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Adicciones

SOCIDROGALCOHOL Sociedad Científica Española de Estudios sobre el Alcohol, el Alcoholismo y las otras Toxicomanías

ISSN 0214-4840

FUNDED BY:
MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD
SECRETARÍA DE ESTADO DE SERVICIOS SOCIALES E IGUALDAD
DELEGACIÓN DEL GOBIERNO PARA EL PLAN NACIONAL SOBRE DROGAS

2015 | Vol. 27 | n.1

FUNDED BY:

adicciones

publishes articles about addictions and their relationship with dual diagnosis (schizophrenia, depression, personality disorders...) and organic pathology

MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD
SECRETARÍA DE ESTADO DE SERVICIOS SOCIALES E IGUALDAD
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PUBLISHER: **SOCIDROGALCOHOL** (Sociedad Científica Española de Estudios sobre el Alcohol, el Alcoholismo y las otras Toxicomanías)

I.S.S.N.: 0214-4840 • **SVPF:** 89010R • **LEGAL DEP.:** V-1543-1989

printing: MARTIN IMPRESORES, S.L., Pintor Jover, 1, 46013 VALENCIA • Permanent paper according to stardard ISO 9706

dirigir correspondencia a: SOCIDROGALCOHOL • Avda. de Vallcarca, 180 • 08023 Barcelona
Tel.: (+34) 932103854 • E-mail: socidrogalcohol@socidrogalcohol.org • www.socidrogalcohol.org

INDEXED IN: ADDICTION ABSTRACTS, C.A.N., C.I.C., CVDD, EMBASE/EXCERPTA MEDICA, ETOH (NIAAA), FAMILY STUDIES DATABASE (NISC), IBECS, I.M.E., INDID, INIST-CNRS, ISOC, MEDLINE, PSICODOC, PSYCINFO, REDALYC, SOCIAL SCIENCES CITATION INDEX (SSCI) & SCIENCE CITATION INDEX EXPANDED (SCIE).TOBACCO AND HEALTH ABSTRACTS (NISC), TOXIBASE

impact factor 2013: 1.167

editorial

originals / originales

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The reduction of alcohol consumption. A new treatment target for low-severity alcoholism

La reducción del consumo de alcohol. Un nuevo objetivo en el tratamiento del alcoholismo de baja gravedad

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The pharmacotherapy of alcoholism, for relapse prevention, goes back more than 60 years, to the introduction of disulfiram. It was probably the very characteristics of the drug that promoted a treatment model based on continuous abstinence, which has remained to the present day.

The acetaldehyde reaction, which can occur if the patient drinks alcohol again, acts as a cognitive deterrent, and helps the recovering patient maintain the commitment to maintain complete and continuous abstention, which in turn helps to protect him or her from relapse (Chick et al., 1992).

This treatment model has been imposed to the extent that for decades no alternative proposal has managed to replace it in our country; moreover, it has created an expectation of what recovery from alcoholism should be like, among patients, their families and professionals, and this has interfered in the development of other options.

What is more, many controlled clinical trials with drugs for the prevention of relapse have equated any alcohol use (however small) with relapse. A return of any kind to drinking has been considered as treatment failure, and has even obliged patients who drink during the treatment to drop out of the study (Naranjo, Dongier, & Bremmer, 1997; Gual & Lehert, 2001).

In fact, it was not until the advent of clinical trials with naltrexone (for the treatment of alcoholism) that a new, less stringent relapse criterion was proposed, overlapping with that of "heavy drinking", which consists of 5 or more drinks per day or at one sitting, or 4 or more in the case of women (Volpicelli, Alterman, Hayashida, & O'Brien, 1992; O'Malley et al., 1992; Guardia et al., 2002).

This progress, from any alcohol consumption at all being considered as relapse, to the acceptance of low-risk drinking as a criterion of improvement, is laying the bases for accepting the concept of reduced alcohol use as a valid outcome target for treatment programmes.

Naltrexone was introduced as an anti-craving drug designed to bring about continuous abstinence from alcohol. However, few clinical trials have confirmed that naltrexone produces a clear reduction in craving, nor that it increases abstinence rates. However, several review studies and meta-analyses have concluded that its most notable therapeutic effect is the reduction of excessive alcohol use (Bouza, Magro, Muñoz, & Amate, 2004; Pettinati et al., 2006; Rösner et a., 2010).

On the other hand, clinical experience shows that while disulfiram can be useful over a certain period for people who have decided to give up drinking, it is likely that after an initial period of continuous abstinence, the alcoholic patient will try a drink, which tends to lead to relapse, just when he/she was at an advanced stage of recovery.

Such late relapses are often unexpected (for both patients and their families), and tend to be associated with immediate negative consequences, which are sometimes so severe that they can be devastating for the patients

Received: October 2014; Accepted: November 2014

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themselves, since they lose confidence in themselves and in the treatment. If in addition to this the family shows rejection, the patient can develop self-destructive behaviours, which may even lead to suicide during relapse crises.

In both studies with laboratory animals and in clinical practice it can be seen that when alcohol consumption is discontinued for a period, it is likely that intake increases considerably (due to loss of control) when the patient starts drinking again. This neurobiological phenomenon has been called alcohol deprivation effect, and is related to the functioning of the opioid system, since the administration of opioid receptor antagonists (such as naltrexone and nalmefene) can attenuate its impact (Kornet, Goosen, & Van Ree, 1990; O'Brien, Volpicelli, & Volpicelli, 1996; Sinclair, 2001).

Treatment oriented towards continuous alcohol abstinence has several drawbacks. Probably the most important of these is the above-mentioned withdrawal effect (which begins on the day the patient starts drinking again); but there may be other, more subtle ones, which will interfere with both patients' understanding and awareness of their addictive disease and the development of effective relapse-prevention strategies.

Patients that are able to stop drinking altogether, for a while, have the illusory perception of being already fully "recovered", because they no longer feel the "need" to drink and they have found it easy to stay abstinent. If moreover they take disulfiram or cyanamide, it is as though alcohol has ceased to exist, since it is no longer "available" to them. In such a situation, the patient does not drink at all and no longer craves for alcohol, and his or her behaviour has returned to normal. Such remission even leads patients to think that they didn't really have an addictive disease, that maybe the doctor made a mistake in the diagnosis, or in any case, that they had an alcohol problem in the past, but that they've now "got over it".

From here on in they begin to think that at some time in the future they can have the odd drink without problems. Even their family and friends might begin to say that, since they have already gone so long without drinking, they have probably now recovered, and they could have a drink without it leading them to drink excessively (Guardia-Serecigni, 2008).

Hence, conventional treatment with disulfiram or cyanamide does not favour understanding or awareness with regard to the underlying addictive disease, which tends to be persistent and can be reactivated by even just one drink, since the first glass can lead to uncontrolled drinking and relapse into heavy drinking, with all the associated negative consequences. Relapse will generate despair and pessimism, and can lead people to think (wrongly), that their alcohol problem has no solution. Such pessimism tends also to affect family members, and even the professionals treating the problem.

The reduction of alcohol use, with the help of nalmefene, is a new treatment target that brings clear advantages for low-severity alcoholic patients who follow closely the corresponding instructions.

If a patient has begun to have "problems", which are negative consequences of his or her excessive alcohol use, and the professionals treating the person help him/her to understand this relationship between such excessive consumption and those problems, it is likely that the patient will be well-disposed to reducing his/her intake.

Patients often decide to stop drinking when they find themselves stressed by these "problems". However, "stopping drinking" is not exactly the same as having the specific target of complete and continuous abstinence: patients tend to leave themselves the option of having the odd drink, in certain situations of celebration or when they meet up with friends and family, especially in their initial attempts to treat their alcoholism (Guardia-Serecigni, 2009; 2012).

Lack of a proper understanding of the withdrawal effect and of the characteristics of the addictive disease lead patients, their families and their friends to think that control or lack of control over their drinking depends exclusively on their "willpower", and they all tend to believe that if the patient were to just "try a bit harder", he or she could manage to control it. Finally, when the patient manages to stay abstinent for a reasonable period of time, everyone thinks along the lines of "time is a great healer", and that the patient will soon be able to have a few drinks without problems. This is the "trap" that usually leads to relapse, and only antagonists of the opioid receptors can protect the patient from a situation where that first drink indeed ends up leading to relapse.

That is, the patient's true objective is actually closer to a reduction in use than to continuous abstinence, since he or she tends to leave open the option of having a few drinks at some point in the future. If the patient has taken an opioid receptor antagonist, the day he or she takes a drink again, he/she can avoid relapse, and may succeed in being able to drink just occasionally and at low risk, which would signify clinical remission from alcoholism.

However, when the patient seeks the euphoria-inducing effects of alcohol, or "needs" to drink so as to mitigate other psychiatric symptoms (anxiety, insomnia, depression, post-traumatic stress, etc.), reducing alcohol use may be more difficult, possible because this quest for the psychoactive effects of alcohol or the effect of self-medication may overpower the limited effect of opioid receptor antagonists. Indeed, clinical trials on treatment with naltrexone have only yielded small or moderate effect sizes (Feinn & Kranzler, 2005).

The efficacy of treatments targeting a reduction in alcohol use has been demonstrated only with nalmefene, in low-severity alcoholic patients (Van den Brink et al., 2013; Van den Brink et al., 2014). Future studies could broaden the severity spectrum of patients who might benefit from this new treatment objective.

Low-severity alcoholic patients are those that do not present alcohol withdrawal effects, nor serious or decompensated medical, psychiatric or addictive comorbidities. The majority of alcoholic patients do not present withdrawal syndrome, but only difficulties for controlling their alcohol intake (which is what leads them to drink to excess), and nor do they present serious or decompensated comorbidities. Therefore, most people who suffer from this disease can be considered as low-severity, and can benefit from treatment with opioid receptor antagonists, targeting the ongoing reduction of their alcohol use – and this represents a paradigm shift in the treatment of low-severity alcoholism (Guardia-Serecigni, 2011).

It is certainly the case that the majority of alcoholic patients are low-severity, given that just 20% present clear withdrawal syndrome (Anton, 2008). Patients with high levels of severity should begin their treatment with a detoxification programme, so as to alleviate the alcohol abstinence symptoms and facilitate their withdrawal from drinking.

When alcoholic patients properly follow the instructions for reducing their drinking, at the same time as taking nalmefene (prior to having an alcoholic drink), the expected reduction effect appears right from the beginning of the treatment, and is maintained long-term, with the possibility, even, of achieving a gradual pharmacological extinction of the addictive behaviour. That is, if every time the patient ingests alcohol the expected reinforcing effect fails to occur, the quest for alcohol and its consumption lose relevance, the patient's "obsession" to drink decreases, and his/her "freedom" to decide whether to have a drink or not increases, on each new potential drinking occasion that comes up.

This "freedom" of decision with respect to alcohol may not seem very important to people who have never had difficulty controlling their drinking, but it is very important for those who have lost the ability to control their alcohol use. Moreover, greater awareness about addiction and lack of control over drinking may increase both the "obsession" to drink and the symptoms of grief, when one is obliged to stop drinking altogether, and this can lead to depression and increase vulnerability to relapse in some patients.

In treatment with opioid receptor antagonists, alcoholic patients will follow a process in whose initial stages they still have the "need" or *craving* for a drink. This will help them to become aware of their addictive disease and also to realize that they should reduce their alcohol intake as much as possible, or even stop drinking altogether. They also learn that they have to protect themselves, taking a pill prior to their first drink after a period of abstinence, if they want to avoid the risk of losing control, of going back to excessive drinking, and of suffering the associated negative consequences. And the professional experts in alcoholism treating them can also play an important role, helping them to be aware of their addictive disease, and working with them on strategies for preventing a return to heavy drinking.

Having reached this point, we can state that alcoholism corresponds to the medical model of illness, and can be treated like any other bodily dysfunction. The great difference is that the cardinal symptom, the "difficulty to control" alcohol intake, is not a bodily symptom but a behavioural one, but the similarity resides in the fact that it also responds to pharmacological treatment – that is, taking the medication at the right time has the effect of neutralizing the symptom and helps the patient to achieve the goal of reducing alcohol intake.

Drawing a parallel with other diseases or bodily dysfunctions such as migraine crises, sea-sickness, insomnia, allergic rhinitis, or epigastric illnesses, we see that the therapeutic procedure normally consists in taking a pill (of the drug in question) at the moment the symptom appears, or even before it does (with the aim of preventing it), in situations in which it is likely that the symptom will reappear.

This medical model involves the use of a treatment option "in case of need" or "on-demand", which might be needed more frequently at first, but as the patient becomes more stabilized, the frequency will decrease, and it may become unnecessary at times. All the same, factors such as stress can contribute to a reappearance of the symptom, so that a further treatment episode is required, until stabilization is achieved once more, and eventually clinical remission.

When the treatment targeting a reduction in alcohol use achieves the stabilization of the patient, or even, going a step further, when the patient finally stops drinking altogether, he or she will no longer need to take medication for a long time. However, it may be that the patient has another relapse at some later date; in that case, the medication will once again be necessary to avoid them falling back into heavy drinking.

If patients manage to stay within the limits of low-risk drinking, on all occasions that they drink, they will also avoid the negative consequences associated with excessive alcohol intake. If the negative consequences disappear, we can consider that the patient is in clinical remission from alcoholism. And if the patient succeeds in maintaining this remission over a long period, in line with the aforementioned medical model of disease, we can consider that he or she has recovered from his/her illness.

From that moment on, the patient can stop worrying about the episode of alcoholism, which he/she has now got over, and get on with resolving other more or less pressing problems.

Conclusions

Clinical trials on the treatment of alcoholism, with opioid receptor antagonists, have provided a new, less stringent relapse criterion, and have demonstrated their utility for the reduction of excessive alcohol intake. Nalmefene helps low-severity alcoholic patients seeking to reduce their alcohol use to achieve their goal. This new treatment approach brings recovery from alcoholism closer to the model of medical illness. If patients attain a significant reduction in their alcohol use, whereby they stay within the limits of low-risk drinking, on all occasions that they drink, this treatment can lead to clinical remission and also to the disappearance of the negative consequences of heavy drinking. Once remission has been achieved, the alcohol addiction ceases to be a source of preoccupation (for both patients and their families), and may well follow a course similar to that of medical disorders.

Conflicts of interests

The author participated as principal investigator in the ESENSE II study and has formed part of the Lundbeck España assessment committee on nalmefene.

References

Anton, R. F. (2008). Naltrexone for the management of alcohol dependence. *The New England Journal of Medicine, 359*, 715-721.

Bouza, C., Magro, A., Muñoz, A., & Amate, J. M. (2004). Efficacy and safety of naltrexone and acamprosate in the treatment of alcohol dependence: a thematic review. *Addiction, 99*, 811-828.

Chick, J., Gough, K., Falkowski, W., Kershaw, P., Hore, B., Metha, B., … Torley, D. (1992). Disulfiram treatment of alcoholism. *British Journal of Psychiatry, 161*, 84-89.

Feinn, R., & Kranzler, H. R. (2005). Does effect size in naltrexone trials for alcohol dependence differ for single-site vs. multi-center studies? *Alcoholism Clinical and Experimental Research, 29*, 983-988.

Gual, A., & Lehert, Ph. (2001). Acamprosate during and after acute alcohol withdrawal: a double–blind placebo-controlled study in Spain. *Alcohol and Alcoholism, 36,* 413-418.

Guardia, J., Caso, C., Arias, F., Gual, A., Sanahuja, J., Ramírez, M., … Casas, M. (2002). A double-blind, placebo-controlled study of naltrexone in the treatment of alcohol-dependence disorder. Results from a multicenter clinical trial. *Alcoholism Clinical and Experimental Research, 26*, 1381–1387.

Guardia Serecigni, J. (2008). Alcoholismo. Guías Clínicas de Socidrogalcohol basadas en la Evidencia Científica. 2ª Edición. Barcelona: Socidrogalcohol.

Guardia Serecigni, J. (2009). Avances en el tratamiento farmacológico del alcoholismo y de la enfermedad adictiva, una vez finalizado el tratamiento de la abstinencia aguda. *JANO, 4*, 21-33.

Guardia Serecigni, J. (2011). Cambio de paradigma en el tratamiento del alcoholismo de baja gravedad. *Adicciones, 23*, 299-316.

Guardia Serecigni, J. (2012). Tratamiento del Alcoholismo. En F. Pascual Pastor, & J. Guardia Serecigni (Eds.). *Monografía sobre el Alcoholismo*, pp. 415-442. Barcelona: Socidrogalcohol.

Kornet, M., Goosen, C., & Van Ree, J. M. (1990). The effect of interrupted alcohol supply on spontaneous alcohol consumption by rhesus monkeys. *Alcohol and Alcoholism, 25,* 407-412.

Naranjo, C. A., Dongier, M., & Bremner, K. E. (1997) Long-acting injectable bromocriptine does not reduce relapse in alcoholics. *Addiction*, *92*, 969-978.

O'Brien, C. P., Volpicelli, L. A., & Volpicelli, J. R. (1996). Naltrexone in the treatment of alcoholism: A clinical review. *Alcohol, 13,* 35-39.

O'Malley, S. S., Jaffe, A., Chang, G., Schottenfeld, R. S., Meyerm R. E., & Rounsaville, B. (1992). Naltrexone and coping skills therapy for alcohol dependence a controlled study. *Archives of General Psychiatry, 49,* 881-887.

Pettinati, H. M., O'Brien, C. P., Rabinowitz, A. R., Wortman, S. P., Oslin, D. W., Kampman, K. M., & Dackis, C. A. (2006). The status of naltrexone in the treatment of alcohol dependence: specific effects on heavy drinking. *Journal of Clinical Psychopharmacology, 26*, 610-625.

Rösner, S., Hackl-Herrwerth, A., Leucht, S., Vecchi, S., Srisurapanont, M., & Soyka, M. (2010). Opioid antagonists dor alcohol dependence. *Cochrane Database Systematic Review, 8*, CD001867. doi: 10.1002/14651858.CD001867.pub2.

Sinclair, J. D. (2001). Evidence about the use of naltrexone and for different ways of using it in the treatment of alcoholism. *Alcohol and Alcoholism*, *36*, 2-10.

Van den Brink, W., Aubin, H. J., Bladström, A., Torup, L., Gual, A., & Mann, K. (2013). Eficacia de nalmefeno administrado a demanda en pacientes con dependencia del alcohol con un nivel de consumo de riesgo como mínimo alto: resultados de un análisis de subgrupos de dos estudios controlados y aleatorizados a 6 meses. *Alcohol and Alcoholism, 48,* 570-578.

Van den Brink, W., Sørensen, P., Torup, L., Mann, K., Gual, A., for the SENSE Study Group. (2014). Long-term efficacy, tolerability and safety of nalmefene as-needed in patients with alcohol dependence: A 1-year, randomised

controlled study. *Journal of Psychopharmacology*, 28, 733-744. doi: 10.1177/026988111452/362.

Volpicelli, J. R., Alterman, A. I., Hayashida, M., & O'Brien, C. P. (1992). Naltrexone in the treatment of alcohol dependence. *Archives of General Psychiatry*, *49*, 876-880.

Do cigarette smoking and alcohol consumption associate with cannabis use and problem gambling among Spanish adolescents?

¿El consumo de cigarrillos y alcohol se relaciona con el consumo de cánnabis y el juego problema en adolescentes españoles?

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Abstract

This article examined the relationship between cigarette smoking or alcohol consumption and cannabis use and problem gambling among a random and representative sample of 1447 Spanish adolescents (797 males and 650 females with an average of 12.8 years). An ad-hoc questionnaire was used to assess cigarette smoking, alcohol consumption (beer, wine and spirits) and cannabis use. Gambling was assessed with the South Oaks Gambling Screen Revised for Adolescents (SOGS-RA). Results indicated a positive and significant association between cigarette smoking and alcohol consumption and the two aforementioned variables. A larger percentage of cigarette smokers and drinkers was found among those participants who had consumed cannabis before or scored significantly in problem gambling. Additionally, multiple regression analysis confirmed that both cigarette smoking and alcohol consumption (beer and wine) were the most determinant variables for cannabis use and problem gambling.

Key words: smoking, alcohol, cannabis, gambling, adolescents.

Resumen

Este estudio examinó la relación entre consumo de tabaco y alcohol, y consumo de cannabis y juego problema en una muestra aleatoria y representativa de 1.447 adolescentes españoles (797 varones y 650 mujeres con una media de edad de 12,8 años). Los participantes respondieron a un cuestionario elaborado a tal efecto que recogía información acerca del consumo de cigarrillos, de alcohol (cerveza, vino y licores) y cannabis. El juego se evaluó con el South Oaks Gambling Screen Revised for Adolescents (SOGS-RA). Los resultados indicaron una asociación positiva y significativa entre el consumo de tabaco y alcohol y las dos variables analizadas. Se halló un mayor porcentaje de fumadores y consumidores de alcohol entre los que habían consumido cánnabis en alguna ocasión así como entre los jugadores problema. Además, el análisis de regresión lineal múltiple mostró que tanto el consumo de cigarrillos como de alcohol (cerveza y vino) se relacionaban positivamente con el inicio en el consumo de cánnabis y con una mayor implicación en el juego.

Palabras clave: tabaco, alcohol, cannabis, juego, adolescentes.

Received: July 2014; Accepted: October 2014

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Cigarette smoking is considered a substantial public health problem and the main global cause of preventable death that is also affecting young people (WHO, 2013). Recently, cigarette consumption has decreased globally, although an increase has been observed among female adolescents in the last Spanish National Survey on Drugs in the School Population (Plan Nacional sobre Drogas, 2011). Given that nicotine is one of the most addictive substances, smoking in adolescence, even in a sporadic fashion, may lead to a serious addiction in adulthood with substantial adverse long-term health consequences (Edwards, 2004; Kandel & Merrick, 2003). Moreover, if in addition to tobacco use there is the consumption of other substances, as can be alcohol use, this can have synergistic effects which increase the risks tobacco has in health (Burke, Hunter, Croft, Cresanta, & Berenson, 1988) or can cause other effects such as poor academic performance (Inglés et al., 2013).

Likewise, the consumption of alcohol has considerable social and health repercussions, and, its use is also increasing among adolescents (Plan Nacional sobre Drogas, 2011). Currently, in Spain the most common pattern of alcohol use involves abusive drinking (binge drinking) on weekends with recreational purposes (Ministerio de Sanidad, Servicios Sociales e Igualdad & Instituto Nacional de Estadística, 2012). Smoking and drinking among adolescents is one of the main concerns for public healthcare systems in most developed countries. Smoking most often occurs in combination with alcohol use; in Spain, as in other countries, alcohol and tobacco are the most consumed legal drugs in adolescence (Hoffman, Welte & Barnes, 2001; Míguez & Becoña, 2006; Orlando, Tucker, Ellickson & Klein, 2005; Plan Nacional sobre Drogas, 2011; Piko, 2006; Reed, McCabe, Lange, Clapp, & Shillington, 2010).

As regards illegally traded substances, cannabis is the substance most widely consumed in Europe (European Monitoring Centre for Drugs and Drug Addiction [EMCDDA], 2011). The last Spanish National Survey on Drugs in the School Population (*Encuesta Estatal sobre uso de Drogas en Estudiantes de Enseñanzas Secundarias*) reveals that among secondary school students surveyed (aged 14 to 18), 17.2% reported having consumed this substance in the previous 30 days (Plan Nacional sobre Drogas, 2011). This implies an increase in the number of adolescents consuming more than one substance at the same time. Alcohol, tobacco and cannabis use is highly prevalent among young people in Spain as compared with most European countries (European Monitoring Centre for Drugs and Drug Addiction [EMCDDA], 2011), with polydrug use being the most prevalent pattern (Plan Nacional sobre Drogas, 2011).

Cigarette smoking and cannabis use often co-occur (Brook, Lee, Finch, & Brown, 2010; Degenhardt, Hall, & Lynskey, 2001). This comorbidity is significant, in that, in addiction to the separate effects of tobacco and cannabis use on psychosocial functioning, concurrent use of these substances can have a cumulative effect on physical functioning (Peters, Budney, & Carroll, 2012). Several mechanisms may explain this strong relatedness. Some researchers have hypothesized that both tobacco and alcohol serve as "gateways" to the use of the illicit drugs initiating with marijuana and progressing to "hard" drugs like cocaine (Kandel and Yamaguchi, 2002; Kandel, Yamaguchi, & Klein, 2006). Tobacco (Agrawal, Silberg, Lynskey, Maes, & Eaves, 2010; Korhonen, Prince van Leeuwen, & Reijneveld, 2010) and alcohol (Willner, 2001) onset have been linked to a higher propensity to start and maintain cannabis use (Fergusson, 2008). Nevertheless, certain researchers (e.g. Patton, Coffey, Carlin, Sawyer, & Lynskey, 2005) have hypothesized that, in some cases, cannabis use may lead to tobacco initiation ("reverse gateway theory").

Another issue among adolescents is *problem gambling* (in this case an addictive behaviour without substance), with an estimated prevalence higher than that of the adult population (Shaffer & Hall, 1996). Problem gambling is circumscribed to non-clinical populations, especially in studies carried out in order to estimate prevalence in the general population. Problem gamblers experience difficulties, originated from their gambling behaviour, which have an impact on many aspects of their daily life (for instance, academic performance, relationships with parents or peers, etc.*)*. One of the consequences of problem gambling in children and adolescents is that it increases the likelihood of the development of pathological gambling in adults. Therefore, it is important to detect it at an early age. Among the variables that have been associated with problem and pathological gambling are alcohol use (Barnes, Welte, Hoffman, & Tidwell, 2009) and/or smoking (Becoña, 2009; McGrath, Barrett, Stewart, & McGrath, 2012). This is due, in part, to the fact that gambling takes place in contexts in which substances such as tobacco and alcohol are available (Arbinaga, 2000).

Different studies have focused on the analysis of the co-occurrence between cigarette smoking or alcohol use and some cannabis use or problem gambling but no research has been carried out in adolescents.

The aim of the present *ex post facto* study was to explore the relationship between tobacco or alcohol use and cannabis use, assess whether the same kind of relationship can be established with problem gambling; and finally, to analyze the level of association between consumption of a legal substances (tobacco or alcohol) and initial consumption of an illegal substance (cannabis) or engagement in gambling. It was hypothesized that there would be a positive and significant relationship between smoking or alcohol use and cannabis experimentation as well as with problem gambling.

Method

Participants

By means of a probabilistic sampling method, a random and representative sample of 1,447 participants aged 11 to 16 from the school population in Galicia (a region in nor-

thern Spain) was recruited, stratified by province and size of municipality. The sample, who participated in a cross-sectional descriptive study, was made up of 650 females and 797 males, with an average of 12.8 years of age (*SD* = 1.2).

Data collection

The study was approved by the regional education authorities of Galicia (Spain) as well as by headmasters and school councils. This was a clustered randomized study. The sample was obtained by random selection of schools from among all public and private schools, using a random number table and with stratification by province and by municipality size (over 50,000 inhabitants, from 20,001 to 50,000 inhabitants, from 10,001 to 20,000 inhabitants, from 5,000 to 10,000, and under 5,000 inhabitants), giving a total of 17 schools selected from different cities and towns in the region. In schools in which there was more than one class for each grade, the class to be included in the study was also randomly selected. In-class anonymous questionnaires were self-administered within a single class period without the presence of the teacher. Participation in this study was voluntary. Data were collected by two trained psychologists. Overall survey response rate was 92.41%.

Measures

For each participant, demographic variables (age, sex), reported cigarette consumption, and alcohol and cannabis use were recorded by an ad-hoc instrument.

The smoking, alcohol and cannabis use questionnaire comprises 17 items assessing the use of these substances in terms of frequency, quantity, and aged of initial use. Consumption of each substance was assessed with the same set of questions. Participants were asked whether they had ever used alcohol, cannabis, or tobacco. In the case of alcohol, type of drink (beer, wine and spirits) was also recorded. If a participant answered "Yes", information on frequency of use was obtained. Response choices ranged from *never smoked/drank this beverage in my life* to *every day* on a 5-point scale (considering the categories "never in my life", "once or twice in my life" "sometimes," "very often" and "daily"). Questions were asked about usual quantities of each substance, i.e., daily and weekly mean consumption (e.g. with regard to beer students were asked "Have you ever drunk beer?" If so, "How many beers do you drink weekly?" and "How many beers do you drink daily?").

In order to assess problem gambling, Winters, Stinchfield, and Fulkerson's (1993) South Oaks Gambling Screen Revised for Adolescents (SOGS-RA) was administered. This questionnaire comprises 12 items, each with two response options (YES/NO). Scores obtained with the SOS-RA provided us with three categories: non-gambler or non-problem gambler (0 or 1 points), at risk gambler (2 or 3 points), and problem gambler (4 points or over). Internal consistency reliability within our sample was good (Cronbach's alpha = 0.83).

Statistical analysis

SPSS Version 18.0 for Windows was used for all the analyses, and statistical significance was considered when $p < 0.05$. The relationship between categorical variables was analyzed by means of the chi-square test, in those cases in which chi-square was significant, Cramer´s V coefficients were calculated for estimating the effect size. Differences in continuous variables were assessed by means of independent Student´s *t* test. Stepwise multiple linear regression analysis was used to examine the association between dependent variables cannabis use and problem gambling (scores on the SOGS-RA) and independent variables age, daily and weekly cigarette consumption, and daily and weekly beer, wine, and spirits consumption.

Results

Tobacco, alcohol and cannabis use

A total of 27.4% (*n*= 397) of the sample reported having smoked tobacco at least once. Of these, 5.6% (*n*= 81) reported smoking daily [5.9% (*n*= 47) were male and 5.2% (*n*= 34) were female (χ^2 (1) = 0.188, p = 0.665)]. The prevalence of weekly smokers was 9.3% (*n*= 135). Of those reporting having smoked at least once, 14.9% said they had smoked just once or twice in their lives, 6.3% smoked sometimes and 3.3% very often. Mean age at which these young people tried their first cigarette was 10.7 (*SD*= 2.3) years, and 94.4% of first contacts with tobacco were between the ages of 10 and 13; males starting earlier than females (10.2 vs. 11.3 years); gender difference was statistically significant (*t*= 3.84, $p< 0.05$).

Regarding to alcohol, 36.4% (*n*= 526) of participants said they had tried some alcoholic beverage, and 7.3% (*n*= 105) recognized drinking alcohol every week. Of the drinks assessed, beer was the most widely consumed (Table 1). Concerning the relationship between alcohol use and smoking, we found a significantly higher percentage of alcohol users among the daily smokers for each of the drinks assessed (Table 2). Thus, 45.7% of the smokers drank beer weekly, compared to 4.5% of the non-smokers (χ^2 (1) = 205.70, $p < 0.001$); wine is drunk by 23.5% of the smokers but by just 3.5% of the non-smokers (χ^2 (1) = 68.86, $p < 0.001$). As far as spirits are concerned, the percentages were 42.0% vs. 2.9% (χ^2 (1) = 240.25, $p < 0.001$).

Taking into account the frequency of smoking, there was a significantly higher percentage of alcohol users among those who reported smoking daily compared to those who smoked sporadically. For each one of the drinks assessed (Figure 1), the greater the involvement in smoking (considering the categories "never," "sometimes," and "daily"), the higher the percentage of alcohol users. Differences between groups were statistically significant for each one of the drinks: beer ($\chi^2(2) = 185.52$, $p < 0.001$); wine ($\chi^2(2) = 45.09$, $p < 0.001$) and spirits ($\chi^2(2) = 221.84$ $p < 0.001$).

Table 1.
Characteristics of sample

	n	%
Gender		
Male	797	55.1
Female	650	44.9
Tobacco use		
At least once	397	27.4
Daily smokers	81	5.6
Weekly smokers	105	7.3
Alcohol use		
Beer weekly	98	6.8
Wine weekly	67	4.6
Spirits weekly	74	5.1
Cannabis use		
At least once	32	2.2
Gambling		
Non-gambler	1234	85.3
At-risk gambler	147	10.1
Problem gambler	66	4.6

Table 2.
Relationship between use of tobacco and alcohol, cannabis and gambling (%)

	Smoker	Non-smoker	χ^2	Cramer's V
Alcohol use				
Beer			205.70***	.38***
No	54.3	95.5		
Yes	45.7	4.5		
Wine			68.86***	.22***
No	76.5	96.5		
Yes	23.5	3.5		
Spirits			240.25***	.41***
No	58.0	97.1		
Yes	42.0	2.9		
Cannabis use			223.13***	.39***
No	74.1	99.2		
Yes	25.9	0.8		
Gambling			45.40***	.18***
Non-gambler	4.2	95.8		
At-risk gambler	9.5	90.5		
Problem gambler	22.7	77.3		

***p< .001

There was a higher percentage of participants who had used cannabis at least once (Table 2) among the smokers (25.9%) than among the non-smokers (0.8%) (χ^2 (1) = 223.25, $p < 0.001$). In this case there were no daily users. The percentage of participants who tried cannabis (Figure 2) is higher among daily smokers (27.9% of the daily smokers, as against 4.5% of the occasional smokers and 0.4% of the non-smokers). Likewise, there was a higher percentage of participants who had used cannabis at least once among alcohol users (Table 3) for each one of the drinks assessed ($p < 0.001$).

Tobacco and alcohol use and problem gambling

The results indicated that 85.3% of the participants belonged to the "non-gambler" category, 10.1% to that of "at risk gambler" and 4.6% to that of "problem gambler" (Table 1). A significant association ($p < .001$) was found between type of gambler and smoker status ("non-smoker" vs. "smoker") and drinker status ("non-drinker" vs. "drinker"). The percentage of smokers in the "non-gambler" group was 4.2%; among "at-risk gamblers" it reached 9.5%; and in the "problem gambler" group it peaked at 22.7%. Thus, the percentage of smokers in the "problem gambler" category is double that in the "at-risk gambler" category and in this latter category it is again twice than that found in the "non-gambler" category. Thus, the percentage of smokers is four times higher in the "problem gambler" category than in the "non-gambler" one (Table 2).

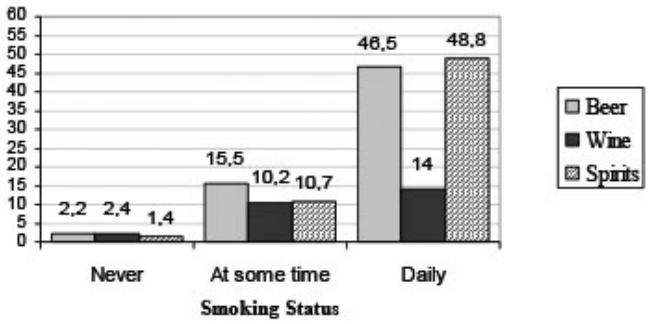

Figure 1. Percentage of weekly alcohol consumers for different beverages, according to smoking frequency

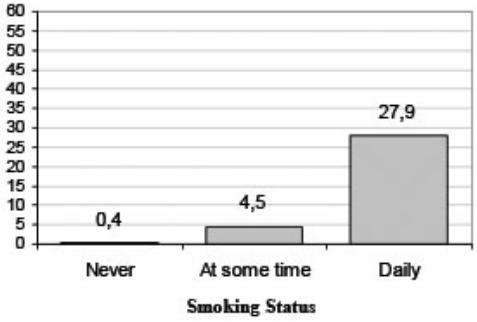

Figure 2. Use of cannabis at least once (%) according to smoking frequency

Table 3.
Relationship between use of alcohol (beer, wine and spirits), cannabis and gambling (%)

	Beer		χ^2	Cramer's V	*Wine*		χ^2	Cramer's V	*Spirits*		χ^2	Cramer's V
	No	Yes			No	Yes			No	Yes		
Cannabis use			199.08***	0.37***			40.90***	0.16***			176.34***	0.34***
No	94.6	5.4			95.9	4.1			96.0	4.0		
Yes	31.3	68.8			71.9	28.1			43.8	56.3		
Gambling			61.93***	0.21***			17.97***	0.11***			26.15***	0.13***
Non-gambler	95.1	4.9			96.0	4.0			95.8	4.2		
At-risk gambler	86.4	13.6			94.6	5.4			93.2	6.8		
Problem gambler	72.7	27.3			84.8	15.2			81.8	18.2		

***p< .001

Table 4.
Results of multiple regression analysis

Model	B	Standard error	Beta	t	p	C.I. (95%)
CANNABIS USE						
Number of daily cigarettes	0.062	0.004	0.387	15.97	0.001	0.054 -0.069
Weekly beer consumption	0.060	0.005	0.293	12.09	0.001	0.050 -0.070
Weekly wine consumption	0.044	0.006	0.161	6.92	0.001	0.031 -0.056
Constant	1.003	0.005		199.22		0.993 -1.013
PROBLEM GAMBLING (scores SOGS-RA)						
Weekly beer consumption	0.341	0.033	0.265	10.44	0.001	0.277 -0.405
Weekly wine consumption	0.096	0.044	0.056	2.17	0.030	0.009 -0.182
Number of daily cigarettes	0.056	0.026	0.056	2.11	0.035	0.004 -0.108
Constant	0.529	0.035		15.09	0.001	0.460 -0.597

Concerning the relationship between alcohol use and problem gambling, we found a significantly higher percentage of alcohol users among the problem gamblers ($p < 0.001$) for each of the drinks assessed (Table 3). The percentage of smokers and alcohol users rises with increasing involvement in gambling.

Quantifying the relationship between cannabis use and problem gambling and significant variables

We carried out two stepwise multiple linear regression analysis in which we included the variables age, number of cigarettes smoked per day, alcohol used (beer, wine and spirits), in order to predict cannabis use and problem gambling. The first multiple regression analysis (Table 4) explained the 25% of the variance with three significant variables of a greater likelihood of cannabis use: higher levels of daily cigarette consumption (*beta*= 0.38; *F*= 255.20, $p< 0.001$), higher levels of weekly beer consumption (*beta*= 0.29; *F*= 213.56, $p< 0.001$), and higher levels of weekly wine consumption (*beta*= 0.16; *F*= 162.96, $p< 0.001$). In the first step, daily cigarette consumption accounted for 15% of the variance, in step 2, weekly beer consumption added an additional 8% of the variance and, in step 3, weekly wine consumption explained 2% of the variance. Regarding the predictors of scores obtained with the SOGS-RA, the regression model explained a lower percentage of variance (7%) with three significant variables: higher levels of weekly beer consumption (*beta*= 0.26; *F*= 108.98, $p< 0.001$), higher levels of weekly wine consumption (*beta*= 0.05; *F*= 56.94, $p< 0.001$) and higher levels of daily cigarette consumption (*beta*= 0.05; *F*= 39.58, $p< 0.001$).

Discussion

The results of this study indicated that smoking in the students of this sample was related to other addictive behaviours. It was observed how among smokers there is a higher percentage of users of alcoholic beverages, so that the greater the involvement in smoking, the greater the use of

alcohol. This relationship was found for all the alcoholic drinks that were assessed (beer, wine and spirits). Thus, as other studies have confirmed, use of cigarettes by adolescents most often co-occurs with use of alcohol, that is, both substances are used concurrently (Hoffman, Welte, & Barnes, 2001; Reed et al., 2010). Likewise, among the smokers, 25.9% reported having used cannabis on some occasion, compared to 0.8% of non-smokers (Table 2). The same positive relationship was found between alcohol consumption and cannabis use. For example, 68.8% of beer drinkers reported having used cannabis on some occasion, compared to 31.3% among those who did not drink beer (Table 3). In accordance with previous studies indicating that early onset of smoking and drinking increases the risk of subsequent use of cannabis or other drugs (Agrawal et al., 2010; Becoña et al., 2011; Fergusson, 2008; Korhonen et al., 2008; 2010; Prince van Leeuwen et al., 2011; Willner, 2001), our results show that tobacco and alcohol use were associated with cannabis use, as hypothesized.

Adolescence is a critical developmental phase that opens a window of vulnerability, especially with regard to substance use. Normally, cannabis use initiation occurs during this life stage. Early onset of cannabis use in adolescence has been associated with a higher risk of experimenting with other substances (Agrawal et al., 2006) and of developing a substance use disorder or dependence (Perkonigg et al., 2008), which makes early detection of alcohol and cigarette use very important.

The second goal of this study was to determine the relationship between tobacco or alcohol use and problem gambling. The results showed a clear association between a greater involvement in gambling and greater cigarette and alcohol use, with clear differences in smoking and drinking between problem gamblers and those who either do not gamble at all or those whose gambling does not reach the level of seriousness of the first group (Tables 2 and 3). Thus, higher percentages of alcohol and cigarette users were found among problem gamblers compared to the other groups, and their daily and weekly cigarette consumption is also higher. Likewise, as hypothesized, in this study both tobacco and alcohol use were related to problem gambling.

Although high rates of comorbidity between smoking and/or drinking and gambling have been documented (Becoña & Míguez, 2001; McGrath & Barret, 2009), little empirical attention has been directed towards investigating the exact nature of this relationship, i.e., how smoking might affect gambling or vice versa. A growing body of literature suggests that smoking and gambling might share similar environmental influences (McGrath & Barret, 2009). For example, in Spain, the sale of tobacco, alcohol and access to gambling premises is prohibited to minors. However, the reality is different, as the prevalence of these behaviours in young people under the age of 18 is high, which is largely the consequence of both the high accessibility to various forms of gambling and the availability of tobacco and alcohol (Harper, 2003). Therefore, there is a need for a strict application of the law.

The results of the present study are consistent with previous research that found an association between adolescent tobacco and alcohol use, drug use and deviant behaviour in general (e.g., Brook, Balka, Ning, Whiteman, & Finch, 2006; Brook et al., 2006; Wanner, Vitaro, Ladouceur, Brendgen, & Tremblay, 2006), described as adolescent problem behaviour syndrome or general deviance syndrome (McGee y Newcomb, 1992; Welte & Barnes, 1987). Concurrent consumption of at least two substances is the most common pattern in Spain (Plan Nacional de Drogas 2011; 2012). Multi-substance use can be understood as an attempt to enhance or compensate the effects of different drugs or simply experience new sensations. In any case, this tendency poses more health risks, social issues and higher treatment attrition.

In this study, it was not possible to establish causal relationships between cigarette smoking and alcohol consumption, on the one hand, and cannabis use and problem gambling on the other. Future research should explore in more depth the possibility of causal connections. Attention should also be paid to previous behaviours and personality factors that could predispose individuals to a series of addictive behaviours (Becoña et al., 2012; Rush, Becker, & Curry, 2009). It is important to analyze this association to determine whether we can speak of a simple relationship, a relationship modulated by other variables, or a causal relationship. The measures to adopt will depend on the nature of these relationships. Nevertheless, it is clear that interventions have to be carried at an early age because the prevalence of smoking and alcohol and cannabis use increases with age during adolescence (Duncan, Gau, Duncan, & Strycker, 2011; Plan Nacional sobre Drogas, 2011).

The present findings should be considered in the context of several limitations. Firstly, this study was cross-sectional and no conclusions about causality can be drawn from our results. It would be necessary to replicate it and carry out a long-term follow-up in order to draw some firmer conclusions. Secondly, the validity of the self-report data in this study cannot be verified, therefore it should be considered with caution (Becoña & Míguez, 2006; Botvin, Botvin, Renick, Filazzola, & Allegrante, 1984), since response bias might have occurred (e.g., tendency to endorse problematic behaviours or tendency to under-report problem behaviours). Although anonymity was guaranteed, a social desirability effect cannot be ruled out, although it must be said that this methodology (main outcome measure: self-reported status at survey) is the most used in this type of studies (Villalbí, Suelves, Saltó y Cabezas, 2011). In any case, the study also has several strengths. It was carried out on a very large sample of young people aged 11 to 16 years. Furthermore, we should point out that whereas the majority of studies focus on the assessment of the relationship between two substances (either tobacco

and/or alcohol and cannabis), here we have also assessed relationships with problem gambling.

In sum, the results of the current study provide a contribution to the literature on the associations between smoking and drinking behaviours and concurrent conditions in adolescents, as well as congruent data with the gateway hypothesis to cannabis consumption and problem gambling behaviour. However, more research is necessary to understand the multi-faceted association between smoking and drinking and the variables analyzed, since both are not isolated behaviours, but rather these are associated with other risk behaviours from very early ages.

Acknowledgements

This research was supported by Grant No. XUGA21105B98 of the Secretaría de Investigación y Desarrollo de la Xunta de Galicia (Spain).

Conflicts of interest

The authors declare no conflict of interest concerning this article.

References

Agrawal A., Grant J.D., Waldron M., Duncan, A.E., Scherrer, J.F., Lynskey, … Heath, A.C. (2006). Risk for initiation of substance use as a function of age of onset of cigarette, alcohol and cannabis use: Findings in a Midwestern female twin cohort. *Preventive Medicine, 43*, 125-128. doi:10.1016/j.ypmed.2006.03.022

Agrawal, A., Silberg, J.L., Lynskey, M.T., Maes, H.H., & Eaves, L.J. (2010). Mechanisms underlying the lifetime co-ocurrence of tobacco and cannabis use in adolescent and young adult twins. *Drug and Alcohol Dependence, 108*, 49-55.

Arbinaga, F. (2000). Consumo de drogas y juego patológico en Punta Umbría (Huelva) [Drug use and pathological gambling in Punta Umbría (Huelva)]. *Revista Española de Drogodependencias, 25*, 301-320.

Barnes, G.M, Welte, J.W, Hoffman, J.H., & Tidwell, M.C. (2009) Gambling, alcohol, and other substance use among youth in the United States. *Journal of Studies on Alcohol and Drugs, 70*, 134-142.

Becoña, E. (2009). Spain. In G. Meyer, T. Hayer, & M. Griffiths (Eds.), *Problem gambling in Europe. Challenges, prevention, and interventions* (pp. 281-299). New York: Springer.

Becoña, E., López-Durán, A., Fernández del Río, E., Martínez, U., Osorio, J., Fraga, J., … Domínguez, M.N. (2011). Borracheras, conducción de vehículos y relaciones sexuales en jóvenes consumidores de cocaína y éxtasis [Drunkness, driving and sexual relations in young cocaine and ecstasy users]. *Adicciones, 23,* 205-218.

Becoña, E., López-Durán, A., Fernández del Río, E., Martínez, U., Fraga, J., Osorio, J., …. Domínguez, M. N. (2012). Can we predict psychostimulant use in youths? A study with structural equation modeling analysis. *Adicciones, 24*, 339-346.

Becoña, E., & Míguez M. C. (2001). Juego problema y juego de riesgo en adolescentes: su relación con el consumo de tabaco y alcohol. *Adicciones, 13*, 279-288.

Becoña, E., & Míguez, M. C. (2006). Concordance of self-reported abstinence and measurement of expired air carbon monoxide in a self-help smoking cessation treatment. *Psychological Reports, 99*, 125-130. doi: 10.2466/pr0.99.1.125-130

Botvin, E. M., Botvin, G. J., Renick, N.L., Filazzola, A. D., & Allegrante, J. P. (1984). Adolescents' self-reports of tobacco, alcohol, and marijuana use: examining the comparability of video tape, cartoon and verbal bogus-pipeline procedures. *Psychological Reports, 55*, 379-386. doi: 10.2466/pr0.1984.55.2.379

Brook, J. S., Balka, E. B., Ning, Y., Whiteman, M., & Finch, S. J. (2006). Smoking involvement during adolescence among African Americans and Puerto Ricans: Risks to psychological and physical well-being in young adulthood. *Psychological Reports, 99*, 421-438. doi: 10.2466/pr0.99.6.421-438

Brook, J. S., Lee, J. Y., Finch, S. J., & Brown E. N. (2010). Course of comorbidity of tobacco and marijuana use: Psychosocial risk factors. *Nicotine & Tobacco Research, 12*, 474-482. doi: 10.1093/ntr/ntq027

Burke, G. L., Hunter, S. M., Croft, J. B., Cresanta, J. L., & Berenson, G. S. (1988). The interaction of alcohol and tobacco use in adolescents and young adults: Bogalusa Heart Study. *Addictive Behaviors, 13,* 387-393. doi: 10.1016/0306-4603(88)90046-9

Degenhardt, L., Hall, W., & Lynskey, M. (2001). The relationship between cannabis use and other substance use in the general population. *Drug and Alcohol Dependence, 64*, 319-327. doi: 10.1016/s0376-8716(01)00130-2

Duncan, S. C., Gau, J. M., Duncan, T. E., & Strycker, L. A. (2011). Development and correlates of alcohol use from ages 13-20. *Journal of Drug Education, 41*, 235-252. doi: 10.2190/DE.41.3.a

Edwards, R. (2004). The problem of tobacco smoking. *British Medical Journal, 328*, 217-219. doi: 10.1136/bmj.328.7433.217

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) (2011). *Annual Report 2011. The state of the drugs problem in Europe*. Luxembourg: Publications Office of the European Union.

Fergusson, D.M., Boden, J.M., & Horwood, L.J. (2008). The developmental antecedents of illicit drug use: Evidence from a 25-year longitudinal study. *Drug and Alcohol Dependence, 96*, 165-177. doi: 10.1016/j.drugalcdep.2008.03.003

Harper, T. (2003). Smoking and gambling: a trance inducing ritual. *Tobacco Control, 12*, 231-233. doi: 10.1136/tc.12.2.231

Hoffman, J. H., Welte, J. W., & Barnes, G. M. (2001). Co-occurrence of alcohol and cigarette use among adolescents. *Addictive Behaviors, 26*, 63-78. doi: 10.1016/S0306-4603(00)00089-7

Inglés, C.J., Torregrosa, M.S., Rodríguez-Marín, J, García del Castillo, J.A., Gázquez, J.J., García-Fernández, J.M., & Delgado, B. (2013). Alcohol and tobacco use and cognitive-motivational variables in school settings: Effects on academic performance in Spanish adolescents. *Adicciones, 25*, 63-70.

Kandel, I., & Merrick, J. (2003). Smoking and adolescence. *International Journal of Adolescent Medicine and Health*, *15*, 365-368. doi: 10.1515/IJAMH.2003.15.4.365

Kandel, D. B., & Yamaguchi, K. (2002). Stages of drug involvement in the U.S. population. In D. B. Kandel (Ed.), *Stages and pathways of drug involvement: Examining the gateway hypothesis* (pp. 65-89). Cambridge: Cambridge University Press.

Kandel D.B., Yamaguchi K., & Klein L.C. (2006).Testing the gateway hypothesis. Addiction, 101, 470–472. doi: 10.1111/j.1360-0443.2006.01426.x

Korhonen, T., Prince van Leeuwen, A., Reijneveld, S.A., Ormel, J., Verhulst, F.C., & Huizink, A.C. (2010). Externalizing behavior problems and cigarette smoking as predictors of cannabis use: The TRAILS study. *Journal of the American Academy of Child and Adolescent Psychiatry, 49*, 61-69.

McGee, L., & Newcomb, M.D. (1992). General deviance syndrome. Expanded hierarchical evaluations at four ages from early adolescence to adulthood. *Journal of Consulting and Clinical Psychology, 60*, 766-776.

McGrath, D. S., & Barrett, S. P. (2009). The comorbidity of tobacco smoking and gambling: a review of the literature. *Drug Alcohol Review, 28,* 676-681.doi: 10.1111/j.1465-3362.2009.00097.x

McGrath, D. S., Barrett, S. P., Stewart, S. H., & McGrath, P. R. (2012). A comparison of gambling behavior, problem gambling indices, and reasons for gambling among smokers and nonsmokers who gamble: Evidence from a Provincial Gambling Prevalence Study. *Nicotine & Tobacco Research, 14*, 833-839. doi: 10.1093/ntr/ntr294

Míguez, M. C., & Becoña, E. (2006). Consumo de tabaco y alcohol en la población escolar de Galicia [Smoking and alcohol use in the school population of Galicia]. *Revista Española de Drogodependencias, 31*, 46-56.

