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Drug and Alcohol Dependence 55 (1999) 117–125

DRUG and ALCOHOL DEPENDENCE

Response patterns of the Spanish version of the 49-item short form of the Addiction Research Center Inventory after the use of sedatives, stimulants, and opioids

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Received 17 July 1998; received in revised form 16 October 1998; accepted 17 November 1998

Abstract

This report examines the validity of the Spanish version of the 49-item short form of the Addiction Research Center Inventory (ARCI) for measuring subjective effects after the use of sedatives, stimulants, and opioids. Data from four clinical trials in which this questionnaire was used have been analyzed. The Spanish ARCI short form was found to be sensitive in measuring subjective effects after the administration of alcohol, triazolam, and flunitrazepam (sedatives), cocaine (stimulants), and morphine, pentazocine, and naloxone (opioids) and to distinguishing among them. The response patterns were similar to those previously reported for the same drugs with the English version of ARCI. It is concluded that Spanish version of the 49-item short form of ARCI is a valid instrument for assessing the subjective effects of psychoactive drugs in the Spanish-speaking population context.

Keywords: Addiction Research Center Inventory (ARCI); Spanish version; Subjective effects; Sedatives; Stimulants; Opioids; Drug abuse

1. Introduction

The classification of drugs and the analysis of abuse liability are closely linked to subjective effects elicited after drug use. The assessment of subjective effects, however, is difficult, not only because these are personal experiences of the individual and therefore not directly accessible to the observer, but also because their description may depend on the private language of users and previous history of drug use. A questionnaire of subjective effects, the Addiction Research Center Inventory (ARCI, Haertzen et al., 1963) was developed to address the problem of the discrepancy of observer/user terminology by constructing the items from empirically validated, solicited responses of former addicts under the influence of various drugs. A series of studies of dose-effects, cross-validation, and test–retest reliability have shown that the complete version ARCI, which consists of 550 true–false items, has a high degree of validity and reliability (Hill et al., 1963).

A short form of ARCI that includes 49 items has also been developed (Martin et al., 1971). It contains five scales: the morphine-benzedrine group (MBG) for the measurement of euphoria, the pentobarbital-chlorpromazine-alcohol group (PCAG) for sedation; the lysergic acid diethylamide specific scale (LSD) for dysphoria, the benzedrine group (BG) which is a stimulant-sensitive scale, and the amphetamine (A) for measuring the effects of *d*-amphetamine. This 49-item short form allows quick administration, repeated measurements, and

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0376-8716/99/$ - see front matter
PII: S0376-8716(98)00185-9

minimum interference with ongoing procedures of pharmacological investigation. It has been successfully used to discriminate among the subjective states induced by psychoactive drugs and to assess the abuse liability that is associated with their consumption (Martin et al., 1971; Jasinski and Henningfield, 1989). This short version has been translated into several languages including French (Warot et al., 1997) and Spanish (Lamas et al., 1994b). In the case of the Spanish version, a preliminary validity study in a population of opiate addicts under drug simulation conditions has been reported (Lamas et al., 1994b). To further validate the Spanish version of the 49-item short form under actual drug conditions, this questionnaire was administered to participants in four different clinical trials, which were conducted to assess the effects of sedatives (alcohol, diazepam, flunitrazepam, and triazolam), stimulants (cocaine, and amphetamine), and opioids (morphine, pentazocine, and the opioid antagonist, naloxone). This report includes data from the four aforementioned studies and describes the pattern response of the Spanish version of ARCI questionnaire to different classes of drugs.

2. Methods

2.1. Study design

This research includes data from four different clinical trials. Three of them have been published previously (Lamas et al., 1994a; Farré et al., 1996, 1997), and one was published as an abstract (Teran et al., 1993). To facilitate cross-drug comparisons, a new statistical analysis of the original data has been performed. This included pairwise contrasts between control group and all other drug conditions.

All studies were randomized, cross-over, double-blind, and placebo controlled. All subjects gave the written informed consent to take part in the study. The protocols were reviewed by the Institutional Ethical Committee and approved by the Spanish Ministry of Health.

Studies 1 and 2 used similar procedures and the same number of male healthy volunteers (10 subjects per study). Study 1 examined the effects of placebo, flunitrazepam 1 and 2 mg, diazepam 5 mg, and *d-l*-amphetamine 10 mg (Teran et al., 1993), whereas study 2 tested the effects of placebo, flunitrazepam 0.5 and 2 mg, and triazolam 0.25 and 0.5 mg (Farré et al., 1996). All drugs were administered as a single dose by the oral route in the form of capsules. Subjects were informed that they may receive a tranquilizer, a stimulant or a placebo, but were not given any specific information as to which of these they were receiving, nor which specific class of drugs or pharmacological agent they were given.

Study 3 was conducted to examine the effects of alcohol, cocaine, and the combination of alcohol and cocaine in eight male healthy subjects with previous experience with intranasal cocaine use and alcohol intoxication (Farré et al., 1997). Alcohol was given as a dose of 0.8 g/kg in a 450 ml drink (vodka and tonic water), ingested over 30 min. Cocaine was given as a 100 mg dose of cocaine hydrochloride in 200 mg of powder (the rest being made up by lactose) that was snorted immediately after the drinking period. At each session, both a drink and a powder were administered, of which none, one, or both were active (double-blind, double-dummy masking).

