Brain 1H MRSI and Formal Thought Disorder in Pediatric Complex Partial Epilepsy

J. O'Neill[1], J. Levitt[1], E. Lanphier[1], C. Bailey[2], S. Gurbani[3], J. Alger[4], R. Caplan[1]

[1]UCLA NPI Child Psychiatry, Los Angeles, CA, United States, [2]UCLA MRRC, Los Angeles, CA, United States, [3]UC Irvine Pediatrics, Irvine, CA, United States, [4]UCLA Neurology, Los Angeles, CA, United States

Introduction: ^{1}H MRS detects metabolite abnormalities, e.g., low NAA, NAA/Cr, and NAA/Cho; high Cho and Cr, in adult and pediatric epilepsy proximal and distal to seizure foci[1]. These abnormalities have been little studied in relation to use of language to organize and formulate thoughts, formal thought disorder (FTD) in children. We assayed ^{1}H MRSI metabolites in 11 brain regions bilaterally in children and adolescents with Complex Partial Seizures (CPS) and investigated potential relations of metabolite measures to metrics of FTD.

Methods: 9 medicated children (5 ♀, 6.7-14.3 yr) with CPS of unknown etiology were compared to 9 unmedicated age- and sex-yoked healthy controls. Patients underwent extensive neuropsychological testing, including evaluation for formal thought disorder (FTD). Whole-brain MRI (axial FSE, sagittal SPGR) and water-suppressed multislice ^{1}H MRSI (IR: TR/TI/TE = 2300/170/272 ms; 10x10x12 mm^3 voxels) were acquired at 1.5 T (GE). ^{1}H MRSI was collected from 3 contiguous axial slices (basal ganglia, ventricular, supraventricular) broadly sampling cortex, white-matter, and subcortex. After FT, each subject's ^{1}H MRSI volume underwent spatial filtering, 2.0-Hz apodization, and automated baseline fitting; voxels with lipid signals exceeding NAA, with NAA SNR < 2.0, with linewidth > 10.0 Hz, or with other artifact were excluded manually. Individual ^{1}H MRSI voxels were interrogated from (left and right): perigenual anterior cingulate, anterior middle cingulate, frontal, parietal, and occipital cortices; caudate head and body, putamen, thalamus; and frontal and parietal white matter, all sites remote from the seizure foci. Structures were identified from FSE PD-weighted images coregistered to MRSI. Voxel tissue composition was obtained from coregistered SPGR T1 MRI segmented into gray matter, white matter, and CSF. Voxels were sought with ≥ 75% cortical gray matter; ≥ 75% white matter, or ≥ 50% subcortical gray matter, according to site. Signal intensities for NAA, Cr, and Cho were adjusted for transmitter and receiver gains, normalized to PD-weighted MRI intensity, and corrected for voxel CSF, yielding absolute metabolite levels (uncorrected for T1, T2) in Institutional Units (IU). Data were processed blind to subject identity. Repeated-measures ANCOVA was performed for NAA, Cr, and Cho for each left-right structure pair with hemisphere as within-subjects factor, group as between-subjects factor, and (as appropriate) voxel volume % gray matter or white matter as covariate. For significant analyses, *post-hoc* comparisons were made with one-way ANOVA. Criterion for significance was $p < 0.05$.