Ministerio de Sanidad, Servicios Sociales e Igualdad, & Instituto Nacional de Estadística (2012). *National Health Survey of Spain 2011/12.*

Orlando, M., Tucker, J.S., Ellickson, P.L, & Klein, D.J. (2005). Concurrent use of alcohol and cigarettes from adolescence to young adulthood: an examination of developmental trajectories and outcomes. *Substance Use & Misuse, 40,* 1051-1069. doi: 10.1081/JA-200030789

Patton, G.C, Coffey, C., Carlin, J.B., Sawyer, S.M., Lynskey, M. (2005). Reverse gateways? Frequent cannabis use as a predictor of tobacco initiation and nicotine dependence. *Addiction. 100*, 1518-1525. doi: 10.1111/j.1360-0443.2005.01220.x

Perkonigg, A., Goodwin, R.D., Fiedler, A, Behrendt, S., Beesdo, K., Lieb, R., Wittchen, H.U. (2008).The natural course of cannabis use, abuse and dependence during the first decades of life. *Addiction, 103*, 439-449. doi: 10.1111/j.1360-0443.2007.02064.x

Peters, E. N., Budney, A.J., & Carroll, K.M. (2012). Clinical correlates of co-ocurring cannabis and tobacco use: a systematic review. *Addiction, 107*, 1404-1417. doi: 10.1111/j.1360-0443.2012.03843.x

Piko, B. F. (2006). Adolescent smoking and drinking: The role of communal mastery and other social influences. *Addictive Behaviors, 31*, 102-114. doi: 10.1016/j.addbeh.2005.04.013

Plan Nacional sobre Drogas (2011). *Encuesta Estatal sobre uso de Drogas en Estudiantes de Enseñanzas Secundarias. ESTUDES, 2010* [*National Survey on Drug Use among Secondary School Students*]. Madrid: Delegación del Gobierno para el Plan Nacional sobre Drogas.

Plan Nacional sobre Drogas (2012). *Encuesta sobre alcohol y drogas en población general en España* [Survey on alcohol and drugs in the general population in Spain] (EDADES 2011-2012). Madrid: Ministerio de Sanidad, Servicios Sociales e Igualdad y Secretaría de Estado de Servicios Sociales e Igualdad.

Prince van Leeuwen, A., Verhulst, F.C., Reijneveld, S.A., Vollebergh, W.A., M., Ormel, J., & Huizink, A.C. (2011). Can the Gateway Hypothesis, the Common Liability Model and/ or the Route of Administration Model predict initiation of cannabis use during adolescence? A survival analysis-The TRAILS Study. *Journal of Adolescence, 48,* 73-78.

Reed, M. B., McCabe, C., Lange, J. E., Clapp, J. D., & Shillington, A. M. (2010). The relationship between alcohol consumption and past-year smoking initiation in a sample of undergraduates. *The American Journal of Drug and Alcohol Abuse, 36*, 202-207. doi: 10.3109/00952990.2010.493591

Rush, Ch. C., Becker, S. J., & Curry, J. F. (2009). Personality factors and styles among college students who binge eat and drink. *Psychology of Addictive Behaviors, 23*, 140-145. doi: 10.1037/a0013167

Shaffer, H. J., & Hall, M. N. (1996). Estimating the prevalence of adolescent gambling disorders: A quantitative synthesis and guide toward standard gambling nomenclature. *Journal of Gambling Studies, 12*, 193-214. doi:10.1007/BF01539174

Wanner, B., Vitaro, F., Ladouceur, R., Brendgen, M., & Tremblay, R. E. (2006). Joint trajectories of gambling, alcohol and marijuana use during adolescence: A person-variable-centered developmental approach. *Addictive Behaviors, 31*, 566-580. doi: 10.1016/j.addbeh.2005.05.037

Villalbí, J.R., Suelves, J.M., Saltó, E., & Cabezas, C. (2011). Valoración de las encuestas a adolescentes sobre consumo de tabaco, alcohol y cannabis en España. *Adicciones, 23*, 11-16.

Welte, J. W., & Barnes, G. M. (1987). Youthful smoking patterns and relationships to alcohol and other drug use. *Journal of Adolescence, 10*, 327-340. doi: 10.1016/S0140-1971(87)80015-5

World Health Organization (2013). *WHO report on the global tobacco epidemic, 2013: Enforcing bans on tobacco advertising, promotion and sponsorship*. Switzerland: World Health Organization.

Willner P. (2001). A view through the gateway: Expectancies as a possible pathway from alcohol to cannabis. *Addiction, 96*, 691–703.

Winters, K. C., Stinchfield, R. D., & Fulkerson, J. (1993). Toward the development of an adolescent gambling problem severity scale. *Journal of Gambling Studies, 9*, 63-84. doi: 10.1007/BF01019925

Evaluation of the psychometric properties of the Gambling Motives Questionnaire in Argentinian young people and adults

Valoración de las propiedades psicométricas del Cuestionario de Motivos de Apuestas en jóvenes y adultos argentinos

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Abstract

The purpose of the present study was to evaluate, in a sample of young people and adults from the general community, the psychometric properties of two models developed for assessing gambling motives (Gambling Motives Questionnaire and Gambling Motives Questionnaire-Financial; GMQ and GMQ-F). Specifically, a confirmatory factor analysis was carried out to assess the fit of the two models to the data. Internal consistency of the scales was then analyzed. A multiple regression analysis was conducted to analyze the utility of gambling motives for predicting levels of gambling problem severity. The final sample was made up of 341 young people and adults, aged 18 to 60, who reported any gambling activity during the last six months. The maximum likelihood (ML) method with robust Satorra-Bentler correction was used to evaluate the fit of the models to the data. The results indicated that both the GMQ and the GMQ-F models show a reasonable fit to the data. All scales have adequate internal consistency values. Enhancement, coping and financial gambling motives were associated with greater severity of gambling problems. Overall, the results indicate that both models have adequate psychometric properties, though the GMQ-F appears to provide a more comprehensive alternative for assessing gambling motives in the general community.

Key Words: gambling motives; young people, adults, psychometric properties.

Resumen

El presente trabajo tuvo como objetivo evaluar, en una muestra de apostadores jóvenes y adultos de la comunidad general, las propiedades psicométricas de estructura y consistencia interna del Cuestionario de Motivos de Apuestas en sus dos versiones: original (GMQ) y revisada (GMQ-F). Específicamente, se efectuó un análisis factorial confirmatorio para evaluar el ajuste de ambos modelos. Luego se analizó la consistencia interna de las escalas y se analizó la utilidad de las escalas para predecir un mayor nivel de severidad en los juegos de apuestas. Participaron 341 jóvenes y adultos, con edades entre 18 y 60 años, que reportaron realizar apuestas en los últimos seis meses. Para evaluar el ajuste de los modelos propuestos se utilizó el método de estimación máxima verosimilitud (ML) con la corrección robusta de Satorra-Bentler. Los resultados indicaron que los modelos GMQ y GMQ-F presentan un ajuste razonable a los datos. Todas las escalas presentan adecuados valores de consistencia interna. Los motivos de mejora, afrontamiento y financieros se relacionan con una mayor severidad de problemas con las apuestas. En general, los resultados indican que ambos modelos cuentan con adecuadas propiedades psicométricas, sin embargo, el GMQ-F se ofrece como una alternativa más completa para la medición de los motivos de apuestas en la comunidad general.

Palabras clave: motivos de apuestas, jóvenes, adultos, propiedades psicométricas.

Received: April 2014; Accepted: September 2014

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In its most recent version, the Diagnostic and Statistical Manual of Mental Disorders (DSM 5; American Psychiatric Association, 2013) situates gambling-related disorders in the category of *addictions*, together with substance-abuse disorders. This new classification of pathological gambling, which in previous versions of the DSM was grouped with impulse-control disorders, is based on the existence of a range of elements common to the two types of disorder, and pathological gambling is clearly defined as a behavioural addiction (Chambers & Potenza, 2003; Clark, 2010). In the clinical medical context, both the DSM and the International Classification of Diseases (ICD) distinguish between pathological and non-pathological gambling, whilst less severe levels of compulsive gambling are not even addressed by these diagnostic classifications.

There are, however, various tools developed for detecting different levels of severity of this behaviour and thus improving our understanding of the disorder. Some of these instruments, such as the *South Oaks Gambling Screen* (SOGS; Lesieur & Blume, 1987) and the *Problem Gambling Severity Index* (PGSI; Ferris & Wynne 2001), permit us to distinguish a problematic mode of gambling that would be situated between the pathological mode and the recreational mode. Betting and gambling as recreational activities are highly prevalent in many countries and cultures (Clark, 2010; Frascella, Potenza, Brown, & Childress, 2010; Ledgerwood, Alessi, Phoenix, & Petry, 2009). The vast majority of people who gamble experience no serious problems or consequences; nevertheless, for a percentage of gamblers their behaviour develops into a disorder (French, Maclean, & Ettner, 2008; Korman, Toneatto, & Skinner, 2006).

Gambling behaviour, then, is understood in terms of a continuum that goes from recreational mode to pathological mode, including qualitative and quantitatively different stages (Hodgins, Stea, & Grant, 2011; Toce-Gerstein, Gerstein, & Volberg, 2003). Indeed, research has highlighted the importance of studying all levels of this continuum for a better understanding of recreational modes, pathological modes and all the stages in between (Dechant, 2014; Toce-Gerstein et al., 2003).

In Argentina, data from epidemiological studies in relation to the prevalence of gambling, be it in recreational, problematic or pathological mode, are scarce. There is evidence, however, that levels of gambling among Argentinian university students (Tuzinkievich, Vera, Caneto, Garimaldi, & Pilatti, 2013a; 2013b) are similar to those in countries such as the United States (Huang, Jacobs, Derevensky, Gupta, & Paskus, 2007) and Canada (Huang & Boyer, 2007; Ladouceur, Dubé, & Bujold, 1994). The studies in question reveal that approximately 60% of the university population have gambled at some time in their life, whilst between 6 and 12% meet the criteria for problem gambling.

People gamble for different reasons, with different motives (Dechant, 2014; Dechant & Ellery, 2011; Steinberg, Tremblay, Zack, Busto, & Zawertailo, 2011; Stewart & Zack, 2008). In the field of alcohol use, the motives are understood as internal or external needs that people seek to satisfy through drinking (Cooper, 1994; Cooper, Russell, Skinner,, & Windle, 1992; Hauck-Filho, Teixeira, & Cooper, 2012; Merrill & Read, 2010; Kuntsche & Kuntsche, 2009; Mazzardis, Vieno, Kuntsche, & Santinello, 2010). The *Drinking Motives Questionnaire* (DMQ; Cooper et al., 1992) postulates a structure of three factors or dimensions accounting for the principal motives for drinking alcohol: social, coping and enhancement. Recently, this theoretical model has been used as a starting point for constructing the *Gambling Motives Questionnaire* (GMQ, Stewart & Zack, 2008). Indeed, the GMQ employs the 15 items of the DMQ (Cooper et al., 1992) to investigate the frequency with which people gamble with a view to obtaining results guided by social, enhancement and coping motives. The GMQ has been used satisfactorily in various studies with samples of gamblers at different levels of severity (MacLaren, Harrigan, & Dixon, 2012; Stewart & Zack, 2008; Parhami, Siani, Campos, Rosenthal, & Fong, 2012).

These studies indicate that gamblers scoring higher on instruments for the detection of severity in gambling also score higher, compared to gamblers with moderate or low severity levels, on the three scales of the GMQ (MacLaren et al., 2012; Parhami et al., 2012; Stewart & Zack, 2008). However, not all the motives show the same prevalence. Specifically, gamblers with scores indicating potentially pathological gambling (Parhami et al., 2012) or high level of severity (MacLaren et al., 2012) appear to gamble more mainly from motives of enhancement, followed by motives of coping, and finally by social motives. Social motives for gambling, like social motives for alcohol use (Merrill & Read, 2010), do not appear to have a direct influence on the development of problematic levels of this disorder (Stewart & Zack, 2008) or on higher frequency of gambling (Dechant, 2014).

As far as the assessment of gambling motives is concerned, some researchers have suggested the need to include items that take into account motives of a financial nature (Dechant & Ellery, 2011; Lee, Chae, Lee, & Kim, 2007). From the work of Dechant and cols. (Dechant & Ellery, 2011; Dechant, 2014) there emerged the GMQ-F, which incorporates a new dimension for measuring gambling frequency in accordance with financial motives (e.g., because I enjoy thinking about what I could with my winnings). Dechant (2014) evaluated, in a sample of adults who had gambled at some time in the year prior to the study, the functioning of the GMQ incorporating items that assessed financial motives. First of all, it was found that the items *it's a way to celebrate* and *to relax* did not load in the respective factors (social and coping), and that the item because it's exciting (from the enhancement motives scale) loaded across two different dimensions. In addition, the Cronbach's alpha

coefficient improved on removing these three items from the respective scales. Once the irrelevant items had been removed, and by means of further structural and internal consistency analysis, the study's authors obtained evidence of the adequate psychometric functioning of the GMQ-F made up of 16 items grouped in four scales: social, enhancement, coping and financial. Through hierarchical regression analysis it was found that the addition of the financial scale improved the prediction of gambling frequency.

In the Argentinian context, to the best of our knowledge, no study to date has evaluated the psychometric properties of either the GMQ (Stewart & Zack, 2008) or the GMQ-F (Dechant, 2014); likewise, researchers in this field have highlighted the need to examine the functioning of these instruments in the general population (Dechant, 2014). Thus, the principal aim of the present work is to examine the psychometric properties of the Spanish language version of the GMQ-F (Dechant, 2014) and the GMQ (Stewart & Zack, 2008). We also set out to determine which scales of these models shows the best fit to the local context, and to carry out a hierarchical regression analysis to decide which of them best predicts gambling severity level in a sample of young and adult gamblers from the general community. Furthermore, and by means of an analysis of variance (ANOVA), we aim to assess the instrument's criterion validity for providing evidence about the capacity of its gambling motives scales for discriminating between participants with different levels of severity in their gambling behaviour.

Method

Participants

The sample was made up of 355 participants (29.3% men and 70.7% women) aged between 18 and 60 (M=29.09±.55). People in this age range from the general community and who reported any kind of gambling activity in the previous six months were invited to take part in the research. The invitation to participate reached potential participants via social media and e-mail. It contained a link so that they could fill out the questionnaire online. Fourteen cases were discarded because they failed to meet the inclusion criteria (e.g., they had not gambled in the last six months). Thus, the final sample included 341 participants (29.3% men and 70.7% women, with a mean age of 29.12±.57). By age subgroup, 59.8% were aged 18-27, 22.3% were aged 28-37, 8.2% were aged 38-47, and 9.7% were aged 48-60. As regards place of residence, 45.5% reported living in the province of Córdoba (though only 31.4% said they were born in that province), 40.5% lived in the province of Buenos Aires and 4.4% in Santa Fe. Place of residence of the remaining 9.6% was distributed across 13 other provinces of Argentina. Sixteen-point-four per cent (16.4%) reported working between 20 and 40 hours per week, 55.1% were university students, and 2.3% were neither working or studying.

Instruments

Problem Gambling Severity Index (PGSI; Ferris & Wynne, 2001): this tool for detecting the severity level of gambling problems is made up of nine items, of which five are associated with behavioural indicators and four with negative consequences. It presents a high correlation with the South Oaks Gambling Screen (SOGS) (Lesieur & Blume, 1987). The original English version of the PGSI shows adequate internal consistency values (α= .84) (Ferris & Wynne, 2001). For the present study, two judges expert in English translated the items into Spanish. These versions were revised until a consensual version was obtained, with special emphasis on linguistic and cultural aspects. After that, cognitive interviews were carried out with seven participants so as to obtain information about how well each item was understood and how appropriate it was for the local context. On the basis of these interviews the necessary modifications were made. The Spanish version used in this study showed adequate internal consistency (α= .88). According to Ferris and Wynne (2001), scores should be interpreted as follows: a score of 8 or more indicates problem gambling with negative consequences and loss of control, scores of between 3 and 7 indicate a moderate level of problems, with some negative consequences, whilst scores of between 0 and 2 indicate a low level of problems, with few negative consequences.

Gambling Motives Questionnaire (GMQ; Stewart & Zack, 2007): this version is made up of 15 items, grouped in three subscales: social, enhancement and coping, which refer to people's different motives for gambling. In addition, we employed the financial scale added to the instrument by Dechant (2014). Specifically, the model proposed by Dechant includes 16 items: twelve corresponding to the GMQ and four referring to financial motives. The GMQ-F, in contrast to the GMQ, does not include the items *it's a way to celebrate* from the social scale, because it's exciting from the enhancement scale and *to relax* from the coping scale. Participants were required to indicate, by means of a Likert-type scale with five response options (from 0 = almost never/never, to 5 = almost always/always), the frequency with which they had gambled in the last year for the reason mentioned in each item. First of all, three experts in the English language each produced their own Spanish translation of the four scales. The three versions were compared and discussed until an agreed version was obtained for each item. In this step the authors took into account the linguistic and cultural differences between the population of origin and the target population of this adapted version. With this first adapted instrument, cognitive interviews were carried out with seven people so as to identify any possible difficulties for understanding the items. Based on the results of these interviews the appropriate language adjustments were made. In this study we applied the 15 items of the GMQ (Stewart & Zack, 2007) together with the four items of the financial scale (Dechant, 2014). Previous studies, using the original English version, have reported

adequate internal consistency values for the GMQ-F (from α = .69 to α = .82) (Dechant, 2014) and for the GMQ (from α = .81 to α = .91) (Stewart & Zack, 2007).

Procedure

Prospective participants followed a link to a secure website belonging to the Survey and Questionnaire Server at the Universidad Nacional de Córdoba (Argentina). On the page for the questionnaire used in this study, the person was first asked to provide informed consent to take part. Filling out the questionnaire took approximately 30 to 40 minutes. Participants received no type of financial reward for responding to the questionnaire.

Data analysis

First of all, the behaviour of the variables was explored by means of univariate analysis, based on frequencies and percentages, in order to describe the level of gambling severity (PGSI). Subsequently, measures of central tendency (Mean) were used to describe participants' scores on each of the gambling motives scales. Furthermore, through a variance analysis, scores on each of the scales were compared between participants with different severity levels. The locus of significant differences was analyzed by means of *post hoc* analysis, using the *Tukey* statistic, and this was followed by a series of confirmatory factor analyses (AFC) with the aim of assessing the internal structure of the model proposed by the GMQ-F and of the model proposed by the GMQ. It was decided to use an AFC rather than an exploratory factor analysis since this permits us to test previous hypotheses about the factor structure of an instrument (Verdejo-García et al., 2012). The GMQ-F Model is composed of the latent factors social, enhancement, coping and financial, and 16 items (four for each scale) as observed variables and their respective measurement errors. The GMQ Model is made up of the factors social, enhancement and coping, and 15 items (five for each scale) as observed variables and their respective measurement errors.

The fit of the two models was examined and compared. For the fit analysis we used the EQS 6.1. software, and the estimation method employed was maximum likelihood (ML) with the Satorra-Bentler (S-B; Bentler, 2006; Satorra, 2002) robust correction. This method is the most appropriate for the estimation of AFC models with observed data on ordinal scales and absence of multivariate normality (Mardia coefficient ≥ 5) (Mezquita et al., 2011). For assessing the fit of the models the following indicators were used: the Comparative Fit Index (CFI) and the Root Mean Square Error of Approximation (RMSEA). The values used for the model's goodness of fit were as follows: for the CFI, values of between .90 and .95 or higher were considered to indicate acceptable to excellent fit for the model, and for the case of RMSEA the respective values were .05 to .08 (Hu & Bentler, 1995). Finally, we took into account the standardized factor loadings (β) of each observed variable in the latent variable (Hair, Black, Babin, Anderson, & Tatham, 2006).

Next, the Cronbach's alpha coefficients were calculated for examining the internal consistency of each sub-scale. Finally, and by means of hierarchical regression analysis, we examined the capacity of each one of the gambling motives sub-scales for predicting the severity level of problem gambling. Specifically, we evaluated separately the independent contribution of each of the three GMQ sub-scales and the four GMQ-F sub-scales (predictor variables) to problem gambling severity (PGSI) (criterion variable). The effects of sex (man = 1, woman = 2) and age were controlled. All the analyses conducted out in relation to level of problem gambling severity were carried out with the sub-sample (n = 270, 29.3% men and 70.7%, women, *M* age = 29.44±10.63) that responded to the PGSI.

Results

Descriptive: prevalence of problem gambling severity and differences in gambling motives according to severity level.

Problem gambling severity: The sample obtained a mean of 1.54±2.97 on the PGSI. Four-point-four per cent (4.4%) (n

Table 1
Mean and standard deviation for each of the scales of the two models analyzed (GMQ and GMQ-F), by severity level.

	GMQ			GMQ-F			
	Enhancement	**Coping**	**Social**	**Enhancement**	**Coping**	**Financial**	**Social**
	M(DS)	M(DS)	M(DS)	M(DS)	M(DS)	M(DS)	M(DS)
JP-CN	13.33 ± 4.89	10.25 ± 4.63	8.75 ± 4.20	10.92 ± 3.92	7.92 ± 3.94	12.16 ± 3.07	7.00 ± 3.46
PM-ACN	10.60 ± 4.29	7.05 ± 2.52	9.23 ± 3.38	8.94 ± 3.79	5.40 ± 1.99	8.80 ± 3.39	7.51 ± 2.87
PB-PCN	8.49 ± 3.29	5.95 ± 1.76	7.99 ± 2.94	7.08 ± 2.90	4.53 ± 1.30	6.72 ± 3.15	6.58 ± 2.54

GMQ: Three-factor model; GMQ-F: Four-factor model; PG-NG: problem gambling with negative consequences and loss of control (scores ≥ 8 on the PGSI); MP-SNC: moderate problem gambling with some negative consequences (scores of 3 to 7 on the PGSI); LP-FNC: low problem gambling with few negative consequences (scores of 0 to 2 on the PGSI).

= 12) of the participants obtained a score of 8 or more, which is considered an indicator of problem gambling with negative consequences and loss of control, whilst 13% (n = 35) scored between 4 and 7, placing them in the category of moderate level of problem gambling with some negative consequences, and the remaining 82.6% (n = 223) obtained scores reflecting a low level of problems with few negative consequences (≤ 2).

Differences in gambling motives according to severity level: Table 1 shows the scores (mean and standard deviation) obtained on each of the scales of the two models analyzed (GMQ and GMQ-F) by severity category (low level of problems, moderate level of problems, and problem gambling with loss of control) according to the values obtained on the PGSI.

GMQ Model: Significant differences were found for the enhancement $F(2, 269) = 15.13$, $p \leq .001$ and coping scales $F(2, 269) = 26.73$, $p \leq .001$ between the groups of gamblers with different severity levels. A posteriori analyses indicated that problem gamblers with higher levels of severity (loss of control), compared to the other two groups of gamblers (low and moderate severity levels), scored higher on the coping scale. Likewise, gamblers with moderate severity level also scored higher on this scale than low-severity gamblers. Furthermore, problem gamblers and moderate-severity gamblers scored higher than low-severity gamblers on the enhancement scale. No significant differences were found in the social motives for gambling.

GMQ-F Model: Significant differences were found between the groups with different severity levels for the enhancement $F(2, 269) = 13.35$, $p \leq .001$, coping $F(2, 269) = 28.41$, $p \leq .001$ and financial scales $F(2, 269) = 21.57$, $p \leq .001$. The *post hoc* analyses showed that gamblers with scores indicating greater severity, compared to those with moderate and low severity, were significantly more likely to gamble from coping and financial motives. Moreover, gamblers with moderate severity scored significantly higher than those with low severity on these two scales. In addition to this, participants with high and moderate gambling severity levels scored significantly higher on the enhancement scale than those with low problem gambling level. No significant differences were found in the social motives for gambling.

Confirmatory factor analysis

First, all the items were inspected in order to assess the quality of the database. No missing cases were observed given the online survey methodology employed in this study. In order to check the assumptions of normality of the sample we carried out skewness and kurtosis analyses for each item. Seven items presented kurtosis and skewness indices greater than +2.00 and -2.00, which according to the literature is inadequate (George & Mallery, 2003); the rest of the items presented values within the bounds of acceptability. Taking into account the Mardia coefficient (≥ 5), we used the maximum likelihood (ML) estimation method with the Satorra-Bentler robust correction.

GMQ Model (three factors, 15 items): The normalized Mardia coefficient value (79.8695) indicated that the items did not follow the multivariate normal distribution. The goodness-of-fit statistics for this model revealed an excellent fit to the data: Satorra–Bentler χ^2 (df = 87) = 247.1645, p<.000; CFI = .970; RMSEA = .074 (90% confidence interval = .063 to .084). The standardized factor loadings ($p \leq .05$) in the social factor ranged from .65 to .74, in the enhancement factor from .70 to .93, and in the coping factor from .65 to .83.

Table 2
Standardized factor loadings of each one of the gambling motives items, for the two models, GMQ and GMQ-F.

	β GMQ	β GMQ-F
SOCIAL		
It's a way to celebrate	.68	-
Because it's what most of my friends do when they meet up	.65	.80
For socializing	.66	.74
Because it's something I do on special occasions	.74	.52
Because it makes a social gathering more fun	.77	.83
ENHANCEMENT		
Because I like the way it makes me feel	.93	.94
Because it's exciting	.79	.77
To bring on a feeling of euphoria	.70	-
Because it's fun	.77	.77
Because it makes me feel good	.85	.86
COPING		
To relax	.77	-
Because it makes me feel more confident and sure of myself	.83	.65
Because it helps me when I feel nervous or depressed	.64	.88
To forget my worries	.80	.80
To make me feel better when I'm in a bad mood	.81	.89
FINANCIAL		
To win money	-	.86
Because I enjoy thinking about what I could do with my winnings	-	.80
Because winning could change my lifestyle	-	.83
To make money	-	.89

GMQ-F Model (four factors, 16 items): The normalized Mardia coefficient value (64.2544) indicated the absence of multivariate normality, whilst the goodness-of-fit statistics revealed an excellent fit of the model to the data: Satorra–Bentler χ^2 (df = 98) = 208.4837, p< .000; CFI = .974; RMSEA = .058 (90% confidence interval = .047 to .068). The standardized factor loadings ($p \leq .05$) for the social factor ranged from .52 to .83, for the enhancement factor from .77 to .86, for the coping factor from .65 to .89, and for the financial factor from .80 to .89.

Table 2 shows the standardized factor loadings for each one of the items that describe different gambling motives in accordance with each of the two models analyzed (GMQ and GMQ-F).

Internal consistency analysis

The results obtained on analyzing the reliability of the sub-scales of the two models (GMQ and GMQ-F) provided evidence of the models' sound functioning. Specifically, the three sub-scales of the GMQ Model yielded adequate internal consistency values: social (α = .75), enhancement (α = .87) and coping (α = .81). In turn, the four sub-scales of the GMQ-F Model also yielded adequate reliability values: social (α = .73), enhancement (α = .84), coping (α = .77) and financial (α= .88). These results indicate that the analyses of the individual reliability of each item carried out on the two models (GMQ and GMQ-F) provide evidence of the sound functioning of all of them.

Multiple regression analysis: concurrent validity

For the hierarchical regression analysis, in the first step we inputted the socio-demographic variables age and sex, and in the second step the gambling motives scales corresponding to each of the two modes analyzed. The criterion variable was problem gambling severity level.

GMQ Model: In the first step, the socio-demographic variables explained .06% of the variance of the criterion variable, F (2, 267) = 8.60 =, p< .001. Male participants (β = -.25, t = 4.13, p< .001) scored higher on the instrument for detecting problem gambling. Participants' age was not associated with greater severity. In the second step, inputting the three GMQ scales (social, coping and enhancement) led to an increase in explained variance to 28% F (3, 264 = 27.33, p< .001. Specifically, greater frequency of gambling from motives of enhancement (β = .23, t = 3.04, p<.01) and of coping (β = .40, t = 5.58, p<.001) was associated with greater severity measured by the PGSI. The social scale had a negative effect on severity level (β = -.22, t = 3.46, p< .001). Furthermore, we observed a reduction in the regression coefficient for sex (from -.25 to -.15), indicating partial mediation of the motives in the effect that being male has on the criterion variable. These results are presented in Table 3.

GMQ-F Model: The socio-demographic variables inputted in the first step explained .06% of the variance of the criterion variable, F (2, 267) = 8.60 =, p< .001. This is based on the fact that male participants (β = -.25, t = 4.13, p< .001) obtained scores indicating higher problem gambling severity. In the second step we inputted the four GMQ-F scales: social, coping, enhancement and financial, and the explained variance increased by 28%, rising to 34% [*F change* (4,263 = 27.59, p< .001]. Higher scores on the scales of enhancement (β = .16, t = 2.37, p< .05), coping (β = .36, t = 5.70, p< .001) and financial motives (β = .24, t = 4.34, p< .001) were associated with higher problem gambling severity levels. The social scale was again found to have a negative effect on severity level (β = -.17, t = 2.73, p< .01). In turn, once again we observed a reduction in the regression coefficient for the socio-demographic variable sex (from -.25 to -.15), indicating partial mediation of the gambling motives on the criterion variable. These results are shown in Table 3.

Table 3
Multiple regression analysis for predicting problem gambling severity.

		GMQ		GMQ-F	
		β	*t*	β	*t*
1st	Sex	-.245	-4.131***	-.245	-4.131***
	Age	-.020	-.343	-.020	-.343
2nd	Sex	-.152	-2.857**	-.155	-3.042**
	Age	-.006	-1.104	-.104	-1.997*
	Enhancement	.225	3.035*	.161	-2.734*
	Social	-.224	-3.462**	-.168	2.374*
	Coping	.399	5.584***	.358	5.695***
	Financial	-	-	.236	4.344***
	Durbin-Watson:	2.089			1.997
	R	.532			.582
	R^2	.283			.338

*** $p \leq .001$; ** $p \leq .005$ y * $p \leq .05$

Discussion

The purpose of the present work was to examine the psychometric properties of the structure and the internal consistency of the Gambling Motives Questionnaire (GMQ; Stewart & Zack, 2007) in its version adapted for Spanish-speaking population. The GMQ, derived from the field of alcohol-use research, has shown adequate functioning in various studies with gamblers (Parhami et al., 2012; MacLaren et al., 2012; Stewart & Zack, 2007). However, it fails to address a motivational aspect that appears to be relevant in gambling: the financial angle (Dechant, 2014; Lee et al.,

2007). In the present study we analyzed, by means of confirmatory factor analysis, the fit of the structure proposed by the GMQ (Stewart & Zack, 2007) and also the structure posited by the GMQ-F (Dechant, 2014), a model incorporating a scale that enquires about the frequency with which one gambles out of motives such as *to win money* or because *winning could change my lifestyle*. Furthermore, and through multiple regression analysis, we analyzed the concurrent validity of the scales of both models for predicting level of problem gambling severity.

An interesting finding is that 17% of the participants (of the total 270 that filled out the PGSI) obtained scores indicating a problem gambling severity level of between moderate and high. This prevalence is somewhat lower than that reported in previous studies with general population (Parhami et al., 2012; Stewart & Zack, 2007) or with gamblers recruited close to horse-racing venues (MacLaren et al., 2012), but higher than that found in previous studies in Argentina (Tuzinkievich et al., 2013a, 2013b). Notably, the sample in the present study was made up of people from the general community that had gambled in any way in the previous six months, whilst previous data on the prevalence of gambling in the local population come exclusively from university students.

Also of interest is the fact that, as observed in previous studies with gamblers, the coping, enhancement (MacLaren et al., 2012; Parhami et al., 2012; Stewart & Zack, 2007) and financial motives (Dechant, 2014) were the most common among gamblers with high problem gambling severity, followed by those with moderate severity level, and finally, by those with low risk of gambling problems. Gambling motives, then, undoubtedly permit us to distinguish between gamblers with different severity levels. Specifically, significant differences were observed in the coping and financial motives among all the groups of gamblers with different severity levels, and in the enhancement motive between those with low severity level and the two highest-severity groups. The social motive, as found in previous studies (Dechant, 2014; MacLaren et al., 2012), did not have the same utility for distinguishing between these groups of gamblers.

The results of the confirmatory factor analysis indicate that the GMQ and GMQ-F show adequate fit to the data for the local population. Specifically, both the model that proposes gambling motives grouped in three dimensions and that which also incorporates financial motives showed excellent fit to the data. Likewise, all the items presented high standardized factor loadings. In addition, all the scales of both models yielded adequate internal consistency values (≤ .70). The GMQ-F, on the other hand, showed better fit than the GMQ according to the root mean square error of approximation (RMSEA).

The concurrent validity analysis indicated, in a similar way to what was found in previous research, that men were more likely to present high severity levels (Stewart and Zack, 2008) or high gambling frequency (Dechant, 2014) than women. In contrast to the findings of Stewart and Zack (2008), but coinciding with those of Dechant (2014), no differences were found in relation to participants' age. The enhancement and coping motives scales, in the case of both the GMQ model and the GMQ-F model, had a positive and significant effect on gambling severity, even after controlling the effects of the socio-demographic variables age and sex. These results provide further evidence about the relation between this cognitive variable and greater presence of gambling problems. In addition, the incorporation of the scale referring to financially-motivated gambling increased the percentage of variance explained by gambling motives from .22% to .28%. These results suggest, in a similar way to those of other studies, that the incorporation of motives referring to financial or monetary aspects improves the prediction of greater gambling frequency (Dechant, 2014) and of problem gambling (Lee et al., 2007). The social scale motives had a significant – though negative – effect on the level of problem gambling. Bearing in mind that this scale presented a null bivariate correlation with severity level (r = .09), this negative effect at a multivariate level may be due to a suppression effect. A similar situation was found in previous studies in relation to the conformity scale of the Drinking Motives Questionnaire (Hauck-Filho et al., 2012; Mezquita et al., 2011).

All in all, the results of the present study indicate that the two models analyzed show an excellent fit to the data from this sample of gamblers from the general community. However, the GMQ-F model allows better discrimination between problem gamblers with different levels of severity. Specifically, gamblers with scores indicating problem gambling with negative consequences and loss of control gamble mainly out of financial motives, and their frequency of gambling in response to these motives distinguishes them from the rest of the gamblers. Moreover, the multiple regression analysis provided more evidence about the utility of this scale for predicting greater problem gambling severity. In sum, although the Spanish versions of both models show adequate psychometric properties, the GMQ-F model emerges as a more comprehensive alternative than the GMQ for measuring gambling motives.

Some limitations should be taken into account on considering the results of this study. First of all, the sample included more women than men, and a majority of young adults (over half the participants were in the age range 18 to 27, and almost 83% were aged between 18 and 37), so there is potential for bias related to sex and age. Furthermore, there may be differences between those who actually filled out the questionnaires and those who read the invitation to participate but, despite meeting the requirements to take part in the study, declined to do so. Such limitations make it difficult to generalize the results to the rest of the population; nevertheless, it is worth highlighting the fact that the results

coincide, in general, with those obtained in samples selected by means of methods using stratification by location, age and sex (Dechant, 2014). A further limitation concerns the simultaneous measurement of gambling motives and problem gambling severity: this aspect undoubtedly restricts the possibility of accurately predicting the problems associated with gambling from the motives to which people attribute their gambling. In this regard, future research should consider the possibility of employing a prospective design in which the motives would be assessed prior to the problems. This type of design would make it possible to determine the utility of gambling motives for predicting the presence of problem gambling.

Regardless of these limitations, though, the results reported here provide evidence on the adequate functioning of the functioning of the GMQ, and especially of the GMQ-F, for measuring gambling motives in peope from the general population.

Acknowledgements

This work was made possible by a grant from the Argentinian National Agency for the Promotion of Science and Technology (Agencia Nacional de Promoción Científica y Tecnológica; FONCyT) to Angelina Pilatti (PICT 2012-1736) and support from the National Council for Scientific and Technical Research (Consejo Nacional de Investigaciones Científicas y Técnicas; CONICET, Argentina).

The authors would like to thank Dr. Marcos Cupani (CONICET-UNC) for his help with the confirmatory factor analyses.

Conflicts of interests

The authors declare that they have no conflicts of interests.

References

Bentler, P. (2006). *EQS 6 structural equations program manual*. Encino, CA: Multivariate Software, Inc.

Chambers, R. A., & Potenza, M. N. (2003). Neurodevelopment, impulsivity, and adolescent gambling. *Journal of Gambling Studies, 19*, 53-83.

Clark, L (2010). Decision-making during gambling: an interaction of cognitive and psychobiological approaches. *Philosophical Transactions of The Royal Society, 365*, 319-330.

Cooper, M. L. (1994). Motivations for Alcohol Use Among Adolescents: Development and Validation of a Four-Factor Model. *Psychological Assessment, 6*, 117-128.

Cooper, M. L., Russell, M., Skinner, J. B., & Windle, M. (1992). Development and validation of a three-dimensional measure of drinking motives. *Psychological Assessment, 4*, 123-132.

Dechant, K. (2014). Show Me the Money: Incorporating Financial Motives into the Gambling Motives Questionnaire. *Journal of Gambling Studies, 30*, 949-965.

Dechant, K., & Ellery, M. (2011). The effect of including a monetary motive item on the gambling motives questionnaire in a sample of moderate gamblers. *Journal of Gambling Studies, 27*, 331-344.

Ferris, J., & Wynne, H. (2001). The Canadian Problem Gambling Index: Final Report. Report to the Canadian Inter-Provincial Advisory. Committee. Downloaded online document on the 6th of June, 2013.

Frascella, J., Potenza, M.N., Brown, L.L., & Childress, A.R. (2010). Shared brain vulnerability open the way for nonsubstance addictions: carving addiction at a new joint? *Anals of the New York Academy of Sciences, Addictions Reviews, 2*, 294-315.

French, M. T., Maclean, J. C., & Ettner, S. L. (2008). Drinkers and bettors: Investigating the complementarity of alcohol consumption and problem gambling. *Drug and Alcohol Dependence, 96*, 155-164.

George, D., & Mallery, M. (2003). *Using SPSS for Windows Step by Step: a simple guide and reference*. Boston, MA: Allyn & Bacon.

Hair, J. F., Black, W. C., Babin, B. J., Anderson, R. E., & Tatham, R. L. (2006). *Multivariate Data Analysis*. New Jersey: Pearson.

Hauck-Filho, N., Teixeira, M. A. P., & Cooper, M. L. (2012). Confirmatory factor analysis of the Brazilian version of the Drinking Motives Questionnaire-Revised (DMQ-R). *Addictive Behaviors, 37*, 524-527.

Hodgins, D. C., Stea, J. N., & Grant, J. E. (2011). Gambling disorders. *The Lancet, 378*, 1874-1884.

Hu, L. & Bentler, P. (1995). Evaluating Model Fit. En R. Hoyle (Ed.). *Structural Equation Modelling: Concepts, Issues and Applications* (pp. 76-99). Thousand Oaks, CA: Sage Publications.

Huang, J. H., & Boyer, R. (2007). Epidemiology of youth gambling problems in Canada: A national prevalence study. *The Canadian Journal of Psychiatry/La Revue Canadienne de Psychiatrie, 52*, 657-665.

Huang, J. H., Jacobs, D. F., Derevensky, J. L., Gupta, R., & Paskus, T. S. (2007). Gambling and health risk behaviors among US college student-athletes: Findings from a national study. *Journal of Adolescent Health, 40*, 390-397.

Korman, L. M.,Toneatto, T., & Skinner, W. (2006). Pathological Gambling. En J. E. Fisher & W. T. O'Donohue (Eds), *Practitioners' guide to evidence-based psychopathology*. New York: Springer.

Kuntsche, E., & Kuntsche, S. (2009). Development and Validation of the Drinking Motive Questionnaire Revised Short Form (DMQ–R SF). *Journal of Clinical Child & Adolescent Psychology, 38*, 899-908.

Ladouceur, R., Dubé, D., & Bujold, A. (1994). Prevalence of pathological gambling and related problems among

college students in the Quebec metropolitan area. *The Canadian Journal of Psychiatry/La Revue Canadienne de Psychiatrie, 39*, 289-293.

Ledgerwood, D.M., Alessi, S.M., Phoenix, N., & Petry, N.M.(2009). Behavioral assessment of impulsivity in pathological gamblers with and without substance use disorder histories versus healthy controls. *Drug and Alcohol Dependence, 105*, 89-96.

Lee, H. P., Chae, P. K., Lee, H. S., & Kim, Y. K. (2007). The five-factor gambling motivation model. *Psychiatry Research, 150*, 21-32.

Lesieur, H.R., & Blume S.B. (1987). The South Oaks Gambling Screen (SOGS): A new instrument for the identification of pathological gamblers. *The American Journal of Psychiatry, 144*, 1184-1188.

MacLaren, V. V., Harrigan, K. A., & Dixon, M. (2012). Gambling motives and symptoms of problem gambling in frequent slots players. *Journal of Gambling Issues, 27*, 1-13.

Mazzardis, S., Vieno, A., Kuntsche, E., & Santinello, M. (2010). Italian validation of the drinking motives questionnaire revised short form (DMQ-R SF). *Addictive Behaviors, 35*, 905-908.

Merrill, J. E., & Read, J. P. (2010). Motivational pathways to unique types of alcohol consequences. *Psychology of Addictive Behaviors, 24*, 705-711.

Mezquita, L., Stewart, S. H., Ibáñez, M. I., Ruipérez, M. A., Villa, H., Moya, J., & Ortet, G. (2011). Drinking motives in clinical and general populations. *European Addiction Research, 17*, 250-261.

Parhami I, Siani A, Campos MD, Rosenthal RJ, & Fong TW (2012). Gambling in the Iranian-American Community and an Assessment of Motives: A Case Study. *International Journal of Mental Health Addiction, 10*, 710-721.

Satorra, A. (2002). Asymptotic robustness in multiple group linear-latent variable models. *Econometric Theory, 18*, 297–312. http://dx.doi.org/10.1017/S0266466602182041

Steinberg, L., Tremblay, A.M., Zack M., Busto, U.E., & Zawertailo, L.A. (2011). Effects of stress and alcohol cues in men with and without problem gambling and alcohol use disorder. *Drug and Alcohol Dependence, 119*, 46-55. doi: 10.1016/j.drugalcdep.2011.05.011.

Stewart, S. H., & Zack, M. (2008). Development and psychometric evaluation of a three-dimensional Gambling Motives Questionnaire. *Addiction, 103*, 1110-1117.

Toce-Gerstein, M., Gerstein, D. R., & Volberg, R. A. (2003).A hierarchy of gambling disorders in the community. *Addiction, 98*, 1661-1672.

Tuzinkievich, F., Vera B. del V., Caneto, F., Garimaldi, J., & Pilatti, A. (2013a). Poster: Ocurrencia de juegos de apuestas en adolescentes y su relación con distorsiones cognitivas y consumo de alcohol. *Libro de Resúmenes VIII Congreso Latinoamericano Interdisciplinario del Adolescente (CLIOA).* ISBN: 978-950-33-1078-6

Tuzinkievich, F., Vera B. del V., Caneto, F., Garimaldi, J., & Pilatti, A. (2013b). Poster: Prevalencia de apuestas y su relación con distorsiones cognitivas e impulsividad en estudiantes universitarios. *Revista Argentina de Ciencias del Comportamiento, Suplemento (Julio)*, 368-369.

Verdejo-García, A., Lozano, O., Moya, M., Alcazar, M.A., & Pérez-García, M. (2010). Psychometric properties of a Spanish version of the UPPS-P impulsive behavior scale: reliability, validity and association with trait and cognitive impulsivity. *Journal of Personality Assessment, 92*, 70-77.

Alcohol consumption, illicit substances, and intimate partner violence in a sample of batterers in psychological treatment

Consumo de alcohol, sustancias ilegales y violencia hacia la pareja en una muestra de maltratadores en tratamiento psicológico

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Abstract

The purpose of this study is to analyze the alcohol and illicit substance consumption characteristics in a sample of 572 batterers in treatment by court order. The results indicate that the prevalence of alcohol consumption in the past year was 89.3%, whereas within illicit substances, the prevalences were higher for cannabis (27.8%), followed by cocaine (20.3%). In order to analyze the possible effect of consumption on levels of perpetration and victimization of partner-aggression, the sample was divided into 4 groups: nonconsumers (16.3%), alcohol consumers (58.6%), illicit drug consumers (3.5%), and consumers of alcohol and illicit drugs (21.7%), finding that the groups of nonconsumers and alcohol consumers presented the lowest level of perpetration of psychological, physical, and sexual aggression and of victimization of psychological and physical aggression, whereas the group of consumers of alcohol and illicit drugs presented the highest levels. The results reveal the need to assess substance consumption when designing intervention protocols with batterers.

Key words: batterers, intimate partner violence, alcohol use, alcohol abuse, substance use.

Resumen

Este estudio tiene como objetivo analizar las características de consumo de alcohol y sustancias ilegales en una muestra de 572 maltratadores en tratamiento por orden judicial. Los resultados indican que la prevalencia de consumo de alcohol en el último año fue de 89,3%, mientras que dentro de las sustancias ilegales las prevalencias más altas fueron para cannabis (27,8%) seguido de cocaína (20,3%). Con el objetivo de analizar el posible efecto del consumo sobre los niveles de perpetración y victimización de agresiones hacia la pareja, se dividió la muestra en 4 grupos: no consumidores (16,3%), consumidores de alcohol (58,6%), consumidores de drogas ilegales (3,5%) y consumidores de alcohol y drogas ilegales (21,7%), encontrándose que el grupo de los no consumidores y el de los consumidores de alcohol son los que presentan los niveles más bajos en perpetración de agresiones psicológicas, físicas y sexuales y victimización de agresiones psicológicas y físicas, mientras que el grupo de consumidores de alcohol e ilegales es el que presenta los niveles más elevados. Los resultados hallados ponen de manifiesto la necesidad de evaluar el consumo de sustancias a la hora de diseñar protocolos de intervención con maltratadores.

Palabras clave: maltratadores, violencia en las relaciones de pareja, consumo de alcohol, abuso de alcohol, consumo de sustancias.

Received: April 2014; Accepted July 2014

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Use of psychoactive substances is a serious risk factor for intimate partner violence (Castillo-Carniglia, Pizarro, Luengo, & Soto-Brandt, 2014; Catalá-Miñana, Lila, & Oliver, 2013; El-Bassel, Gilbert, Wu, Go, & Hill, 2005; Moore & Stuart, 2004; Stuart, Temple, & Moore, 2007); however, our knowledge of which specific substances are most clearly associated with such violence remains quite limited. Langenderfer (2013) carried out a meta-analysis with 8 studies on intimate partner violence and use of alcohol, concluding that rates of perpetration of violent acts by men on their partners ranged from 4% to 78.1% (Cunradi, 2009; Hove, Parkhill, Neighbors, McConchie, & Fossos, 2010; Lipsky & Caetano, 2011; McKinney, Caetano, Ramisetty-Mikler, & Nelson, 2009; Rhodes et al., 2009; Taft, Schumm, Orazem, Meis, & Pinto, 2010), while of those men who reported having been violent towards their partners, between 9% and 59.7% reported having got drunk (5 or more alcoholic drinks) (Cunradi, 2009; Lipsky & Caetano, 2011; McKinney et al., 2009), and between and 17.8% and 50% said they had sometimes drunk excessively (Lipsky & Caetano, 2011; Rhodes et al., 2009). Finally, Langenderfer (2013) points out that alcohol problems correlate to a statistically significant degree with intimate partner violence (Hove et al., 2010).

In another meta-analysis, Foran and O'Leary (2008) analyzed 47 studies on the relation between alcohol use and abuse and intimate partner violence, concluding that the effect size of this relation was .23, a result consistent with the effect size of .24 found in a previous meta-analysis by Stith, Smith, Penn, Ward and Tritt (2004), and in the same line as the .22 found by Lipsey, Wilson,

Cohen and Derzon (1997). These results indicate a significant but moderate relation between alcohol use and intimate partner violence (Bushman & Cooper, 1990; Pernanen, 1991).

As regards the use of other substances, the association between the use of illicit drugs and intimate partner violence has been less widely studied. Some research indicates that men who assault their partners report more frequent use of cannabis and cocaine, compared to non-violent men (Chermack, Fuller, & Blow, 2000), whilst other research (Walton, Chermack, & Blow, 2002) found that those men who after receiving treatment for substance use continued to mistreat their partners reported greater consumption of cannabis than those who reported not having repeated such assaults since the treatment. In a similar line, other studies with men in treatment for drug use concluded that the use of cannabis, cocaine and stimulants, as well as the consequences of such use, predicted the perpetration of intimate partner violence (Chermack et al., 2000; Murphy, O'Farrell, Fals-Stewart, & Feehan, 2001). Moore et al. (2008), for their part, carried out a meta-analysis with 96 studies that analyzed intimate partner violence and use of drugs, finding that cocaine was the substance that presented the greatest effect size in relation to aggressive behaviour; in fact, cocaine was the illicit substance associated with the commission of most psychological, physical and sexual violence, whist marijuana use was related to intimate partner psychological violence but not physical violence.

However, few studies have analyzed the relation between illicit substance use and intimate partner violence in samples of batterers in treatment. One of these is that carried out by Brown, Werk, Caplan and Seraganian (1999), who found in a sample of batterers undergoing therapy that those who used drugs presented higher levels of psychological violence, compared to non-consumers, but no significant differences as far as levels of physical aggression were concerned. On the other hand, Moore and Stuart (2004), with a sample of 151 batterers in treatment by court order, concluded that, after controlling the possible effect of alcohol use, the consumption of illicit drugs continued to be a clear predictor of perpetration and victimization for psychological, physical and sexual violence, as well as actual harm.

As regards victimization, it would seem that this is also related to alcohol use, even though the results are not altogether consistent (Breiding, Black, & Ryan, 2008; Coker et al., 2002; El-Bassel et al., 2005; Kilpatrick, Acierno, Resnick, Saunders, & Best, 1997; Testa, Livingston, & Leonard, 2003). Coker et al. (2002) found, in a sample of couples in the US, that in the case of women victimization was associated with alcohol abuse and use of analgesics, but not with illicit substances, whilst in men victimization was associated with use of analgesics and other drugs, but not with alcohol abuse. More recently, Smith, Homish, Leonard and Cornelius (2012) analyzed the relation between intimate partner violence and use of alcohol, cannabis, cocaine and opiates, using data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (2004-2005) (Grant & Kaplan, 2005), concluding that alcohol and cocaine use were more closely associated with the perpetration of intimate partner violence, whilst cannabis and opiates use were more closely associated with victimization.

Although these results indicate that the use of illicit substances is related to the perpetration of intimate partner violence and to victimization, it would be interesting to explore whether this relation is still found after controlling for the effects of alcohol, as Moore and Stuart (2004) concluded. If illicit substance use has an independent effect on levels of aggression towards one's partner, the implications would be highly relevant to interventions with this type of population, first of all highlighting the importance of assessing the use of these other substances, not only of alcohol, and second, making pos-

sible the adaptation of psychological intervention programmes – in case of need – to the presence of problems of use and abuse of different substances. In fact, those mean who achieve stable sobriety show significant reductions in levels of intimate partner violence and are less likely to be violent again, compared to those who relapse (O'Farrell, Fals-Stewart, Murphy, & Murphy, 2003; O'Farrell & Murphy, 1995). Moreover, an important fact to take into account is that those batterers in therapy who are drug users, especially those with more serious problems and higher levels of use, are more likely to drop out of therapy and/or to strike again after the treatment programme has finished, by comparison with those that do not present drug-use problems (Bennett, Goodman, & Dutton, 2000; Gordon & Moriarty, 2003). These data permit us to conclude that the efficacy of psychological intervention programmes with batterers will also depend on the presence of substance use and on the work carried out in relation to this problem.

