TRYPTOPHAN ACUTE DEPLECTION TEST IN COCAINE DEPRESSED PATIENTS

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Introduction

Major depression is the most common psychiatric comorbidity in cocaine dependent (CD) subjects. A major challenge is to know if the comorbid depression episode is primary (PMD) or induced by the substance. Serotonergic system is one of the neurochemical systems implicated in both independent major depression and substance use disorders. Acute tryptophan depletion (ATD) has been used to evaluate serotonin function [1]. ATD response could be a useful biomarker to differentiate primary from induced depression.
The aim of the study is to assess the ATD response in cocaine dependent patients with PMD and cocaine-induced major depression (C-IMD).

Subjects and methods

23 cocaine dependent patients (DSM-IV-TR) (14 with PMD and 9 with comorbid C-IMD and 21 healthy controls (DSM-IV-TR) have been assessed by ATD in a randomized double-blind crossover study. Mood changes during ATD by the Hamilton Rating Scale for Depression (HRSD), tryptophan (TRP) plasma levels and ratio of tryptophan and large neutral amino acids (LNAA) plasma levels (that limits the transport of tryptophan across the blood brain barrier by competition [1]). Were evaluated at baseline (T0) and at 5 hs (T5). The data were analyzed with repeated measures ANOVA.

Results

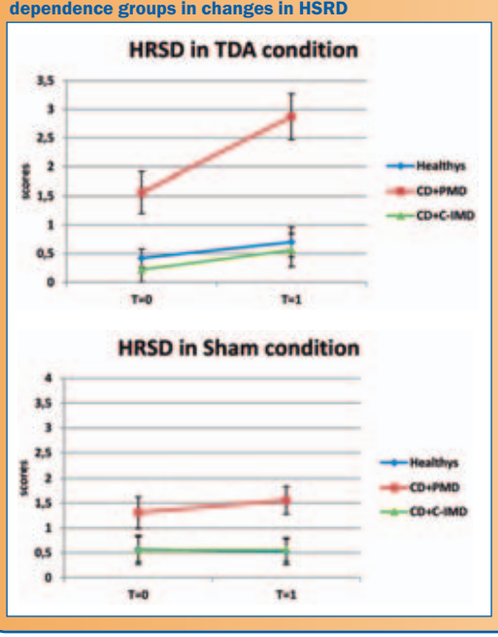
In cocaine dependent subjects, those with PMD depression showed that ATD induces changes in HRSD total scores in T5. No changes were found in C-IMDgroup neither in control group. In TRP plasma levels decrease in TDA-session and in Control-session but there were no differences between the controls and cocaine dependence group. Even in TRP/LNAA ratio plasma levels were decrease in TDA and but not in sham session, but there was no differences between groups. The most important results are shown in the following **table 1 and graphics 1-6**:

Table 1. The most important results between healthy and cocaine dependence group in TDA condition or shame condition.

