Subjects affected by a substance use disorder with or without a comorbid mental disorder: looking for differential factors

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Introduction

The coexistence in the same subject of substance use disorders (SUD) with other psychiatric disorders it is a major health problem. These "dual patients" or "drug addicts with psychiatric co-morbidity" are a high risk group from the clinical and social perspective; they are frequenters of emergency services , require more psychiatric admissions , have a high risk of infections such as HIV [3] and respond poorly to treatment [4]. From a social perspective have high social unrest with high unemployment and marginalization. Prevalence studies in general population and in clinical samples estimate it is between 30-50% in psychiatric population and between 47% and 87% in drug-dependent population. This high prevalence along with their clinical and social gravity has prompted the study of factors related to the pathogenesis and development of new treatments for dual diagnosis as a priority line of research. Factors such as personality traits (eg impulsivity, sensation seeking, harm avoidance) or psychiatric co-morbidity may also contribute to the development of a SUD [5].

Objectives

To study the genetic variability of subjects with SUD depending if they have co-morbidity with non SUD psychiatric disorders (dually diagnosed subjects, DD) or not (SD).

Material and Methods

This is a case-control association study of 160 SD subjects as controls and 153 DD subjects as cases. Individuals included in the study were substance abusers collected from CIDI-TOX study (National Plan 2005) and identified as white Europeans. All patients were diagnosed according the Spanish validated version of Psychiatric Research Interview for Substance and Mental Disorders (PRISM-IV). The personality characteristics were evaluated using the Spanish version of the Cloninger's Temperament and Character Inventory (TCI-R). We genotyped 768 SNPs located in 57 genes involved in addiction using the GoldenGate Assay (Illumina) (Fig 1). Statistical analyses were performed using different software packages (Haploview, SNPassoc and PLINK) and the significance of the results were assessed by permutation procedure.

Results

- Compared with SD group, DD subjects were older, more prevalence of single status, lower academic levels as well as a higher frequency of psychiatric and addictive family background. According to SUD, DD subjects showed higher occurrence of alcohol and cocaine use disorders and a lower cannabis use disorders.
- With respect to personality dimensions, subjects with dual diagnosis scored significantly higher in terms of 'harm avoidance' and 'self-transcendence', and a lower score on 'self-direction' (Table 1).
- The association study of DD vs. SD showed no significantly associated SNP. Also, haplotype analysis did not reveal any combination of SNPs as more frequent in DD than in SD.

Table 1. Sociodemographic and clinical characteristics among the group of subjects with substance use disorders (SD) and the dual group (DD).

	SD (n=160)	DD (n=153)	*P**
Age inyears, mean (SD)	25 (10)	36 (12)	**<0,001**
Men (%)	119 (74,4)	99 (64,7)	0,066
Single (%)	154 (96,3)	129 (84,3)	**<0,001**
Educational level (high school or superior) (%)	123 (76,9)	99 (64,7)	**0,019**
Parental Psychiatric Background	17 (10,6)	31 (20,3)	**0,019**
Parental Drug Misuse Background	12 (7,5)	30 (19,6)	**0,003**
Cannabis SUD (%)	123 (76,9)	77 (50,3)	**<0,001**
Alcohol SUD (%)	74 (46,3)	108 (70,6)	**<0,001**
Cocaine SUD (%)	32 (20)	71 (46,4)	**<0,001**
Other SUD (%)	3 (1,9)	3 (2)	0,956
TCI temperamental scales, mean (SD)			
Harm Avoidance	49,8 (12,3)	55,3 (12,4)	**<0,001**
Novelty Seeking	56,8 (8,4)	57,1 (10,8)	0,814
Reward Dependence	47,3 (9,5)	47,5 (9,1)	0,832
Persistence	46,6 (11,2)	48,4 (12,2)	0,202
TCI character scales, mean (SD)			
Self-Directness	43,6 (10,3)	37,9 (11)	**<0,001**
Cooperativeness	44,9 (9,3)	43,4 (10,5)	0,229
Self-Transcendence	50,5 (10,7)	55,7 (13)	**<0,001**

Figure 1. Comprehensive list of genes included in this study.