Taking into account these implications at a clinical level, the aim of the present work is to analyze, first of all, the characteristics of use in a sample of batterers referred by court order to psychological treatment, and secondly, to ascertain whether those who use drugs or alcohol, or both, present higher levels of intimate partner violence and of victimization, compared to non-users.

Method

This study was approved by the Deontological Committee of the Psychology Faculty at the Universidad Complutense of Madrid, on 30th May 2009. Likewise, written informed consent was obtained from all participants, all of them being informed of the aims of the research, as well the procedure to be followed and the estimated duration of the treatment.

Participants

Participants in the study were men from the Madrid Autonomous Region (Comunidad de Madrid) that had been sentenced to less than two years' prison for intimate partner violence, the sentence having been substituted by a programme of psychological treatment, as set down in Section IV of Law1/2004, on Measures of Comprehensive Protection against Gender Violence, which in its article 35 on the substitution of sentences states that: *"In cases in which the detainee has been sentenced for an offence related to gender violence,…, the Judge or Court shall in addition oblige him to attend specific programmes of re-education and psychological treatment…".*

The total sample was made up of 572 men aged between 18 and (mean 38.61 years; *SD* = 10.49). As regards marital status, 32.2% (n = 184) were married or registered civil partners, 35.3% (n = 202) were single, and 32.5% (n = 186) were widowed, separated or divorced). Regarding educational level, 40.9% (n = 234) had only primary education, 40.6% (n = 232) secondary education, and 18.5% (n = 106) university education. By occupation, 18.5% (n = 106) fell into the category of managers or directors/businessmen/public administration employees, 16.8% (n = 96) into that of unemployed/pensioners, and 64.7% (n = 370) into that of construction workers/catering and bar or restaurant sector workers/industrial workers. As far as nationality is concerned, more than half (58.4% (n = 334) were Spanish, 34.1% (n = 195) were from South American countries, and 7.5% (n = 43) were of other nationalities. Finally, the majority (87.2%, n = 499) had been sentenced for physical aggression, and 12.8% (n = 73) for offences of a psychological nature.

Procedure

The pre-treatment assessment phase was carried out individually, with two therapists trained in the application of the assessment protocol. Each participant received between four and eight 60-minute sessions, which included the following activities:

a. In the first session the therapist explained the conditions and objectives of the research and obtained the informed consent.
b. Collection of socio-demographic data and analysis of the offence for which the person had been required to take the psychological treatment programme.
c. Application of the scales described in the *Measures* section, reading the instructions aloud to the patient, doing the first item of each instrument as an example, and resolving any doubts arising. All the questionnaires were self-administered, and all the questions referred to violence against the partner for which they had been sentenced, who was not necessarily the partner they at the time of the assessment.
d. During the assessment phase work was done on treatment adherence, increasing motivation levels, and highlighting the benefits of the treatment programme, which include seeing justice done, getting to know more about one's form of relating to women, and learning about the function of aggression in intimate partner relationships.

Measures

Socio-demographic data was collected by means of an interview, and information related to the offence through the analysis of the judicial records. In addition, the following instruments were applied.

Severity and frequency of the intimate partner violence were measured by means of the Revised Conflict Tactics Scale-CTS2 (Straus, Hamby, Boney-McCoy, & Sugarman, 1996, Spanish adaptation by Loinaz, Eche-

burúa, Ortiz-Tallo, & Amor, 2012). This scale consists of 78 items, 39 of which assess perpetration and the other 39 victimization, by asking about what occurred over the last year of the relationship with the partner who pressed charges. There are 5 scales: negotiation, psychological violence, physical violence, sexual coercion and actual harm, and the instrument shows a reliability of between .79 and .95 (Straus et al., 1996). Cronbach's *alpha* in the present study was .81 for perpetration and .86 for victimization.

To evaluate use of alcohol and illicit substances, we used the *EuropASI* (Kokkevi & Hartgers, 1995; McLellan et al., 1992; Spanish adaptation by Bobes, González, Sáiz, & Bousoño, 1996), which collects information in relatively brief fashion on the possible use of multiple substances. Data is gathered by means of a semi-structured interview, and this instrument is highly advantageous for clinical practice, as it allows the detection of possible use-related problems, analyzing multiple substances, frequency of use, and so on. For each of the substances analyzed information is obtained on the number of months the substance was used that year and of days it was used in the last month (in both cases referring to the period of the intimate partner relationship in which the relevant violence took place). As regards the psychometric properties of the instrument, the data show high levels of reliability and validity (Ravndal, Vaglum, & Lauritzen, 2005; Roa, 1995). Cronbach's *alpha* in this study was .75 for the set of questions referring to use in the last month and the last year.

Statistical analyses

All the statistical analyses were carried out using the *SPSS 15.0* statistics package. First of all, we calculated the reliability indices of the scales used in the study by means of Cronbach's *alpha*. Secondly, we calculated the percentages of prevalence of use of all the substances evaluated. We then formed 4 groups according to use of alcohol and illegal drugs (non-users, alcohol users, illicit substance users and users of both alcohol and illicit substances), with the aim of analyzing whether these 4 groups differed with regard to levels of perpetration and victimization. To this end we performed, first, an ANOVA with post-hoc (Bonferroni) comparisons to detect significant differences between the 4 groups in the age variable and a Pearson *Chi-squared* test for qualitative variables, specifically the socio-demographic variables (educational level, occupation, marital status, nationality) and the offence for which the participant was sentenced. Lastly, we performed another ANOVA with post-hoc (Bonferroni) comparisons to determine whether among these 4 groups there were significant differences in perpetration and victimization, without taking into account the possible effect of age.

Results

Prevalences of use and comparison with a community sample

The first objective of this study was to examine in a sample of 572 batterers the characteristics of use of alcohol and illicit substances. To this end we used two measures, prevalence of use in the last year and prevalence of use in the last month.

The results show that 89.3% of the sample had used alcohol in the last year, while 72.4% had done so in the last month. As regards use of alcohol in large quantities, 44.2% of the sample had consumed large amounts of alcohol in the last year, while 19.8% had done so in the last month. As for the rest of the rest of the substances, prevalences of use are shown in Table 1; as it can be seen, the highest, in both the last year and the last month, are for cannabis (year 27.8%; month 14.2%), followed by cocaine (year 20.3%; month 10%).

On the other hand, comparing the prevalences of use of the sample of batterers in this study with those of men from the community in Spain (Delegación del Gobierno para el Plan Nacional sobre Drogas, 2012), it is observed that for all substances the sample of abusers presents higher prevalences of consumption, both in the last year and the last month, except in the case of alcohol and heroin in the last month, where prevalences for the sample of batterers and that of community men are similar (see Table 1).

Relation between substance use and perpetration and victimization

The second objective of this study was to explore whether there are differences in the levels of perpetration

Table 1
Prevalences of use of different psychoactive substances in the sample of batterers in this study and in men in the general Spanish community

	Batterers in the study		Spanish population	
PSYCHOACTIVE SUBSTANCE	Last year	Last month	Last year	Last month
Alcohol	89,3 %	72,4 %	83,2 %	73,2 %
Alcohol (large quantities)	44,2 %	19,8 %	25,9 %	20,7 %
Heroin	7,7 %	0 %	0,2 %	0,1 %
Hypnosedatives	9,3 %	7 %	7,6 %	5,2 %
Cocaine	20,3 %	10 %	3,6 %	1,8 %
Amphetamines	8,6 %	5,2 %	0,9 %	0,4 %
Cannabis	27,8 %	14,2 %	13,6 %	10,2 %
Hallucinogens	7,7 %	5,4 %	0,6 %	0,2 %
Inhalants	6,6 %	0 %	0,1 %	0 %

and victimization, as regards intimate partner violence, between on the one hand, those abusers who use alcohol, illicit substances or both, and on the other, those who do not consume any substances. To this end, participants were divided into 4 groups: non-users, that is, those who had not used any substances in the last year (16.3%); alcohol users – those that had used only alcohol in the last year (58.6%); illicit substance users – those that had in the last year of the relation in question used some illicit substance from among those listed in Table 1 (other than alcohol (3.5%); and users of both alcohol and any other substance the relevant period (one year) (21.7%).

Analyzing the socio-demographic characteristics of the 4 groups, it can be seen that there are no statistically significant differences regarding occupation and type of violence involved in the offence; on the other hand significant differences were indeed found for the marital status variable ($\chi 2(6) = 26.48$, $p = .000$), the proportion of married men being significantly higher in the alcohol users and significantly lower in the group that uses both illicit drugs and alcohol), whilst the proportion of single men is significantly lower in the group of alcohol users and significantly higher in the group that uses both (see Table 2).

Table 2
Distribution of socio-demographic variables by user group

	Non-users (N = 93) (1)	Alcohol users (N = 335) (2)	Illicit substances (N = 20) (3)	Alcohol plus illicit substances (N = 124) (4)	$F_{(3,568)}/\chi 2$ Bonferroni
AGE (years)	41 ± 10,37	39,07 ± 10,86	35,15 ± 6,37	36,12 ± 9,49	4,99 (p = ,002) 1 > 4 (p = ,004) 2 > 4 (p = ,042)
Spaniards R.C. = C.R.	57 % (R.C. = -0,3)	52,2 % (R.C. = -3,5)	70 % (R.C. = -1,1)	74,2 % (R.C. = 4)	29,01[a] (p = ,000)
South Americans	30,1 % (R.C. = -0,9)	41,8 % (R.C. = 4,6)	20 % (R.C. = -1,4)	18,5 % (R.C. = -4,1)	
Other nationalities	12,9 % (R.C. = 2,2)	6 % (R.C. = -1,7)	10 % (R.C. = 0,4)	7,3 % (R.C. = -0,1)	
Primary Education	45,2 % (R.C. = 0,9)	34,9 % (R.C. = -3,5)	55 % (R.C. = 1,3)	51,6 % (R.C.= 2,7)	14,33 [a] (p = ,026)
Secondary Education	35,5 % (R.C. = -1,1)	45,7 % (R.C. = 3)	25 % (R.C. = -1,4)	33,1 % (R.C.= -1,9)	
University education	19,4 % (R.C. = 0,2)	19,4 % (R.C. = 0,6)	20 % (R.C. = 0,2)	15,3 % (R.C. = -1)	
Managers or directors/ businessmen/public administration employees	16,1 % (R.C. = -0,7)	19,1 % (R.C. = 0,4)	15 % (R.C. = -0.4)	19,4 % (R.C. = 0,3)	4,86 [a] (p = ,562)
Unemployed/pensioners	10,8 % (R.C. = -1,7)	17,9 % (R.C. = 0,9)	25 % (R.C. = 1)	16,9 % (R.C. = 0,1)	
Construction workers/ catering and bar or restaurant sector workers/ industrial workers	73,1 % (R.C. = 1,9)	63 % (R.C. = -1)	60 % (R.C. = -0,4)	63,7 % (R.C. = -0,3)	
Married or registered civil partners	37,6 % (R.C. = 1,2)	36,1 % (R.C. = 2,4)	25 % (R.C. = -0,7)	18,5 % (R.C. = -3,7)	26,48 [a] (p = ,000)
Single	28 % (R.C. = -1,6)	30,1 % (R.C. = -3,1)	50 % (R.C. = 1,4)	52,4 % (R.C. = 4,5)	
Widowed, separated or divorced	34,4 % (R.C. = 0,4)	33,7 % (R.C. = 0,7)	25 % (R.C. = 0,7)	29 % (R.C. = -0,9)	
Physical offence	89,2 % (R.C. = 0,6)	87,2 % (R.C. = 0,4)	70 % (R.C. = -2,4)	87,1 % (R.C. = -0,1)	5,76 [b] (p = ,124)
Psychological offence	10,8 % (R.C. = -0,6)	12,2 % (R.C. = -0,4)	30 % (R.C. = 2,4)	12,9 % (R.C. = 0,1)	

Note. The data correspond to mean ± standard deviation (*SD*), except in those cases in which they refer to percentages.
C.R. = corrected residuals.
[a]*df = 6;* [b]*df = 3*.

Differences between the 4 groups were also found for educational level ($\chi 2(6) = 14.33$, $p = .026$), where the proportion of those with primary education was significantly lower in the alcohol-only group, and significantly higher in the group that used both alcohol and illegal drugs, whilst the proportion of those with secondary education was significantly higher in the group that used only alcohol (see Table 2).

With regard to nationality ($\chi 2(6) = 29.01$, $p = .000$) the proportion of Spaniards is significantly lower in the group of alcohol users and significantly higher in the "users of both" group, while the proportion of South Americans is significantly higher in the alcohol users and significantly lower in the group that uses both alcohol and illicit drugs (see Table 2).

Finally, in relation to age, statistically significant differences were also found according to user group (F (3,568) = 4.99, $p = 002$), the mean ages of non-users and of alcohol-only users being significantly higher than that of the group that used both alcohol and illicit drugs (see Table 2).

To analyze whether the 4 groups differed in levels of perpetration and victimization, we performed an analysis of covariance (ANCOVA) controlling the effect of the age variable. As shown in Table 3, there were statistically significant differences between groups on the scales of perpetration of psychological violence (F (3,567) = 9.19, $p = .000$) physical violence (F (3,567) = 6.64, $p =. 000$) and sexual coercion (F (3,567) = 11.24, $p = .000$). Specifically, the group of illicit substance users and the group that used both illicit substances and alcohol were those with significantly higher means in psychological and sexual violence compared to non-users and the alcohol-only group; as for physical violence, it was the group that consumed both alcohol and illicit drugs that presented higher levels of violence compared to non-users and alcohol-only users (see Table 3).

On analyzing the results for victimization, statistically significant differences were observed on the scales of psychological violence (F (3,567) = 7.75, $p = .000$) and physical violence (F (3,567) = 7.59, $p = .000$). Specifically, non-users and alcohol-only users reported experiencing significantly fewer physical assaults by their partners, compared to the users of both alcohol and illicit drugs, whilst the non-users and alcohol users also reported fewer cases of psychological violence compared to the illicit drugs and "both" groups (see Table 3).

Table 3
Comparison of levels of intimate partner violence and victimization in users and non-users of psychoactive substances

	Non-users (N = 93) (1)	Alcohol users (N = 335) (2)	Illicit substances (N = 20) (3)	Alcohol plus illicit substances (N = 124) (4)		
Variable	*M* (± *SD*)	*M* (± *SD*)	*M* (± *SD*)	*M* (± *SD*)	$F_{(3, 567)}$	Bonferroni
CTS2 – Perpetration						
Psychological violence	16,12 ± 22,82	15,95 ± 23,71	39,95 ± 41,55	25,27 ± 26,84	9,19 (p = ,000)	1 < 3 (p = ,001) 2 < 3 (p = ,000) 2 < 4 (p = ,003)
Physical violence	2,95 ± 5,44	3,94 ± 9,53	7,51 ± 9,21	7,78 ± 11,65	6,64 (p = ,000)	1 < 4 (p = ,001) 2 < 4 (p = ,001)
Sexual coercion	0,58 ± 2,77	1,93 ± 7,48	5,19 ± 7,62	5,41 ± 7,29	11,24 (p = ,000)	1 < 3 (p = ,043) 1 < 4 (p = ,000) 2 < 4 (p = ,000)
Harm	1,96 ± 7,77	1,42 ± 4,88	1,32 ± 2,79	1,56 ± 4	0,27 (p = ,847)	
CTS2 – Victimization						
Psychological violence	17,40 ± 23,97	24,99 ± 31,12	40,87 ± 41,91	36,28 ± 37,21	7,75 (p = ,000)	1 < 3 (p = ,019) 1 < 4 (p = ,000) 2 < 4 (p = ,005)
Physical violence	6,59 ± 17,05	8,23 ± 18,35	16,71 ± 14,75	18,03 ± 31,63	7,59 (p = ,000)	1 < 4 (p = ,001) 2 < 4 (p = ,000)
Sexual coercion	0,70 ± 3,13	1,67 ± 8,61	1,24 ± 5,57	2,81 ± 11,11	1,12 (p = ,342)	
Harm	0,83 ± 1,57	1,64 ± 4,40	1,29 ± 2,46	1,36 ± 3,48	1,13 (p = ,338)	

Note. The data correspond to mean ± standard deviation (*SD*).
CTS2 = Revised Conflict Tactics Scale.

Discussion

The results of this study allow us to conclude, first of all, that there are high levels of psychoactive substance use among batterers. Comparing the prevalences of consumption in the last year in this sample with those of men the general Spanish community (Delegación del Gobierno para el Plan Nacional sobre Drogas, 2012), the sample of batterers presents higher prevalences of use in the last year for all the substances analyzed. These data are in line with those of numerous previous studies linking both alcohol use (Klostermann & Fals-Stewart, 2006; Langenderfer, 2013; Smith et al., 2012) and use of illegal drugs (Moore & Stuart, 2004; Moore et al., 2008; Smith et al., 2012) with intimate partner violence.

The prevalences of use found in this research are similar to those found by Moore and Stuart (2004), who analyzed drug use in the last year in a sample of batterers in treatment, except in relation to cannabis use, which was 53% in the last year, compared to 27.8% in the present study – though other studies refer to prevalence rates for cannabis use in the last year ranging from 32% to 88% (Brown et al., 1999; Logan, Walker, & Leukefeld, 2001; Roberts, 1987; Stuart & Holtzworth-Munroe, 1996). For the rest of substances, Moore and Stuart (2004) obtained 23.8% for cocaine in the last year, versus to 20.3% in the present study; hallucinogens 14.6% versus 7.7%; amphetamines 6.6% versus 8.6%; hypnosedatives 11.3% versus 9.3%; and heroin 7.9% versus 7.7%. Finally, in relation to the use of alcohol in large quantities, prevalence in the last month in this study was 19.8%, versus the 17.8% (prevalence of abusive alcohol consumption in the last month) found by Lipsky and Caetano (2011) and the 17% (prevalence of alcohol abuse in the last month) obtained by Cunradi (2009). The prevalence of alcohol use in large quantities in the past year in this study was 44.2%, compared to the 59.7% found in the study by McKinney et al. (2009). These data are similar to those of other international studies, and highlight the importance of alcohol and drug use in the perpetration of violent behaviour in intimate partner relationships, as indicated by several studies included in recent meta-analyses (Foran & O 'Leary, 2008; Stith et al., 2004), which conclude that the probability of assault is 8-11 times higher on days that alcohol and drugs are consumed compared to days on which they are not consumed (Fals-Stewart, 2003).

On comparing the levels of perpetration and victimization 4 groups of perpetrators (non-users, alcohol users, illegal drug users and users of both alcohol and illegal drugs), the results indicate that of the 4 groups, that presenting the highest levels of violence (perpetration and victimization) is that made up of users of both illegal drugs and alcohol, and this result is in line with those of other research that found higher levels of perpetration and victimization of aggression in batterers that use illegal drugs (Moore & Stuart., 2004; Moore et al., 2008; Smith et al., 2012).

The most important distinguishing aspect of the present research is that both the consumption of illegal drugs and their use in conjunction with alcohol significantly increase the probability of committing acts of psychological violence, physical violence and sexual coercion in the intimate partner relationship, compared to the cases of non-users or alcohol-only users. As regards victimization, the results are in the same line, and it is users of illegal drugs together with alcohol who are most likely to be victims of psychological and physical violence from their partners. Men belonging to these two groups are largely younger and unmarried and maintain more unstable relationships. The use of illegal drugs affects one's lifestyle and conception of what an intimate partner relationship means, which from the results appears to be different from that of the first two groups.

Furthermore, the results suggest that alcohol consumption alone has no significant effect on aggression, and also that men in this group are the most numerous, are older and married – similarly to the case of non-users. These data suggest that alcohol use appears to be quite normalized (alcohol is of course mostly easily accessible) and that it is well integrated in our culture and patterns of socio-interpersonal relations, and that this is in contrast to the cases of the other two use patterns (illicit substances/alcohol plus illicit substances) and to the situations in other countries (Bloomfield, Stockwell, Gmel, & Rehn, 2003).

From an applied point of view, the data from this study imply that, with regard to treatment, it is important to analyze substance use in detail. In the case of confirming that there is use of either illicit drugs alone or illicit drugs plus alcohol, it would be necessary to develop an alternative treatment programme or refer the case to specialized help services. On the other hand, if there is only alcohol use within parameters in line with those of the community population, it will be a case of applying, as part of treatment programmes for batterers, specific modules with the aim of raising participants' awareness about the potential effects of alcohol on violent behaviours, as well addressing possible mistaken expectations about alcohol use, providing realistic information on alcohol and its effects, and finally, motivating participants to undergo specific treatment for alcohol use, in case of need.

Looking to future research, in addition to analyzing the effect of use of specific substances on levels of violence and victimization in situations of intimate partner relationships, it would be interesting to carry out longitudinal analyses on substance use and its effect on the efficacy of interventions and levels of reoccurrence.

Acknowledgements

This research was supported by the Spanish Ministry of Science and Innovation (Plan Nacional I+D+I; Ref.: PSI2008-02215).

Conflicts of interests

The authors declare that there are no conflicts of interests.

References

Bennett, L., Goodman, L., & Dutton, M. A. (2000). Risk assessment among batterers arrested for domestic assault: The salience of psychological abuse. *Violence Against Women, 6,* 1190-1203. doi: 10.1177/10778010022183596.

Bloomfield, K., Stockwell, T., Gmel, G., & Rehn, N. (2003). International comparisons of alcohol consumption. *Alcohol Research & Health, 27,* 95-109.

Bobes, J., González, M. P., Sáiz, P. A., & Bousoño, M. (1996). *Índice europeo de la severidad de la adicción: EuropASI. Versión española.* IV Reunión Interregional de Psiquiatría Minutes (pp. 201-218).

Breiding, M. J., Black, M. C., & Ryan, G. W. (2008). Chronic disease and health risk behaviors associated with intimate partner violence–18 U.S. states/territories, 2005. *Annals of Epidemiology, 18,* 538-544. doi: 10.1016/j.annepidem.2008.02.005.

Brown, T. G., Werk, A., Caplan, T., & Seraganian, P. (1999). Violent substance abusers in domestic violence treatment. *Violence and Victims, 14*, 179-190.

Bushman, B. J., & Cooper, H. M. (1990). Effects of alcohol on human aggression: An integrative research review. *Psychological Bulletin, 107*, 341-354. doi: 10.1037//0033-2909.107.3.341.

Castillo-Carniglia, A., Pizarro, E., Luengo, D., & Soto-Brandt, G. (2014). Consumo de alcohol y autoinforme de eventos violentos en Chile. *Adicciones, 26*, 46-53.

Catalá-Miñana, A., Lila, M., & Oliver, A. (2013). Consumo de alcohol en hombres penados por violencia contra la pareja: factores individuales y contextuales. *Adicciones, 25*, 19-28.

Chermack, S. T., Fuller, B. E., & Blow, F. C. (2000). Predictors of expressed partner and non-partner violence among patients in substance abuse treatment. *Drug and Alcohol Dependence, 58,* 43-54. doi: 10.1016/S0376-8716(99)00067-8.

Coker, A. L., Davis, K. E., Arias, I., Desai, S., Sanderson, M., Brandt, H. M., & Smith, P. H. (2002). Physical and mental health effects of intimate partner violence for men and women. *American Journal of Preventive Medicine, 23,* 260-268. doi: 10.1016/S0749-3797(02)00514-7.

Cunradi, C. (2009). Intimate partner violence among Hispanic men and women: The role of drinking, neighborhood disorder, and acculturation-related factors. *Violence and Victims, 24*, 83-97. doi: 10.1891/0886-6708.24.1.83.

Delegación del Gobierno para el Plan Nacional sobre Drogas (2012). *Informe Nacional 2012 (datos del 2011) al OEDT por el Punto Focal Nacional Reitox. España. Evolución, Tendencias y Cuestiones Particulares.* Madrid: Ministerio de Sanidad, Servicios Sociales e Igualdad.

El-Bassel, N., Gilbert, L., Wu, E., Go, H., & Hill, J. (2005). Relationship between drug abuse and intimate partner violence: A longitudinal study among women receiving methadone. *American Journal of Public Health, 95,* 465-470. doi: 10.2105/AJPH.2003.023200.

Fals-Stewart, W. (2003). The occurrence of partner physical aggression on days of alcohol consumption: A longitudinal diary study. *Journal of Consulting and Clinical Psychology, 71*, 41-52. doi: 10.1037/0022-006x.71.1.41.

Foran, H. M., & O'Leary, K. D. (2008). Alcohol and intimate partner violence: A meta-analytic review. *Clinical Psychology Review, 28,* 1222-1234. doi: 10.1016/j.cpr.2008.05.001.

Gordon, J. A., & Moriarty, L. J. (2003). The effects of domestic violence batterer treatment on domestic violence recidivism. *Criminal Justice and Behavior, 30,* 118-134. doi: 10.1177/0093854802239166.

Grant, B. F., & Kaplan, K. (2005). *Source and accuracy statement for wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC*). Rockville, MD: National Institute on Alcohol Abuse and Alcoholism.

Hove, M. C., Parkhill, M. R., Neighbors, C., McConchie, J. M., & Fossos, N. (2010). Alcohol consumption and intimate partner violence perpetration among college students: The role of self-determination. *Journal of Studies on Alcohol and Drugs, 71*, 78-85.

Kilpatrick, D. G., Acierno, R., Resnick, H. S., Saunders, B. E., & Best, C. L. (1997). A 2-year longitudinal analysis of the relationships between violent assault and substance use in women. *Journal of Consulting and Clinical Psychology, 65,* 834-847. doi: 10.1037//0022-006X.65.5.834.

Klostermann, K., & Fals-Stewart, W. (2006). Intimate partner violence and alcohol use: Exploring the role of drinking in partner violence and its implications for intervention. *Aggression and Violent Behavior: A Review Journal, 11*, 587-597. doi: 10.1016/j.avb.2005.08.008.

Kokkevi, A., & Hartgers, C. (1995). European adaptation of a multidimensional assessment instrument for drug and alcohol dependence. *European Addiction Research, 1*, 208-210. doi: 10.1159/000259089.

Langenderfer, L. (2013). Alcohol use among partner violent adults: reviewing recent literature to inform intervention. *Aggression and Violent Behavior, 18*, 152-158. doi: 10.1016/j.avb.2012.11.013.

Ley Orgánica 1/2004 (2004). Medidas de Protección Integral Contra la Violencia de Género. *Boletín Oficial*

del Estado núm. 313 (29 de Diciembre, 2004). Retrieved from http://www.boe.es/boe/dias/2004/12/29/pdfs/A42166-42197.pdf.

Lipsey, M. W., Wilson, D. B., Cohen, M. A., & Derzon, J. H. (1997). Is there a causal relationship between alcohol use and violence? A synthesis of evidence. En M. Galanter (Ed.), *Recent developments on alcoholism: Vol. 13. Alcohol and violence* (pp. 245-282). New York, NY: Plenum Press.

Lipsky, S., & Caetano, R. (2011). Intimate partner violence perpetration among men and emergency department use. *The Journal of Emergency Medicine, 40*, 696-703. doi: 10.1016/j.jemermed.2008.04.043.

Logan, T. K., Walker, R., & Leukefeld, C. G. (2001). Intimate partner and nonintimate violence history among drug-using, incarcerated men. *International Journal of Offender Therapy and Comparative Criminology, 45*, 228-243. doi: 10.1177/0306624X01452008.

Loinaz, I., Echeburúa, E. Ortiz-Tallo, M., & Amor, P. (2012). Propiedades psicométricas de la Conflict Tactics Scales (CTS-2) en una muestra española de agresores de pareja. *Psicothema, 24*, 142-148.

McKinney, C. M., Caetano, R., Ramisetty-Mikler, S., & Nelson, S. (2009). Childhood family violence and perpetration and victimization of intimate partner violence: Findings from a national population-based study of couples. *Annals of Epidemiology, 19*, 25-32. doi: 10.1016/j.annepidem.2008.08.008.

McLellan, A. T., Kushner, H., Metzger, D., Peters, R., Smith, I., Grissom, G.,… Argeriou, M. (1992). The Fifth Edition of the Addiction Severity Index. *Journal of Substance Abuse Treatment, 9*, 199-213. doi: 10.1016/0740-5472(92)90062-S.

Moore, T., & Stuart, G. (2004). Illicit substance use and intimate partner violence among men in batterers' intervention. *Psychology of Addictive Behaviors, 18*, 385-389. doi: 10.1037/0893-164X.18.4.385.

Moore, T. M., Stuart, G. L., Meehan, J. C., Rhatigan, D. L., Hellmuth, J. C., & Keen, S. M. (2008). Drug abuse and aggression between intimate partners: A meta-analytic review. *Clinical Psychology Review, 28*, 247-274. doi: 10.1016/j.cpr.2007.05.003.

Murphy, C. M., O'Farrell, T. J., Fals-Stewart, W., & Feehan, M. (2001). Correlates of intimate partner violence among male alcoholic patients. *Journal of Consulting and Clinical Psychology, 69,* 528-540. doi: 10.1037//0022-006X.69.3.528.

O'Farrell, T. J., Fals-Stewart, W., Murphy, M., & Murphy, C. M. (2003). Partner violence before and after individually-based alcoholism treatment for male alcoholic patients. *Journal of Consulting and Clinical Psychology, 71*, 92-102. doi: 10.1037//0022-006X.71.1.92.

O'Farrell, T. J., & Murphy, C. M. (1995). Marital violence before and after alcoholism treatment. *Journal of Consulting and Clinical Psychology, 63*, 256-262. doi: 10.1037//0022-006X.63.2.256.

Pernanen, K. (1991). *Alcohol in human violence*. New York: Guilford Press.

Ravndal, E., Vaglum, P., & Lauritzen, G. (2005). La finalización del tratamiento de internamiento a largo plazo para drogadictos: Estudio prospectivo de 13 unidades. *RET, Revista de Toxicomanías, 44*, 25-30.

Rhodes, K. V., Houry, D., Cerulli, C., Straus, H., Kaslow, N., & McNutt, L. (2009). Intimate partner violence and comorbid mental health conditions among urban male patients. *Annals of Family Medicine, 7*, 47-55. doi: 10.1370/afm.936.

Roa, A. (1995). *Evaluación en psicología clínica y de la salud.* Madrid: CEPE.

Roberts, A. R. (1987). Psychosocial characteristics of batterers: A study of 234 men charged with domestic violence offenses. *Journal of Family Violence, 2*, 81-93. doi: 10.1007/BF00976372.

Smith, P., Homish, G., Leonard, K., & Cornelius, J. (2012). Intimate partner violence and specific substance use disorders: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychology of Addictive Behaviors, 26*, 236-245. doi: 10.1037/a0024855.

Stith, S. M., Smith, D. B., Penn, C. E., Ward, D. B., & Tritt, D. (2004). Intimate partner physical abuse perpetration and victimization risk factors: A meta-analytic review. *Aggression and Violent Behavior, 10*, 65-98. doi: 10.1016/j.avb.2003.09.001.

Straus, M. A., Hamby, S. L., Boney-McCoy, S., & Sugarman, D. B. (1996). The revised Conflict Tactics Scales (CTS2): Development and preliminary psychometric data. *Journal of Family Issues, 17*, 283-316. doi: 10.1177/019251396017003001.

Stuart, G. L., & Holtzworth-Munroe, A. (1996). *A multimethod assessment of impulsivity and related constructs in maritally violent and non-violent men.* Poster presentado en la 30th annual meeting of the Association for the Advancement of Behavior Therapy, New York, NY.

Stuart, G. L., Temple, J. R., & Moore, T. M. (2007). Improving batterer intervention programs through theory-based research. *Journal of the American Medical Association, 298,* 560-562. doi: 10.1001/jama.298.5.560.

Taft, C., Schumm, J., Orazem, R. J., Meis, L., & Pinto, L. A. (2010). Examining the link between posttraumatic stress disorder symptoms and dating aggression perpetration. *Violence and Victims, 25*, 456-469. doi: 10.1891/0886-6708.25.4.456.

Testa, M., Livingston, J. A., & Leonard, K. E. (2003). Women's substance use and experiences of intimate partner violence: A longitudinal investigation among a community sample. *Addictive Behaviors, 28,* 1649-1664. doi: 10.1016/j.addbeh.2003.08.040.

Walton, M. A., Chermack, S. T., & Blow, F. C. (2002). Correlates of received and expressed violence persistence following substance abuse treatment. *Drug and Alcohol Dependence, 67,* 1-12. doi: 10.1016/S0376-8716(02)00016-9.

Smoking cessation after 12 months with multi-component therapy

Abstinencia a los 12 meses de un programa multicomponente para dejar de fumar

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Abstract

Smoking is one of the most important causes of morbidity and mortality in developed countries. One of the priorities of public health programmes is the reduction of its prevalence, which would involve millions of people quitting smoking, but cessation programs often have modest results, especially within certain population groups. The aim of this study was to analyze the variables determining the success of a multicomponent therapy programme for smoking cessation. We conducted the study in the Smoking Addiction Unit at the Hospital of Manresa, with 314 patients (91.4% of whom had medium or high-level dependency). We observed that higher educational level, not living with a smoker, following a multimodal programme for smoking cessation with psychological therapy, and pharmacological treatment are relevant factors for quitting smoking. Abstinence rates are not associated with other factors, such as sex, age, smoking behaviour characteristics or psychiatric history. The combination of pharmacological and psychological treatment increased success rates in multicomponent therapy. Psychological therapy only also obtained positive results, though somewhat more modest.

Key words: multimodal treatment, smoking cessation, mental disorders, heavy smokers.

Resumen

El tabaquismo es una de las causas de morbimortalidad más importantes en los países desarrollados. Uno de los objetivos prioritarios de los programas de salud pública es la disminución de su prevalencia lo que implica que millones de personas dejen de fumar, sin embargo los programas de cesación a menudo tienen resultados discretos, especialmente con algunos grupos de población. El objetivo de este estudio fue analizar la eficacia de un tratamiento de cesación tabáquica multicomponente realizado en una unidad de tabaquismo hospitalaria. Fue realizado en la Unidad de Tabaquismo del Hospital de Manresa, e incluyó 314 pacientes (91,4% presentaban un nivel de dependencia medio o alto). Se observó que el nivel de estudios, no convivir con fumadores, seguir la terapia multicomponente y utilizar tratamiento farmacológico son factores relevantes en el éxito al dejar de fumar. La tasa de abstinencia no se asocia con otras características como el sexo, la edad, las características del hábito tabáquico o el presentar antecedentes psiquiátricos. La combinación del tratamiento farmacológico y psicológico aumentó las tasas de éxito en la terapia multicomponente. La terapia psicológica única también obtuvo resultados positivos aunque más modestos.

Palabras clave: tratamiento multicomponente, deshabituación tabáquica, trastornos mentales, pacientes con alta dependencia.

Received: June 2014; Accepted: October 2014

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Among the most challenging aspects involved in interventions with smokers are the chronicity of this addiction and the apparent limitations of programmes designed to help people quit smoking. In order to design interventions with maximal levels of efficiency, it is of the utmost importance to consider previous studies that can contribute data for analyzing the conditions and characteristics of efficacious treatments, the predictors of good results, the characteristics of participants and their success or failure in smoking cessation programmes.

There are a range of different types of smoking cessation interventions: brief advice from a health professional (the person is advised and encouraged to give up smoking), self-help courses and materials, the prescription of pharmacological treatments with or without follow-up, motivational interventions, and multicomponent therapy (Hays, Ebbert, & Sood 2009; Hays, Leischow, Lawrence, & Lee 2010; Stead & Lancaster 2012). The last in this list may be the most intensive of such interventions, since it combines psychological and pharmacological interventions of proven efficacy. The results of smoking cessation treatments currently available are modest: the most efficacious have achieved no more than 30-40% abstinence rates at the one-year follow-up (Ranney, Melvin, Lux, McClain, & Lohr, 2006) in general population.

Pharmacological treatment and smoking cessation advice have been widely analyzed in the scientific literature, and the majority of studies concur that they increase the likelihood of success in quitting smoking (PHS Guideline Update Panel, Liaisons, and Staff, 2008; Silagy, Lancaster, Stead, Mant, & Fowler, 2004; Wilkes, 2008). Various studies have shown that sociodemographic variables (sex, educational level, socioeconomic level) influence the results, as well as the characteristics of the smoking addiction and the person's health antecedents (Nerin, Novella, Beamonte, Gargallo, Jimenez-Muro, & Marqueta, 2007; Ramon & Bruguera, 2009). However, there is scarcely any research analyzing these aspects in multicomponent therapy, whose efficacy has indeed been studied, but not the influence on it of these variables (Bauld, Bell, McCullough, Richardson, & Greaves, 2010; Hays et al., 2009).

Addictive disorders are complex entities that affect human behaviour with physiological, psychological and sociological bases. The comprehensive approach involved in multicomponent therapy is that which has yielded the best outcomes in the medium and long term (PHS Guideline Update Panel, 2008; Alonso-Perez, Alonso-Cardeñoso, Garcia-Gonzalez, Fraile-Cobos, Lobo-Llorente, & Secades-Villa, 2013; Stead & Lancaster 2005). Thus, the aim of the present study was to analyze the efficacy of a multicomponent smoking cessation treatment carried out in a hospital Smoking Addiction Unit and how its outcomes were influenced by the characteristics of participants and their addiction, social factors, different pharmacological treatments, and psychological therapy.

Method

Design and participants

Longitudinal study of 314 patients who attended the Smoking Addiction Unit at the Hospital de Manresa (Manresa, Spain) to try and quite smoking between January 2001 and December 2009. This unit takes in patients referred from other departments in the same hospital or from primary care services, where all have received brief interventions for smoking cessation, and more than 65% have received specific interventions that have failed (carried out by specialist nurses working in primary care, cardiology units, pulmonary units, etc.). Included in the study were all those patients treated in the unit that followed multicomponent therapy; inclusion was in accordance with order of registration on the waiting list, where they remained for an average of nine months. Exclusion criteria for the multicomponent treatment were: psychiatric illness in an acute phase or a psychotic disorder, reading and/or writing problems, and other disorders that would make it difficult to follow the therapy. The majority of the patients referred to this programme were from the central area of Catalonia (Manresa and the surrounding area).

Procedure

A one-year follow-up was carried out, counting from the point at which the patient gave up or should have given up smoking, which for the patients meant a mean of 14 months of therapy. A total of 90% of the patients received the multicomponent therapy in group format, while just 10% did so on an individual basis. The structure of the therapy was the same for the group and individual formats. In principle, all patients were assigned to the group mode, the individual format being employed only in exceptional cases (pregnant patients who could not wait for the start of group programme, or people with difficulties for following the group timetable). The therapy was implemented by the same professionals (a psychologist and a lung specialist) throughout the study. The multicomponent treatment programme brings together all those strategies that have shown themselves to be efficacious (Alonso-Perez et al., 2014; Fiore, Jaen, Baker, Bailey, Benowitz, & Curri, 2009): psychological treatments based on behavioural, cognitive, motivational and relapse prevention techniques combined with pharmacological treatment based on nicotine replacement (Becoña & Míguez, 2008; Ranney et al., 2006), bupropion and varenicline (Wu, Wilson, Dimoulas, & Mills, 2006; Tinich & Sadler 2007; Cahill, Stevens, & Lancaster 2014). Multicomponent therapy consists of three phases: a) "preparation", which involves psychoeducation about addiction, motivation to quit, changing habits, and monitoring of tobacco use with or without reduction in six weekly 75-minte sessions; b) "cessation", in which pharmacological treatment is introduced where applicable

and the therapists work on coping with the day the patient gives up ("D-Day"), withdrawal syndrome and craving, in four two-weekly 60-minute sessions; and c) "relapse prevention", following the models of Marlatt, Curry and Gordon (1988) and Baer and Marlatt (1991), in 10 monthly 60-minute sessions.

The therapy involved no direct financial cost for the patients, except for the pharmacological treatment, for which they had to pay. All the patients received the same psychological therapy and assignment to one type of pharmacological treatment or another was in line with clinical criteria, taking into account at each moment the treatment that could most benefit the patient in accordance with availability, previous experience, personal health antecedents and pharmacological interactions with other treatments he or she might be undergoing at that time. Some patients decided not to take up the treatment, and this group also includes those who did not receive treatment because they dropped out of the programme before beginning it (n=69).

Those patients that did not take up the treatment for whatever reason remained in the study, and were contacted by telephone or personally for the purpose of obtaining the necessary follow-up data. The distribution of the patients across the different treatment modes and retention up to the 12-month follow-up are shown in detail in Figure 1.

Information on sociodemographic variables, heath antecedents and smoking characteristics were obtained at the first visit (which was always individual) based on the patient interview and the data from the person's clinical records. Information on how the patient was developing and the drugs used was recorded in the first, third, sixth and twelfth month after "D-Day". All patients were contacted in person at the hospital or by telephone for the follow-up (months 1, 3, 6 and 12) and all the relevant information recorded. All the patients who claimed to remain abstinent were given an appointment to take a carbon monoxide test.

Instruments

The objective measure of abstinence used was level of carbon monoxide (CO) in expired air, or co-oximetry (abstinent if CO≤6ppm) (Middleton & Morice, 2000). The instrument employed for this purpose was a co-oximeter (Bedfont Pico Smokerlyzer®).

For the data analysis, the following variables were taken into account: sex, age, educational level, living with other smokers or not, occupation, number of cigarettes smoked per day, years smoked, level of dependence according to Fagerström Test (low dependence ≤4; medium=5; high ≥6), psychiatric antecedents (yes/no), multicomponent therapy (yes/no), pharmacological treatment (yes/no), and drug used for smoking cessation.

Statistical analysis

The categorical variables are shown as absolute value and relative frequency. The continuous variables are shown with the mean and standard deviation. We calculated the accumulated incidence of abstinence, both global and according to multicomponent programme, at 1, 3, 6 and 12 months, together with its 95% confidence interval. The variables associated with relapse at 12 months were examined using bivariate and multivariate logistic regression models. In the multivariate logistic regression model we introduced the covariables found to be significant in the bivariate analysis, or with evidence of their association. We used a stepwise exclusion strategy controlled by the researcher. The

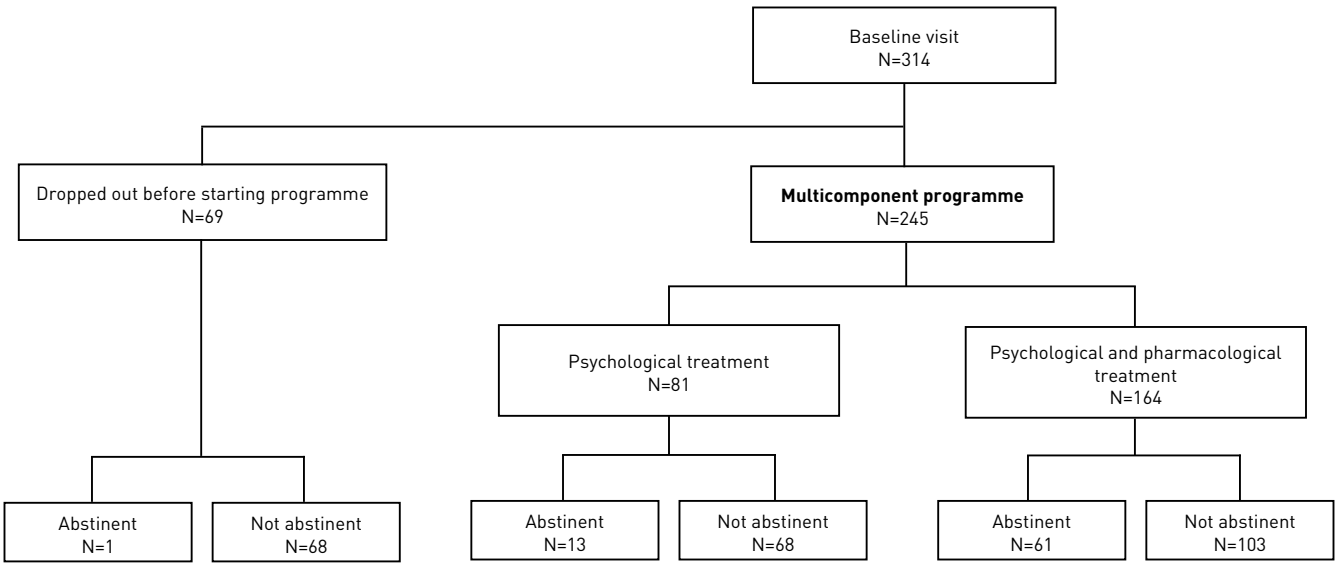

Figure 1. Patient flow

raw and adjusted odds ratios (OR) and the 95% confidence intervals (CI 95%) were calculated. Statistical significance level was bilateral 5% (p<0.05).

The programs used in the statistical analysis were IBM® SPSS® Statistics for Windows v.22 (IBM Corporation, Armonk, New York, USA) and Stata® v.10 (StataCorp LP, College Station, Texas, USA).

Results

Mean age of the patients was 48.5 years; 61.8% were men, 61.9% had only elementary education and 32.6% were skilled workers or professionals. As regards smoking characteristics, 50.3% lived with other smokers, 34.4% had been smoking for 35 years or more, 48.2% smoked 21 or more cigarettes per day, and 68.8% had high nicotine dependence (score ≥6) according to the Fagerström Test. Furthermore, 57.1% of the patients had made two or more previous attempts to quit smoking, 85% had been referred to the programme from other hospital departments where they were being treated for illnesses associated with smoking, and 58% had psychiatric antecedents (Table 1).

Of the total 314 patients, we included all those who during the studied period put their names down on the waiting list and came to the first appointment when called; of these, 69 dropped out of the programme before the first session of multicomponent therapy and the remaining 245 began the multicomponent therapy (Figure 1). Of these 245 patients, 81 did not receive the pharmacological treatment, on their own or the doctors' decision (n=29) or because they gave up the therapy before completing the first phase (n=52).

Abstinence for the whole sample was 50.3% at the one-month follow-up, 38.5% at three months, 29.0% at six months and 23.9% at 12 months. Patients who received psychological and pharmacological treatment obtained the highest abstinence rates at all the follow-up points, showing an abstinence rate at 12 months of 37.2%, followed by those who received psychological therapy only, with a rate of 16%, and those who received no type of treatment (1.4%) (Table 2).

In the bivariate analysis, sex, age, years smoked, dependence (score on Fagerström Test) and psychiatric antecedents, did not appear as relapse risk factors. A trend towards significance was observed, with higher relapse rate, among younger patients (OR 0.98) and those who had been smoking for 20 years or less (OR 1.96). Having at least

Table 1.
Baseline characteristics of participants (n=314)

	n=(%)
Mean age [standard deviation]	48,5±[12,1]
Sex	
Man	194 (61,8)
Woman	120 (38,2)
Educational level	
Primary	192 (61,9)
Secondary	63 (20,3)
University	55 (17,7)
Living with smokers	
No	156 (49,7)
Yes	158 (50,3)
Years smoked	
≤ 20	68 (21,7)
21-35	138 (43,9)
> 35	108 (34,4)
Fagerström Test	
< 4 Low	27 (8,6)
4-5 Medium	71 (22,6)
≥ 6 High	216 (68,8)
Psychiatric antecedents	
No	132 (42,0)
Yes	182 (58,0)
Multicomponent programme	
Neither psychological nor pharmacological treatment	69 (22,0)
Psychological treatment	81 (25,8)
Psychological and pharmacological treatment	164 (52,2)
Nicotine replacement therapy	84 (51,2)
Bupropion	30 (18,3)
Varenicline	50 (30,5)

Table 2.
Abstinence (global and according to multicomponent programme) at 1, 3, 6 and 12 months

	n	1 month[a]	3 months[a]	6 months[a]	12 months[a]
Global	314	50,3 (44,6-56,0)	38,5 (33,1-44,2)	29,0 (24,0-34,3)	23,9 (19,3-29,0)
According to multicomponent programme					
Neither psychological nor pharmacological treatment	69	2,9 (0,4-10,1)	1,4 (0,04 -7,8)	1,4 (0,04 -7,8)	1,4 (0,04 -7,8)
Psychological treatment	81	27,2 (17,9-38,2)	23,5 (14,8-24,2)	16,0 (8,8-25,9)	16,0 (8,8-25,9)
Psychological and pharmacological treatment	164	81,7 (74,9-87,3)	61,6 (53,7-69,1)	47,0 (39,1-54,9)	37,2 (29,8-45,1)
Nicotine replacement therapy	84	83,3 (73,6-90,6)	61,9 (50,7-72,3)	50,0 (38,9-61,1)	44,0 (33,2-55,3)
Bupropion	30	83,3 (65,3-94,4)	70,0 (50,6-85,3)	50,0 (31,3-68,7)	36,7 (19,9-53,9)
Varenicline	50	78,0 (64,0-88,5)	56,0 (41,3-70,0)	40,0 (26,4-54,8)	26,0 (14,6-40,3)

[a] % (95% Confidence Interval)

Table 3.
Risk factors for relapse at 12 months. Bivariate analysis.

	Abstinence[a] n=75	Relapses[a] n=239	Raw OR (95% CI)	p value
Mean age [standard deviation]	50,7±[12,0]	47,8±[12,0]	0,98 (0,96-1,00)	0,068
Sex				
Man	51 (26,3)	143 (73,7)	1[b]	
Woman	24 (20,0)	96 (80,0)	1,43 (0,82-2,47)	0,205
Educational level				
Primary	35 (18,2)	157 (81,8)	1[b]	
Secondary	23 (36,5)	40 (63,5)	0,39 (0,21-0,73)	0,003
University	16 (29,1)	39 (70,9)	0,54 (0,27-1,08)	0,082
Living with smokers				
No	47 (30,1)	109 (69,9)	1[b]	
Yes	28 (17,7)	130 (82,3)	2,00 (1,18-3,41)	0,011
Years smoked				
> 35	32 (29,6)	76 (70,4)	1[b]	
21-35	31 (22,5)	107 (77,5)	1,45 (0,82-2,58)	0,202
<= 20	12 (17,6)	56 (82,4)	1,96 (0,93-4,15)	0,077
Fagerström Test				
<4 Low	7 (25,9)	20 (74,1)	1[b]	
4-5 Medium	24 (33,8)	47 (66,2)	0,68 (0,25-1,85)	0,455
<= 6 High	44 (20,4)	172 (79,6)	1,37 (0,54-3,44)	0,505
Psychiatric antecedents				
No	36 (27,3)	96 (72,7)	1[b]	
Yes	39 (21,4)	143 (78,6)	1,38 (0,82-2,32)	0,231
Multicomponent programme				
Neither psychological nor pharmacological treatment	1 (1,4)	68 (98,6)	1[b]	
Psychological treatment	13 (16,0)	68 (84,0)	0,08 (0,01-0,60)	0,015
Psychological and pharmacological treatment	61 (37,2)	103 (62,8)	0,02 (0,003-0,18)	< 0,001
Nicotine replacement therapy	37 (44,0)	47 (56,0)	1[b]	
Bupropion	11 (36,7)	19 (63,3)	1,36 (0,58-3,21)	0,483
Varenicline	13 (26,0)	37 (74,0)	2,24 (1,04-4,81)	0,039

[a] Number of individuals (% of row). [b] Reference category
OR: *Odds Ratio*; 95% CI: 95% Confidence Interval .

secondary education, not living with smokers, and receiving multicomponent therapy with psychological treatment alone or in conjunction with pharmacological treatment emerged as predictors of success ($p<0.05$). As regards pharmacological treatments, nicotine replacement therapy is found to be the best predictor of success, with significant differences compared to varenicline, though not compared to bupropion (Table 3).