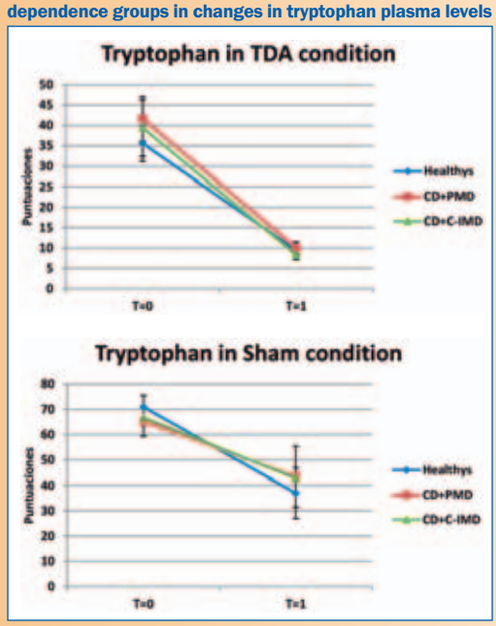
	TDA			No- TDA		
	T0	T5	ANOVA	T0	T5	ANOVA
Healthys	M±S.D	M±S.D	P/*Bonferroni	M±S.D	M±S.D	P/*Bonferroni
HRDS total (n=20/21)	0,42±0,75	0,70±1,17	0,102	0,57±1,21	0,52±1,17	0,329
Tryptophan (n=17)	35,54±17,99	9,40±5,44	0,001/a	70,91±44,15	36,98±19,07	0,000/a
Ratio TRP/LNAA	0,083±0,043	0,006±0,003	0,000/a	0,048±0,027	0,089±0,040	0,000/a
PMD						
HRDS total	1,56±1,46	2,87±2,00	0,002/a	1,31±1,11	1,56±1,31	0,137
Tryptophan (n=14)	41,65±20,52	9,99±5,72	0,000/a	65,25±37,98	43,40±22,03	0,003/a
Ratio TRP/LNAA	0,082±0,036	0,008±0,010	0,000/a	0,049±0,027	0,085±0,040	0,001/a
C-IMD						
HRDS total	0,22±0,67	0,56±0,88	0,271	0,56±0,73	0,56±0,88	0,361
Tryptophan	39,40±20,81	8,31±3,50	0,016/a	66,64±36,07	42,79±19,21	0,010/a
Ratio TRP/LNAA	0,082±0,038	0,007±0,004	0,003/a	0,046±0,025	0,089±0,038	0,001/a
One way- ANOVA	p/*	p/*		p/*	p/*	
HRDS total	0,013/b,d	0,000/ b,d		0,922	0,69	
Tryptophan	0,682	0,412		0,951	0,956	
Ratio TRP/LAAN	0,992	0,554		0,1	0,025/d	

PMD: Cocaine Dependence + comorbid primary major depression; C-IMD: CD + comorbid cocaine-induced major depression
*P. Bonferroni: ANOVA time factor) a= statistically significant differences between T0 and T5;
One-way ANOVA (group factor) b= statistically significant differences between healthys and PMD; c= statistically significant differences between healthys and C-IMD; d= statistically significant differences between PMD and C-IMD.

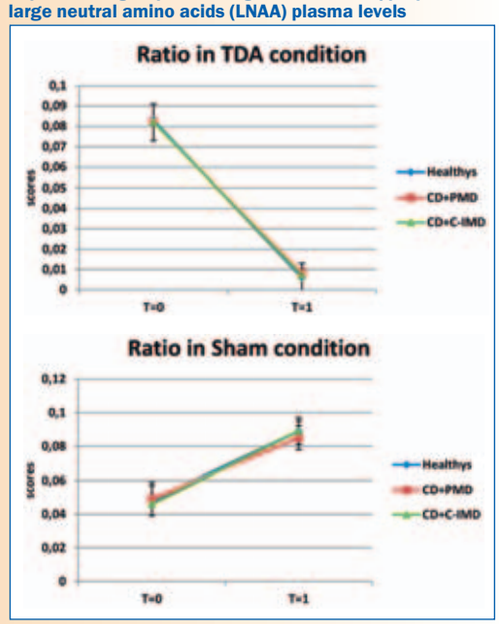
Graphic 1. Differences between Healthy and cocaine dependence groups in changes in HSRD



Graphic 2. Differences between Healthy and cocaine dependence groups in changes in tryptophan plasma levels



Graphic 3. Differences between Healthy and cocaine dependence groups in changes in ratio of tryptophan and large neutral amino acids (LNAA) plasma levels



Conclusions

These preliminary results show a different response to ATD test between independent or cocaine-induced major depression in HRSD scores. These data support differences in the serotonergic system among independent and substance- induced depression.

Bibliography

[1]. Moreno, FA., Parkinson, D., Palmer, C., Castro, WL., Misiaszek, J., El Khoury, A., Mathé, AA., Wright, R., Delgado, PL.,2010 CSF neurochemicals during tryptophan depletion in individuals with remitted depression and healthy controls. Eur Neuropsychopharmacol Jan;20(1):18-24.

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