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Differences in the subjective effects of drugs in patients with a first psychotic episode. Preliminary results

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Introduction. The study of the subjective effects of abuse substances may facilitate comprehension of the high prevalence of substance abuse in psychosis.

Objective. To assess the subjective effects of psychoactive substances in psychotic patients with substance use disorder in a prospective open study with a 6 month evaluation.

Methods. Thirty patients consecutively admitted for the first time to a psychiatric hospital because of a psychotic disorder (DSM-IV) were included. Socio-demographic data, substance use history, drug urine test, and severity of psychotic symptoms measured by BPRS, SANS, and SAPS were evaluated. The subjective effects of drugs were assessed with the short form of the ARCI questionnaire. Patients were re-assessed at six months follow-up.

Results. Sixty-three percent of patients were male, mean age 29.2 years. A total of 46.6 % presented at least one substance use disorder. Differences between substance users group (SUG) and non-substance users group (non SUG) were only related to sex (more male in SUG), and no other sociodemographic and clinical differences were found. The main abuse drugs found were: 86 % cannabis, 17 % cocaine, 17 % alcohol, 3 % heroin and 3 % hypnosedatives. Fifty percent only consumed cannabis. The psychotic patients with substance use disorder showed higher punctuation in MBG scale (euphoria scale); no differences in other ARCI scales were found. At six months follow-up, 83.3 % patients were re-assessed and no differences were found.

Conclusions. The psychotic patients with substance use disorder showed a higher subjective effect of euphoria than non-substance user psychotics, suggesting that drug use is mainly related to obtaining euphoria-like effects than sedatives in this group.

Key words:
Psychotic disorders. Schizophrenia. Self-medication. Substance use disorders. Euphoria.

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Diferencias en los efectos subjetivos de la drogas en pacientes con primer brote psicótico. Resultados preliminares

Introducción. El estudio de los efectos subjetivos de las sustancias de abuso puede facilitar la comprensión de la elevada prevalencia de consumo de drogas en la psicosis.

Objetivo. Estudiar los efectos subjetivos a las sustancias psicoactivas en psicóticos con abuso/dependencia en un estudio prospectivo y abierto con evaluación a los 6 meses.

Métodos. Se estudiaron 30 pacientes ingresados consecutivamente por primera vez por síndrome psicótico. Se evaluaron datos sociodemográficos, historia de consumo de sustancias psicoactivas, tóxicos en orina al ingreso y evolución de escalas de gravedad de psicosis (BPRS, SANS y SAPS). Los efectos subjetivos de las sustancias se evaluaron mediante la versión reducida del ARCI. Se reevaluaron a los 6 meses.

Resultados. El 63 % eran varones; edad media: 29,2 años. El 46,6 % presentaban abuso/dependencia de alguna sustancia. Excepto en el sexo (predominio de varones entre los consumidores), no hubieron diferencias en el perfil sociodemográfico y clínico entre el grupo de psicóticos con consumo de sustancias y el grupo de no consumidores. Las drogas principales de abuso fueron: 86 % cannabis, 17 % cocaína, 17 % alcohol, 3 % opiáceos y 3 % hipnosedantes. El 50 % únicamente consumía cannabis. Los consumidores presentaban mayor puntuación en la escala MBG, que valora principalmente la euforia, sin diferencias en otras escalas del ARCI. A los 6 meses se reentrevistaron el 83,3 % de casos sin diferencias en la evolución.

Conclusiones. Los psicóticos con abuso de drogas presentan unos efectos subjetivos de euforia superiores a los no consumidores, sugiriendo que en ellos el consumo se relaciona más con la obtención de efectos euforizantes que sedantes.

Palabras clave:
Trastorno psicótico. Esquizofrenia. Automedicación. Trastorno por uso de sustancia. Euforia.

INTRODUCTION

The high prevalence of psychoactive substance consumption in patients with psychosis is an area of growing interest[1-3]. One of the hypotheses that has been related with this consumption is the self-medication theory[4]. According to this theory, some subjects consume drugs in an attempt to improve their psychotic symptoms[5], decreasing the depressive and negative ones[8-12], or the collateral effects induced by the neuroleptics, mainly the extrapyramidal ones[13]. However, some studies have obtained contradictory results[14,15], probably due to the diversity of the sample studied and the methodology used. Until there are new technological advances, probably in the neuroimaging field, that make it possible to study the relationship between substance consumption and psychosis, one approach could be the study of the subjective effects of the different psychoactive substances in these subjects.