In the multivariate analysis, the factors found to protect against relapse were having a secondary or university education, not living with smokers, and receiving some type of smoking cessation treatment, be it psychological only or psychological plus pharmacological (Table 4).

Table 4.
Risk factors for relapse at 12 months. Multivariate analysis.

	Adjusted OR (95% CI)	p value
Age	0,98 (0,96-1,01)	0,169
Sex		
Man	1[a]	
Woman	1,36 (0,69-2,66)	0,371
Educational level		
Primary	1[a]	
Secondary	0,36 (0,18-0,73)	0,005
University	0,41 (0,19-0,89)	0,024
Living with smokers		
No	1[a]	
Yes	2,03 (1,12-3,68)	0,020
Multicomponent programme		
Neither psychological nor pharmacological treatment	1[a]	
Psychological treatment	0,06 (0,01-0,51)	0,010
Psychological and pharmacological treatment	0,02 (0,003-0,17)	<0,001

[a] OR: *Odds Ratio*; 95% CI: 95% Confidence Interval.

Discussion

As a result of a multicomponent smoking cessation programme, 1 in 4 smokers with high levels of dependence remained abstinent at the 12-month follow-up. These results are independent of sex, age, psychiatric antecedents or smoker characteristics. On the other hand, social factors such as educational level or living/not living with other smokers did indeed influence the results of this type of therapy. Furthermore, receiving multicomponent therapy with or without pharmacological treatment clearly increases the likelihood of success, though patients who also receive pharmacological treatment achieve better abstinence rates.

The results obtained in this study raise a number of points for discussion. Some of the findings are at odds with those of previous research. Thus, for example, the abstinence rates are somewhat lower than might be expected for a high-intensity therapy, while aspects such as participant's sex or psychiatric antecedents, which in the majority of studies affect the success of the treatment (Fernández, García, Schiaffino, Borràs, Nebot, & Segura, 2001; Nerín et al., 2007; Perkins & Scott, 2008; Piper et al., 2010) do not yield differences in this respect in our study.

These low abstinence rates compared to those of other studies (Becoña & Vazquez, 1998; Nerín et al., 2007) may be due to the fact that the sample is not from the general population; indeed, it is highly selective: the study took place in a hospital smoking cessation unit, with participants who had failed in previous attempts to quit smoking, with high levels of nicotine dependence and who had been referred from other hospital departments because they presented smoking addiction-related pathologies. Some authors refer to such people as recalcitrant smokers (Wilson, Wakefield, Owen, & Roberts, 1992). Moreover, the results were analyzed on an "intent-to-treat" basis, which makes it difficult to compare this study with previous ones that exclude those patients who gave up after the first visit. We found no differences between men and women at any of the follow-ups or at the end of the treatment. Although some previous studies refer to sex differences (Bjornson et al., 1995) in success rates for smoking cessation, more recent studies with populations in phase IV of smoking dependence report no such differences (Villalbí, Rodriguez-Sanz, Villegas, Borrell, 2009; Wilson et al., 1992). The absence of sex differences in our study may be attributable to this, or to the intensive intervention involved in multicomponent therapy. Although some studies have found a higher incidence of relapse in women (Heatherton, Kozlowsky, Frecker, & Fagerström, 1991), others report a substantial improvement in women's results when psychological therapy is added to pharmacological treatment (Nerín & Jané, 2007) – but this is an aspect requiring further research.

Educational level is associated with success of the therapy, as various studies have shown (Fernández et al., 2001; Piper et al., 2010), and the fact of receiving multicomponent therapy does not reduce the weight of this variable. In the univariate analysis we observed that it is only significant to have secondary education, and that having a university education does not attain statistical significance, even though this aspect does emerge as significant in the multivariate analysis. This is probably due to the fact that in the subgroup with university education there is a higher proportion of young people, in whom we already saw a greater tendency for relapse; therefore, when we adjust for age, having a university education also shows up as significant. Thus, educational level is significant as a predictor of success in multicomponent therapy. Bearing in mind that various studies have shown how people with higher levels of education respond better to psychological therapy of whatever kind (Haustein, 2004; Piper et al., 2010; Siahpush, McNeill, Borland, & Fong, 2006), all of this would be in support of the hypothesis that psychological aspects play a relevant role in attempts to quit smoking (Likura, 2010).

Occupational or professional level was also analyzed, though it only yielded significant differences in the first and sixth months, and not at the 12-month follow-up. Educational level is stable in adults, while the occupation variable can show considerable instability over the course of life (Belleudi et al., 2006), which would explain why the former yields greater significance and more robust results than the latter, as the previously-cited studies have also shown (Fernández et al., 2006; Yanez, Leiva, Gorreto, Estela, Tejera, & Torrent, 2013).

Level of dependence presented differences in the results, as observed in previous studies (Baer & Marlatt, 1991; Fernández et al., 1998), though these differences were only significant at the one-month and three-month follow-ups. This is probably due to the effect of the pharmacological treatment. The Fagerström Test is a good indicator of the smoker's level of physical dependence, but it is not reliable for measuring psychological dependence (Nerín et al., 2007). People with high levels of physical dependence are those that most benefit from pharmacological treatment (De Leon, Diaz, Bevona, Gurpegui, Jurado, Gonzalez-Pinto, 2003). However, in the medium and long term after the pharmacological treatment is finished, what could be determining relapse is not so much the physical dependence level as the degree of psychological dependence and the capacity for developing relapse prevention strategies (Hajek, Stead, West, Jarvis, Hartmann-Boyce, & Lancaster, 2013; Siahpush et al., 2006).

The majority of studies to date with psychiatric patients (Killen et al., 2008) have found them to have more difficulty giving up smoking and to present higher relapse rates. In our study, however, no such differences were appreciated. Various factors could explain this: first of all, the broad concept of psychiatric antecedents we employed, considering a patient to fall into this category if they had at any time in their life received a psychiatric diagnosis and been treated, and this covers a wide range of levels of severity. Secondly,

the fact that patients with schizophrenia or severe psychotic disorders were directly excluded. Though perhaps the most relevant factor is the environment in which the treatment programme took place, since the smoking cessation unit is part of the hospital's mental health department in which patients receive psychiatric follow-up. We believe that this may have led to greater adherence to the treatment and the sessions, as well as better monitoring and adjustment of the psychiatric treatment according to patients' progress towards giving up the habit, facilitated by the coordination between the professionals at the smoking cessation unit and the mental health department. Previous studies in similar environments, indeed, have found higher rates of smoking cessation in these types of patient (Cepeda-Benito et al., 2004; Fagerström & Aubin, 2009). Finally, it is reasonable to think that the intensive treatment involved in multicomponent therapy improves the results of these patients, as some authors have already suggested (Brown et al., 2001; Himelhoch & Daumit, 2003).

In the present study, multicomponent therapy with or without pharmacological treatment improves abstinence rates at the 12-month follow-up. If we focus on the 81 patients that opted for psychological treatment only, we can observe a substantial smoking cessation rate that reveals the effect of psychological therapy even without its reinforcement with pharmacological treatment, as also shown in several previous studies (Killen et al., 2008). Given that the data were analyzed on an "intent-to-treat" basis, the group of 81 participants that received the therapy without pharmacological treatment incudes patients who dropped out during the first phase of the treatment, so that we may actually be underestimating the results yielded by psychological therapy without pharmacological treatment. Focusing on the differences between abstinence at one month and at twelve months, it can be seen that the "psychological treatment only" group lost 11% of patients to relapse, while the psychological plus pharmacological treatment group lost 44%. This leads us to think that those who achieve abstinence in the first month without pharmacological treatment are keener to maintain their abstinence than those who achieve it with the help of pharmacological treatment, though it would be necessary to carry out more studies with experimental design to be able to confirm this hypothesis.

As regards pharmacological treatments, it was found that all of the play an important role in all phases of the process (Hajek, Stead, West, Jarvis, Hartmann-Boyce, & Lancaster, 2013; Tinich & Sadler, 2007). The results suggest that pharmacological treatment increases the likelihood of success in quitting smoking in the first three months, and that once a period of abstinence has been attained, the probability of maintaining abstinence in the medium and long term increases substantially (PHS Guideline Update Panel 2008). A study with experimental design in patients with characteristics similar to those in our study showed that following psychological therapy after the third smoking-free month is effective for the maintenance of abstinence (Hajek et al., 2013). Likewise, various reviews have shown how group therapy, cognitive-behavioural therapy and interventions with intensive follow-up are more efficacious in the long term (Bauld et al., 2010; Hall, Humfleet, Muñoz, Reus, Robbins, Prochaska, 2009).

We observed a clear advantage of nicotine replacement therapy compared to varenicline. Given that this was a descriptive study, it should be borne in mind that there may be bias in relation to the selection of pharmacological options, since they were not assigned randomly; hence, we cannot draw the kinds of causal conclusions that could be drawn from a study with experimental design. These differences may be due to the fact that greater efficacy of varenicline for reducing symptoms of craving (Stapleton et al., 2008) would hinder the learning of coping strategies for craving on the part of these patients. This is why after the end of the pharmacological treatment we see a higher relapse rate. Since we are talking about patients with serious difficulties for quitting smoking, there may be an influence of poor ability to apply relapse-prevention strategies. If this were indeed the case, nicotine replacement therapy would emerge as the most appropriate pharmacological treatment for multicomponent therapy interventions with these types of patients, while varenicline would be more suitable for patients who had not previously tried and failed to quit, who would not be followed-up after the pharmacological treatment, or who did not receive psychological treatment, though this hypothesis would need to be tested with specially designed studies.

It would be useful to analyze therapy adherence according to the characteristics of participants who completed the treatment, since this would provide information on predictors of adherence to multicomponent therapy and would help in the consideration of possible aspects to improve with a view to increasing it.

The main limitation of the present study concerns the time dimension. The fact of the sample being recruited over a long period (9 years) means that socio-cultural variables (e.g., legislative changes with regard to the prohibition of smoking in public spaces, changes in society's perception of the risks involved in smoking) could be having an effect that we have not controlled for. Thus, it may be that the 2005 legislation restricting smoking in public had some influence on people's motivation to give up smoking. On the other hand, though, the fact that the smokers in our sample had homogeneous characteristics (high level of dependence, many with previous pathologies, several attempts to quit) brings some correctional elements, so that this aspect does not influence the results as much as it would in a study with the general population. Another limitation is not having a record of the exact date of relapse, as this prevents us from knowing whether a patient starts smoking again and

therefore drops out of the programme, or first drops out of the programme which in turn leads to smoking relapse.

An advantageous aspect of the study is the fact of its using co-oximetry to confirm abstinence, as it gives much greater validity to the results than if we had only the patient-reported information.

The restricted geographical context of the study may seem like a limitation, given that the whole sample is concentrated in the same smoking cessation unit, which attends to a population with particular socio-cultural characteristics and served by a specific health-service structure, and this could limit the generalization potential of the results. Nevertheless, the population is a heterogeneous one in terms of socio-cultural characteristics, since both rural and urban regions are represented: Manresa is a city of over 70,000 inhabitants, situated within the third ring of the Barcelona metropolitan area and with an urban culture, while other parts of the sample are drawn from regions of central Catalonia with primarily rural socio-economic environments.

The fact of being a clinical study carried out in a real and natural context, that it seeks the most appropriate treatment according to the patient's characteristics and that the data analysis is carried out on an intent-to-treat basis are relevant aspects of the present study, enabling it to provide information that complements the results obtained in clinical trials conducted in ideal conditions (Brown et al., 2001; Garrison & Dugan, 2009; Tinich et al., 2007). In sum, we believe that this study permits as to contribute data on the effectiveness of multicomponent therapy in the clinical context, with heavy smokers and in a real environment.

The results obtained in the present study show how multicomponent therapy facilitates smoking cessation at one, three, six and twelve months. Socio-environmental characteristics such as higher educational level and not living with smokers predicted success in quitting smoking through multicomponent therapy, but this was not the case for other variables, such as sex, smoker characteristics and personal psychiatric antecedents. The combination of pharmacological and psychological treatment increased success rates in the multicomponent therapy, and psychological therapy alone also yielded positive results, though they were more limited in this case. In the light of these results, which require confirmation through experimental studies with better control of other possible determinants of dropout and success, we might consider a more generalized application of this type of therapy, especially with heavy or recalcitrant smokers.

Acknowledgements

Thanks to Anna Arnau, Rosa Cobacho, Joan Taberner and Alejandro Gella for their help at different stages of the study.

Antònia Raich, Jose M. Martínez-Sanchez and Esteve Fernández received funding from the Instituto de Salud Carlos III (RETICC, *beca* RD12/0036/0053) and the *Departament d'Economia i Coneixement de la Generalitat de Catalunya* (2009 SGR 192).

This work received the *XVI Premi del Bages de Ciències Mèdiques* (XVI Bages Prize for Medical Science), awarded by the *Acadèmia de Ciencies Mèdiques de Catalunya filial del Bages* and the *Collegi Oficial de Metges de Barcelona.*

Conflicts of interests

The authors declare that there are no conflicts of interests.

References

Alonso-Pérez, F., Alonso-Cardeñoso, C., García-González, J. V., Fraile-Cobos, J. M., Lobo-Llorente, N., & Secades-Villa, R. (2014). Effectiveness of a multicomponent smoking cessation intervention in primary care. *Gaceta Sanitaria, 28*, 222-224.

Baer J. S., & Marlatt G. A. (1991). Maintenance of smoking cessation. *Clinics in Chest Medicine, 12*, 793-800.

Bauld, L., Bell, K., McCullough, L., Richardson, L., & Greaves, L. (2010). The effectiveness of NHS smoking cessation services: a systematic review. *Journal of Public Health, 32*, 71-82.

Becoña E., & Vazquez F. L. (1998).The course of relapse across 36 months for smokers from a smoking-cessation program. *Psychological Reports*; *82*:143-146.

Becoña, E., & Míguez, M. C. (2008). Group behavior therapy for smoking cessation. *Journal of Groups in Addiction & Recovery, 3*, 63-78.

Belleudi, V., Bargagli, A. M., Davoli, M., Di Pucchio, A., Pacifici, R., Pizzi, E., ... Perucci, C. A. (2006). Characteristics and effectiveness of smoking cessation programs in Italy. Results of a multicentric longitudinal study. *Epidemiologia e Prevenzione, 31*, 148-157.

Bjornson, W., Rand, C., Connett, J. E., Lindgren, P., Nides, M., Pope, F., ... O'Hara, P. (1995). Gender differences in smoking cessation after 3 years in the Lung Health Study. *American Journal of Public Health, 85*, 223-230.

Brown, R. A., Kahler, C. W., Niaura, R., Abrams, D. B., Sales, S. D., Ramsey, S. E., ... Miller, I. W. (2001). Cognitive–behavioral treatment for depression in smoking cessation. *Journal of Consulting and Clinical Psychology, 69*, 471-480.

Cahill, K., Stevens, S., & Lancaster, T. (2014). Pharmacological treatments for smoking cessation. *JAMA, 311*, 193-194.

Cepeda-Benito, A., Reynoso, J. T., & Erath, S. (2004). Meta-analysis of the efficacy of nicotine replacement therapy for smoking cessation: differences between men and women. *Journal of Consulting and Clinical Psychology, 72*, 712-722.

de Leon, J., Diaz, F. J., Becoña, E., Gurpegui, M., Jurado, D., & Gonzalez-Pinto, A. (2003). Exploring brief measures

of nicotine dependence for epidemiological surveys. *Addictive Behaviors, 28*, 1481-1486.

Fagerström, K., & Aubin, H. J. (2009). Management of smoking cessation in patients with psychiatric disorders. *Current Medical Research and Opinion, 25*, 511-518.

Fernández, E., Carné, J., Schiaffino, A., Borràs, J., Saltó, E., Tresserras, R., ... Segura, A. (1998). Determinants of quitting smoking in Catalonia, Spain. *Gaceta Sanitaria, 13*, 353-360.

Fernandez, E., Garcia, M., Schiaffino, A., Borras, J. M., Nebot, M., & Segura, A. (2001). Smoking initiation and cessation by gender and educational level in Catalonia, Spain. *Preventive Medicine, 32*, 218-223.

Fernández, E., Schiaffino, A., Borrell, C., Benach, J., Ariza, C., Ramon, J. M., ... Kunst, A. (2006). Social class, education, and smoking cessation: long-term follow-up of patients treated at a smoking cessation unit. *Nicotine & Tobacco Research, 8*, 29-36.

Fiore, M. C., Jaén, C. R., Baker, T. B., Bailey, W. C., Benowitz, N. L., & Curry, S. J. (2009). Treating Tobacco Use and Dependence: 2008 Update. Rockville, MD: US Department of Health and Human Services; May 2008.

Garrison, G. D., & Dugan, S. E. (2009). Varenicline: a first-line treatment option for smoking cessation. *Clinical Therapeutics, 31*, 463-491.

Hajek, P., Stead, L. F., West, R., Jarvis, M., Hartmann-Boyce, J., & Lancaster, T. (2013). Relapse prevention interventions for smoking cessation. *Cochrane Database Syst Rev, 8*.

Hall, S. M., Humfleet, G. L., Muñoz, R. F., Reus, V. I., Robbins, J. A., & Prochaska, J. J. (2009). Extended treatment of older cigarette smokers. *Addiction, 104*, 1043-1052.

Haustein, K. O. (2004). Smoking and low socio-economic status. *Gesundheitswesen (Bundesverband der Arzte des Offentlichen Gesundheitsdienstes (Germany)), 67*, 630-637.

Hays, J. T., Ebbert, J. O., & Sood, A. (2009). Treating tobacco dependence in light of the 2008 US Department of Health and Human Services clinical practice guideline. In *Mayo Clinic Proceedings, 84*, 730-736.

Hays, J. T., Leischow, S. J., Lawrence, D., & Lee, T. C. (2010). Adherence to treatment for tobacco dependence: Association with smoking abstinence and predictors of adherence. *Nicotine & Tobacco Research, 12*, 574-581.

Heatherton, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerström, K. O. (1991). The Fagerström test for nicotine dependence: a revision of the Fagerström Tolerance Questionnaire. *British Journal of Addiction, 86*, 1119-1127.

Himelhoch, S., & Daumit, G. (2003). To whom do psychiatrists offer smoking-cessation counseling?. *American Journal of Psychiatry, 160*, 2228-2230.

Killen, J. D., Fortmann, S. P., Schatzberg, A. F., Arredondo, C., Murphy, G., Hayward, C., ... Pandurangi, M. (2008). Extended cognitive behavior therapy for cigarette smoking cessation. *Addiction, 103*, 1381-1390.

Likura, Y. (2010). Classification of OCD in terms of response to behavior therapy, manner of onset, and course of symptoms. *Seishin Shinkeigaku Zasshi= Psychiatria et Neurologia Japonica, 113*, 28-35.

Marlatt, G. A., Curry, S., & Gordon, J. R. (1988). A longitudinal analysis of unaided smoking cessation. *Journal of Consulting and Clinical Psychology, 56*, 715-720.

Middleton, E. T., & Morice, A. H. (2000). Breath carbon monoxide as an indication of smoking habit. *CHEST Journal, 117*, 758-763.

Nerín I., & Jané M. (2007). Libro blanco sobre mujeres y tabaco. Comite Nacional para la prevención del Tabaquismo. Zaragoza: Ministerio de Sanidad y Consumo.

Nerín I., Novella P., Beamonte A., Gargallo P., Jimenez-Muro A., & Marqueta A.(2007) Results of smoking cessation therapy in a specialist unit. *Archives of Bronconeumology, 43*, 669-673.

Perkins, K. A., & Scott, J. (2008). Sex differences in long-term smoking cessation rates due to nicotine patch. *Nicotine & Tobacco Research, 10*, 1245-1251.

PHS Guideline Update Panel, Liaisons, and Staff. Treating tobacco use and dependence: (2008) update U.S. public health service clinical practice guideline executive summary. *Respiratory Care, 53*, 1217-1222.

Piper, M. E., Cook, J. W., Schlam, T. R., Jorenby, D. E., Smith, S. S., Bolt, D. M., & Loh, W. Y. (2010). Gender, race, and education differences in abstinence rates among participants in two randomized smoking cessation trials. *Nicotine & Tobacco Research, 12*, 647-657.

Ramon, J. M., & Bruguera, E. (2009). Real world study to evaluate the effectiveness of varenicline and cognitive-behavioural interventions for smoking cessation. *International Journal of Environmental Research and Public Health, 6*, 1530-1538.

Ranney, L., Melvin, C., Lux, L., McClain, E., & Lohr, K. N. (2006). Systematic review: smoking cessation intervention strategies for adults and adults in special populations. *Annals of Internal Medicine, 145*, 845-856.

Siahpush, M., McNeill, A., Borland, R., & Fong, G. T. (2006). Socioeconomic variations in nicotine dependence, self-efficacy, and intention to quit across four countries: findings from the International Tobacco Control (ITC) Four Country Survey. *Tobacco Control, 15*(suppl 3), iii71-iii75.

Silagy, C., Lancaster, T., Stead, L., Mant, D., & Fowler, G. (2004). Nicotine replacement therapy for smoking cessation. *Cochrane Database Systematic Reviews, 3,* CD000146.

Stead, L. F., & Lancaster, T. (2005). Group behaviour therapy programmes for smoking cessation. *Cochrane Database Systematic Review, 2*, CD001292.

Stead, L. F., & Lancaster, T. (2012). Behavioural interventions as adjuncts to pharmacotherapy for smoking cessation. *Cochrane Database Systematic Reviews, 12,* CD009670.

Stapleton, J. A., Watson, L., Spirling, L. I., Smith, R., Milbrandt, A., Ratcliffe, M., & Sutherland, G. (2008). Varenicline in the routine treatment of tobacco dependence: a pre–post comparison with nicotine replacement therapy and an evaluation in those with mental illness. *Addiction, 103*, 146-154.

Tinich, C., & Sadler, C. (2007). What strategies have you found to be effective in helping patients to stop smoking?. *ONS Connect, 22*, 14.

Villalbí, J. R., Rodriguez-Sanz, M., Villegas, R., & Borrell, C. (2009). Changes in the population smoking patterns: Barcelona, 1983-2006. *Medicina Clinica, 132*, 414-419.

Wilkes, S. (2008). The use of bupropion SR in cigarette smoking cessation. *International Journal of Chronic Obstructive Pulmonary Disease, 3*, 45-53.

Wilson, D., Wakefield, M., Owen, N., & Roberts, L. (1992). Characteristics of heavy smokers. *Preventive Medicine, 21*, 311-319.

Wu, P., Wilson, K., Dimoulas, P., & Mills, E. J. (2006). Effectiveness of smoking cessation therapies: a systematic review and meta-analysis. *BMC Public Health, 6*, 300.

Yáñez, A., Leiva, A., Gorreto, L., Estela, A., Tejera, E., & Torrent, M. (2013). El instituto, la familia y el tabaquismo en adolescentes. *Adicciones, 25*, 253-259.

PIUS-a: Problematic Internet Use Scale in adolescents. Development and psychometric validation

EUPI-a: Escala de Uso Problemático de Internet en adolescentes. Desarrollo y validación psicométrica

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Abstract

Adolescents' use of the Internet is becoming a matter of great concern for different sectors of society. The psychological and behavioural consequences of problematic Internet use in young people demands quick and effective answers. One of the major challenges in this context is the development of empirically validated tools, which would facilitate early detection and screening for potential risk cases. This is precisely the aim of this paper. Based on a sample of 1,709 secondary-school students from Galicia (a region in northern Spain) aged 11 to 17 (M = 13.74, SD = 1.43), the analysis carried out permitted us to present a brief and simple tool (with just 11 items). It has substantial theoretical support, since both the existing background information and the views of experts from the academic and professional spheres were taken into account in the course of its development. The scale is adapted to the Spanish cultural context and to the language of young people. It has satisfactory psychometric properties in terms of reliability of the scores (α = .82), evidence of its internal structure (tested via a Confirmatory Factorial Analysis), sensitivity (81%), and specificity (82.6%). Moreover, its use enables the gradation of adolescents on a risk or problematic Internet use continuum. In our view, all of this lends it enormous applied potential in both the educational and clinical contexts.

Key words: addiction, adolescents, early detection, Internet, problematic use, screening.

Resumen

El uso que los adolescentes hacen de Internet viene suscitando una enorme preocupación en diferentes sectores de la sociedad. Las consecuencias a nivel psicológico y conductual que el uso problemático de la Red provoca entre los más jóvenes demandan una respuesta tan rápida como eficaz. Uno de los grandes retos en este contexto es el desarrollo de herramientas validadas empíricamente, que permitan hacer un cribado o detección precoz de posibles casos de riesgo. Ese es precisamente el objetivo de este trabajo. A partir de una muestra de 1709 escolares de Enseñanza Secundaria Obligatoria de la comunidad gallega, de edades comprendidas entre los 11 y los 17 años (M = 13,74; DT = 1,43), los análisis realizados permiten presentar una herramienta breve y sencilla (compuesta por solo 11 ítems), que goza de un importante aval teórico, ya que para su elaboración se tuvieron en cuenta tanto los antecedentes existentes en la literatura, como las opiniones de expertos del ámbito académico y profesional. Dicha escala, además de estar adaptada al contexto cultural español y al lenguaje de los adolescentes, presenta unas propiedades psicométricas satisfactorias, tanto en términos de fiabilidad de las puntuaciones (α = ,82) y evidencias de su estructura interna (probada a través de un Análisis Factorial Confimatorio), como de sensibilidad (81%) y especificidad (82,6%), permitiendo "escalar" a los adolescentes en un continuum de riesgo o uso problemático de Internet. Todo ello le confiere, a nuestro modo de ver, un notable potencial a nivel aplicado, tanto en el contexto educativo como clínico.

Palabras clave: adicción, adolescentes, cribado, detección precoz, Internet, uso problemático.

Received: May 2014; Accepted: November 2014

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One of the defining characteristics 21st-century society is the generalized use of so-called *New Technologies* (NT) or *Information and Communications Technology* (ICT). According to Spain's National Institute of Statistics (Instituto Nacional de Estadística [INE], 2014), in Spain 92% of minors aged 10 to 15 are Internet users. The Web provides access to multiple sources of information, learning, leisure and personal, academic and professional development, as well as to innovative forms of communication, relation and expression. Without questioning its benefits, we should not overlook the fact that its use also involves certain associated risks and dangers (loss of privacy, contact with strangers, isolation), in addition to disconcerting practices such as cyberbullying, grooming or sexting, which are affecting increasing numbers of adolescents, considered one of the most vulnerable groups in this new environment (Castellana, Sánchez-Carbonell, Graner, & Beranuy, 2007; Echeburúa & Corral, 2010; Yang & Tung, 2007).

The use that teenagers make or are able to make of Internet is a topic of concern in Spain and elsewhere (Oliva et al., 2012; Puerta-Cortés & Carbonell, 2014; Ruiz-Olivares, Lucena, Pino, & Herruzo, 2010; Smahel et al., 2012; Tsitsika, Tzavela, Mavromati and EU consortium NET ADB, 2012; Valedor do Pobo, 2011). This general concern has been heightened in recent years by the sometimes sensationalist way in which the subject is treated in the media. This has helped to create some degree of social alarm and no little scepticism among researchers and professionals, who do not consider it appropriate to speak of Internet addiction per se (Estallo, 2001; Grohol, 1999; Matute, 2001). However, others have indeed taken this step, attempting to scientific credibility to the use of this term (Cao & Su, 2007; Young, 1998). Various studies have tried to provide evidence that the behaviour of some individuals in relation to the Web fulfils the general criteria of an addiction (Echeburúa, 1999; Griffiths, 1998), or even proposed diagnostic criteria (Ko, Yen, Chen, Chen, & Yen, 2005; Tao et al., 2010; Young, 1996). And while it is true that neither of the diagnostic manuals of reference (CIE-10 and DSM-5) currently includes such a category, it is interesting to mention two innovations that appear in the DSM-5 (American Psychiatric Association [APA], 2013): on the one hand, *Internet Gaming Disorder* has been included in Section III of the manual, reserved for potential new diagnostic categories that require further research and evidence from clinical contexts; on the other hand, *compulsive gambling* has been classified as a *behavioural addiction*, which leads us to think, in line with other authors (Cía, 2014; Petry & O'Brien, 2013), that other behaviours capable of generating the psychopathology characteristic of addiction could also be fully incorporated into coming editions of the manual.

Despite the enormous amount of scientific work that this area has been generating for almost two decades now, there is still a degree of controversy (García, Beltrán, & Pérez, 2012; Douglas et al., 2008; Rial, Gómez, Braña, & Varela, 2014; Sánchez-Carbonell, Beranuy, Castellana, Chamarro, & Oberst, 2008; Spada, 2014). An example of this is the disparity in the prevalence figures estimated by different studies. In the Spanish context the data range from *0.76%* of adolescents and young people *with severe level of Internet addiction* to *21.88% with moderate addiction* (Oliva et al., 2012), or *3.3% of problematic users* and *43.3% of risk users* in young people aged 14 to 18 (Estévez, Bayón, de la Cruz, & Fernández-Líria, 2009), to *19.9% of problematic users* among secondary-school students (Gómez, Rial, Braña, Varela, & Barreiro, 2014).

In the case of Europe-wide studies, the data range from *1% of pathological levels of Internet use* found in children aged 11 to 16 (Smahel et al., 2012), or the *1.2% of* adolescents aged 14 to 17 with *Internet addiction behaviours* and *12.7% at risk* (Tsitsika et al., 2012), to *4.4% of pathological Internet users* and *13.5% of maladaptive users* (Durkee et al., 2012)

The figures in studies outside Europe also show disparities: Cao, Sun, Wan, Hao and Tao (2011) report *8.1%* of *problematic users of Internet* among Chinese adolescents, whilst Lam, Peng, Mai and Jing (2009) speak, in relation to Chinese secondary-school students, of *10.2% moderately addicted* and *0.6% severely addicted* to the Web. At the same time, the range of prevalence found in studies with adolescents and university students in the USA is from *0%* to *26.3%* (Moreno, Jelenchick, Cox, Young, & Christakis, 2011).

In sum, although more and more research is being done on this no., the data are confusing, and at times even contradictory. The "risk" estimated in each case tends to be an excessively diffuse term, given the underlying conceptual controversy that must be resolved first: what do we actually want to assess? It is necessary to clarify what we are talking about: *Internet addiction* (Chou & Hsiao, 2000; Young, 1996), *compulsive use* (Greenfield, 1999; Meerkerk, Van Den Eijnden, Vermulst, & Garretsen, 2009), *pathological use* (Davis, 2001; Morahan-Martin & Schumacher, 2000), *problematic use* (Caplan, 2002; Shapira et al., 2003), *excessive use* (Hansen, 2002), *unregulated use* (LaRose, Lin, & Eastin, 2003) or *Internet dependence* (Anderson, 2001; Scherer, 1997). Do these terms form part of a single *continuum* of risk? And if so, what sequence do they follow? Which of them accounts for the highest level of risk? Where should we set the boundaries between one concept and another? The heterogeneity of terms makes it seriously difficult to compare and integrate results, so that the first task for research teams and the scientific-professional community is to reach a consensus on both the term to use and its defining criteria. Thus,

although it might be acceptable to speak of *addiction* to Internet, in the name of rigour and orthodoxy (and pending the necessary consensus), a prudent solution would be to employ the term *problematic use*. Authors such as Ceyhan, Ceyhan and Gürcan (2007), Pulido-Rull, Escoto-de la Rosa and Gutiérrez-Valdovinos (2011) or Thatcher and Goolam (2005) advocate the use of this expression.

But beyond this controversy, what is certain is that signs are increasing of the existence of the problem, so that it must be addressed as soon as possible. In this context, one of the greatest challenges for research is the development of screening instruments, permitting early detection or the identification of possible risk cases, which would redound to the benefit of prevention initiatives.

The Appendix to this article includes a list of the principal instruments or tests developed to date. Its length serves only to highlight the enormous degree of heterogeneity there is, from both the conceptual and methodological points of view. Despite the large number of scales available, if our goal is to develop a tool with sound guarantees that permits early detection of cases of problematic Internet use among adolescents, the truth is that many of them present some kind of limitation: (1) they are not adapted to the adolescent population or the items are unsuitable for the specific reality of this age group (Armstrong, Phillips, & Saling, 2000; Nichols & Nicki, 2004); (2) they do not provide sufficient data on their psychometric properties, or they are not as reliable as they should be (Frangos, Frangos, & Sotiropoulos, 2012; García et al., 2008; Orman, 1996); (3) the samples used for their empirical validation are too small (Lam-Figueroa et al., 2011; Morahan-Martin & Schumacher, 2000); (4) their factor structure is unclear (Chang & Law, 2008; Widyanto & McMurran, 2004); (5) they are difficult to use as *screening tools*, given their large numbers of items (Davis, Flett, & Besser, 2002; Li & Yang, 2007) or because they do not provide cut-off points (Beranuy, Chamarro, Graner, & Carbonell, 2009; Meerkerk et al., 2009); (6) there is no suitably adapted version in Spanish (Demetrovics, Szeredi, & Rózsa, 2008); or (7) they were developed in a culture very different from that of Spain (Chen, Weng, Su, Wu, & Yang, 2003; Huang, Wang, Qian, Zhong, & Tao, 2007).

The objective of the present work is precisely to develop a screening scale for *problematic Internet use in* adolescents, with sufficient theoretical and empirical guarantees, and that is both brief and easy to use. Such a scale must integrate the different antecedents from the literature and present acceptable psychometric properties, with regard to score reliability, evidence of validity, sensitivity and specificity. In addition to being brief and simple, its items must be in accordance with the language and cultural context of adolescents.

Method

Participants

To achieve our objective we used purposive sampling, in an effort to access the largest and most heterogeneous sample possible. Through contact with 11 secondary schools in 7 different municipalities (both urban and rural) of the province of A Coruña (north-western Spain), it was possible to assemble a sample of 1709 adolescents (835 girls and 874 boys) aged 11-17 (M = 13.74; SD = 1.43). Of these, 30.2% were in the first grade (1º de ESO), 25.2% in the second grade, 23.8% in the third grade and 20.8% in the fourth grade. As regards parents' educational level, 4% of fathers and 3.2% of mothers had no formal education, whilst 36.9% of fathers and 34.5% of mothers had primary education. Those with secondary/high-school education accounted for 48.6% of the fathers and 46.3% of the mothers, and 10.4% of fathers and 15.9% of mothers had a university education.

Instruments

For the construction and development of the scale we followed the phases set down in the American Educational Research Association's *Standards (Ame*rican Psychological Association and National Council on Measurement in Education, 1999). First of all, we defined the purpose of the scale, which was to produce a *screening instrument for problematic Internet use in* adolescents, as well as defining the scope of the construct or domain to be measured. We next specified certain aspects of the scale, such as item format, response format and the procedure for calculating the scores obtained by each participant. Specifically, it was decided that the items would be statements in the first person, and that the response format would be based on a Likert-type scale with 5 options, since this maximizes score reliability and improves the chances of obtaining good validity evidence. For calculating the scores we established a range of 0 to 4 in the 5 categories of the agreement scale, 0 signifying *Totally disagree and* 4 signifying *Totally disagree*. Next, we implemented the phase of development, assessment and selection of the items, and finally, we drew up the final version of the scale and carried out its empirical evaluation.

These four phases were developed through three complementary strategies. The first of these involved a review of the extensive literature on the subject, summarized in the Appendix, which lists the main scales previously proposed and their defining characteristics. We also took into account the DSM-5 diagnostic criteria for pathological gambling and Internet Gaming Disorder.

The second strategy was the development of a qualitative study, which involved the creation of a multidisciplinary team of experts consisting of 12 professionals (3 clinical psychologists, 3 psychiatrists, 3 community edu-

cation workers and 3 experts in drug-dependence prevention), with three specific objectives: (1) To carry out a critical review of the existing literature, highlighting the current limitations in this area; (2) To provide evidence of the content validity of the scale and the items making it up; and (3) To establish criteria for analyzing its discriminative capacity, given the absence of consensus-based diagnostic criteria.

For the work with the experts we used the Delphi technique, structured in three phases: the initial meeting was for discussing the state of the no. and the possible criteria indicating the problem; the experts then individually presented their reflections on the problem and their considered proposals for the items to be included in the scale and the response format to be used; finally, they agreed on the indicators or reference criteria for considering an adolescent's behaviour as "risk", as well as other, more technical elements such as the order of presentation of the items.

Furthermore, we took into account the results of the preliminary study by Gómez et al. (2014), which presented an 8-item scale that can be considered the starting point of the scale used in the present study. Nevertheless, it should be noted that, given its additional contributions, the present scale can be considered a priori a more comprehensive and rigorous instrument, with greater theoretical support (thanks to the extensive literature review and the work carried out with the experts).

As a result of the four phases mentioned above and the three complementary strategies used, we drew up an initial version of the 14-item scale, as shown in Table1.

Table 1
Items of the scale and sources

ITEMS OF THE SCALE	SOURCES
1. When I'm online I feel that time flies and hours pass without me realizing it	- Beranuy et al., 2009 - Huang et al., 2007 - Preliminary study - Expert group
2. I've sometimes tried to control or reduce my Internet use, but I couldn't	- Echeburúa, 1999 - Young, 1996 - Internet Gaming Disorder - Gambling Disorder
3. I sometimes prefer to be online than to be with people (family or friends)	- Chen et al., 2003 - García et al., 2008 - Young, 1998 - Preliminary study - Expert group
4. I've sometimes even managed to neglect certain tasks or perform below par (in exams, sport, etc.) because I put connecting to Internet first	- De García et al., 2008 - Internet Gaming Disorder - Preliminary study
5. I'm starting to like more and more spending hours connected to Internet	- Chen et al., 2003 - Greenfield, 1999 - Internet Gaming Disorder - Gambling Disorder
6. I sometimes get irritated or in a bad mood because I can't connect to Internet or because I have to disconnect	- Demetrovics et al., 2008 - Young, 1998 - Internet Gaming Disorder - Gambling Disorder - Preliminary study
7. I prefer that my parents don't know how long I spend online because they would think it was too much	- Huang et al., 2007 - Morahan-Martin & Schumacher, 2000 - Internet Gaming Disorder - Gambling Disorder - Expert group
8. I've stopped going to places or doing things that interested me before so as to connect to the Internet	- Armstrong et al., 2000 - Internet Gaming Disorder - Preliminary study - Expert group
9. Connecting to the Internet helps me to not think about problems and to relax	- Beranuy et al., 2009 - Huang et al., 2007 - Internet Gaming Disorder - Gambling Disorder
10. I've even put relationships or important things at risk because of the Internet	- Beranuy et al., 2009 - De Gracia et al., 2002 - Internet Gaming Disorder - Gambling Disorder - Preliminary study
11. I've sometimes got into trouble because of the Internet	- Caplan, 2002 - Morahan-Martin& Schumacher, 2000 - Expert group

(continues)

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12. It annoys me to spend hours without connecting to Internet	- Young, 1998 - Internet Gaming Disorder - Gambling Disorder - Preliminary study - Expert group
13. When I can't connect I can't stop thinking that I might be missing something important	- Caplan, 2002 - Labrador, Becoña& Villadangos, 2008 - Internet Gaming Disorder - Gambling Disorder
14. I say or do things on Internet that I wouldn't be capable of saying/doing in person	- Caplan, 2002 - Carbonell et al., 2012 - Expert group

Procedure

Data were collected in the classrooms of the schools participating in the study, in small groups (20 or less), after the corresponding instructions had been given. Collection of the information was carried out by the experts in drug-dependence prevention who developed the education for health programmes at the different schools, as an extra activity of the same programme, within the module on responsible use of New Technologies. A training session was held with technicians who assisted with data collection in order to standardize the procedure as much as possible and resolve any doubts at the technical level. Special emphasis was placed on the confidentiality of information and anonymity of responses was guaranteed, since at no time were the adolescents asked about their names or personal information. The cooperation and consent of both the schools' head teachers and parents' associations were obtained. Participation in the study was completely voluntary and unpaid. Rate of refusal to participate in the study was 1.2%. Finally, it should also be pointed out that the study was approved by the Bioethics Committee of the University of Santiago de Compostela.

Data analysis

First of all we carried out a missing values analysis. Once confirmed the low percentage of missing values for each of the variables (ranging between 0% and 1.8%), and the randomness of such values, we decided to remove from the analysis those participants with missing values in any of their answers. Thus, an initial sample of 1772 adolescents became a final sample of 1709 adolescents for the analysis. We then calculated the descriptives (M, SD, skewness and kurtosis) for each scale item, as well their corrected homogeneity indices (HIc). The multivariate normal distribution was evaluated by means of the Mardia coefficient and the internal consistency with Cronbach's alpha. To study the dimensionality or factor structure of the scale we carried out first of all an Exploratory Factor Analysis (EFA), followed by a first-order Confirmatory Factor Analysis (CFA). Given the absence of consensus-based diagnostic criteria with which to define problematic Internet use among adolescents, in order to explore the scale's capacity for screening, we first divided the total sample into two groups: (a) a first group whose use of Internet could be considered moderate, and (b) a second group whose use could be considered problematic (they go online every day, usually for more than 5 hours a day, and report frequent arguments with their parents for this reason). Next, based on this categorization as moderate or problematic users, we calculated the sensitivity and specificity values for different cut-off points, and complementary to this, we carried out a ROC curve analysis. Finally, in addition to providing the descriptive statistics of the final scale for the total sample, we made comparisons of means by the adolescents' sex (through application of the Student *t test*) and age (through a one-factor ANOVA and a Tukey *post-hoc* comparison). All the analyses were carried out using IBM SPSS Statistics 20.0 (IBM Corp. Released, 2011) and IBM SPSS AMOS 21.0 (Arbuckle, 2012).

A large part of the decisions made on a methodological level took as a reference studies such as those of Cuenca-Royo, Torrens, Sánchez-Niubó, Suelves and Domingo-Salvany (2013) or Muñiz and Fonseca-Pedrero (2008).

Results

Table 2 shows the descriptive statistics for each one of the 14 items in the initial version. The highest averages correspond to items 1 (When I'm online I feel that time flies and hours pass without me realizing it) with a mean of 2.62, followed by item 9 (Connecting to the Internet helps me to not think about problems and to relax), with an average of 1.69. The lowest average corresponds to item 8 (I've stopped going to places or doing things that interested me before so as to connect to the Internet), with a mean of 0.27, and item 10 (I've even put relationships or important things at risk because of the Internet), with 0.39. As regards the variability of responses, the item that presents the most heterogeneous responses (with a standard deviation of 1.45) is item 9, while item 8 is the most homogeneous, with a standard deviation of 0.71. As regards the standardized skewness values, we can observe a marked positive skewness in all the items, except in the case of the first one, which presents marked negative skewness. Regarding the kurtosis, many of the items show a leptokurtic distribution (items

2, 3, 6, 7, 8, 10, 11, 12 and 14), though some have a platykurtic distribution (items 1, 5, 9 and 13). However, only four of the items have a value above 10, the rest falling within reasonable limits (Kline, 2005). The Mardia multivariate normality coefficient is 77.97, which leads to rejection of the multivariate normality hypothesis. The corrected homogeneity index (HIc) of the items ranges from .37 to .59 and the internal consistency of the initial scale is in general highly acceptable, with a Cronbach's alpha coefficient of .83. As Pardo and Ruíz (2001) state, "values of over .80 are generally considered sound, and those of over .90, excellent" (p. 598).

To study the factor structure of the scale we began by dividing the aggregate sample into two random halves of the same size. With the first we carried out an Exploratory Factor Analysis (EFA), and with the second, a Confirmatory Factor Analysis (CFA), in an effort to confirm or validate the structure found. It was also found that there

Table 2
Descriptive Statistics for the Elements of the Initial Scale

Ítem	M	SD	Skewness	Kurtosis	HIc
1	2,62	1,27	-6,983	-5,694	0,39
2	0,81	1,13	18,378	5,584	0,43
3	0,53	0,94	26,332	21,018	0,42
4	1,00	1,21	14,567	,138	0,49
5	1,22	1,24	10,801	-2,533	0,56
6	0,88	1,20	17,896	4,108	0,57
7	0,91	1,33	17,708	1,808	0,51
8	0,27	0,71	44,471	74,563	0,40
9	1,69	1,45	4,210	-8,748	0,37
10	0,39	0,91	35,935	41,721	0,42
11	0,48	1,01	31,099	28,493	0,38
12	0,96	1,20	15,854	1,807	0,57
13	1,11	1,35	13,674	-2,362	0,59
14	0,93	1,29	16,994	1,629	0,42

were no significant differences in the composition of the two subsamples, or by sex (χ^2 = 0.02; p = .88), or age (t = 1.27; p = .20).

For carrying out the EFA we used the Principal Components Method. The KMO index value was .88, and that of the Bartlett Sphericity Test, 2539.47 (p <.01). The analysis provided three factors, which together accounted for 49.40% of the variance of the data, even though the first one explained 32.90%, the other two factors showing a much more residual character, which fits at a theoretical level with the unidimensional nature of the Gomez et al. (2014) scale that was used as a basis. Following this first analysis we conducted a CFA, starting out from a theoretical model with a single dimension. Despite the absence of normality, for parameter estimation we used the Maximum Likelihood (ML) method, since works such as those of Curran, West and Finch (1996) or Thomas and Oliver (1998) have indicated that this method is sufficiently robust against non-fulfilment of this assumption when samples are large, as in this case (n = 1709). In any case, and in accordance with Levy, Martin and Norman (2006), we used complementarily other methods, such as Generalized Least Squares (GLS), Unweighted Least Squares (ULS) and Asymptotically Distribution Free (ADF), obtaining very similar results. The estimated parameters were statistically significant (p <.01) and the factor loadings greater than .40, except in the case of item 9 (see Figure 1).

Goodness of fit of the model was assessed by means of different indices, as recommended by Byrne (2009) or Kline (2005): χ^2, χ^2/df, *Goodness of Fit Index* (GFI), *Adjusted Goodness of Fit Index* (AGFI), *Comparative Fit Index* (CFI), *Normed Fit Index* (NFI), *Tucker Lewis Index* (TLI) and *Root Mean Square Error of Approximation* (RMSEA). Following the recommendations of Steiger (1998), we also included the 90% confidence intervals in the case of RMSEA. The

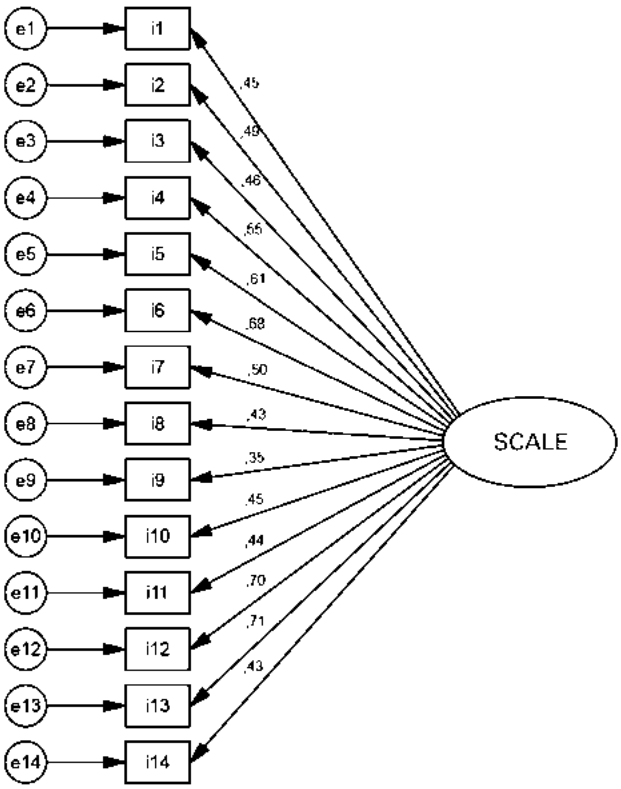

Figure 1. Estimated standardized parameters of the Initial CFA Model

different indices show that the scale fits only moderately with the unidimensional theoretical model (see Table 3). Although the GFI and AGFI values were over .90, those of the NFI, TLI and CFI were around .85, and the RMSEA value was .074. The low HIc values of some items (3, 9 and 10) and their low factor loadings (.46, .35, and .45, respectively), together with the modification indices provided by the program, advised a respecification of the initial model, deleting the 3 items mentioned.

Table 3
Goodness of fit indicators of the CFA Model for the Screening Tool

	χ^2	df	p	χ^2/df	GFI	AGFI	NFI	TLI	CFI	RMSEA [CI]*
Initial model	325.38	77	←.001	4.22	.93	.90	.84	.85	.87	.074 [.066-.083]
Respecified model	118.39	44	←.001	2.69	.96	.95	.92	.94	.95	.054 [.042-.065]

Note: * 90% Confidence Interval for the RMSEA statistic

Next, on the re-specified model with only 11 elements, a new CFA was conducted, giving a better overall fit of the scale, with a GFI value of .96, AGFI, NFI, TLI and CFI values of between .92 and .95, and an RMSEA value of under .06, as recommended by Hu and Bentler (1999). It should be borne in mind that even differences below 0.1 in the GFI or AGFI can be considered as relevant (Levy, Martin, & Norman, 2006). All estimated parameters were statistically significant (p <.01) (Figure 2). Finally, the internal consistency of the final scale was analyzed, yielding a Cronbach's alpha of .82. Additionally, since the response format used was an ordered categorical scale, the ordinal alpha index (Elosúa & Zumbo, 2008) was calculated, yielding a slightly higher value (83).

As regards the total descriptive statistics for the final 11-item scale, for a theoretical minimum score of 0 and a maximum of 44, the average score attained for the whole sample was 11.18, and the standard deviation was 7.70. As shown in Table 4, no significant differences were found by sex, but there were differences according to age group (F = 10.32; p <.001), with a higher average on the scale in the older age groups.

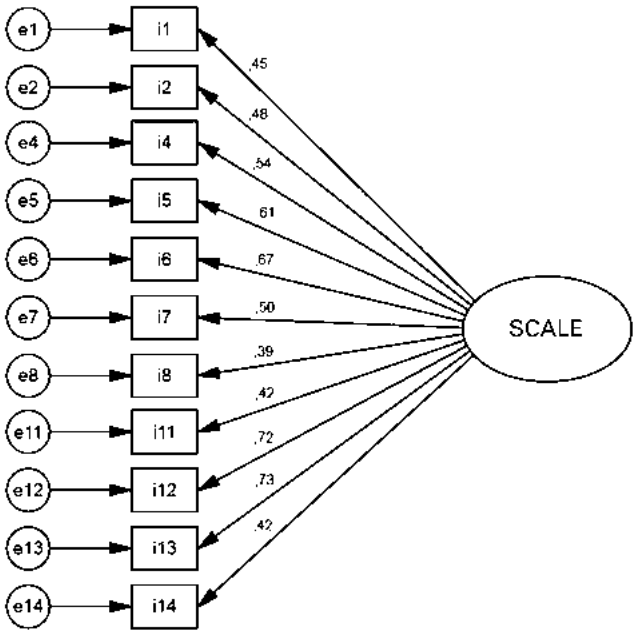

Figure 2. Estimated standardized parameters of the Final CFA Model

To study the scale's capacity for screening, in the absence of consensus-based diagnostic which could enable us to have a clinical sample, the total sample was divided into two groups: (a) a first group whose Internet use could be considered moderate, and (b) a second group whose use could be considered problematic. This second group would be made up those adolescents who: 1) connect the Internet every day, 2) are usually online for more than 5 hours a day, and 3) report frequent arguments with their parents for this reason. The sensitivity and specificity values obtained for different cut-off points are shown in Figure 3. As it can be seen, values 15 and 16 permit the attainment of a balance between these two indicators. Specifically, if we use as a cut-off point a score of 16, we obtain a sensitivity of 81% and a specificity of 82.6%. In other words, the screening instrument is capable of detecting true positives in 81% of cases and of rejecting true negatives in 82.6% of cases, both results being highly acceptable. By way of a complement, we carried out a ROC curve (Receiver Operating Characteristic) analysis, obtaining an area under the curve of 0.88.

