Assessment of Normative Metabolite Variations in Fronto-Cerebellar Voxels using ^{1}H MRS

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Introduction

Chronic alcohol abuse has been correlated to anatomical, functional and metabolic brain abnormalities, and these effects have been most frequently reported in the frontal lobe and cerebellum. Previously, alterations of N-acetyl aspartate (NAA) and choline-containing compounds have been studied using ^{1}H spectroscopy in these areas [1]. Advances in high field clinical spectrometers and pulse sequences have made it possible to measure levels of the major inhibitory neurotransmitter γ-aminobutyric acid (GABA) in various brain regions such as the anterior cingulate and cerebellar vermis, to augment the metabolite profiles routinely accessible from these areas. The purpose of this study was to establish normative concentrations of metabolites in these areas using a J-difference spectroscopic technique specifically aimed at quantifying GABA. The data were used to quantify GABA, glutamate (Glu), NAA, total creatine (tCr), aspartate (Asp), N-acetyl aspartylglutamate (NAAG), myo-inositol (MI), and taurine (Tau). The detection of GABA by this method is confounded by the presence of co-edited compounds with similar chemical shifts and coupling networks, such as homocarnosine and macromolecules. Given these concerns and the paucity of data regarding variations due to anatomy and pathology of co-edited compounds, reported here are GABA* concentrations.

Methods

22 healthy volunteers (24.8 +/ 8.7 years) were studied in accordance with procedures approved by the Vanderbilt University Institutional Review Board. All experiments were performed on a 3 Tesla Philips Achieva spectrometer (release 2.1.3) with the standard 30.0 cm T/R volume coil. 256 transients were acquired from 7.32 and 6.10 mL (FWHM) voxels located in the anterior cingulate (AC) and cerebellar vermis (CV), respectively, using the MEGA-PRESS pulse sequence [2] with 2.5 second recycle delays, 2048 complex points, and 2 kHz receiver bandwidth. Prior to FFT, time-domain spectra were apodized with a 2 Hz exponential function. Selective inversion pulse durations were 15.64 ms sinc-center pulses (64 Hz FWHM bandwidth). The carrier frequency was maintained within ~2 Hz using the manufacturer ^1H_2O navigator-based frequency drift compensation option and free-induction decays were retrospectively corrected for susceptibility-induced frequency and phase variations [3]. Metabolite concentration ratios were obtained using LCModel [4] with basis sets generated from density matrix simulations employing ideal and real slice-selective and editing radiofrequency pulses, respectively, and fids were sampled from 10^4 magnetic field gradient points to account for the differential impact of crusher gradients in the presence of spectrally selective editing pulses.

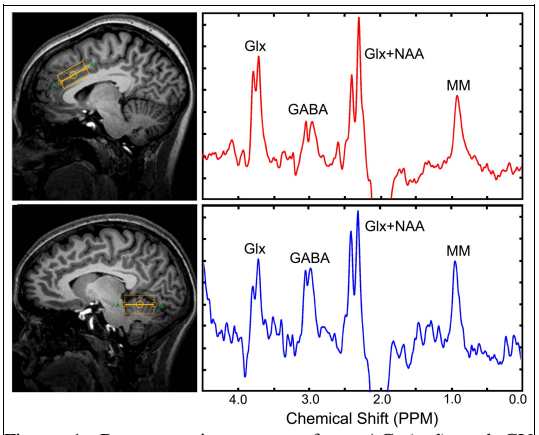

Figure 1. Representative spectra from AC (red) and CV (blue). Glx equals glutamate + glutamine and MM refers to co-edited macromolecular resonances.

Results and Discussion

Representative AC and CV spectra are shown in Figure 1 and metabolite profiles and standard deviations are summarized in Table 1. Difference spectra are uniformly characterized by flat baselines and the edited GABA peak at 3.01 ppm was consistent with the pseudo doublet line-shape as predicted from theory. The largest mean Cramer-Rao lower bound (CRLB) for these metabolites was 15.4 % (AC Tau) and the corresponding values for GABA in the AC and CV are 6.7 (4.5) and 5.7 (2.7), respectively. The mean [GABA*]/[tCr] ratios in the AC and CV were 0.32 +/- 0.08 and 0.23 +/- 0.06, respectively. AC and CV [GABA*]/[tCr] were not correlated (P = 0.41). As indicated in Table 1, statistically significant differences also existed between these regions for Glu and NAA with both relatively elevated in the AC. In summary, mean [GABA*]/[tCr] is ~140 % higher and more variable (based on CRLB's) in the AC relative to the CV in this set of healthy volunteers.

Met/tCr	GABA*	Glu	NAA	Asp	NAAG	MI	Tau
AC	0.32 (0.08)	1.13 (0.14)	1.46 (0.15)	0.23 (0.08)	0.14 (0.07)	0.72 (0.15)	0.17 (0.04)
CV	0.23 (0.06)	0.68 (0.13)	0.93 (0.15)	0.14 (0.05)	0.11 (0.03)	0.66 (0.09)	0.19 (0.04)

Table 1. Ratios of metabolites with total creatine in the AC and CV.

References

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