Studying the subjective effects of drugs is one of the crucial points of the investigation of abuse potential of the different substances in humans[16,17]. These studies are based on the fact that the subjective effects may be measured reliably and quantitatively and that the subjective experiences of a drug in humans are related systematically with its abuse potential. Specifically, it is assumed that «positive» and «euphorizing» effects are a measure of the reinforcing effect of the drug[18]. The scales of subjective effects used most are: Addiction Research Center Inventory (ARCI)[18-20], Single Dose Questionnaire (SDQ)[21], Profile of Mood States (POMS)[22] and Visual Analogue Scales[23]. All these scales contain measurements of the type «I like it», «good effect of the drug», «positive mood». The profile of the negative subjective effects may also be relevant since it may limit the substance's abuse potential, although this causes some positive effects[24].

However, the possibility of drug abuse is not only determined by its pharmacological characteristics but also by the characteristics of the individual who consumes it and the context in which it is consumed[25]. As such, the risk profile for a substance would be different in subjects with psychiatric disorders. This is determined by the interaction of the psychiatric disorder and the pharmacological properties of the substance in question. It can be argued that individuals with certain psychiatric disorders would be «vulnerable» subjects.

Based on the hypothesis that psychotic patients with abuse/dependence of psychoactive substances report different subjective effects in regards to the drugs than those who have not been diagnosed of abuse/dependence, although they have tried it, we have designed a prospective and longitudinal study of the subjective effects to the drugs in patients with acute psychotic disorder and disorder due to abuse and/or dependence of psychoactive substances. To do so, we used a control group made up of those patients with psychotic disorders who, although they had tried them, were not diagnosed or abuse or dependence.

METHODOLOGY

A prospective and open study was performed on 30 patients of both genders, admitted to a psychiatric hospital consecutively. They fulfilled the following inclusion criteria: first psychiatric admission due to a psychotic syndrome, including the following diagnosis according to the DSM-IV: schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder, induced psychotic disorder, non-specific psychotic disorder and bipolar disorder in manic episode. Due to the site's characteristics, patients under 18 years of age were excluded. Drug consumption was defined as the presence of abuse and/or dependence of psychoactive substances according to DSM-IV criteria with active consumption during the six months prior to admission, reported by the patient and/or family or by the detection of toxics in urine on admission. Nicotine dependence disorder was not included in the group's definition. Thus, the subjects were classified into two groups: consumers of psychoactive substances (C), and non-consumers (NoC). The study was approved by the center's IRB. Informed and written consent was requested from all the patients.

Measurements

A specific protocol of sociodemographic data (age, gender, civil status, occupational situation, studies, living arrangements and social class), somatic, psychiatric, personal and family background, and a history of psychoactive substance consumption: consumption at some time, onset age, consumption in the last 12 months and in the last 30 days was used to assess all the subjects. A urine sample was collected on admission for the detection of cannabis, cocaine, heroin, amphetamines and hallucinogens.

Psychotic symptoms were evaluated using the Spanish versions of the Brief Psychiatric Rating Scale (BPRS)[26,27] and the Scale for the Assessment of Positive and Negative symptoms of schizophrenia (SANS and SAPS)[28-31].

All the subjects who reported that they had consumed some of the psychoactive substances at some time were administered the reduced and Spanish version of the ARCI questionnaire[32] in relationship with the substance in question so that they would give a self-report response under a simulated condition of the drug effect. Previous studies have demonstrated that when the subjects are given oral advice to respond to the test describing the recall of their feelings at the time in which they were under the effects of the psychoactive substance in question, they report subjective effects similar to the situation of real consumption[32,33]. The Spanish version of the ARCI questionnaire has 49 items and 5 scales. These are: the Pentobarbital-Chlorpromazine-Alcohol Group (PCAG) scale, which scores the intensity of the effect from 0 to 15, the maximum effect being 15. It also measures sedation, it being especially sensitive to alcohol and sedatives of the central nervous system; the Morphine-Benzedrine Group

scale (MBG, score from 0 to 16) that measures euphoria and is especially sensitive to heroin, cocaine, amphetamines and alcohol; the Lysergic acid Dyethylamide Scale (LSD, score from 0 to 14), that measures dysphoria and somatic type symptoms and is especially sensitive to alcohol and hallucinogens; the Benzedrine Group scale (BG, score from 0 to 13), that measures stimulation and mainly consists in items related with intellectual efficiency and energy, and is especially sensitive to stimulants, mainly cocaine and, finally, the Amphetamine scale (A, score from 0 to 11) which is a scale derived from the MBG and BG, of empirical phenomena, sensitive to the effects of d-amphetamine.