Gen	Simbolo	N° de SNPs
ATP-binding cassette, sub-family B, member 1	ABCB1	5
Actinin, alpha 1	ACTN1	1
Alcohol dehydrogenase 1C (class I), gamma polypeptide	ADH1C	11
Alcohol dehydrogenase 4 (class II), pi polypeptide	ADH4	4
Alcohol dehydrogenase 1B (class I), beta polypeptide	ADH1B	8
Aldehydedehydrogenase 2 family	ALDH2	6
Ankyrin repeat and kinase domain containing 1	ANKK1	10
Bobby soxhomolog	BBX	1
Brain-derivedneurotrophic factor	BDNF	8
Calcium/calmodulin-dependent protein kinase I	CAMK1	1
Cannabinoid receptor 1	CNR1	14
Catechol-O-methyltransferase	COMT	17
Cytochrome P450, family 2, subfamily A, polypeptide 6	CYP2A6	12
Cytochrome P450, family 2, subfamily D, polypeptide 6	CYP2D6	11
Cytochrome P450, family 2, subfamily E, polypeptide 1	CYP2E1	11
Cholinergic receptor, muscarinic 2	CHRM2	46
Cholinergic receptor, nicotinic, alpha polypeptide 3	CHRNA3	4
Cholinergic receptor, nicotinic, alpha polypeptide 4	CHRNA4	7
Cholinergic receptor, nicotinic, alpha polypeptide 5	CHRNA5	2
Cholinergic receptor, nicotinic, beta 2	CHRNB2	1
Dopamine beta-hydroxylase	DBH	29
Dopa decarboxylase	DDC	5
Dopamine receptor D2	DRD2	23
Dopamine receptor D3	DRD3	13
Dopamine receptor D4	DRD4	4
Fattyacidamidehydrolase	FAAH	10
Gamma-aminobutyricacid (GABA) A receptor, alpha 1	GABRA1	8
Gamma-aminobutyricacid (GABA) A receptor, alpha 2	GABRA2	17
Gamma-aminobutyricacid (GABA) A receptor, alpha 6	GABRA6	6
Gamma-aminobutyricacid (GABA) A receptor, beta 1	GABRB1	13
Gamma-aminobutyricacid (GABA) A receptor, gamma 1	GABRG1	12
Growth hormone secretagogue receptor 1A	GHS-R1A	2
Glutamate receptor, ionotropic, N-methyl D-aspartate 2A	GRIN2A	96
Glutathione S-transferase theta 1, 2 and 2B	GSTT1-2-2B	9
5-Hydroxytryptamine (serotonin) receptor 1B	HTR1B	9
5-Hydroxytryptamine (serotonin) receptor 2A	HTR2A	50
Interleukin 10	IL10	7
Monoamine oxidase A	MAOA	8
5,10-methylenetetrahydrofolate reductase (NADPH)	MTHFR	1
Myocardin	MYOCD	2
Neuropeptide Y	NPY	6
Neurexin 1	NRXN1	2
Neurexin 3	NRXN3	1
Neurotrophic tyrosine kinase, receptor, type 2	NTRK2	4
Opioid receptor, delta 1	OPRD1	1
Opioid receptor, kappa 1	OPRK1	13
Opioid receptor, mu 1	OPRM1	74
Prodynorphin	PDYN	18
Proteininteractingwith PRKCA 1	PICK1	2
Neurotransmitter transporter, dopamine	SCL6A3	23
Neurotransmitter transporter, serotonin	SLC6A4	9
Taste receptor, type 2, member 16	TAS2R16	1
Tyrosinehydroxylase	TH	11
Tryptophanhydroxylase 1	TPH1	9
Tryptophanhydroxylase 2	TPH2	28
Transient receptor potential cation channel, subfamily C, member 5	TRPC5	1
Zinc fingerprotein 505	ZNF505	1
	Total general	768

Conclusions

Some differential characteristics were observed between PD and SD subjects in sociodemograhical, clinical and personality profiles but we were not able to find genetical variants that could discriminate between both samples.

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