* = 2.09 for abstainers, and *M* = 5.88, *SD* = 1.97, for smokers; *t* = -4.30, *p* < .001).

On NWS and craving post-treatment, significant differences were observed by final smoking status. Abstainers presented lower NWS (*M* = 8.15, *SD* = 5.08 for abstainers, and *M* = 10.98, *SD* = 6.58 for smokers; *t* = -3.94, *p* < .001), and lower craving (*M* = 1.84, *SD* = 1.13 for abstainers, and *M* = 2.73, *SD* = 1.05 for smokers; *t* = -6.84, *p* < .001), than smokers.

Smoking status at 3 months follow-up and its relationship with NWS and craving

Taking as a reference the number of participants who were abstinent at the end of the treatment (n = 201), we obtained complete data for 162 participants on NWS and craving pre-treatment, post-treatment and at 3 months follow-up. Of these 106 (65.43%) remained abstinent and 56 (34.57%) relapsed by 3 months follow-up.

At 3 months follow-up, we found significant differences on NWS and craving assessment between abstainers and relapsers. Those participants who relapsed at 3 months follow-up presented higher NWS (*M* = 6.02, *SD* = 6.30 for abstainers, and *M* = 9.75, *SD* = 6.77 for relapsers; *t* = -3.46, *p* < .001), and higher craving (*M* = 0.81, *SD* = 1.05 for abstainers, and M = 2.66, *SD* = 1.08 for relapsers; *t* = -10.53, *p* < .001), than participants who remained abstinent at 3 months follow-up.

Evolution of craving and NWS from the beginning to the end of treatment (n = 312)

Among end-of-treatment abstainers (n = 201), we observed that the pattern of change of craving was different than that of NWS. Craving in abstainers decreased until reaching values below pre-treatment levels (2.97 pre-treatment vs. 1.84 post-treatment; *t* = -11.08, *p* < .001). However, NWS increased (6.53 pre-treatment, vs. 8.15 post-treatment; *t* = -3.64; *p* < .001).

Among continuing smokers, craving remain stable (2.89 pre-treatment vs. 2.73 post-treatment; *t* = 1.31, n.s.), but NWS increased significantly (8.04 pre-treatment vs. 10.98 post-treatment; *t* = - 4.19, p < .001).

Evolution of craving and NWS from treatment onset to the 3 months follow-up (n = 201)

As seen in Table 2 we found no differences between those who abstained versus relapsed at 3-months on either pre-treatment craving or NWS. At posttreatment, only NWS differed between the groups (7.34 for abstainers vs. 9.89 for relapsers). By 3 months follow-up, we observed significant differences between abstainers and relapsers on both variables. Those who relapsed had a higher craving and higher NWS than those who remained abstinent.

With respect to NWS, the ANOVA indicated a significant effect of the time factor (pre, post and 3 months) and of the group factor (abstainers and relapsers), and a significant time x group interaction. Thus, among relapsers (n = 56), after the application of post hoc Bonferroni correction (see Figure 1), we found significant differences between NWS pre and post (*p* < .001) and NWS pre and 3 months follow-up (*p* < .05), but no differences between NWS post and 3 months follow-up. In abstainers (n =106), no significant differences were found on NWS across the different time points.

With respect to craving, we found a significant time effect, a significant group effect, and a significant time x group interaction. Among relapsers (see Figure 2), a signifi-

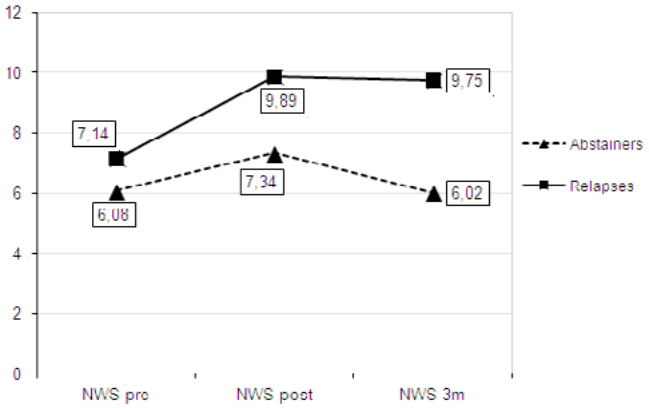

Figure 1. Nicotine withdrawal syndrome (NWS) over the three time points among relapsers and abstainers.

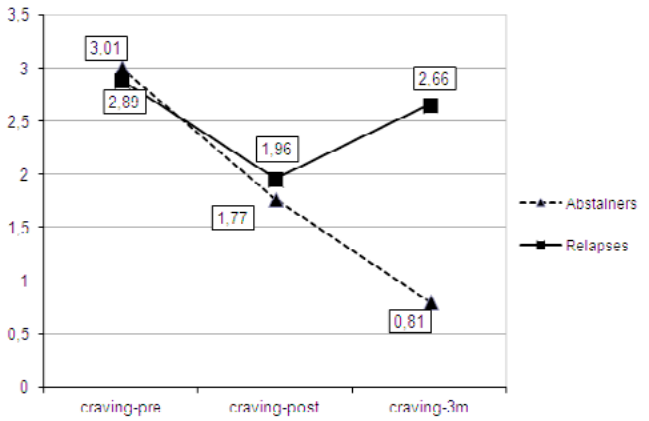

Figure 2. Craving over the three time points among relapsers and abstainers.

Table 2
Differences in craving and nicotine withdrawal syndrome (NWS) at three time points (pre-treatment, post-treatment, and 3 months follow-up) among abstainers and relapsers

	3 months follow-up (n = 162)					
	Abstainers (n = 106; 65.43%)	Relapsers (n = 56; 34.57%)	t	95% CI		d
				Lower	Upper	
Pre-treatment assessment						
NWS, Mean (*SD*)	6.08 *(5.41)*	7.14 *(5.49)*	-1.19	-2.84	0.70	
Craving, Mean (*SD*)	3.01 *(0.82)*	2.89 *(0.99)*	0.76	-0.19	0.42	
Post-treatment assessment						
NWS, Mean (*SD*)	7.34 *(4.89)*	9.89 *(5.52)*	-3.02**	-4.22	-0.88	0.23
Craving, Mean (*SD*)	1.77 *(1.12)*	1.96 *(1.04)*	-1.06	-0.55	0.17	
3 month follow-up assessment						
NWS, Mean (*SD*)	6.02 (*6.30*)	9.75 (*6.77*)	-3.49***	-5.84	-1.62	0.27
Craving, Mean (*SD*)	0.81 (*1.05*)	2.66 (*1.08*)	-10.53***	-2.20	-1.50	0.64
NWS	Anova Time (pre, post, 3 months)	F (2,159) = 7.28***				
	Group (abstainer, relapses)	F (1,160) = 11.83***				
	Interaction (time x group)	F (2,159) = 3.14*				
Craving	Anova Time (pre, post, 3 months)	F (2,159) = 68.74***				
	Group (abstainer, relapses)	F (1,160) = 37.56***				
	Interaction (time x group)	F(2,159) = 43.27***				

Note. NWS = nicotine withdrawal syndrome.
* p <.05;** p < .01;***p < .001.

Table 3
Logistic regression analysis output as predictors of smoking status at the end of treatment (n = 312) and at 3 months follow-up (n = 162)

	B[a]	Wald	*p* value	*OR*	OR (95% CI)
End of the treatment					
ND, FTND (≥ 6) pre-treatment	0.828	11.772	.001	2.28	1.42-3.67
Constant	-0.986	33.289	.001	0.37	
3 months of follow-up					
NWS-post	0.094	8.258	.004	1.09	1.03-1.02
Constant	-1.445	18.555	.001	0.23	

Note. CI = confidence interval; FTND = Fagerström Test for Nicotine Dependence; ND = nicotine dependence; OR = odds ratio.
[a] The groups were coded into the model as Smokers = 1 and Abstainers = 0.

cant decrease was observed in craving from pre to post-treatment, followed by a significant increase by 3 month. However, pre-treatment and at 3 months craving did not differ. In contrast, among abstainers, we found progressive decline in craving between the 3 time points with all differences statistically significant at $p < .001$.

Predictors of smoking status at the end of the treatment and relapse at 3 months follow-up

For analysing predictors of smoking status at the end of the treatment, binary logistic regression was conducted using those 312 participants with end-of-treatment data, as the criterion variable smoking or abstinent and the predictor variables ND, NWS-pre, and craving-pre. We found that ND was significantly associated with smoking at the end of the treatment. Having high ND (*OR* = 2.28) was associated with a significantly increased likelihood of smoking at the end of the treatment (see Table 3).

We also examined predictors of relapse at 3 months follow-up, using a binary logistic regression analysis using the 162 participants with follow-up data out of the 201 who had reached abstinence at the end of the treatment. Adopting as the criterion variable smoking or abstinent, and as predictor variables ND, craving-pre, NWS-pre, craving-post, and NWS-post, we found that NWS post was associated with a higher risk of relapse. That is, higher NWS at the end of the treatment was associated with a significantly increased likelihood of smoking 3 months later (*OR* = 1.09; see Table 3).

Discussion

Role of NWS, craving, and ND on the treatment outcome

We found that those participants who did not quit smoking at the end of the treatment presented a higher post-treatment NWS and craving for cigarettes than those participants who achieved abstinence. This same result has been found in previous studies (e.g., Ferguson et al., 2006; Tiffany et al., 2009) in which high scores in NWS and craving were associated with failures when quitting smoking. We also observed that high pre-treatment ND predicted failure to quit smoking by the end of the treatment. These results are consistent with the robust role of ND in the maintenance of smoking behavior (Benowitz, 2010) and the predictive power of ND (Ferguson et al., 2003). These results support the statement that both NWS and craving, as well as nicotine dependence in general, are related to treatment outcome. Indeed, these results are consistent with previous studies that established craving and NWS as symptoms of dependence and predictors of smoking cessation success (Hughes et al., 1990; Tiffany et al., 2009), consistent with DSM-5 criteria. Moreover, these relationships between craving, ND, and smoking cessation outcomes are consistent with Robinson et al. (2011) who found that more dependent smokers also experienced greater craving, and Baker et al. (2012), who considered craving as a NWS symptom and as the symptom most associated with tobacco dependence.

With respect to the concurrent relationship between craving and NWS with smoking at 3 months follow-up, those participants who had relapsed presented with significantly higher NWS and craving than those who remained abstinent. This is contrary to many smokers' expectations that craving and withdrawal symptoms will decrease if they return to smoking. However, these uncomfortable effects in fact appear more likely to decline if they remain abstinent.

With respect to predicting relapse among smoker who achieved end-of-treatment abstinence, we observed that high post-treatment NWS was associated with a greater risk of relapse at 3 months. Therefore, as Piasecki et al. (2003b) and Shiffman et al. (2004) had pointed out, the NWS that a smoker suffers when quitting appears to play an important role in the maintenance of abstinence versus relapse. This suggests that greater emphasis on controlling NWS, via pharmacotherapy, education, and coping skills training, may be advisable in general, and particularly for those smokers who present with high NWS during treatment.

Evolution of craving and NWS

We found different patterns of change in these two variables, among both abstainers and continuing smokers between pre- and post-treatment. Consistent with other studies, we found that among abstainers craving decreased whereas NWS increased (Etter, 2005; Gilber et al., 1998; Hughes, 1992; Shiffman et al., 1997) finding different patterns of change in craving and NWS among abstaining smokers. The increase in NWS is a normal fact giving that they have quit smoking and, although the treatment is based on a gradual cessation, any reduction in nicotine intake carries on the presence of NWS regardless of a higher or lower intensity. Thus, it is necessary to work during the treatment with the aim of decreasing NWS as far as possible to avoid relapse due to the discomfort generated by these symptoms. An important aspect that should be included in the treatment is craving decrease. One of the most frequent expectations among smokers is that if they give up smoking, craving or the desire for the consumption is going to be very intense.

Among continuing smokers, we also found an increase NWS, but no change in craving. The increase in NWS among continuing smokers may reflect the reduction in smoking (and, therefore, likely nicotine intake) that most of the smokers experienced during treatment.

With respect to the change in craving and NWS from the onset of the treatment until the 3 months follow-up, our results showed that craving decreased significantly among abstainers. On the other hand, in those who relapse, an increase in craving in the 3 months follow-up was found. A similar result was reported by Schlam, Piper, Cook, Fiore, and Baker (2012), in which craving continued

decreasing in the group of abstainers compared to those who continue smoking at one year follow-up. The finding of craving increases among relapsers is consistent with studies showing that relapses often occur in the presence of an intense craving (Shiffman et al., 1997). Regarding NWS, only abstainers showed a decline by 3 months. The continuing NWS among relapsers may reflect their continued attempts to control their smoking, rather than simply immediately resuming their pretreatment patterns of use. It would be very interesting to analyze in future studies if this result is due to the characteristics of this type of treatment for smoking cessation in which the smoker learns different strategies to control their smoking behavior or whether NWS remains high when relapsing regardless of the method used.

Limitations

The study has several limitations. First, we must take care with generalizing the results obtained from this treatment study, with specific inclusion and exclusion criteria, to the general population of smokers. Moreover, it would be interesting to analyze the evolution of craving and NWS in smokers who gave up smoking without attending a specific treatment and see if there are differences with those who used specific procedures. On the other hand, that this specific sample of Spanish smokers in treatment produced results consistent with previous research with very different samples supports the robustness and generalizability of the roles of craving and nicotine withdrawal. Second, the size of the sample of relapsers was modest, which may have limited our power to detect effects. Finally, our findings are based on retrospective, self-reports. However, we employed a widely-accepted and reliable instrument for the assessment of NWS (Shiffman et al., 2004).

Conclusions

In summary, evidence indicates that craving decreases as the time without smoking increases, but that relapse is associated with craving increase. In the case of NWS, a slight increase happens when giving up smoking and it decreases as length of abstinence increases, whereas it remains high among relapsers. Moreover, we found that at the end of the treatment, NWS is higher in persons who later relapse than among those who do not, although the levels of craving are similar between the groups.

In conclusion, our findings among a Spanish sample of smokers provide further support for the robust role of craving and NWS in smoking cessation and relapse.

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Conflict of interest

None declared.

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Physiological and psychological effects of a high dose of alcohol in young men and women

Efectos fisiológicos y psicológicos de una alta dosis de alcohol en hombres y mujeres jóvenes

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Resumen

El objetivo de este estudio fue evaluar los efectos de una dosis alta de alcohol sobre parámetros fisiológicos y psicológicos en hombres y mujeres jóvenes con historia previa de consumo de alcohol. La presión sanguínea sistólica y diastólica, la frecuencia cardiaca, la ansiedad estado, el procesamiento atencional, la estimación temporal y la destreza manual fueron registradas antes (fase 1) y después (fase 2) de la ingesta de alcohol (38,4 g) o de una bebida no alcohólica. La ansiedad rasgo fue registrada solamente en la fase 2. Los resultados mostraron que el consumo agudo de una dosis alta de alcohol: i) en hombres, mejora el procesamiento atencional (aunque la ejecución de los consumidores no fue mejor que la de los no consumidores); ii) en mujeres, bloquea el fenómeno de habituación observado en la presión sanguínea sistólica de los sujetos controles; iii) en ambos sexos, bloquea la mejoría en la ejecución en destreza manual (asociada a la experiencia en los no consumidores). Por otro lado, los hombres consumidores de alcohol mostraron una frecuencia cardiaca menor que los no consumidores, independientemente de la fase en la que se encuentren; mientras que en las mujeres se observó una mayor ansiedad estado y una peor ejecución en procesamiento atencional entre las consumidoras de alcohol, independientemente de la fase. Estos resultados ayudan a comprender la magnitud del deterioro en diversas medidas producido por el alcohol, tras un consumo de riesgo, en hombres y mujeres jóvenes.

Palabras clave: alcohol, hombres, mujeres, medidas fisiológicas, medidas psicológicas

Abstract

The objective of this study was to evaluate the effects of a high dose of alcohol on physiological and psychological parameters in young men and women with a previous history of alcohol consumption. Systolic and diastolic blood pressure, heart rate, state anxiety, attention, time estimation and manual dexterity were registered before (phase 1) and after (phase 2) intake of alcohol (38.4 g) or a non-alcoholic beverage. Trait anxiety was registered in phase 2 only. The results showed that acute consumption of a high dose of alcohol: i) improves attention in men (although the performance of alcohol consumers was not better than that of non-consumers); ii) blocks the systolic blood pressure habituation phenomenon (observed in controls) in women; and iii) blocks the improvement in manual dexterity (associated with experience in non-consumers) in both sexes. On the other hand, male consumers had a lower heart rate than non-consumers, independently of the phase, while female consumers had a higher state anxiety and performed worse in attention than controls, also independently of the phase. These results help to understand the extent of performance impairment of different tasks produced by risk alcohol consumption in young men and women.

Keywords: alcohol, men, women, physiological measures, psychological measures

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Alcohol is one of the most widely consumed psychoactive substances in the world, especially among young people and adolescents, among whom heavy drinking is becoming increasingly frequent, particularly in the case of 15- to 24-year-olds, whose alcohol consumption in the past 12 months is high (78.5%) (OEDT, 2012). In general, men show a higher prevalence of alcohol consumption than women, but these differences are less marked among 15- to 24-year-olds, due to the rising numbers of girls that drink in many countries. In Spain, alcohol consumption in adolescence is more frequent among women than among men (14-18 year-olds) (Observatorio Español sobre Drogas, 2013). As a consequence, the level of heavy episodic drinking among European adolescents has grown slowly but continuously over recent years (Chavez, Nelson, Naimi, & Brewer, 2011; Hibell, Guttormsson, Ahlström, Balakireva, Bjarnason, Kokkevi, & Kraus, 2007; Sánchez Pardo, 2002).

The World Health Organization and the Spanish Ministry of Health define risk alcohol consumption as upwards of 2.5 standard drink units (25 g of alcohol) for women and upwards of 4 standard drink units (40 g of alcohol) for men (Ministerio de Sanidad y Consumo, 2008). Consumption of the same amount of alcohol in men and women produces a significantly lower blood alcohol concentration (BAC) in the former sex, due to the lower metabolism rate of women and their higher sensitivity to this drug (Courtney & Polich, 2009). Similarly, animal studies show that females are more vulnerable than males to the neurotoxic/neuroinflammatory effects of ethanol, supporting the view that women are more susceptible than men to the medical consequences of alcohol abuse (Alfonso-Loeches, Pascual, & Guerri, 2013). This fact, together with a lack of studies of adolescent female social drinkers, make this latter group a risk population in whom the effects of alcohol need to be studied in a more exhaustive manner according to pattern of consumption (acute intake of a high dose and a long-term consumption history).

