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Substance use disorder comorbidity with schizophrenia in families of Mexican and Central American Ancestry

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Abstract

Objectives—The aims of this study were to estimate the frequency and course of substances use disorders in Latino patients with schizophrenia and to ascertain risk factors associated with substance use disorders in this population.

Method—We studied 518 subjects with schizophrenia recruited for a genetic study from the Southwest United States, Mexico, and Central America (Costa Rica and Guatemala). Subjects were assessed using structured interviews and a best estimate consensus process. Logistic regression, χ^2 , t- test, Fisher's exact test, and Yates' correction, as appropriate, were performed to assess the

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The data and results reported in the presented paper have not been previously reported.

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sociodemographic variables associated with dual diagnosis. We defined substance use disorder as either alcohol or substance abuse or dependence.

Results—Out of 518 patients with schizophrenia, 121 (23.4%) had substance use disorders. Comorbid substance use disorders were associated with male gender, residence in the United States, immigration of Mexican men to the United State, history of depressive syndrome or episode, and being unemployed. The most frequent substance use disorder was alcohol abuse/dependence, followed by marijuana abuse/dependence, and solvent abuse/dependence.

Conclusion—This study provides data suggesting that depressive episode or syndrome, unemployment, male gender, and immigration of Mexican men to the United States were factors associated with substance use disorder comorbidity in schizophrenia. Binary logistic regression showed that country of residence was associated with substance use disorder in schizophrenic patients. The percentage of subjects with comorbid substance use disorders was higher in the Latinos living in the United States compared with subjects living in Central America and Mexico.

Keywords

Alcohol; drug abuse; substance misuse; dual diagnosis; Schizophrenia; Latino populations

1. Introduction

There is little data on dual diagnosis (DD) of schizophrenia (SC) and substance use disorders (SUD) in the Latino population. The aims of this paper were to estimate the frequency of comorbid alcohol and drug use disorders in Latinos with SC from Mexican and Central American ancestry, and to describe the risk factors associated with SC in this population.

Lifetime prevalence rates of SUD have ranged from 14.6% to 26.6% in the general United States (US) population (Baumeister and Härter, 2007; Kessler et al., 1994, 2005a), and from 9.9% to 18.7% in Europe (Bijl et al., 1998; Jacobi et al., 2004). In studies from the US, lifetime prevalence of SUD in Latinos (11.2% to 16.1%) (Alegría et al., 2008; Breslau et al., 2006) is lower than in non-Latino Whites (Alegría et al., 2006; Zhang and Snowden, 1999). In Latinos living outside of the US, lifetime prevalence of SUD is also lower than in the general US population (Andrade et al., 2000; Medina-Mora et al., 2007).

Persons with SC have substantially higher lifetime risk of having SUD than do persons from the general population (McCreadie, 2002; Kessler et al., 2005; Regier et al., 1990; Ringen et al., 2008; Soyka et al., 2001; Swartz et al., 2006), ranging from 40% to 60% (Cantor-Graae et al., 2001). In the US, an epidemiologic study found lifetime history of comorbid SUD was 47% for persons with SC or schizophreniform disorder, a rate 4.6 times higher than for the general population (Kavanagh et al., 2004). In a recent nation-wide study of SC in the US, even higher rates of SUD were found: 60.3% of 1460 persons with SC reported a SUD (Rosenman et al., 2000). Similar high rates of SUD with SC have been found in studies from Europe (Dervaux et al., 2001; Fowler et al., 1998; Kavanagh et al., 2004; Menezes et al., 1996; Ringen et al., 2008; Rosenman et al., 2000; Verma et al., 2002).

Despite recent interest in how rates of psychiatric disorders vary in Latinos (Breslau et al., 2006; Grant et al., 2004; Vega and Sribney, 2003) there are only a couple of studies, which have looked specifically at comorbidity of SUD in SC as a function of ethnicity. Montross et al. (2005) found the prevalence of DD was lower in Latino Americans than in European and African Americans in San Diego County (US). An epidemiologic study conducted in Mexican Americans found the lifetime prevalence of SUD in those subjects with comorbid psychotic symptoms was 20% for immigrants and 49% for those born in the US (Vega et al., 2006). Outside of these two studies there are no published reports of SC and SUD comorbidity rates

in samples of Latino subjects and no epidemiologic studies that have investigated these comorbidities in an international sample.