Study 4 was conducted to examine the agonist/antagonist properties of pentazocine in relation to naloxone and morphine in six opioid dependent male subjects who were maintained on methadone (the daily oral dose of 30 mg of methadone was administered ≈ 20 h before the start of each session, Lamas et al., 1994a). This study was cross-over, double-blind and placebo controlled, but in this case a randomized block method was used to arrange the sessions in the order of ascending doses for safety. In the first block, subjects received placebo, morphine (20 mg), naloxone (0.1 mg), and pentazocine (45 mg). In the second block subjects received morphine (40 and 60 mg), naloxone (0.2 mg), and pentazocine (60 mg). When effects in the first block were so intense as to cause ethical concerns, the study could be discontinued. Drug preparations were made by dilution in sterile physiological saline solution to reach a constant volume of 3 ml and were injected through the intramuscular route. Subjects were told that the purpose of the study was to evaluate the effects of several classes of opioid drugs and that during experimental sessions they would experience effects resembling those of opioid agonists such as heroin or methadone and/or opioid withdrawal symptoms. They were given no other information. All subjects had previous experience with a wide range of drugs of abuse and knew what effects opioid antagonists produce in opioid-dependent individuals. Only 5 of the 8 original drug conditions were used in this analysis (placebo, 40 and 60 mg of morphine, 0.2 mg of naloxone, and 45 mg of pentazocine).

2.2. Subjective effects questionnaires

A Spanish validated version of a shortened 49-item form of the ARCI (Lamas et al., 1994b) was administered to all participants. The five scales were PCAG (a mesure of sedation), MBG (a measure of euphoria), LSD (a measure of dysphoria and somatic symptoms), BG (a stimulant scale consisting mainly of items related to intellectual efficiency and energy), and A (an empirically derived scale sensitive to the effects of *d*-amphetamine).

Table 1
Mean ARCI scores obtained after the administration of different drugs (studies 1–4)[a]

	PCAG	MBG	LSD	BG	A
Study 1 ($n = 10$)					
Flunitrazepam 1 mg	6.100**	2.100	2.200	−0.900	2.000
Flunitrazepam 2 mg	8.100**	2.300	2.800	−4.100*	1.800
Diazepam 5 mg	2.100	1.300	1.100	−0.700	0.600
Amphetamine 10 mg	0.500	1.600	1.000	1.900	2.000
Placebo	1.000	0.200	1.600	−0.700	0.200
Study 2 ($n = 10$)					
Triazolam 0.25 mg	5.200**	−0.500	0.500	−2.700**	0.500
Triazolam 0.5 mg	6.200**	0.400	1.500	−3.200**	0.900
Flunitrazepam 0.5 mg	4.300**	0.700	1.400	−2.000**	0.500
Flunitrazepam 2 mg	8.100**	2.300	3.500*	−4.100**	1.500
Placebo	0.900	0.200	1.100	0.500	0.300
Study 3 ($n = 8$)					
Cocaine 100 mg	0.125	2.750*	1.750	0.625	2.125**
Alcohol 0.8 g/kg	6.125**	0.375	2.500	−2.375	0.250
Placebo	1.625	0.125	−0.250	−0.625	−0.125
Study 4 ($n = 6$)					
Morphine 40 mg	0.500	4.000*	−0.667*	1.333	1.333
Morphine 60 mg	0.000	5.667**	−0.500*	2.167*	2.167
Naloxone 0.2 mg	6.333**	−1.167	8.167**	−4.333	−0.333
Pentazocine 45 mg	5.833*	−1.000	8.000**	−3.833	1.833
Placebo	1.333	−1.167	2.833	−2.000	0.333

[a] Values are peak effects (differences from baseline).
* $P < 0.05$ (post-hoc Dunnett's test).
** $P < 0.01$ (post-hoc Dunnett's test).

The response pattern of the 49-item form of the ARCI was compared with effects rated by subjects on a series of visual analog scales (100 mm) labeled with different adjectives marked at opposite ends with "not at all" and "extremely" (Fischman and Foltin, 1991). Subjects rated effects as "high", "any effect", "good effects", "bad effects", "liking", "feeling good", "sedated", "drowsy", "drunk", and "content". Furthermore, subjects were requested to identify the class of drug that they had received (studies 1, 2, and 4). For this purpose a pharmacological class questionnaire was used, according to which subjects identify the effect of one of 12 classes of psychoactive drugs (with examples of names of common compounds used in Spain) including placebo, opioid agonists, neuroleptics, barbiturates, benzodiazepines, hallucinogens, amphetamine-like stimulants, cocaine, alcohol, cannabinoids, and other as the most similar to that experienced in the experimental session.

2.3. Data analysis

For the purpose of this study, a comparison of active treatment with placebo was made from data of all studies. In study 3, only pure drug conditions were considered in the analysis, so that the combination of alcohol and cocaine was excluded. In study 4, pentazocine 45 mg, naloxone 0.2 mg, and morphine 40 and 60 mg were taken into account. All values were calculated as peak effects (greatest change from baseline regardless of the direction of the change) and analyzed by repeated measures ANOVA. When significant differences were observed post-hoc comparisons with placebo were made by the Dunnett's test. Statistical significance was set at $P < 0.05$.

3. Results

The scores obtained by the different drug conditions on ARCI scales are shown in Table 1.