Ethanol produces a wide variety of behavioral and physiological effects in the body, but exactly how it acts to produce these effects is still poorly understood (Harris, Trudell, & Mihic, 2008). Alcohol impairs the functioning of a variety of domains throughout the life cycle (Espert & Gadea, 2012), including brain development (Guerri & Pascual, 2010), attentional processing (Marinkovic, Rickenbacher, Azma, & Artsy, 2012), memory (Squeglia, Schweinsburg, Pulido, & Tapert, 2011), academic performance (Inglés, Torregrosa, Rodríguez-Marín, García del Castillo, Gázquez, García-Fernández & Delgado, 2013), and motor performance (Marczinski, Fillmore, Henges, Ramsey, & Young, 2012; Modig, Fransson, Magnusson, & Patel, 2012), and it alters physiological parameters, as well as anxiety (Vinader-Caerols, Monleón, Carrasco, & Parra, 2012).

In a previous study in our laboratory, a low dose of alcohol (15.8 g in women and 18.7g in men) on physiological parameters and anxiety in a young population (mean age: 20.34 ± 2.34 years) produced a decrease in diastolic but not systolic blood pressure, and no alteration of the heart rate (Vinader-Caerols et al., 2012). These findings challenged previously published data suggesting that alcohol consumption increases blood pressure (Taylor, Irving, Baliunas, Roerecke, Patra, Mohapatra, & Rehm, 2009; Xin, He, Frontini, Ogden, Motsamai, & Whelton, 2001). In addition, we observed higher levels of state anxiety in alcohol consumers than in control subjects. However, no differences in state anxiety were detected in the former group when levels were compared before and after the acute intake of alcohol (Vinader-Caerols et al., 2012).

The aim of the present study was to evaluate the effects of a high dose of alcohol on core physiological and psychological parameters in young male and female social consumers. The physiological measures were systolic and diastolic blood pressure (SBP and DBP) and heart rate (HR), and the psychological measures were state anxiety (SA), trait anxiety (TA), attention (ATT), time estimation (TE) and manual dexterity (MD). The first two psychological parameters are measures of anxiety, the following two measure attentional processing, and the last measures motor behaviour. The novelty of the present study lies in that it combines the population sample (late adolescents with a history of risk alcohol consumption during the previous year), the consumption of a high dose of alcohol (38.4 g) in a short period of time (15-20 min), and the reproduction of the conditions under which alcohol is normally consumed. Following the rationale used by other researchers (Hindmarch, Rigney, Stanley, Quinlan, Rycroft, & Lane, 2000), we believe that administering alcohol to experimental subjects as it is usually ingested in "real life" is a more appropriate method of evaluating its effects in a risk population.

Method

Subjects

Twenty-two healthy male and 24 healthy female undergraduate students at the University of Valencia, Spain participated in the study (mean age: 19.36 ± 0.21 years old and 19.5± 0.48 years old, respectively). They were recruited as experimental subjects according to their consumption habits and general health status, which were determined by a self-report in which the following controlled variables were measured: consumption of drugs, frequency and level of consumption, hours and quality of sleep, physical health (e.g. normotensive subjects) and psychological health (e.g. no previous history of episodes of anxiety). Participants were classified as abstemious subjects or social consumers of alcohol (≥ 3 standard drink units for women and ≥ 4 standard drink units for men, consumed in a short period of time –over a weekend– on a regular basis during the previous year) whose alcohol consumption had begun at an early age (mean age: 15.00 ± 0.39 years old). A telephone

interview was then conducted with each selected subject in order to confirm the information provided in the self-report and to fix the date and time of the test.

Informed consent was obtained from all participants the test day and the study was conducted in accordance with the guidelines for human experimentation of the Ethics Committee of the University of Valencia and with those of the Helsinki Declaration. The following inclusion criteria were determined: 18 years old or older; and body mass index of 18-28 and good health, according to the data obtained through the self-report and subsequently checked in the interview. The exclusion criteria were as follows: being on medication; a history of mental disorders; an irregular sleep pattern; or a history of substance abuse, including caffeine and tobacco. Subjects (the consumers) were told to abstain from drinking alcohol and performing heavy physical exercise during the evening/night prior to the experiment, and all subjects were instructed to follow their normal sleep patterns. All the participants were right-handed.

Tests and Apparatus

A digital automatic blood pressure monitor (M10-IT, OMRON, Spain) was used to measure SBP (mmHg), DBP (mmHg) and HR in all the subjects.

The State-Trait Anxiety Inventory (STAI) (Spielberger, 1984) was used to measure anxiety. This is a questionnaire consisting of 20 items referring to self-reported SA and 20 items referring to TA. All subjects completed the standardized Spanish version of the STAI.

The Stroop task was used to measure attentional processing. This test measures the ability to focus attention on relevant stimuli while ignoring distracters and to suppress a prepotent response (i.e. word reading) in favour of an atypical one (i.e. colour naming) (Stroop, 1935). A standard printed version of this task consisting of three parts or sheets was employed. Sheet 1 (a page of words with the names of colours printed in black ink) and sheet 2 (a page printed with coloured 'Xs') are congruent conditions; in this case, the subject is instructed to read the words (sheet 1) or name the colours (sheet 2) as quickly as possible within a time limit of 45 s. Sheet 3 (a page of words from the first page printed in the colours appearing on from the second page) is the incongruent condition, as the colour and the word do not match (e.g. the word red is printed in blue ink); in this case the subject is told to name the ink colour rather than the word. Three scores (based on the number of items completed on each sheet) are provided, with the score for sheet 3 being the most relevant. An additional interference score known as the "Stroop effect" is also calculated [Stroop effect = score3 – (score1 * score2 / score1 + score2)]; the higher the Stroop effect value, the lower the interference effect. Taking into consideration the relevance of these measures, only sheet 3 and Stroop effect scores were analysed in the present study.

The time estimation task, an integrated computerized procedure used to provide time estimation trials and to record results, was also performed by the subjects. The programme and protocol were the same as those described in detail elsewhere (Somoza & Parra, 1995). Subjects were also asked to estimate a short time interval (10 s) without feedback in a prospective paradigm. In this time estimation task, subjects were asked to press a key when they believed that 10 s had elapsed following a "beep" sound. Ten experimental trials (per subject) were preceded by two practical trials in which the computer demonstrated a 10 s interval. No feedback on performance was offered. The intertrial interval was variable (mean = 5; range = 3-7 s).

A standard version of the Purdue Pegboard test was used to provide a global assessment of manual dexterity (Tiffin & Asher, 1948). The pegboard is equipped with pins, collars and washers placed in four cups at the top of the board. Four separate scores were obtained with this test: (1) right hand; (2) left hand; (3) both hands; and (4) assembly. For the first three measures, subjects were instructed to place as many round pegs (3 mm x 25 mm) as possible in the board within a short period of time (30 s), while for the last measure, they were told to assemble pins, collars, and washers using both hands simultaneously within a period of 1 min. The whole test lasted roughly 10 min.

An alcoholmeter (Alcoquant® 6020, Envitec, Germany) was employed to measure the concentration of alcohol in the air exhaled by the social consumers of alcohol before and after intake of a drink.

The Alcohol Use Disorders Identification Test (AUDIT) (Saunders, Aasland, Babor, de la Fuente, & Grant, 1993) was also employed to measure alcohol dependency among the subjects. The AUDIT consists of 10 questions that evaluate the quantity and frequency of alcohol intake and alcohol-related behaviours and consequences. It uses a range of 0-40, in which a score of 8 or more indicates a problematic use of alcohol. A higher score is related to greater severity of alcohol dependence.

Procedure

The experimental procedure was approved by the Ethics Committee of the University of Valencia. The subjects were allocated by sex to two treatment groups according to their consumption habits: control group (C) and alcohol group (A). The C groups consisted of 11 male and 12 female abstemious individuals respectively, who received 100 ml of a lime- or orange-flavoured refreshment. The A groups consisted of 11 male and 12 female social consumers respectively, who were administered 38.4 g of alcohol in the form of vodka mixed with a refreshment (120 ml of vodka diluted in 100 ml of a lime- or orange-flavoured refreshment) that they were instructed to drink within a period of 15-20 min. The dose of alcohol was selected according to the consumption habits of the subjects. After finishing the drink, all subjects rinsed their mouths with water.

The body weight of C and A groups did not significantly differ for men (C group: 67.91 ± 1.06 kg; A group: 70.64 ± 1.55 kg) or women (C group: 58.25 ± 1.29 kg; A group: 57.33 ± 1.05 kg). Similarly, body mass index (BMI) did not significantly differ for men (C group: 20.8 ± 0.39; A group: 22.39 ± 0.43) or women (C group: 21.4 ± 0.55; A group: 20.85 ± 0.48). According to the body weight mean of A group, the mean alcohol intake was 0.55 g/kg in men and 0.66 g/kg in women, which is considered a medium-high dose of alcohol (Ogden, Wearden, Gallagher, & Montgomery, 2011). Body weight, BMI, drinking duration, and sex differences in metabolism were taken into account in this experimental procedure, as they are critical factors in the within-subject variability of blood alcohol concentration levels (Lange & Voas, 2001).

Each subject participated in two phases separated by a 35-min interval consisting of treatment (15-20 min) and wait (15 min). In the first phase, SBP, DBP, HR, SA, ATT, TE and MD were registered for all subjects. Alcohol concentration was measured in the social consumers using an alcoholmeter. Following the wait interval, a second phase took place in which, in addition to the aforementioned parameters, TA and alcoholic dependence were measured in social consumers of alcohol by the AUDIT test (mean score: 6,5 ± 1.12 in men and 6,64 ± 0.89 in women). The concentrations of alcohol in exhaled air were 0.00 mg/L for men and women before the alcoholic drink, and 0.22 ± 0.016 mg/L for men and 0.32 ± 0.021 mg/L for women after drinking. Subjects were told to follow their usual breakfast routine at least one hour before the experimental session. All the tests were performed between 10:30 a.m. and 12:30 p.m. and members of the A groups remained on the premises until their alcohol concentration dropped to legal limits for driving.

Statistical Analyses

After checking that data met the criteria for normality and homogeneity of variances, they were subjected to parametric analysis. Taking into account that alcohol concentration differed significantly in men and women, separate ANOVAs were performed for each sex. An ANOVA was performed for each measure (SBP, DBP, HR, SA, TA, ATT, TE and MD), with the between-subjects factor "Treatment" and the within-subjects factor "Phase" as independent variables. When their interaction was statistically significant, further analyses were carried out with Student's *t*-tests for dependent and independent samples. All analyses were performed using the "SPSS" Statistics software package, version 19.0 for Windows (IBM, 2010).

Results

A summary of significant ANOVA results for physiological (SBP, DBP and HR) and psychological (SA, TA, ATT, TE and MD) parameters is provided in table 1.

Table 1
Summary of significant ANOVAs for physiological (SBP, DBP and HR) and psychological (SA, ATT and MD) parameters.

MEASURE	Mean (±SEM) PHASE 1	Mean (±SEM) PHASE 2	PHASE	TREATMENT	PHASE X TREATMENT
SBP Men	C = 12.24 (±0.38) A = 12.28 (±0.26)	C = 11.89 (±0.40) A = 11.88 (±0.25)	n.s.	n.s.	n.s.
SBP Women	C = 11.32 (±0.23) A = 10.64 (±0.28)	C = 10.27 (±0.18) A = 10.27 (±0.17)	***	n.s.	*
DBP Men	C = 7.26 (±0.23) A = 7.44 (±0.37)	C = 6.91 (±0.30) A = 6.61 (±0.29)	**	n.s.	n.s.
DBP Women	C = 7.37 (±0.24) A = 6.94 (±0.21)	C = 6.94 (±0.22) A = 6.65 (±0.14)	***	n.s.	n.s.
HR Men	C = 77.00 (±4.53) A = 66.45 (±2.75)	C = 72.36 (±3.43) A = 64.18 (±2.21)	*	*	n.s.
HR Women	C = 83.58 (±1.93) A = 74.83 (±3.08)	C = 80.17 (±2.71) A = 76.92 (±1.72)	n.s.	n.s.	n.s.
SA Men	C = 22.32 (±4.21) A = 19.86 (±3.00)	C = 16.04 (±3.25) A = 18.23 (±4.76)	n.s.	n.s.	n.s.
SA Women	C = 13.58 (±3.54) A = 27.75 (±5.00)	C = 13.83 (±4.98) A = 42.83 (±7.12)	n.s.	**	n.s.
ATT (Sheet 3) Men	C = 58.45 (±2.49) A = 61.64 (±1.08)	C = 63.27 (±2.69) A = 66.27 (±1.13)	***	n.s.	n.s.
ATT (Sheet 3) Women	C = 60.25 (±1.59) A = 53.17 (±2.05)	C = 67.58 (±2.19) A = 56.42 (±2.41)	***	***	n.s.
ATT (Stroop Effect) Men	C = 59.18 (±1.70) A = 55.64 (±1.75)	C = 59.82 (±2.09) A = 63.00 (±1.94)	**	n.s.	*
ATT (Stroop Effect) Women	C = 58.33 (±1.81) A = 54.25 (±1.29)	C = 62.58 (±2.01) A = 58.25 (±1.42)	***	*	n.s.
MD (Right-hand) Men	C = 15.00 (±0.53) A = 14.91 (±0.54)	C = 15.14 (±0.59) A = 15.55 (±0.53)	n.s.	n.s.	n.s.
MD (Right-hand) Women	C = 15.44 (±0.38) A = 16.00 (±0.50)	C = 17.00 (±0.44) A = 15.92 (±0.43)	*	n.s.	*
MD (Left-hand) Men	C = 12.57 (±0.78) A = 13.91 (±0.45)	C = 14.00 (±0.49) A = 14.09 (±0.41)	n.s.	n.s.	n.s.
MD (Left-hand) Women	C = 14.78 (±0.32) A = 13.92 (±0.40)	C = 15.67 (±0.50) A = 14.92 (±0.48)	*	n.s.	n.s.
MD (Assembly) Men	C = 7.43 (±0.57) A = 8.18 (±0.50)	C = 8.43 (±0.48) A = 7.73 (±0.43)	n.s.	n.s.	**
MD (Assembly) Women	C = 8.00 (±0.29) A = 9.42 (±0.45)	C = 9.56 (±0.67) A = 8.83 (±0.47)	n.s.	n.s.	**

Note. SBP = systolic blood pressure, DBP = diastolic blood pressure, HR = heart rate, SA = state anxiety, ATT = attention (Stroop test), MD = manual dexterity (Purdue test). C = control group, A = alcohol group. * $p < .05$; ** $p < .01$; *** $p < .005$.

Blood pressure

The ANOVA for SBP in women revealed that the factor "Phase" was significant, with a decrease observed in the second phase, $F(1, 22) = 18.56$, $p < .0001$. The factor "Treatment" was not significant, while the interaction "Phase" x "Treatment" was statistically significant $F(1, 22) = 4.32$, $p < .05$. Comparison of dependent samples revealed a decrease of SBP in the C group $t(11) = 5.73$, $p < .0001$, but not in the A group (see Figure 1). Neither the main factors nor their interaction were significant in men.

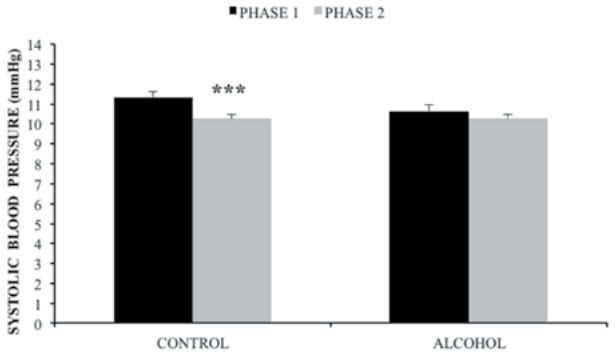

Figure 1. Mean (+SEM) systolic blood pressure (mmHg) in Control and Alcohol women. *** p < .005 versus phase 1.

In the case of DBP, the factor "Phase" was significant in men, $F(1, 20) = 7.6$, $p < .05$, and women, $F(1, 22) = 11.13$, $p < .005$. A decrease was observed in the second phase in both sexes. The factor "Treatment" and the interaction "Phase" x "Treatment" were not significant with respect to DBP in either men or women.

Heart rate

The ANOVA for HR in men revealed that the factor "Phase" was significant, with a decrease observed in the second phase, $F(1, 20) = 4.4$, $p < .05$. "Treatment" was also significant in men, $F(1, 20) = 4.45$, $p < .05$, with alcohol consumers showing a lower HR than control subjects. The interaction "Phase" x "Treatment" was not significant. Neither the main factors nor their interaction were significant in women.

State-Trait anxiety

The factor "Treatment" was significant for SA in women, $F(1, 22) = 11.42$, $p < .005$, with higher values recorded for alcohol consumers. Neither the factor "Phase" nor the interaction "Phase" x "Treatment" was significant with respect to SA in women. Neither the main factors nor their interaction were significant in men.

"Treatment" was not significant with respect to TA in either men or women.

Attention

In sheet 3 of the Stroop task (incongruent condition), the "Phase" factor was significant in men, $F(1, 20) = 18.9$, $p < .0001$, who showed an improvement in the second phase, while neither the factor "Treatment" nor the interaction "Phase" x "Treatment" was significant. In women, the factor "Phase" was significant, $F(1, 22) = 14.01$, $p < .001$, as an improvement was detected in the second phase. "Treatment" was also significant $F(1, 22) = 12.52$, $p < .005$, as the C group performed better than the treatment group. The interaction was not statistically significant.

The Stroop effect highlighted that there was less interference in the second phase than in the first phase in both men, $F(1, 20) = 8.62$, $p < .01$, and women $F(1, 22) = 11.23$, $p < .005$. The factor "Treatment" was not significant in men but was so in women, $F(1, 22) = 4.46$, $p < .05$, among whom control subjects exhibited less interference than their alcohol-consuming counterparts. The interaction "Phase" x "Treatment" was not statistically significant in women but was so in men $F(1, 20) = 6.09$, $p < .05$. The comparison of dependent samples revealed a minor interference in the second versus first phase in the A group $t(10) = 3.77$, $p < .005$, but not in C group (see Figure 2).