The present analyses utilized the largest known sample of systematically assessed subjects with SC from the Latino population, drawn from the NIMH Genetics of Schizophrenia in Latino Populations study, to estimate the frequency of DD in the subjects in this study. In addition, the present study describes the clinical characteristics of subjects with comorbid SUD in these Latino subjects and compares rates of DD across three geographic regions (the Southwest United States, Mexico, and Central America). We also tested several hypotheses regarding SUD comorbidity in SC subjects within this sample. These hypotheses included that SUD comorbidity would be higher in the US subjects compared to those from Mexico and Central America and that rates of comorbidity would be, in general, less than previous studies of SC in non-Latino populations. Based on studies conducted in other samples (Bartels et al., 1993; Menezes et al., 1996; Soyka et al., 2001; Swartz et al., 2006; Weaver et al., 1999), we also hypothesized that gender, marital status, employment status, and immigration to the US from Mexico would be associated with comorbidity in this sample. We hypothesized that increased lifetime history of depression and level of deterioration would be associated with comorbid SUD in SC subjects from the current study. Finally, we investigated the ages of onset of SUD and SC in comorbid cases, to better understand how these comorbidities develop in Latino/a men and women.

2. Methods

2.1. Subjects

All participants were recruited in accordance with the principles of the Declaration of Helsinki and with approval from the Institutional Review Boards of each participating site, as part of a family based linkage study of SC and schizoaffective disorder. Recruitment teams were located in San Antonio (Texas, US), Los Angeles and San Diego (California, US), Monterrey and Mexico City (Mexico), Guatemala City (Guatemala), and San José (Costa Rica). All sites participated in group training sessions to standardize assessments using the Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et al., 1994), the Family Interview for Genetic Studies (FIGS) (Maxwell, 1992), and a review of psychiatric records. Families were eligible for study if they had at least two siblings with hospital or clinical diagnoses of SC or schizoaffective disorder. Subjects included in the study were all over 18 age of year, willing to contribute a blood sample, and complete a diagnosis interview. Subjects were recruited if their parents had ancestry from Central America or Mexico. Subjects were also asked to describe their parents's ethnicity, as part of the DIGS interview (see description in Results). After complete description of the study to the subjects, written informed consent was obtained.

2.2. Diagnosis

Subjects were diagnosed according to the DSM-IV by a best estimate consensus process, using a DIGS, a FIGS and review of all available medical records, this best estimate procedure has been described in detail (Escamilla et al., 2007). Each best estimator was a bilingual, bicultural clinician (psychiatrist or psychologist) and cases were diagnosed independently, followed by a discussion of any differences in diagnosis, and a final consensus was completed for specific disorders, syndromes, and ages of onset. After completion of the best estimate consensus process, 518 subjects (from 284 separate families) met DSM-IV criteria for SC. Tables shown in this article are for the entire sample of affected participants. SUD was defined as either alcohol or substance abuse or dependence by best estimate consensus. Best estimators also determined age of onset of each SUD, as well as the age when each subject first met full DSM-IV criteria for SC, and whether or not each subject had ever met criteria for a full depressive episode or syndrome, using DSM-IV criteria. Best estimators independently rated the level of

deterioration experienced by subjects using the measure included in the Lifetime Dimension of Psychosis Scale (Levinson et al., 2002), and the rater average was used in these analyses. Other demographic variables were captured in the DIGS. Best estimators were not aware of any of the specific hypotheses being tested in this paper.

2.3. Data analysis

Statistical analysis was carried out with the program Statistical Procedures for Science Society, version 15.0. To test specific hypotheses, we used a subset of the full sample (one subject with SC per family), to avoid bias that could be caused by potential correlations between relatives. The single individual per family with SC was selected using the random number generator function in Microsoft Excel. Since each hypothesis tested was a specific one, based on previous analyses, we considered probability values ≤ 0.05 to be statistically significant. All tests were two-tailed. When a chi-square could not be calculated, a 2×2 table was built and its significance was determined by means of the Fisher test, or Yates' correction test as appropriate.