Table 4
Comparison of total scores on the scale by sex and age

		M	*SD*	*t*	*p*
Sex	Men	10,76	7,24	-1,87	,062
	Women	11,60	8,13		
		M	*SD*	*t*	*p*
Age group	11 – 13 years	10,18	7,43	10,321	< ,001
	14 – 15 years	11,78	7,92		
	16 – 17 years	13,18	7,61		

Finally, participants' response pattern was analyzed by comparing the profile of adolescents who make moderate use of the Internet with those who use is problematic. As can be seen in Table 5, at both the global score level and that of each of the items individually, the two groups showed statistically significant differences (p <.01). This confirms the capacity of each of the items for detecting problematic Internet use and justifies their presence in the final version of the scale.

Discussion

One the main concerns among professionals and researchers in the field of addictions today is adolescents' problematic use of the Internet. In this context, various authors have highlighted the need to reach a consensus, from both the conceptually and methodological points of view, on the denomination, definition and evaluation of

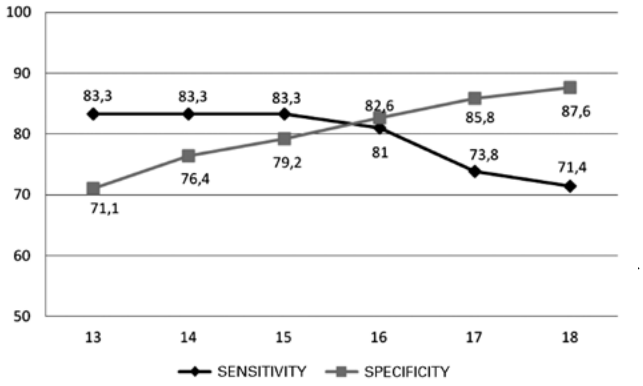

Figure 3. Sensitivity and Specificity values for the different cut-off points

Table 5
Comparison between adolescents with moderate use and problematic use

	Item	*Moderate use*	*Problematic use*	*t*	*p*
1	When I'm online I feel that time flies and hours pass without me realizing it	2,50	3,25	-4,59	< ,001
2	I've sometimes tried to control or reduce my Internet use, but I couldn't	0,72	1,43	-3,22	< ,01
3	I've sometimes even managed to neglect certain tasks or perform below par (in exams, sport, etc.) because I put connecting to Internet first	0,86	2,09	-5,67	< ,001
4	I'm starting to like more and more spending hours connected to Internet	1,12	2,32	-4,99	< ,001
5	I sometimes get irritated or in a bad mood because I can't connect to Internet or because I have to disconnect	0,69	2,16	-6,13	< ,001
6	I prefer that my parents don't know how long I spend online because they would think it was too much	0,72	2,32	-6,37	< ,001
7	I've stopped going to places or doing things that interested me before so as to connect to the Internet	0,19	0,67	-2,88	< ,01
8	I've sometimes got into trouble because of the Internet	0,36	1,28	-3,66	< ,001
9	It annoys me to spend hours without connecting to Internet	0,82	1,89	-4,56	< ,001
10	When I can't connect I can't stop thinking that I might be missing something important	0,97	2,41	-6,32	< ,001
11	I say or do things on Internet that I wouldn't be capable of saying/doing in person	0,81	1,84	-4,09	< ,001
	TOTAL	9,67	21,62	-9,70	< ,001

lation, or fail to provide data on their psychometric properties. Sometimes the samples used for their validation are too small, their factor structure is unclear, they are too long, or they or simply do not provide the cut-off points needed for their used as screening instruments.

Analyses carried out with a sample of 1709 schoolchildren in the Spanish region of Galicia made it possible to present a new scale (PIUS-a) that may prove extremely useful for practitioners and researchers in this field. This scale was developed on the basis of a thorough review of the literature and enriched by the contributions from a multidisciplinary team of experts; moreover, it has highly acceptable psychometric properties, in terms of both internal consistency (α = .81), and evidence of internal structure and content, attaining an interesting balance between levels of sensitivity (81%) and specificity (82.6%), as far as screening capacity is concerned. In short, the work carried out has made available to researchers, clinicians and community education workers a brief and simple scale (with just 11 items), adapted to the cultural context of our country and the language of young people – qualities that lend it great potential for everyday practice.

Although in this paper we have been prudent and chosen to use the term problematic Internet use, it would not be unreasonable, as various authors have proposed, to employ terms such as pathological Internet use or Internet addiction (Durkee et al., 2012; Tsitsika et al., 2012; Young, 1996). The facts that the selection of scale items was made on the basis of previous work along these lines, that we took into account the judgements of experts in the clinical and educational spheres, and that we used as references the criteria for diagnostic categories of a similar nature, makes the use of these terms quite plausible. Official recognition of a pathology associated with the use of Internet and the availability of clinical samples, as is the case in the Asian context (Huang et al., 2007; Ko, Yen, Yen et al., 2005), would help resolve these types of controversy.

Moreover, despite the unidimensionality of the scale developed, we cannot discard the possibility of a multidimensional approach, given the complexity of the pro-

blem at hand. However, many of the works that adopt a multidimensional approach (Günüç & Kayri, 2010; Widyanto & McMurran, 2004) provide a global α, which implicitly entails some unidimensionality. Furthermore, the fact that the calculation of an overall score and the setting of a cut-off point are necessary to enable screening for possible cases of risk makes it preferable to opt initially for the existence of a single factor.

However, this study does have some limitations. First, all the variables are self-reported, so it is impossible to know the extent to which the adolescents may have underestimated or overestimated their Internet use. On the other hand, self-report questionnaires on the use of alcohol and other drugs have shown themselves to be reliable and even comparatively better than other detection methods in the field of substance use (Babor, Kranzler, & Lauerman, 1989; Winters, Stinchfield, Henly, & Schwartz, 1990), so that self-report measures may well be relevant in this context also. It is also true that the use of a social desirability scale or an instrument for the detection of random response patterns could of great use. Moreover, given the still-unresolved conceptual controversy and lack of consensus on the defining criteria of the problem, the sensitivity and specificity values were calculated based on criteria established by the authors, even though it must be said that they have been used in works and endorsed by the group of experts. The availability in the future of duly consensus-based criteria will be what finally permits the validation of the instruments developed, which from a purely psychometric perspective is not currently possible.

It is important to note, finally, that the scale presented constitutes a tool for screening, and never for diagnosis, as the latter must be based on the clinical act itself. Such instruments would play a complementary role, facilitating the early detection of adolescents whose use of the Internet could constitute a problem, on interfering in a crucial way in their everyday life. The scale is specifically designed for use by counsellors, community education workers and drug-prevention experts in the school context, in which it has been validated empirically. Future research would need to test its behaviour in clinical settings, linked in (as occurs in other countries) to primary care services.

Acknowledgements

This study was supported by the Valedor do Pobo institution, a part of the Galician Regional Administration (Xunta de Galicia).

Conflicts of interests

The authors declare that there are no conflicts of interests.

References

American Educational Research Association, American Psychological Association & National Council on Measurement in Education (1999). *Standards for educational and psychological testing*. Washington, DC: American Educational Research Association.

American Psychiatric Association [APA]. (2013). *Diagnostic and statistical manual of mental disorders. Fifth edition.* Washington, DC: American Psychiatric Publishing.

Anderson, K. J. (2001). Internet use among college students: An exploratory study. *Journal of American College Health, 50*, 21-26.

Arbuckle, J. L. (2012). *AMOS 21.0*. Crawfordville, FL: Amos Development Corporation.

Armstrong, L., Phillips, J., & Saling, L. (2000). Potential determinants of heavier Internet usage. *International Journal of Human-Computer Studies, 53*, 537–550.

Babor, T. F., Kranzler, H. R., & Lauerman, R. J. (1989). Early detection of harmful alcohol consumption: comparison of clinical, laboratory, and self-report screening procedures. *Addictive Behaviors*, *14*, 139-157.

Beard, K. W. (2005). Internet addiction: A review of current assessment techniques and potential assessment questions. *CyberPsychology & Behavior, 8*, 7-14. doi:10.1089/cpb.2005.8.7

Beranuy, M., Chamarro, A., Graner, C., & Carbonell, X. (2009).Validación de dos escalas breves para evaluar la adicción a Internet y el abuso de móvil. *Psicothema, 21*, 480-485.

Brenner, V. (1997). Psychology of computer use: XLVII. Parameters of Internet use, abuse and addiction: the first 90 days of the internet usage survey. *Psychological Reports, 80*, 879-882. doi:10.2466/pr0.1997.80.3.879

Byrne, B.M. (2009). *Structural equation modeling with AMOS: Basic concepts, applications, and programming* (2nd ed.). London: Psychology Press.

Byun, S., Ruffini, C., Mills, J. E., Douglas, A. C., Niang, M., Stepchenkova, S.,… Blanton, M. (2009). Internet addiction: metasynthesis of 1996-2006 quantitative research. *CyberPsychology & Behavior*, *12*, 203–207. doi:10.1089/cpb.2008.0102

Cao, F., & Su, L. (2007). Internet addiction among Chinese adolescents: prevalence and psychological features. *Child: Care, Health and Development*, *33*, 275–281. doi:10.1111/j.1365-2214.2006.00715.x

Cao, H., Sun, Y., Wan, Y., Hao, J., & Tao, F. (2011). Problematic Internet use in Chinese adolescents and its relation to psychosomatic symptoms and life satisfaction. *BMC Public Health, 11*, 802. doi:10.1186/1471-2458-11-802

Caplan, S. E. (2002). Problematic Internet use and psychosocial well-being: Development of a theory-based cognitive-behavioral measurement instrument. *Computers in Human Behavior, 18*, 553–575.

Caplan, S. E. (2010). Theory and measurement of generalized problematic Internet use: A two-step approach. *Computers in Human Behavior, 26*, 1089-1097. doi:10.1016/ j.chb.2010.03.014

Castellana, M., Sánchez-Carbonell, X., Graner, C., & Beranuy, M. (2007). El adolescente ante las tecnologías de la información y la comunicación: Internet, móvil y videojuegos. *Papeles del Psicólogo, 28*, 196-204.

Ceyhan, E., Ceyhan, A. A., & Gürcan, A. (2007). The validity and reliability of the Problematic Internet Usage Scale. *Educational Sciences: Theory & Practice, 7*, 411–416.

Chang, M. K., & Law, S. P. M. (2008). Factor structure for Young's Internet Addiction Test: A confirmatory study. *Computers in Human Behavior, 24*, 2597-2619. doi:10.1016/ j.chb.2008.03.001

Chen, S. H., Weng, L. C., Su, Y. J., Wu, H. M., & Yang, P. F. (2003). Development of Chinese Internet Addiction Scale and its psychometric study. *Chinese Journal of Psychology, 45*, 279–294.

Cho, H., Kwon, M., Choi, J. H., Lee, S. K., Choi, J.S., Choi, S. W., & Kim, D. -J. (2014). Development of the Internet Addiction Scale based on the Internet Gaming Disorder criteria suggested in DSM-5. *Addictive Behaviors, 39,* 1361-1366. doi:10.1016/ j.addbeh.2014.01.020

Chou, C., Chou, J., & Tyan, N. N. (1998, febrero). *An Exploratory Study of Internet Addiction, Usage and Communication Pleasure.* Trabajo presentado en el Annual meeting of the Association for educational communications and technology, St. Louis, MO.

Chou, C., & Hsiao, M. C. (2000). Internet addiction, usage, gratification, and pleasure experience: The Taiwan college student's case. *Computers & Education, 35*, 65–80.

Chow, S. L., Leung, G. M., Ng, C., & Yu, E. (2009). A Screen for Identifying Maladaptive Internet Use. *International Journal of Mental Health & Addiction, 7*, 324-332. doi:10.1007/s11469-008-9170-4

Cía, A. H. (2014). Las adicciones no relacionadas a sustancias (DSM-5, APA, 2013): un primer paso hacia la inclusión de las Adicciones Conductuales en las clasificaciones categoriales vigentes. *Revista de Neuro-Psiquiatría, 76*, 210 - 217.

Cuenca-Royo, A.M., Torrens, M., Sánchez-Niubó, A., Suelves, J.M., & Domingo-Salvany, A. (2013). Comorbilidad psiquiátrica en jóvenes-adultos consumidores de cannabis. *Adicciones, 25*, 45-54.

Curran, P. J., West, S. G., & Finch, J. F. (1996). The robustness of test statistics to nonnormality and specification error in confirmatory factor analysis. *Psychological Methods, 1*, 16-29.

Davis R. A. (2001). A cognitive–behavioral model of pathological Internet use. *Computers in Human Behavior, 17*, 187–195.

Davis, R. A., Flett, G. L., & Besser, A. (2002). Validation of a new scale for measuring problematic Internet use: implications for pre-employment screening. *CyberPsychology & Behavior, 5*, 331–345. doi:10.1089/109493102760275581

De Gracia, M., Vigo, M., Fernández, J., & Marcó, M. (2002). Problemas conductuales relacionados con el uso de Internet: Un estudio exploratorio. *Anales de Psicología, 18*, 273-292.

Del Miglio, C., Gamba, A., & Cantelmi, T. (2001). Costruzione e validazione preliminare di uno strumento UADI per la rilevazione delle variabili psicologiche e psicopatologiche correlate all'uso di Internet. *Giornale Italiano di psicopatologia, 7*, 293-306.

Demetrovics, Z., Szeredi, B., & Rózsa, S. (2008). The three-factor model of Internet addiction: The development of the Problematic Internet Use Questionnaire. *Behavior Research Methods, 40*, 563-574. doi:10.3758/ BRM.40.2.563

Douglas, A. C., Mills, J. E., Niang, M., Stepchenkova, S., Byun, S., Ruffini, C.,… Blanton, M. (2008). Internet addiction: Meta-synthesis of qualitative research for the decade 1996–2006. *Computers in Human Behavior, 24*, 3027–3044. doi:10.1016/j.chb.2008. 05.009

Durkee, T., Kaess, M., Carli, V., Parzer, P., Wasserman, C. Floderus, B.,… Wasserman, D. (2012). Prevalence of pathological internet use among adolescents in Europe: demographic and social factor. *Addiction, 107*, 2210-2222. doi:10.1111/j.1360-0443.2012.03946.x

Echeburúa, E. (1999). *L*as nuevas adicciones: juego, sexo, comida, compras, trabajo, internet. Bilbao: Desclée de Brouwer.

Echeburúa, E., & de Corral, P. (2010). Adicción a las nuevas tecnologías y a las redes sociales en jóvenes: un nuevo reto. *Adicciones, 22*, 91-96.

Elosúa, P., & Zumbo, B. D. (2008). Coeficientes de fiabilidad para escalas de respuesta categórica ordenada. *Psicothema, 20,* 896-901.

Estallo, J. A. (2001). Usos y abusos de internet. *Anuario de Psicología, 32*, 95-108.

Estévez, L., Bayón, C., de la Cruz, J., & Fernández-Líria, A. (2009). Uso y abuso de Internet en adolescentes. En E. Echeburúa, F. J. Labrador y E. Becoña (Eds.), *Adicción a las nuevas tecnologías en adolescentes y jóvenes* (pp. 101-130). Madrid: Ediciones Pirámide.

Ferraro, G., Caci, B., D'amico, A., & Di Blasi, M. (2007). Internet Addiction Disorder: An Italian study. *CyberPsychology & Behavior, 10*, 170-175. doi:10.1089/cpb.2006.9972

Fortson, B. L., Scotti, J. R., Chen, Y., Malone, J., & Del Ben, K. S. (2007). Internet use, abuse, and dependence among students at a Southeastern Regional University. *Journal of American College Health, 56*, 137-144.

Frangos, C. C., Frangos, C. C., & Sotiropoulos, I. (2011). Problematic internet use among Greek university students: an ordinal logistic regression with risk factors of negative psychological beliefs, pornographic sites, and

online games. *Cyberpsychology, Behavior, and Social Networking, 14*, 51-58. doi:10.1089/cyber.2009.0306

Frangos, C. C., Frangos, C. C., & Sotiropoulos, I. (2012). A meta-analysis of the reliabilty of Young's Internet Addiction Test. En S. I. Ao, L. Gelman, D. W. L. Hukins, A. Hunter y A. M. Korsunsky (Eds.), *Proceedings of the World Congress on Engineering: Vol. 1*. The 2012 International Conference of Computational Statistics and Data Engineering (pp. 368-371). Londres, Reino Unido: Newswood Limited.

García, A., Beltrán, P., & Pérez, C. (2012). Uso y consumo de redes sociales e Internet entre los adolescentes españoles. Características y prácticas de riesgo: Revisión bibliográfica. *Documentación de las Ciencias de la Información, 35*, 253-273.

García, J. A., Terol, M. C., Nieto, M., Lledó, A., Sánchez, S., Martín-Aragón, M., & Sitges, E. (2008). Uso y abuso de Internet en jóvenes universitarios. *Adicciones, 20,* 131-142.

Goldberg, I. (1995*). Internet addictive disorder (IAD) diagnostic criteria*. Retrieved from www.psycom.net/iadcriteria.html

Gómez, P., Rial, A., Braña, T., Varela, J., & Barreiro, C. (2014). Evaluation and early detection of problematic Internet use in adolescents. *Psicothema, 26*, 21-26. doi:10.7334/ psicothema2013.109

Greenfield, D. N. (1999). Psychological characteristics of compulsive Internet use: a preliminary analysis. *CyberPsychology & Behavior, 2*, 403-412.

Griffiths, M. (1998). Internet addiction: does it really exist? En J. Gackenbach (Ed.), *Psychology and the Internet: intrapersonal, interpersonal, and transpersonal implications*. New York: Academic Press.

Grohol, J. M. (1999). *Internet Addiction Guide*. Retrieved from http://psychcentral.com/ netaddiction/

Günüç, S., & Kayri, M. (2010). The profile of internet dependency in Turkey and development of internet addiction scales: study of validity and reliability. *Hacettepe* Üniversitesi *Egitim Fakültesi Dergisi, 39*, 220–232.

Hansen, S. (2002). Excessive Internet usage or "Internet addiction"? The implications of diagnostic categories for student users. *Journal of Computer Assisted Learning, 18*, 232–236. doi:10.1046/j.1365-2729.2002.t01-2-00230.x

Hawi, N. S. (2013). Arabic validation of the Internet Addiction Test. *Cyberpsychology, Behavior, and Social Networking, 16*, 200-204. doi:10.1089/cyber.2012.0426

Hu, L., & Bentler, P. M. (1999). Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. *Structural Equation Modeling: A Multidisciplinary Journal, 6,* 1-55. doi:10.1080/10705519909540118

Huang, Z., Wang, M., Quian, M., Zhong, J., & Tao, R. (2007). Chinese Internet addiction inventory: Developing a measure of problematic Internet use for Chinese college students. *CyberPsychology & Behavior, 10*, 805-812. doi:10.1089/cpb.2007.9950

IBM Corp. Released (2011). *IBM SPSS Statistics for Windows, Version 20.0*. Armonk, NY: IBM Corp.

Instituto Nacional de Estadística [INE]. (2014). *Encuesta sobre equipamiento y uso de tecnologías de información y comunicación en los hogares (TIC- H)*. Madrid: Instituto Nacional de Estadística. Retrieved from http://www.ine.es/prensa/np864.pdf

Jelenchick, L. A., Eickhoff, J., Christakis, D. A., Brown, R. L., Zhang, C., Benson, M., & Moreno, M. A. (2014). The Problematic and Risky Internet Use Screening Scale (PRIUSS) for adolescents and young adults: Scale development and refinement. *Computers in Human Behavior, 35*, 171–178. doi:10.1016/j.chb.2014.01.035

Jenaro, C., Flores, N., Gómez-Vela, M., González-Gil, F., & Caballo, C. (2007). Problematic Internet and cell-phone use: Psychological, behavioral and health correlates. *Addiction Research & Theory, 15*, 309-320. doi:10.1080/16066350701350247

Kline, R. B. (2005). *Principles and Practice of Structural Equation Modeling* (2ª ed.). New York: The Guilford Press.

Ko, C. H., Yen, J. Y., Chen, C. C., Chen, S. H., & Yen, C. F. (2005). Proposed diagnostic criteria of Internet Addiction for adolescents. *The Journal of Nervous and Mental Disease, 193*, 728–733. doi:10.1097/01.nmd.0000185891.13719.54

Ko, C. H., Yen, J. Y., Yen, C. F., Chen, C. C., Yen, C. N., & Chen, S. H. (2005). Screening for Internet addiction: an empirical study on cut-off points for the Chen Internet Addiction Scale. *The Kaohsiung Journal of Medical Sciences, 21*, 545-551. doi:10.1016/S1607-551X(09)70206-2

Koronczai, B., Urbán, R., Kökönyei, G., Paksi, B., Papp, K., Kun, B.,… Demetrovics, Z. (2011). Confirmation of the three-factor model of problematic internet use on off-line adolescent and adult samples. *Cyberpsychology, Behavior, and Social Networking, 14*, 657–664. doi:10.1089/cyber.2010.0345

Labrador, F.J., Villadangos, S., Crespo, M., & Becoña, E. (2013). Desarrollo y validación del cuestionario de uso problemático de nuevas tecnologías (UPNT). *Anales de Psicología, 29,* 836-847. doi:10.6018/analesps.29.3.159291

Lam, L. T., Peng, Z., Mai, J., & Jing, J. (2009). Factors associated with Internet addiction among adolescents. *CyberPsychology & Behavior, 12*, 551–555. doi:10.1089/cpb.2009.0036

Lam-Figueroa, N., Contreras-Pulache, H., Mori-Quispe, E., Nizama-Valladolid, M., Gutiérrez, C., Hinostroza-Camposano, W.,... Hinostroza-Camposano, W.D. (2011). Adicción a Internet: desarrollo y validación de un instrumento en escolares adolescentes de Lima, Perú. *Revista Peruana de Medicina Experimental y Salud Pública, 28*, 462-469. doi:10.1590/S1726-46342011000300009

LaRose, R., Lin, C.A., & Eastin, M. S. (2003). Unregulated Internet Usage: Addiction, Habit, or Deficient Self-Regulation? *Media Psychology, 5*, 225-253. doi:10.1207/S1532785XMEP0503_01

Lee, K., Lee, H. K., Gyeong, H., Yu, B., Song, Y. M., & Kim, D. (2013). Reliability and validity of the Korean version of the Internet Addiction Test among college students. *Journal of Korean Medical Sciences, 28*, 763-768. doi:10.3346/jkms.2013.28.5.763

Lévy, J.P., Martín, M.T., & Román, M.V. (2006). Optimización según estructuras de covarianzas. En J.P. Lévy & J. Varela (Eds.), *Modelización con estructuras de covarianzas en ciencias sociales* (pp. 11-30). A Coruña: Netbiblo.

Li, L., & Yang, Y. (2007). The development and validation of Adolescent Pathological Internet Use Scale. *Acta Psychologica Sinica, 39*, 688- 696.

Lopez-Fernandez, O., Freixa-Blanxart, M., & Honrubia-Serrano, M. L. (2013). Problematic Internet Entertainment Use Scale for Adolescents: prevalence of problem Internet use in Spanish high school students. *Cyberpsychology, Behavior, and Social Networking, 16*, 108-118. doi:10.1089/cyber.2012.0250

Matute, H. (2001). *La adicción a Internet no existe*. Retrieved from http://eciencia.com/blog/ divulgacion/la adiccion a internet_no_existe_195/

Meerkerk, G. J., Van Den Eijnden, R. J. J. M., Vermulst, A. A., & Garretsen, H. F. L. (2009). The Compulsive Internet Use Scale (CIUS): Some psychometric properties. *CyberPsychology & Behavior, 12*, 1-6. doi:10.1089/cpb.2008.0181

Mitchell, K. J., Sabina, C., Finkelhor, D., & Wells, M. (2009). Index of problematic online experiences: Item characteristics and correlation with negative symptomatology. *CyberPsychology & Behavior, 12*, 707–711. doi:10.1089/cpb.2008.0317

Morahan-Martin, J., & Schumacher, P. (2000). Incidence and correlates of pathological Internet use among college students. *Computers in Human Behavior, 16*, 13–29.

Moreno, M. A., Jelenchick, L., Cox, E., Young, H., & Christakis, D. A. (2011). Problematic Internet Use among US youth: A systematic review. *Archives of Pediatrics & Adolescent Medicine, 165*, 797-805. doi:10.1001/archpediatrics.2011.58

Muñiz, J., & Fonseca-Pedrero, E. (2008). Construcción de instrumentos de medida para la evaluación universitaria. *Revista de Investigación en Educación, 5*, 13-25.

Nichols, L. A., & Nicki, R. (2004). Development of a psychometrically sound Internet Addiction Scale: a preliminary step. *Psychology of Addictive Behaviors, 18*, 381-384. doi:10.1037/0893-164X.18.4.381

Oliva, A., Hidalgo, M. V., Moreno, C., Jiménez, L., Jiménez, A., Antolín, L., & Ramos, P. (2012). *Uso y riesgo de adicciones a las nuevas tecnologías entre adolescentes y jóvenes andaluces*. Sevilla: Editorial Agua Clara.

Orman, M. (1996). *Internet Stress Scale o test d'Orman*. Retrieved from http://www.stresscure.com/hrn/addiction.html

Pardo, A., & Ruíz, M. A. (2001). *SPSS 11. Guía para el análisis de datos*. Madrid: McGraw-Hill.

Petry, N. M., & O'Brien, C. P. (2013). Internet gaming disorder and the DSM-5. *Addiction, 108*, 1186–1187. doi:10.1111/add.12162

Pratarelli, M. E., Browne, B. L., & Johnson, K. (1999). The bits and bytes of computer/Internet addiction: A factor analytic approach. *Behavior Research Methods, Instruments, & Computers, 31*, 305-314.

Puerta-Cortés, D. X., & Carbonell, X. (2014). El modelo de los cinco grandes factores de personalidad y el uso problemático de Internet en jóvenes colombianos. *Adicciones, 26*, 54-61.

Puerta-Cortés, D. X., Carbonell, X., & Chamarro, A. (2013). Análisis de las propiedades psicométricas de la versión en español del Internet Addiction Test. *Trastornos Adictivos, 14*, 99-104.

Pulido-Rull, M. A., Escoto-de la Rosa, R., & Gutiérrez-Valdovinos, D. M. (2011). Validez y confiabilidad del Cuestionario de Uso Problemático de Internet (CUPI). *Journal of Behavior, Health & Social Issues, 3*, 25–34. doi:10.5460/jbhsi.v3.1.27681

Rial, A., Gómez, P., Braña, T., & Varela, J. (2014). Actitudes, percepciones y uso de Internet y las redes sociales entre los adolescentes de la comunidad gallega (España). *Anales de Psicología, 30,* 642-655. doi: 10.6018/analesps.30.2.159111

Rotunda, R. J., Kass, S. J., Sutton, M. A., & Leon, D. T. (2003). Internet use and misuse. Preliminary findings from a new assessment instrument. *Behavior Modification, 27*, 484-504. doi:10.1177/0145445503255600

Ruiz-Olivares, R., Lucena, V., Pino, M. J., & Herruzo, J. (2010). Análisis de comportamientos relacionados con el uso/abuso de Internet, teléfono móvil, compras y juego en estudiantes universitarios. *Adicciones, 22*, 301-310.

Sánchez-Carbonell, X., Beranuy, M., Castellana, M., Chamarro, A., & Oberst, U. (2008). La adicción a Internet y al móvil: ¿moda o trastorno? *Adicciones, 20*, 149-160.

Scherer, K. (1997). College life on-line: healthy and unhealthy Internet use. *Journal of College Student Development, 38*, 655-665.

Shapira, N. A., Lessig, M. C., Goldsmith, T. D., Szabo, S. T., Lazoritz, M., Gold, M. S., & Stein, D. J. (2003). Problematic internet use: Proposed classification and diagnostic criteria. *Depression and Anxiety, 17*, 207–216. doi:10.1002/da.10094

Smahel, D., Helsper, E., Green, L., Kalmus, V., Blinka, L., & Ólafsson, K. (2012). *Excessive internet use among European children*. London: EU Kids Online, London School of Economics & Political Science.

Spada, M. M. (2014). An overview of problematic Internet use. *Addictive Behaviors, 39*, 3-6. doi:10.1016/j.addbeh.2013.09.007

Steiger, J. H. (1998). A note on multiple sample extensions of the RMSEA fit index. *Structural Equation Modeling: A Multidisciplinary Journal, 5*, 411-419.

Tao, R., Huang, X., Wang, J., Zhang, H., Zhang, Y., & Li, M. (2010). Proposed diagnostic criteria for internet addiction. *Addiction*, *105*, 556–564. doi:10.1111/j.1360-0443.2009.02828.x

Thatcher, A., & Goolam, S. (2005). Development and psychometric properties of the Problematic Internet Use Questionnaire. *South African Journal of Psychology, 35*, 793-809.

Tomás, J. M., & Oliver, A. (1998). Efectos de formato de respuesta y método de estimación en el análisis factorial confirmatorio. *Psicothema, 10*, 197-208.

Tsai, C. C., & Lin, S. S. J. (2001). Analysis of attitudes toward computer networks and Internet addiction of Taiwanese adolescents. *CyberPsychology & Behavior, 4*, 373-376. doi:10.1089/109493101300210277

Tsitsika, A., Tzavela, E., Mavromati, F., & el consorcio EU NET ADB. (Ed.). (2012). *Research on Internet addictive behaviours among European adolescents (Proyecto EU NET ADB)*. Athens: National and Kapodestrian University of Athens.

Valedor do Pobo. (2011). *Informe extraordinario: Adolescentes e Internet en Galicia*. Santiago de Compostela: Valedor do Pobo. Retrieved from http://www.valedordopobo.com/index.php?s=115&i=104&l=es

Watters, C. A., Keefer, K. V., Kloosterman, P. H., Summerfeldt, L. J., & Parker, J. D. A. (2013). Examining the structure of the Internet Addiction Test in adolescents: A bifactor approach. *Computers in Human Behavior, 29*, 2294-2302.

Widyanto, L., & McMurran, M. (2004). The psychometric properties of the Internet Addiction Test. *CyberPsychology & Behavior, 7*, 443-450. doi:10.1089/1094931041774578

Winters, K. C., Stinchfield, R.D., Henly, G.A., & Schwartz, R.H. (1990). Validity of adolescent self-report of alcohol and other drug involvement. *International Journal of the Addictions, 25*, 1379-1395. doi:10.3109/10826089009068469

Yang, S. C., & Tung, C. -J. (2007). Comparison of Internet addicts and non-addicts in Taiwanese high school. *Computers in Human Behavior*, *23*, 79–96. doi:10.1016/j.chb.2004.03.037

Young, K. S. (1996, August). *Internet addiction: The emergence of a new clinical disorder*. Work presented at the 104th Annual Convention of the American Psychological Association, Toronto, Canadá.

Young, K. S. (1998). *Caught in the Net: How to recognize the signs of Internet addiction and a winning strategy for recovery*. New York, NY: John Wiley & Sons, Inc.

Yuen, C. N., & Lavin, M. J. (2004). Internet dependence in the collegiate population: the role of shyness. *CyberPsychology & Behavior, 7*, 379 – 383. doi:10.1089/1094931041774587

Yuen, C. N. y Lavin, M. J. (2004). Internet dependence in the collegiate population: the role of shyness. *CyberPsychology & Behavior, 7*, 379 – 383. doi:10.1089/1094931041774587

Appendix. Table A1
Compilation of the most relevant assessment tools or screening instruments published

YEAR	AUTHORS	INSTRUMENTS	COUNTRY	VALIDATION SAMPLE	CONSTRUCT	Nº ITEMS	Nº FACTORS
1995	Goldberg	Internet Addiction Disorder scale – Qualitative scale	USA	-	Internet addiction	7 criteria	-
1996	Orman	Internet Stress Scale (ISS)	USA	-	Internet addiction	9 YES/NO items	-
1996	Young	Young's Diagnostic Questionnaire (YDQ)	USA	496 participants online (Adult population)	Internet addiction	8 YES/NO items	1
1997	Brenner	Internet-Related Addicitive Behavior Inventory (IRABI)	USA	563 users (Mean age: 34 years)	Internet addiction	32 TRUE/FALSE items	1
1997	Scherer	Clinical symptoms of Internet dependency (CSID)	USA	531 university students	Internet dependence	10 clinical symptoms	-
1998	Chou, Chou & Tyan	Chinese Internet-Related Addicitive Behavior Inventory version I (C- IRABI- I)	Taiwan	104 participants online (Mean age: 22,3 years; *SD*= 3.13)	Internet addiction	32 TRUE/FALSE items	1
1998	Griffiths	Addiction Core components criteria	UK	5 case studies (ages 15 to 35 years)	Addiction	6 principal components of addiction	-
1998	Young	Internet Addiction Test (IAT)	USA	-	Internet addiction	20 items (Likert 5-point scale)	-
1999	Pratarelli, Browne & Johnson	Computer Use Survey	USA	341 university students (Mean age: 22.8 years; *SD*= 5.88)	Internet addiction	55 items	4
1999	Greenfield	Virtual Addiction Survey (VAS)	USA & Canada	17251 participants online	Compulsive Internet use	36 YES/NO items	-
1999	Echeburúa	Test de Adicción a Internet	Spain	-	Internet addiction	9 YES/NO items	-
2000	Chou & Hsiao	Chinese Internet-Related Addicitive Behavior Inventory version II (C- IRABI- II)	Taiwan	910 university students (Mean age: 21.11 years; *SD*= 210)	Internet addiction	37 items (Likert 4-point agreement scale)	6
2000	Morahan-Martin & Schumacher	Pathological Internet Use Scale (PIUs)	USA	277 university students (Mean age: 20.72 years; *SD*= 2.35)	Pathological Internet use	13 TRUE/FALSE items	-
2000	Armstrong et al.	Internet Related Problem Scale (IRPS)	Australia	50 participants (75% aged 25 to 30 years)	Internet addiction	20 questions (Likert 10-point agreement scale)	-
2001	Tsai & Lin	Internet Addiction Scale for Taiwan high school students (IAST)	Taiwan	753 secondary-school students (Age range: 16-17 years)	Internet addiction	29 items (Likert 4-point scale)	4
2001	Anderson	Sin nombre	USA	1302 university students	Internet dependence	7 YES/NO items	-
2001	Del Miglio, Gamba & Cantelmi	Use, Abuse and Dependence on the Internet inventory (UADI scale)	Italy	244 participants (Age range: 13-57 years; Mean age: 28.7 years)	Internet dependence	75 items (Likert 5-point scale)	5
2002	Caplan	Generalized Problematic Internet Use Scale (GPIUS)	USA	386 university students (Age range: 18-57 years; Mean age: 20 years; *SD*= 2.22)	Generalized problematic Internet use	29 items (Likert 5-point agreement scale)	7

YEAR	AUTHORS	INSTRUMENTS	COUNTRY	VALIDATION SAMPLE	CONSTRUCT	Nº ITEMS	Nº FACTORS
2002	Davis et al.	Online Cognition Scale (OCS)	Canadá	211 Psychology students (Mean age: 21.73 years; *SD*= 4.4)	Problematic Internet use	36 items (Likert 7-point agreement scale)	4
2002	De Gracia, Vigo, Fernández & Marcó	*Problemas Relacionados con Internet (PRI)*	Spain	1664 Self-selected internauts (Age range: 15- 54 years)	Problematic Internet use	19 items (Likert frequency scale)	-
2003	LaRose et al.	Deficient Internet self-regulation	USA	465 university students	Unregulated Internet use	7 items (Likert 7-point scale)	-
2003	Rotunda, Kass, Sutton & Leon	Internet Use Survey (IUS)	USA	393 university students (Age range: 18-81 years; Mean age: 276 years)	Abuse of Internet	*Impairment index* of the IUS: 32 items (Likert 5-point frequency scale)	4
2003	Chen et al.	Chinese Internet Addiction Scale (CIAS)	Taiwan	-	Internet addiction	26 items (Likert 4-point scale)	5
2004	Yuen & Lavin	No name	USA	283 university students (adults	Internet dependence	7 items adapted from the DSM- IV criteria for substance dependence (Likert 5-point agreement scale)	-
2004	Nichols & Nicki	Internet Addiction Scale (IAS)	Canada	233 university students	Internet addiction	31 items (Likert 5-point frequency scale)	1
2004	Widyanto & McMurran	Internet Addiction Test (IAT)	UK	86 participants online (Age range: 13-67 years; Mean age men: 25.45 years (*SD* = 8.91); Mean age women: 31.44 years (*SD* = 10.34))	Internet addiction	20 items (Likert 5-point scale)	6
2005	Beard	Screening Interview Assessing Problematic Internet Use	USA	-	Problematic Internet use	72 questions	-
2005	Thatcher & Goolam	Problematic Internet Use Questionnaire (T- PIUQ)	South Africa	Pilot study: 279 participants; Validation: 1795 participants	Problematic Internet use	20 items (Likert 5-point scale)	3
2007	Fortson, Scotti, Chen, Malone & Del Ben	Reported Behaviors Related to Internet Abuse and Dependence	USA	411 university students (Age range: 18-56 years; Mean age: 20.4 years; *SD*= 3.2)	Internet abuse and/or dependence	9 items (Likert scale)	-
2007	Li & Yang	Adolescent Pathological Internet Use Scale	China	1331 secondary-school students and 30 Adolescents diagnosed as pathological users	Pathological Internet use	38 items (Likert 5-point scale)	6
2007	Ceyhan et al.	Problematic Internet Usage Scale (PIUS)	Turkey	1658 university students	Problematic Internet use	33 items (Likert 5-point scale)	3
2007	Huang et al.	Chinese Internet Addiction Inventory (CIAI)	China	Study 1: 516 university students (Age range: 17-24 years; mean age: 20.5 years; *SD*= 1.47); Study 2: 513 university students (Age range: 17-24 years; Mean age: 20.7 years; *SD*= 1.51); Study 3: 54 participants (27 clinical sample)	Internet addiction	31 items (Likert 5-point frequency scale)	3

YEAR	AUTHORS	INSTRUMENTS	COUNTRY	VALIDATION SAMPLE	CONSTRUCT	Nº ITEMS	Nº FACTORS
2007	Ferraro, Caci, D'amico & Di Blasi	Internet Addiction Test (IAT)	IItaly	236 participants online (Age range: 13-50 years; Mean age: 23.9 years; *SD* = 6.5)	Internet addiction	20 items (Likert 5-point scale)	6
2007	Jenaro, Flores, Gómez-Vela, González-Gil & Caballo	Internet Over-use scale (IOS)	Spain	377 university students	Pathological Internet use	23 items (Likert 6-point scale)	-
2008	Demetrovics et al.	Problematic Internet Use Questionnaire (D- PIUQ)	Hungary	1037 participants online (Mean age: 23.3 years; *SD*= 9.1)	Problematic Internet use	18 items (Likert 5-point scale)	3
2008	Labrador, Becoña & Villadangos	*Cuestionario de Detección de Nuevas Adicciones (DENA)*	Spain	Pilot study: 140 secondary-school students; Study 2: 1710 minors (Age range: 12-17 years)	Internet addiction	50 items. Block of 12 items referring to Internet use	-
2008	García et al.	*Cuestionario de Uso y Abuso de Internet*	Spain	391 university students (Age range: 18-47 years; Mean age: 19.59 years; *SD*= 2.83)	Internet abuse	47 items (Likert 5-point scale)	-
2008	Chang & Law	Internet Addiction Test (IAT)	China	410 university students	Internet addiction	20 items (Likert 5-point scale)	3
2009	Chow, Leung, Ng & Yu	Internet-user Assessment Screen	China	Phase 1: 378 adolescents (Mean age: 12.84 years; *SD*= 1.53); Phase 2: 3523 adolescents (Mean age men: 12.33 years; *SD*= 1.66. Mean age women: 12.5 years; *SD*= 1.6)	Maladaptive Internet use	26 items (20 items with Likert 5-point agreement scale)	9
2009	Meerkerk et al.	The Compulsive Internet Use Scale (CIUS)	Holland	Study 1: 447 intensive Internet users (Mean age: 38.5 years; *SD*=12.5); Study 2: 229 participants from the previous study; Study 3: 16,925 participants online (Age range: 11-80 years; Mean age: 25.3; *SD*= 10.0)	Compulsive Internet use	14 items (Likert 5-point frequency scale)	1
2009	Beranuy et al.	*Cuestionario de Experiencias Relacionadas con Internet (CERI)*	Spain	1879 secondary-school and university students (Mean age: 15.52; *SD*=2.434)	Internet addiction	10 items (Likert 4-point scale)	2
2009	Mitchell, Sabina, Finkelhor & Wells	Index of Problematic Online Experiences (I-POE)	USA	563 university students (Mean age: 19.86 years)	Problematic Internet use	26 YES/NO items	-
2010	Caplan	Generalized Problematic Internet Use Scale 2 (GPIUS2)	USA	785 participants (Age range: 18-70 years. Mean age: 33.14 years; *SD*= 15.25)	Generalized problematic Internet use	15 items (Likert 8-point agreement scale)	5 first-order factors (2 of them form a 2nd-order factor)
2010	Günüç & Kayri	Tukish Internet Addiction Scale	Turkey	754 secondary-school students	Internet addiction	35 items (Likert 5-point scale)	4
2011	Frangos, Frangos & Sotiropoulos	Problematic Internet Use Diagnostic Test (PIUDT)	Greece	2293 university students (adults)	Problematic Internet use	38 items	4
2011	Lam- Figueroa et. al.	*Escala de la Adicción a Internet de Lima (EAIL)*	Peru	248 secondary-school students	Internet addiction	11 items (Likert 4-point frequency scale)	2

YEAR	AUTHORS	INSTRUMENTS	COUNTRY	VALIDATION SAMPLE	CONSTRUCT	Nº ITEMS	Nº FACTORS
2011	Pulido-Rull et al.	*Cuestionario de Uso Problemático de Internet (CUPI)*	Mexico	697 university students (Mean age: 22.68 years; *SD*= 4)	Problematic Internet use	18 items (Likert 5-point scale)	5
2013	Lopez-Fernandez, Freixa-Blanxart & Honrubia-Serrano	Problematic Internet Entertainment Use Scale for Adolescents (PIEUSA)	Spain	1131 adolescents (Age range: 12-18 years. Mean age: 14.55 years; *SD*= 1.816)	Problematic Internet use	30 items (Likert 7-point agreement scale)	5
2013	Labrador, Villadangos, Crespo & Becoña	*Cuestionario de Uso Problemático de Nuevas Tecnologías (UPNT)*	Spain	2747 students (from 5th-grade Primary to 5th-year degree)	Problematic Internet use	26 items (Internet subscale: 7 items)	7
2013	Watters, Keefer, Kloosterman, Summerfeldt & Parker	Internet Addiction Test (IAT)	Canada	1948 secondary-school students (Age range: 16-18 years; Mean age: 17.07 years; *SD* = 0.84)	Internet addiction	20 items (Likert 5-point scale)	2
2013	Puerta-Cortés, Carbonell & Chamarro	Internet Addiction Test (IAT)	Colombia	1117 participants online (Age range: 14-67 years; Mean age = 20.93 years; *SD* = 4.84)	Internet addiction	20 items (Likert 5-point scale)	3
2013	Hawi	Internet Addiction Test (IAT)	Republic of Lebanon	817 middle and secondary school students (Age range: 10-22 years; Mean age: 15 years; *SD* = 2.12)	Internet addiction	20 items (Likert 5-point scale)	1
2013	Lee, Lee, Gyeong, Yu, Song & Kim	Korean version of the Internet Addiction Test (KIAT)	Republic of Korea	279 university students (Mean age: 19.9 years; *SD* = 2.7)	Internet addiction	20 items (Likert 5-point scale)	4
2014	Gómez et al.	Screening Scale of Problematic Internet Use in adolescents	Spain	2339 secondary-school students (Age range: 11-18 years. Mean age: 13.77; *SD*= 1.34)	Problematic Internet use	8 items (Likert 5-point agreement scale)	1
2014	Cho et al.	Internet Addiction Scale (IAS) based on the Internet Gaming Disorder Criteria (DSM-5)	Republic of Korea	1082 secondary-school students (Age range: 13-14 years)	Internet addiction	26 items	7
2014	Jelenchick et al.	Problematic and Risky Internet Use Screening Scale (PRIUSS)	USA	714 university students (Age range: 18-25 years; Mean age: 19.7 years; *SD* = 1.4)	Problematic Internet use	18 items (Likert 5-point frequency scale)	3

Neuropsychological impairments associated with the relation between cocaine abuse and violence: neurological facilitation mechanisms

Déficits neuropsicológicos asociados a la relación entre abuso de cocaína y violencia: mecanismos neuronales facilitadores

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Abstract

Introduction. Cocaine abuse, as well as prenatal exposure to cocaine, could be key factors in the expression of violent behaviour. Neuropsychological impairments, sex differences and the concurrent abuse of cocaine and alcohol have been suggested as facilitation mechanisms. **Aims.** To review and recapitulate the results obtained on the relationship between neuropsychological deficits due to cocaine abuse and/or prenatal exposure and the expression of violence. Furthermore, we analyze the roles of sex, concurrent alcohol abuse and possible brain damage as risk markers in this relationship. **Development.** The scientific literature was reviewed using Google Scholar, PsycINFO, PubMed, Medline and ISI Web of Knowledge. **Conclusions**. Cocaine facilitates the expression of violence due to neuropsychological deficits in emotional decoding, abstract reasoning and inhibitory control, as well as in mnemonic and verbal skills, and such impairments might also explain problems in decision-making. Both the deficits and the expression of violence appear to be more pronounced in men than in women. However, despite the fact that the combination of cocaine and alcohol use may increase the risk of violent reactions, the deficits would not be greater than those resulting from the separate use of each substance. The impairments might be caused by functional abnormalities of certain regions of the frontal (especially the prefrontal) and parietal lobes and some subcortical structures, such as the amygdala. All of this would provide a basis for the development of intervention strategies focusing on these cognitive domains.

Keywords: alcohol, cocaine, gender, neuropsychology, violence.

Resumen

Introducción. El abuso de la cocaína, así como la exposición prenatal a la misma parece ser un factor relevante en el desencadenamiento de comportamientos violentos. Los déficits neuropsicológicos, así como el género y la combinación con el alcohol, serían los posibles mecanismos facilitadores. **Objetivo.** Revisar y recapitular los resultados obtenidos sobre los déficits neuropsicológicos debidos al abuso o a la exposición prenatal a la cocaína y relacionarlos con la expresión de la violencia. Además, se enfatiza el papel del género y el abuso del alcohol junto a la cocaína, así como la posible existencia de daño orgánico cerebral como mecanismos facilitadores. **Desarrollo.** Se ha revisado la bibliografía científica usando los buscadores Google Scholar, PsycINFO, PubMed, Medline e ISI Web of Knowledge. **Conclusiones.** La cocaína facilitaría la expresión de la violencia debido a los déficits en la decodificación emocional, la capacidad de abstracción e inhibición, así como en las habilidades verbales y mnémicas. Esto explicaría, además, los problemas en la toma de decisiones. Los déficits y la expresión de la violencia parecen ser más evidentes en los hombres. Sin embargo, a pesar de que la combinación de la cocaína con el alcohol incrementaría el riesgo de reaccionar de forma violenta, los déficits no serían mayores que el consumo de cada una de ellas por separado. Estos déficits podrían ser producto de un funcionamiento anormal de algunas áreas del lóbulo frontal (especialmente el prefrontal) y el parietal, así como estructuras subcorticales como la amígdala. Todo ello permitiría planificar estrategias de intervención cuyos objetivos serían estos dominios cognitivos.

Palabras clave: alcohol, cocaína. género, neuropsicología, violencia.

Received: June 2014; Accepted: October 2014

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Substance addiction is known to be a key factor in the triggering of antisocial and/or violent behaviour. However, addictions are not always linked to violence, and addictions can be found without the manifestation of violence, since there is no causal relation between them (Gómez et al., 2008; Romero-Martínez, & Moya-Albiol, 2013). Indeed, violent behaviour tends to precede drug use (Collins & Messerschmidt, 1993; Farrington, 1994).

Several studies have reported a positive relationship between cocaine use and violent behaviour (Brody, Slovis, & Wrenn, 1990; Moore et al., 2008; Kraanen, Vedel, Scholing, & Emmelkamp, 2014; Pennings, Leccese, & Wolff, 2002), as well highlighting the seriousness of such behaviour (Chermack & Blow, 2002). Violent responses can be facilitated either directly, as a result of acute cocaine use (Licata, Taylor, Berman, & Cranston, 1993) or indirectly, due to cognitive deficits caused by high prenatal exposure to this substance (Bendersky & Lewis, 1998; 2001; Mayes, Bornstein, Chawarska, Haynes, & Granger, 1996), or by its chronic use in adulthood (Volkow et al., 1997).

Both sex and poly-drug use (including cocaine) are considered as triggers for violence (Delaney-Black et al., 2004). The relationship between cocaine use and violence is more evident in men (Chermack et al., 2010); also, cocaine and alcohol tend to be consumed at the same time (Alcázar-Córcoles & Bezos-Saldaña, 2011; Chermack et al., 2008; Chérrez-Bermejo & Alás-Brun, 2014), with the result that the euphoria-inducing effects of cocaine use increase in duration and intensity, increasing in turn the the risk of violent reactions (Heinz, Beck, Meyer-Lindenberg, Sterzer, & Heinz, 2011; Lizasoain, Moro, & Lorenzo, 2001; McCance-Katz, Kosten, & Jatlow, 1998).

The absence of a well-defined and systematized theoretical framework regarding the mediating factors between cocaine use/abuse/dependence and the triggering of violence, and more specifically regarding the neuropsychological deficits that can facilitate violent reactions, hinders a comprehensive understanding of the mechanisms involved. In the light of the above, and with the aim of providing a synthesis of the scientific literature focusing on the analysis of mediating variables between the exposure to or consumption of cocaine and the facilitation of aggressive behaviour, we shall first describe the main findings on the neuropsychological domains altered in people that abuse or are dependent on cocaine and those that were prenatally exposed to this substance. Next, we shall discuss the most relevant findings on the role of the main contributory variables, such as sex and alcohol and cocaine abuse/dependence. Finally, and taking into account previous data on the altered functioning of several brain structures underlying these deficits, the we shall analyze the possible existence of organic damage or hypofunctionality in the central nervous system (CNS).

Parameters of the literature search

We have Google Scholar, PsycINFO, PubMed, Medline and ISI Web of Knowledge to review the scientific literature on the relationship between neuropsychological deficits and the expression of aggressive behaviour in cocaine users. The initial search encompassed the following terms: *aggressive behaviour, cocaine, biological correlates, cognitive deficits, empathy, emotion recognition, executive functions, intelligence, neuropsychology* and *violence*. Articles dealing with biological variables only, with no direct or indirect mention of the expression of violence, were not considered in our review.