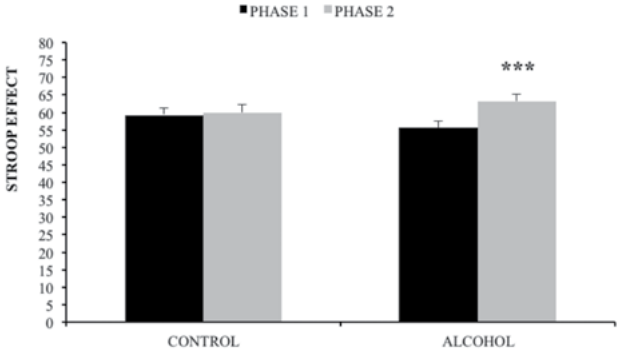

Figure 2. Mean (+SEM) score for Stroop effect in Control and Alcohol men. *** p < .005 versus phase 1.

Time estimation

Neither the main factors nor their interaction were significant in men or women.

Manual dexterity

The results obtained for each measure in the Purdue Pegboard test were as follows:

Right hand. In women, the factor "Phase" was significant, $F(1, 19) = 5.15$, $p < .05$, as subjects obtained a higher score in the second phase. The factor "Treatment" was not significant, while the interaction was, $F(1, 19) = 6.38$, $p < .05$. The comparison of dependent samples revealed an improvement in the C group, $t(8) = 3.5$, $p < .01$, that was not observed in the A group (see Figure 3). Neither the main factors nor their interaction were significant in men.

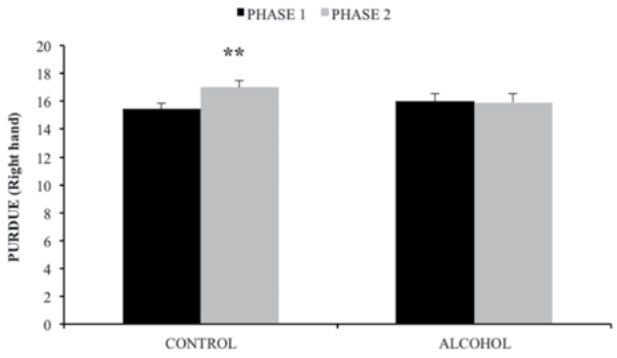

Figure 3. Mean (+SEM) score for right-hand Purdue task in Control and Alcohol women. ** p < .01 versus phase 1.

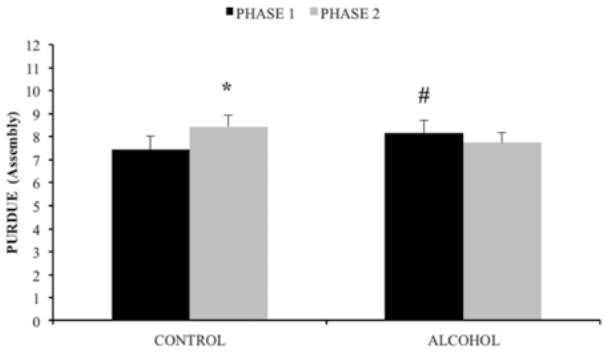

Figure 5. Mean (+SEM) score for assembly Purdue task in Control and Alcohol women. * p < .05 versus phase 1; # p < .05 versus Control in the same phase.

Left hand. The factor "Phase" was significant, with higher scores being obtained in the second phase by men, $F(1, 16) = 4.29$, $p < .05$, and women, $F(1, 19) = 6.13$, $p < .05$. Neither "Treatment" nor the interaction of the two factors was significant in either sex.

Both hands. Neither the main factors nor their interaction was statistically significant with respect to this measure in men or in women.

Assembly. The main factors "Phase" and "Treatment" were not significant in either sex, though their interaction was significant in both men, $F(1,16) = 7.73$, $p < .01$, and women, $F(1,19) = 7.56$, $p < .01$.

In men, comparison of dependent samples revealed an improvement among controls in the second versus first phase, $t(6) = 4.58$, $p < .005$, a result that was not observed in the alcohol consumers (see Figure 4).

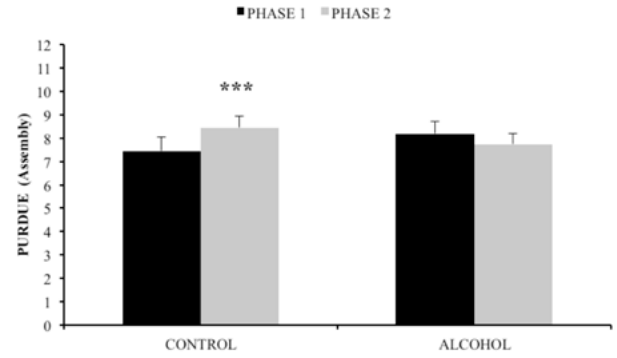

Figure 4. Mean (+SEM) score for assembly Purdue task in Control and Alcohol men. *** p < .005 versus phase 1.

In women, comparison of dependent samples revealed an improvement among controls in the second versus first phase, $t(8) = 2.8$, $p < .005$, that was not observed among the alcohol consumers. Comparison of independent samples revealed a better performance among alcohol consumers than control subjects in the first phase, $t(19) = 2.44$, $p < .05$ (see Figure 5).

Discussion

Alcohol consumption is highly prevalent during adolescence and youth in many countries, and an increase in heavy episodic drinking has become apparent among young people, and especially women, over recent years (Chavez et al., 2011; Hibell et al., 2007; Observatorio Español sobre Drogas, 2013). With this context in mind, the present study set out to evaluate the effects of a high dose of alcohol on physiological and psychological parameters in young male and female social consumers with a previous history of alcohol consumption.

In terms of physiological parameters, no differences were observed in SBP among men in either of the groups. In the case of women, SBP was found to be lower in control subjects after drinking the non-alcoholic beverage, while it did not change in alcohol consumers. This reduction observed in the second phase is likely to be a result of habituation to the experimental situation, which was prevented by alcohol consumption. This habituation phenomenon was also observed with respect to SBP in women and with respect to DBP in both sexes, as a reduction of blood pressure was observed in the second phase, independently of the treatment received. Furthermore, DBP was not affected by a high dose of alcohol (38.4 g) in either men or women. Our findings challenge previously published data associating total habitual alcohol consumption, consumption of specific alcoholic drinks, and binge drinking with higher mean blood pressure in adults (Abramson Lewis, & Murrah, 2010; Briasoulis, Agarwal, & Messerli, 2012; Xin et al., 2001). A meta-analysis by Taylor et al. (2009) concluded that the risk of hypertension increases linearly with alcohol consumption. Nevertheless, the relation between alcohol consumption and hypertension is still unclear (Halanych, Safford, Kertesz, Pletcher, Kim, Person, Lewis, & Kiefe, 2010).

HR was lower in male alcohol consumers than in male controls, while HR was similar in female control subjects and alcohol consumers, in contrast to the findings of other studies reporting an increase in this respect (e.g. Spaak, Tom-

linson, McGowan, Soleas, Morris, Picton, Notarius & Floras, 2010). Besides the reduction of HR produced by alcohol in men, the habituation phenomenon was also observed with respect to this measure in the second phase (lower HR, independently of treatment). However, no such habituation was observed in women.

Higher SA was observed among in female alcohol consumers than their control counterparts, independently of the phase. Other authors have reported an association between symptoms of anxiety and an increased risk of alcohol use disorders in early adulthood (e.g. Liang & Chikritzhs, 2011; McKenzie, Jorm, Romaniuk, Olsson, & Patton, 2011). For example, Blumenthal, Leen-Feldner, Frala, Badour, and Ham (2010) found that socially anxious youths drink alcohol to manage their anxious arousal. As expected, control and alcohol consumers of both sexes exhibited similar TA in our study. In view of this finding, it is reasonable to believe that the differences observed in SA were due to a history of alcohol consumption rather than stable individual differences of personality (Vinader-Caerols et al, 2012).

The effects on psychological parameters of a high dose of alcohol administered in conditions that simulate those under which alcohol is normally consumed by the population sample have not been well studied. The neural basis of alcohol's effects on cognitive control is also poorly understood, despite evidence of impaired ability to evaluate competing demands and to inhibit maladaptive responses (Marinkovic et al., 2012). The Stroop test is an appropriate task for evaluating this aspect. Our results show that the habituation phenomenon was advantageous to both men and women in the sheet 3 and Stroop effect, with both sexes performing better in the second phase than in the first (independently of the treatment received). On the other hand, female -but not male- alcohol consumers performed worse than control subjects in the sheet 3 test and displayed a higher interference effect in the attentional processing evaluated by this task. Furthermore, men with a history of alcohol consumption showed a lower interference effect (higher Stroop effect score) under the effects of alcohol (second phase). However, it is important to point out that the performance of alcohol consumers was not superior to that of non-consumers. Past research has indicated an impairment of attentional process under the effects of alcohol (e.g. Marinkovic et al., 2012), and we do not have a logical explanation to the apparent improvement in the male alcohol consumers' performance in our study.

In the case of TE, alcohol consumption did not significantly affect this measure in men or women. Published data regarding the effects of alcohol on TE are somewhat discrepant (Heishman, Aresteh, & Stitzer, 1997; Lapp, Collins, Zywiak, & Izzo, 1994; Tinklenberg, Roth, & Kopell, 1976). Tinklenberg et al. administered ethanol to subjects who were instructed to indicate when 30 s, 60 s and 120 s had passed and found that the estimations were longer than the stipulated time intervals. The opposite was reported by Lapp et al., whose subjects' estimations were shorter than the stipulated time intervals of 5 s, 10 s and 30 s. Heishman et al. failed to detect an effect of alcohol on the estimations of intervals from 5 to 80 s, results that are in accordance with those of the present study.

In terms of manual dexterity, control men and women showed an improvement in the assembly measure of the Purdue task, whilst alcohol seemed to block this improvement. In the right-hand measure, the same pattern was observed in women, but not in men. Marczinski et al. have reported that alcohol impairs simple and complex motor coordination in the same task. The negative impact of alcohol in our study was obvious in an impairment of the adaptive response (improved performance in the second phase) normally observed in control subjects. The improvement in the right-hand (and not in the left-hand) component of the Purdue task cannot be due to the fact that all our participants were right-handed, as this effect was observed only in women.

Furthermore, our female subjects benefitted from the habituation phenomenon, as they performed better in the second phase (independently of the treatment received) in both right- and left-hand measures of the Purdue task.

BAC obtained in the present study was a significantly higher in women and the blood pressure and manual dexterity measures were affected by alcohol consumption in this sex. Despite the fact that men had a lower BAC after consuming the same quantity of alcohol, two measures - attention and manual dexterity- were affected in their case.

The results obtained in women in the present study and previous findings by our group (Vinader-Careols et al., 2012) are in line; namely: i) a decrease in SBP and DBP, independently of treatment, was observed in the second phase; ii) HR and TA was not affected by either treatment or phase; and iii) SA levels were higher among alcohol consumers. On the other hand, in contrast to the findings of our previous study, in the present work the decrease of SBP occurred specifically in control subjects but not in alcohol consumers, while no reduction of DBP was observed in the latter group.

In summary, taking into account that the present study is mainly descriptive and that the results have been obtained by mimicking the consumption habits of young people and reproducing the conditions under which they normally consume alcohol, it can be affirmed that:

i. In men, acute alcohol consumption improves ATT (although the performance of alcohol consumers was not better than that of non-consumers).
ii. In women, acute alcohol consumption blocks the habituation phenomenon with respect to SBP observed in controls.
iii. In both sexes, acute alcohol consumption blocks the improvement in MD performance associated with experience in non-consumers.

These results help to understand the extent of performance impairment produced by risk alcohol consumption in young men and women. They reinforce the idea that the adolescent brain is especially sensitive to the impact of ethanol exposure during this critical developmental period (Maldonado-Devincci, Badanich, & Kirstein, 2010). Moreover, they support the hypothesis that the phenomenon of habituation and the improvement in performance associated with experience can be blocked by alcohol.

Future research with larger samples of young men and women and alternative experimental designs is required to understand better the effects of alcohol on young people with consumption habits established in adolescence.

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Conflict of interest

All authors have no conflicts of interest to declare.

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Duration of Internet use and adverse psychosocial effects among European adolescents

Tiempo de uso de Internet y efectos psicosociales adversos en adolescentes europeos

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Resumen

A pesar de las importantes contribuciones de los estudios realizados sobre la prevalencia del uso problemático de Internet (PIU) entre los adolescentes europeos, sigue existiendo dudas importantes con respecto a las consecuencias adversas del PIU. El objetivo de este estudio fue evaluar la relación entre la duración del uso de Internet y los efectos psicosociales adversos en adolescentes de seis países europeos. La muestra final estuvo compuesta por 7.351 adolescentes (50,8 % varones y 49,2 % mujeres, edad media: 14,6 años ± 1,90) reclutados en escuelas seleccionadas al azar dentro de los seis países del estudio. Los resultados mostraron que el 12,9% de los adolescentes utilizaba Internet más de 20 horas a la semana. Se encontró una relación estadísticamente significativa entre la duración del uso de Internet y la frecuencia de uso de alcohol, tabaco, cannabis y otras drogas ilegales. La duración del uso de Internet también se asoció significativamente con problemas escolares, con el uso de las máquinas tragaperras y con otros problemas psicosociales. Estos resultados ponen de relieve la necesidad de fortalecer los esfuerzos en prevención para reducir el uso problemático de Internet y las consecuencias asociadas entre los adolescentes.

Palabras Clave: Internet, adolescentes, problemas psicosociales.

Abstract

Despite the significant contributions from previous studies about the prevalence of problematic Internet use (PIU) among adolescents in Europe, important questions remain regarding adverse consequences of PIU. This study aims to assess the relation between duration of Internet use and adverse psychosocial effects among adolescents from six European countries. The final sample included 7,351 adolescents (50.8% male and 49.2% female; mean age: 14.6±1.90) recruited from randomly selected schools within the six study sites. Results showed that 12.9% of adolescents used Internet more than 20 hours per week. There was a significant relationship between duration of Internet use and frequency of alcohol, tobacco, cannabis and other illegal drug use. Duration of Internet use is also significantly associated with school problems, with use of slot machines and with other psychosocial problems. These findings highlight the need to strengthen preventive efforts for reducing PIU and related consequences among adolescents.

Key Words: Internet, adolescents, psychosocial problems.

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Using the Internet has become one of the most popular leisure-time activities in Western societies. Particularly among adolescents, the Internet is observed to be increasingly adopted as a readily accessible means for information retrieval, entertainment, and socialization (Kormas, Critselis, Janikian, Kafetzis, & Tsitsika, 2011). For the majority of Internet users, the World Wide Web represents a tremendous wellspring of opportunity that enhances well-being. However, for some people the Internet can lead to psychosocial problems, including mental disorders (Aboujaoude, 2010).

Due to the lack of consensus on diagnostic criteria and the dearth of large epidemiological studies, the prevalence of problematic Internet use (PIU) in the adolescent population has not been well established. The results can vary widely and are difficult to compare, due to differences in Internet access, recruitment methodology, the exact age bracket studied, and the definitions utilized (Aboujaoude, 2010).Considering only relatively large and offline studies, research has yielded prevalence estimates ranging between 2% and 11% (Cao & Su, 2007; Ghassemzadeh, Shahraray, & Moradi, 2008; Johansson & Gotestam, 2004; Kim et al., 2006; Park, Kim, & Cho, 2008; Siomos, Dafouli, Braimiotis, Mouzas, & Angelopoulos, 2008).In particular, among European adolescents, the prevalence of PIU has been observed to range between 2% and 15.1% (Durkee et al., 2012; Johansson & Gotestam, 2004; Niemz, Griffiths, & Banyard, 2005; Pallanti, Bernardi, & Quercioli, 2006; Sasmaz et al., 2013; Siomos et al., 2008). PIU in adolescence has been associated with a wide range of adverse psychosocial and mental health conditions such as attention-deficit/hyperactivity disorder (ADHD) (Yoo et al., 2004), psychosomatic symptoms (Cao, Sun, Wan, Hao, & Tao, 2011; Jenaro, Flores, Gómez-Vela, González-Gil, & Caballo, 2007), inappropriate dietary behavior and poor diet quality (Kim et al., 2010), interpersonal problems (Seo, Kang, & Yom, 2009), aggressive behaviors (Ko, Yen, Yen, et al., 2008) or depressive symptoms (Morrison & Gore, 2012).

Despite the significant contributions from previous studies, important questions remain regarding adverse consequences of PIU in adolescence. For example, findings from previous studies have often been constrained by their focus on specific geographic locations or examined a limited number of psychosocial variables. No published study has examined consequences of PIU in adolescence usually associated with addiction, such as multiple substance use or impairment in family and social activity. The vast majority of studies were conducted in Asia, most of them in China and very few studies have been conducted in Europe. Thus, more research needs to be performed in other regions of the world for eventual cross-cultural comparisons (Carli et al., 2011).

We sought to address these gaps in knowledge by identifying the relation between Internet use and psychosocial problems by drawing on data from community samples from six regions in Europe. Due that the duration of Internet use has a close relationship with Internet addiction and PIU, and the longer the Internet using time the more risk there is to be addicted (Cao et al., 2011; Carli et al., 2011; Durkee et al., 2012; Grohol, 1999), we used duration of Internet use as a proxy of PIU. The specific goals of the present study were to assess the association between duration of Internet use and: 1) use of tobacco, alcohol and illegal drugs, 2) school problems, 3) use of slot machines; and 4) other problematic behaviors such as stop playing sports/hobbies, injured after drinking, trouble with police, have family problems, sexually transmitted diseases, lost friends and have gained weight.

Methods

Study design and participants

A survey was carried out between October 2010 and February 2011 in sixty-nine middle schools from six European regions (23.9% from Coimbra in Portugal, 13% from Ljubljana in Slovenia, 22.7% from Mallorca Island in Spain, 10.8% from Merseyside in UK, 15.9% from Prague in Czech Republic, and 13.6% from Stockholm in Sweden). For all countries we used a common protocol to select the sample, procedures to be followed in the survey, collection of incidents, management and delivery of questionnaires to be included in the database. We used a stratified and incidental school sample taking into account if it was a public or private school, the size and the location of the school, according with the real distribution of schools in each region. There could be only one classroom per school year for each school. The procedure for obtaining consent from participants differs in each country. In total, 7,701 children's surveys were included in the analysis. Approximately 350 were excluded for reasons including non-completion of major sections (substance use) and illegibility of responses. A total of 50.8% of the participants were boys and 49.2% were girls. Mean age of the sample was 14.6 years (s = 1.90; range: 11-19 years).