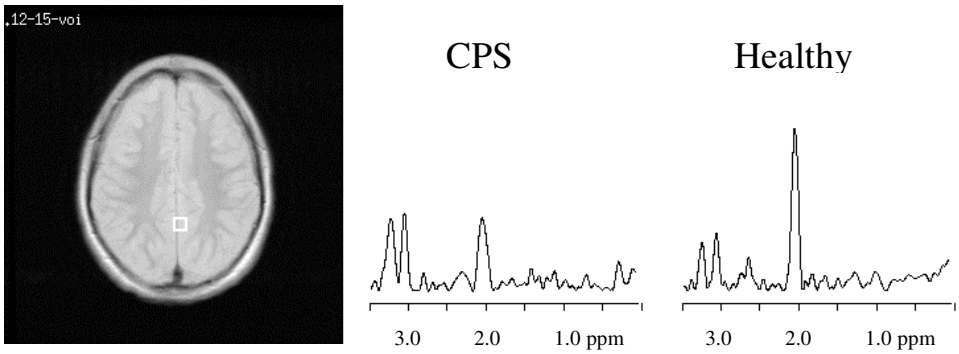
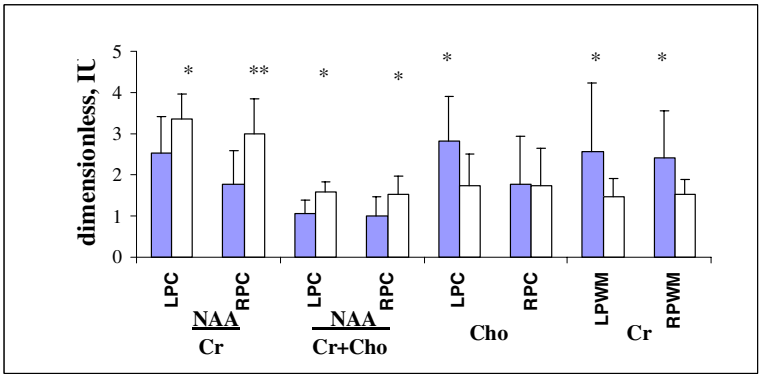


Fig. 1. Superventricular-level axial PD-weighted brain MRI (*left*) of 9.3-yr-old girl with CPS with left-sided focus. White box marks ^{1}H MRSI voxel in left parietal cortex, remote from focus. Local baseline-corrected spectra from patient (*middle*) and yoked control (*right*). Note elevated Cho (3.24 ppm) and Cr (3.01 ppm) relative to NAA (2.01 ppm) in patient.

Fig. 2. Selected parietal-lobe metabolite ratios and absolute levels (means ± SD) in CPS (*solid*) and controls (*open*). Note lower NAA/Cr, NAA/(Cr+Cho); higher Cr, Cho in patients. *p < 0.05,**p < 0.01 (ANCOVA). L: left, R: right; PC: parietal cortex, PWM: parietal white matter.



Results: Fig. 1 shows above-normal Cr and Cho, below-normal NAA in a sample CPS spectrum. In left parietal cortex (Fig. 2), NAA/Cr (24.3%) and NAA/(Cr+Cho) (32.7%) were lower, Cho (64.3%) was higher in CPS than in controls; in right parietal cortex NAA/Cr (41.2%) and NAA/(Cr+Cho) (34.4%) were also lower in CPS. Cr was higher in CPS in left (73.0%) and right (56.8%) parietal white matter. Within CPS, NAA/Cr in left parietal cortex ($r = 0.99$, $p = 0.01$) and Cr in left parietal white matter ($r = 0.92$, $p = 0.03$) correlated with FTD. Lower NAA/(Cr+ Cho) (35.5%, $p = 0.01$) and higher Cr (49.0%, $p = 0.003$) in right caudate body and higher Cho (43.2%, p = 0.02) in right putamen were also observed in CPS. Right putaminal Cho in CPS also correlated with FTD ($r = 0.98$, $p = 0.02$). Finally, Cho was elevated in CPS in right anterior middle cingulate (71.7%, $p = 0.03$).

Discussion: Consistent with prior brain MRS investigations of epilepsy in children and adults[1], this long-TE ^{1}H MRSI study identified below-normal NAA/Cr and NAA/(Cr+Cho) and above-normal Cr and Cho in patients. Bilateral parietal lobes and right striatum appear to be impacted extrafocal regions. The metabolite abnormalities evidenced may reflect local damage to neurons and/or gliosis. This pathology may contribute to formal thought disorder in children with CPS. Study limitations include low subject numbers and medication of patients. **References:** 1. Briellman et al. In: Gillard et al. Clinical MR Neuroimaging, Cambridge University Press, Cambridge 488-508 (2005). Supported by grants NS32070 and MH067187 (RC).