3.1. PCAG scale

Significant differences among active drugs and placebo were observed for PCAG scale. The dose-response curves for all conditions in PCAG scale are shown in Fig. 1. Post-hoc analysis showed that PCAG scores increased with all studied doses of flunitrazepam (0.5, 1, and 2 mg, $P < 0.01$), with both doses of triazolam (0.25 and 0.5 mg, $P < 0.01$), alcohol ($P < 0.01$), naloxone 0.2 mg ($P < 0.01$) and pentazocine (60 mg) ($P < 0.05$). Results of VAS were similar, i.e. flunitrazepam 2 mg and triazolam 0.5 mg determined a

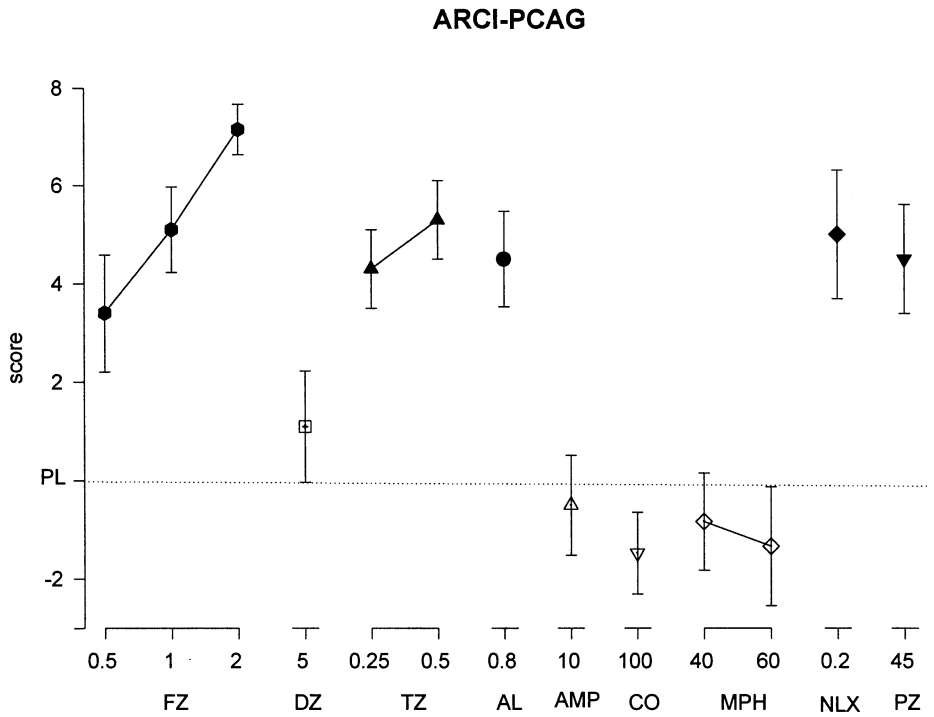

Fig. 1. Peak effects of studied drug conditions on the scale PCAG of the ARCI. Values reported represent the differences between obtained by active drugs and those obtained after placebo administration scores (mean ± S.E.). Filled symbols are presented when differences relative to placebo are significant ($P < 0.05$). Doses shown are in mg, except for alcohol which is in g/kg. Flunitrazepam 2 mg scores are the mean of the two different studies. PL: placebo; FZ: flunitrazepam; DZ: diazepam; TZ: triazolam; AL: alcohol; AMP: amphetamine; CO: cocaine; MPH: morphine; NLX: naloxone; PZ: pentazocine.

statistically significant increase ($P < 0.01$) in the "drowsy" scale, and flunitrazepam 1 and 2 mg in the "sedated" scale. Subjects identified both doses of flunitrazepam as a tranquilizer (90 and 100% of the cases for the 1 and 2 mg doses, respectively) and the high dose of triazolam was identified as a tranquilizer by 70% of subjects.

3.2. MBG scale

The dose–response curves for all conditions in MBG scale are shown in Fig. 2. Scores increased for cocaine ($P < 0.05$) and for both doses of morphine (40 mg, $P < 0.05$, 60 mg, $P < 0.01$). In the VAS, cocaine increased the scales of "high", "good effects", and "liking" ($P < 0.01$), as well as "good effects" after the administration of morphine 60 mg ($P < 0.05$). Both doses of morphine (40 and 60 mg) were correctly classified as an opioid agonist by 4 and 5 subjects, respectively (maximum possible number was 6).

3.3. LSD scale

The dose–response curves for all conditions in the LSD scale are shown in Fig. 3. Significant increases were observed on the LSD scale after flunitrazepam 2 mg ($P < 0.05$), naloxone 0.2 mg ($P < 0.01$), and pentazocine 45 mg ($P < 0.01$). By contrast, morphine decreased LSD scores at both doses, 40 and 60 mg ($P < 0.05$). Flunitrazepam 2 mg increased the VAS scales of "drunken" and "bad effects" ($P < 0.01$), and pentazocine and naloxone increased the "bad effects" scale ($P < 0.01$ and $P < 0.05$, respectively). The 45 mg dose of pentazocine was identified as an opioid antagonist by 2 subjects, as hallucinogen by 2, as stimulant by 1, and alcohol by 1 of the subjects. Also the 0.2 mg dose of naloxone was identified as an opioid antagonist by four of the subjects. One participant classified naloxone as a benzodiazepine and one classified it as alcohol (maximum possible number was 6).

