Glutamate Correlations Between the Anterior Cingulate and Cerebellar Vermis

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Introduction

Structural, functional and resting state studies suggest that dysregulated function of distributed circuits may underlie a variety of neuropsychiatric and neurological disorders. In particular, disrupted fronto-thalamo-cerebellar circuitry is a consistent finding in schizophrenia [1]. As a first step towards investigating whether disruptions in inter-regional functional and/or structural connections have neurometabolic correlates, we have investigated the degree to which metabolite concentrations, particularly those that reflect neurotransmitter tone (glutamate, GABA) and neuronal density (NAA), exhibit inter-regional correlations in healthy normal volunteers, focusing on the anterior cingulate (AC) and cerebellar vermis (CV), which have been identified consistently as nodes of the fronto-thalamo-cerebellar circuit.

Methods

19 volunteers (11 females and 8 males, age = 24.6 +/ 6.4 yrs) were studied in accordance with procedures approved by the Vanderbilt University Institutional Review Board. Experiments were performed on a 3 Tesla Philips Achieva (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 AC and CV, respectively, using the MEGA-PRESS pulse sequence [2] with 2 second recycle delays. 2048 complex points were sampled with 2 kHz receiver bandwidth, and, 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). 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 custom 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.

Results and Discussion

Mean AC and CV GABA:tCr ratios were 0.31 (0.08) and 0.23 (0.06), respectively, while corresponding Glu levels were 1.16 (0.10) and 0.70 (0.07), respectively. Glu was correlated between the AC and the CV (Figure 2) (r = 0.61, p = 0.01 and p = 0.06 when adjusted for multiple comparisons). Inter-regional correlations were not observed for other metabolites, minimizing the possibility of a referencing bias to tCr. Intraregional correlations were observed between NAA and Glu (AC: r = 0.66, p = 0.01 and p = 0.06 when adjusted for multiple comparisons; CV: r = 0.64, p = 0.01 and p = 0.06 when adjusted for multiple comparisons). Correlations between and within these regions are potentially interesting and may enable further differentiation among disorders that involve AC and CV steady-state functional linkages. Data quality was highly consistent between exams - as illustrated in Figure 3, the spectrum from the AC of all volunteers combined shows higher SNR but is otherwise identical to individual acquisitions (Figure 1). As a consequence, data analysis was purely nonparametric and to our knowledge represents the first observations of Glu correlations between brain regions.
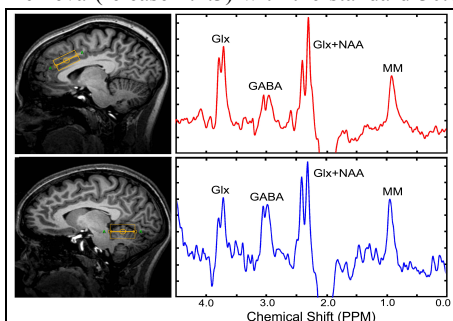

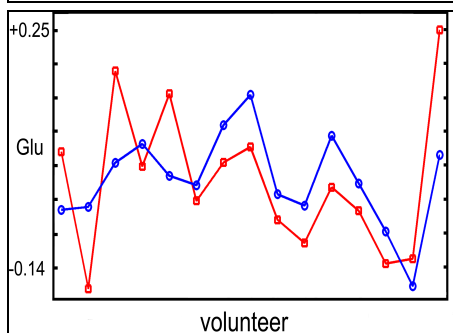Figure 1. Representative spectra from AC (red) and CV (blue).

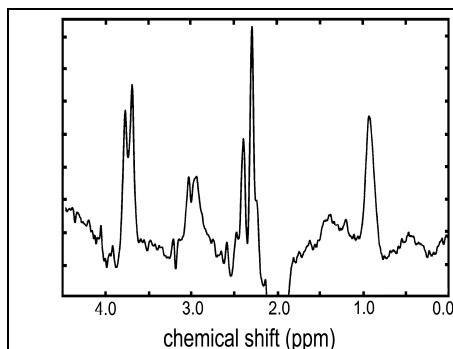Figure 2. Mean-shifted correlations in Glu between the AC and CV.

Figure 3. Combined spectrum of the anterior cingulate from 19 volunteers.

References

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