

Supplementary material

Hippocampal proton magnetic resonance spectroscopy and symptom severity in medication-naïve children with attention-deficit/hyperactivity disorder: an exploratory retrospective cross-sectional study

Liping Yang, Yunjie Li, Wenqi Chen, Heli Li, Xiaolin Hu, Min Chen*

Correspondence: Min Chen; Email: 806956762@qq.com

Supplementary Table S1. Complete SNAP-IV correlation matrix. Pearson r with Benjamini-Hochberg FDR q in parentheses. FDR correction was applied across all 72 SNAP-IV tests; * q < 0.05. n is the number of children with both the metabolite ratio and SNAP-IV score available.

Region: ratio	n	Inattention	Hyperactivity/impulsivity	Oppositional defiant	Mean score
Left head: NAA/Cr	55	-0.521 (0.003)*	-0.325 (0.185)	-0.208 (0.706)	-0.455 (0.012)*
Left head: NAA/Cho	55	-0.159 (0.730)	-0.266 (0.514)	0.031 (0.912)	-0.203 (0.706)
Left head: NAA/(Cho+Cr)	55	-0.467 (0.012)*	-0.343 (0.150)	-0.164 (0.730)	-0.437 (0.016)*
Left body: NAA/Cr	31	0.097 (0.887)	0.176 (0.730)	-0.032 (0.929)	0.140 (0.799)
Left body: NAA/Cho	31	-0.070 (0.887)	0.075 (0.887)	-0.095 (0.887)	-0.036 (0.925)
Left body: NAA/(Cho+Cr)	31	0.042 (0.912)	0.139 (0.799)	-0.064 (0.887)	0.069 (0.887)
Left tail: NAA/Cr	26	-0.307 (0.706)	-0.226 (0.730)	-0.066 (0.887)	-0.276 (0.730)
Left tail: NAA/Cho	26	-0.306 (0.706)	-0.174 (0.730)	-0.258 (0.730)	-0.288 (0.730)
Left tail: NAA/(Cho+Cr)	26	-0.343 (0.706)	-0.200 (0.730)	-0.176 (0.730)	-0.301 (0.706)
Right head: NAA/Cr	43	0.199 (0.730)	0.024 (0.930)	0.170 (0.730)	0.158 (0.730)
Right head: NAA/Cho	43	0.149 (0.730)	0.091 (0.887)	0.135 (0.730)	0.154 (0.730)
Right head: NAA/(Cho+Cr)	43	0.159 (0.730)	0.052 (0.887)	0.146 (0.730)	0.143 (0.730)
Right body: NAA/Cr	29	0.178 (0.730)	0.075 (0.887)	-0.061 (0.887)	0.113 (0.887)
Right body: NAA/Cho	29	0.126 (0.884)	-0.015 (0.960)	0.179 (0.730)	0.095 (0.887)
Right body: NAA/(Cho+Cr)	29	0.251 (0.730)	0.049 (0.912)	0.067 (0.887)	0.168 (0.730)
Right tail: NAA/Cr	27	0.325 (0.706)	0.117 (0.887)	0.084 (0.887)	0.216 (0.730)
Right tail: NAA/Cho	27	0.097 (0.887)	-0.014 (0.960)	-0.111 (0.887)	-0.025 (0.940)
Right tail: NAA/(Cho+Cr)	27	0.220 (0.730)	0.047 (0.912)	-0.010 (0.962)	0.098 (0.887)

Supplementary Table S2a. Hippocampal MRS ratios versus QCD total score. Pearson correlations. FDR q was corrected across the complete functional matrix of 126 tests (QCD total plus six CPRS-48 scores).

Region: ratio	n	r	p	FDR q
Left head: NAA/Cr	16	-0.351	0.182	0.994
Left head: NAA/Cho	16	-0.378	0.149	0.994
Left head: NAA/(Cho+Cr)	16	-0.366	0.164	0.994
Left body: NAA/Cr	5	-0.148	0.813	0.994
Left body: NAA/Cho	5	-0.037	0.953	0.994
Left body: NAA/(Cho+Cr)	5	-0.071	0.910	0.994
Left tail: NAA/Cr	5	-0.345	0.569	0.994
Left tail: NAA/Cho	5	-0.535	0.353	0.994
Left tail: NAA/(Cho+Cr)	5	-0.465	0.430	0.994
Right head: NAA/Cr	11	-0.134	0.694	0.994
Right head: NAA/Cho	11	0.187	0.583	0.994
Right head: NAA/(Cho+Cr)	11	0.043	0.900	0.994
Right body: NAA/Cr	6	0.162	0.760	0.994
Right body: NAA/Cho	6	0.364	0.479	0.994

Region: ratio	n	r	p	FDR q
Right body: NAA/(Cho+Cr)	6	0.279	0.592	0.994
Right tail: NAA/Cr	6	0.000	1.000	1.000
Right tail: NAA/Cho	6	-0.108	0.839	0.994
Right tail: NAA/(Cho+Cr)	6	-0.063	0.906	0.994

Supplementary Table S2b. Hippocampal MRS ratios versus CPRS-48 scores. Each cell shows Pearson r with FDR q in parentheses. FDR correction was applied across the complete functional matrix of 126 tests. No association survived correction. Conduct, conduct problems; Psychosom., psychosomatic; Imp-hyper, impulsive-hyperactive; Hyper-idx, hyperactivity index.