Procedures

On admission, all the patients were evaluated by the protocol and the psychotic symptom severity scales (BPRS, SANS and SAPS). The ARCI was administered for each substance during admission when the patient's clinical condition made it possible.

Treatment was that indicated by the reference psychiatrist. Admission duration was maintained independent of the study, it only being based on clinical criteria related with the severity of the psychotic symptoms. At the end of the admission, and prior to discharge, the patients were re-evaluated with the BPRS, SANS and SAPS.

The patients were contacted at six months of admission for a re-evaluation interview. The interview was performed personally when the subjects accepted the interview and by telephone if they were not available. In the follow-up interview, *an ad hoc* questionnaire was administered in which they were asked on the regularity of the out-patient follow-up, treatment administration and number of admissions required during this period as well as information reported by the patient on the consumption of different substances during this period. They were also administered the SANS, SAPS and BPRS scales.

Statistical analysis

The chi squared test or alternatively the Fisher's exact test was used for the qualitative variables and the Student's *t* test for continuous variables. The analysis of the variance for repeated measurements was used for the changes produced over time. Statistical significance was established when p was < 0.05. The SPSS statistical program was used.

RESULTS

Baseline

The sample studied was made up of 30 patients, 63% men, with a mean age of 29.20 (SD: 10.58) years, who were diagnosed of psychotic disorder (DSM-IV). The diagnoses were schizophrenic disorder in 11 cases, schizophreniform disorder in seven cases, bipolar affective disorder (manic episode) in four cases, substance induced psychotic disorder in three cases, schizoaffective disorder in two cases, brief psychotic disorder in two cases and not otherwise specified psychotic disorder in a single case. A total of 46.6% of the cases (14/30) fulfilled the conditions of psychoactive substance consumers (C) and 16 were non-consumers (NoC). Table 1 describes the baseline characteristics of both groups, no significant differences being observed in the sociodemographic data, except in relationship to gender, with a clear predominance of men in group C (85.7%, p=0.017). No significant diagnostic differences were found between the consumer and non-consumer group. The scores on the SANS, SAPS and BPRS scales regarding psychotic symptom severity are shown in table 2. On admission, no differences were observed between the two groups.

Table 1 Sociodemographic characteristics of 30 psychotic patients who consume and do not consume drugs

Variables	C n = 14 N (%)	NoC n = 16 N (%)	p
Male gender	12 (85.7)	7 (43.8)	0.017*
Active work	8 (57.1)	12 (75)	0.44
Married civil status	0 (0)	4 (25)	0.13
Lives with parents	11 (78.6)	11 (68.8)	0.25
Middle social class	9 (64.3)	11 (68.8)	1
Secondary studies	6 (42.9)	7 (43.8)	0.38
Personal psychiatric background	8 (57.1)	8 (50)	0.69
Family psychiatric background	6 (42.9)	8 (50)	0.35
Involuntary admission type	10 (71.4)	11 (68.8)	0.59
Mean age (years) (x ± SD)	26.5 ± 6.97	31.56 ± 12.71	0.19

C: psychoactive substance consumers; NoC: non-consumers of psychoactive substances; N: number of subjects; SD: standard deviation. *p < 0.05.

In regards to the consumption of psychoactive substances, all the subjects of the C group and only 50 % (n=8) of the NoC group were nicotine dependent (p=0.002). Regarding the other substances, the group C subjects fulfilled diagnostic criteria of abuse and/or cannabis in 12 cases (85.7%), of cocaine abuse/dependence in five (35.7%), of alcohol abuse/dependence in five (35.7%). There was one case of opiate dependence and one case of hypnosedative dependence. No case of abuse or dependence on amphetamines and/or derivatives, designer drugs (ecstasy type) hallucinogens, or inhalants was diagnosed. A total of 50% consumed cannabis as the only abuse substance.

Table 2 Results of the BPRS, SAPS and SANS scales on admission and discharge.