Measures

A team of four people, specially trained for this study, was sent to each school to talk to the participants about the aims of the study and the confidentiality of the data. All students filled out an anonymous questionnaire in their classrooms and during school time. Duration of Internet use was determined by asking respondents about "approximately, how much time are you using Internet at home each week (in hours)". For evaluating the Internet sited use we included the following predefined and not exclusive categories: social networking, chat room use, downloading movies, music, watching TV, shopping, email, gaming and school work. Extensive questions covered drug use. For the evaluation of the adolescents' alcohol use the item used was: "How frequently do you drink alcohol?", and the response options being: "I have never drank alcohol", "Less than once a month", "Once a month", "Once a week", "2-4 times a week" and "Every day,

or almost". Frequency of drunkenness was determining by asking individuals: How many times have you been drunk in the last month?" For the assessment of smoking we used the item: "Read the following statements and tick the box for that which best describes you: I have never smoked, I have only tried smoking once, I have smoked once or twice in the past but now I don't, I smoke cigarettes but not more than one a week, I smoke between one and six cigarettes a week, In general I smoke more than six cigarettes a week". For the evaluation of cannabis use we asked: "Have you ever used cannabis?", the response options being: "No", "Yes, at some time in my life", "Yes, in the last 12 months" and "Yes, in the last 30 days". For the evaluation of illegal drug use we used a dichotomous response question: "Have you ever used illegal drugs (cocaine, ecstasy, amphetamine, heroin, others..)?".

The school variables have been classified into three different dimensions: Performance ("It is difficult to pay attention in class", "I forget things" and "I have trouble keeping up with homework"), Absenteeism ("I missed class because I feel sick", "I go to school but sometimes I miss some classes", "Sometimes I'm not going to school because I do not want to go", and "Sometimes I'm not going to school because my parents/caregivers not let me go to school") and Satisfaction("I am happy to be at school/college/university" and "I feel safe at school/college/university").

For the evaluation of other different psychosocial problems the question used was: "Have you experienced any of these problems during the past six months?" The items were:, "injured after drinking", "having trouble with the police", "having family problems", "regret having had sex with someone, "sexually transmitted diseases", "have lost friends, "put on weight". Responses were categorized as "yes" or "no". Finally, slot machines use was determined by asking respondents about "how often do you play on slot machines". Response options were: "never", "a few times a year", "once or twice a month", "at least once a month" and "almost every day".

Data analyses

Various descriptive and frequency analyses in relation to participants' characteristics were carried out. The relationship between different variables measured by the questionnaire and frequency of Internet use were analyzed using chi-squared tests. Effect sizes of principal comparisons were calculated using phi ($_{\Phi}$) for χ^2 tests, in order to maintain values for small, medium and large effects (.10, .30 and .50). Confidence level was 95%, and the statistical package used was the SPSS-15.

Results

Duration of Internet use and Internet sited used

Ninety-four percent of adolescents use the Internet at home. Rates of Internet use were as follows: 3.0% of adolescents never used Internet, 36.2% used Internet between 1 and 5 hours per week; 29.3% used Internet between 6 and 10 hours per week; 18.7% used Internet between 11 and 20 hours per week and 12.9% used Internet more than 20 hours per week. Seventy-five percent of adolescents used social networking (e.g. Facebook), 28.6% chat rooms, 62.25% downloading movies, music, etc., 28.8% for watching TV, 15.2% for shopping, 53.8% to email, 41.5% for gaming and 64.8% for school work. Fifty six percent of respondents reported that parents do not limit the time they can use the Internet.

Duration of Internet use and drug use

There is a statistically significant relationship (p= .000) between duration of Internet use and alcohol use (Table 1). Among adolescents who use the Internet less time (1-5 hours) the frequency of alcohol consumption is lower than expected. The opposite trend occurs with adolescents who use the Internet more than 20 hours a week. Chi-square tests also showed a significant positive relationship between duration of Internet use and tobacco use (p= .000).

Adolescents who use the Internet more time per week tend to use more cannabis (p= .000) and other illegal drugs (p= .000). Specifically, among those who use the Internet more than 20 hours per week are twice more likely to be cannabis users than expected by chance. In contrast, among those who use the Internet between 1-5 hours are half as many likely to be regular users than expected by chance (Table 1).

Table 1
Relationship between duration of Internet use and drug use

Drug use	Chi square*	N	Df	P	Effect size ($_{\Phi}$)
Alcohol use	411.273	6678	24	.000	.248
Frequency of drunkenness	115.880	3594	80	.005	.180
Tobacco use	220.509	7439	20	.000	.172
Cannabis use	186.707	7294	12	.000	.160
Other illegal drugs	108.096	7556	4	.000	.120

* With Yates continuity correction

Table 2
Relationship between duration of Internet use and school factors

School factors	Chi square*	N	Df	P	Effect size (Φ)
Problem paying attention in class	233.749	7565	16	.000	.176
Forget things	123.979	7552	12	.000	.128
Trouble keeping up with homework	129.406	7528	12	.000	.131
Missed class because sickness	68.014	7524	12	.000	.095
Sometimes miss some classes	162.507	7535	12	.000	.147
Sometimes not going to school because do not want to go	185.773	7539	12	.000	.157
Sometimes not going to school because my parents/caregivers let me not go to school	145.391	7544	12	.000	.139
Happy to be at school	140.408	7529	12	.000	.137
Feel safe at school	127.848	7481	12	.000	.131

* With Yates continuity correction

Table 3
Relationship between duration of Internet use and interpersonal and psychosocial problems

Psychosocial problems	Chi square*	N	Df	P	Effect size (Φ)
Injured after alcohol	109.441	7557	4	.000	.120
Trouble with police	95.049	7556	4	.000	.112
Family problems	47.066	7554	4	.000	.79
Had regretted sex	63.761	7546	4	.000	.092
Losing friends	41.925	7538	4	.000	.075
Put on weight	22.685	7503	4	.000	.055
Sexually transmitted diseases	115.510	7544	4	.000	.124

* With Yates continuity correction

Duration of Internet use and school factors

There is a significant relationship between duration of Internet use and school problems (p= .000) (Table 2). In all cases, adolescents using more than 20 hours of Internet per week have a lower school performance and school satisfaction, and higher rates of absenteeism than expected by chance.

Duration of Internet use and interpersonal and psychosocial problems

There are statistically significant relationships between duration of Internet use and the following problems: injured after drinking, trouble with police, family problems, regretted having sex with someone, losing friends, put on weight and have sexually transmitted diseases (Table 3). In all cases, the likelihood of such problems is higher than expected by chance among teens who use the Internet more than 20 hours per week. Conversely, the likelihood of problems is lower than expected by chance among those who use the Internet between 1-5 hours (Table 3).

Duration of Internet use and use of slot machines

There is a statistically significant relationship between duration of Internet use and the frequency of playing on slot machines χ^2 (16, N = 7411) = 113.100, p= .000; Φ= .124. We also performed the same analysis but collapsing the variable 'frequency slot game' in two categories: 0 (never) and 1 (other cases, from 'a few times a year' to 'almost every day'). The results also show a statistically significant relationship between the two variables χ^2 (4, N = 7411) = 70.346, p= .000; Φ= .097.

Discussion

To our knowledge, this is the first study to examine the relation between duration of Internet use and psychosocial problems in an adolescent community sample from several regions in Europe. The study findings suggest that adolescents who use the Internet for longer are more likely to concomitantly exhibit psychosocial problems. Specifically,

we emphasized five major results: 1) A high percentage of the study population is at risk of PIU, as the number of hours per week using the Internet is very high; 2) adolescents who use the Internet excessively compared to their peers are at greater risk to use drugs; 3) adolescents who use Internet for longer have poorer school performance and miss more school classes; 4) the odds of psychosocial problems are greater among adolescents who use the Internet more than 20 hours per week; and 5) the frequency of gambling among those who use the Internet more hours is greater than among adolescents who use Internet less time.

In line with other studies, our results showed that excessive Internet use is very high. There is increasing evidence that PIU among adolescents is emerging due to easy access to the Internet (Gómez Salgado, Rial Boubeta, Braña Tobío, & Varela Mallou, 2014). Adolescents may be particularly vulnerable to the development of PIU and addictive behavioral patterns in general (Griffiths & Wood, 2000; Pallanti et al., 2006; Puerta-Cortés, & Carbonell, 2014; van den Eijnden, Spijkerman, Vermulst, van Rooij, & Engels, 2010).

Consistent with findings from previous studies (Fisoun, Floros, Siomos, Geroukalis, & Navridis, 2012; Kim, 2012; Lam, Peng, Mai, & Jing, 2009; Liu, Desai, Krishnan-Sarin, Cavallo, & Potenza, 2011; Pawlikowski, Nader, Burger, Stieger, & Brand, 2013), we found an association between the duration of Internet use and drug use. Those who use the Internet excessively compared to their peers were seen to be at increased risk of drug use: alcohol, tobacco, cannabis and other illegal drugs. The results also showed that the more adolescents use the Internet the more often they reported being drunk. There are several possible mechanisms explaining this association. Out-of-control gambling, eating, and Internet use may share the same neurobiological mechanism with substance dependence and can be termed "behavioral addiction" (Holden, 2001). Thus, if the Internet had the potential to be addictive, adolescents with vulnerability to drug use would be vulnerable to excessive Internet use and PIU. Alternatively, the co-occurrence of excessive Internet use and drug use may also be due to shared risk factors such as neurobehavioral disinhibition, high novelty-seeking and low reward dependence (Lam et al., 2009), low self-esteem, low family function, and low life satisfaction (Ko et al., 2008b). It is also possible that one behavior may cause the other.

Using the Internet for over 20 hours per week was associated with increased risk of lower school performance, lower satisfaction and higher absenteeism. Several factors may contribute to the high risk of school problems among adolescents who spend much time connected to Internet. The poor mental health can affect school performance and several studies reported strong association between PIU and depression (Ceyhan & Ceyhan, 2008; Kim et al., 2006; Yen, Ko, Yen, Chang, & Cheng, 2009),and between PIU and ADHD (Ko, Yen, Chen, Chen, & Yen, 2008; Yoo et al., 2004). Previous studies also suggest that individuals with Internet addiction exhibit more impulsivity than those who use the Internet less frequently(Cao & Su, 2007). Adolescents tend to use the Internet as a medium for socializing (Carballo, Perez-Jover, Espada, Orgiles, & Piqueras, 2012), but PIU can result in individuals spending ever-increasing amounts of time in online activities (Cao et al., 2011; Gámez-Guadix, Orue, & Calvete, 2013), leading to school problems. Late night use of the Internet can cause sleep deprivation and fatigue, which can adversely affect academic performance (Flisher, 2010).

Our results are consistent with previous work (Cao & Su, 2007; Seo et al., 2009) documenting that higher use of Internet is associated with increased risk of having interpersonal or psychosocial problems such as injured after drinking, trouble with the police, family problems, regretted having sex with someone, loss of friends and have gained weight. Several studies have reported significant correlations between PIU and hostility and aggressive behavior (Ko, Yen, Chen, Yeh, & Yen, 2009; Xiuqin et al., 2010). For adolescents with interpersonal conflict or rejection, the Internet could provide a more accessible world, free and virtual interpersonal difficulties escape from real life. Also, many Internet activities, especially in online games offer a world in which they learn to express hostility and violence perpetrated without restriction (Ko et al., 2008). Spending much time on the Internet can lead to social isolation, self-neglect, poor nutrition, and family problems. A sedentary lifestyle can increase risk of obesity and its associated complications.

Previous studies identified association between PIU and gambling and our results are in agreement with them. The availability of the Internet as a medium for gambling practices among adolescents may contribute to increase and generalize the overall gambling behaviors (Tsitsika, Critselis, Janikian, Kormas, & Kafetzis, 2011). It is also plausible that some pre-existing problem gamblers may more readily adopt this accessible medium for the purposes of gambling. However, it is also upheld that internet gambling may potentially confound the development of problematic Internet use. Additional longitudinal studies are necessary in order to elucidate the etiological association between gambling, internet gambling practices and the development of PIU among adolescents (Tsitsika et al., 2011).

Our study has the limitations common to most large-scale surveys. First, the cross-sectional design prevents any attribution of causality between Internet using time and psychosocial problems. Second, measures of Internet time use and the other study variable were based on self-reports, rather than on direct observation of the respondents' behavior or confirmation by third parties. However, it would be difficult to obtain such information in sample as large as the one that comprises the present study. Third, the results of this study were based on schools and their students, so adolescents who do not go to school are excluded from the list of subjects for investigation. There is a possibility that adolescents who do not go to school might have different Internet use

and this fact needs to be considered in interpretation of the results of this study. Fourth, this study focused on time spent on the Internet per week. However, previous studies showed that the frequency spent using the Internet per week is highly associated with PIU (Carli et al., 2011; Durkee et al., 2012), suggesting a high degree of overlap between these two categories. However, from what has been said above, it should be concluded that in the future, for public health studies and policies concerning adolescent Internet problems, both Internet addiction and Internet using time need to be considered (Kim, 2012).

Despite these limitations, our study indicates that excessive time spent on the Internet (and probably the risk of PIU) is common among European adolescents, and that duration of Internet use was significantly associated with drug use, school problems, gambling and a variety of psychosocial problems. These findings highlight the need to strengthen preventive efforts for reducing PIU and related consequences among adolescents. Particularly, Internet-specific parenting practices (van den Eijnden et al., 2010) may help prevent internet-related problems among this population.

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Conflict of interest

Authors declare no interest conflict.

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Patología dual en trastornos de ansiedad: recomendaciones en el tratamiento farmacológico

Dual diagnosis in anxiety disorders: pharmacologic treatment recommendations

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Resumen

Los trastornos por uso de sustancias y los trastornos de ansiedad presentan una gran comorbilidad (entre el 18% y 37%), lo cual complica el tratamiento y empeora el pronóstico de los pacientes (incluido mayor riesgo de suicidio). Son pocos los trabajos de investigación terapéutica que hayan abordado de forma específica el tratamiento farmacológico de los trastornos de ansiedad en caso de patología dual. La mayor parte de los autores apuestan por el abordaje de ambos trastornos de forma integral y simultánea. Los datos procedentes de la revisión de la literatura indican que los fármacos recomendados habitualmente en el tratamiento para los trastornos de ansiedad también son eficaces en el tratamiento de la ansiedad dual. Los antidepresivos ISRS constituyen el tratamiento de primera línea en los trastornos de ansiedad duales, mientras que las benzodiacepinas son fármacos a evitar. En los últimos años se observa una gran tendencia a utilizar fármacos antiepilépticos de última generación, los cuales muestran resultados prometedores en estudios abiertos y series de casos, en especial la pregabalina en el trastorno de ansiedad generalizada.

Palabras Clave: trastornos de ansiedad, patología dual, comorbilidad, tratamiento, recomendaciones.

Abstract

Anxiety disorders and substance use disorders are highly comorbid (between 18% and 37%), and such comorbidity complicates treatment and worsens prognosis (including higher suicide risk). There are not many research works on the specific pharmacologic treatment of dual comorbid anxiety disorders. Most authors recommend a simultaneous approach of both, anxiety and substance use, disorders. Research data on pharmacotherapy suggest that psychotropics used in the treatment of anxiety disorders are also effective in dual diagnosis. SSRIs are considered first-line therapy in the treatment of dual anxiety while benzodiacepines should be avoided. New generation antiepileptic have shown efficacy in case series and open label studies in the latest years, thus being a promising treatment option for dual comorbid anxiety disorders, specially pregabalin in generalized anxiety disorder.

Key Words: anxiety disorders, dual diagnosis, comorbidity, therapeutics, recommendations.

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Los pacientes con trastornos de ansiedad (TA) son muy vulnerables a desarrollar otras patologías comórbidas. Tanto los grandes estudios epidemiológicos como estudios clínicos muestran una elevada asociación entre los distintos trastornos de ansiedad (TA) y los trastornos por uso de sustancias (TUS), que oscila entre el 18% y el 37% (Buckley y Brown, 2006; Fatseas, Denis, Lavie y Auriacombe, 2010; Grant et al., 2004; Kessler et al., 2006; Marmorstein, 2012; Merikangas et al., 1996; Regier et al., 1990). Esta asociación es especialmente llamativa cuando se consideran los trastornos relacionados con el uso de alcohol (Arias et al., 2013a) y trastornos de ansiedad específicos como la agorafobia o el trastorno de pánico (ver Tabla 1 donde se resumen los datos epidemiológicos de la asociación entre TA y TUS en diversos estudios realizados en población general). De igual modo ocurre con el cannabis y los trastornos de ansiedad generalizada o de pánico (Arias et al., 2013b). Cabe reseñar que las prevalencias de TA asociado a TUS, varían en función del ámbito de realización del estudio y de las sustancias incluidas en el mismo. En general, la asociación es menor en población general que en población clínica, ya que la presencia de un trastorno mental facilita una mayor oportunidad de diagnóstico y tratamiento de la patología dual. No obstante, existen estudios que ponen de manifiesto que en muchas ocasiones existe infratratamiento de la patología comórbida (Terra et al., 2006).

La presencia de comorbilidad entre TA y TUS complica el tratamiento y empeora el pronóstico de ambos tipos de trastorno (Madoz, García, Luque, y Ochoa, 2013). Por ejemplo, se ha demostrado cómo la comorbilidad entre el uso de alcohol y el trastorno obsesivo compulsivo aumenta el riesgo de suicidio, o cómo los pacientes dependientes con trastornos de ansiedad no tratados tienen más posibilidad de recaídas (Ochoa, Salvador, Vicente, y Madoz, 2010; Pasche, 2012).

