Glutamate and Choline Levels Predict Individual Differences in Reading Ability in Emergent Readers

Pugh et al, 2014

Background : Reading Disability (RD)

- Reading Disability (RD) is as a **brain-based developmental disorder** associated with deficits in **phonological processing**

- **Phonological awareness** - the metalinguistic understanding that spoken words are made of smaller units

Background : Reading Disability (RD)

- **Possible Genes:** DYX1C1, DCDC2, KIAA0319, GRIN2A, and ROBO1, as well as common variations, e.g., COMT
- **Structural Differences**
  - **DTI –** Differences in FA (Fractional Anisotropy)
  - **Volumetric -** White/Grey Matter Volume
- **Functional Differences**
  - Activation (fMRI)
  - Connectivity (Active, Resting State)

Background: MRS & Neurochemistry (Common Links)

- Magnetic Resonance Spectroscopy (MRS)
  - **Noninvasive in vivo -** measures of *neurometabolites* including N-acetyl-aspartate, choline, creatine, GABA, and glutamate.
  - **Abnormal Choline** → reflect abnormal white matter organization and/or cell membrane turnover
  - **Abnormal Glutamate** → hyperexcitability

Current Study

- This study examines neurochemistry early in the process of learning to read, which is critical for understanding the functional significance of neurometabolite-reading relations.

Materials & Methods

- **Participants:** Seventy-five speakers of English (47 males; 28 females)
- **Behavioral Testing:** behavioral battery to characterize their reading, language, and general cognitive skills (e.g.

Table 1. Descriptive statistics for the entire sample and for RD and TD subsets

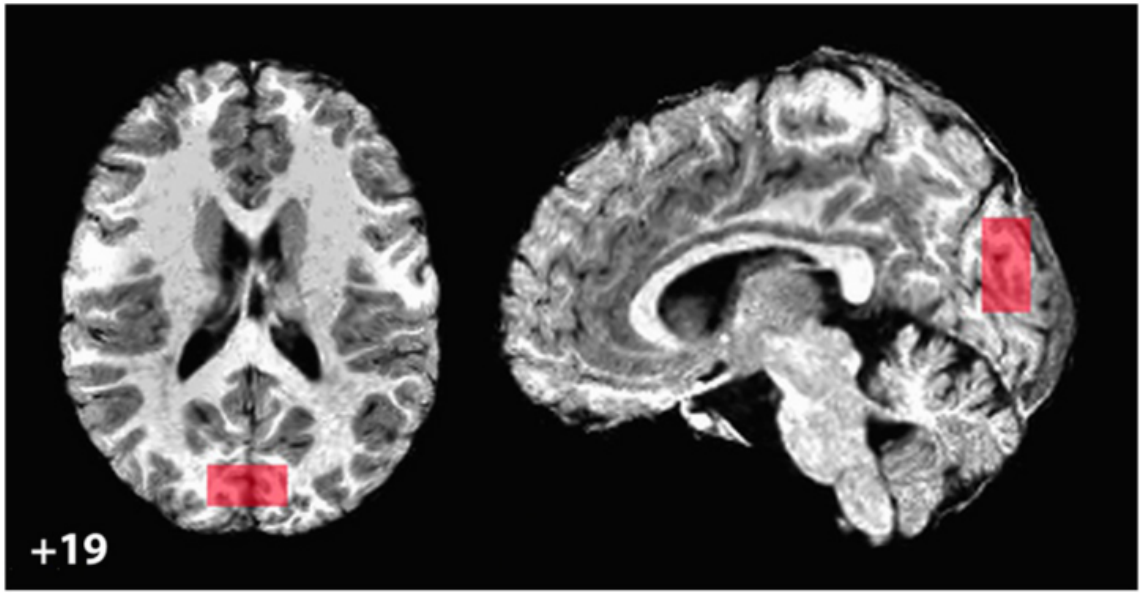
	Mean (SD)		
	Entire sample	RD	TD
N	75	10	47
Gender	47 M; 28 F	6 M; 4 F	28 M; 19 F
Age	7.68 (0.70)	7.45 (0.56)	7.59 (0.67)
Age-normed standard scores			
TOWRE SWE	106.16 (15.65)	84.00 (3.94)	115.70 (11.02)**
TOWRE PDE	103.68 (14.15)	84.60 (4.60)	111.40 (11.61)**
TOWRE WRE	106.09 (17.50)	81.20 (3.22)	116.55 (12.96)**
WJ-III LWID	111.40 (15.25)	92.40 (4.43)	120.36 (11.52)**
WJ-III PC	105.27 (13.70)	88.60 (3.95)	113.09 (10.17)**
CTOPP BW	10.93 (2.46)	10.00 (2.16)	11.31 (2.70)
CTOPP EL	11.63 (3.29)	8.10 (2.23)	12.44 (3.34)**
PPVT III	112.00 (12.88)	107.50 (8.91)	113.30 (13.98)
WASI block design	109.64 (17.23)	102.10 (20.15)	112.07 (17.53)
Metabolite concentrations (ratios to Cr)			
GABA	0.18 (0.02)	0.18 (0.02)	0.18 (0.02)
Glu	0.97 (0.21)	1.10 (0.19)	0.94 (0.21)*
Cho	0.18 (0.02)	0.19 (0.01)	0.18 (0.02)*
NAA	0.95 (0.07)	0.97 (0.06)	0.94 (0.07)