Scales	C n = 14		NoC n = 16		ANOVA		
	Mean	SD	Mean	SD	i F (gl) p	g F (gl) p	t F (gl) p
Overall BPRS					2.94 (1) NS	< 0.01 (1) NS	148.24 (1) < 0.001*
Admission	22.68	9.82	20.35	7.02			
Discharge	3.81	3.27	6.14	3.37			
Overall SANS					0.52 (1) NS	0.01 (1) NS	10.25 (1) 0.003*
Admission	3.93	3.37	3.71	3.64			
Discharge	2.12	3.07	2.57	2.27			
Compound SANS					0.11 (1) NS	< 0.01 (1) NS	14.18 (1) 0.001*
Admission	16.96	13.46	16.00	16.37			
Discharge	9.06	11.16	9.42	9.38			
Overall SAPS					2.78 (1) NS	0.07 (1) NS	144.05 (1) < 0.001*
Admission	8.25	2.17	7.14	3.73			
Discharge	0.50	0.89	1.28	1.13			
Compound SAPS					0.79 (1) NS	0.11 (1) NS	113.92 (1) < 0.001*
Admission	31.31	11.28	30.14	15.90			
Discharge	2.12	2.91	5.28	4.14			

C: consumers of psychoactive substances; NoC: non-consumers of psychoactive substances; N: number of subjects; SD: standard deviation; t: time effect on the group; i : different effect of time in each group; g: intergroup differences with independence of time factor; F: Schnedecor F; gl: degrees of freedom. BPRS: Brief Psychiatric Rating Scale. SANS and SAPS: positive and negative symptoms scales of schizophrenia. *p < 0.01.

In regards to the conditions used to apply the ARCI under the supposition of consumption, nine of the 14 subjects in group C could evaluate alcohol, 14 cannabis and nine cocaine. Although the abuse/dependence criteria were not fulfilled in the NoC group, some subjects had tried different substances and 13 could evaluate alcohol, seven cannabis and three cocaine. Not all the subjects could evaluate all the substances that they had tried at some time because, in some cases, consumption had been joint (for example, cannabis and alcohol) and they did not know how to distinguish the effects of each one. Table 3 shows the results of the ARCI questionnaire. No differences were found on comparing the subjective effects of each drug intergroup (alcohol, cannabis and cocaine). However, on assessing the global results of the ARCI, independently of the substance evaluated, there were differences between the group C subjects and the NoC group; the group C subjects had a higher score on the MBG scale, that mainly assesses the sensation of euphoria, than the NoC group subjects. No differences were observed in the remaining scales.

Evolution of admission

From the pharmacological treatment point of view, all the patients received antipsychotic treatment according to the reference physician's criterion, no differences being observed between both groups in regards to type of antips-

Table 3 Results of ARCI questionnaire in the patients who have responded for each drug

n/N ARCI	Alcohol		Cannabis		Cocaine		t (gl) p
	C 9/14	NoC 13/16	C 14/14	NoC 7/16	C 9/14	NoC 3/16	
PCAG	7	7.69	10.14	10.5	3	3.66	-0.911 (26) 0.374
MBG	7.5	6.30	7.78	4.28	13.44	12.66	2.216 (26) 0.036*
LSD	6.11	7.46	5.14	6	5.53	6.66	-1.368 (26) 0.183
BG	4.55	4.38	4.28	4.14	10.11	9.66	1.371 (26) 0.182
A	5.12	4	5.14	3.85	7.33	7.66	1.941 (26) 0.063

C: consumers of psychoactive substances; NoC: non-consumers of psychoactive substance; n/N: indicates the number of patients who have responded to the ARCI for the drug, over the total number of patients of the group in question (14 DC and 16 NDC). t: Student's *t*; gl: degrees of freedom. ARCI: Spanish version of ARCI questionnaire, that is made up of five scales: PCAG: Pentobarbital-Chlorpromazine-Alcohol Group; MBG: Morphine-Benzedrine Group; LSD: Lysergic acid Dyethylamide Scale; BG: Benzedrine Group; A: Amphetamine. *p<0.05.

ychotic administered (classic: 79% in group C and 75% in NoC; atypical: 43% in group C and 56% in group NoC). Some patients underwent combined antipsychotic treatment with the classical and atypical ones. No differences were observed in regards to use of associated benzodiazepines (43% in group C and 50% in NoC). In most of the cases, extrapyramidal symptoms were detected (93% in group C and 94% in NoC). Antidepressants were not indicated for any patient during admission.