Hipótesis explicativas de la relación entre TUS y TA

De forma general, se consideran cuatro modos de asociación entre TUS y TA(Pasche, 2012):

1. el TA es primario y las sustancias se utilizan a modo de "automedicación" para paliar los síntomas de ansiedad: para poder confirmar la hipótesis de la automedicación, en primer lugar hay que establecer la secuencia temporal de la comorbilidad, de manera que

Tabla 1
Riesgo de patología dual (TUS y TA) en población general

Trastorno primario	ECA (Regier et al., 1990)		NESARC (Conway et al., 2006; Hasin et al., 2007)		NCS-R (Marmorstein, 2012)		ESEMeD (Alonso et al., 2004)	
	Prevalvida	OR* (IC 95%)	Prevalvida	OR* (IC 95%)	OR* (IC 95%)		OR* (IC 95%)	
					Abuso	Dependencia	Abuso	Dependencia
TA y desarrollo de algún TUS	23.7%	1.7						
Fobias	22.9%	1.6						
TP	35.8%	2.9						
TOC	32.8%	2.5						
TUS (alcohol) y desarrollo de TA	19.4%	1.5		2.3				
Fobia		1.4						
-Fobia social				2.3	3.03	4.01	2.7 (1.5-4.7)	2.7 (0.6-12.3)
-Fobia específica				2.2			2.0 (1.3-3.2)	3.3 (1.3-8.4)
TP		2.6		2.4	3.71	4.93	3.3 (1.8-5.8)	6.8 (2.2-21.1)
-Con agorafobia				2.5				
-Sin agorafobia				2.3				
Agorafobia					3.50	4.29	2.9 (1.2-6.6)	10.7 (3.0-38.5)
TAG				2.2	2.67	3.39	2.5 (1.3-5.1)	11.2 (3.8-32.9)
TOC		2.1						
TEPT							1.9 (1.0-3.6)	3.1 (1.0-9.5)
TUS (otras sustancias) y desarrollo de TA	28.3%	2.5 2.2	29.9%	2.5				
Fobia			10.7%	2.7	3.54	5.54		
-Fobia social			17.1%	2.2				
-Fobia específica		3.2			3.39	4.07		
TP			3.6%	4.6				
-Con agorafobia			9.0%	2.8				
-Sin agorafobia			9.2%	3.3	2.84	3.11		
TAG		3.7						
TOC								

*Riesgo de padecer trastorno comórbido del grupo expuesto frente al no expuesto
Nota. IC = Intervalo de confianza; OR = Odds ratio; TA = Trastorno de ansiedad; TAG = Trastorno de ansiedad generalizada; TEPT = Trastorno por estrés postraumático; TOC = Trastorno obsesivo-compulsivo; TP = Trastorno de pánico; TUS = Trastorno por uso de sustancias

el TUS debería ser posterior al TA. Existen estudios a gran escala que han tratado de dilucidar la naturaleza de los patrones de comorbilidad entre los TA y los TUS. En concreto, el International Consortium in Psychiatric Epidemiology ha presentado datos en los que el inicio de los TA suele preceder al TUS (Marquenie et al., 2007; Merikangas et al., 1998).

2. el TUS es primario y los síntomas de ansiedad son consecuencia del uso o de la abstinencia de la sustancia: TAs como el trastorno de ansiedad generalizada o el trastorno por estrés postraumático, frecuentemente son secundarios al consumo de alcohol u otras sustancias. En estos casos, la pérdida de control sobre los consumos y/o la alteración de determinados sistemas de neurotransmisión facilitarían la aparición de determinados trastornos de ansiedad. En cambio, la agorafobia o el trastorno de pánico pueden aparecer de forma primaria o secundaria al TUS (Marmorstein, 2012; Sareen, Chartier, Paulus, y Stein, 2006). En este sentido, existen datos recientes que ponen de manifiesto que la dependencia de cannabis (Zvolensky et al., 2006), el consumo de más de un paquete diario de tabaco (Johnson et al., 2000), o el uso de alucinógenos (Bonn-Miller, Bernstein, Sachs-Ericsson, Schmidt y Zvolensky, 2007) se asocia con un riesgo incrementado de padecer, posteriormente, ataques de pánico.
3. el TA y el TUS no están relacionados pero interfieren entre sí, alterando la presentación y pronóstico mutuamente: en líneas generales, suele aceptarse que los trastornos fóbicos (sobre todo la fobia social) preceden al uso patológico de alcohol (Brady et al., 2005; Buckner et al., 2008; Marmorstein, 2012; Schneier et al., 2010; Terra et al., 2006) u otras sustancias (Buckner et al., 2008; Buckner y Schmidt, 2009; Marmorstein, 2012) por sus posibles efectos ansiolíticos, estando dicha comorbilidad asociada con una mayor gravedad del abuso o dependencia de la sustancia y con una menor tasa de búsqueda activa de tratamiento, más fracasos terapéuticos, mayores costes sanitarios por ingresos, consultas, y tiempo de tratamiento (Arias Horcajada, 2009; Scheneier et al., 2010).
4. el TA y el TUS son consecuencia de una base biológica o psicosocial común: los hallazgos actuales, en ocasiones contradictorios (Van Laar, van Dorsselaer, Monshouwer y de Graaf, 2007), sugieren que tanto el TUS como los TA pueden inducir el otro trastorno (Cosci, Schruers, Abrams y Griez, 2007). Así, por ejemplo, en el caso del alcohol se ha propuesto la existencia de un círculo vicioso en el que, a corto plazo, existe una disminución de la ansiedad inducida por el alcohol)que favorece su consumo, mientras que el consumo crónico y la abstinencia del mismo inducen síntomas de ansiedad, lo cual también refuerza los consumos (Kushner, Abrams y Borchardt, 2000), posiblemente en relación con mecanismos de hipersensibilidad al CO_2 (Cosci et al., 2007). De igual modo, para complicar más aún el tema, hay que señalar la existencia de estudios que ponen de manifiesto la existencia de una agregación y transmisión familiar entre el trastorno por uso de alcohol y el trastorno de pánico (Goodwin et al., 2006; Cosci et al., 2007), lo cual indicaría que ambos trastornos comparten una causa común.

Etiopatogenia de la ansiedad dual

Estudios recientes ponen de manifiesto que el estrés podría ser un factor clave en la etiopatogenia del consumo de sustancias, así como de las recaídas, habiéndose demostrado cómo la exposición a situaciones estresantes en la infancia, o la presencia de estrés sostenido a lo largo de la vida, genera un mayor riesgo de comportamientos adictivos o aumenta la recompensa por consumo de ciertas sustancias (Cleck y Blendy, 2008).

Una de las hipótesis que explicaría esta relación desde un punto de vista neurobiológico la encontramos en el eje hipotálamo-hipófiso-adrenal (HPA). Durante los últimos años, diversos estudios han demostrado que la funcionalidad de este eje es modulada por el consumo de sustancias. El eje HPA se activa en roedores y primates tras la administración de la mayoría de sustancias de abuso produciendo un incremento de los niveles de ACTH y corticosterona plasmáticos (Kreek y Koob, 1998), que a su vez se correlacionan de modo positivo con conductas de autoadministración (Piazza et al., 1991). Por otra parte, la administración crónica de sustancias de abuso en animales da lugar a un incremento sostenido de la funcionalidad HPA, en el caso de los psicoestimulantes, o un descenso respecto a los efectos activadores iniciales de la droga, en el caso de morfina, nicotina o alcohol (Cleck y Blendy, 2008). De modo similar, los estudios realizados en humanos encuentran que la administración aguda de alcohol, cocaína, y nicotina se acompaña de un incremento de niveles de cortisol, mientras que la exposición aguda a opiáceos se acompaña de un descenso de los mismos. Por otra parte, la activación HPA persiste tras la adicción a cocaína, mientras que en el caso de adicción a opiáceos la respuesta HPA se va reduciendo a lo largo del tiempo (Cleck y Blendy, 2008).

Los datos obtenidos de estudios genéticos también apoyan esta relación, tras descubrirse cómo determinados polimorfismos implicados en la regulación del Eje HPA (Chong et al., 2006; Uhart, McCaul, Oswald, Choi y Wand, 2004; Wust et al., 2004) se asocian con la aparición de dependencia de alcohol (Oslin et al., 2003; Radel et al., 2005).

La influencia del eje HPA en las adicciones se ha explicado por la relación que existe entre la funcionalidad del eje HPA y el sistema dopaminérgico mesolímbico que, a su vez, podría contribuir a explicar la existencia de diferencias individuales en relación a la vulnerabilidad a la adicción (Uhart y Wand, 2009). El incremento de niveles séricos de

glucocorticoides inducido por situaciones de estrés produce un incremento de la DA mesolímbica y a su vez facilita el consumo de psicoestimulantes y opiáceos en ratas (Piazza et al., 1990). Además, los niveles de cortisol tras la exposición a un estresor se correlacionan con los efectos subjetivos de las anfetaminas (Wand et al., 2007).

En resumen, un aumento de secreción de glucocorticoides o una mayor sensibilidad a los mismos, como sucedería en los pacientes con ansiedad, determinaría una mayor vulnerabilidad de la persona a desarrollar una dependencia a través de una potenciación de la actividad del sistema dopaminérgico mesolímbico (Manzanares et al., 2010) en los estadíos tempranos del consumo, mientras que el estrés crónico (que se acompaña de una situación de hipercortisolismo) se asocia a una disminución de la respuesta dopaminérgica mesolímbica, y crearía un estado de afecto negativo que facilitaría la continuidad de los consumos (Uhart y Wand, 2009).

Otro sistema de neurotransmisión que se ha relacionado con los trastornos de ansiedad es el endocannabinoide. La elevada prevalencia de TA entre consumidores habituales de cannabis ha dado lugar a diversas hipótesis que tratan de explicar dicha relación (ver Crippa et al., 2009). El uso de cannabis puede precipitar de modo agudo la ansiedad tanto por la acción directa de su principal principio psicoactivo, el delta-9-tetrahidrocannabinol, así como por la afectación cognitiva secundaria a la intoxicación aguda por cannabis.

Protocolo de intervención

Evaluación diagnóstica

Dada la frecuente asociación entre TA y TUS y que el diagnóstico y tratamiento precoz de dichas patologías mejora el pronóstico de ambas, es prioritario realizar un diagnóstico correcto e investigar la posibilidad de comorbilidad en pacientes que demandan tratamiento por problemas de ansiedad o TUS.

Una vez establecido el diagnóstico de comorbilidad sería necesario situar el diagnóstico de TA en una categoría específica (primario, efectos esperados o inducidos por sustancias). Para ello se recomienda tener presente las pautas de ayuda para el diagnóstico diferencial entre trastorno primario e inducido especificadas en la Tabla 9.

Uno de los métodos más reconocido para poder hacer esta distinción consiste en la observación del paciente durante un periodo de abstinencia, si bien no existe unanimidad en cuanto a la duración más apropiada del mismo. Se entiende que ante el consumo de sustancias de vida media larga como la metadona o ciertas BZD se requerirían tiempos de observación más prolongados que cuando se usan sustancias de vida media más corta como la cocaína. En general se recomienda 2-4 semanas de abstinencia con controles analíticos que aseguren que no hay consumo de sustancias. La persistencia de los síntomas de ansiedad después de este periodo, así como una historia familiar y/o personal de este tipo de trastornos y la constatación del inicio de la sintomatología ansiosa con antelación al uso de sustancias, serían datos a favor de un trastorno de ansiedad primario. Para una adecuada constatación de todo ello una evaluación clínica comprehensiva y que incluya una historia toxicológica exhaustiva es fundamental.

Por otra parte, hay que tener presente que para establecer un adecuado diagnóstico los instrumentos de evaluación psicométrica constituyen un elemento fundamental de ayuda (García-Portilla et al., 2011). Por ese motivo, en la Tabla 10 se resumen de modo simplificado una serie de instrumentos útiles tanto desde el punto de vista diagnóstico como para determinar la gravedad de las patologías existentes. Cabe reseñar que, la Asociación Americana de Psiquiatría, en la nueva versión de su Manual Diagnóstico y Estadístico de los Trastornos Mentales (DSM-5), recomienda diferentes instrumentos psicométricos para la facilitación de la evaluación diagnóstica y de la gravedad subyacente a los distintos trastornos. No obstante, dado que, en los trastornos que nos atañen, la mayoría de dichos instrumentos propuestos aún no han sido adaptados y validados al español, simplemente remitimos al lector interesado a la página web donde puede localizarlos (http://www.psychiatry.org/practice/dsm/dsm5/ online-assessment-measures#Disorder).

Intervención terapéutica

Uno de los aspectos claves del tratamiento de la ansiedad dual es el tratamiento específico del TUS. Por dicho motivo deben iniciarse las intervenciones farmacológicas y psicosociales necesarias para conseguir la abstinencia y el posterior mantenimiento de la misma.

No obstante, hay que tener presente que el tratamiento del TA es otro aspecto fundamental para mejorar el pronóstico de los pacientes y evitar el riesgo de recaídas en los consumos. En la Figura 1 se muestran, de modo resumido, los posibles pasos a seguir en el abordaje terapéutico de la ansiedad dual.

En caso de un TA inducido la propia abstinencia de las sustancias consumidas junto con el apoyo psicológico (y/o far-

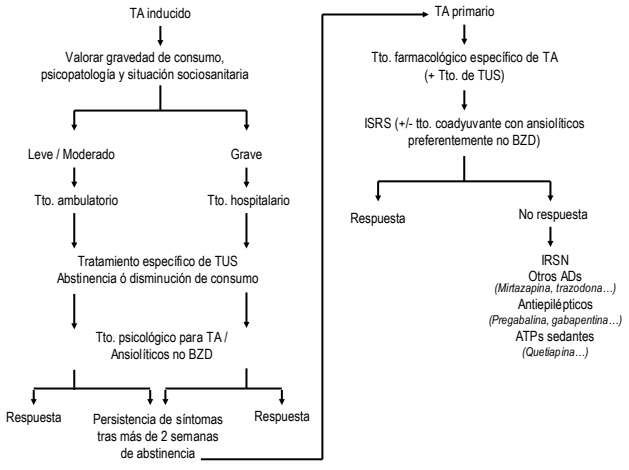

Figura 1. Algoritmo terapéutico de la ansiedad dual

macológico) puede ser suficiente. En general, como ya se ha comentado con anterioridad, se recomienda el uso de ansiolíticos no BZD, siendo opciones adecuadas los antidepresivos de perfil sedativo (por ej., mirtazapina o trazodona), algunos antiepilépticos (pregabalina o gabapentina) o antipsicóticos atípicos de perfil sedativo a dosis bajas (por ej., la quetiapina).

En el caso de los TA primarios es necesario su abordaje terapéutico teniendo en cuenta las recomendaciones específicas realizadas para cada TA. No obstante, en líneas generales, cabe señalar que los ISRS a las dosis adecuadas para cada trastorno podrían ser una buena opción de inicio terapéutico, teniendo presente que en ocasiones puede ser necesario el tratamiento coadyuvante con otros fármacos ansiolíticos. En dicho caso la opción más segura sería la adición de fármacos no BZD. En el caso de falta de respuesta al ISRS (una vez que éste ha sido usado en dosis y tiempo adecuado), podría procederse al cambio por un IRSN (venlafaxina o duloxetina), otros antidepresivos de perfil sedativo (preferentemente mirtazapina o trazodona) o a la adición de otros fármacos de perfil ansiolítico como pregabalina o gabapentina o antipsicóticos de perfil sedativo. No obstante, hay que tener presente cual es el TA primario para, en función de el mismo, elegir las opciones terapéuticas más adecuadas.

Abordaje terapéutico

El abordaje terapéutico de los trastornos duales presenta importantes dificultades derivadas de las particulares características de estos trastornos, con tendencia a la recidiva y cronicidad, y de los patrones de conducta y relación interpersonal propios de los pacientes drogodependientes (Arias et al., 2013c).

Por lo tanto, el tratamiento ideal debería llevarse a cabo en un sistema asistencial integrado en el que se incluyan equipos multidisciplinares capaces de atender todas las necesidades terapéuticas del paciente a nivel psicopatológico, físico y social. Sin embargo, en la mayoría de los casos, la existencia de redes asistenciales diferentes y paralelas genera una gran dificultad para la atención de los pacientes con patología dual (Rubio, López-Muñoz y Álamo, 2002).

Los tratamientos utilizados en los pacientes duales suelen ser semejantes a los que utilizan cuando se presenta una sola patología y, en general, se considera que los tratamientos eficaces para tratar un determinado trastorno mental (distinto del TUS) también tienden a ser eficaces en los pacientes duales y viceversa (Ochoa et al., 2010).

Recomendaciones farmacológicas generales para el manejo de la ansiedad dual

En el momento actual carecemos de suficientes pruebas científicas de tipo I (ensayos clínicos controlados, metaanálisis o revisiones sistemáticas) o II (estudios controlados no aleatorizados bien diseñados) procedentes de estudios que hayan abordado de forma conjunta el tratamiento de los TA y TUS, de modo que la mayoría de aportaciones proceden de las recomendaciones de expertos (Watkins, Hunter, Burnam, Pincus y Nicholson, 2005).

Los fármacos antidepresivos constituyen el tratamiento de primera línea en los TA (Ministerio de Sanidad y Consumo, 2008) y existen datos que ponen de manifiesto que el uso de determinados ISRS, como la paroxetina y la sertralina son eficaces en la reducción de la ansiedad en pacientes con dependencia de alcohol y TA comórbido, si bien los resultados sobre la dependencia de alcohol son dispares (Brady et al., 2005; Schadé et al., 2005).

Por otra parte, los antiepilépticos de nueva generación han demostrado eficacia tanto en el tratamiento de los diferentes TA como en el TUS. En las Tablas 2 a 7 se resumen los hallazgos en este sentido, y se puede apreciar cómo el TAG es el trastorno en el que se dispone de mejor nivel de pruebas científicas sobre la eficacia de los antiepilépticos, siendo la pregabalina el fármaco con más aval científico. En el caso de los TUS, las evidencias más notables se obtendrían, con la gabapentina, la pregabalina y el topiramato en la dependencia de alcohol, y con el topiramato en la dependencia a cocaína.

Las benzodiacepinas deben evitarse en este tipo de pacientes por el potencial desarrollo de tolerancia y dependencia al fármaco, como se ha destacado en diferentes estudios realizados en nuestro país (Secades et al., 2003; OECD, 2012), de manera que las guías clínicas desaconsejan su uso y, en caso de ser necesario, realizarlo sólo en tratamientos a corto plazo (Giner, 2005; NICE, 2011; San Molina, 2004).

En base a los datos existentes en la actualidad sobre el tratamiento de los TA con patología dual, se puede establecer una serie de recomendaciones terapéuticas generales que se recogen en forma de decálogo en la Tabla 8.

