A J-resolved, Two Dimensional MRS Study of Brain GABA and NAA Levels in Cocaine Dependent Subjects-Before and After Treatment

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Introduction

Decreased brain GABA levels in cocaine dependent 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 newly developed quantitative method based on J-resolved 2D MRS technique [4], we have recently measured frontal lobe GABA level in 37 cocaine dependent subjects and10 controls. For patients, 2D MRS data was acquired before and after an eight-week period of drug abuse treatment. Our results demonstrate differences in GABA and NAA levels between patients and controls, as well as their changes after treatment.

Methods

Using quantitative J-resolved 2D MRS methods, in vivo 2D MR spectra were acquired from a voxel of 18.75cm3 centered on the left dorsolateral prefrontal cortex in 37 cocaine dependent (25 male, age: 45+/-6.8 yr.; 12 female, age: 38+/-6.2 yr.) subjects and 10 healthy controls (4 male, 6 female, age: 31+/-5 yr) using a GE SIGNA 1.5 T scanner and a home-built phased array receiver [5]. Acquisition parameters included TR = 2.64sec, minimum TE = 48 msec, and 64 TE values, which ranged from 48ms to 678 ms with an increment of 10 ms. These parameters yield a bandwidth of 100Hz and frequency resolution of 0.78Hz for the second frequency dimension with 2X zero filling. With the use of phased array receiver for this frontal lobe voxel, receiver sensitivity was increased by approximately 4 fold compared with a standard quadrature head coil. All 2D 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 14+/-7 years. Prior to enrollment in 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, Cre and Choline resonance intensities were estimated from their J-resolved 2D MR spectra. Results are reported by sub group: light cocaine users (<10 days/30day, n=12), moderate cocaine users (10-20 days/30days, n=20) and heavy cocaine user (>20days/30day, n=5). Assuming a mean creatine concentration of 6.4ìM/cm3 for frontal gray matter [6], our mean metabolite levels are listed in Table 1. All patients have lower GABA levels than controls before treatment (B.T.) (0.81 ìM/cm3 vs. 1.07 ìM/cm3, p=0.005). Light cocaine users had an increase in their GABA and NAA levels after treatment (A.T.), while heavy cocaine users did not.

Discussion

Based on preliminary results, cocaine dependent subjects have lower brain GABA and NAA levels within dorsolateral prefrontal cortex compared with normal controls. Light cocaine users appear to increase both GABA and NAA. Heavy cocaine users were not observed to have changes in chemistry during treatment. These results suggest that significant decrements in brain GABA and NAA levels are present in cocaine dependent subjects and these neurochemical alterations may complicate efforts to develop effective pharmacotherapies.

References

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Table 1: GABA and NAA levels for controls and cocaine users. All numbers are in unit of µM/cm3

	Subjects	GABA	NAA
	Control (n=10)	1.07+/-0.13	9.58+/-0.48
	L. cocaine users (n=12, B.T.)	0.79+/-0.08	8.66+/-0.86
	L. cocaine users (n=11, A.T.)	0.82+/-0.09	9.98+/-0.72
	H. cocaine users (n=5, B.T.)	0.90+/-0.17	7.72+/-0.69
	H. cocaine users (n=3, A.T.)	0.74+/-0.08	6.96+/-1.23