Neuropsychological domains

Empathy

Cocaine-dependent subjects have empathy-related deficits, specifically in perspective-taking, emotional decoding and emotional empathy (Kemmis, Hall, Kingston, & Morgan, 2007; Preller et al., 2014; Roselli & Ardila, 1996; Verdejo-García, Rivas-Perez, Vilar-López, & Pérez-García, 2007). In addition, they present high levels of alexithymia, that is, deficits in the ability to identify and verbalize their own emotions (Keller, Carroll, Nick, & Rounsaville, 1995; Li &Sinha, 2006).

Emotional decoding or recognition processes (of both facial expressions and prosody) are essential for cognitive empathy and for inferring one's own and others' thoughts, intentions and feelings (Babcock, Green, & Webb, 2008; Kemmis, Hall, Kingston, & Morgan, 2007; Preller et al., 2014; Roselli & Ardila, 1996; Verdejo-García et al., 2007), and so determining subsequent behaviour (Calder & Young, 2005). In this regard, greater severity of cocaine use has been associated with poorer emotional recognition. More specifically, the greater the level of cocaine use and the higher the number of years of its consumption, the poorer the recognition of facial expressions of fear and anger (Fernández-Serrano, Lozano, Pérez-García, & Verdejo-García, 2010). Research results also show that young adults who use cocaine occasionally and/or for recreational purposes, together with users currently abstinent, presented particular deficits in the recognition of fear in the "eyes task", which assesses the extent to which people can "read the mind" from the other's facial expression (Kemmis et al., 2007). Furthermore, such deficits could be relatively stable, since they have been observed in users of several substances (cocaine among them) in abstinence periods ranging from 3 to 20 months (Foisy et al., 2007).

Studies in children prenatally exposed to cocaine are in the same line, as 3- to 6-year-olds that were prenatally exposed displayed less reactivity to the crying of other children and of their own mothers. They even showed less competence in cooperation tasks than non-prena-

tally exposed children (Jones, Field, Davalos, & Hart, 2004).

Deficits in empathic processes, as well as lack of remorse, have often been associated with antisocial behaviour (Moya-Albiol, Herrero, & Bernal, 2010; Preller et al., 2014). A possible explanation for this is that deficits in basic empathic processes, such as those of emotional decoding, are related to poor emotional regulation (Schipper & Petermann, 2013), which in turn affects decision-making. Moreover, cocaine users show poorer emotional and behavioural regulation during early abstinence (Fox, Axelrod, Paliwal, Sleeper, & Sinha, 2007). This might facilitate the expression of violence in these people, who fail to foresee and correctly interpret the consequences of their own actions (Blair, 2003).

Children prenatally exposed to cocaine have poor impulse control and emotion regulation and higher irritability than non-cocaine-exposed children (Bendersky & Lewis, 1998; 2001; Campbell, Bliven, Silveri, Snyder, & Spear, 2000; Fox, Calkins, Schmidt, Rubin, & Coplan, 1996; Mayes et al., 1996). Such poor behavioural regulation could increase the likelihood of their manifesting sustained disruptive behaviour, which would become more evident and serious as the socialization of the child/teenager runs its course over time (Allen, Bennett, Carmody, Wang, & Lewis, 2014; Rao et al., 2007).

Executive functioning

Chronic use of cocaine is related to poorer executive functioning, affecting capacity for inhibition, mental flexibility, planning ability, alternation of cognitive sets and decision-making (Colzato et al., 2009; Madoz-Gúrpide, Blasco-Fontecilla, & Baca-García, 2011; Morie, De Sanctis, & Foxe, 2014; Pike, Stoopsa, Fillmore, & Rush, 2013; Verdejo-García & Pérez-García, 2007; van der Plas et al., 2009; Woicik et al., 2009; 2011). This altered functioning has not only been found in adults: children and teenagers prenatally exposed to high levels of cocaine also present such deficits (Betancourt et al., 2011; Bridgett & Mayes, 2011; Grewen et al., 2014; Landi et al., 2012).

The executive functions are critical for to good social adaptation, so that deficits in these mental processes facilitate the expression of violence (Krämer, Kopyciok, Richter, Rodriguez-Fornells, & Münte, 2011; Raaijmakers et al., 2008). Whilst studies in adults that use cocaine and are violent have focused on the analysis of decision -making and mental flexibility, research in children and adolescents teenagers prenatally exposed to high levels of this substance have focused on inhibition processes.

One study revealed that cocaine users with higher levels of violence and antisocial traits committed fewer perseverative errors in the Wisconsin card sorting test than those who were less violent (Rosse, Miller, & Deutsch, 1993). The same study also suggested that a greater mental flexibility (or fewer perseverations) in cocaine-abusing subjects with antisocial traits and high levels of violence could increase the chances of their committing an offence but avoiding any negative consequences of such behaviour (Rosse et al., 1993). However, the results are at odds with those for other subgroups of violent individuals (men serving sentences for domestic abuse and psychiatric population), which tend to show less mental flexibility (Miura, 2009; Romero-Martínez, Lila, Catalá-Miñana, Williams, & Moya-Albiol, 2013; Romero-Martínez, Lila, Sariñana-González, González-Bono, & Moya-Albiol, 2013; Romero-Martínez & Moya-Albiol, 2013). This could be explained by methodological errors in the mentioned study, by inadequate sample size or even by the instruments used in the assessment of antisocial traits.

A study that assessed decision-making through the Iowa Gambling Task revealed that abstinent cocaine users showed a behavioural pattern similar to those of violent subgroups, such as sex offenders, drug dealers and people arrested for drunk-driving. These people gave great importance to gains and rewards while disregarding losses and punishments (Yechiam et al., 2008). Thus, they would have deficits in reward processing, failing to consider all the relevant information and focusing only on that related to the greatest and most immediate rewards, and dismissing losses (Yechiam et al., 2008).

Children and teenagers exposed to cocaine during their mother's pregnancy often have a difficult temperament (Bendersky, Bennett, & Lewis, 2006; Moilanen, Shaw, & Fitzpatrick, 2010), which can lead to behavioural no.s such as externalizing behaviour and/or risk or criminal behaviour (Allen et al., 2014; Bennett, Marini, Berzenski, Carmody, & Lewis, 2013; Delaney-Black et al., 2000; Min et al., 2014). Poor inhibitory control might explain this, since the lower the capacity for inhibitory control, the more serious the violence perpetrated (Bendersky et al., 2006; Carmody, Bennettb, & Lewis, 2011; Holler & Kavanaugh, 2013; Pawliczek et al., 2013; Schafer & Fals-Stewart, 1997).

Memory

Several studies have revealed that adult cocaine users have deficits in memory, both immediate and delayed. They also have working memory deficits (Fox, Jackson, & Sinha, 2009; Spronk, van Wel, Ramaekers, & Verkes, 2013; Woicik et al., 2009), whose functions provide the foundation for other high-level cognitive processes, such as executive functioning (McCabe, Roediger, McDaniel, Balota, & Hambrick, 2010). These results have been replicated in children and teenagers that were prenatally exposed to high levels of cocaine (Bridgett & Mayes, 2011; Buckingham-Howes, Berger, Scaletti, & Black, 2013; Riggins et al., 2012). Moreover, such children show delayed development in the aforementioned abilities compared

to controls of the same age (Betancourt et al., 2011; Buckingham-Howes et al., 2013).

With regard to the relationship between cocaine use, memory deficits and violence, only one study has analyzed it in adults, reporting that in heterosexual couples with a history of poly-substance abuse (cocaine included), the greater the deficit in the delayed recollection of words in the *California Verbal Learning Test*, the poorer the recollection of episodes of violence against their partners (Medina, Schafer, Shear, & Armstrong, 2004). Therefore, there is no direct relationship between memory deficits and violence; rather, deficits in delayed recall could more likely associated with deficits in executive functioning, which in turn could be more strongly related to the expression of violence (Krämer et al., 2011; Raaijmakers et al., 2008).

Attention

Several studies have revealed that cocaine abuse in adults is related to deficits in sustained attention and problems for fixating and shifting attentional focus (Spronk et al., 2013; Woicik et al., 2009). On the other hand, studies in children that were prenatally exposed to high levels of cocaine have revealed that, regardless of their sex and from age 3 to 7, they made more omissions in the *Visual Continuous Performance Test* than non-cocaine-exposed children (Bandstra, Morrow, Anthony, Accornero, & Fried, 2001). Furthermore, such deficits may be specifically circumscribed to the processing of visual information in the right hemisphere, as demonstrated by results from the *sustained visual orienting task* (SVOT) (Bandstra et al., 2001; Heffelfinger, Craft, & Shyken, 1997). Finally, such attention deficits may be caused by alterations in arousal regulation, affecting processing, learning and memorization (Heffelfinger, Craft, White, & Shyken, 2002).

Studies that have analyzed the relationship between attention deficits, cocaine and violence have focused on children and teenagers prenatally exposed to high levels of cocaine. Such studies concluded that children and teenagers with prenatal cocaine exposure tend to have greater attention deficits – especially in relation to sustained attention – and higher levels of externalizing behaviours (Bada et al., 2012; Carmody et al., 2011; Min et al., 2014). As is the case with memory, there is no direct relationship between attention and violence; rather, the relationship would be mediated by the executive functions (Tirapu-Ustárroz, Ríos-Lago, & Maestú-Unturbe, 2011).

Sex and concurrent use of alcohol and cocaine: precipitants and facilitators of violent behaviour

Sex is important on analyzing the effects of cocaine, since boys that were exposed to cocaine during gestation have more behaviour problems and cognitive deficits (central processing of information, motor skills and abstract thinking) as they grow up than non-cocaine-exposed boys. Prenatally exposed girls, on the other hand, do not differ from non-exposed-girls in this respect. Moreover, the greater the exposure the more pronounced the behaviour problems and cognitive deficits (Delaney-Black et al., 2004). Comparisons between prenatally exposed boys and girls reveal that show more externalizing, risk and/or aggressive behaviour than girls (Allen et al., 2014; Carmody et al., 2011; Delaney-Black et al., 2000). Inhibitory control increases as the children grow older (from 7.5 to 11.5 years of age), even among boys; girls, however, have better prognosis as they improve earlier (Bridgett & Mayes, 2011; Carmody et al., 2011). Therefore, the neurotoxic effects of cocaine can cause more damage to the CNS in men than in women (Allen et al., 2014; Carmody et al., 2011; Chang, Ernst, Strickland, Mehringer, & Mark, 1999).

Generally, the relationship between the use and/or abuse of cocaine and violence is more evident in men than in women (Allen et al. 2014; Chermack et al., 2010), as men are more prone to being physically aggressive in general and against women in particular. In women, the aggression is verbal, and is usually directed at her offspring (Gómez et al., 2008). In both men and women the relationship between antisocial personality disorder and aggressive behaviour is clearer when there is abuse of substances, such as cocaine (Lewis, 2011; Mattson, O'Farrell, & Lofgreen, Cunningham & Murphy, 2012).

With regard to the concurrent use of cocaine and alcohol, the risk of displaying violent behaviour and an increase in violent thoughts is greater than that produced by the separate effects of each one of these substances (Chermack & Blow, 2002; Chérrez-Bermejo & Alás-Brun, 2014; Kraanen et al., 2014). This could be explained by the fact that the combination of the two substances can lead to the formation of a metabolite called *cocaethylene,* which inhibits the reuptake of dopamine in the systems of impulse control, such as the nucleus accumbens (Chermack & Blow, 2002; Soler-González, Balcells-Oliveró, & Gual-Solé, 2014). As stated earlier, neuropsychological deficits can play an important role in the facilitation of violent behaviour. Nonetheless, on comparing different cognitive domains in three groups of former users (cocaine, alcohol and alcohol-cocaine) there were statistically significant differences only between ex-cocaine users and ex-alcohol users. In fact, the group of ex-cocaine users showed less mental flexibility (assessed through the *Bexley-Maudsley Category Sorting Test*), poorer short-term/working memory for visual information and lower processing speed (assessed through the Sternberg Task and the Processing Speed Index [PSI] of the WAIS-R) than ex-alcohol users and consumers of both substances (Lawton-Craddock, Nixon & Tivis, 2003). Thus, the neuropsy-

chological deficits in people that abuse cocaine and alcohol and would ot be as pronounced as in those that use cocaine exclusively.

In addition to these two factors, there are others that come into play, such as socio-economic status, which is a mediating factor in the relationship between cocaine abuse and violence. In general, people from the lower socio-economic status strata and those who are divorced, single or unemployed would be at greater risk of their cocaine abuse facilitating the expression of violence (Tardiff, Marzuk, Leon, Portera, & Weiner, 1997).

Neuronal correlates

Neurotransmission

It is has been hypothesized that cocaine facilitates aggression by inhibiting the reuptake of monoamines such as dopamine, noradrenaline, and serotonin or by overstimulating the postsynaptic receptors (Cunningham & Anastasio, 2014; Grewen et al., 2014; Moore et al., 2008; Patkar et al., 2003; 2006). Hence, the levels of monoamines in the synaptic space might increase (Cooper, Bloom, & Roth, 1991; Matuskey et al., 2014) in different areas of the prefrontal cortex and limbic system, which play a key role in the regulation of behaviour and emotions (Davis, 1996). Serotonin could be an important mediator in the relationship between the expression of violence and cocaine abuse (Patkar et al., 2006). Cocaine users presenting greater levels of violence show alterations in both the transporters of this neurotransmitter and in the postsynaptic receptors (Patkar et al., 2003; 2006). Such alterations in the monoaminergic system were corroborated by studies that analyzed the concentration of monoamine metabolites and monoamines in the cerebrospinal fluid of children with prenatal exposure to cocaine, concluding that these children presented higher levels of noradrenaline and its precursors and reductions in dopamine metabolites (Mayes et al., 1998; Needlman, Zuckerman, Anderson, Mirochnick, & Cohen, 1993).

Brain structures

Cocaine users have deficits in emotional decoding that might be due to the small size of their amygdala, as has been observed by some authors (Makris et al., 2004). In addition, these individuals might display less physiological activation, assessed through the amount of pupillary response, with regard to social interaction (Preller et al., 2014). Weaker activation of the medial orbitofrontal cortex could be a neural correlate of this kind of interpersonal interaction. Lower activation of this region would be associated with smaller social networks (Preller et al., 2014).

The high prevalence of impulsiveness and violence, as well as the greater reactivity and increased anger in response to stress observed in briefly abstinent cocaine users may be linked to poor neurocognitive inhibitory control (Bell, Foxe, Ross, & Garavan, 2014; Fox et al., 2007; Fox, Hong, Siedlarz, & Sinha, 2008). Low activity of the following structures would be the neural correlate of such deficient control: the medial and inferior frontal gyri of the right hemisphere, the right inferior parietal lobe, the bilateral insula, the medial cingulate cortex and the supplementary motor cortex, whose hypoactivation could affect the regulation of behaviour through its interaction with the limbic regions (Bell et al., 2014; Pawliczek et al., 2013). Furthermore, these users also display low activation of the lateral orbitofrontal cortex and the ventral striatum, which is associated with greater anger expression (Goldstein et al., 2005), as well as poorer emotional recognition of anger (Calder, Keane, Lawrence, & Manes, 2004; Murphy et al., 2003). On the other hand, chronic cocaine users display less mental flexibility, which is linked to greater connectivity between the left medial frontal gyrus and the nucleus accumbens in periods of repose (Camchong et al., 2011).

In turn, cocaine-dependent adults have less grey matter and less activation of the anterior rostral cingulate cortex, and this would be subjacent to the low behavioural self-awareness and/or self-monitoring these people usually display (Moeller et al., 2014). All of this, together with the deficits in empathic processes, would affect decision-making processes, given the role they play as somatic markers of behaviour (Verdejo-Garcia & Bechara, 2009).

Lastly, children and teenagers (of both genders) exposed to high levels of cocaine have less grey matter and more cerebrospinal fluid in the prefrontal and frontal superior cortex (especially dorsal), the superior frontal gyrus, the precuneus and the parietal, limbic and paralimbic cortex than those not exposed to cocaine. Such structural deficits might explain their poor behaviour regulation and their sub-par executive functioning (Grewen et al., 2014; Rando, Chaplin, Potenza, Mayes. & Sinha, 2013). Furthermore, children aged 3-6 that were prenatally exposed to cocaine are less empathic to the crying of other babies and the discomfort of their mothers and show poorer capacity for cooperation, and this could be explained by a greater activation of the frontal right hemisphere (Moilanen et al., 2010). These results would be consistent with the deficits found in adult cocaine users that are prone to being violent.

Conclusions

The deficits described so far provide us with a deeper understanding of the perpetration of violence by cocaine users. The majority of studies have focused on deficits in empathy and executive functions, as these are important for social adaptation. Deficiencies in the decoding of

emotions (which could be explained by poor sustained attention capacity) may be subjacent to an inability or low ability to comprehend others' feelings and thoughts and for decision-making, as these people would not properly appreciate the consequences of their actions. Furthermore, it should be noted that the risk of violence is higher when one's abilities to verbalize emotions and think abstractly are severely altered. Thus, cocaine users may have difficulties for thinking logically, increasing the risk of their using violence, as they are unable to appropriately channel or express these internal states. Greater activation in different cortical regions of the right hemisphere regarding empathic processes might be considered as an indicator of greater right lateralization of emotional processing. However, the scientific literature to date claims that cortical processing of positive emotions is lateralized in the left hemisphere, whilst that of negative emotions is lateralized in the right. In consequence, this abnormal activation pattern characteristic of aggressive cocaine users would underlie the bias towards hostile processing of emotional information. Poor emotion regulation, whose neural correlate is a smaller amygdala than that of non-users, and poor inhibitory control and decision-making, defined by hypoactivation of different regions of the prefrontal cortex, could explain such excessively violent responses. Such deficits appear to be more evident in men, their effects at a neurological level having poorer prognosis than in the case of women. Despite that the concurrent use of cocaine with other substances, such as alcohol, would increase the risk of violent reactions, the related neuropsychological effects do not seem to be as marked as in other scenarios. An important limitation of the studies conducted to date is the variability of the populations used, since most of the studies have a very small sample size, and have considered different periods of abstinence, different socio-economic levels, different types of drug-use history. The present article, together with another addressing the neuropsychological profile of men convicted for intimate partner violence (Romero-Martínez & Moya-Albiol, 2013), highlights the importance of a certain homogeneity in the deficits presented by violent drug users. Thus, it would be of great utility to develop a single neuropsychological battery for the assessment of the propensity for violence in the absence or presence of drug abuse, adjusting it to a series of tests tailored to this population subgroup. This, together with the consideration of diverse psychobiological variables shown to be relevant in violent people (Romero-Martínez et al., 2013a; 2013b; Romero-Martínez, González-Bono, Lila, & Moya-Albiol, 2013; Romero-Martínez, Lila, Conchell, González-Bono, & Moya-Albiol, 2014; Romero-Martínez, Lila, Williams, González-Bono, & Moya-Albiol, 2013), would permit the development of intervention strategies that focus on these specific cognitive domains.

Acknowledgements

This study was made possible by funding from the Spanish Ministry of Health, Social Services and Equality (2012/001), and the Council for Education, Culture and Sport of the *Generalitat Valenciana* (PROMETEO/2011/048) and beca VALi+d (ACIF/2011/075).

The authors wish to thank Miguel Pallás Miralles for improving the use of English in the manuscript.

References

Allen, J.W., Bennett, D.S., Carmody, D.P., Wang, Y., & Lewis, M. (2014). Adolescent risk-taking as a function of prenatal cocaine exposure and biological sex. *Neurotoxicology and Teratology*, *41*, 65-70. doi: 10.1016/j.ntt.2013.12.003.

Alcázar-Córcoles, M.A., & Bezos-Saldaña, L. (2011). Cocaetileno y Violencia: Influencia de la Interacción Cocaína-Alcohol en la Conducta Antisocial. *Anuario de Psicología Jurídica*, *21*, 49-55. doi: 10.5093/jr2011v21a5

Babcock, J.C., Green, C.E., & Webb, S.A. (2008). Decoding deficits of different types of batterers during presentation of facial affect slides. *Journal of Family Violence*, *23*, 295-302. doi: 10.1007/s10896-008-9151-1

Bandstra, E.S., Morrow, C.E., Anthony, J.C., Accornero, V.H., & Fried, P.A. (2001). Longitudinal investigation of task persistence and sustained attention in children with prenatal cocaine exposure. *Neurotoxicology and Teratology*, *23*, 545-559. doi:10.1016/S0892-0362(01)00181-7

Bell, R.P., Foxe, J.J., Ross, L.A., & Garavan, H. (2014). Intact inhibitory control processes in abstinent drug abusers (I): a functional neuroimaging study in former cocaine addicts. *Neuropharmacology*, *82*, 143-150. doi: 10.1016/j.neuropharm.2013.02.018.

Bendersky, M., Bennett, D.S., & Lewis, M. (2006). Aggression at age 5 as a function of prenatal exposure to cocaine, gender, and environmental risk. *Journal of Pediatric Psychology*, *31*, 71–84. doi: 10.1093/jpepsy/jsj025

Bendersky, M., & Lewis, M. (1998). Prenatal cocaine exposure and impulse control at two years. *Annals of the New York Academy of Sciences, 846*, 365–367.

Bendersky, M., & Lewis, M. (2001). Effects of prenatal cocaine exposure on arousal recovery at 30 months. Poster presented at the annual meeting of the Eastern. Washington, DC: Psychological Association.

Bennett, D.S., Marini, V.A., Berzenski, S.R., Carmody, D.P., & Lewis, M. (2013). Externalizing problems in late childhood as a function of prenatal cocaine exposure and environmental risk. *Journal of Pediatric Psychology*, *38*, 296-308. doi: 10.1093/jpepsy/jss117.

Betancourt, L.M., Yang W, Brodsky, N.L., Gallagher, P.R., Malmud, E.K., Giannetta, J.M., … Hurt, H. (2011).

Adolescents with and without gestational cocaine exposure: longitudinal analysis of inhibitory control, memory and receptive language. *Neurotoxicology and Teratology, 33*, 36–46. doi: 10.1016/j.ntt.2010.08.004.

Blair, R.J. (2003). Facial expressions, their communicatory functions and neurocognitive substrates. *Philosophical Transactions of the Royal Society B: Biological, 358*, 561–572.

Bridgett, D.J., & Mayes, L.C. (2011). Development of inhibitory control among prenatally cocaine exposed and non-cocaine exposed youths from late childhood to early adolescence: The effects of gender and risk and subsequent aggressive behavior. *Neurotoxicology and Teratology, 33*, 47-60. doi: 10.1016/j.ntt.2010.08.002.

Brody, S.L., Slovis, C.M., & Wrenn, K.D. (1990). Cocaine-related medical problems: consecutive series of 233 patients. *American Journal of Medicine, 88*, 325-331. doi: http://dx.doi.org/10.1016/0002-9343(90)90484-U

Calder, A.J., Keane, J., Lawrence, A.D., & Manes, F. (2004). Impaired recognition of anger following damage to the ventral striatum. *Brain, 127*, 1958–1969. doi: 10.1093/brain/awh214.

Calder, A.J., & Young, A.W. (2005). Understanding the recognition of facial identity and facial expression. *Nature Review Neuroscience, 6*, 641-651. doi:10.1038/nrn1724.

Camchong, J., MacDonald, A.W., 3rd, Nelson, B., Bell, C., Mueller, B.A., Specker, S., & Lim, K.O. (2011). Frontal hyperconnectivity related to discounting and reversal learning in cocaine subjects. *Biological Psychiatry*, 69, 1117-1123. doi: 10.1016/j.biopsych.2011.01.008.

Campbell, J.O., Bliven, T.D., Silveri, M.M., Snyder, K.J., & Spear, L.P. (2000). Effects of prenatal cocaine on behavioral adaptation to chronic stress in adult rats. *Neurotoxicology and Teratology, 22*, 845–850. doi:10.1016/S0892-0362(00)00104-5.

Carmody, D.P., Bennett, D.S., & Lewis, M. (2011). The effects of prenatal cocaine exposure and gender on inhibitory control and attention. *Neurotoxicology and Teratology, 33*, 61-68. doi: 10.1016/j.ntt.2010.07.004.

Chang, L., Ernst, T., Strickland, T., Mehringer, C., & Mark, M. (1999). Gender effects on persistent cerebral metabolite changes in the frontal lobes of abstinent cocaine users, *American Journal of Psychiatry, 156*, 716-722.

Chermack, S.T., & Blow, F.C. (2002). Violence among individuals in substance abuse treatment: the role of alcohol and cocaine consumption. *Drug and Alcohol Dependence, 66*, 29–37. doi: http://dx.doi.org/10.1016/S0376-8716(01)00180-6

Chermack, S.T., Grogan-Kaylor, A., Perron, B.E., Murray, R.L., De Chavez, P., & Walton, M.A. (2010). Violence among men and women in substance use disorder treatment: a multi-level event-based analysis. *Drug and Alcohol Dependence, 112*, 194-200. doi: 10.1016/j.drugalcdep.2010.06.005.

Chermack, S.T., Murray, R.L., Walton, M.A., Booth, B.A., Wryobeck, J., & Blow, F.C. (2008). Partner aggression among men and women in substance use disorder treatment: correlates of psychological and physical aggression and injury. *Drug and Alcohol Dependence, 98*, 35–44. doi: 10.1016/j.drugalcdep.2008.04.010.

Chérrez-Bermejo, C., & Alás-Brun, R. (2014). A descriptive study of substance abuse and mental health disorders in intimate partner violence abusers in prison. *Revista Española de Sanidad Penitenciaria, 16*, 29-37. doi: 10.4321/S1575-06202014000200002.

Collins, J.J., & Messerchmidt, M.A. (1993). Epidemiology of alcohol-related violence. *Alcohol Health & Research World, 17*, 93–100.

Colzato, L.S., Huizinga, M., & Hommel, B. (2009). Recreational cocaine polydrug use impairs cognitive flexibility but not working memory. *Psychopharmacology, 207*, 225–234. doi: 10.1007/s00213-009-1650-0

Cooper, J., Bloom, F., & Roth, R. (1991). The Biochemical Basis of Neuropharmacology, 6th ed. New York: Oxford University Press.

Cunningham, K.A., & Anastasio, N.C. (2014). Serotonin at the nexus of impulsivity and cue reactivity in cocaine addiction. *Neuropharmacology, 76*, 460-478. doi: 10.1016/j.neuropharm.2013.06.030.

Davis, W.M. (1996). Psychopharmacologic violence associated with cocaine abuse: kindling of a limbic dyscontrol syndrome? *Progress in Neuropsychopharmacology & Biological Psychiatry, 20*, 1273–1300. doi:10.1016/S0278-5846(96)00126-1.

Delaney-Black, V., Covington, C., Nordstrom, B., Ager, J., Janisse, J., Hannigan, J.H., … Sokol, R.J. (2004). Prenatal cocaine: quantity of exposure and gender moderation. *Journal of Developmental & Behavioral Pediatrics, 25*, 254-263.

Delaney-Black, V., Covington, C., Templin, T., Ager, J., Nordstrom-Klee, B., Martier, S., … Sokol, R. J. (2000). Teacher assessed behavior of children prenatally exposed to cocaine. *Pediatrics, 106*, 782–791.

Farrington, D. (1994). Early developmental prevention of juvenile delinquency. *Criminal Behavior and Mental Health, 4*, 209–227.

Fernández-Serrano, M.J., Lozano, O., Pérez-García, M., & Verdejo-García, A. (2010). Impact of severity of drug use on discrete emotions recognition in polysubstance abusers. *Drug and Alcohol Dependence, 109*, 57-64. doi: 10.1016/j.drugalcdep.2009.12.007.

Foisy, M.L., Kornreich, C., Fobe, A., D'Hondt, L., Pelc, I., Hanak, C., … Philippot, P. (2007). Impaired emotional facial expression recognition in alcohol dependence: do these deficits persist with midterm abstinence? *Al-*

coholism: Clinical and Experimental Research, 31, 404–410. doi:10.1111/j.1530-0277.2006.00321.x

Fox, H.C., Axelrod, S.R., Paliwal, P., Sleeper, J., & Sinha, R. (2007). Difficulties in emotion regulation and impulse control during cocaine abstinence. *Drug and Alcohol Dependence, 89*, 298-301. doi:10.1016/j.addbeh.2007.10.002

Fox, N.A., Calkins, S.D., Schmidt, L., Rubin, K.H., & Coplan, R.J. (1996). The role of frontal activation in the regulation and dysregulation of social behavior during the preschool years. *Development and Psychopathology, 8*, 89-102.

Fox, H.C., Hong, K.I., Siedlarz, K., & Sinha, R. (2008). Enhanced sensitivity to stress and drug/alcohol craving in abstinent cocaine-dependent individuals compared to social drinkers. *Neuropsychopharmacology, 33*, 796-805. doi:10.1038/sj.npp.1301470.

Fox, H.C., Jackson, E.D., & Sinha, R. (2009). Elevated cortisol and learning and memory deficits in cocaine dependent individuals: relationship to relapse outcomes. *Psychoneuroendocrinology, 34*, 1198-1207. doi: 10.1016/j.psyneuen.2009.03.007.

Goldstein, R.Z., Alia-Klein, N., Leskovjan, A.C., Fowler, J.S., Wang, G.J., Gur, R.C., … Volkow, N.D. (2005). Anger and depression in cocaine addiction: association with the orbitofrontal cortex. *Psychiatry Research, 138*, 13-22. DOI: http://dx.doi.org/10.1016/j.pscychresns.2004.10.002.

Gómez, J., Valderrama-Zurián, J.C., Tortajada, S., Girva, T., Clari, E., & Saiz, A. (2008). Cocaína, violencia y género desde el punto de vista de los profesionales. *Revista Española de Drogodependencias, 33*, 180-194.

Grewen, K., Burchinal, M., Vachet, C., Gouttard, S., Gilmore, J.H., Lin, W., …Gerig, G. (2014). Prenatal cocaine effects on brain structure in early infancy. *Neuroimage, 101*, 114-123. doi: 10.1016/j.neuroimage.2014.06.070.

Heffelfinger, A., Craft, S., & Shyken, J. (1997). Visual attention in children prenatally exposed to cocaine. *Journal of the International Neuropsychological Society, 3*, 237-245.

Heffelfinger, A., Craft, S. White, D., & Shyken, J. (2002). Visual attention in preschool children prenatally exposed to cocaine: Implications for behavioral regulation. *Journal of the International Neuropsychological Society, 8*, 12-21.

Heinz, A.J., Beck, A., Meyer-Lindenberg, A., Sterzer, P., & Heinz, A. (2011). Cognitive and neurobiological mechanisms of alcohol-related aggression. *Nature Review Neuroscience, 12*, 400-413. doi: 10.1038/nrn3042.

Holler, K., & Kavanaugh, B. (2013). Physical aggression, diagnostic presentation, and executive functioning in inpatient adolescents diagnosed with mood disorders. *Child Psychiatry and Human Development, 44*(4), 573-581. doi: 10.1007/s10578-012-0351-9.

Jones, N.A., Field, T., Davalos, M., & Hart, S. (2004). Greater right frontal EEG asymmetry and nonemphathic behavior are observed in children prenatally exposed to cocaine. *International Journal of Neuroscience, 114*(4), 459-480. doi:10.1080/00207450490422786.

Kemmis, L., Hall, J.K., Kingston, R., & Morgan, M.J. (2007). Impaired fear recognition in regular recreational cocaine users. *Psychopharmacology, 194*, 151–159.

Keller, D.S., Carroll, K.M., Nick, C., & Rounsaville, B.J. (1995). Alexithymia in Cocaine Abusers. Response to Psychotherapy and Pharmacotherapy. *American Journal of Addictions, 4,* 234-244. doi: http://dx.doi.org/10.3109/10550499509038108.

Krämer, U.M., Kopyciok, R.P., Richter, S., Rodriguez-Fornells, A., & Münte, T.F. (2011). The role of executive functions in the control of aggressive behavior. *Frontiers in Psychology, 2*,152. doi: 10.3389/fpsyg.2011.00152.

Kraanen, F.L., Vedel, E., Scholing, A., & Emmelkamp, P.M. (2014). Prediction of intimate partner violence by type of substance use disorder. *Journal of Substance Abuse Treatment, 46*(4), 532-539. doi: 10.1016/j.jsat.2013.10.010.

Lawton-Craddock, A., Nixon, S.J., & Tivis, R. (2003). Cognitive efficiency in stimulant abusers with and without alcohol dependence. *Alcoholism Clinical Experimental Research, 27*(3), 457-464. doi: 10.1097/01.ALC.0000056620.98842.E6

Lewis, C.F. (2011). Substance use and violent behavior in women with antisocial personality disorder. *Behavioral Sciences & Law, 29*(5), 667-676. doi: 10.1002/bsl.1006.

Li, C.S., & Sinha, R. (2006). Alexithymia and stress-induced brain activation in cocaine-dependent men and women. *Journal of Psychiatry & Neuroscience, 31*(2), 115-121.

Licata, A., Taylor, S., Berman, M., & Cranston, J. (1993). Effects of cocaine on human aggression. *Pharmacology Biochemistry and Behavior, 45*, 549–552. doi:10.1016/0091-3057(93)90504-M.

Lizasoain, I., Moro, M.A., & Lorenzo, P. (2001). Cocaína: aspectos farmacológicos. *Adicciones, 13*, 37-45.

Madoz-Gúrpide, A., Blasco-Fontecilla, H., Baca-García, E., & Ochoa-Mangado, E. (2011). Executive dysfunction in chronic cocaine users: an exploratory study. *Drug and Alcohol Dependence, 117*(1), 55-58. doi: 10.1016/j.drugalcdep.2010.11.030.

Makris, N., Gasic, G.P., Seidman, L.J., Goldstein, J.M., Gastfriend, D.R., Elman, I., … Breiter, H.C. (2004). Decreased absolute amygdala volume in cocaine addicts. *Neuron, 44*, 729–740.

Mattson, R.E., O'Farrell, T.J., Lofgreen, A.M., Cunningham, K., & Murphy, C.M. (2012). The role of illicit substance use in a conceptual model of intimate partner violence in men undergoing treatment for alcoholism. *Psychology of Addictive Behaviors, 26*(2), 255-264. doi: 10.1037/a0025030.

Matuskey, D., Gallezot, J.D., Pittman, B., Williams, W., Wanyiri, J., Gaiser, E., … Ding, Y.S. (2014). Dopamine D_3 receptor alterations in cocaine-dependent humans imaged with [^{11}C](+)PHNO. *Drug and Alcohol Dependence, 139*, 100-105.

Mayes, L., Bornstein, M., Chawarska, K., Haynes, M., & Granger, R. (1996). Impaired regulation of arousal in 3 month-old infants exposed prenatally to cocaine and other drugs. *Development and Psychopathology, 8*, 29-42. doi: 10.1017/S0954579400006957

Mayes, L.C., Grillon, C., Granger, R., & Schottenfeld, R. (1998). Regulation of arousal and attention in preschool children exposed to cocaine prenatally. *Annals of the New York Academy of Sciences, 846*, 126-143.

McCabe, D.P., Roediger, H.L., McDaniel, M.A., Balota, D.A., & Hambrick, D.Z. (2010). The relationship between working memory capacity and executive functioning: evidence for a common executive attention construct. *Neuropsychology, 24*(2), 222-243. doi: 10.1037/a0017619.

McCance-Katz, E. F., Kosten, T. R., & Jatlow, P. (1998). Concurrent use of cocaine and alcohol is more potent and potentially more toxic than use of either alone – A multiple-dose study. *Biological Psychiatry, 44*, 250-259. doi: http://dx.doi.org/10.1016/S0006-3223(97)00426-5.

Medina, K.L., Schafer, J., Shear, P.K., & Armstrong, T.G. (2004). Memory ability is associated with disagreement about the most recent conflict in polysubstance abusing couples. *Journal of Family Violence, 19*, 381-390. doi: 10.1007/s10896-004-0683-8.

Min, M.O., Minnes, S., Lang, A., Weishampel, P., Short, E.J., Yoon, S., & Singer, L.T. (2014). Externalizing behavior and substance use related problems at 15 years in prenatally cocaine exposed adolescents. *Journal of Adolescence, 37*(3), 269-279. doi: 10.1016/j.adolescence.2014.01.004.

Miura, H. (2009). Differences in frontal lobe function between violent and nonviolent conduct disorder in male adolescents. *Psychiatry and Clinical Neurosciences, 63*(2), 161-166. doi: 10.1111/j.1440-1819.2009.01935.x.

Moeller, S.J., Konova, A.B., Parvaz, M.A., Tomasi, D., Lane, R.D., Fort, C. … Goldstein, R.Z. (2014). Functional, structural, and emotional correlates of impaired insight in cocaine addiction. *JAMA Psychiatry, 71*(1), 61-70. doi: 10.1001/jamapsychiatry.2013.2833.

Moilanen, K.L., Shaw, D.S., & Fitzpatrick, A. (2010). Self-regulation in early adolescence: Relations with maternal regulatory supportive parenting, antagonism, and mother-son relationship quality. *Journal of Youth and Adolescence, 39*, 1357-1367. doi: 10.1007/s10964-009-9485-x.

Moore, T. M., Stuart, G. L., Meehan, J. C., Rhatigan, D. L., Hellmuth, J. C., & Keen, S. M. (2008). Drug abuse and aggression between intimate partners: A meta-analytic review. *Clinical Psychology Review, 28*, 248–275. doi:10.1016/j.cpr.2007.05.003

Morie, K.P., De Sanctis, P., Garavan, H., & Foxe, J.J. (2014). Executive dysfunction and reward dysregulation: a high-density electrical mapping study in cocaine abusers. *Neuropharmacology, 85*, 397-407. doi: 10.1016/j.neuropharm.2014.05.016.

Moya-Albiol, L., Herrero, N., & Bernal, M.C. (2010). Bases neurales de la empatía. *Revista Neurología, 50*, 89-100.

Murphy, F.C, Nimmo-Smith, I., & Lawrence, A.D. (2003). Functional neuroanatomy of emotions: A meta-analysis. *Cognitive, Affective, & Behavioral Neuroscience, 3*, 207–233.

Needlman, R., Zuckerman, B., Anderson, G.M., Mirochnick, M., & Cohen, D.J. (1993). Cerebrospinal fluid monoamine precursors and metabolites in human neonates following in utero cocaine exposure: a preliminary study. *Pediatrics, 92*(1), 55-60.

Patkar, A.A., Gottheil, E., Berrettini, W.H., Hill, K.P., Thornton, C.C., & Weinstein, S.P. (2003) Relationship between platelet serotonin uptake sites and measures of impulsivity, aggression, and craving among African-American cocaine abusers. *American Journal on Addictions, 12*, 432–437.

Patkar, A.A., Mannelli, P., Peindl, K., Hill, K.P., Gopalakrishnan, R., & Berrettini, W.H. (2006). Relationship of disinhibition and aggression to blunted prolactin response to meta-chlorophenylpiperazine in cocaine-dependent patients. *Psychopharmacology, 185*(1), 123-132.

Pawliczek, C.M., Derntl, B., Kellermann, T., Kohn, N., Gur, R.C., & Habel, U. (2013). Inhibitory control and trait aggression: neural and behavioral insights using the emotional stop signal task. *Neuroimage, 79*, 264-274. doi: 10.1016/j.neuroimage.2013.04.104.

Pennings, E.J., Leccese, A.P., & Wolff, F.A. (2002). Effects of concurrent use of alcohol and cocaine. *Addiction, 97*, 773-783. doi: 10.1046/j.1360-0443.2002.00158.x

Pike, E., Stoops, W.W., Fillmore, M.T, & Rush, C.R. (2013). Drug-related stimuli impair inhibitory control in cocaine abusers. *Drug and Alcohol Dependence, 133*(2), 768-771. doi: 10.1016/j.drugalcdep.2013.08.004.

Preller, K.H., Hulka, L.M., Vonmoos, M., Jenni, D., Baumgartner, M.R., Seifritz, E., … Quednow, B.B. (2014). Impaired emotional empathy and related social network deficits in cocaine users. *Addiction Biology, 19*(3), 452-66. doi: 10.1111/adb.12070.

Raaijmakers, M.A., Smidts, D.P., Sergeant, J.A., Maassen, G.H., Posthumus, J.A., van Engeland, H., … Matthys, W. (2008). Executive functions in preschool children with aggressive behavior: impairments in inhibitory control. *Journal of Abnormal Child Psychology, 36*(7), 1097-107. doi: 10.1007/s10802-008-9235-7.

Rao, H., Wang, J., Giannetta, J., Korczykowski, M., Shera, D., Avants, B.B., … Hurt, H. (2007). Altered resting cerebral blood flow in adolescents with in utero cocaine exposure revealed by perfusion functional MRI. *Pediatrics, 120*(5), e1245-1254. doi: 10.1542/peds.2006-2596.

Rando, K., Chaplin, T.M., Potenza, M.N., Mayes, L., & Sinha, R. (2013). Prenatal cocaine exposure and gray matter volume in adolescent boys and girls: relationship to substance use initiation. *Biological Psychiatry, 74*(7), 482-489. doi: 10.1016/j.biopsych.2013.04.030.

Romero-Martínez, A., González-Bono, E., Lila, M., & Moya-Albiol, L. (2013). Testosterone/cortisol ratio in response to acute stress: a possible marker of risk for marital violence. *Social Neuroscience, 8*(3), 240-247. doi: 10.1080/17470919.2013.772072.

Romero-Martínez, A., Lila, M., Catalá-Miñana, A., Williams, R.K., & Moya-Albiol, L. (2013a). The contribution of childhood parental rejection and early androgen exposure to impairments in socio-cognitive skills in intimate partner violence perpetrators with high alcohol consumption. *International Journal of Environmental Research in Public Health, 10*(8), 3753-3770. doi:10.3390/ijerph10083753.

Romero-Martínez, A., Lila, M., Conchell, R., González-Bono, E., & Moya-Albiol, L. (2014). Immunoglobulin A response to acute stress in intimate partner violence perpetrators: The role of anger expression-out and testosterone. *Biological Psychology, 96*, 66-71. doi: 10.1016/j.biopsycho.2013.11.009.

Romero-Martínez, A., Lila, M., Sariñana-González, P., González-Bono, E., & Moya-Albiol, L. (2013b). High testosterone levels and sensitivity to acute stress in perpetrators of domestic violence with low cognitive flexibility and impairments in their emotional decoding process: a preliminary study. *Aggressive Behavior, 39*(5), 355-369. doi: 10.1002/ab.21490.

Romero-Martínez, A., Lila, M., Williams, R.K., González-Bono, E., & Moya-Albiol, L. (2013). Skin conductance rises in preparation and recovery to psychosocial stress and its relationship with impulsivity and testosterone in intimate partner violence perpetrators. *International Journal of Psychophysiology, 90*(3), 329-333. doi: 10.1016/j.ijpsycho.2013.10.003.

Romero-Martínez, A., & Moya-Albiol, L. (2013). Neuropsychology of perpetrators of domestic violence: the role of traumatic brain injury and alcohol abuse and/or dependence. *Revista Neurología, 57*(11), 515-522.

Rosse, R.B., Miller, M.W., & Deutsch, S.I. (1993). Violent antisocial behavior and Wisconsin Card Sorting Test performance in cocaine addicts. *American Journal Psychiatry, 150*(1), 170-171.

Roselli, M., & Ardila, A. (1996). Cognitive effects of cocaine and polydrug abuse. *Journal of Clinical and Experimental Neuropsychology, 18*, 122–135. doi:10.1080/01688639608408268

Schafer, J., & Fals-Stewart, W. (1997). Spousal violence and cognitive functioning among men recovering from multiple substance abuse. *Addictive Behaviors, 22*, 127-130. doi:10.1016/S0306-4603(96)00012-3.

Schipper, M., & Petermann, F. (2013). Relating empathy and emotion regulation: do deficits in empathy trigger emotion dysregulation? *Social Neuroscience, 8*(1), 101-107. doi: 10.1080/17470919.2012.761650.

Soler-González, C., Balcells-Oliveró, M., & Gual-Solé, A. (2014). Alcohol related brain damage. State of the art and a call for action. *Adicciones, 26*(3), 199-207.

Spronk, D.B., van Wel, J.H., Ramaekers, J.G., & Verkes, R.J. (2013). Characterizing the cognitive effects of cocaine: a comprehensive review. *Neuroscience & Biobehavioral Reviews, 37*(8), 1838-1859. doi: 10.1016/j.neubiorev.2013.07.003.

Tardiff, K., Marzuk, P.M., Leon, A.C., Portera, L., & Weiner, C. (1997). Violence by patients admitted to a private psychiatric hospital. *American Journal of Psychiatry, 154*(1), 88-93.

Tirapu-Ustárroz, J., Ríos-Lago, M., & Maestú-Unturbe, F. (2011). Manual de Neuropsicología. Barcelona: Viguera.

van der Plas, E.A., Crone, E.A., van den Wildenberg, W.P., Tranel, D., & Bechara, A., (2009). Executive control deficits in substance-dependent individuals: a comparison of alcohol, cocaine, and methamphetamine and of men and women. *Journal of Clinical and Experimental Neuropsychology 31*, 706–719. doi: 10.1080/13803390802484797.

Verdejo-García, A., & Bechara, A. (2009). A somatic marker theory of addiction. *Neuropharmacology, 56* (1), 48–62. doi: 10.1016/j.neuropharm.2008.07.035.

Verdejo-García, A., Rivas-Pérez, C., Vilar-López, R., & Pérez-García, M. (2007). Strategic self-regulation, decision-making and emotion processing in poly-substance abusers in their first year of abstinence. *Drug and Alcohol Dependence, 86*, 139–146. doi: http://dx.doi.org/10.1016/j.drugalcdep.2006.05.024

Volkow, N.D., Wang, G.J., Fowler, J.S., Logan, J., Gatley, S.J., Hitzemann, R., … Pappas, N. (1997). Decreased striatal dopaminergic responsiveness in detoxified cocaine-dependent subjects. *Nature, 386*, 830–833. doi:10.1038/386830a0.

Yechiam, E., Kanz J, Bechara, A., Stout, J.C., Busemeyer, J.R., Altmaier, E.M., & Paulsen, J. (2008). Neurocognitive deficits related to poor decision-making in people behind bars. *Psychonomic Bulletin and Review, 15*, 44-51.

Woicik, P.A., Moeller, S.J., Alia-Klein, N., Maloney, T., Lukasik, T.M., Yeliosof, O., … Goldstein, R.Z. (2009). The neuropsychology of cocaine addiction: recent cocaine use masks impairment. *Neuropsychopharmacology, 34*(5), 1112-1122. doi: 10.1038/npp.2008.60.

Woicik, P.A., Urban, C., Alia-Klein, N., Henry, A., Maloney, T., Telang, F., … Goldstein, R.Z. (2011). A pattern of perseveration in cocaine addiction may reveal neurocognitive processes implicit in the Wisconsin Card Sorting Test. *Neuropsychologia, 49*, 1660–1669. doi: 10.1016/j.neuropsychologia.2011.02.037.

Core research areas on addiction: the need for a broader view

Núcleos y ámbitos de investigación sobre adicciones: necesidad de una visión más amplia

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Dear Editor,

It is becoming increasingly important to explore in more depth the diverse aspects related to scientific research in the field of health. Until quite recently, the focus was mainly on what was being studied, who was studying it, the impact factor of the journal, the researcher's institution, and his or her h-index. This is useful for obtaining knowledge about research activity in a given field, and can contribute to better decision-making in relation to the assignment of resources or university places. In particular, we have made a series of contributions in this field that have thrown light on the research situation in our respective areas of specialization (Burbano et al., 2013; Miró & Burillo-Putze, 2012; Miró, Montori, Ramos, Galicia, & Nogué, 2009).

Today, it is also of great interest to have access to more information about the links between researchers. Hence, our interest was drawn to a recent publication in ADICCIONES (González-Alcaide, Calafat, & Becoña, 2014), which for the first time identifies the core areas and networks of Spanish research on substance abuse and addictions over the last 14 years. But the snapshot these authors provide is, in our opinion, quite biased, on being confined – as the authors themselves indeed acknowledge – to a search for documents published only in the *Substance Abuse* category of *Journal Citation Reports* (JCR) within the *Web of Science (WoS)*, that is, a total of 18 journals.

The world of addictions is highly cross-sectional, and many specialists are involved in the care of addiction-related patients. If we think, for example, about psychologists, psychiatrists, neurologists, emergency doctors, critical care specialists and toxicologists, to mention just 6 specialities clearly related to the care of those addicted to substances of abuse, one could have included the same number of JCR categories (*Psychology*, *Psychiatry*, *Neuroscience*, *Emergency medicine*, *Critical Care Medicine* and *Toxicology*), which altogether yield 599 journals, that is, 33 times more than those explored in the mentioned article. Therefore, we believe that the perspective emerging from their work is, despite its pioneering nature, somewhat incomplete. By way of example of the possible biases it contains, we might point out that while alcohol constitutes the target of 17 (57%) of the 30 core research areas identified, cocaine has a high presence in just 6 of the mentioned foci. Without wishing to deny the undoubted importance of alcohol addiction in the Spanish population, this methodological bias related to the group of journals selected reduces the true impact of cocaine addiction in our context, including all the visits to emergency

Received: October 2014; Accepted: January 2015;

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departments generated by acute adverse reactions to a drug or its adulterants, the associated hospitalizations, and the mortality directly derived from drug use – all the object as well, of clinical and epidemiological research, particularly by specialists in emergency care (Galicia et al., 2012; Galicia, Nogué, & Burillo-Putze, 2014; Galicia, Nogué, & Miró, 2012; López-Rincón et al., 2013). And for the same reason, nor do we find references to research related to the use of gamma- hydroxybutyrate (GHB, liquid ecstasy), amphetamine derivatives or other drugs with emerging use in Spain (Caudevilla-Gálligo et al., 2013; Galicia, Nogué, & Miró, 2011).

What we propose is that an alternative search approach, based on key words rather than on journals, might perhaps give us a better picture of the true situation. Thus, following the methodology presented by the authors, we carried out a search in WoS, confining it to the period 2000-2013, using as key words "cocaine or ecstasy or GHB or heroine or methadone or ethanol or alcohol" (we limited the search to these few, but agreement could be reached on which to include), and indicating ourselves as authors. The results was 32 documents signed by one of the two (14 if one considers those documents signed by both at the same time). We do not know whether, following the methodology described by the authors to whom this letter refers, the activity would achieve the proposed definition of research cluster or core area, though we do think that this methodological alternative should be explored.

In any case, we acknowledge that the step forward, and in the right direction, made by the cited authors is a fundamental one, and constitutes another link in the chain that can provide a better understanding of the broad field of Spanish research on addictions. But perhaps what is needed is an extra effort so as not to exclude any relevant actor.

Conflicts of interests

None.

References

Burbano, P., Martín-Sánchez, F. J., Burillo-Putze, G., Fernández-Pérez, C., Del Prado-González, N., & Miró, O. (2013). Producción y repercusión científica de un grupo de urgenciólogos españoles seleccionados por su trayectoria investigadora. *Emergencias, 25*, 245-254.

Caudevilla-Gálligo, F., Quintana-Mathé, P., Fornís-Espinosa, I., & Ventura-Vilamala, M. (2013). Metanfetamina vendida como MDMA (3,4- metilendioximetanfetamina, éxtasis). *Emergencias, 25*, 154-155.