3.4. BG scale

Morphine 60 mg increased scores in the BG scale ($P < 0.05$). By the opposite, BG scores decreased with flunitrazepam 0.5 mg ($P < 0.01$) and 2 mg ($P < 0.05$), and with triazolam 0.25 and 0.5 mg ($P < 0.01$). The dose–response curves for all conditions are shown in Fig. 4.

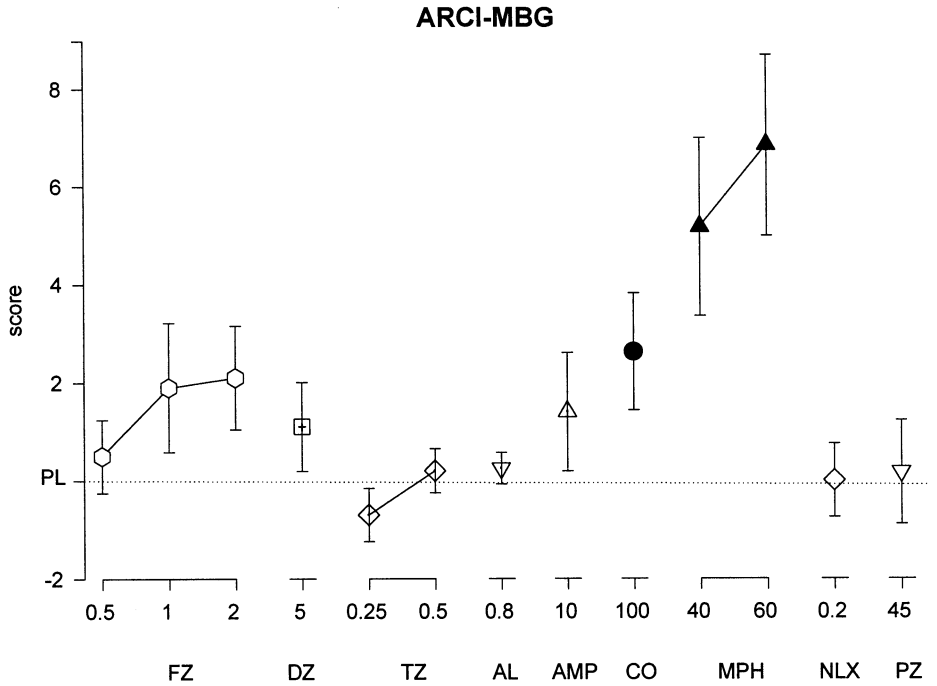

Fig. 2. Peak effects of studied drug conditions on the scale MBG of the ARCI. Other details of the figure are similar to those for Fig. 1.

3.5. A scale

The A scores increased only with cocaine ($P < 0.01$).

4. Discussion

The results of all four studies show that the Spanish translation of the ARCI is a valid instrument for assessing the subjective effects of at least three major classes of psychotropic drugs. For each class—sedative-hypnotics, stimulants, and opioids—one or more representative drug(s) was examined at a range of doses. Additionally, in order to assess the relative sensitivity of the ARCI to changes in the subjective effects, other subjective measures such as the VAS and a drug classification scale were also included. A similar method has been used by Warot et al. (1997) to validate the sensitivity and specificity to amphetamine of the French version of the 49-item form of the ARCI.

In relation to the PCAG scale, scores are generally expected to increase in persons complaining of fatigue, weakness, and sluggishness and represent the characteristic pattern for sedative drugs such as benzodiazepines. The fact that these scores were significantly increased by flunitrazepam, triazolam, alcohol, naloxone, and pentazocine indicates that the PCAG scale of the Spanish version of ARCI is sensitive to detect differences between these drugs and placebo. Moreover, the magnitude of the increase in the PCAG scores in study 1 was the same as that following the same dose in study 2 for flunitrazepam. These results are confirmed by the scale "drowsiness" of the VAS that increased with flunitrazepam 2 mg, and with triazolam 0.5 mg. The majority of the subjects identified the substance as a tranquilizer. Although no ARCI published profiles are available for flunitrazepam, the effects of triazolam on the ARCI scores in normal subjects reported by others (Rush et al., 1993a,b; Oliveto et al., 1994) are similar to the present results.

On the other hand, diazepam 5 mg did not produce a significant increase in the PCAG scores. This dose is generally considered low, so the absence of an increase in the PCAG scores may be explained by this reason. Some studies (Heishman and Henningfield, 1991; Chutuape and de Wit, 1995) have found an effect at higher doses. However, de Wit et al. (1986a,b) found an effect with the 5 mg dose. Whether inconsitency between our data and results of de Wit et al. (1986a,b) were due to differential sensitivity of the Spanish version of the ARCI, we would expect other measures of the strength of drug effect to be similar between the two studies. Our study and those of de Wit et al. (1986a,b) included similar drug identification tasks. Only 20% of our subjects identified diazepam as a tranquilizer, whereas 56% of the subjects in the study of de Wit et al. (1986a) did so. The same dose of diazepam produced stronger subjective effects in the study by de Wit et al. (1986a), and the absence of an increase in the PCAG scores in our study does not seem to be due to a lower sensitivity of our questionnaire version. We believe that the different procedures used in our study may, at least

