Acute tryptophan depletion response in cocaine dependent subjects with comorbid depression

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Abstract

An important challenge in substance use is to discriminate between induced and independent depression. Serotonergic system is one of the neurochemical systems implicated in both independent major depression and substance use disorders. Acute tryptophan depletion test (ATD) has been used to evaluate serotonin function. ATD response could be a useful biomarker to differentiate primary from induced depression.

(1) Substance dependent patients (SDP) (2) with independent major depression (SMD) or (3) substance-induced major depression (SIMD), (4) matched-healthy controls (HC), and (5) patients with major depression (MD).

Subjects participated in two double-blind randomized sessions (ATD and non-ATD). A total of 83 subjects participated: 20 subjects with induced depression (9 cocaine induced depression and 11 alcohol induced depression), 21 subjects with substance use disorder and primary major depression (15 cocaine and 6 alcohol), 20 subjects with substance use disorder, without depression (9 cocaine and 11 alcohol), 5 subjects with major depression (without substance use) and 17 healthy controls. ATD test was performed and mood changes were evaluated by the Hamilton Rating Scale for Depression (HRSD) at baseline (T0) and after 5 hours (T2).

Differences on tryptophan concentrations between T0 and T2 were statistically significant for all groups evaluated ($p<0.01$). An increase in T2 HDRS total scores was observed in two groups of comorbid major depression, both induced and primary, and no changes were found in the other groups.

These preliminary results show a different response to ATD test between independent depression and cocaine-induced major depression and alcohol-induced major depression supporting the idea of a different implication of the serotonergic system in substance-induced depressions.

Introduction

Substance use disorders present high prevalence of comorbidity with depressive disorder [1]. An important challenge in cocaine/alcohol dependent subjects is to discriminate between induced and independent major depression. Differences in antidepressant response have been described between both types of depression [2]. Also, poorer outcomes at discharge have been described in induced depressions [3]. Serotonergic system is one of the neurochemical systems involved in both independent major depression and substance use disorders [4]. Acute tryptophan depletion test (ATD) has been used to evaluate serotonin function [5]. ATD response could be a useful biomarker to differentiate primary from induced depression.

The aim of the present study was to assess the ATD response in five groups: (1) substance dependent patients (SDP) (2) with independent major depression (SMD) or (3) substance-induced major depression (SIMD), (4) matched-healthy controls (HC), and (5) patients with major depression (MD).

Methods

Subjects participated in two double-blind randomized sessions (ATD and non-ATD) A total of 83 subjects participated: 20 subjects with induced depression (9 cocaine induced depression and 11 alcohol induced depression), 21 subjects with substance use disorder and primary major depression (15 cocaine and 6 alcohol), 20 subjects with substance use disorder, without depression (9 cocaine and 11 alcohol), 5 subjects with major depression (without substance use) and 17 healthy controls.

DSM-IV-TR diagnoses were obtained by PRISM interview. ATD test was performed and mood changes were evaluated by the Hamilton Rating Scale for Depression (HRSD) at baseline (T0) and after 5 hours (T2).

The data were analyzed with Paired sample T-test and repeated measures ANOVA and post hoc analysis using the Bonferroni test.

Results

The main characteristics of included subjects are described in Table 1. There were no differences in gender, or race, but healthy controls were younger and substance use subjects present more prevalence of single status.

In the ATD session, differences on tryptophan concentrations between T0 and T2 were statistically significant for all groups evaluated (Table 2). An increase in T2 HDRS total scores was observed in two groups of comorbid major depression, both induced and primary, and no changes were found in the other groups (Table 3).

When we analyzed the sample dividing by the type of substance used (alcohol or cocaine), we observed that the differences in the HDRS scores were statistically increased from T0 to T2 in the cocaine primary depression group and in the alcohol induced depression group (Figure 1).