To test hypotheses that gender, age, living situation, employment status, marital status, deterioration or history of depressive disorders are associated with SUD in these subjects, we used a T-test for age at interview, years of school, and deterioration. Fischer's exact test was used for gender, depressive syndrome or episode, marital status, employment, and migration status. Yates' correction test was used for relative onset of SC and SUD. Binary logistic regression was used to model the relationship between the dependent variable SUD and predictor variable living situation. To control for confounding effects of SUD and gender in sociodemographic variables such as marital status and employment, logistic regression methods were used for each outcome variable. In order to test whether country of residence was associated with different rates of SUD logistic regression methods were utilized.

3. Results

Ethnicity of the participants in this study was by self report. Costa Rican subjects reported 100% bilineal ancestry from Costa Rica, with two subjects reporting partial Nicaraguan ancestry. Guatemalan subjects reported 100% bilineal ancestry from Guatemala, with two of the subjects reporting partial known European ancestry (Belgian and Spanish ancestry). Of the 310 subjects from Mexico who reported on their ancestry, 100% reported bilineal Mexican ancestry, with four reporting partial known ancestry from Western Europe (Spain, France), 3 reporting partial known ancestry from Eastern Europe (Poland), and one reporting partial known ancestry from Puerto Rico. Subjects from the United States reported primarily bilineal Mexican ancestry (94% of subjects), with 5% reporting half Mexican ancestry (one parent) and half non-Hispanic white ancestry (other parent with Anglo-Saxon or Western European ancestry) and 1 person reporting Mexican ancestry from one parent and Puerto Rican ancestry from the other parent. Of the subjects from the United States, 4 reported known partial Native American ancestry, one reported Guatemalan ancestry, and 3 additional subjects with bilineal Mexican ancestry reported partial known European ancestry.

Sample characteristics are described in Table 1. Out of 518 SC subjects, 23.4% had DD (SC and SUD). Of 178 female subjects with SC, 7.9% had SUD comorbidity and out of 340 male subjects with SC, 31.5% had comorbid SUD. The proportion of subjects who reported a history of depressive syndrome or episode was large among those who had SUD. Regardless of history of SUD, the majority of subjects had never married.

History of marriage frequencies was essentially the same for women with and without a history of SUD (38.5% of DD women, 39.4% of SC only women). For men, those with a history of DD had higher frequencies of ever having been married (22.1% of DD men had been married, versus 13.9% of SC only men). The variable "ever married" included those who were married,

separated, divorced or widowed. Rates of ever marrying were higher for women than for men, regardless of SUD comorbidity history.

Unemployment rates were higher for SC subjects with a history of DD, but this was primarily due to differences in males. Only 29.5% of men with a DD were employed, compared to 43.8% of men with SC only. Employment rates for women were 53.8% and 51% respectively for DD cases and SC only cases. Regardless of DD history, males were more frequently unemployed than females. It is important to note, however, that the variable “employed” included any type of employment including ‘housewife,’ which may explain the higher employment rates for women in this sample.

Table 2 shows the lifetime prevalence of SUD, by gender and country of residence, in the total sample. For both genders, the most frequent substance of abuse/dependence was alcohol, followed by marijuana. In the whole sample one in four of the men had history of alcohol abuse or dependence, and almost one in six men had history of marijuana abuse or dependence. Inhalant misuse and cocaine misuse occurred in approximately 4 % of the men. All other substances had lifetime abuse/dependence rates below 1% in men. For women, the same four substances were the substances with lifetime misuse rates greater than 1%, although the rates were much less than the equivalent rates in men.

As shown in Table 3, for men with DD histories, the mean age of onset of SUD was 2.6 years earlier than the mean age of onset of SC. For females with DD history, the mean onset of SUD was 3.5 years after the onset of SC.