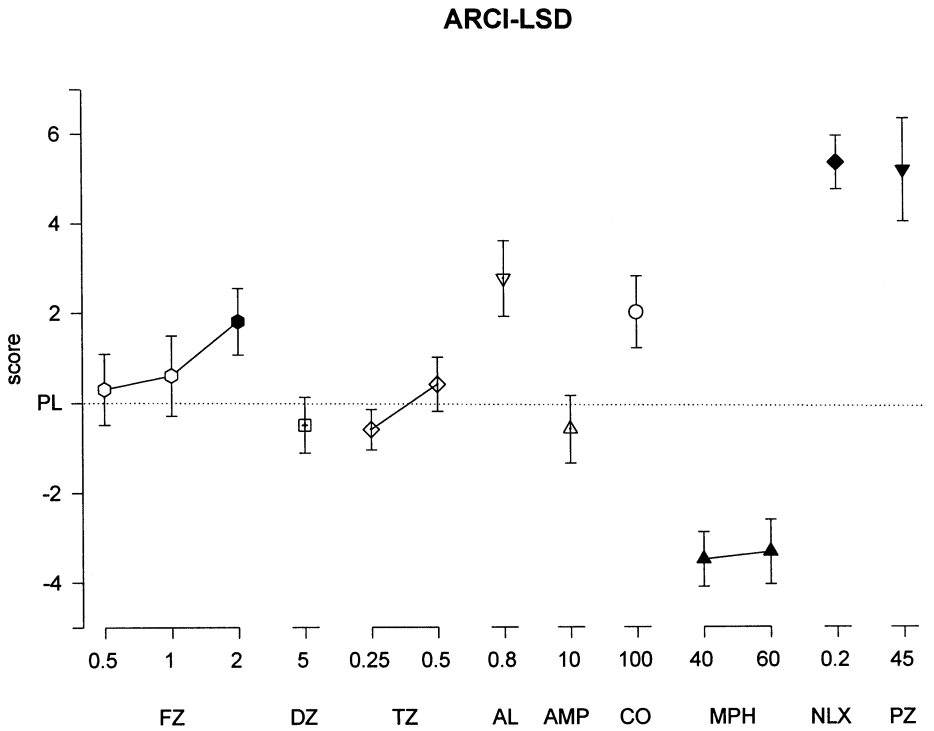

Fig. 3. Peak effects of studied drug conditions on the scale LSD of the ARCI. Other details of the figure are similar to those for Fig. 1.

in part, account for the differences in results. Most importantly, de Wit et al. (1986a) used a choice procedure in their study, entailing the repeated administration of diazepam (two to five times), which may have trained the subjects to be more sensitive to drug effects and, therefore, elevated the scores on the appropriate scales. Also, de Wit et al. (1986a) did not require the subjects to remain in the laboratory, once they had ingested the drug. In contrast, our study required the subjects to remain in the laboratory for the full experimental session. This may have constituted a discrepancy in task-requirements between our study and those of de Wit et al. (1986a) and could affect subjective measures. Finally, subjects of the de Wit study (de Wit et al., 1986a) included those chosen for their high level of anxiety and, therefore, with subject characteristics that were different than the subjects in our study.

Alcohol produced a significant increase in the PCAG scores, which is the typical pattern that has been found in previous research (Haertzen and Hickey, 1987; Chutuape and de Wit, 1995; Doty and de Wit, 1995). In study 4, increased PCAG scores were obtained with naloxone and pentazocine. Some studies with naloxone also report an increase in the PCAG scores (Preston et al., 1987, 1990; Preston and Jasinski, 1991; Eissenberg et al., 1995). The same results have been found with pentazocine (Jasinski et al., 1970).

With regard to the MBG scale, cocaine produced an increase in MBG scores. The results of the studies that have examined the subjective effects of inhaling intranasal cocaine powder measured by the ARCI, are not consistent, showing either an increase (Fischman and Schuster, 1980) or no change (Foltin et al., 1993). The increase in MBG scores is almost always found after intravenous administration of cocaine (Fischman et al., 1976; Foltin and Fischman, 1991), but there are some studies in which no differences were detected (Preston et al., 1993; Walsh et al., 1994). However, the increase in MBG scores are in agreement with some changes in scales of the VAS like "high", "good effects", "liking", "feeling good" and "content". Morphine, at 40 and 60 mg, also increased the MBG scores, although only the higher dose of morphine increased the scale of "good effects" on the VAS. In a meta-analysis of 33 studies, Lamas et al. (1994c) showed that MBG scale was the variable which presented most consistent results across studies as shown by non-significant heterogeneity, MBG appears to be the most consistent measure of morphine subjective effects.

Flunitrazepam did not increase significantly the MBG scale of ARCI, but this drug increased some similar scales of the VAS as "good effects", "high", and "liking". This discrepancy has been previously reported by Rush et al. (1993a,b) when triazolam and lorazepam were given to healthy volunteers, and by Preston et al. (1989b, 1992) in sedative abusers who received lorazepam and methocarbamol. Increases in the MBG scores have been described when some benzodiazepine compounds (lorazepam, triazolam, diazepam) were administered to sedative abusers or to subjects