Tratamiento farmacológico de los trastornos de ansiedad específicos

Trastorno de pánico. Existe cierta controversia acerca de si es necesario un tratamiento ansiolítico específico para los pacientes con abuso de sustancias primario, especialmente si se presentan crisis de angustia durante las primeras semanas de abstinencia. Sin embargo, si las crisis de angustia continúan en intensidad y frecuencia, estaría justificado un diagnóstico de trastorno de pánico (Gorman et al., 2006).

Muchos tipos de medicamentos han demostrado eficacia para el tratamiento del trastorno de pánico, como los ISRS, los ATC, IMAO y BZD. Sin embargo, no se dispone de estudios sistemáticos que evalúen la eficacia de estos tratamientos cuando el trastorno de pánico va asociado al abuso de sustancias. No obstante, los ISRS han mostrado un modesto efecto en la reducción del consumo de alcohol en algunos subgrupos de pacientes (Pettinati et al., 2000), no tienen potencial de abuso, son bien tolerados y relativamente seguros, por lo que son la elección más lógica en pacientes con este tipo de patología dual a las dosis habitualmente indicadas.

Tabla 2
Antiepilépticos y trastorno de pánico (TP)

Fármaco / estudio	Tipo de estudio (Nivel de evidencia)	Dosis utilizada	Eficacia	Comentarios
Gabapentina				
Himmerich et al. (2007)	1 caso clínico (III)	300mg/día	Eficaz y bien tolerado	Dependencia a alprazolam e intolerancia a carbamacepina
Spila y Szumillo (2006)	6 casos clínicos (III)	300mg/día	Eficaz y bien tolerado	Tto coadyuvante en TP
Pande et al. (2000)	ECACP (I)	600-3600mg/día	Eficaz y bien tolerado	Monoterapia en TP
Tiagabina				
Zwanzger et al. (2009)	Control placebo (II)	----------	No diferencia entre grupos	Monoterapia en TP
Sheehan et al. (2007)	Abierto (III)	2-20mg/día	Eficacia escasa y bien tolerado, en general	Monoterapia en TP ± agorafobia

Nota. ECACP = Ensayo clínico aleatorizado con placebo; TBP = Trastorno bipolar

Ahora bien, cuando se utilizan en este tipo de pacientes conviene acentuar las precauciones que se toman al principio del tratamiento para evitar el agravamiento de los síntomas de pánico debido al efecto activador de los ISRS, ya que en pacientes duales un empeoramiento de los síntomas de ansiedad podría incrementar el riesgo de recaídas en los consumo. La regla general de proceder a instaurar el tratamiento de modo progresivo, con un incremento paulatino desde dosis bajas, está especialmente indicado en estos pacientes ya que parecen presentar una sensibilidad mayor a este efecto y con ello un mayor riesgo de recaída.

Se debe prestar atención al periodo de latencia de inicio del efecto terapéutico de estos fármacos (2 a 6 semanas hasta alcanzar el efecto máximo) por el riesgo de recaídas en esta etapa (Brady y Verduin, 2005). En este tiempo se podría asociar una BZD, preferentemente de vida media larga (Rubio et al, 2002). Por ejemplo, el clonazepam ha sido utilizado con éxito en el tratamiento de crisis de angustia en pacientes consumidores de cocaína.

Existe cierta experiencia acerca de la eficacia de los ATC para el tratamiento del trastorno de pánico en pacientes bebedores de alcohol (Kranzler, 1996; Nunes, McGrath y Quitkin, 1995), pero han sido desplazados por los ISRS por la menor frecuencia y gravedad de los efectos secundarios.

De los inhibidores de recaptación de serotonina y noradrenalina (IRSN), la venlafaxina de liberación prolongada ha demostrado su eficacia en el tratamiento del trastorno de pánico con dosis entre 75 y 225 mg/día (Bradwejn, Ahokas y Stein, 2005). Además, hay experiencia de su utilización en abusadores de alcohol con síntomas depresivos, observándose que es un fármaco bien tolerado, seguro, con escaso potencial de abuso e incluso con capacidad para mejorar los problemas relacionados con la dependencia del alcohol (García-Portilla et al., 2005).

A pesar de que las BZD han demostrado eficacia en el tratamiento del trastorno de pánico con o sin agorafobia, hay una tendencia a evitar su uso en pacientes con TUS y a usarlas con cautela en aquellos con antecedentes de este tipo de trastornos. No obstante, no existen datos publicados que avalen dicha práctica y se recomienda que la decisión de prescribir BZD en estos pacientes se tome en base a una valoración cuidadosa de las ventajas e inconvenientes de cada caso particular (Posternak y Mueller, 2001).

Aunque se ha sugerido la utilidad potencial de diversos fármacos antiepilépticos (carbamacepina, valproato, lamotrigina, gabapentina, pregabalina, tiagabina, topiramato) en el tratamiento del trastorno de pánico, sólo existen pruebas de nivel I en el caso de la gabapentina (ver Tabla 2). La principal ventaja de este tipo de fármacos, en especial los de más reciente introducción, radica en su buen perfil de seguridad, tolerabilidad y escaso potencial de abuso.

Trastorno de ansiedad generalizada (TAG). Los síntomas característicos del trastorno de ansiedad generalizada están presentes tanto en la intoxicación como en el síndrome de abstinencia de distintas sustancias (Chambless, Cherney y Caputo, 1987), lo cual complica de forma significativa el diagnóstico de TAG (Brady y Verduin, 2005), de manera que no debe realizarse hasta la completa remisión de la intoxicación y/o abstinencia (Back y Brady, 2008). En el caso de sustancias de vida media corta como la cocaína, el diagnóstico de TAG se puede hacer tras una semana de abstinencia, mientras que sustancias de vida media larga como la metadona o algunas benzodiacepinas requieren una demora de 4 a 8 semanas de abstinencia para poder realizar el diagnóstico de TAG (McKeehan y Martin, 2002).

En cuanto al tratamiento, numerosos fármacos han demostrado eficacia en el tratamiento del TAG, como los ISRS, IRSN, ATC, BZD, buspirona (retirada del mercado español) o antiepilépticos. Sin embargo, se recomienda evitar las BZD en el TAG en pacientes duales y, si se utilizan, debería de hacerse con mucha cautela respetando las indicaciones de la circular de 2000 de la Agencia Española del Medicamento, evitando superar las 8-12 semanas de tratamiento (Giner, 2005; San Molina, 2004).

Tabla 3
Antiepilépticos y trastorno de ansiedad generalizada (TAG)

Fármaco / estudio	Tipo de estudio (Nivel de evidencia)	Dosis utilizada	Eficacia	Comentarios
Pregabalina				
Lydiard et al. (2010)	ECACP (I)	150-600mg/día	Eficaz en ansiedad (dosis ↗ 300mg/día) y bien tolerado	Monoterapia en TAG. Incluye 6 ECACP previos
Montgomery et al. (2009)	ECACP (I)	150-600mg/día	Eficaz en insomnio y ansiedad (dosis ↗ 300mg/día)	Monoterapia en TAG. Incluye 6 ECACP previos
Stein et al. (2009)	ECACP (I)	150-600mg/día	Eficaz en síntomas GI y ansiedad (dosis ↗ 300mg/día	Monoterapia en TAG. Incluye 6 ECACP previos
Stein et al. (2008)	ECACP (I)	150-600mg/día	Eficaz en síntomas depresivos asociados a TAG (300-450mg/día)	Monoterapia en TAG. Incluye 6 ECACP previos
Feltner et al. (2008)	ECACP (I)	450mg/día	Eficaz en prevención de recaídas	Monoterapia en TAG
Tiagabina				
Pollack et al. (2008)	ECACP (I)	4-16mg/día	No eficaz	Monoterapia TAG. Incluye 3 ECACP previos

Nota. ECACP = Ensayo clínico aleatorizado con placebo

Los ISRS y los IRSN son los fármacos más utilizados por la eficacia y seguridad en el TAG comórbido con TUS, si bien la trazodona también se ha utilizado con buenos resultados. Entre los nuevos antiepilépticos, la pregabalina (300-600 mg/día), es el único fármaco que acumula pruebas científicas de nivel I (ver Tabla 3). Su seguridad, tolerabilidad, escasas interacciones y bajo potencial de abuso, contribuyen a que este fármaco tenga las mejores perspectivas para el tratamiento del TAG en pacientes con TUS.

De igual modo, aunque con un nivel de evidencia más limitado, los antipsicóticos de segunda generación con perfil sedativo (quetiapina, olanzapina y risperidona), a dosis bajas, podrían constituir otra alternativa para el tratamiento sintomático de la ansiedad (Gao, Sheehan y Calabresse, 2009; Sattar, Schultz, Arndt, Soundy y Petty, 2007).

Trastorno por estrés postraumático (TEPT). El TEPT es uno de los trastornos de ansiedad más frecuentes en sujetos con TUS (Donovan et al., 2001). La presencia de TEPT incrementa entre dos y cuatro veces la posibilidad de abusar de sustancias (Back y Brady, 2008) del mismo modo que los consumidores de sustancias tienen un riesgo

Tabla 4
Antiepilépticos y trastorno por estrés postraumático (TEPT)

Fármaco / estudio	Tipo de estudio (Nivel de evidencia)	Dosis utilizada	Eficacia	Comentarios
Valproato				
Hamner et a.l (2009)	ECACP (I)	----------	No eficaz	Monoterapia en TEPT crónico
Davis et al (2008)	ECACP (I)	Media = 2309mg/día	No eficaz	Monoterapia en TEPT crónico
Gabapentina				
Stein et al (2007)	ECACP (I)	----------	No eficaz en prevención	Prevención de TEPT
Oxcarbazepina				
Malek-Ahmadi y Hanretta (2004)	1 Caso clínico (III)	1500mg/día	Eficaz en síntomas TEPT	TBP comórbido con TEPT
Pregabalina				
Pae et al (2009)	Abierto (III)	Dosis flexible	Eficaz y bien tolerado	Coadyuvante de ADT en TEPT
Tiagabina				
Davidson et al (2007)	ECACP (I)	4-16mg/día	No eficaz, bien tolerado	Monoterapia en TEPT
Topiramato				
Alderman et al (2009)	Abierto (III)	50-200mg/día	Mejoría sintomática. ↓ nº pacientes con consumo excesivo de alcohol	Tto coadyuvante en TEPT
Lindley et al (2007)	ECACP (I)	Dosis flexible	No eficaz, bien tolerado	Tto coadyuvante en TEPT
Tucker et al (2007)	ECACP (I)	400mg/día	↓ algunos síntomas	Monoterapia en TEPT

Nota. ADT = Antidepresivos; ECACP = Ensayo clínico aleatorizado con placebo; TBP = Trastorno bipolar

más elevado de TEPT, con prevalencias hasta del 50% en algunos estudios (North et al., 2002).

Además, la coexistencia de ambos trastornos dificulta notablemente el diagnóstico. Las manifestaciones clínicas del TEPT se pueden modificar por la intoxicación o la abstinencia de las distintas sustancias. Los pensamientos intrusivos pueden aumentar por la acción de sustancias estimulantes, alcohol, cannabis, y con la abstinencia de sedantes o estimulantes. El estado de alerta y activación se pueden reforzar con estimulantes o cannabis, o en los estados de abstinencia de éstas y también de alcohol, opiáceos o BZD. En general, la acción de sustancias estimulantes agrava los síntomas, mientras que las de acción depresora los alivian (Brady et al., 2005; Schäfer y Najavits 2007).

Los fármacos más utilizados en el tratamiento del TEPT por su eficacia, seguridad y tolerabilidad son los ISRS. Asimismo, se han obtenido buenos resultados con mirtazapina, trazodona, venlafaxina y bupropion, pero sin pruebas concluyentes de eficacia. También se ha observado cierta mejoría en los síntomas del TEPT con diversos antiepilépticos (ver Tabla 4), así como con antipsicóticos atípicos como la olanzapina, quetiapina y risperidona, especialmente útiles en casos graves con síntomas psicóticos (Ursano et al., 2006).

En los pocos estudios realizados para determinar los tratamientos más eficaces en pacientes con TEPT y TUS, los ISRS vuelven a ser los fármacos de elección por eficacia y escaso potencial de abuso (San Molina et al., 2005). Un estudio doble ciego con sertralina (150 mg/día) en pacientes con TEPT y alcoholismo puso de manifiesto la capacidad del fármaco para aliviar los síntomas del TEPT y para reducir el consumo de alcohol comparado con placebo (Brady et al., 2005). La venlafaxina podría utilizarse cuando predominan síntomas de ansiedad, y la mirtazapina o trazodona, dotados de un buen perfil sedativo, para el manejo del insomnio. En casos resistentes se han utilizado eutimizantes como valproato, así como los antipsicóticos atípicos con perfil ansiolítico. No se recomiendan las BZD en pacientes con este trastorno dual (San Molina, 2004).

Existen estudios que han evaluado el efecto del tratamiento de sustitución con metadona en adictos a opiáceos con TEPT, y el del disulfiram y naltrexona en alcohólicos con dicho trastorno, apreciando que tales tratamientos eran eficaces para disminuir el uso de las sustancias problema pero sin efecto claro sobre los síntomas del TEPT (Schäfer y Najavits, 2007).

Fobia social (trastorno de ansiedad social) (TAS).

Las personas con TAS tienen unas altas tasas de comorbilidad con otros trastornos psiquiátricos, en especial con TUS (Brady et al., 2005). La elevada asociación entre TAS y consumo de alcohol (entre 2 y 3 veces mayor que la población general) puede explicarse con la hipótesis de la automedicación (Back y Brady, 2008). Según esta hipótesis el alcohol se utilizaría para disminuir la ansiedad en las interacciones sociales. En la mayoría de los casos el TAS es previo a los problemas por el uso de alcohol (Terra et al., 2006).

El diagnóstico precoz del TAS en usuarios de sustancias es de gran importancia porque el trastorno puede impedir una adecuada adherencia al tratamiento, especialmente a las actividades psicoterapéuticas. En estos casos no es necesario un largo periodo de observación en abstinencia pues el miedo a las interacciones sociales no es una característica específica de la intoxicación o del síndrome de abstinencia de sustancias, e incluso en los casos en los que aparece, como puede ocurrir en el contexto de consumo de cannabis o estimulantes, no cumple criterios de fobia social (Brady et al., 2005).

Al igual que en el resto de TA, apenas hay datos sobre la farmacoterapia del TAS cuando se asocia a uso de sustancias. No obstante, la paroxetina podría ser de utilidad en base a los resultados obtenidos en un estudio doble ciego aleatorizado y controlado con placebo, en pacientes con TAS y uso de alcohol, que puso de manifiesto una capacidad

Tabla 5
Antiepilépticos y fobia social

Fármaco / estudio	Tipo de estudio (Nivel de evidencia)	Dosis utilizada	Eficacia	Comentarios
Valproato Kinrys et al (2003)	Abierto (III)	500-2500mg/día	Eficaz	Monoterapia en fobia social
Gabapentina Pande et al (1999)	ECACP (I)	900-3600mg/día	Eficaz	Monoterapia en fobia social
Pregabalina Pande et al (2004)	ECACP (I)	150 / 600mg/día	Eficaz (600mg/día) y bien tolerado	Monoterapia en fobia social
Tiagabina Dunlop et al (2007)	Abierto (III)	4-16mg/día	Eficaz y bien tolerado	Monoterapia en fobia social
Topiramate Van Ameringen et al (2004)	Abierto (III)	400mg/día	Eficaz	Monoterapia en fobia social

Nota. ECACP = Ensayo clínico aleatorizado con placebo

mayor que placebo para mejorar la ansiedad social, pero no se apreciaron cambios en la cantidad y frecuencia del consumo de alcohol. Sí se observó que en los pacientes sin paroxetina el consumo de alcohol estaba ligado a la intensidad de la ansiedad, mientras que en los pacientes tratados con paroxetina no se observaba esta relación (Thomas, Randall, Book y Randall, 2008). Otras opciones terapéuticas serían el resto de ISRS o la venlafaxina. Las BZD deben usarse con cautela, si bien pueden asociarse a los ISRS durante el periodo de latencia de inicio del efecto terapéutico (Brady et al., 2005).

Los nuevos antiepilépticos, especialmente la gabapentina y la pregabalina, podrían ser una excelente alternativa al uso de BZD, sobre todo en el caso del TAS asociado con trastorno por uso de alcohol (ver Tablas 5 y 7). Se ha publicado algún caso de eficacia de gabapentina en la reducción del craving y de la intensidad de la adicción en TUS con TAS comórbido (Verduin, McKay y Brady, 2007). A pesar de la utilidad de los IMAO en el TAS no se recomiendan cuando hay uso de alcohol u otras sustancias de abuso por las dificultades de manejo. En este caso, los inhibidores reversibles de la monoaminooxidasa (RIMA) son una alternativa si fracasan los tratamientos de primera línea.

Trastorno obsesivo-compulsivo (TOC). Existen cuantiosos datos acerca de la frecuente comorbilidad del TOC con otros trastornos mentales, sin embargo los datos de prevalencia de TOC y TUS, en población general, son más limitados que en otras patologías duales (Brady y Verduin, 2005). No obstante, cuando se presenta no suele plantear problemas diagnósticos porque los síntomas de TOC no se solapan con los de intoxicación o abstinencia de sustancias. Por ello, no suele ser necesario un periodo de observación prolongado en ausencia de consumo de sustancias para establecer el diagnóstico.

En cuanto al tratamiento farmacológico, no hay ensayos clínicos sobre el uso de psicofármacos en esta patología dual. Como en todos los casos de comorbilidad con uso de sustancias, se recomienda usar fármacos con escaso potencial de abuso, evitando, si es posible, el empleo de BZD. Los ISRS son las fármacos de primera elección a las dosis recomendadas para el TOC (Tiet y Mausbach, 2007), recordando que la acción terapéutica suele iniciarse entre la 6ª y 8ª semanas, y la eficacia máxima no se alcanza hasta la 12ª semana. Si no hay respuesta se recomienda cambiar a otro ISRS; y en caso de que el cambio tampoco resulte efectivo, asociar o cambiar a clomipramina. En caso de asociar las dosis deben ser inferiores a las usadas en monoterapia. La clomipramina presenta mayor capacidad de disminuir el umbral convulsivo, así como de presentar interacciones con el alcohol, estimulantes y depresores del SNC (Brady y Verduin, 2005).