In regards to the evolution of the psychotic symptoms, the scores on the SANS, SAPS and BPRS scales during admission showed a clear decrease of within subject symptoms for all the scales, both those that assess positive as well as negative symptoms, without intergroup differences and a different influence of time for each group was not observed (table 2).

The average stay was 21.40 days without differences between both groups (22.07 ± 4.68 days in group C and 20.81 ± 16.87 days in group NoC) and the medical discharge was 93% and 94% respectively.

Evaluation at 6 months

At 6 months, 25 cases (83.3%) were re-interviewed. Four cases did not accept the interview and one could not be located; 3 were from group C and 2 from NoC. The evaluation was performed by personal interview in 53% and the rest were interviewed by telephone.

A total of 57.1% of group C and 81.3% of the NoC group had out-patient control and regular treatment at 6 months, there being no differences between both groups. Three patients (10%) required hospital readmission in an acute psychiatric unit during the 6 month period after the first admission: 1 C and 2 NoC. Another patient of this first group required admission in a subacute unit after the discharge.

Regarding the results of the clinical scales at 6 months, no differences were found between both groups, except in relationship to the decrease of the within subject psychotic symptoms for all the scales over time. Significance was also found in the global SAPS scale in the group-time interaction. It seems that the latter affects both groups differently, but this difference is not maintained for the remaining scales.

In group C, toxic consumption was only detected at 6 months in one subject, who presented alcohol, cannabis and cocaine abuse. All of them maintained nicotine dependence in situation of active consumption. Among the NoC, two individuals reported toxic abuse: one to cannabic derivatives and another to cocaine. On the contrary to what could be expected, there were no differences in relationship with drug consumption or non-consumption.

CONCLUSIONS

The finding that 47% of the first consecutive admissions due to psychosis in a psychiatric hospital also had a diagnosis of psychoactive substance abuse/dependence verifies the epidemiological studies that find a high substance of consumption in psychotic patients[34]. The observation that the psychotic patients consuming psychoactive substance had greater subjective effects of euphoria in regards to different substances than those psychotic patients who, although they had tried them, did not usually consume them, supports the study hypothesis. Because this was the first psychiatric admission due to psychosis in all of the cases, the lack of differences between both groups in regards to the psychotic symptoms and in the other ARCI scales, especially the PCAG one, that measures sedation, suggests that drug consumption in psychotic subjects is more related with obtaining euphorizing effects than with sedative effects. Thus, these patient could be searching more for the compensation of negative or depressive symptoms than the reduction of anxious symptoms. Some authors[5,12,35] have already previously described this possible relationship.

On comparing the sociodemographic characteristics between both groups of patients, it was observed that those subjects who consumed drugs tended to be younger than those who did not consume them. This tendency has already been described in other studies[36,37] suggesting that substance consumption could have acted as a precipitating factor of the psychotic disorder[38-41]. The absence of differences in both clinical characteristics of the psychotic picture[42] and in the response to the pharmacological treatment observed[15] also coincides with results found in previous studies. In regards to the psychoactive substances, it was observed that cannabis, alcohol and cocaine were the most common, coinciding with the previous studies[2,43]. Since the study of the characteristics of the first psychotic episodes and their prodromic phases has special interest for the advance in knowledge of psychosis[44,45], the relationship between substance consumption and the subjective effects that these produce in psychotic subjects may contribute new research pathways.

The study's main limitation is related with the sample size, which is why these preliminary results must be verified in larger samples of patients. Other limitations are related with the type of patients studied. These were subjects with psychotic symptoms who required admission for the first time, those subjects who could receive treatment in out-patient regime being excluded. On the other hand, that fact that it was difficult to re-interview all the patients at six months due to early treatment drop-out limits the interpretation of the follow-up results.

Finally, this study has made it possible to verify the feasibility of administering questionnaires on subjective effects of drugs in subjects with psychiatric disorder (in this case psychosis) who are under a supposed consumption. These

questionnaires were initially designed to be applied in subjects who regularly consume drugs who are under the effect of the substance administration. This situation is similar to that performed in the design of scales on abuse potential[46], since the administration of psychoactive substances with abuse potential in this type of patients would pose important ethical problems.

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