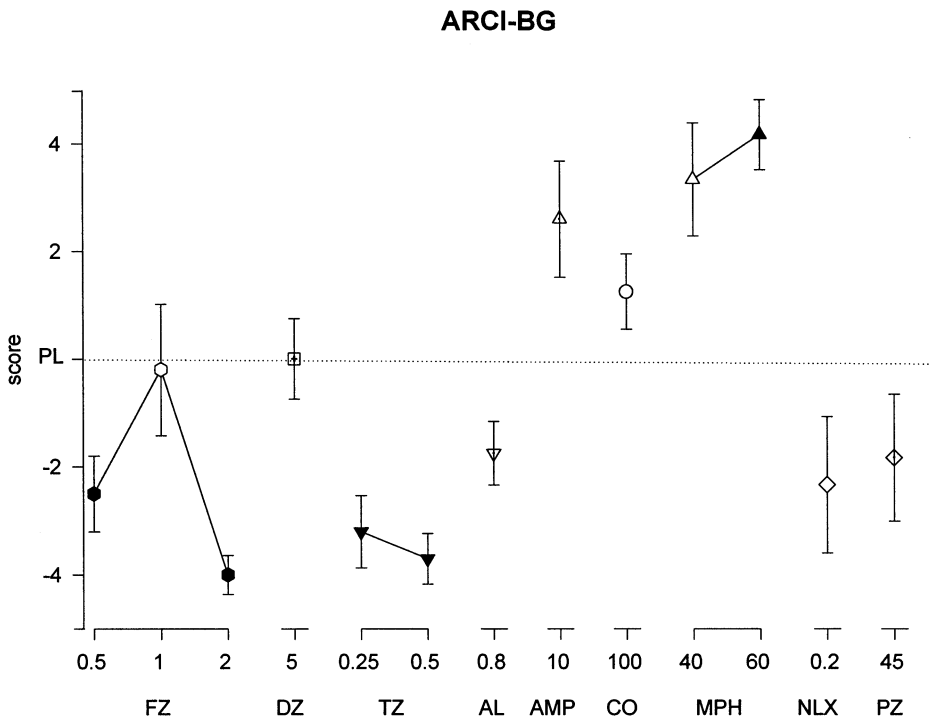

Fig. 4. Peak effects of studied drug conditions on the scale BG of the ARCI. Other details of the figure are similar to those for Fig. 1.

with previous or current history of opiate abuse/dependence, but not in healthy non-abuser subjects (Roache and Griffiths, 1985; de Wit and Griffiths, 1991).

In relation to the LSD scale, in two of three experiments reported by Rush et al. (1993a,b) the 0.5 mg dose of triazolam significantly increased LSD scores, whereas in our study only the higher dose of flunitrazepam (study 2) produced changes in this scale. On the other hand, the scale of "bad effects" and "drunken" of the VAS increased with flunitrazepam (2 mg). These data add evidence to previous studies showing that some benzodiazepines could produce increases in the LSD scale when administered to healthy volunteers (Rush et al., 1993a,b; de Wit et al., 1984). Alcohol increased LSD scores. The same result was found by Doty and de Wit (1995), and, in the same way, also increased the scale of "bad effects" of the VAS. Pentazocine increased LSD scores, in agreement with other studies (Bickel et al., 1989; Preston et al., 1989a; Preston and Jasinski, 1991). Naloxone (0.2 mg) also increased LSD scores. Although the administration of naloxone alone is not associated with any change on the ARCI scales in non-dependent subjects (Haertzen and Hickey, 1987), the additional observation of an increase in the antagonists effects scales in our study indicates that naloxone precipitated a withdrawal syndrome, as is also corroborated with the elevations of the scores of "bad effects" on the VAS. The precipitated withdrawal in opioid dependent volunteers after the administration of naloxone (Preston et al., 1987, 1988; Strain et al., 1993; Eissenberg et al., 1995) and with pentazocine (Strain et al., 1993) has already been reported.

In the BG and A scales, decreases in BG scores were found after the use of flunitrazepam 0.5 and 2 mg and after for both doses of triazolam (0.25 and 0.5 mg). Other studies corroborate this results for triazolam (Oliveto et al., 1994), but others do not show changes in BG scale after the use of this type of drugs (Rush et al., 1993a,b).

Cocaine increased the scores of the A scale, which is the scale specifically developed for measuring the effects of stimulants and, therefore, constitutes the typical effect of this class of drugs. Because A scale is derived from items of MBG and BG scales, the increase in A scale could be consequence in part of the increase in MBG scores. Amphetamine did not produce any significant changes on BG and A scales which are associated with amphetamine administration. However, it should be noted that the pattern changes established for amphetamine have been obtained with one or more of the following factors: large number of subjects (Haertzen et al., 1963), moderate to high doses (Haertzen et al., 1963; Martin et al., 1971), *d*-amphetamine, which is more potent than *d*-*l*-amphetamine (Martin et al., 1971), and parenteral route of administration (Haertzen et al., 1963). The only exceptions are the studies of de Wit et al. (1986a,b) which showed an increase in the BG and A scores after a 5 mg dose of orally administered *d*-*l*-amphetamine, and which may

not be suitable for comparison with our study mainly due to methodological differences in the study design.

The ARCI short form was effective in distinguishing the effects of sedatives, stimulants, and opioids from placebo. Each of the drugs affected the ARCI scales in a pattern that is typically associated with their respective pharmacological class and, therefore, would have allowed to classify the drugs correctly. In addition, it should be noted that the ARCI short form produced a similar pattern of response when the same drug was administrated in different studies. In this way, the scores obtained when flunitrazepam was administered at 2 mg dose were almost identical in studies 1 and 2, and very similar when the same dose of flunitrazepam was administered in another clinical trial (data not shown, Farré et al., 1998). The characteristic effects of the drugs that were observed on the ARCI are in contrast with results of other subjective measures, such as visual analog scales that produced less consistent results and, in some cases, subjective effects were more difficult to interpret.