Galicia, M., Nogué, S., & Burillo-Putze, G. (2014). Diez años de asistencias urgentes a consumidores de cocaína en España. *Medicina Clínica, 143*, 322-326. doi: 10.1016/j.medcli.2013.11.023.

Galicia, M., Nogué, S., & Miró, O. (2011). Liquid ecstasy intoxication: clinical features of 505 consecutive emergency department patients. *Emergency Medicine Journal, 28*, 462-466. doi: 10.1136/emj.2008.068403.

Galicia, M., Nogué, S., & Miró, O. (2012). The role of the emergency department in detecting high-risk cocaine users. *European Journal of Emergency Medicine, 19*, 205-206. doi: 10.1097/MEJ.0b013e32834dd305.

Galicia, M., Nogué, S., Casañas, X., Iglesias, M. L., Puiguriguer, J., Supervía, A.,... Miró, O. (2012). Multicenter assessment of the revisit risk for a further drug-related problem in the emergency department in cocaine users (MARRIED-cocaine study). *Clinical Toxicology, 50*, 176-182. doi: 10.3109/15563650.2012.658917.

González-Alcaide, G., Calafat, A., & Becoña, E. (2014). Nucleos y ámbitos de investigación sobre adicciones en España a través del análisis de los enlaces bibliográficos en la Web of Science (2000-2013). *Adicciones, 26*, 168-183.

López-Rincón, R. M., Martínez, F., Parreño, D., Plaza-Lloret, M., Aladrén, M., & Pardo, M. G. (2013). Obstrucción intestinal por bolas de cocaína líquida. *Emergencias, 25*, 155-156.

Miró, O., & Burillo-Putze, G. (2012). Research in emergency medicine in Europe. *European Journal of Emergency Medicine, 19*, 63-68. doi: 10.1097/MEJ.0b013e32834749a0.

Miró, O., Montori, E., Ramos, X., Galicia, M., & Nogué, S. (2009). Trends in research activity in toxicology and by toxicologists in seven European countries. *Toxicology Letters, 189*, 1-4. doi: 10.1016/j.toxlet.2009.04.029.

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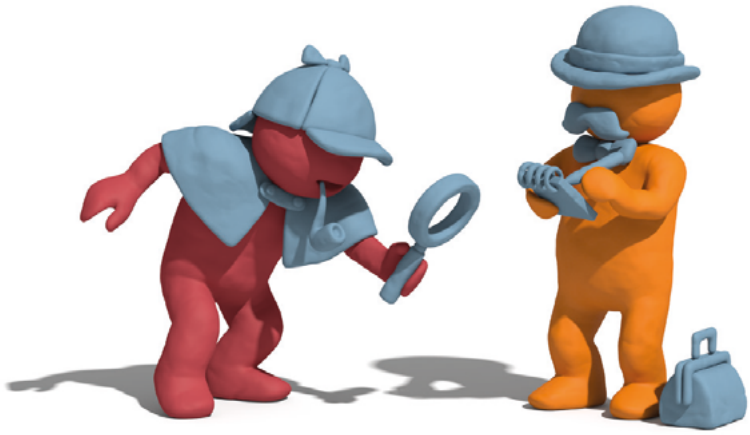

EFICACIA PARA SENTIRSE BIEN

FARMACOCINÉTICA[1, 2]

EFICACIA[1]

SIN SUPLEMENTACIÓN ORAL[3]

MONOTERAPIA[1, 4, 5]

TOLERABILIDAD CONTRASTADA[3, 6-9] *

SIN METABOLISMO HEPÁTICO[3]

CLARIDAD DE PENSAMIENTO[10-13]

FLEXIBILIDAD DE PAUTA POSOLÓGICA[3]

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1. NOMBRE DEL MEDICAMENTO. XEPLION 50 mg suspensión inyectable de liberación prolongada. XEPLION 75 mg suspensión inyectable de liberación prolongada. XEPLION 100 mg suspensión inyectable de liberación prolongada. XEPLION 150 mg suspensión inyectable de liberación prolongada. **2. COMPOSICIÓN CUALITATIVA Y CUANTITATIVA.** XEPLION 50 mg. Cada jeringa precargada contiene 78 mg de palmitato de paliperidona equivalentes a 50 mg de paliperidona. XEPLION 75 mg. Cada jeringa precargada contiene 117 mg de palmitato de paliperidona equivalentes a 75 mg de paliperidona. XEPLION 100 mg. Cada jeringa precargada contiene 156 mg de palmitato de paliperidona equivalentes a 100 mg de paliperidona. XEPLION 150 mg. Cada jeringa precargada contiene 234 mg de palmitato de paliperidona equivalentes a 150 mg de paliperidona. Para consultar la lista completa de excipientes ver sección 6.1. **3. FORMA FARMACÉUTICA.** Suspensión inyectable de liberación prolongada. La suspensión es de color blanco a blanquecino. La suspensión tiene un pH neutro (aproximadamente 7,0). **4. DATOS CLÍNICOS. 4.1. Indicaciones terapéuticas.** XEPLION está indicado para el tratamiento de mantenimiento de la esquizofrenia en pacientes adultos estabilizados con paliperidona o risperidona. En determinados pacientes adultos con esquizofrenia y respuesta previa a paliperidona o risperidona oral, XEPLION puede ser utilizado sin necesidad de estabilización previa con tratamiento oral si los síntomas psicóticos son leves o moderados y es necesario un tratamiento con un inyectable de acción prolongada. **4.2. Posología y forma de administración.** Posología. Se recomienda iniciar XEPLION con una dosis de 150 mg en el día 1 de tratamiento y 100 mg una semana después (día 8), ambos administrados en el músculo deltoides para alcanzar concentraciones terapéuticas rápidamente (ver sección 5.2). La dosis de mantenimiento mensual recomendada es de 75 mg; algunos pacientes pueden beneficiarse de dosis inferiores o superiores dentro del rango recomendado de 25 a 150 mg en función de la tolerabilidad y/o eficacia individual del paciente. Los pacientes con sobrepeso u obesos pueden requerir dosis situadas en la parte superior del intervalo (ver sección 5.2). Después de la segunda dosis, las dosis de mantenimiento mensuales se pueden administrar tanto en el músculo deltoides como en el glúteo. El ajuste de la dosis de mantenimiento se puede hacer mensualmente. Al realizar ajustes de la dosis, se deben tener en cuenta las características de liberación prolongada de XEPLION (ver sección 5.2), dado que el pleno efecto de las dosis de mantenimiento puede no resultar evidente durante varios meses. *Cambio desde paliperidona oral o risperidona oral.* El tratamiento recibido previamente con paliperidona oral o risperidona oral puede ser interrumpido en el momento de iniciar el tratamiento con XEPLION. XEPLION debe iniciarse según se describe al principio de la sección 4.2 anterior. *Cambio desde Risperidona inyectable de acción prolongada.* Al realizar el cambio de tratamiento de los pacientes desde risperidona inyectable de acción prolongada, inicie el tratamiento con XEPLION en lugar de la siguiente inyección programada. A partir de entonces, XEPLION se debe continuar en intervalos mensuales. No es necesario seguir el régimen de dosificación inicial de una semana incluyendo las inyecciones intramusculares (día 1 y 8, respectivamente) según se describe en la sección 4.2 anterior. Los pacientes previamente estabilizados con diferentes dosis de risperidona inyectable de acción prolongada pueden alcanzar una exposición similar a paliperidona en estado estacionario durante el tratamiento de mantenimiento con dosis mensuales de XEPLION según se describe a continuación:

Dosis de risperidona inyectable de acción prolongada y XEPLION necesaria para alcanzar una exposición a paliperidona similar en estado estacionario

Dosis previa de risperidona inyectable de acción prolongada	Inyección de XEPLION
25 mg cada 2 semanas	50 mg mensualmente
37,5 mg cada 2 semanas	75 mg mensualmente
50 mg cada 2 semanas	100 mg mensualmente

La interrupción de los medicamentos antipsicóticos debe realizarse de acuerdo a una apropiada información de prescripción. En caso de interrupción de XEPLION, se deben considerar sus características de liberación prolongada. Tal y como se recomienda con otros medicamentos antipsicóticos, se ha de reevaluar periódicamente la necesidad de continuar con la administración de los medicamentos actuales para el tratamiento de los síntomas extrapiramidales (SEP). Dosis omitidas. *Medidas para evitar la omisión de dosis.* Se recomienda que la segunda dosis de iniciación de XEPLION se administre una semana después de la primera dosis. Para evitar la omisión de esta dosis, los pacientes pueden recibir la segunda dosis 4 días antes o después del momento de administración semanal (día 8). Del mismo modo, se recomienda administrar mensualmente la tercera inyección y las siguientes después del régimen de iniciación. Para evitar la omisión de la dosis mensual, los pacientes pueden recibir la inyección hasta 7 días antes o después del momento de administración mensual. Si se omite la fecha límite para la segunda inyección de XEPLION (día 8±4 días), el momento de reinicio recomendado depende del tiempo que haya transcurrido desde la primera inyección del paciente. *Omisión de la segunda dosis de iniciación (<4 semanas desde la primera inyección).* Si han transcurrido menos de 4 semanas desde la primera inyección, se le debe administrar al paciente la segunda inyección de 100 mg en el músculo deltoides tan pronto como sea posible. Se debe administrar una tercera inyección de XEPLION de 75 mg en el músculo deltoides o en el glúteo 5 semanas después de la primera inyección (independientemente del momento en el que se haya administrado la segunda inyección). A partir de entonces, se debe seguir el ciclo normal de inyecciones mensuales, ya sea en el músculo deltoides o en el glúteo, de 25 mg a 150 mg en función de la tolerabilidad y/o eficacia individual del paciente. *Omisión de la segunda dosis de iniciación (entre 4 y 7 semanas desde la primera inyección).* Si han transcurrido entre 4 y 7 semanas desde la primera inyección de XEPLION, reanude la administración con dos inyecciones de 100 mg de la siguiente manera: 1. una inyección en el deltoides tan pronto como sea posible, 2. otra inyección en el deltoides una semana más tarde, 3. reanudación del cido normal de inyecciones mensuales, ya sea en el músculo deltoides o en el glúteo, de 25 mg a 150 mg en función de la tolerabilidad y/o eficacia individual del paciente. *Omisión de la segunda dosis de iniciación (>7 semanas desde la primera inyección).* Si han transcurrido más de 7 semanas desde la primera inyección de XEPLION, inicie la administración según las pautas recomendadas para la iniciación de XEPLION recogidas anteriormente. *Omisión de la dosis de mantenimiento mensual (1 mes a 6 semanas).* Tras la iniciación, el cido de inyección recomendado de XEPLION es mensual. Si han transcurrido menos de 6 semanas desde la última inyección, entonces se debe administrar la dosis previamente estabilizada tan pronto como sea posible, seguida de inyecciones a intervalos mensuales. *Omisión de la dosis de mantenimiento mensual (>6 semanas a 6 meses).* Si han transcurrido más de 6 semanas desde la última inyección de XEPLION, la recomendación es la siguiente: *Para los pacientes estabilizados con dosis de 25 a 100 mg:* 1. una inyección en el deltoides tan pronto como sea posible, de la misma dosis en la que el paciente se estabilizó previamente. 2. otra inyección en el deltoides (misma dosis) una semana más tarde (día 8). 3. reanudación del ciclo normal de inyecciones mensuales, ya sea en el músculo deltoides o en el glúteo, de 25 mg a 150 mg en función de la tolerabilidad y/o eficacia individual del paciente. *Para los pacientes estabilizados con 150 mg:* 1. una inyección en el deltoides tan pronto como sea posible, de una dosis de 100 mg. 2. otra inyección en el deltoides una semana más tarde (día 8) de una dosis de 100 mg. 3. reanudación del ciclo normal de inyecciones mensuales, ya sea en el músculo deltoides o en el glúteo, de 25 mg a 150 mg en función de la tolerabilidad y/o eficacia individual del paciente. *Omisión de la dosis de mantenimiento mensual (>6 meses).* Si han transcurrido más de 6 meses desde la última inyección de XEPLION, inicie la administración según las pautas recomendadas para la iniciación de XEPLION recogidas anteriormente. Poblaciones especiales. Población de edad avanzada. No se ha establecido la eficacia y la seguridad en la población de edad avanzada >65 años. En general, la dosis recomendada de XEPLION en los pacientes de edad avanzada con función renal normal es la misma que para los pacientes adultos más jóvenes con función renal normal. Sin embargo, ya que los pacientes de edad avanzada pueden tener disminuida la función renal, puede ser necesario ajustar la dosis (ver *Insuficiencia renal* más adelante para conocer las recomendaciones de dosificación en pacientes con insuficiencia renal). *Insuficiencia renal.* No se ha estudiado XEPLION sistemáticamente en los pacientes con insuficiencia renal (ver sección 5.2). En los pacientes con insuficiencia renal leve (aclaramiento de creatinina ≥50 a <80 ml/min), se recomienda iniciar XEPLION con una dosis de 100 mg el día 1 del tratamiento y 75 mg una semana después, ambos administrados en el músculo deltoides. La dosis de mantenimiento mensual recomendada es de 50 mg con un rango de 25 a 100 mg, en función de la tolerabilidad y/o eficacia individual del paciente. XEPLION no está recomendado en pacientes con insuficiencia renal moderada o grave (aclaramiento de creatinina <50 ml/min) (ver sección 4.4). *Insuficiencia hepática.* Basándose en la experiencia con paliperidona oral, no es preciso ajustar las dosis en los pacientes con insuficiencia hepática leve o moderada. Dado que paliperidona no se ha estudiado en pacientes con insuficiencia hepática grave, se recomienda precaución en estos pacientes. *Otras poblaciones especiales.* No se recomienda ajustar la dosis de XEPLION por motivos de sexo, raza o tabaquismo. *Población pediátrica.* No se ha establecido la seguridad y la eficacia de XEPLION en niños <18 años de edad. No hay datos disponibles. Forma de administración. XEPLION se utiliza únicamente para uso intramuscular. Se debe inyectar lentamente, profundamente en el músculo. Cada inyección debe ser administrada por un profesional sanitario. La administración debe realizarse en una sola inyección. La dosis no se debe administrar en inyecciones divididas. La dosis no se debe administrar por vía intravascular o subcutánea. Las dosis de iniciación del día 1 y del día 8 se deben administrar ambas en el músculo deltoides para alcanzar concentraciones terapéuticas rápidamente (ver sección 5.2). Después de la segunda dosis, las dosis de mantenimiento mensuales se pueden administrar tanto en el músculo deltoides como en el glúteo. Se debe cambiar del glúteo al deltoides (y viceversa) en caso de dolor en el lugar de inyección si no se tolera bien el malestar en el lugar de inyección (ver sección 4.8). También se recomienda alternar entre los lados izquierdo y derecho (ver más adelante). Para consultar las instrucciones de uso y manipulación de XEPLION, ver prospecto (información destinada únicamente a médicos o profesionales del sector sanitario). *Administración en el músculo deltoides.* El tamaño de la aguja recomendado para la administración inicial y de mantenimiento de XEPLION en el músculo deltoides viene determinado por el peso del paciente. En los pacientes ≥90 kg, se recomienda la aguja de calibre 22 de 1½ pulgadas (38,1 mm x 0,72 mm). En los pacientes <90 kg, se recomienda la aguja de calibre 23 de 1 pulgada (25,4 mm x 0,64 mm). Las inyecciones en el deltoides se deben alternar entre los dos músculos deltoides. *Administración en el músculo glúteo.* El tamaño de la aguja recomendado para la administración mantenimiento de XEPLION en el músculo glúteo es el de una aguja de calibre 22 de 1½ pulgadas (38,1 mm x 0,72 mm). La administración se debe realizar en el cuadrante superior externo de la zona glútea. Las inyecciones en el glúteo se deben alternar entre los dos músculos glúteos. **4.3. Contraindicaciones.** Hipersensibilidad al principio activo, a risperidona o a alguno de los excipientes incluidos en la sección 6.1. **4.4. Advertencias y precauciones especiales de empleo.** Uso en pacientes que se encuentran en un estado sumamente agitado o psicótico grave. XEPLION no se debe utilizar para el tratamiento de estados agitados agudos o psicóticos graves cuando esté justificado el control inmediato de los síntomas. Intervalo QT. Se debe tener precaución al recetar paliperidona a pacientes con enfermedad cardiovascular conocida o antecedentes familiares de prolongación del intervalo QT, y en caso de uso concomitante con otros medicamentos que prolonguen el intervalo QT. Síndrome neuroléptico maligno. Se han notificado casos del Síndrome Neuroléptico Maligno (SNM), que se caracteriza por hipertermia, rigidez muscular, inestabilidad autonómica, alteración de la consciencia y elevación de los niveles séricos de creatina fosfocinasa relacionados con paliperidona. Otros signos clínicos pueden ser mioglobinuria (rabdomiólisis) e insuficiencia renal aguda. Si un paciente desarrolla signos o síntomas indicativos del SNM, se debe interrumpir la administración de todos los antipsicóticos, incluido paliperidona. Discinesia tardía. Los medicamentos con propiedades antagonistas del receptor de la dopamina se han asociado con la inducción de discinesia tardía, caracterizada por movimientos rítmicos involuntarios, predominantemente de la lengua y/o la cara. Si aparecen signos y síntomas de discinesia tardía, se debe considerar la interrupción de la administración de todos los antipsicóticos, incluido paliperidona. Leucopenia, neutropenia y agranulocitosis. Se han notificado casos de leucopenia, neutropenia y agranulocitosis con antipsicóticos, incluido XEPLION. La agranulocitosis ha sido notificada en muy raras ocasiones (<1/10.000 pacientes) durante la experiencia postcomercialización. Pacientes con un historial de un bajo recuento de glóbulos blancos clínicamente significativo (GB) o una leucopenia/neutropenia inducida por el medicamento deben ser monitorizados durante los primeros meses de tratamiento y se considerará discontinuar el tratamiento con XEPLION si aparecen los primeros signos de disminución clínicamente significativa de GB, en ausencia de otros factores causales. Pacientes con neutropenia clínicamente significativa deben ser cuidadosamente monitorizados por la fiebre u otros síntomas o signos de infección y se deben tratar inmediatamente en caso de aparecer estos síntomas o signos. En pacientes con neutropenia grave (recuento total de neutrófilos $<1x10^9$/L) se debe discontinuar el tratamiento con XEPLION y controlar los niveles de GB hasta la recuperación. Hiperglucemia y diabetes mellitus. Se ha notificado hiperglucemia, diabetes mellitus y exacerbación de diabetes pre-existente durante el tratamiento con paliperidona. En algunos casos, se ha notificado un aumento de peso previo que puede ser un factor de predisposición. Se ha notificado en muy raras ocasiones la asociación con cetoacidosis y en raras ocasiones con coma diabético. Se recomienda una monitorización clínica adecuada de acuerdo con las guías antipsicóticas utilizadas. A los pacientes tratados con antipsicóticos atípicos, incluido XEPLION, se les deben monitorizar los síntomas de la hiperglucemia (tales como polidipsia, poliuria, polifagia y debilidad) y a los pacientes con diabetes mellitus se les debe monitorizar regularmente el empeoramiento del control de glucosa. Aumento de peso. Se ha notificado un aumento de peso significativo con el uso de XEPLION. El peso debe controlarse regularmente. Hiperprolactinemia. Los estudios de cultivo de tejidos sugieren que prolactina puede estimular el crecimiento de células en los tumores de mama humanos. Aunque hasta ahora los estudios clínicos y epidemiológicos no han demostrado la existencia de una asociación dara con la administración de antipsicóticos, se recomienda precaución en pacientes con antecedentes patológicos de interés. Paliperidona debe utilizarse con precaución en pacientes con posibles tumores dependientes de prolactina. Hipotensión ortostática. Paliperidona puede inducir hipotensión ortostática en algunos pacientes sobre la base de su actividad alfa-bloqueante. Según los datos agrupados de los tres ensayos controlados con placebo, de dosis fijas y 6 semanas de duración con comprimidos orales de paliperidona de liberación prolongada (3, 6, 9 y 12 mg), el 2,5% de los pacientes tratados con paliperidona oral comunicaron hipotensión ortostática, en comparación con el 0,8% de los sujetos tratados con placebo. XEPLION debe utilizarse con precaución en pacientes con enfermedad cardiovascular conocida (p. ej., insuficiencia cardíaca, infarto de miocardio o isquemia, trastornos de la conducción), enfermedad cerebrovascular o afecciones que predispongan al paciente a la hipotensión (p. ej. deshidratación e hipovolemia). Convulsiones. XEPLION debe utilizarse con precaución en pacientes con antecedentes de convulsiones u otros trastornos que potencialmente puedan reducir el umbral convulsivo. Insuficiencia renal. Las concentraciones plasmáticas de paliperidona aumentan en pacientes con insuficiencia renal y por tanto, se recomienda un ajuste de la dosis en pacientes con insuficiencia renal leve. XEPLION no está recomendado en pacientes con insuficiencia renal moderada o grave (aclaramiento de creatinina <50 ml/min) (ver secciones 4.2 y 5.2). Insuficiencia hepática. No se dispone de datos en pacientes con insuficiencia hepática grave (clase C de Child-Pugh). Se recomienda precaución si se utiliza paliperidona en dichos pacientes. Pacientes de edad avanzada con demencia. No se ha estudiado XEPLION en pacientes de edad avanzada con demencia. XEPLION se debe utilizar con precaución en pacientes de edad avanzada con demencia y con factores de riesgo de padecer ictus. La experiencia con risperidona citada más adelante se considera válida también para paliperidona. *Mortalidad global.* En un metanálisis de 17 ensayos clínicos controlados, los pacientes de edad avanzada con demencia tratados con otros antipsicóticos atípicos, tales como risperidona, aripiprazol, olanzapina y quetiapina, tenían un mayor riesgo de mortalidad en comparación con placebo. Entre los pacientes tratados con risperidona, la mortalidad fue del 4% frente al 3,1% con placebo. *Reacciones adversas cerebrovasculares.* Se ha observado un aumento de aproximadamente 3 veces del riesgo de reacciones adversas cerebrovasculares en los ensayos clínicos aleatorizados controlados con placebo en la población con demencia al utilizar algunos antipsicóticos atípicos, tales como risperidona, aripiprazol y olanzapina. Se desconoce el mecanismo de este aumento del riesgo. Enfermedad de Parkinson y demencia con cuerpos de Lewy. Los médicos deben sopesar los riesgos y los beneficios de prescribir XEPLION a los pacientes con enfermedad de Parkinson o Demencia con Cuerpos de Lewy (DCL), ya que ambos grupos pueden tener mayor riesgo de padecer Síndrome Neuroléptico Maligno, así como tener una mayor sensibilidad a los antipsicóticos. Las manifestaciones de este aumento de la sensibilidad pueden incluir confusión, obnubilación, inestabilidad postural con caídas frecuentes, además de síntomas extrapiramidales. Priapismo. Se ha notificado que los medicamentos antipsicóticos (incluida risperidona) con efectos de bloqueo alfa adrenérgico inducen priapismo. Durante la vigilancia post-comercialización, también se han notificado casos de priapismo con paliperidona oral, que es el metabolito activo de risperidona. Se ha de informar a los pacientes de la necesidad de acudir al médico urgentemente en caso de que el priapismo no haya sido resuelto en el transcurso de 3 a 4 horas. Regulación de la temperatura del organismo. Se ha atribuido a los medicamentos antipsicóticos la interrupción de la capacidad del organismo para reducir la temperatura corporal central. Se aconseja proceder con especial cautela cuando se prescriba XEPLION a pacientes que vayan a experimentar circunstancias que puedan contribuir a una elevación de la temperatura corporal central, p. ej. ejercicio físico intenso, exposición a calor extremo, que reciban medicamentos concomitantes con actividad anticolinérgica o que estén sujetos a deshidratación. Tromboembolismo venoso. Se han notificado casos de tromboembolismo venoso (TEV) con medicamentos antipsicóticos. Dado que los pacientes tratados con antipsicóticos suelen presentar factores de riesgo adquiridos de TEV, se han de identificar todos los posibles factores de riesgo de TEV antes y durante el tratamiento con XEPLION y adoptar medidas preventivas. Efecto antiemético. Se observó un efecto antiemético en los estudios precínicos con paliperidona. Este efecto, si se produce en humanos, puede enmascarar los signos y síntomas de la sobredosis de determinados medicamentos o de enfermedades como la obstrucción intestinal, el síndrome de Reye y los tumores cerebrales. Administración. Se debe tener cuidado para evitar la inyección involuntaria de XEPLION en un vaso sanguíneo. Síndrome del Iris Flácido Intraoperatorio. Se ha observado síndrome del iris flácido intraoperatorio (IFIS) durante la cirugía de cataratas en pacientes tratados con medicamentos con efecto antagonista alfa1a-adrenérgico, como XEPLION (ver sección 4.8). El IFIS puede aumentar el riesgo de complicaciones oculares durante y después de la intervención. El oftalmólogo debe ser informado del uso actual o pasado de medicamentos con efecto antagonista alfa1a-adrenérgico antes de la cirugía. El beneficio potencial de la interrupción del tratamiento con bloqueantes alfa antes de la cirugía de cataratas no ha sido establecido y debe ser sopesado frente al riesgo de interrumpir el tratamiento antipsicótico. **4.5. Interacción con otros medicamentos y otras formas de interacción.** Se recomienda precaución al prescribir XEPLION con medicamentos que prolonguen el intervalo QT, p. ej. antiarrítmicos de clase IA (p. ej., quinidina, disopiramida) y antiarrítmicos de clase III (p. ej. amiodarona, sotalol), algunos antihistamínicos, algunos otros antipsicóticos y algunos antipalúdicos (p. ej. mefloquina). Esta lista es indicativa y no exhaustiva. Posibilidad de que XEPLION afecte a otros medicamentos. No se espera que paliperidona produzca interacciones farmacocinéticas clínicamente relevantes con medicamentos que sean metabolizados por las isoenzimas del citocromo P-450. Dado que los efectos principales de paliperidona se ejercen sobre el sistema nervioso central (SNC) (ver sección 4.8), XEPLION debe utilizarse con precaución en combinación con otros medicamentos de acción central, p. ej., ansiolíticos, la mayoría de los antipsicóticos, hipnóticos, opiáceos, etc. o con el alcohol. Paliperidona puede antagonizar el efecto de levodopa y otros agonistas de dopamina. Si se considera necesario administrar esta combinación, sobre todo para la enfermedad de Parkinson terminal, se debe recetar la dosis mínima eficaz de cada tratamiento. Debido a la posibilidad de que induzca hipotensión ortostática (ver sección 4.4), se puede observar un efecto aditivo si se administra XEPLION con otros tratamientos que también tengan esta posibilidad, p.ej., otros antipsicóticos, tricíclicos. Se recomienda precaución cuando se coadministre paliperidona junto con otros medicamentos que disminuyan el umbral convulsivo (es decir, fenotiazinas o butirofenonas, tricíclicos o ISRS, tramadol, mefloquina, etc.). La administración concomitante de comprimidos orales de paliperidona de liberación prolongada en estado estacionario (12 mg una vez al día) con comprimidos de divalproex sódico de liberación prolongada (de 500 mg a 2000 mg una vez al día) no afectó a la farmacocinética en estado estacionario de valproato. No se ha realizado ningún estudio de interacción entre XEPLION y el litio, sin embargo, no es probable que se produzca una interacción farmacocinética. Posibilidad de que otros medicamentos afecten a XEPLION. Los estudios *in vitro* indican que las enzimas CYP2D6 y CYP3A4 pueden tener una intervención mínima en el metabolismo de la paliperidona, pero no hay indicios *in vitro* ni *in vivo* de que esas isoenzimas desempeñen un papel significativo en el metabolismo de paliperidona. La administración conjunta de paliperidona oral con paroxetina, un potente inhibidor de la CYP2D6, no tuvo un efecto clínicamente significativo sobre la farmacocinética de paliperidona. La administración concomitante de paliperidona oral de liberación prolongada una vez al día y carbamazepina 200 mg dos veces al día originó una disminución de aproximadamente un 37% de la media de la C_{max} y del AUC en el estado estacionario de paliperidona. Esta disminución se debe en gran parte a un aumento de un 35% del aclaramiento renal de paliperidona, probablemente como resultado de la inducción de la P-gp renal por carbamazepina. Una disminución menor de la cantidad del principio activo inalterado excretado en la orina sugiere que durante la administración concomitante con carbamazepina, hubo un efecto mínimo en el metabolismo del CYP o en la biodisponibilidad de paliperidona. Con dosis más altas de carbamazepina, podrían aparecer disminuciones mayores de las concentraciones plasmáticas de paliperidona. Al inicio del tratamiento con carbamazepina, se debe reevaluar y aumentar la dosis de XEPLION, si es necesario. Por el contrario, en caso de interrupción del tratamiento con carbamazepina, se debe reevaluar y disminuir la dosis de XEPLION, si es necesario. La administración concomitante de una sola dosis de un comprimido de paliperidona oral de liberación prolongada de 12 mg con comprimidos de divalproex sódico de liberación prolongada (dos comprimidos de 500 mg una vez al día) tuvo como resultado un aumento de aproximadamente el 50% en la C_{max} y el AUC de paliperidona, probablemente como resultado de un aumento de la absorción oral. Dado que no se observó ningún efecto sobre el aclaramiento sistémico, no se espera que se produzca una interacción clínicamente significativa entre los comprimidos

de divalproex sódico de liberación prolongada y la inyección intramuscular de XEPLION. Esta interacción no se ha estudiado con XEPLION. Uso concomitante de XEPLION y risperidona. Risperidona administrada por vía oral o intramuscular se metaboliza en un grado variable a paliperidona. Se debe proceder con cautela en caso de administración concomitante de risperidona o paliperidona oral con XEPLION. **4.6. Fertilidad, embarazo y lactancia.** Embarazo. No existen datos suficientes sobre la utilización de paliperidona durante el embarazo. El palmitato de paliperidona inyectado por vía intramuscular y paliperidona administrada por vía oral no fueron teratógenos en estudios en animales, pero se observaron otros tipos de toxicidad reproductiva (ver sección 5.3). Los recién nacidos expuestos a antipsicóticos (como paliperidona) durante el tercer trimestre de embarazo están en peligro de sufrir reacciones adversas como síntomas extrapiramidales y/o síndromes de abstinencia que pueden variar en gravedad y duración tras la exposición. Se han notificado casos de síntomas de agitación, hipertonía, hipotonía, temblor, somnolencia, dificultad respiratoria o alteraciones alimenticias. Por consiguiente, se debe vigilar estrechamente a los recién nacidos. XEPLION no se debe utilizar durante el embarazo salvo que sea claramente necesario. Lactancia. Paliperidona se excreta por la leche materna en tal medida que es probable que se produzcan efectos en el lactante si se administra en dosis terapéuticas a mujeres lactantes. XEPLION no debe utilizarse durante la lactancia. Fertilidad. No se observaron efectos relevantes en estudios no clínicos. **4.7. Efectos sobre la capacidad para conducir y utilizar máquinas.** La influencia de paliperidona sobre la capacidad para conducir y utilizar máquinas es pequeña o moderada debido a sus posibles efectos sobre el sistema nervioso y la vista, tales como sedación, somnolencia, síncope, visión borrosa (ver sección 4.8). Por tanto, se debe aconsejar a los pacientes que no conduzcan ni utilicen máquinas hasta conocer su sensibilidad individual a XEPLION. **4.8. Reacciones adversas.** Resumen del perfil de seguridad. Las reacciones adversas a medicamentos (RAMs) notificadas con más frecuencia en los ensayos clínicos fueron insomnio, cefalea, ansiedad, infección de las vías respiratorias altas, reacción en el lugar de la inyección, parkinsonismo, aumento de peso, acatisia, agitación, sedación/somnolencia, náuseas, estreñimiento, mareos, dolor musculoesquelético, taquicardia, temblor, dolor abdominal, vómitos, diarrea, fatiga y distonía. De estas, la acatisia y la sedación/somnolencia parecían estar relacionadas con la dosis. Tabla de reacciones adversas. A continuación se recogen todas las RAMs notificadas con paliperidona en función de la frecuencia estimada de ensayos clínicos llevados a cabo con XEPLION. Se aplican los siguientes términos y frecuencias: *muy frecuentes* (≥1/10), *frecuentes* (≥1/100 a <1/10), *poco frecuentes* (≥1/1000 a <1/100), *raras* (≥1/10.000 a <1/1000), *muy raras* (<1/10.000), y *frecuencia no conocida* (no puede estimarse a partir de los datos disponibles).

Clasificación por órganos y sistemas	Reacción adversa al medicamento				
	Frecuencia				
	Muy frecuentes	Frecuentes	Poco frecuentes	Raras	No conocidas
Infecciones e infestaciones		infección de las vías respiratorias superiores, infección del tracto urinario, gripe	neumonía, bronquitis, infección del tracto respiratorio, sinusitis, cistitis, infección de oídos, infección de ojos, amigdalitis, celulitis, acarodermatitis, absceso subcutáneo	onicomicosis	
Trastornos de la sangre y del sistema linfático			disminución del recuento de glóbulos blancos, anemia, disminución del hematocrito, aumento del recuento de eosinófilos	agranulocitosis[e] neutropenia, trombocitopenia	
Trastornos del sistema inmunológico			hipersensibilidad	reacción anafiláctica[e]	
Trastornos endocrinos		hiperprolactinemia[a]		secreción inapropiada de la hormona antidiurética	presencia de glucosa en orina
Trastornos del metabolismo y de la nutrición		hiperglucemia, aumento de peso, disminución de peso, aumento de los triglicéridos en sangre	diabetes mellitus[c], hiperinsulinemia, aumento del apetito, anorexia, disminución del apetito, aumento del colesterol en sangre	intoxicación por agua[e], cetoacidosis diabética[e], hipoglucemia, polidipsia	
Trastornos psiquiátricos	insomnio[d]	agitación, depresión, ansiedad	trastorno del sueño, manía, estado de confusión, disminución de la líbido, nerviosismo, pesadillas	embotamiento afectivo[e], anorgasmia	
Trastornos del sistema nervioso	cefalea	parkinsonismo[b], acatisia[b], sedación/somnolencia, distonia[b], mareos, discinesia[b], temblor	discinesia tardía, convulsión[e], síncope, hiperactividad psicomotora, mareo postural, alteración de la atención, disartria, disgeusia, hipoestesia, parestesia	síndrome neuroléptico maligno, isquemia cerebral, sin respuesta a estímulos, pérdida de la consciencia, disminución del nivel de consciencia, coma diabético[e], trastorno del equilibrio, coordinación anormal[e], titubeo de la cabeza[e]	
Trastornos oculares			visión borrosa, conjuntivitis, sequedad de ojos	glaucoma[e], trastornos del movimiento del ojo, giros de los ojos, fotofobia, aumento del lagrimeo, hiperemia ocular	
Trastornos del oído y del laberinto			vértigo, acúfenos, dolor de oído		
Trastornos cardiacos		bradicardia, taquicardia	fibrilación auricular, bloqueo auriculoventricular, QT prolongado en el electrocardiograma, síndrome de taquicardia postural ortostática, anomalías del electrocardiograma, palpitaciones	arritmia sinusal	
Trastornos vasculares		hipertensión	hipotensión, hipotensión ortostática	embolismo pulmonar[e], trombosis venosa, isquemia[e], rubor	
Trastornos respiratorios, torácicos y mediastínicos		tos, congestión nasal	disnea, congestión pulmonar, sibilancias, dolor faringeolaríngeo, epistaxis	síndrome de apnea del sueño[e], hiperventilación[e], neumonía por aspiración[e], congestión del tracto respiratorio disfonía[e]	
Trastornos gastrointestinales		dolor abdominal, vómitos, náuseas, estreñimiento, diarrea, dispepsia, dolor de muelas	malestar abdominal, gastroenteritis, sequedad de boca, flatulencia	pancreatitis, obstrucción del intestino[e], íleo, hinchazón de la lengua, incontinencia fecal, fecaloma, disfagia, queilitis[e]	
Trastornos hepatobiliares		aumento de las transaminasas	aumento de la gamma-glutamiltransferasa, aumento de las enzimas hepáticas	ictericia[e]	
Trastornos de la piel y del tejido subcutáneo		erupción cutánea	urticaria, prurito, alopecia, eccema, sequedad de la piel, eritema, acné	angioedema[e], erupción debida al medicamento, hiperqueratosis, decoloración de la piel[e], dermatitis seborreica[e], caspa	
Trastornos musculoesqueléticos y del tejido conjuntivo		dolor musculoesquelético, dolor de espalda	espasmos musculares, rigidez en las articulaciones, dolor de cuello, artralgia	rabdomiólisis[e], aumento de la creatina fosfoquinasa en sangre, anomalía postural[e], inflamación de las articulaciones, debilidad muscular	
Trastornos renales y urinarios			incontinencia urinaria, polaquiuria, disuria	retención urinaria	
Embarazo, puerperio y enfermedades perinatales				síndrome de abstinencia neonatal (ver sección 4.6)[e]	
Trastornos del aparato reproductor y de la mama			disfunción eréctil, trastorno de la eyaculación, amenorrea, retraso en la menstruación, trastornos menstruales[d], ginecomastia, galactorrea, disfunción sexual, secreción vaginal	priapismo[e], dolor de las mamas, malestar de las mamas, congestión de las mamas, aumento de las mamas, secreción mamaria	
Trastornos generales y alteraciones en el lugar de administración		pirexia, astenia, fatiga, reacción en el lugar de la inyección	edema facial, edema[e], alteración de la marcha, dolor de pecho, malestar de pecho, malestar, endurecimiento	hipotermia, disminución de la temperatura corporal[e], escalofríos, aumento de la temperatura corporal, sed, síndrome de abstinencia a medicamentos[e], absceso en el lugar de la inyección, celulitis en el lugar de la inyección, quiste en el lugar de la inyección[e], hematoma en el lugar de la inyección	
Lesiones traumáticas, intoxicaciones y complicaciones de procedimientos terapéuticos			caídas		

[a]Referido a "Hiperprolactinemia" a continuación. [b]Referido a "Síntomas extrapiramidales" a continuación. [c]En ensayos controlados con placebo, se notificó diabetes mellitus en un 0,32% de los pacientes tratados con XEPLION comparado con un 0,39% del grupo placebo. En general, la incidencia en todos los ensayos clínicos fue de un 0,47% en todos los pacientes tratados con XEPLION. [d]**Insomnio incluye:** insomnio inicial, insomnio medio; **Convulsión incluye:** convulsión del gran mal; **Edema incluye:** edema generalizado, edema periférico, edema con fóvea. **Trastornos menstruales incluyen:** menstruación irregular, oligomenorrea. [e]No se observaron en estudios clínicos de XEPLION pero sí en la experiencia tras la comercialización con paliperidona.

Reacciones adversas notificadas con las formulaciones de risperidona. Paliperidona es el metabolito activo de risperidona, por lo tanto, los perfiles de las reacciones adversas de estos compuestos (incluyendo ambas formulaciones la oral y la inyectable) son relevantes entre sí. Además de las reacciones adversas anteriormente mencionadas, se han notificado las siguientes reacciones adversas con el uso de risperidona, las cuales se espera que aparezcan con XEPLION. **Trastornos del sistema nervioso:** trastorno cerebrovascular. **Trastornos oculares:** síndrome del iris flácido (intraoperatorio). **Trastornos respiratorios, torácicos y mediastínicos:** estertores. **Trastornos generales y alteraciones en el lugar de administración:** (observadas con la formulación inyectable de risperidona): necrosis en el lugar de la inyección, úlcera en el lugar de la inyección. Descripción de algunas reacciones adversas. *Reacción anafiláctica.* Durante la experiencia post comercialización, en raras ocasiones se han notificado casos de una reacción anafiláctica después de la inyección de XEPLION en pacientes que previamente han tolerado risperidona oral o paliperidona oral. *Reacciones en el lugar de la inyección.* La reacción adversa relacionada con el lugar de la inyección notificada con mayor frecuencia fue el dolor. La mayoría de estas reacciones se notificaron con gravedad de leve a moderada. Las evaluaciones del dolor en el sitio de la inyección en los sujetos, basada en una escala analógica visual, indican que el dolor tiende a disminuir en frecuencia e intensidad con el tiempo en todos los estudios de fase 2 y 3. Las inyecciones en el músculo deltoides se perciben como un poco más dolorosas que las correspondientes inyecciones en el glúteo. Otras reacciones en el lugar de la inyección fueron en su mayoría de intensidad leve e incluyeron induración (frecuente), prurito (poco frecuente) y nódulos (raro). *Síntomas extrapiramidales (SEP).* SEP incluye un análisis agrupado de los siguientes términos: parkinsonismo (incluye hipersecreción salival, rigidez musculoesquelética, parkinsonismo, babeo, rigidez en rueda dentada, bradicinesia, hipocinesia, facies en máscara, tensión muscular, acinesia, rigidez de la nuca, rigidez muscular, modo de andar parkinsoniano y reflejo de la glabella anormal, temblor en reposo parkinsoniano), acatisia (incluye acatisia, inquietud, hipercinesia y síndrome de las piernas inquietas), discinesia (discinesia, calambres musculares, coreatetosis, atetosis y miodonía), distonía (incluye distonía, hipertonía, tortícolis, contracciones musculares involuntarias, contracturas musculares, blefarospasmo, giro ocular, parálisis lingual, espasmo facial, laringoespasmo, miotonía, opistótonos, espasmo orofaríngeo, pleurotótonos, espasmo lingual y trismo) y temblor. Hay que destacar que se incluye un espectro más amplio de síntomas que no tienen forzosamente su origen en el trastorno extrapiramidal. *Aumento de peso.* En el estudio de 13 semanas de duración que incluyó un régimen de dosificación inicial de 150 mg, la proporción de sujetos con un aumento anormal de peso ≥7% mostró una tendencia relacionada con la dosis, con una tasa de incidencia del 5% en el grupo placebo, en comparación con tasas del 6%, 8%, y 13% en los grupos tratados con 25 mg, 100 mg y 150 mg de XEPLION, respectivamente. Durante el período abierto de transición/mantenimiento de 33 semanas de duración del ensayo de prevención de recidivas a largo plazo, el 12% de los pacientes tratados con XEPLION cumplieron este criterio (aumento de peso de ≥7% desde la fase doble ciego hasta el final del estudio); la media (DE) del cambio de peso desde el nivel basal del periodo abierto fue de +0,7 (4,79) kg. *Hiperprolactinemia.* En ensayos clínicos, se observaron medianas de aumento de la prolactina sérica en sujetos de ambos sexos que recibieron XEPLION. Las reacciones adversas que pueden sugerir un aumento de los niveles de prolactina (p. ej., amenorrea, galactorrea, alteraciones de la menstruación, ginecomastia) se notificaron en <1% de los sujetos. Efectos de clase. Con antipsicóticos puede aparecer prolongación del QT, arritmias ventriculares (fibrilación ventricular, taquicardia ventricular), muerte súbita inexplicable, parada cardíaca y Torsades de pointes. Se han notificado casos de tromboembolismo venoso, incluidos casos de embolismo pulmonar y de trombosis venosa profunda, con el uso de medicamentos antipsicóticos (frecuencia no conocida). Notificación de sospechas de reacciones adversas. Es importante notificar sospechas de reacciones adversas al medicamento tras su autorización. Ello permite una supervisión continuada de la relación beneficio/riesgo del medicamento. Se invita a los profesionales sanitarios a notificar las sospechas de reacciones adversas a través del Sistema Español de Farmacovigilancia de Medicamentos de Uso Humano: https://www.notificaram.es. **4.9. Sobredosis.** En general, los signos y síntomas previstos son los resultantes de la exageración de los efectos farmacológicos conocidos de paliperidona, es decir, somnolencia y sedación, taquicardia e hipotensión, prolongación del intervalo QT y síntomas extrapiramidales. Se han notificado Torsades de pointes y fibrilación ventricular en un paciente en relación con la sobredosis de paliperidona oral. En caso de sobredosis aguda, se debe tener en cuenta la posibilidad de que estén implicados varios medicamentos. Al evaluar el tratamiento necesario y la recuperación hay que tener en cuenta la naturaleza de liberación prolongada del medicamento y la prolongada vida media de eliminación de paliperidona. No hay ningún antídoto específico para paliperidona. Se utilizarán medidas de apoyo generales. Hay que establecer y mantener una vía respiratoria despejada y garantizar que la oxigenación y la ventilación sean adecuadas. El control cardiovascular debe empezar inmediatamente e incluir un control electrocardiográfico continuo para controlar posibles arritmias. La hipotensión y el fracaso circulatorio deben tratarse con las medidas terapéuticas adecuadas, como administración de líquidos por vía intravenosa y/o de simpaticomiméticos. En caso de síntomas extrapiramidales intensos, se administrará medicación anticolinérgica. Se debe mantener una supervisión y un control estrictos hasta que el paciente se recupere. **5. PROPIEDADES FARMACOLÓGICAS. 5.1. Propiedades farmacodinámicas.** Grupo farmacoterapéutico: psicolépticos, otros antipsicóticos. Código ATC: N05AX13. XEPLION contiene una mezcla racémica de paliperidona (+) y (-). Mecanismo de acción. Paliperidona es un agente bloqueante selectivo de los efectos de las monoaminas, cuyas propiedades farmacológicas son diferentes de las de los neurolépticos tradicionales. Paliperidona se une firmemente a los receptores serotoninérgicos 5-HT2 y dopaminérgicos D2. Paliperidona también bloquea los receptores adrenérgicos alfa1 y bloquea, en menor medida, los receptores histaminérgicos H1 y los adrenérgicos alfa2. La actividad farmacológica de los enantiómeros (+) y (-) de paliperidona es similar desde el punto de vista cualitativo y cuantitativo. Paliperidona no se une a los receptores colinérgicos. Aunque paliperidona es un antagonista D2 potente, motivo por el que se cree que alivia los síntomas positivos de la esquizofrenia, produce menos catalepsia y reduce las funciones motrices en menor medida que los neurolépticos tradicionales. La preponderancia del antagonismo central de la serotonina puede reducir la tendencia de paliperidona a producir efectos secundarios extrapiramidales. Eficacia clínica. *Tratamiento agudo de la esquizofrenia.* La eficacia de XEPLION en el tratamiento agudo de la esquizofrenia fue establecida en cuatro ensayos doble ciego, aleatorizados, controlados con placebo, de dosis fija, a corto plazo (uno de 9 semanas y tres de 13 semanas de duración) en pacientes adultos ingresados con recidiva aguda que cumplían los criterios para la esquizofrenia del DSM-IV. Las dosis fijas de XEPLION en estos estudios se administraron en los días 1, 8, y 36 en el estudio de 9 semanas de duración, y, además, el día 64 en los estudios de 13 semanas de duración. No fue necesario administrar suplementos antipsicóticos orales adicionales durante el tratamiento agudo de la esquizofrenia con XEPLION. El criterio principal de eficacia del estudio se definió como una reducción de las puntuaciones totales de la Escala de los Síndromes Positivo y Negativo (PANSS), como se muestra en la siguiente tabla. La PANSS es un inventario multi-elemento validado compuesto por cinco factores destinados a evaluar los síntomas positivos, los síntomas negativos, el pensamiento desorganizado, la hostilidad/excitación incontrolada y la ansiedad/depresión. La función se evaluó mediante la escala de Funcionamiento Personal y Social (PSP). La PSP es una escala homologada que mide la capacidad del paciente para desempeñar sus actividades personales y sociales en cuatro áreas del comportamiento: las actividades socialmente útiles (incluidos el trabajo y el estudio), las relaciones personales y sociales, el cuidado personal y los comportamientos disruptivos y agresivos. En un estudio de 13 semanas de duración (n=636) que comparó tres dosis fijas de XEPLION (inyección inicial en el deltoides de 150 mg seguida por tres dosis en el glúteo o en el deltoides de cualquiera de 25 mg/4 semanas, 100 mg/4 semanas o 150 mg/4 semanas) con placebo, las tres dosis de XEPLION fueron superiores a placebo en términos de la mejoría de la puntuación total de la PANSS. En este estudio, tanto los grupos de tratamiento con 100 mg/4 semanas como con 150 mg/4 semanas, pero no el 25 mg/4 semanas, demostraron una superioridad estadística respecto a placebo en cuanto a la puntua-

ción de PSP. Estos resultados respaldan la eficacia a lo largo de toda la duración del tratamiento y la mejoría de la PANSS, que se observaron ya en el día 4, con una separación significativa respecto a placebo en los grupos tratados con 25 mg y 150 mg de XEPLION en el día 8. Los resultados de los otros estudios arrojaron resultados estadísticamente significativos a favor de XEPLION, a excepción de la dosis de 50 mg en un estudio (ver tabla siguiente).

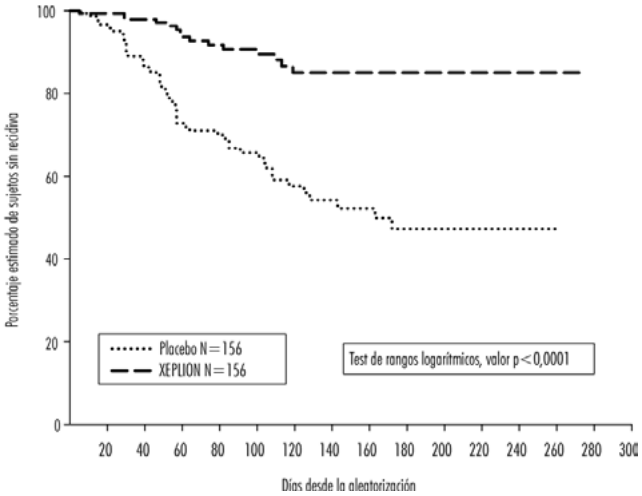
Puntuación total de la escala de los síndromes positivo y negativo de la esquizofrenia (PANSS). Variación entre el momento basal y el final del estudio-LOCF para los estudios R092670-SCH-201, R092670-PSY-3003, R092670-PSY-3004 y R092670-PSY-3007: Grupo de análisis del criterio principal de valoración de la eficacia

	Placebo	25 mg	50 mg	100 mg	150 mg
R092670-PSY-3007*	n=160	n=155		n=161	n=160
Media basal (DE)	86,8 (10,31)	86,9 (11,99)	--	86,2 (10,77)	88,4 (11,70)
Variación media (DE)	-2,9 (19,26)	-8,0 (19,90)		-11,6 (17,63)	-13,2 (18,48)
Valor p (frente a placebo)	--	0,034		<0,001	<0,001
R092670-PSY-3003	n=132		n=93	n=94	n=30
Media basal (DE)	92,4 (12,55)	--	89,9 (10,78)	90,1 (11,66)	92,2 (11,72)
Variación media (DE)	-4,1 (21,01)		-7,9 (18,71)	-11,0 (19,06)	-5,5 (19,78)
Valor p (frente a placebo)	--		0,193	0,019	--
R092670-PSY-3004	n=125	n=129	n=128	n=131	
Media basal (DE)	90,7 (12,22)	90,7 (12,25)	91,2 (12,02)	90,8 (11,70)	--
Variación media (DE)	-7,0 (20,07)	-13,6 (21,45)	-13,2 (20,14)	-16,1 (20,36)	
Valor p (frente a placebo)	--	0,015	0,017	<0,001	
R092670-SCH-201	n=66		n=63	n=68	
Media basal (DE)	87,8 (13,90)	--	88,0 (12,39)	85,2 (11,09)	--
Variación media (DE)	6,2 (18,25)		-5,2 (21,52)	-7,8 (19,40)	
Valor p (frente a placebo)	--		0,001	<0,0001	

*En el estudio R092670-PSY-3007, se administró una dosis de iniciación de 150 mg a todos los sujetos de los grupos de tratamiento con XEPLION el día 1 y, a partir de entonces, la dosis asignada. Nota: un cambio negativo de la puntuación denota mejoría.