En casos resistentes podría ser de utilidad el tratamiento coadyuvante con fármacos antiepilépticos (ver Tabla 8) o con antipsicóticos atípicos de perfil más sedativo a dosis bajas. Estos fármacos podrían usarse en combinación con antidepresivos serotoninérgicos en pacientes en los que hayan fracasado otros tratamientos.

Tabla 6
Antiepilépticos y trastorno obsesivo compulsivo (TOC)

Fármaco / estudio	Tipo de estudio (Nivel de evidencia)	Dosis utilizada	Eficacia	Comentarios
Carbamacepina				
Aggarwal et al. (2009)	1 caso clínico (III)	1200mg/día	Mejoría + escitalopram (20mg/día)	TOC sin respuesta a ISRS
Da Rocha et al. (2009)	1 caso clínico (III)	1200mg/día	Eficaz + clobazam (20mg/día)	TOC 2º a epilepsia de lóbulo temporal
Lamotrigina				
Uzun (2010)	1 caso clínico (III)	150mg/día	Mejoría + clomipramina (225mg/día)	TOC resistente a clomipramina
Pregabalina				
Oulis et al. (2008a)	1 caso clínico (III)	450mg/día	Mejoría	TOC inducido por BZD
Oulis et al. (2008b)	1 caso clínico (III)	600mg/día	Mejoría + sertralina (400mg/día) + risperidona (2mg/día)	TOC resistente a setralina + risperidona
Tiogabina				
Oulis et al. (2009)	1 caso clínico (III)	15mg/día	Mejoría + flovoxamina (400mg/día) + risperidona (1mg/día)	TOC resistente a fluvoxamina + risperidona
Topiramate				
Berlin et al. (en prensa)	ECACP (I)	50-400mg/día	Mejoría de compulsiones	Tto coadyuvante en TOC resistente a ISRS
Hollander y Dell'Osso (2006)	1 caso clínico (III)	150mg/día	Mejoría + paroxetina (40mg/día)	TOC resistente a paroxetina
Van Ameringen et al. (2006)	Serie de casos (III)	Media = 253mg/día	Mejoría	Tto coadyuvante en TOC resistente a ISRS

Nota. ECACP = Ensayo clínico aleatorizado con placebo

Tabla 7
*Nuevos antiepilépticos y TUS**

Fármaco / estudio	Tipo de estudio (Nivel de evidencia)	Dosis utilizada	Eficacia	Comentarios
Gabapentina				
Brower et al. (2008)	ECACP (I)	1500mg/día	Retrasa el inicio de ingesta excesiva	Dependencia alcohol + Insomnio
Furieri et al. (2007)	ECACP (I)	600mg/día	↓ consumo de alcohol y craving	Dependencia alcohol
González et al. (2007)	ECACP (I)	2400mg/día	No eficaz	Dependencia cocaína + tratamiento con metadona
Bisaga et al. (2006)	ECACP (I)	3200mg/día	No eficaz	Dependencia cocaína
Martínez-Raga et al. (2004)	Abierto (III)	1800mg/día	Eficaz y bien tolerado	Coadyuvante en sd abstinencia heroína
Bonnet et al. (2003)	ECACP (I)	1600mg/día	No eficaz	Sd abstinencia alcohol
Lamotrigina				
Rubio et al. (2006)	Abierto (III)	300mg/día	↓ CDT y craving	Dependencia alcohol + TBP
Brown et al. (2006)	Abierto (III)	300mg/día	↓ consumo y craving	Dependencia cocaína + TBP
Berger et al. (2005)	Abierto controlado con placebo (II)	Reserpina = 0.5mg/día Gabapentina = 1800mg/día	Todas más eficaces que placebo y bien toleradas	Dependencia cocaína
Brown et al. (2003)	Abierto (III)	Lamotrigina = 150 mg/día	↓ craving y bien tolerado	Dependencia cocaína + TBP
Rosen et al. (1998)	Abierto (III)	300mg/día 250-400mg/día	No eficaz y bien tolerado	Sd abstinencia heroína precipitado por naloxona
Oxcarbacepina				
Martinotti et al. (2007)	Abierto aleatorizado controlado con naltrexona (II)	OXC = 1500-1800mg/día OXC = 600-900mg/día NTX = 50mg/día	Eficaz a dosis 1500-1800mg/día	Prevención de recaídas en dependencia alcohol
Koethe et al. (2007)	ECACP (I)	----------	No eficaz	Sd abstinencia alcohol
Llopis y Castillo (2008)	Observacional (III)	600-900mg/día	↓ consumo, craving e impulsividad	Uso/dependencia cocaína
Croissant et al. (2005)	Estudio de casos	----------	Eficaz	Desintoxicación de BZD
Pregabalina				
Di Nicola et al. (2010)	Abierto (III)	200-450mg/día	↓ síntomas abstinencia y craving. Bien tolerado	Desintoxicación alcohólica
Martinotti et al. (2010a)	ECACP (I)	150-450mg/día	Igual de eficaz que naltrexona	Dependencia alcohol
Martinotti et al. (2010b)	ECACP (I)	450mg/día	Eficaz y bien tolerado	Sd abstinencia alcohol
Tiagabina				
Paparrigopoulos et al. (2009)	Abierto aleatorizado controlado (II)		Menor tasa de recaídas y bien tolerado	Coadyuvante de psicoterapia en dependencia alcohol
González et al. (2007)	ECACP (I)	24mg/día	Eficaz en reducción consumo de cocaína	Dependencia cocaína + tratamiento con metadona
Winhusen et al. (2007)	ECACP (I)	20mg/día	No eficaz	Dependencia cocaína
Winhusen et al. (2005)	ECACP (I)	20mg/día	Mejoría de medidas subjetivas	Dependencia cocaína
González et al. (2003)	ECACP (I)	12-24mg/día	Eficaz (dosis 24mg/día) y bien tolerado	Dependencia cocaína + tratamiento con metadona
Topiramato				
Florez et al. (2010)	Abierto (III)	TPM = 200-400mg/día NTX = 50 mg/día	Más eficaz que naltrexona	Dependencia alcohol
Rubio et al. (2009)	ECACP (I)	----------	Eficaz y bien tolerado	Dependencia alcohol
Baltieri et al. (2009)	ECACP (I)	300mg/día	Eficaz en prevención de recaídas	Dependencia alcohol
Flórez et al. (2008)	Abierto controlado con naltrexona (II)	TPM = 200-400mg/día NTX = 50 mg/día	Igual de eficaz que naltrexona	Dependencia alcohol
Reis et al. (2008)	Abierto (III)	25-300mg/día	↓ craving y bien tolerado	Dependencia cocaína
Bobes et al. (2004)	Abierto (III)	Máxima 400mg/día	↓ consumo y craving	Dependencia cocaína / opiáceos
Kampman et al. (2004)	ECACP (I)	200mg/día	↑ abstinencia	Dependencia cocaína
Zullino et al. (2002)	Tres casos (III)	----------	Eficaz	Coadyuvante en sd abstinencia heroína

Nota. CDT = Transferrina deficiente en carbohidratos; ECACP = Ensayo clínico aleatorizado con placebo; TBP = Trastorno bipolar
*Sólo se incluyen los estudios con nivel más elevado de evidencia para cada grupo

Tabla 8
Recomendaciones terapéuticas generales para el manejo de la ansiedad dual

1. El tratamiento ha de ser individualizado, teniendo presentes los recursos asistenciales disponibles en el entorno y las expectativas del paciente.
2. El tratamiento de ambos trastornos debería realizarse de modo simultáneo. No obstante, es importante establecer una adecuada secuenciación de los tratamientos debido a la frecuencia con la que la abstinencia se acompaña de síntomas de ansiedad y para evitar interacciones.
3. Se debe controlar la adherencia al tratamiento así como supervisar el posible mal uso o abuso de los psicofármacos pautados para manejar situaciones de estrés.
4. Se recomiendan apoyo psicosocial y entrenamiento en estrategias de afrontamiento para trastornos de ansiedad inducidos, reservándose el uso de medicación para ansiedad persistente y trastornos de ansiedad primarios.
5. Se debe maximizar el uso de los abordajes no-farmacológicos. La psicoterapia cognitivo-conductual ha demostrado eficacia en el abordaje de ambos tipos de trastorno, y un adecuado entrenamiento en relajación puede interrumpir el ciclo de la automedicación.
6. El tratamiento farmacológico de la ansiedad dual es, en general, semejante al de los TA no comórbidos, no estando contraindicado ningún psicofármaco. Al elegir la medicación se deben tener en cuenta las interacciones con la sustancia de abuso en caso de recaída, así como usar fármacos con el menor potencial de abuso.
7. Los ISRS son los fármacos de elección en el tratamiento de la ansiedad comórbida con el TUS, por el bajo potencial de abuso, escasas interacciones y relativa seguridad en caso de sobredosis. Las dosis son las mismas que la que se emplea en población sin TUS, cuidando las interacciones con otros fármacos habituales en pacientes abusadores de sustancias (metadona, antirretrovirales, aversivos del alcohol, etc.).
8. Los antidepresivos tricíclicos y tetracíclicos (ATC) deben utilizarse con precaución, dados los efectos secundarios e interacciones, así como el potencial para disminuir el umbral convulsivo, circunstancia a tener en cuenta en pacientes alcohólicos, con antecedentes de convulsiones o lesión cerebral. Debido a las interacciones con fármacos y alimentos, se desaconseja el empleo de los inhibidores de la monoaminooxidasa (IMAO).
9. Las benzodiacepinas (BZD) deben evitarse por el potencial de abuso (especialmente el alprazolam) y las peligrosas interacciones con alcohol, opiáceos y otros depresores del SNC. Están indicadas para el tratamiento de los cuadros de abstinencia y en las desintoxicaciones de alcohólicos o con dependencia a hipnosedantes. La Agencia Española del Medicamento (circular 3/2000) indica que la duración del tratamiento no debe de superar las 8-12 semanas, incluyendo el tiempo de retirada progresiva de las mismas.
10. 10. Los nuevos antiepilépticos podrían constituir un buen tratamiento alternativo al uso de BZD en el tratamiento de esta patología dual. De igual modo, aunque con evidencias más limitadas, los antipsicóticos con perfil sedativo a dosis bajas podrían constituir otra posible alternativa para el tratamiento sintomático.

Tabla 9
Pautas de ayuda para el diagnóstico diferencial entre trastorno primario ("independiente") e inducido

Trastorno primario / "independiente"	**Trastorno inducido**
Edad de inicio de adicción posterior	Edad de inicio de adicción previo
Antecedentes personales psiquiátricos	No antecedentes personales de otros trastornos mentales
Antecedentes familiares psiquiátricos	Antecedentes familiares de adicciones
Persiste tras la abstinencia de sustancias	Remite con la abstinencia
Curso más recurrente	Curso menos recurrente (si no hay consumo)
Síntomas característicos del trastorno	Cuadros clínicos atípicos
Síntomas diferentes de lo esperable según tipo/cantidad de droga consumida	Síntomas se corresponden con el perfil de la droga consumida
Mejor estructura familiar	Mayor desestructuración familiar

Modificado de Arias Horcajada (2009)

Tabla 10
Pautas guía para la evaluación psicométrica de la ansiedad dual en la práctica clínica cotidiana

Area evaluada	**Instrumento (autor)**	**Aspectos evaluados**	**Validación española**
Orientación diagnóstica	MINI Entrevista Neuropsiquiátrica Internacional (MINI) (Sheehan et al., 1997)	Principales trastornos psiquiátricos del eje I (criterios DSM-IV y CIE-10)	L. Ferrando, J. Bobes, J. Gibert, M. Soto, O. Soto
	Entrevista de Investigación Psiquiátrica para Trastornos Mentales y por Sustancias (PRISM) (Hasin et al., 1996)	Comorbilidad psiquiátrica en pacientes con consumo de alcohol y otras sustancias. Discrimina trastornos mentales primarios, inducidos por sustancias, efectos de intoxicación y abstinencia.	Torrens et al. (2004)
Gravedad TA			
- TP	Escala de Pánico y Agorafobia de Bandelow (PAS) (Bandelow, 1995)	Gravedad del trastorno de pánico	No existe
- TAG	Escala de Detección del TAG (Carroll y Davidson, sin publicar)	Identificación del trastorno de ansiedad generalizada	Bobes et al. (2006)
- TEPT	Escala para el TEPT Administrada por el Clínico (CAPS) (Blake et al., 1990)	Presencia y gravedad de los síntomas del trastorno por estrés postraumático	Bobes et al. (2000)
- TAS	Escala de Ansiedad Social de Liebowitz (LSAS) (Liebowitz, 1987)	Gravedad de la fobia social	Bobes et al. (1999)
- TOC	Escala de Obsesiones y Compulsiones de Yale-Brown (Y-BOCS) (Goodman et al., 1989)	Gravedad de los síntomas del trastorno obsesivo compulsivo	Nicolini et al. (1996)
Gravedad TUS			
- General	Indice de Gravedad de la Adicción (versión 6.0) (ASI6) (Alterman, sin publicar)	Gravedad de la adicción entendida como necesidad de tratamiento	Díaz Mesa et al. (2010)
- Alcohol	Test AUDIT (Saunders et al., 1993) Escala para la Evaluación de la Abstinencia Alcohólica (revisada) (CIWA-Ar) (Sullivan et al., 1989)	Detección de bebedores de riesgo Gravedad del síndrome de abstinencia de alcohol	Rubio et al. (1998) No existe
- Opiáceos	Escala Breve de Abstinencia a Opiáceos (SOWS) (Gossop, 1990)	Gravedad de la abstinencia a opiáceos	No existe
- Cocaína	Cuestionario de Craving de Cocaína (CCQ) (Tiffany et al., 1993)	Intensidad del craving de cocaína	Tejero et al. (2003a)
	Escala de Valoración de la Gravedad Selectiva para Cocaína (CSSA) (Kampman et al., 1998)	Sintomatología inicial de la abstinencia a cocaína	Tejero et al. (2003b)
- BZD	Cuestionario de Síntomas de Retirada de BZD (BWSQ) (Tyrer et al., 1990)	Gravedad del síndrome de retirada de benzodiacepinas	No existe
Suicidabilidad	Escala SAD PERSONS (Patterson et al., 1983)	Riesgo de comportamiento suicida en base a factores clínicos y sociodemográficos	No existe
	Escala Columbia para Evaluar el Riesgo de Suicidio (Posner et al., 2011)	Evaluación conjunta de pensamientos suicidas (ideación suicida) y de comportamientos suicidas	En fase de realización
	Escala de Intencionalidad Suicida de Beck (SIS) (Beck et al., 1974)	Características de la tentativa suicida realizada	No existe

Modificado de García-Portilla et al (2011) y Sáiz et al (2011)

Nota. BZD = Benzodiacepinas; TA = Trastorno de ansiedad; TAG = Trastorno de ansiedad generalizada; TAS = Fobia social; TEPT = Trastorno por estrés postraumático; TOC = Trastorno obsesivo-compulsivo; TP = Trastorno de pánico; TUS = Trastorno por uso de sustancias

Tratamiento psicológico de la ansiedad dual

Si bien el abordaje psicológico de los TA duales no es objeto de revisión en el presente trabajo, nunca se debe olvidar la necesidad de hacer un enfoque integral bio-psicosocial en el abordaje de este tipo de trastornos.

En este sentido, merece la pena hacer una breve referencia a la psicoterapia cognitivo-conductual, dada su eficacia demostrada en el tratamiento de los TA (Baker, Thornton, Hiles, Hiles y Lubman, 2012; Hesse, 2009).

Al igual que ocurre con los tratamientos farmacológicos, apenas existen estudios sobre el tratamiento psicológico de los TA con TUS comórbidos (Baker et al., 2012), y los datos de estos trabajos no son concluyentes (Hobbs, Kushner, Lee, Reardon y Maurer, 2011). La psicoterapia cognitivo-conductual unida a la entrevista motivacional, han resultado eficaces en el tratamiento del abuso de alcohol en pacientes con ansiedad comórbida, especialmente cuando se realizan programas de intervención prolongados (Baker et al., 2012), si bien existen estudios en los que no se demuestra que el tratamiento psicológico simultáneo de TA y TUS aporte ventajas (Hesse, 2009; Randall, Thomas y Thevos, 2001). De hecho, alguno de estos trabajos recomienda que la intervención psicológica se haga de forma secuencial o escalonada (Baker et al., 2012).

Limitaciones de la revisión

Para la elaboración del presente trabajo, se ha realizado una búsqueda bibliográfica en Medline, revisando más de 70 estudios con diferente metodología. La variedad de estudios, así como la participación de cada autor en partes específicas del trabajo, ha imposibilitado la inclusión en las tablas de las medidas eficacia y de significación estadística de los estudios referenciados. Para acceder a esta información con mayor detalle, se remite al lector a las diferentes referencias bibliográficas.

Conflicto de intereses

No existen conflictos de intereses en la elaboración de este artículo de revisión. Los autores no han recibido financiación para la elaboración de este trabajo.

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NUEVOS EVENTOS

15ª Escuela de Otoño (Valencia, 27 a 29 de Noviembre 2014)

Tras los excelentes resultados obtenidos en la 14ª Escuela de Otoño, se está trabajando en la oferta de talleres para la próxima edición de la Escuela, tratando de atender a la demanda de formación que hacen llegar los socios de Socidrogalcohol a través de la web.

Como cada año se intentará superar el interés y la calidad del anterior.

Pueden consultarse los talleres en nuestra web www.socidrogalcohol.org. También se puede contactar con la Secretaría Técnica de la Escuela "C&EVENTS SOLUCIONES", Tef. 960914545; e-mail: soluciones@cevents.es

XLII Jornadas Nacionales 2015 (Logroño, 12 a 14 de Marzo 2015)

El Comité Organizador de dichas Jornadas está trabajando en la elaboración del programa, que podéis consultar en la web www.socidrogalcohol.org. Es importante que todos los profesionales interesados hagan llegar las propuestas de mesas dentro de los períodos previstos y siguiendo las normas establecidas. Esto permitirá confeccionar un programa atractivo y representativo de los intereses de los diferentes profesionales de las adicciones.