Overall, the present results are in agreement with the original ARCI studies conducted by Haertzen et al. (1963) and with other studies using the English version of the ARCI short form (Haertzen and Hickey, 1987). The Spanish version of this shortened questionnaire seems to be sensitive in distinguishing the changes induced by different classes of psychoactive drugs and confirms its validity for the assessment of subjective drug effects in the Spanish-speaking population. For this reason, the questionnaire is currently being used as a standard method to evaluate drug effects in abuse liability studies carried out by our research group. We believe that the Spanish version of the 49-item short form of the ARCI will be increasingly useful globally, particularly in countries which may have rapidly increasing Spanish-speaking populations.

Acknowledgements

These studies were supported in part by grants from 'Fondo de Investigación Sanitaria' (FIS) 91/0686, 92/0152, and 95/0231, CIRIT grant GRQ93-9303, IMIM 'Beca X. Lamas' and CITRAN Foundation. We thank Marta Pulido, MD, for editing the manuscript and editorial assistance.

References

Bickel, W.K., Bigelow, G., Preston, K., Liebson, I., 1989. Opioid drug discrimination in humans: stability, specificity, and relation to self-reported drug effect. J. Pharmacol. Exp. Ther. 251, 1053–1063.

Chutuape, M.A.D., de Wit, H., 1995. Preferences for ethanol and diazepam in anxious individuals: and evaluation of the self-medication hypothesis. Psychopharmacology 121, 91–103.

de Wit, H., Griffiths, R.R., 1991. Testing the abuse liability of anxiolytic and hypnotic drugs in humans. Drug Alcohol Depend. 28, 83–111.

de Wit, H., Johanson, C.E., Uhlenhuth, E.H., 1984. Reinforcing properties of lorazepam in normal volunteers. Drug Alcohol Depend. 13, 31–41.

de Wit, H., Uhlenhuth, E.H., Hedeker, D., McCracken, S.G., Johanson, C.E., 1986a. Lack of preference for diazepam in anxious volunteers. Arch. Gen. Psychiat. 43, 533–541.

de Wit, H., Uhlenhuth, E.H., Johanson, C.E., 1986b. Individual differences in the reinforcing and subjective effects of amphetamine and diazepam. Drug Alcohol Depend. 16, 341–360.

Doty, P., de Wit, H., 1995. Effect of setting on the reinforcing and subjective effects of ethanol in social drinkers. Psychopharmacology 118, 19–27.

Eissenberg, T., Greenwald, M.K., Johnson, R.E., Liebson, I.A., Bigelow, G.E., Stitzer, M.L., 1995. Buprenorphine's physical dependence potential: antagonist-precipitated withdrawal in humans. J. Pharmacol. Exp. Ther. 276, 449–459.

Farré, M., de la Torre, R., González, M.L., Terán, M.T., Roset, P.N., Menoyo, E., Camí, J., 1997. Cocaine and alcohol interactions in humans: neuroendocrine effects and cocaethylene metabolism. J. Pharmacol. Exp. Ther. 283, 164–176.

Farré, M., Terán, M.T., Camí, J., 1996. A comparison of the acute behavioral effects of flunitrazepam and triazolam in healthy volunteers. Psychopharmacology 125, 1–12.

Farré, M., Roset, P.N., Mas, M., Menoyo, E., de la Torre, R., Hernández, C., Camí, J., 1998. Flunitrazepam abuse potential in relation to rate of onset of effects and dose administered. In: Harris, L. (Ed.), Problems of drug dependence. NIDA Res. Monogr. 178, 1998 p. 75.

Fischman, M.W., Foltin, R.W., 1991. Utility of subjective-effects measurement in assessing abuse liability of drugs in humans. Br. J. Addiction 86, 1563–1570.

Fischman, M.W., Schuster, C.R., 1980. Cocaine effects in sleep-deprived humans. Psychopharmacology 722, 1–8.

Fischman, M.W., Schuster, C.R., Resnekov, L., 1976. Cardiovascular and subjective effects of intravenous cocaine administration in humans. Arch. Gen. Psychiatry 33, 983–989.

Foltin, R.W., Fischman, M.W., Pippen, P.A., Kelly, T.H., 1993. Behavioral effects of cocaine alone and in combination with ethanol or marijuana in humans. Drug Alcohol Depend 32, 93–106.

Foltin, R.W., Fischman, M.W., 1991. Acute tolerance to the effects of smoked and intravenous cocaine in humans. J. Pharmacol. Exp. Ther. 257, 247–261.

Haertzen, C.A., Hickey, J.E, 1987. Addiction Research Center Inventory (ARCI): measurement of euphoria and other drug effects. In: Bozarth, M.A. (Ed.), Methods of assessing the reinforcing properties of abused drugs. Springer-Verlag, New York, pp. 489–520.

Haertzen, C.A., Hill, H.E., Belleville, R.E., 1963. Development of the Addiction Research Center Inventory (ARCI): selection of items that are sensitive to the effects of various drugs. Psychopharmacology 4, 155–166.

Heishman, S.J., Henningfield, J.E., 1991. Discriminative stimulus effects of *d*-amphetamine, methylphenidate, and diazepam in humans. Psychopharmacology 103, 436–442.