Table 1. Main characteristics of the studied groups

	Healthy N= 17	Depression N= 5	SUD Primary depression N= 20	SUD induced depression N= 21	SUD N= 20	p
Males n(%)	11 (65)	5 (100)	15 (75)	17 (81)	16 (80)	NS
Age mean (SD)	32 (5)	44 (14)	40 (9)	47 (8)	40 (13)	0.001
Whites n(%)	17 (100)	5 (100)	20 (100)	21 (100)	19 (95)	NS
Single n(%)	9 (53)	2 (40)	9 (45)	7 (33)	14 (70)	0.043

SUD: substance use disorder; SD: standard deviation

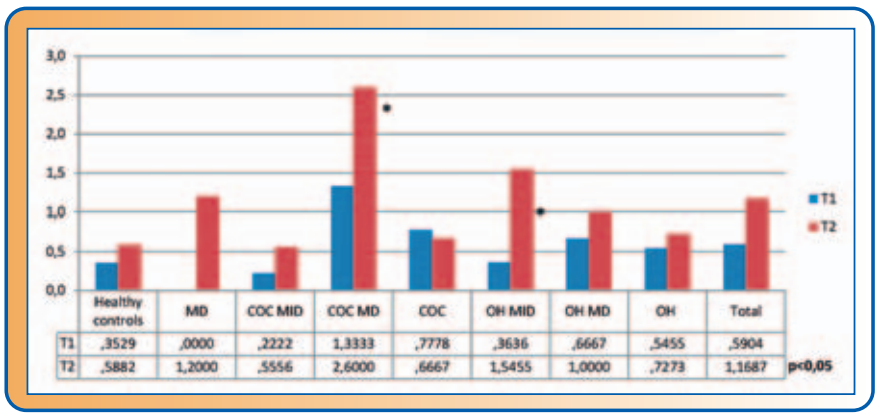
Table 2. Differences in tryptophan concentrations (µMol/L) in the ATD session.

	T-T0	T-T2	p
Healthy	35.5 (17.9)	9.4 (5.4)	<0.001
Depression	59.5 (8.9)	5.8 (0.9)	0.001
SUD Primary depression	43.7 (19.5)	7.5 (3.2)	<0.001
SUD induced depression	46.7 (22.8)	10.6 (7.4)	<0.001
SUD	69.1 (31.6)	7.9 (2.3)	<0.001

Table 3. Differences HDRS scores in the ATD session.

	T-T0	T-T2	p
Healthy	0.4 (0.79)	0.6 (1.1)	NS
Depression	0 (0)	1.2 (1.8)	NS
SUD Primary depression	0.3 (0.7)	1.1 (1.3)	0.009
SUD induced depression	1.1 (1.1)	2.1 (1.8)	0.005
SUD	0.7 (1.3)	0.7 (1.2)	NS

Figure 1. HDRS mean scores in the depletion session. Significant differences in HRSD were found in the COC MD and OH MID groups.



HRSD: Hamilton Rating Scale for Depression; MD: Major depression; COC MID: cocaine induced major depression; COC MD: cocaine major depression; COC: cocaine; OH MID: alcohol induced major depression; OH MD: alcohol major depression; OH: alcohol.

Discussion

As expected, decreases in plasmatic concentrations of tryptophan were detected after the ATD session for all patient's groups. At clinical level, measuring with HDRS, only significant differences were found in the primary and induced substance depression. The lack of significant results in the HDRS in the major depression (without substance abuse) group would be related to the reduced sample size of this group.

Interestingly, when primary and induced depressions were divided depending on the primary drug of abuse, changes in HDRS were only observed in cocaine primary depression and in alcohol induced major depression. These results could be associated with differences in the implication of serotonergic system in the depressions associated with substance use depending on the neurobiological effect of different substances.

Conclusions

These preliminary results show a different response to ATD test between cocaine independent depression and cocaine-induced major depression, and also between alcohol independent and alcohol induced major depression, but with in opposite directions.

These results support the idea of a different implication of the serotonergic system in substance-induced depressions.

More studies, with bigger sample size is assured to better define this different serotonergic behavior.

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