Among men and women with DD, each gender had cases where either SUD or SC occurred first, but there were clear differences in these patterns between genders (Table 4).

There were clear differences in SUD comorbidity between the different geographic regions in this collaborative study (Table 5). All sites showed higher rates of comorbid SUD in men than in women. For men, SUD comorbidity was highest in Latinos living in the US (51%), lowest in Latinos from Mexico (23.3%), and intermediate in Latinos from Central America (31.9%). For women, SUD comorbidity was 27.3% in Latinas from the US, and very low in both Latinas from Mexico and Central America (3.4% and 3.5% respectively).

Regarding migration status, in the whole sample, 36 subjects migrated from their original countries. Out of those 36 subjects, 34 migrated from Mexico to the US, 1 from Guatemala to the US, and 1 from the US to Costa Rica.

Out of 36 subjects who migrated, 15 met criteria for DD, of those 15 subjects 13 migrated from Mexico to the US, one migrated from Guatemala to the US and another one from US to Costa Rica.

Table 6 shows that out of 34 Mexican-born subjects who migrated to the U.S, 13 (38.2%) met lifetime criteria for SUD whereas out of 293 Mexican-born subjects who did not migrate and reside in their own country (Mexico) 45 (15.4%) had a lifetime history of SUD. For individuals whose country of residence was the US, 47% (N=31) of the US-born subjects had lifetime SUD while 40% (N=14) of the immigrants met criteria for lifetime SUD.

Specific hypotheses were tested using one subject per family. We found that male gender was significantly associated with comorbid SUD (Fischer’s exact test, $\chi^2=2.116$, $p<0.001$) and that history of depression was significantly associated with SUD (Fischer’s exact test, $\chi^2=6.479$, $p=0.013$). Furthermore, individuals with SUD had a higher rate of unemployment than individuals with SC only (Fischer’s exact test, $\chi^2=6.773$, $p=0.010$). Binary logistic regression showed that SUD was a significant predictor of unemployment (SUD: $B=0.746$, $Wald=5.774$,

df=1, $p=0.016$, odd ratio=2.159). Gender was not related to unemployment. In this procedure we used the variable employment as a dependent variable and predictors were SUD and gender.

The three countries were significantly different in their rates of DD ($\chi^2=18.349$, $p<0.001$). When binary logistic regression was used to analyze country of residence Mexican and Central American schizophrenic patients were less likely to be diagnosed with SUD than subjects from the US (Mexico: $B=-1.337$, Wald $\chi^2=17.225$, df= 1, $p<0.001$, odd ratios=0.263; Central American: $B=-0.818$, Wald $\chi^2=4.444$, df=1, $p=0.035$, odd ratios=0.441); therefore, country of residence was a significant predictor of SUD.

Mexican-born men who migrated to the US had a significantly higher rate of DD than those who did not emigrate (Fischer's exact test, $\chi^2=6.057$, df=1, $p=0.02$).

Deterioration, current living situation, and marital status were not associated with comorbid diagnoses. For marital status binary logistic regression showed that gender was a significant predictor of marital status because females compared with males were more likely to be married ($B=-1.104$, Wald $\chi^2=12.278$, $p<0.001$, exp (B)=0.331) and SUD was not associated with marital status ($p=0.198$). In this model marital status was the dependent variable and "never married" was selected as the reference category with covariables being SUD and gender, with any SUD and male as predictor variables.

Comorbid SUD did not contribute to earlier onset of SC. The difference in the means of age of onset of SC in participants with and without SUD was not statistically significant when the t test was used ($t=0.853$, df=282, $p=0.394$). In participants with comorbid SC and SUD, subjects were more likely to have the SUD occur before or at the same time as the SC, rather than after onset of SC ($\chi^2=5.657$, Yates' correction=3.850, $p=0.050$), although this was driven largely by men in this sample.

