Brain GABA Levels in Cocaine Dependent Subjects Increased After the Treatment for Cocaine Dependence

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Introduction

Abnormal brain GABA levels in cocaine dependent (CD) subjects may affect response to drug abuse treatment. Using MR spectral editing techniques, decreased brain GABA levels have been reported in ethanol [1] and cocaine [2, 3] dependent persons. Using a quantitative method based on J-resolved 2D MRS technique [4], we have measured frontal lobe GABA level in 35 cocaine dependent subjects and 20 controls. For patients, the MRS data were acquired before and after an eight-week treatment for cocaine dependence. Our results revealed some significant differences in GABA levels between patients and controls, as well as the GABA levels before and after the treatment in CD subjects.

Method

Using the quantitative J-resolved 2D MRS methods, in vivo 2D MR spectra were acquired from a voxel of 18.75cm^3 centered on the left dorsolateral prefrontal cortex in 35 cocaine dependent subjects (26 male, 9 female, age: 43.1±7.3 yr.) and 20 healthy controls (7 male, 13 female, age: 39.1±8.0 yr) on a GE SIGNA 1.5 T scanner with a home-built phased array receiver [5]. Acquisition parameters included TR = 2.32sec, TE_{min} = 48 msec, and 64 TE values ranging from 48ms to 678 ms with an increment of 10 ms. These parameters yield a bandwidth of 100Hz and frequency resolution of 0.78Hz in the J frequency dimension with 2X zero filling. The sensitivity of phased array receiver used for this frontal lobe voxel was approximately 4 fold higher than a standard quadrature head coil receiver. All MR spectra were processed and analyzed using modified Felix nD (MSI, San Diego) software and Statview.

For the cocaine dependent subjects, lifetime cocaine use was reported to be 15.7±8.1 years. Prior to enrollment in this NIDA-sponsored treatment study, cocaine was used during 20±8 days out of thirty days. Each patient went through an eight-week treatment trial on one of separate medications or placebo at VA Boston Health System. The 2D MR spectra were acquired before and after the treatment for each patient. Number of days using cocaine was estimated based on patient self-report and their urine sample tests.

Results

All GABA, NAA, Creatine and Choline resonance intensities were estimated from their J-resolved 1D MR spectra [4]. Results are compared in sub groups: control vs. cocaine dependent, patients receiving active treatment drug (Pramipexole and Venlafaxine) (N=18) vs. those having placebo (N=10). Assuming a mean creatine concentration of 6.4μM/cm^3 at frontal gray matter [6], some mean GABA level results are listed in Table 1. All patients have lower GABA levels than controls before treatment (0.88 μM/cm^3 vs. 1.36 μM/cm^3, t=2.56, p=0.015). The GABA levels of CD subjects who received active drugs increased by 23.5% after the treatment, in contrast, there was only a 2.1% increase of GABA level in CD subjects who received placebo (t=2.21, p=0.036) in the treatment.

Table 1: GABA levels (in unit of μM/cm^3) of cocaine dependent and control groups:

	Baseline				Endpoint					
	Cocaine (N=28)		Compare (N=21)		Cocaine (N=28)		Compare (N=9)			
Measure	Mean	SD	Mean	SD	Mean	SD	Mean	SD	t	p
GABA	0.88	0.24	1.36	0.48	1.04	0.24	1.44	0.24	2.56	0.015

Conclusion:

Cocaine dependent subjects have lower brain GABA levels within dorsolateral prefrontal cortex compared with normal controls. Significant increase of GABA level in cocaine dependent subjects who were treated with active drug suggests that pharmacotherapies designed specifically to increase brain GABA levels or to modify the activity of GABA system may prove efficacious for the treatment of cocaine dependence.

References:

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