Region: ratio	n	Conduct	Psychosom.	Anxiety	Learning	Imp-hyper	Hyper-idx
Left head: NAA/Cr	21	0.30 (0.99)	0.11 (0.99)	-0.13 (0.99)	0.26 (0.99)	0.29 (0.99)	0.42 (0.99)
Left head: NAA/Cho	21	0.30 (0.99)	0.07 (0.99)	-0.11 (0.99)	0.30 (0.99)	0.31 (0.99)	0.43 (0.99)
Left head: NAA/(Cho+Cr)	21	0.32 (0.99)	0.11 (0.99)	-0.12 (0.99)	0.30 (0.99)	0.32 (0.99)	0.45 (0.99)
Left body: NAA/Cr	10	0.01 (1.00)	-0.28 (0.99)	0.01 (1.00)	0.28 (0.99)	0.06 (0.99)	0.16 (0.99)
Left body: NAA/Cho	10	-0.20 (0.99)	-0.51 (0.99)	0.21 (0.99)	-0.15 (0.99)	-0.03 (0.99)	-0.10 (0.99)
Left body: NAA/(Cho+Cr)	10	-0.10 (0.99)	-0.44 (0.99)	0.11 (0.99)	0.17 (0.99)	0.04 (0.99)	0.08 (0.99)
Left tail: NAA/Cr	9	0.12 (0.99)	-0.20 (0.99)	-0.32 (0.99)	-0.23 (0.99)	0.08 (0.99)	0.04 (0.99)
Left tail: NAA/Cho	9	0.45 (0.99)	-0.02 (0.99)	-0.20 (0.99)	-0.22 (0.99)	0.26 (0.99)	0.23 (0.99)
Left tail: NAA/(Cho+Cr)	9	0.34 (0.99)	-0.09 (0.99)	-0.25 (0.99)	-0.23 (0.99)	0.19 (0.99)	0.16 (0.99)
Right head: NAA/Cr	16	-0.20 (0.99)	-0.02 (0.99)	0.00 (1.00)	0.24 (0.99)	0.05 (0.99)	0.07 (0.99)
Right head: NAA/Cho	16	-0.37 (0.99)	-0.23 (0.99)	-0.09 (0.99)	0.38 (0.99)	0.06 (0.99)	0.05 (0.99)
Right head: NAA/(Cho+Cr)	16	-0.29 (0.99)	-0.13 (0.99)	-0.02 (0.99)	0.32 (0.99)	0.05 (0.99)	0.06 (0.99)
Right body: NAA/Cr	10	0.13 (0.99)	-0.46 (0.99)	-0.32 (0.99)	-0.16 (0.99)	0.28 (0.99)	0.08 (0.99)
Right body: NAA/Cho	10	-0.16 (0.99)	-0.56 (0.99)	0.14 (0.99)	-0.09 (0.99)	0.10 (0.99)	-0.01 (1.00)
Right body: NAA/(Cho+Cr)	10	-0.03 (0.99)	-0.57 (0.99)	-0.09 (0.99)	-0.10 (0.99)	0.23 (0.99)	0.07 (0.99)
Right tail: NAA/Cr	10	-0.10 (0.99)	-0.33 (0.99)	-0.39 (0.99)	-0.33 (0.99)	0.09 (0.99)	-0.15 (0.99)
Right tail: NAA/Cho	10	-0.29 (0.99)	-0.46 (0.99)	-0.03 (0.99)	-0.40 (0.99)	0.03 (0.99)	-0.20 (0.99)
Right tail: NAA/(Cho+Cr)	10	-0.25 (0.99)	-0.44 (0.99)	-0.17 (0.99)	-0.38 (0.99)	0.05 (0.99)	-0.19 (0.99)

Supplementary Table S3. MRSinMRS reporting checklist. Items not recoverable from the retrospective archive are stated explicitly.

Category	Item	This study
Hardware	Field strength	3.0 T
Hardware	Manufacturer/model	GE Healthcare / Discovery MR750
Hardware	RF coil	Manufacturer's clinical head coil; specific model/channel count not recoverable
Acquisition	Nucleus	¹ H
Acquisition	Localization/sequence	Single-voxel vendor sequence SVS-SE-30; exact implementation not recoverable from archived export
Acquisition	TR/TE	1500/30 ms
Acquisition	Signal averages	256

Category	Item	This study
Acquisition	Voxel size	1.5 × 1.0 × 0.75 cm (approximately 1.1 mL)
Acquisition	Water suppression/shimming	Vendor automatic prescan
Analysis	Analysis software	GE workstation integrated spectroscopy software; version not recoverable
Analysis	Quantification	Peak-area metabolite ratios: NAA/Cr, NAA/Cho and NAA/(Cho+Cr)
Analysis	Reference	Creatine internal reference; no water-referenced or absolute quantification
Analysis	Metabolites reported	NAA, Cr and Cho; mI localized but not exported in analytic dataset
Data quality	Signal-to-noise ratio	Not available
Data quality	Linewidth (FWHM)	Not available
Data quality	CRLB/fit-quality threshold	Not available
Data quality	Spectral quality-control method	Visual inspection of baseline stability and lineshape
Data quality	Data excluded for quality	Region-specific exclusion counts not uniformly recoverable; for the left hippocampal head, 7 spectra were excluded for unacceptable visual quality

CRLB, Cramér-Rao lower bound; FWHM, full width at half maximum; mI, myo-inositol; MRS, magnetic resonance spectroscopy; NAA, N-acetylaspartate; TR/TE, repetition time/echo time.