4. Discussion

The lifetime prevalence of comorbid SUD in this Latino sample of subjects with SC was on the low end compared to rates documented in previous studies from Europe and non-Latino US populations (Cantor-Graae et al., 2001). However, the prevalence rates of comorbidity varied among Latinos based on the country they were living in. Latinos living in the US had lifetime rates of DD similar to what has described for SC subjects in the US (Cantor-Graae et al., 2001; Kessler et al., 2005; Regier et al., 1990). In contrast, Latinos living in Central America and Mexico had much lower rates of comorbid SUD, which were comparable with studies of with DD in Latino populations (Montross et al., 2005; Vega et al., 2006).

The country of residence with the highest frequency of DD was the US, followed by Central America and finally Mexico and these differences were statistically significant. Immigration from Mexico to the US was significant associated with an increase in the diagnosis of SUD. These increased rates of SUD in US residents and in Mexican subjects that immigrated to the US, compared to subjects living in Mexico, is consistent with the data of Vega (Vega and Sribney, 2003) and others who suggest that acculturation to the US might be associated with increased psychiatric comorbidity for both genders, as well as a risk factor for SUD in non-psychiatric samples (Buchanan and Smokowski, 2009; Prado et al., 2009). It has been suggested that the more typical interconnectedness of large families and other cultural factors among Latinos may represent protective dynamics contributing to lower rates of DD among Latinos and that these factors may begin to break down or have less effect once Latinos are exposed to a different culture through residence in the US (Alegria et al., 2006; Montross et al., 2005; Vega et al., 2009). Since this study was done uniformly across sites, our findings suggest that environment (country of residence) indeed plays a significant role in development of SUD in schizophrenic individuals among Latinos/Latinas.

In the current study, male gender and unemployed status were significantly associated risk factors for DD, as has been reported in previous investigations in other cultures (Ringgen et al., 2008; Swartz et al., 2006; Verma et al., 2002). Although our sample of DD women was small, the finding that women were older compared to men at the outset of SUD is also in agreement with the literature (Cantor-Graae et al., 2001; Gearon et al., 2003). For men, our results suggest that the vast majority will have the onset of SUD prior to or in the same year as they develop the full diagnosis of SC. In women, there is a smaller prevalence of SUD, and when it occurs the SUD is as likely to occur after the onset of full SC as before. This suggests that for men, SUD may be more likely to act as a “trigger” for onset of SC, whereas for women it is equally likely that SUD may occur after SC has already started.

In the Latino populations from the present study, alcohol was the most frequently abused substance, which is similar to what has been found in previous studies conducted in the US, and other countries (Cantor-Graae et al., 2001; Regier et al., 1990; Rossi Menezes and Ratto, 2004; Verma et al., 2002). The second most frequently described SUD in this sample was marijuana. Given recent findings on possible involvement of the cannabinoid receptor in SC (Chavarría-Siles et al., 2008), it is intriguing to note the prominence of this SUD in the DD cases studied here. The third most common type of SUD in our study was for solvent abuse or dependence, a problem that others have suggested is a particular problem in Latino populations (Padilla et al., 1979). Cocaine SUD occurred in a relatively small number of subjects, contrary to what is presented in the literature for other populations, which have reported cocaine abuse as one of the most frequent SUDs (Lammertink et al., 2001; Mueser et al., 2000; Soyka et al., 2001). Newer drugs (i.e. ecstasy) and drugs thought to play a role in SC risk in previous eras or different cultures (i.e. lysergic acid, hallucinogens, PCP) were negligible in the current study sample.

We found in this research that depression was correlated with SUD in SC clients in accord with previous studies that have showed that depressive symptoms may be a risk factor for SUD in patients with SC (Addington and Duchak, 1997; Dixon et al., 1990). The association of depression and SUD in our sample could represent use of SUD to self-medicate depressive mood or, alternately depressogenic effects of SUD. Longitudinal studies would be necessary to better tease out the reason for this interesting association.

The strengths of this research include that this study was conducted in a sample of Latino subjects with SC from three different geographic areas in the same time period, using standardized interviews conducted by psychiatrists, the same diagnostic system across sites, and a consensus process for diagnosis. Few international studies using large, well diagnosis samples have been carried out since WHO's International Study took place decades ago (Sartorius et al., 1972).