Mantenimiento del control de los síntomas y retraso de la recidiva de la esquizofrenia. La eficacia de XEPLION en el mantenimiento del control de los síntomas y el retraso de la recidiva de la esquizofrenia se determinó en un estudio doble ciego, controlado con placebo, de dosis flexible, con un plazo más largo, en el que participaron 849 sujetos adultos no ancianos que cumplían los criterios para la esquizofrenia del DSM-IV. Este estudio incluyó un tratamiento abierto agudo de 33 semanas de duración y una fase de estabilización, una fase aleatorizada, doble ciego, controlada con placebo para observar la recidiva, y un período de extensión abierto de 52 semanas. En este estudio, las dosis de XEPLION fueron 25, 50, 75 y 100 mg administrados mensualmente; la dosis de 75 mg solamente estaba permitida en la extensión abierta de 52 semanas. Inicialmente, los sujetos recibieron dosis flexibles (25-100 mg) de XEPLION durante un período de transición de 9 semanas de duración, seguido de un período de mantenimiento de 24 semanas, en el que los sujetos debían tener una puntuación PANSS ≤75. Los ajustes de la dosis sólo se permitieron en las primeras 12 semanas del período de mantenimiento. Se realizó la asignación aleatoria de un total de 410 pacientes estabilizados a XEPLION (mediana de la duración de 171 días [intervalo de 1 día a 407 días]) o a placebo (mediana de la duración de 105 días [intervalo de 8 días a 441 días]) hasta que experimentaran una recidiva de los síntomas de la esquizofrenia en la fase doble ciego de duración variable. El ensayo se suspendió antes de tiempo por motivos de eficacia, dado que se observó un tiempo significativamente más largo hasta la recidiva (p<0,0001, Figura 1) en los pacientes tratados con XEPLION en comparación con el placebo (cociente de riesgos=4,32; IC 95%: 2,4-7,7).

Figura 1: Gráfico de Kaplan-Meier del tiempo hasta la recidiva. Análisis intermedio (grupo de análisis intermedio por intención de tratar)



Población pediátrica. La Agencia Europea de Medicamentos ha eximido al titular de la obligación de presentar los resultados de los ensayos realizados con XEPLION en los diferentes grupos de la población pediátrica en esquizofrenia. Ver sección 4.2 para consultar la información sobre el uso en población pediátrica. **5.2. Propiedades farmacocinéticas.** Absorción y distribución. Palmitato de paliperidona es el profármaco en forma de éster de palmitato de la paliperidona. Debido a su hidrosolubilidad extremadamente baja, el palmitato de la paliperidona se disuelve lentamente después de la inyección intramuscular antes de ser hidrolizado a paliperidona y se absorbe en la circulación sistémica. Después de una dosis única por vía intramuscular, las concentraciones plasmáticas de paliperidona se elevan gradualmente hasta alcanzar las concentraciones plasmáticas máximas a una mediana de T_{max} de 13 días. La liberación de la sustancia activa se inicia desde el día 1 y tiene una duración de al menos 4 meses. Después de la inyección intramuscular de dosis únicas (de 25 mg a 150 mg) en el músculo deltoides, en promedio, se observó una C_{max} un 28% superior en comparación con la inyección en el músculo glúteo. Las dos inyecciones iniciales intramusculares en el deltoides de 150 mg el día 1 y 100 mg en el día 8 contribuyen a alcanzar concentraciones terapéuticas rápidamente. El perfil de liberación y el régimen de dosificación de XEPLION se traducen en concentraciones terapéuticas mantenidas. La exposición total de paliperidona tras la administración de XEPLION fue proporcional a la dosis en un rango de dosis de 25 mg a 150 mg, y menos que proporcional a la dosis en el caso de la C_{max} para dosis superiores a 50 mg. El promedio del pico en el estado estacionario: a través del ratio para una dosis de 100 mg de XEPLION fue de 1,8 después de la administración en el glúteo y de 2,2 después de la administración en el deltoides. La mediana de la vida media aparente de paliperidona tras la administración de XEPLION a lo largo del rango de dosis de 25 mg a 150 mg osciló entre 25 y 49 días. La biodisponibilidad absoluta del palmitato de paliperidona tras la administración de XEPLION es del 100%. Tras la administración de palmitato de paliperidona, los enantiómeros (+) y (-) de paliperidona se interconvierten, de modo que se alcanza un cociente de AUC (+) a (-) de aproximadamente 1,6-1,8. La unión a proteínas plasmáticas de paliperidona racémica es del 74%. Biotransformación y eliminación. Una semana después de la administración de una sola dosis oral de 1 mg de paliperidona de liberación inmediata marcada con C^{14}, el 59% de la dosis fue eliminada intacta por la orina, lo que indica que paliperidona no experimenta un intenso metabolismo por el hígado. Se recuperó aproximadamente el 80% de la radiactividad administrada en la orina y el 11% en las heces. Se han identificado cuatro vías metabólicas *in vivo*, ninguna de las cuales representó más del 6,5% de la dosis: desalquilación, hidroxilación, deshidrogenación y escisión de benzisoxazol. Aunque en estudios *in vitro* se señaló que las enzimas CYP2D6 y CYP3A4 pueden intervenir en el metabolismo de paliperidona, no hay datos *in vivo* que demuestren que estas isoenzimas desempeñen un papel significativo en el metabolismo de paliperidona. En los análisis de farmacocinética de la población no se observó ninguna diferencia apreciable del aclaramiento aparente de paliperidona tras la administración de paliperidona oral entre los metabolizadores rápidos y lentos de los sustratos de la CYP2D6. En estudios *in vitro* realizados con microsomas hepáticos humanos se demostró que la paliperidona no inhibe sustancialmente el metabolismo de los medicamentos metabolizados por las isoenzimas del citocromo P450, como CYP1A2, CYP2A6, CYP2C8/9/10, CYP2D6, CYP2E1, CYP3A4 y CYP3A5. En estudios *in vitro* se ha demostrado que paliperidona es un sustrato de la P-gp y un inhibidor débil de la P-gp a altas concentraciones. No existen datos de estudios *in vivo* y se desconoce la importancia clínica. Inyección de palmitato de paliperidona de acción prolongada en comparación con paliperidona oral de liberación prolongada. XEPLION está diseñado para liberar paliperidona a lo largo de un período mensual, mientras que la paliperidona oral de liberación prolongada se administra a diario. El régimen de iniciación de XEPLION (150 mg/100 mg en el músculo deltoides en el día 1 /día 8) ha sido diseñado para alcanzar rápidamente las concentraciones de estado estacionario de paliperidona al iniciar el tratamiento sin necesidad de administrar suplementos orales. En términos generales, los niveles plasmáticos globales de iniciación con XEPLION se encontraron dentro del intervalo de exposición observado con entre 6 y 12 mg de paliperidona oral de liberación prolongada. El uso del régimen de iniciación de XEPLION permitió a los pacientes permanecer dentro de este margen de exposición de entre 6 y 12 mg de paliperidona oral de liberación prolongada incluso en los días de concentración mínima previos a la dosis (días 8 y 36). Debido a la diferencia en la mediana de los perfiles farmacocinéticos entre los dos medicamentos, se debe tener precaución al realizar una comparación directa de sus propiedades farmacocinéticas. Insuficiencia hepática. Paliperidona no se metaboliza ampliamente en el hígado. Aunque XEPLION no se ha estudiado en pacientes con insuficiencia hepática, no es preciso ajustar las dosis en los pacientes con insuficiencia hepática leve o moderada. En un estudio con paliperidona oral en pacientes con insuficiencia hepática moderada (Child-Pugh clase B), las concentraciones plasmáticas de paliperidona libre fueron similares a los de individuos sanos. Paliperidona no se ha estudiado en pacientes con insuficiencia hepática grave. Insuficiencia renal. La eliminación de una sola dosis de un comprimido de 3 mg de paliperidona de liberación prolongada se estudió en sujetos con diversos grados de función renal. La eliminación de la paliperidona disminuye si lo hace el aclaramiento de creatinina estimado. El aclaramiento total de la paliperidona disminuyó un promedio del 32% en sujetos con insuficiencia renal leve (CrCl=50 a <80 ml/min), un 64% en sujetos con insuficiencia renal moderada (CrCl=30 a <50 ml/min) y un 71% en sujetos con insuficiencia renal grave (CrCl =10 a <30 ml/min), lo que corresponde con un aumento promedio de la exposición (AUC_{inf}) de 1,5, 2,6 y 4,8 veces, respectivamente, en comparación con los sujetos sanos. Sobre la base del número limitado de observaciones con XEPLION en sujetos con insuficiencia renal leve y de los resultados de las simulaciones farmacocinéticas, se recomienda administrar una dosis reducida (ver sección 4.2). Población de edad avanzada. No se recomienda ajustar la dosis únicamente en función de la edad. Sin embargo, puede ser necesario realizar el ajuste de la dosis debido a las disminuciones en el aclaramiento de creatinina relacionadas con la edad (ver Insuficiencia renal más arriba y la sección 4.2). Peso. Los estudios farmacocinéticos con palmitato de paliperidona han demostrado unas concentraciones plasmáticas de paliperidona algo menores (entre el 10% y el 20%) en pacientes con sobrepeso u obesidad en comparación con los pacientes con un peso normal (ver sección 4.2). Raza. En el análisis farmacocinético de los datos de la población procedentes de los ensayos con paliperidona oral, no se observaron indicios de que existan diferencias relacionadas con la raza en la farmacocinética de la paliperidona tras la administración de XEPLION. Sexo. No se han observado diferencias clínicamente significativas entre hombres y mujeres. Tabaquismo. Según estudios *in vitro* realizados con enzimas hepáticas humanas, paliperidona no es sustrato de la CYP1A2; por lo tanto, el consumo de tabaco no debería afectar a la farmacocinética de paliperidona. Un análisis farmacocinético de la población basado en los datos obtenidos con comprimidos orales de paliperidona de liberación prolongada mostró una exposición ligeramente más baja a paliperidona en fumadores en comparación con los no fumadores. No obstante, se cree que es poco probable que la diferencia tenga relevancia clínica. No se evaluó el tabaquismo con XEPLION. **5.3. Datos preclínicos sobre seguridad.** Los estudios de toxicidad a dosis repetidas de palmitato de paliperidona inyectado por vía intramuscular y paliperidona administrada por vía oral en ratas y perros mostraron efectos principalmente farmacológicos, como sedación y efectos mediados por la prolactina, en las glándulas mamarias y en los genitales. En los animales tratados con palmitato de paliperidona, se observó una reacción inflamatoria en el lugar de la inyección intramuscular. Se produjo la formación ocasional de abscesos. En estudios sobre la reproducción de las ratas utilizando risperidona oral, que se convierte masivamente a paliperidona en ratas y en seres humanos, se observaron efectos adversos en el peso al nacer y de la supervivencia de las crías. No se observó embriotoxicidad ni malformaciones tras la administración intramuscular de palmitato de paliperidona a ratas preñadas a la dosis más alta (160 mg/kg/día), correspondiente a 4,1 veces el nivel de exposición en humanos a la dosis máxima recomendada de 150 mg. Otros antagonistas de la dopamina han tenido efectos negativos en el desarrollo motor y del aprendizaje en las crías cuando se administraron a animales preñados. Palmitato de paliperidona y paliperidona no fueron genotóxicos. En estudios sobre el poder carcinógeno de risperidona oral en ratas y ratones se observaron aumentos de los adenomas hipofisarios (ratón), de los adenomas del páncreas endocrino (rata) y los de adenomas de las glándulas mamarias (en ambas especies). Se evaluó el potencial carcinogénico de palmitato de paliperidona inyectado por vía intramuscular en ratas. Se constató un aumento estadísticamente significativo en los adenocarcinomas de las glándulas mamarias en las ratas hembras a dosis de 10, 30 y 60 mg/kg/mes. Las ratas macho mostraron un aumento estadísticamente significativo de los adenomas y carcinomas de las glándulas mamarias a las dosis de 30 y 60 mg/kg/mes, que equivalen a 1,2 y 2,2 veces el nivel de exposición en humanos a la dosis máxima recomendada de 150 mg. Estos tumores pueden estar relacionados con el antagonismo prolongado de la dopamina D2 y con la hiperprolactinemia. Se desconoce la trascendencia de estos hallazgos tumorales en roedores para el riesgo en seres humanos. **6. DATOS FARMACÉUTICOS. 6.1. Lista de excipientes.** Polisorbato 20. Polietilenglicol 4000. Ácido cítrico monohidrato. Fosfato ácido disódico anhidro. Fosfato diácido de sodio monohidratado. Hidróxido de sodio (para ajuste del pH). Agua para preparaciones inyectables. **6.2. Incompatibilidades.** Este medicamento no debe mezclarse con otros medicamentos. **6.3. Periodo de validez.** 2 años. **6.4. Precauciones especiales de conservación.** No conservar a temperatura superior a 30°C. **6.5. Naturaleza y contenido del envase.** Jeringa precargada (cíclico-olefina-copolímero) con un tapón de tipo émbolo, tope trasero y un protector para la punta (goma de bromobutilo) con una aguja de seguridad del calibre 22 de 1½ pulgadas (0,72 mm x 38,1 mm) y una aguja de seguridad del calibre 23 de 1 pulgada (0,64 mm x 25,4 mm). Tamaños de envase: El envase contiene 1 jeringa precargada y 2 agujas. **Presentaciones y precios.** XEPLION 50 mg suspensión inyectable de liberación prolongada: PVL: 197,72 €; PVP: 243,63 €; PVP (IVA): 253,38 €. XEPLION 75 mg suspensión inyectable de liberación prolongada: PVL: 287,86 €; PVP: 338,77 €; PVP (IVA): 352,32 €. XEPLION 100 mg suspensión inyectable de liberación prolongada: PVL: 345,43 €; PVP: 396,34 €; PVP (IVA): 412,19 €. XEPLION 150 mg suspensión inyectable de liberación prolongada: PVL: 449,06 €; PVP: 499,97 €; PVP (IVA): 519,97 €. **Condiciones de prescripción y dispensación.** Con receta médica. Aportación reducida. Con visado de inspección para pacientes mayores de 75 años. **6.6. Precauciones especiales de eliminación.** La eliminación del medicamento no utilizado y de todos los materiales que hayan estado en contacto con él, se realizará de acuerdo con la normativa local. **7. TITULAR DE LA AUTORIZACIÓN DE COMERCIALIZACIÓN.** Janssen-Glag International NV. Turnhoutseweg 30. B-2340 Beerse. Bélgica. **8. NÚMERO(S) DE AUTORIZACIÓN DE COMERCIALIZACIÓN.** XEPLION 50 mg: EU/1/11/672/002. XEPLION 75 mg: EU/1/11/672/003. XEPLION 100 mg: EU/1/11/672/004. XEPLION 150 mg: EU/1/11/672/005. **9. FECHA DE LA PRIMERA AUTORIZACIÓN/RENOVACIÓN DE LA AUTORIZACIÓN.** 04 de marzo de 2011. **10. FECHA DE LA REVISIÓN DEL TEXTO.** 10/2014. La información detallada de este medicamento está disponible en la página web de la Agencia Europea de Medicamentos http://www.ema.europa.eu.

Bibliografía:

1. Pandina GJ, et al., A randomized, placebo-controlled study to assess the efficacy and safety of 3 doses of paliperidone palmitate in adults with acutely exacerbated schizophrenia. J Clin Psychopharmacol. 2010;30: 235-244.
2. Samtani MN et al. Population Pharmacokinetics of intramuscular paliperidone palmitate in patients with schizophrenia. Clin Pharmacacokinet. 2009; 48 (9): 585-600.
3. Ficha Técnica de Xeplion®.
4. Mesones Peral JE et al. Comparative analysis of the prevention of relapse in psycotic patients following the introduction of Paliperidone Palmitate. XVI Congreso Mundial de Psiquiatría. Madrid, España, 14-18 de septiembre de 2014. Póster 309.
5. Benito A et al. Outcomes económicos del tratamiento con palmitato de paliperidona: Dos años de seguimiento. XVI Congreso Mundial de Psiquiatría. Madrid, España, 14-18 de septiembre de 2014. Póster 393.
6. Jones MP et al. Efficacy and tolerability of paliperidone ER and other oral atypical antipsychotics in schizophrenia.International Journal of Clinical Pharmacology and Therapeutics. 2010; 48 (6): 383-399.
7. Manzano Callejo JM et al. Antipsicóticos atípicos, esquizofrenia y síndrome metabólico. Póster presentado en el XVII Congreso Nacional de Psiquiatría. Sevilla, 2013.
8. Bergmans P, et al. Flexibly dosed paliperidone palmitate in non-acute but symptomatic patients with schizophrenia previously unsuccessfully treated with long-acting injectable risperidone. Póster presentado en el Congreso DGPPN, 27-30 de noviembre de 2013, Berlín, Alemania, Póster P003 (sesión P-06).
9. Montalvo I et al. Changes in prolactin levels and sexual function in young psychotic patients after switching from long-acting injectable risperidone to paliperidone palmitate. Int Clin Psychophacol. 2012; 28: 46.49.
10. Schreiner A. Paliperidone palmitate in acute patients with schizophrenia - Treatment response, safety and tolerability: a prospective flexible dose study in patients previously unsuccessfully treated with oral antipsychotics. Póster presentado en congreso internacional del Royal College of Psychiastrists, 2-5 de julio de 2013, Edimburgo, Reino Unido.
11. Vázquez JM, et al. Evolución de la Brief Psychiatric Rating Scale (BPRS) y la UdvalgfürKliniskeUndersogelser (UKU) en pacientes con trastorno por uso de sustancias y diagnóstico adicional en el espectro psicótico: "Palmitato de Paliperidona versus antipsicóticos orales / R.I.L.". Póster presentado en el XVII Congreso Nacional de Psiquiatría. Sevilla, 2013.
12. Schreiner A, et al. Paliperidone palmitate - Impact on negative, disorganized and depressive symptoms, subjective well-being and patient satisfaction in non-acute patients with schizophrenia previously unsuccessfully treated with oral antipsychotics. Póster presentado en el congreso DGPPN, 27-30 de noviembre de 2013, Berlín, Alemania, póster P006 (sesión P-08).
13. Hargarter L, et al. Functional outcomes with once monthly paliperidone palmitate in acute and non-acute patients with schizophrenia: data from a prospective fexible dose study in patients with schizophrenia previously unsuccessfully treated with oral antipsychotics. Póster presentado en el congreso del Royal College of Psychiastrists's International, 2-5 de julio de 2013, Edimburgo, Reino Unido.

Reducir para ganar

Único fármaco indicado para la reducción del consumo de alcohol[2]

(2) Ficha técnica Selincro 2013

Lundbeck

Selincro®
nalmefeno

Ficha técnica

Selincro® nalmefeno

▼Este medicamento está sujeto a seguimiento adicional, lo que agilizará la detección de nueva información sobre su seguridad. Se invita a los profesionales sanitarios a notificar las sospechas de reacciones adversas. Ver la sección 4.8, en la que se incluye información sobre cómo notificarlas. **1. NOMBRE DEL MEDICAMENTO** Selincro 18 mg comprimidos recubiertos con película. **2. COMPOSICIÓN CUALITATIVA Y CUANTITATIVA** Cada comprimido recubierto con película contiene 18,06 mg de nalmefeno (como dihidrato de hidrocloruro). Excipiente con efecto conocido: cada comprimido recubierto con película contiene 60,68 mg de lactosa. Para consultar la lista completa de excipientes, ver sección 6.1. **3. FORMA FARMACÉUTICA** Comprimido recubierto con película (comprimido). Comprimido recubierto con película de color blanco, ovalado, biconvexo, de 6,0 x 8,75 mm y grabado con "S" en una cara. **4. DATOS CLÍNICOS 4.1 Indicaciones terapéuticas** Selincro está indicado para la reducción del consumo de alcohol en pacientes adultos con dependencia del alcohol que presentan un nivel de consumo de alcohol de alto riesgo (NCR) [ver sección 5.1], sin síntomas de abstinencia físicos y que no requieran una desintoxicación inmediata. Selincro solo se debe prescribir junto con apoyo psicosocial mantenido dirigido a incrementar la adherencia al tratamiento y a reducir el consumo de alcohol. El tratamiento con Selincro se debe iniciar únicamente en los pacientes que mantienen un NCR alto dos semanas después de la evaluación inicial. **4.2 Posología y forma de administración** Posología En la visita inicial, se deben evaluar el estado clínico, la dependencia del alcohol y el nivel de consumo de alcohol del paciente (según el paciente). Por lo tanto, se debe solicitar al paciente que registre su consumo de alcohol durante aproximadamente dos semanas. En la siguiente visita, se puede iniciar el tratamiento con Selincro en los pacientes que mantienen un NCR alto, (ver sección 5.1) durante este periodo de dos semanas, junto con una intervención psicosocial dirigida a incrementar la adherencia al tratamiento y a reducir el consumo de alcohol. Durante los ensayos clínicos pivotales la principal mejoría se observó durante las 4 primeras semanas. Se debe evaluar la respuesta del paciente al tratamiento y la necesidad de mantener farmacoterapia con regularidad (p. ej., mensualmente) (ver sección 5.1). El médico debe seguir evaluando la evolución del paciente en cuanto a la reducción del consumo de alcohol, el funcionamiento general, la adherencia al tratamiento y los posibles efectos adversos. Se dispone de datos clínicos para el uso de Selincro en condiciones controladas y aleatorizadas para un periodo de 6 a 12 meses. Se recomienda precaución al prescribir Selincro durante más de 1 año. Selincro se toma a demanda: cada día que el paciente perciba un riesgo anticipado de consumo de alcohol debe tomar un comprimido, preferiblemente 1-2 horas antes del momento de consumo. Si el paciente ha empezado a beber alcohol sin haber tomado Selincro, el paciente debería tomar un comprimido lo antes posible. La dosis máxima de Selincro es un comprimido al día. Selincro se puede tomar con o sin alimentos (ver sección 5.2). *Poblaciones especiales Población de edad avanzada (≥ 65 años de edad)* No se recomienda el ajuste de la dosis para este grupo de pacientes (ver secciones 4.4 y 5.2). *Insuficiencia renal* No se recomienda el ajuste de la dosis para los pacientes con insuficiencia renal leve o moderada (ver secciones 4.4 y 5.2). *Insuficiencia hepática* No se recomienda el ajuste de la dosis para los pacientes con insuficiencia hepática leve o moderada (ver secciones 4.4 y 5.2). *Población pediátrica* No se ha establecido la seguridad y eficacia de Selincro en niños y adolescentes de < 18 años. No se dispone de datos (ver sección 5.1). Forma de administración Selincro es un medicamento que se administra por vía oral. El comprimido recubierto con película se debe tragar entero. El comprimido recubierto con película no se debe dividir ni aplastar porque el nalmefeno puede provocar sensibilización cutánea en contacto directo con la piel (ver sección 5.3). **4.3 Contraindicaciones** Hipersensibilidad al principio activo o a alguno de los excipientes incluidos en la sección 6.1. Pacientes en tratamiento con analgésicos opioides. Pacientes con una actual o reciente adicción a opiáceos. Pacientes con síntomas agudos de abstinencia de opiáceos. Pacientes con sospecha de uso reciente de opiáceos.Pacientes con insuficiencia hepática grave (clasificación de Child-Pugh). Pacientes con insuficiencia renal grave (eGFR < 30 ml/min por 1,73 m2). Pacientes con historia reciente de síndrome de abstinencia del alcohol agudo (incluyendo alucinaciones, convulsiones y delirium tremens). **4.4 Advertencias y precauciones especiales de empleo** Selincro no está indicado en pacientes cuyo objetivo terapéutico sea la abstinencia inmediata. La reducción del consumo de alcohol es un objetivo intermedio en el camino hacia la abstinencia. Administración de opiáceos En una situación de urgencia en la que se deban administrar opiáceos a un paciente que toma Selincro, la cantidad de opiáceo requerida para lograr el efecto deseado puede ser superior a la habitual. El paciente se debe someter a un estricto control para detectar síntomas de depresión respiratoria como consecuencia de la administración de opiáceos, así como otras reacciones adversas. Si se precisan opiáceos en una urgencia, la dosis siempre se debe ajustar de forma individual. Si se requieren dosis excepcionalmente altas, será necesaria una estrecha observación.El tratamiento con Selincro se debe interrumpir temporalmente 1 semana antes del uso previsto de opiáceos (p. ej., cuando se vayan a utilizar analgésicos opioides en una intervención quirúrgica programada). El médico prescriptor deberá advertir a los pacientes de la importancia de informar a su médico de la última toma de Selincro en caso de que sea necesario el uso de opiáceos. Se debe tener precaución cuando se utilicen medicamentos que contengan opiáceos (p. ej., antitusígenos, analgésicos opioides (ver sección 4.5)). Comorbilidad *Trastornos psiquiátricos* Se han registrado efectos psiquiátricos en estudios clínicos (ver sección 4.8). Si los pacientes presentan síntomas psiquiátricos no asociados al inicio del tratamiento con Selincro, y/o que no son transitorios, el médico prescriptor deberá considerar otras causas de los síntomas y valorar la necesidad de continuar el tratamiento con Selincro. Selincro no se ha investigado en pacientes con enfermedad psiquiátrica inestable. Se debe proceder con precaución al prescribir Selincro a pacientes con comorbilidad psiquiátrica presente como el trastorno depresivo mayor.*Trastornos convulsivos* Se dispone de experiencia limitada en pacientes con antecedentes de trastornos convulsivos, incluidas las convulsiones por abstinencia de alcohol. Se recomienda precaución si se inicia un tratamiento para reducir el consumo de alcohol en estos pacientes. *Insuficiencia renal o hepática* Selincro se metaboliza principalmente en el hígado y se elimina predominantemente por la orina. Por lo tanto, se debe tener precaución cuando se prescriba Selincro a pacientes con insuficiencia renal o hepática leve o moderada, por ejemplo, realizando controles más frecuentes. Se debe proceder con precaución al prescribir Selincro a pacientes con valores altos de ALAT o ASAT (> 3 veces el LSN), ya que estos pacientes fueron excluidos del programa de desarrollo clínico. Pacientes de edad avanzada (≥ 65 años de edad) Se dispone de datos clínicos limitados sobre el uso de Selincro en pacientes ≥ 65 años de edad con dependencia del alcohol. Se debe tener precaución al prescribir Selincro a pacientes ≥ 65 años de edad (ver secciones 4.2 y 5.2). Otras Se recomienda precaución si Selincro se administra conjuntamente con un inhibidor potente de la enzima UGT2B7 (ver sección 4.5). Lactosa Los pacientes con intolerancia hereditaria a galactosa, insuficiencia de lactasa de Lapp o problemas de malabsorción de glucosa o galactosa no deben tomar este medicamento. **4.5 Interacción con otros medicamentos y otras formas de interacción** No se han llevado a cabo estudios de interacción farmacológica *in vivo*. Según estudios *in vitro*, no se prevén interacciones clínicamente relevantes entre el nalmefeno, o sus metabolitos, y medicamentos administrados simultáneamente metabolizados por las enzimas más comunes CYP450 y UGT o transportadores de membrana. La administración conjunta con medicamentos que sean inhibidores potentes de la enzima UGT2B7 (p. ej., diclofenaco, fluconazol, acetato de medroxiprogesterona, ácido meclofenámico) puede aumentar significativamente la exposición a nalmefeno. Es improbable que esto suponga un problema con el uso ocasional, pero si se inicia un tratamiento a largo plazo simultáneo con un inhibidor potente de la UGT2B7, no se puede descartar la posibilidad de un aumento en la exposición a nalmefeno (ver sección 4.4). Por el contrario, la administración conjunta con un inductor de la UGT (p. ej., dexametasona, fenobarbital, rifampicina, omeprazol) puede dar lugar a concentraciones plasmáticas subterapéuticas de nalmefeno. Si se toma Selincro de manera simultánea con agonistas opioides (p. ej., algunos tipos de antitusígenos y antigripales, determinados antidiarreicos, y analgésicos opioides), puede que el paciente no se beneficie del agonista opioide. No existe ninguna interacción farmacocinética clínicamente relevante entre el nalmefeno y el alcohol. Se produce un pequeño deterioro en la función cognitiva y psicomotora tras la administración de nalmefeno. No obstante, el efecto de la combinación de nalmefeno y alcohol no superó la suma de los efectos de cada uno de ellos por separado.El consumo simultáneo de alcohol y Selincro no previene los efectos de la intoxicación del alcohol. **4.6 Fertilidad, embarazo y lactancia** Embarazo No hay datos o estos son limitados (menos de 300 resultados en embarazos) relativos al uso de nalmefeno en mujeres embarazadas. Los estudios en animales han mostrado toxicidad en la reproducción (ver sección 5.3). No se recomienda Selincro durante el embarazo. Lactancia Los datos farmacodinámicos/toxicológicos disponibles en animales muestran que nalmefeno/metabolitos se excretan en la leche (ver sección 5.3). Se desconoce si nalmefeno se excreta en la leche materna. No se puede excluir el riesgo en recién nacidos/lactantes. Se debe decidir si es necesario interrumpir la lactancia o interrumpir/abstenerse de iniciar el tratamiento con Selincro tras considerar el beneficio de la lactancia para el niño y el beneficio del tratamiento para la madre. Fertilidad En estudios de fertilidad en ratas, no se observaron efectos de nalmefeno sobre la fertilidad, el apareamiento, el embarazo o los parámetros espermáticos. **4.7 Efectos sobre la capacidad para conducir y utilizar máquinas** No se ha estudiado la influencia de nalmefeno sobre la capacidad para conducir y utilizar máquinas. Selincro puede provocar reacciones adversas como náuseas, mareo, insomnio y cefalea. La mayoría de estas reacciones fueron leves o moderadas, relacionadas con el inicio del tratamiento y tuvieron una corta duración. La influencia de Selincro sobre la capacidad para conducir y utilizar máquinas es nula o insignificante. **4.8 Reacciones adversas** Resumen del perfil de seguridad Más de 3.000 pacientes han sido expuestos a nalmefeno en estudios clínicos. En general, el perfil de seguridad concuerda en todos los estudios clínicos realizados. Las frecuencias de las reacciones adversas en la Tabla 1 se calcularon basándose en tres estudios aleatorizados, a doble ciego y controlados con placebo en pacientes con dependencia del alcohol (1.144 pacientes expuestos a Selincro a demanda y 797 expuestos a placebo a demanda). Las reacciones adversas más frecuentes fueron náuseas, mareo, insomnio y cefalea. La mayoría de estas reacciones fueron leves o moderadas, estuvieron relacionadas con el inicio del tratamiento y tuvieron una corta duración.En los estudios clínicos se comunicaron estados confusionales y, en raras ocasiones, alucinaciones y disociación. La mayoría de estas reacciones fueron leves o moderadas, estuvieron relacionadas con el inicio del tratamiento y tuvieron una corta duración (de unas pocas horas a unos pocos días). La mayoría de estas reacciones adversas se resolvieron con el tratamiento continuo y no recurrieron con la administración repetida. Si bien estos acontecimientos tuvieron generalmente una corta duración, podrían tratarse de psicosis alcohólica, síndrome de abstinencia alcohólica o enfermedad psiquiátrica comórbida.Tabla de reacciones adversas Las frecuencias se definen como: muy frecuentes (≥1/10), frecuentes (≥1/100 a <1/10), poco frecuentes (≥1/1.000 a <1/100), raras (≥1/10.000 a <1/1.000), muy raras (<1/10.000) o frecuencia no conocida (no puede estimarse a partir de los datos disponibles). Notificación de sospechas de reacciones adversas Es importante notificar sospechas de reacciones adversas al medicamento tras su autorización. Ello permite una

Tabla 1. Frecuencias de las reacciones adversas

Sistema de clasificación de órganos	*Frecuencia*	*Reacción adversa*
Trastornos del metabolismo y de la nutrición	Frecuente	Apetito disminuido
Trastornos psiquiátricos	Muy frecuente	Insomnio
	Frecuente	Trastorno del sueño
		Estado confusional
		Inquietud
		Libido disminuida (incluida la pérdida de líbido)
	No conocida	Alucinación (incluidas alucinaciones auditivas, alucinaciones táctiles, alucinaciones visuales y alucinaciones somáticas)
		Disociación
Trastornos del sistema nervioso	Muy frecuente	Mareo
		Cefalea
	Frecuente	Somnolencia
		Temblor
		Alteración de la atención
		Parestesia
		Hipoestesia
Trastornos cardiacos	Frecuente	Taquicardia
		Palpitaciones
Trastornos gastrointestinales	Muy frecuente	Náuseas
	Frecuente	Vómitos
		Boca seca
Trastornos de la piel y del tejido subcutáneo	Frecuente	Hiperhidrosis
Trastornos musculoesqueléticos y del tejido conjuntivo	Frecuente	Espasmos musculares
Trastornos generales y alteraciones en el lugar de administración	Frecuente	Fatiga
		Astenia
		Malestar general
		Sensación anormal
Exploraciones complementarias	Frecuente	Peso disminuido

supervisión continuada de la relación beneficio/riesgo del medicamento. Se invita a los profesionales sanitarios a notificar las sospechas de reacciones adversas a través del sistema Español de Farmacovigilancia de medicamentos de Uso Humano: https://www.notificaran.es. **4.9 Sobredosis** En un estudio en pacientes diagnosticados de ludopatía, se investigaron dosis de nalmefeno de hasta 90 mg/día durante 16 semanas. En un estudio en pacientes con cistitis intersticial, 20 pacientes recibieron 108 mg/día de nalmefeno durante más de 2 años. Se ha registrado la toma de una dosis única de 450 mg de nalmefeno sin cambios en la tensión arterial, la frecuencia cardiaca y respiratoria o la temperatura corporal. No se ha observado un patrón atípico de reacciones adversas en estos contextos, si bien la experiencia es limitada. En caso de sobredosis, se recomienda realizar un tratamiento sintomático y someter al paciente a observación. **5. PROPIEDADES FARMACOLÓGICAS 5.1 Propiedades farmacodinámicas** Grupo farmacoterapéutico: Otros fármacos del sistema nervioso utilizados en la dependencia del alcohol. Código ATC: N07BB05 Mecanismo de acción El nalmefeno es un modulador del sistema opioide con un perfil definido de receptores μ, δ y κ. - Estudios *in vitro* han demostrado que el nalmefeno es un ligando selectivo de los receptores opioides con actividad antagonista en los receptores μ y δ y actividad agonista parcial en el receptor κ. - Estudios *in vivo* han demostrado que el nalmefeno reduce el consumo de alcohol, posiblemente como resultado de la modulación de las funciones corticomesolímbicas. Los datos de estudios no clínicos, estudios clínicos y literatura médica no indican ninguna forma de posible dependencia o abuso de Selincro. Eficacia clínica y seguridad En dos estudios de eficacia se evaluó la eficacia de Selincro en la reducción del consumo de alcohol en pacientes con dependencia del alcohol (DSM-IV). Se excluyó a los pacientes con antecedentes de delirium tremens, alucinaciones, convulsiones, comorbilidad psiquiátrica significativa, o alteraciones significativas de la función hepática así como a aquellos que presentaban síntomas de abstinencia físicos apreciables en la selección o la aleatorización. La mayoría (80%) de los pacientes incluidos tenían un NCR alto o muy alto (consumo de alcohol > 60 g/día en hombres y > 40 g/día en mujeres según los NCR de alcohol de la OMS) en la selección, y de estos el 65% mantuvieron un NCR alto o muy alto entre la selección y la aleatorización. Ambos estudios fueron aleatorizados, a doble ciego, con grupos paralelos y controlados con placebo, y al cabo de 6 meses de tratamiento, los pacientes que recibieron Selincro se volvieron a aleatorizar para recibir placebo o Selincro durante un periodo de lavado final de 1 mes. La eficacia de Selincro también se evaluó en un estudio aleatorizado, a doble ciego, con grupos paralelos, controlado con placebo y de 1 año de duración. En conjunto, en los estudios participaron 1.941 pacientes, de los cuales 1.144 fueron tratados con Selincro 18 mg a demanda. En la visita inicial se evaluaron el estado clínico, la situación social y el patrón de consumo de alcohol de los pacientes (según la información del paciente). En la visita de aleatorización, que tuvo lugar al cabo de 1 a 2 semanas se reevaluó el NCR, y se inició el tratamiento con Selincro junto con una intervención psicosocial (BRENDA) dirigida a incrementar la adherencia al tratamiento y a reducir el consumo de alcohol. Selincro se prescribió a demanda, y los pacientes lo tomaron, de promedio, aproximadamente la mitad de los días. La eficacia de Selincro se evaluó utilizando dos criterios de valoración principales: el cambio desde la visita basal al mes 6 en el número de días de consumo excesivo de alcohol (DCE) al mes y el cambio desde la visita basal al mes 6 en el consumo de alcohol total diario (CAT). Un DCE se definió como un día con un consumo ≥ 60 g de alcohol puro en hombres y ≥ 40 g en mujeres. Se produjo una reducción significativa del número de DCE y CAT en algunos pacientes en el periodo entre la visita inicial (selección) y la aleatorización debido a efectos no farmacológicos. En los estudios 1 (n = 579) y (n = 655) 2, el 18% y el 33% de la población total, respectivamente, redujeron considerablemente su consumo de alcohol en el periodo comprendido entre la selección y la aleatorización. Con respecto a los pacientes con un NCR alto o muy alto en la visita basal, el 35% de los pacientes experimentaron mejorías debido a los efectos no farmacológicos en el período entre la visita inicial (selección) y la aleatorización. En la aleatorización, estos pacientes consumían una cantidad tan baja de alcohol que era poco el margen para seguir mejorando (efecto suelo). Por lo tanto, los pacientes que mantuvieron un NCR alto o muy alto en la aleatorización se definieron a posteriori como la población objetivo. En esta población post hoc, el efecto terapéutico fue mayor en comparación con el de la población total. La eficacia y relevancia clínicas de Selincro se analizaron en pacientes con un NCR alto o muy alto en la selección y la aleatorización. En la visita basal, los pacientes tenían, de promedio, 23 DCE al mes (11% de los pacientes tenían menos de 14 DCE al mes) y consumían 106 g/día. La mayoría de los pacientes tenían una dependencia del alcohol baja (55% con una puntuación de 0 a 13) o intermedia (36% con una puntuación de 14 a 21) según la Escala de Dependencia de Alcohol. *Análisis post-hoc de la eficacia en pacientes que mantuvieron un NCR alto o muy alto en la aleatorización* En el estudio 1, el porcentaje de abandonos fue más elevado en el grupo de Selincro que en el grupo de placebo (50% frente a 32%, respectivamente). En cuanto a los DCE, se registraron 23 días/mes en la visita basal en el grupo de Selincro (n = 171) y 23 días/mes en la visita basal en el grupo de placebo (n = 167). Respecto a los pacientes que continuaron en el estudio y proporcionaron datos de eficacia en el mes 6, el número de DCE fue de 9 días/mes en el grupo de Selincro (n = 85) y 14 días/mes en el grupo de placebo (n = 114). El CAT fue de 102 g/día en la visita basal en el grupo de Selincro (n = 171) y 99 g/día en la visita basal en el grupo de placebo (n = 167). Respecto a los pacientes que continuaron en el estudio y proporcionaron datos de eficacia en el mes 6, el CAT fue de 40 g/día en el grupo de Selincro (n = 85) y 57 g/día en el grupo de placebo (n = 114). En el estudio 2, el porcentaje de abandonos fue superior en el grupo de Selincro que en el grupo de placebo (30% frente a 28%, respectivamente). En cuanto a los DCE, se registraron 23 días/mes en la visita basal en el grupo de Selincro (n = 148) y 22 días/mes en la visita basal en el grupo de placebo (n = 155). Respecto a los pacientes que continuaron en el estudio y proporcionaron datos de eficacia en el mes 6, el número de DCE fue de 10 días/mes en el grupo de Selincro (n = 103) y 12 días/mes en el grupo de placebo (n = 111). El CAT fue de 113 g/día en la visita basal en el grupo de Selincro (n = 148) y 108 g/día en la visita basal en el grupo de placebo (n = 155). Respecto a los pacientes que continuaron en el estudio y proporcionaron datos de eficacia en el mes 6, el CAT fue de 44 g/día en el grupo de Selincro (n = 103) y 52 g/día en el grupo de placebo (n = 111). Los análisis de respondedores con los datos agrupados de los dos estudios se incluyen en la Tabla 2. Se dispone de datos limitados sobre Selincro en el periodo de lavado final de 1 mes. *Estudio de 1 año* En este estudio participaron un total de 665 pacientes: 52% de ellos tenían un NCR alto o muy alto en la visita basal, y de estos el 52% (que representan el 27% de la población total) siguieron teniendo un NCR alto o muy alto en la aleatorización. En esta población objetivo post-hoc, abandonaron más pacientes que recibían nalmefeno (45%) que aquellos que recibían placebo (31%). En cuanto a los DCE, se registraron 19 días/mes en la visita basal en el grupo de Selincro (n = 141) y 19 días/mes en la visita basal en el grupo de placebo (n = 42). Respecto a los pacientes que continuaron en el estudio y proporcionaron datos de eficacia al cabo de 1 año, el número de DCE fue de 5 días/mes en el grupo de Selincro (n = 78) y 10 días/mes en el grupo de placebo (n = 29) E l CAT fue de 100 g/día en la visita basal en el grupo de Selincro (n = 141) y 101 g/día en la visita basal en el grupo de placebo (n = 42). Respecto a los pacientes que continuaron en el estudio y proporcionaron datos de eficacia al cabo de un año, el CAT fue de 24 g/día en el grupo de Selincro (n = 78) y 47 g/día en el grupo de placebo (n = 29). Población pediátrica La Agencia Europea de Medicamentos ha eximido al titular de la obligación de presentar los resultados de los ensayos realizados con Selincro en los diferentes grupos de la población pediátrica en el tratamiento de la dependencia del alcohol (ver sección 4.2 para consultar la información sobre el uso en la población pediátrica). **5.2 Propiedades farmacocinéticas** Absorción El nalmefeno se absorbe rápidamente tras una única administración oral de 18,06 mg, con una concentración máxima (Cmax) de 16,5 ng/ml al cabo de aproximadamente 1,5 horas, y una exposición (AUC) de 131 ng*h/ml. La biodisponibilidad oral absoluta de nalmefeno es del 41%. La administración de alimentos ricos en grasas aumenta la exposición total (AUC) en un 30% y la concentración máxima (Cmax) en un 50%; el tiempo hasta la concentración máxima (tmax) se retrasa 30 minutos (tmax es de 1,5 horas). Se considera poco probable que este cambio tenga relevancia clínica. Distribución La fracción media de nalmefeno unida a proteínas en plasma es de aproximadamente el 30%. El volumen de distribución (Vd/F) estimado es de aproximadamente 3200 l. Los datos de ocupación obtenidos en un estudio PET tras la administración diaria única y repetida de 18,06 mg de nalmefeno muestran un 94-100% de ocupación de los receptores 3 horas después de la administración, lo que indica que el nalmefeno atraviesa fácilmente la barrera hematoencefálica. Biotransformación Tras la administración oral, el nalmefeno sufre un extenso y rápido metabolismo para formar su principal metabolito, el nalmefeno-3-O-glucurónido, siendo la enzima UGT2B7 la principal responsable de la conversión, y con las enzimas UGT1A3 y UGT1A8 como factores contribuyentes secundarios. Un pequeño porcentaje de nalmefeno se convierte en nalmefeno-3-O-sulfato por sulfatación y en nornalmefeno por CYP3A4/5. El nornalmefeno se convierte posteriormente en nornalmefeno 3 O glucurónido y nornalmefeno-3-O-sulfato. Se considera que los metabolitos no contribuyen con un efecto farmacológico significativo sobre los receptores opioides en humanos, salvo en el caso de nalmefeno-3-O-sulfato, que posee una potencia comparable a la de nalmefeno. No obstante, el nalmefeno-3-O-sulfato está presente a concentraciones inferiores al 10% de la de nalmefeno, por lo que es muy poco probable que constituya un factor contribuyente principal en el efecto farmacológico de nalmefeno. Eliminación El metabolismo por conjugación del glucurónido es el principal mecanismo de aclaramiento de nalmefeno, y la excreción renal es la principal vía de eliminación de nalmefeno y sus metabolitos. El 54% de la dosis total se elimina por la orina en forma de nalmefeno-3-O-glucurónido, mientras que el nalmefeno y sus otros metabolitos están presentes en la orina en cantidades inferiores al 3% cada uno. Se calcula que el aclaramiento oral de nalmefeno (CL/F) es de 169 l/h y la semivida de eliminación de 12,5 horas. De los datos de distribución, metabolismo y eliminación se desprende que el nalmefeno tiene un coeficiente de extracción hepática elevado. Linealidad/No linealidad El nalmefeno muestra un perfil farmacocinético lineal independiente de la dosis en el intervalo de dosis de 18,06 mg a 72,24 mg, con un aumento de 4,4 veces en la Cmax y un aumento de 4,3 veces en el AUCo-tau (en estado estacionario o casi). El nalmefeno no muestra diferencias farmacocinéticas importantes entre sexos, entre jóvenes y ancianos, o entre diferentes grupos étnicos. Sin embargo, el tamaño corporal parece afectar mínimamente al aclaramiento de nalmefeno (el aclaramiento aumenta cuanto mayor es el tamaño corporal), si bien se considera poco probable que tenga relevancia clínica. Insuficiencia renal No se dispone de datos tras la administración oral en pacientes con insuficiencia renal. La administración IV de 1 mg de nalmefeno en pacientes con insuficiencia renal grave produjo una exposición 1,6 veces mayor (AUCinf ajustada por dosis), y una menor Cmax (en un factor de aproximadamente 2,1 a 4,6) que en voluntarios sanos. La semivida de eliminación (26 horas) fue más larga que la de los voluntarios sanos (10 horas) (ver secciones 4.3 y 4.4). Insuficiencia hepática La administración de una dosis única de 18,06 mg de nalmefeno a los pacientes con insuficiencia hepática leve o moderada aumentó la exposición respecto a la de los voluntarios sanos. En pacientes con insuficiencia hepática leve, la exposición aumentó 1,5 veces y el aclaramiento oral se redujo en aproximadamente un 35%. En pacientes con insuficiencia hepática moderada, la exposición aumentó 2,9 veces para el AUC y 1,7 veces para la Cmax, mientras que el aclaramiento oral se redujo en cerca del 60%. No se observaron cambios clínicamente relevantes en el tmax o la semivida de eliminación en ninguno de los grupos. No se dispone de datos farmacocinéticos tras la administración oral de nalmefeno a pacientes con insuficiencia hepática grave (ver secciones 4.3 y 4.4). Pacientes de edad avanzada No se ha realizado ningún estudio específico con administración oral en pacientes de ≥ 65 años. Un estudio con administración IV indicó que no existen cambios relevantes en la farmacocinética en pacientes de edad avanzada en comparación con adultos más jóvenes (ver secciones 4.2 y 4.4). **5.3 Datos preclínicos sobre seguridad** El nalmefeno ha mostrado potencial de sensibilización cutánea en el ensayo de ganglio linfático local en ratones tras la aplicación tópica. Los estudios en animales no sugieren efectos perjudiciales directos con respecto a la fertilidad, el embarazo, el desarrollo embrionario o fetal, el parto o el desarrollo posnatal. En un estudio de toxicidad para el desarrollo realizado en conejos, se observaron efectos en los fetos en términos de reducción de peso fetal y retraso en la osificación, pero no anomalías graves. La AUC a dosis máximas sin efecto adverso observado (NOAEL), para estos efectos fue inferior a la exposición en humanos a la dosis clínica recomendada. Se observó un aumento de la viabilidad natal y una disminución de la viabilidad posnatal de las crías en estudios de toxicidad prenatal y posnatal en ratas. Este efecto se consideró un efecto indirecto relacionado con la toxicidad materna. Los estudios en ratas han mostrado excreción de nalmefeno o sus metabolitos en leche. Los datos no clínicos no muestran riesgos especiales para los seres humanos según los estudios convencionales de farmacología de seguridad, toxicidad a dosis repetidas, genotoxicidad o potencial carcinogénico. **6. DATOS FARMACÉUTICOS 6.1 Lista de excipientes** Núcleo del comprimido. Celulosa microcristalina. Lactosa anhidra. Crospovidona, tipo A. Estearato de magnesio. Recubrimiento del comprimido. Hipromelosa. Macrogol 400. Dióxido de titanio (E171). **6.2 Incompatibilidades** No procede. **6.3 Periodo de validez** 3 años. **6.4 Precauciones especiales de conservación** Este medicamento no requiere condiciones especiales de conservación. **6.5 Naturaleza y contenido del envase** Blísters transparentes de PVC/PVdC/aluminio en cajas de cartón. Tamaños de envases de 7, 14, 28, 42, 49 y 98 comprimidos recubiertos con película. Puede que solamente estén comercializados algunos tamaños de envases. **6.6 Precauciones especiales de eliminación** La eliminación del medicamento no utilizado y de todos los materiales que hayan estado en contacto con él se realizará de acuerdo con la normativa local. **7. TITULAR DE LA AUTORIZACIÓN DE COMERCIALIZACIÓN** H. Lundbeck A/S Ottiliavej 9 DK-2500 Valby Dinamarca **8. NÚMERO(S) DE AUTORIZACIÓN DE COMERCIALIZACIÓN** EU/1/12/815/001 7 comprimidos. EU/1/12/815/002 14 comprimidos. EU/1/12/815/003 28 comprimidos. EU/1/12/815/004 42 comprimidos. EU/1/12/815/005 98 comprimidos. EU/1/12/815/006 49 comprimidos. EU/1/12/815/007 14 comprimidos, tarjeta. EU/1/12/815/008 28 comprimidos, tarjeta. **9. FECHA DE LA PRIMERA AUTORIZACIÓN/RENOVACIÓN DE LA AUTORIZACIÓN** Fecha de la primera autorización: 25 de Febrero de 2013. **10. PRESENTACIÓN Y PRECIO PVP (IVA)** Selincro 18 mg, envase con 14 comprimidos. P.V.P 63,04€ P.V.P iva 65,57€ **11. CONDICIONES DE DISPENSACIÓN POR LA SEGURIDAD SOCIAL** Con receta médica. Especialidad reembolsable por el Sistema Nacional de Salud. Con visado de inspección. Cícero de aportación reducida. **12. FECHA DE LA REVISIÓN DEL TEXTO:** 11/2014. La información detallada de este medicamento está disponible en la página web de la Agencia Europea de Medicamentos http://www.ema.europa.eu/.

Tabla 2 Resultados de los análisis de respondedores con datos agrupados de pacientes con un NCR alto o muy alto en la selección y la aleatorización

Respuesta[a]	*Placebo*	*Nalmefeno*	*Odds ratio (IC del 95%)*	*Valor p*
CAT R70[b]	**19,9%**	**25,4%**	**1,44 (0,97; 2,13)**	**0,067**
0-4 DCE[c]	**16,8%**	**22,3%**	**1,54 (1,02; 2,35)**	**0,040**

a En el análisis se trata a los pacientes que abandonaron como no respondedores.
b Reducción del CAT ≥ 70% respecto al valor basal en el mes 6 (periodo de 28 días).
c De 0 a 4 DCE/mes en el mes 6 (periodo de 28 días)

Reducir para ganar

Único fármaco indicado para la reducción del consumo de alcohol[2]

(2) Ficha técnica Selincro 2013

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