EVENTOS RECIENTES

Simposium Científico sobre Opiáceos (Cartagena, 29 a 30 de Mayo)

Este Symposium se enmarca dentro del objetivo de formación continuada que tiene la Sociedad desde hace años. En esta ocasión, y favoreciendo que los socios de diferentes comunidades pudieran acceder con facilidad a la formación propuesta y tras atender a la demanda efectuada desde la propia Comunidad, se decidió realizar este curso en Cartagena. El mismo supuso una puesta a punto con carácter multidisciplinar de esta temática puntual. Puede consultarse la web www.socidrogalcohol.org para obtener información detallada. Al igual que en otros eventos que organiza la Sociedad, en este caso, también se premiaron los mejores trabajos en formato poster.

OTROS ASPECTOS DE INTERÉS

Relaciones Internacionales

Del 5 al 9 de mayo se celebró en Montevideo (Uruguay) el Seminario anual así como la Asamblea General de la **RIOD** (*Red Iberoamericana de Organizaciones no Gubernamentales que Trabajan en Drogodependencias*), en la que nos ha representado la Dra. Enriqueta Ochoa. En este Seminario se ha designado a Socidrogalcohol representante del NODO España.

Gabinete de Prensa

Bajo la coordinación del periodista Josep Dalmau, Socidrogalcohol ha creado un gabinete de prensa, con el objetivo de informar y dar a conocer la imagen de la sociedad y de sus productos fundamentales: Jornadas Nacionales, Escuela de Otoño y la producción editorial (revista, guías, monografías, etc).

Como "producto estrella" del gabinete destaca el **NEWS de Socidrogalcohol** que todos los socios e instituciones relevantes relacionadas con las adicciones, tanto nacionales como internacionales, reciben vía correo electrónico.

Si no es así y estáis interesados en recibirlo, por favor, facilitadnos vuestra dirección de correo electrónico a socidrogalcohol@socidrogalcohol.org o por correo ordinario a Socidrogalcohol, Avda. de Vallcarca 180 08023 Barcelona.

WEB de Socidrogalcohol

Os invitamos a entrar en la WEB de Socidrogalcohol: www.socidrogalcohol.org que periódicamente es actualizada y ampliada intentando ser un espacio de encuentro de interés para todos.

Además de los contenidos que ya estaban disponibles anteriormente, la WEB de Socidrogalcohol, cuenta actualmente con la posibilidad de enlazar con otras WEBS internacionales como NIDA, NIAAA y otras.

También se pueden consultar Monografías, Guías Clínicas y otros documentos de Socidrogalcohol en pdf, además de algunos informes epidemiológicos de organismos nacionales e internacionales, así como los programas de las últimas Jornadas Nacionales.

Con la finalidad de que podamos mejorar el contacto y la comunicación entre nosotros, es muy importante que **nos hagáis llegar vuestra dirección de correo electrónico**.

Podéis hacerlo utilizando nuestro mail socidrogalcohol@socidrogalcohol.org o por correo ordinario a Socidrogalcohol, Avda. de Vallcarca 180, 08023 Barcelona.

Desde el año 2012 sólo se admite la normativa APA.

Ante la preparación de un artículo de cara a su publicación se deben revisar y aplicar las normas extensas, que pueden ser consultadas en www.adicciones.es

Adicciones está editada por Socidrogalcohol, Sociedad Científica Española de Estudios sobre el Alcohol, el Alcoholismo y otras Toxicomanías. Adicciones publica artículos originales sobre el tratamiento, la prevención, estudios básicos y descriptivos en el campo de las adicciones de cualquier tipo, procedentes de distintas disciplinas (medicina, psicología, investigación básica, investigación social, etc.). Todos los artículos son seleccionados después de pasar un proceso de revisión anónimo hecho por expertos en cada tema. Adicciones publica 4 números al año. Adicciones tiene las secciones de editorial, artículos originales, informes breves, artículos de revisión y cartas al director. La revista se publica en español, aunque admite artículos en inglés. Cuando publica un artículo en inglés, puede exigir su traducción también al español, pero no es la norma.

Papel. La revista Adicciones está impresa en papel estucado fabricado con pastas libres de cloro (TCF).

Conflictos de intereses. La política de la revista es que en todos los artículos y editoriales conste expresamente la existencia o no de conflicto de intereses en el apartado correspondiente. Todos los conflictos de interés son importantes, pero especial cuidado hay que poner en el caso de haber recibido para el estudio financiación de la industria farmacéutica, alcoholera, tabaquera, etc. La revista Adicciones sigue en este tema las recomendaciones de ISAJE (International Society of Addiction Journals Editors). Tener conflicto de intereses no significa no poder publicar el artículo. En caso de duda sobre esta cuestión se debe contactar con el editor.

Autoría. Es muy importante que únicamente se consideren autores aquellos que han hecho sustanciales contribuciones: 1) a la concepción y diseño, adquisición de datos, o el análisis e interpretación de datos; 2) a la redacción del artículo o a su revisión crítica; y 3) que ha dado su aprobación de la versión que se publicará. Los autores deben asegurarse de que partes significativas del material aportado no ha sido publicado con anterioridad. En caso de que puedan tener dudas sobre el cumplimiento de esta norma, deberán presentar copias de lo publicado o de lo presentado para publicación a otras revistas antes de poder ser considerado el artículo para su revisión. En caso de dudas sobre alguno de los aspectos anteriores los autores deben consultar el acuerdo de Farmington al que está adherida la revista Adicciones (Anexo 1), las normas de "Sponshorship, authorship, and accountability" del International Committee of Medical Journal Editors (www.icmje.org/sponsor.htm) o las normas de publicación de la American Psychological Association, 6ª edición (2010) (www.apastyle.org). El editor de la revista puede dirigirse a los autores del artículo para que especifiquen cual ha sido la contribución de cada uno de ellos.

Preparación de manuscritos. Los autores deben seguir exclusivamente para la presentación de sus manuscritos las Normas de Publicación de la American Psychological Association (6ª edición, 2010; http://www.apastyle.org). Las excepciones a esta regla son mínimas y dependen sólo de las diferencias que puede haber en el uso del español y del inglés. Por ejemplo, los ingleses utilizan en la bibliografía el signo '&' antes del último autor, mientras que en español dicho signo se corresponde exactamente con la 'y' (por tanto los artículos en español utilizarán solo la 'y'); otra diferencia puede ser en los títulos de los artículos, puesto que en inglés se pone en mayúscula la primera letra de muchas de las palabras, mientras que en español sólo ponemos la primera…

NO existe un límite exacto de palabras para los trabajos que se presenten. Pero deberá cuidarse mucho que toda la información que se incluya sea estrictamente la necesaria.

Es importante que los artículos sean interesantes para la comunidad científica del campo de las adicciones. Se evitarán trabajos que se refieran a realidades muy concretas –a menos que precisamente en ello resida su interés-, o que sean básicamente descriptivos –a menos, nuevamente, que se trate de algo novedoso.

Artículos originales. Serán preferentemente trabajos de investigación clínicos o experimentales sobre el campo de las drogodependencias o las adicciones. Pero también pueden ser aceptados trabajos teóricos o de otro tipo.

Informes breves. En esta sección se considerarán los trabajos de investigación que por sus características especiales (series con número reducido de observaciones, casos clínicos, trabajos de investigación con objetivos y resultados muy concretos, estudios epidemiológicos descriptivos, primeros resultados de un estudio amplio, etc.) pueden ser publicados de forma abreviada y rápida.

Artículos de revisión. Presentarán la actualización de un tema de forma rigurosa y exhaustiva. Deberán regirse normalmente por metodologías sistematizadas. El contenido del artículo podrá llevar los apartados necesarios para la mejor comprensión de los lectores. En su parte final debe aparecer un apartado de discusión o conclusiones. La extensión preferiblemente no debería superar las 5.000 palabras, pero siempre que esté justificado, se admitirían revisiones más largas.

Cartas al Director. Tendrán normalmente un máximo de 800 palabras, 10 referencias y una tabla o figura. Pueden consistir en una presentación breve sobre algo novedoso, una investigación original, o la contestación o matización a un artículo publicado en la revista. Cuando sea éste el caso la carta tendrá que recibirse dentro de las 6 semanas subsiguientes a la publicación del artículo en el número de la revista

PRESENTACIÓN DE LOS TRABAJOS

Envío electrónico. La forma más rápida y preferente de enviar artículos para su revisión editorial es a través de www.adicciones.es. Allí encontrará todas las instrucciones a seguir y la forma de adjuntar el original. Todo el seguimiento del proceso de revisión y editorial se realizará a través de la web (a través de la plataforma de RECYT). Ésta es la única forma prevista para envío de artículos (pero si tiene alguna duda puede comunicarse con secretaria@adicciones.es). Será muy útil para facilitar el proceso de revisión que en el momento del envío del artículo proporcione a través de la misma plataforma información sobre por lo menos dos posibles revisores para su artículo (nombre, institución y correo electrónico). Estos revisores deberán ser expertos en el tema y no estar ligados a la investigación que se desarrolla en el trabajo presentado. Tampoco podrán pertenecer al actual Comité de Redacción o Editorial. La revista se reserva la decisión de utilizar o no dichos revisores propuestos. El editor señalará además normalmente otros revisores. Recordar que el proceso de revisión es anónimo para los autores. Caso de que no fuese posible por alguna razón o tuviese algún problema con el envío del artículo a través de la web, le agradeceremos que se ponga en contacto con secretaria@adicciones.es o al teléfono (+34) 971727434 o a Editor de Adicciones. Rambla, 15, 2ª, 3ª. 07003 Palma de Mallorca.

ESTRUCTURA DE LOS TRABAJOS ENVIADOS A LA REVISTA

Todas las hojas deberán ir numeradas correlativamente en la parte superior derecha. Cada parte del manuscrito empezará una página en el siguiente orden:

1. En la *primera página* del artículo se indicarán, en el orden que aquí se cita, los siguientes datos:

- Título del artículo, en minúsculas (en castellano e inglés) excepto la letra inicial.
- Nombre de los autores completo (no sólo iniciales), y uno o dos apellidos del/los autor/es (p. ej.: Miguel García o Miguel García Rodríguez o bien Miguel García-Rodríguez, teniendo en cuenta que la forma que hayan utilizado los autores es la que se enviará a las bases de datos) en minúsculas, excepto la letra inicial. Los distintos autores vendrán separados por punto y coma. Detrás del apellido de cada autor, sin espacio intermedio y en superíndice, deberá ir un asterisco de llamada (1 asterisco para el primero, 2 para el segundo, etc.). Estos asteriscos son necesarios para indicar en el siguiente punto la institución donde se ha realizado el trabajo.
- Precedidos por un asterisco o los que fuesen necesarios –según el punto anterior– se indicarán el nombre/s del centro/s donde se ha realizado el trabajo o donde trabajan los autores.

Al final de la primera página (no como 'nota al pie') se colocará este texto: "Enviar correspondencia a: ...", indicando el nombre, la dirección postal, correo electrónico u otra información mediante la cual el autor elegido podrá ser contactado. Este será

el autor al cual la secretaría se dirigirá durante el proceso de revisión, a menos que se acuerde mutuamente otra solución.

2. La *segunda hoja* del artículo incluirá un resumen del trabajo presentado, tanto en español como en inglés. Dicho resumen tendrá alrededor de 250 palabras. Siguiendo las normas de publicación internacional ya citadas, el resumen debe especificar los objetivos del estudio o investigación; la metodología fundamental utilizada; los principales resultados; y las conclusiones más importantes y/o novedosas. El resumen debe redactarse en uno o varios párrafos siguiendo las normas de publicación de la APA, sin atender a las divisiones de antecedentes, método, etc.

Después del resumen se incluirá un listado de alrededor de 5 Palabras clave en español y luego en inglés (Key words) en minúsculas y separadas por comas que, a ser posible, se adapten a las normalmente utilizadas en los índices al uso (ej., Index Medicus, Psychological Abstracts, Índice Médico Español).

3. La *tercera hoja* dará inicio al texto del artículo. Se recomienda la redacción del texto en impersonal. Conviene dividir claramente los trabajos en apartados, siguiendo, siempre que sea posible por las características del estudio, el esquema general siguiente: Introducción (no obstante la palabra introducción no se pondrá, pues se da por supuesta), Método, Resultados, Discusión, Reconocimientos, Conflicto de intereses y Referencias.

Introducción. Será breve y deberá proporcionar sólo la explicación necesaria para que el lector pueda comprender el texto que sigue a continuación. No debe contener tablas ni figuras, a menos que sean imprescindibles para la comprensión del texto. Debe incluir un último párrafo en el que se exponga de forma clara el o los objetivos del trabajo. Siempre que se pretenda publicar una observación muy infrecuente, debe precisarse en el texto el método de pesquisa bibliográfica, las palabras claves empleadas, los años de cobertura y la fecha de actualización.

Métodos. Se describirá claramente la metodología empleada (selección de la muestra, como se recogieron los datos, instrumentos de recogida de datos o de evaluación, temporalización,… Se deben identificar los métodos, instrumentos de evaluación, tratamientos, fármacos utilizados, aparatos, sistema de evaluación, pruebas estadísticas si son novedosas, métodos nuevos, etc. Debe especificarse el tipo de estudio (descriptivo, epidemiológico, experimental, ensayo clínico, etc.), sistema de asignación de los sujetos a grupos, aleatorización, etc. Cuando haya un protocolo debe citarse. Cuando los experimentos son realizados con animales o el ensayo es experimental en humanos debe especificarse explícitamente que se han seguido las normas éticas deontológicas, de investigación y que se han cumplido los convenios internacionales de experimentación animal o humana. Debe especificarse el tipo de análisis estadístico que se va a utilizar, describirlo cuando éste sea nuevo o poco conocido, e indicar el paquete estadístico que se va a utilizar. Se valorará positivamente si se ha conseguido la aprobación del estudio por algún comité ético o se podrá exigir cuando el estudio realizado lo requiera.

Resultados. Los resultados deben presentarse en una secuencia lógica en el texto, tablas y figuras. Utilice sólo aquellas tablas y figuras estrictamente necesarias, que expresen claramente los resultados del estudio. No duplique los datos en tablas y figuras. No repita en el texto todos los datos de las tablas y figuras, sólo los más importantes. Enfatice y resuma sólo las observaciones más importantes. Adicciones adopta el sistema convencional del 5% como valor para la significación estadística y no acepta tener en cuenta las tendencias para valores menores.

Los ensayos clínicos aleatorizados deben adecuarse a las guías CONSORT (www.consort-statement.org) y los estudios con diseños no experimentales a las guías TREND (www.trend-statement.org/asp/trend.asp) para la mayor claridad de los lectores y revisores del trabajo. Igualmente, se presentarán los estadísticos del tamaño del efecto.

Discusión. Enfatizará los aspectos nuevos e importantes del estudio y las conclusiones que se derivan del mismo. No repita en detalle los resultados que ha presentado en la sección anterior ni en la introducción. Destaque lo más importante y controvertido y relacionelo con otros estudios relevantes sobre el tema. No haga suposiciones si no se ven apoyadas por los datos. Cuando sea apropiado pueden incluirse recomendaciones. Indique las implicaciones de sus hallazgos y sus limitaciones (estas preferiblemente formarán un párrafo al final del artículo).

Reconocimientos. Este apartado se situará al final del texto del artículo y justo antes del apartado de Referencias. Cuando se considere necesario se citará a las personas, centros o entidades que hayan colaborado o apoyado la realización del trabajo. Pueden incluirse todas aquellas personas que hayan ayudado en la preparación del artículo, pero no con la intensidad requerida para ser considerados autores. Si el trabajo ha sido financiado se indicará la entidad financiadora.

Conflicto de intereses. Todos los artículos, editoriales, comentarios, opiniones, reseñas de libros y cartas que se publican en la revista estarán acompañados por una declaración sobre los posibles o reales conflictos de interés o una declaración de que los autores no tienen conflictos de intereses que declarar.

Referencias. Seguirán de forma estricta las normas de la American Psychological Association [American Psychological Association (2010). Publication Manual of the American Psychological Association (6th ed.). Washington, DC. http://www.apastyle.org

Tablas y figuras. Irán al final del texto, numeradas, y cada una en una página distinta, siguiendo el diseño propio de la APA.

EL PROCESO DE REVISIÓN DEL MANUSCRITO

Los artículos son enviados a la revista a través de la www.adicciones.es. Los autores reciben al enviar el artículo unas claves para poder entrar en la web y revisar la situación de su artículo. No obstante el editor de la revista enviará un mensaje cuando tenga una decisión tomada o quiera preguntar alguna cuestión. Una vez recibido el manuscrito en la Redacción de la Revista Adicciones empezará el proceso de revisión.

El Editor, normalmente consultando con los editores asociados, puede desestimar de entrada un artículo que entienda que claramente no reúne la calidad suficiente o no entra dentro de las prioridades de la revista. El editor puede rechazar de entrada aquellos artículos que no cumplan estrictamente dicha normativa, sin pasarlo a revisión.

Los manuscritos serán enviados por el Editor o los Editores Asociados a dos o más expertos en el tema (revisores), que harán los comentarios pertinentes sobre el mismo y que requerirán aquellos cambios que estimen necesarios; también pueden dar su opinión sobre la aceptación o rechazo del artículo. La última decisión, basada en el informe de los revisores, o del editor asociado que se hubiese responsabilizado de la revisión, será tomada por el Editor de la revista, que podrá consultar además a los Editores asociados. En todo el proceso de revisión se mantendrá el principio de confidencialidad por parte de los revisores hacia el trabajo que revisan, así como la confidencialidad de los nombres de los revisores entre ellos o ante los autores del manuscrito.

El resultado de la revisión del manuscrito será enviado al autor de correspondencia que viene en el artículo indicándole su aceptación, rechazo o la necesidad de someterse a una nueva revisión una vez tenidos en cuenta los comentarios de los revisores o del editor. El autor, si es el caso, deberá hacer los cambios señalados –cuando esté de acuerdo con ellos–, enviando:

- Una copia del manuscrito revisado.
- Otro documento en donde se exponga de forma detallada las principales modificaciones efectuadas, así como sus propios comentarios sobre los principales aspectos de la revisión, con los que obviamente puede estar en desacuerdo.

Una vez aceptado el artículo, se enviará a los autores las pruebas de imprenta para que las corrijan. Los autores son totalmente responsables de la versión final que se publique. Los autores pueden hacer el uso que crean pertinente para la difusión del artículo, siempre que quede clara toda la información necesaria acerca de la revista donde ha sido publicado.

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