The limitations in this study are several. First, the study sample is not representative of all SC subjects from these populations, but represents a sample of SC subjects from families where there are multiple SC cases. Whether SC in multiplex families is different from SC observed in sporadic cases is not known. The current sample is also not representative of all Latinos, as it does not include South Americans, Puerto Ricans or other Caribbean ancestry Latinos. Further studies about the relationship of SC and SUD in additional Latino populations and in more randomly ascertained subjects would be necessary to have data representative of the larger Latin American population.

In conclusion, the present study finds that there is high comorbidity of SUD in Latinos (particularly men) with SC, and that this varies across countries. Male gender and history of depression are important risk factors for comorbidity in these Latino populations. The substances of abuse/dependence that are most frequent are alcohol, cannabis, solvents, and

cocaine. The sequence of onset of SUD in comorbid cases also suggest that potential preventative strategies may be of use in men (prior to onset of SC) and that SUD prevention in women may be especially important after the development of SC. Further exploration and study of the “protective” aspects of Latino culture in Latino countries and the increased risk associated with Latinos living in the US will be valuable in treating and preventing SUD in subjects with SC.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Abbreviations

DD	dual diagnosis
SC	Schizophrenia
SUD	Substance use disorders
US	United States
NIHM	National Institute of Mental Health
DIGS	Diagnostic Interview for Genetics Studies
FIGS	Family Interview for Genetics Studies
DSM-IV	The Diagnostic and Statistical Manual of Mental Disorders 4th. Edition
PCP	phenylcyclohexylpiperidine
LCD	lysergic acid diethylamide

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Table 1

Demographic Characteristics

Characteristics	Substance Use Disorder and <i>schizophrenia</i>				<i>Schizophrenia only</i>				All Subjects			
	N	%	Mean	SD	N	%	Mean	SD	Mean	SD	Mean	SD
Demographic characteristics												
Count	121	23.4			397	76.6					518	
Male	107	31.5			233	68.5					340	
Female	14	7.9			164	92.1					178	
Age at Interview			38.2	10.5			37.7	10.9			37.8	11.3
Years of education			9.1	3.6			8.9	3.8			8.9	3.8
Deterioration ^a			3.2	0.8			3.1	0.9			3.1	0.8
Depressive Syndrome/Episode												
YES	64	52.9			161	40.5					225	43.4
NO	57	47.1			236	59.5					293	56.6
Living Situation ^b												
Alone	7	6.0			19	4.9					26	5.1
With family or other people	102	87.2			355	91.7					457	90.7
In residential treatment facility	3	2.5			10	2.6					13	2.6
Other	5	4.3			3	0.8					8	1.6
Marital Status ^c											All subjects (adjusted by sex) %	
Never Married	89	76.1			295	75.6					69.7%	
Ever Married	28	23.9			95	24.4					30.3%	

^a11 missing^b14 missing^c11 missingGender: Fischer's exact test, $\chi^2 = 12.116$, $p < 0.001$ Depression: Fischer's exact test, $\chi^2 = 6.479$, $p < 0.013$ Age at interview, years of education, Deterioration, Living situation, Marital status= $p > 0.05$.

Table 2
Frequency of each substance misuse in the Latino Schizophrenic sample by country of residence and gender. (N=518)

Gender	US (N=111)				Mexico (N= 310)				Costa Rica (N= 65)				Guatemala (N=32)				All sample			
	Male N=78	Female N=33	Male N=193	Female N=117	Male N=48	Female N=17	Male N=21	Female N=11	Male N=340	Female N=118										
Type of SUD	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%				
Alcohol	30	38.5	5	15.2	36	18.7	2	1.7	13	27.1	1	5.9	6	28.6	0	0	85	25.0	8	4.5
Marijuana	23	29.5	3	9.1	25	13.0	4	3.4	4	8.3	0	0	1	4.8	0	0	53	15.6	7	3.9
Inhalant/Solvent	6	7.7	1	3.0	8	4.1	1	0.9	1	2.1	0	0	0	0	0	0	15	4.4	2	1.1
Cocaine	7	9.0	2	6.1	6	3.1	0	0	1	2.1	0	0	0	0	0	0	14	4.1	2	1.1
Amphetamine	3	3.8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0.9	0	0
Opitoid	1	1.3	1	3.0	1	0.5	0	0	0	0	0	0	0	0	0	0	2	0.6	1	0.6
LSD	1	1.3	1	3.0	0	0	0	0	0	0	0	0	0	0	0	0	1	0.3	1	0.6
Other Drugs	1	1.3	0	0	1	0.5	1	0.9	0	0	0	0	0	0	0	0	2	0.6	1	0.6