Hill, H.E, Haertzen, C.A, Wolbach, A.B., Miner, E.J, 1963. The Addiction Research Center Inventory: standardization of scales which evaluate subjective effects of morphine, amphetamine, pentobarbital, alcohol, LSD-125, pyrahexyl and chlorpromazine. Psychopharmacology 4, 167–183.

Jasinski, D., Henningfield, J.E., 1989. Human abuse liability assessment by measurement of subjective and physiological effects. In: Fischman, M.W., Mello, N.K. (Eds.), Testing for abuse liability of drugs in humans. NIDA Res. Monogr. 92, 1989, pp. 73–100.

Jasinski, D., Martin, W., Hoedtke, R., 1970. Effects of short and long-term administration of pentazocine in man. Clin. Pharmacol. Ther. 11, 385–403.

Lamas, X., Farré, M., Camí, J., 1994a. Acute effects of pentazocine, naloxone and morphine in opioid-dependent volunteers. J. Pharmacol. Exp. Ther. 268, 1485–1492.

Lamas, X., Farré, M., Llorente, M., Camí, J., 1994b. Spanish version of the 49-item short form of the Addiction Research Center Inventory (ARCI). Drug Alcohol Depend. 35, 203–209.

Lamas, X., Farré, M., Moreno, V., Camí, J., 1994c. Effects of morphine in postaddict humans: a meta-analysis. Drug Alcohol Depend. 36, 147–152.

Martin, W., Sloan, J., Sapira, J., Jasinski, D., 1971. Physiologic, subjective, and behavioral effects of amphetamine, methamphetamine, ephedrine, phenmetrazine, and methylphenidate in man. Clin. Pharmacol. Ther. 12, 245–258.

Oliveto, A.H., Warren, K.B., Kamien, J.B., Hughes, J.R., Higgins, S.T., 1994. Effects of diazepam and hydromorphone in triazolam-trained humans under a novel-response drug discrimination procedure. Psychopharmacology 114, 417–423.

Preston, K.L., Bigelow, G.E., Bickel, W.K., Liebson, I.A., 1987. Three-choice drug discrimination in opioid-dependent humans: hydromorphone, naloxone and saline. J. Pharmacol. Exp. Ther. 243, 1002–1009.

Preston, K.L., Bigelow, G.E., Bickel, W.K., Liebson, I.A., 1989a. Drug discrimination in human postaddicts: agonist-antagonist opioids. J. Pharmacol. Exp. Ther. 250, 184–196.

Preston, K.L., Bigelow, G.E., Liebson, I.A., 1988. Butorphanol-precipitated withdrawal in opioid-dependent human volunteers. J. Pharmacol. Exp. Ther. 246, 441–448.

Preston, K.L., Bigelow, G.E., Liebson, I.A., 1990. Discrimination of butorphanol and nalbuphine in opioid-dependent humans. Pharmacol. Biochem. Behav. 37, 511–522.

Preston, K.L., Guarino, J.J., Kirk, W.T., Griffiths, R.R., 1989b. Evaluation of the abuse liability of methocarbamol. J. Pharmacol. Exp. Ther. 248, 1146–1157.

Preston, K.L., Jasinski, D., 1991. Abuse liability studies for opioid agonist-antagonist in humans. Drug Alcohol Depend. 28, 49–82.

Preston, K.L., Wolf, B., Guarino, J.J., Griffiths, R.R., 1992. Subjective and behavioural effects of diphenhydramine, lorazepam, and methocarbamol: evaluation of abuse liability. J. Pharmacol. Exp. Ther. 262, 707–720.

Preston, K.L., Sullivan, J.T., Berger, P., Bigelow, G.E., 1993. Effects of cocaine alone with combination with mazindol in human cocaine abusers. J. Pharmacol. Exp. Ther. 267, 296–307.

Roache, J.D., Griffiths, R.R., 1985. Comparison of triazolam and pentobarbital: performance impairment, subjective effects and abuse liability. J. Pharmacol. Exp. Ther. 234, 120–133.

Rush, C.R., Higgins, S.T., Bickel, W.K., Hughes, J.R., 1993a. Acute effects of triazolam and lorazepam on human learning, performance and subject ratings. J. Pharmacol. Exp. Ther. 264, 1218–1226.

Rush, C.R., Higgins, S.T., Hughes, J.R., Bickel, W.K., 1993b. A comparison of the acute effects of triazolam and temazepam in normal volunteers. Psychopharmacology 112, 407–414.

Strain, E.C., Preston, K.L., Liebson, I.A., Bigelow, G.E., 1993. Precipitated withdrawal by pentazocine in methadone-maintained volunteers. J. Pharmacol. Exp. Ther. 267, 624–634.

Teran, M.T., Farré, M., Lamas, X., Ugena, B., Camí, J., 1993. Subjective and psychomotor effects of flunitrazepam in healthy volunteers. In: Harris, L. (Ed.), Problems of Drug Dependence. NIDA Res. Monogr. 132, 1993, p. 348.

Walsh, S.L., Preston, K.L., Sullivan, J.T., Fromme, R., Bigelow, G.E., 1994. Fluoxetine alters the effects of intravenous cocaine in humans. J. Clin. Psychopharmacol. 14, 396–407.

Warot, D., Danjou, P., Payan, C., Puech, A.J., 1997. Sensitivity and specificity to amphetamine of a French version of the 49-item form of the Addiction Research Center Inventory. Drug Alcohol Depend. 45, 177–183.