US, United States; SUD, Substance Use Disorder; PCP, phenylcyclohexylpiperidine; LCD, lysergic acid diethylamide. None of the subjects was diagnosed with abuse/dependence of ecstasy, heroin or PCP.

Table 3

Age of Onset of Substance use Disorder, SC in comorbid subject and Schizophrenia only

Age of Onset	Total subjects					
	Male			Female		
	Mean	SD	N	Mean	SD	N
Schizophrenia (in subjects with comorbidity)*	20.9	6.0	121	19.6	5.8	121
Substances Use Disorder (in subjects with comorbidity)	18.3	5.2	121	23.1	8.3	121
Schizophrenia only*	20.2	7.0	397	20.9	7.3	397

*
t test = p>0.05

Table 4

Relative Onset of Schizophrenia and Substance Misuse by Gender

	Gender					
	Male			Female		
Relative Onset	N	%	N	%	N	%
Onset of Substance misuse came first	74	69.2	5	35.7	79	65.3
Onset of Schizophrenia came first	23	21.5	7	50.0	30	24.8
Equal Age Onset SC and Substance misuse	10	9.3	2	14.3	12	9.9
Total	107	100.0	14	100.0	121	100.0

 $\chi^2=5.657$, Yates' correction=3.850, $p=0.05$

Table 5

Frequency of Dual Diagnosis in 518 schizophrenic subjects, by country of residence and gender.

Gender	US (N=111)			Mexico (N=310)			Central America (N=97)			total		
	SC + SUD		N	SC only		N	SC + SUD		N			
	%	N		%	N		%	N				
Male	51.3	38	48.7	45	23.3	148	76.7	22	31.9	47	68.1	340
Female	27.3	24	72.7	4	3.4	113	96.6	1	3.6	27	96.4	178
Total sample	44.1*	62	55.8	49	15.8*	261	84.2	23	23.7*	74	76.3	518

* Fisher's exact test: $\chi^2 = 18.349$, $p = 0.001$;

Mexico: $B = -1.337$, Wald $\chi^2 = 17.225$, $df = 1$, $p < 0.001$, odd ratios = 0.263

Central American: $B = -0.818$, Wald $\chi^2 = 4.444$, $df = 1$, $p = 0.035$, odd ratios = 0.441

Table 6
Characteristics of Migration Status in the schizophrenic sample by dual diagnosis and gender.

Gender	Male						Female						Total	
	Dual Diagnosis			SC Only			Dual Diagnosis			SC Only				
Diagnosis	N	%	N	%	N	%	N	%	N	%	N	%	N	N
Mexican-born Subjects <i>a, c</i>														
Migrated to US	12	44.4	15	55.6	1	14.3	6	85.7	34					
Residing in Mexico	41	22.4	142	77.6	4	3.6	106	96.4	293					
US residents <i>b, d</i>	N	%	N	%	N	%	N	%	N	%	N	%	N	N
Immigrants	13 ^e	46.4	15	53.6	1 ^f	14.3	6	85.7	35					
US-born	24	55.8	19	44.2	7	30.4	16	69.6	66					

^aMexican-born men by Dual Diagnosis or Schizophrenia only: Fischer's exact test, $\chi^2 = 6.057$, $df=1$, $p=0.02$
^bUS residents by Dual Diagnosis or Schizophrenia only = $p>0.05$.
^c17 missing: it was unknown where 17 of the subjects residing in México were born.
^d10 missing: it was unknown where 10 subjects residing in US where born.
^eSubjects migrated from México
^fSubjects migrated from Guatemala.
US = United States.