Standard scores mean = 100, SD = 15 except for CTOPP, for which mean = 10, SD = 3. TOWRE, Tests of Word Reading Efficiency (sight word efficiency, phonemic decoding efficiency); WJ-III, Woodcock-Johnson Tests of Achievement (letter word identification, passage comprehension); CTOPP, Comprehensive Test of Phonological Processing (elision, blending words); PPVT III, Peabody Picture Vocabulary Test; WASI, Wechsler Abbreviated Scales of Intelligence.

$^{**}p < 0.001$; $^{*}p < 0.05$.

Materials & Methods

- **MR Spectroscopy:** NAA, Cho, Glu, and GABA levels (relative to a Cr baseline)



Materials & Methods

- **Brain-Behavior Analyses**
  - **Reading Composite:** raw scores on TOWRE sight word efficiency, TOWRE phonemic decoding efficiency, and WJ III
  - **Phonological Awareness Composite:** CTOPP BW, EL

RESULTS

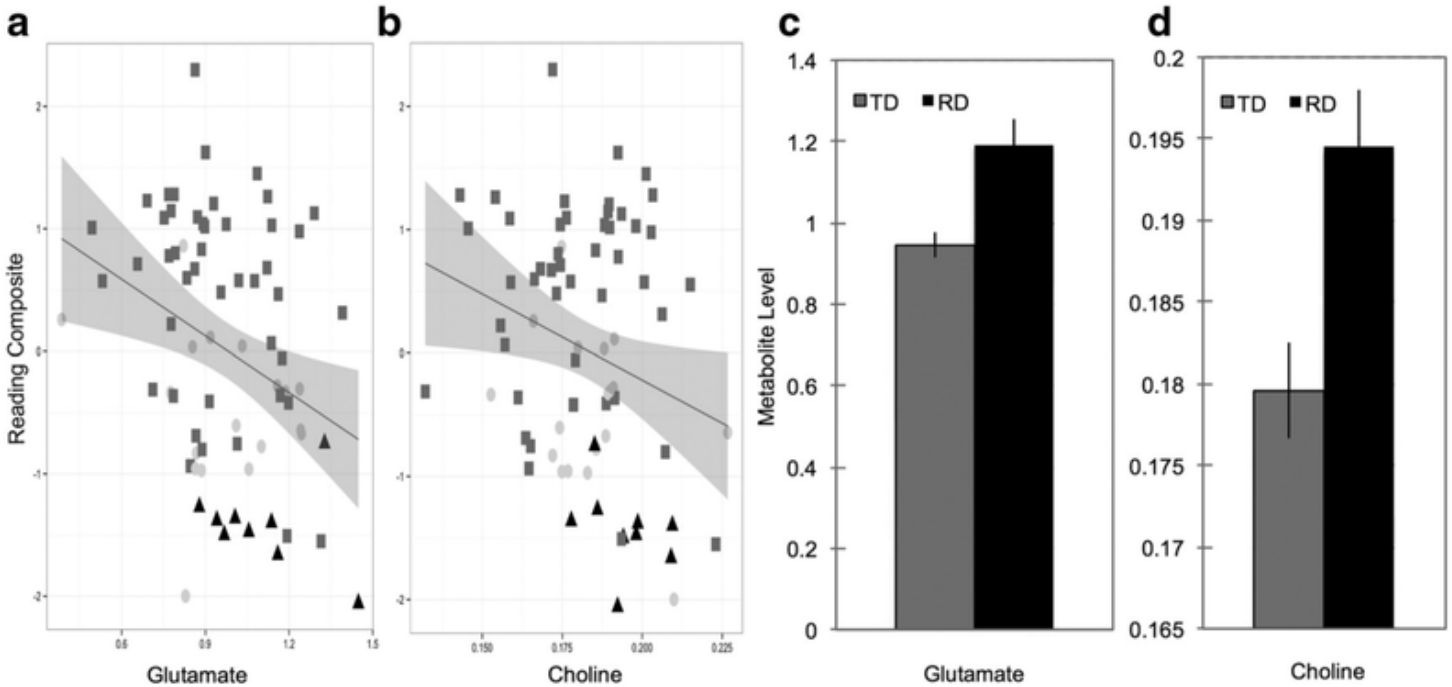
Table 2. Correlations among metabolites ratios and composite reading score, composite PA score, vocabulary, and nonverbal IQ scores

	Reading composite	PA composite	Vocabulary	Nonverbal IQ
Glu	**−0.32 (−0.25)**	**−0.35 (−0.30)**	**−0.31 (−0.23)**	−0.11 (−0.06)
	N* = 72, *p* = 0.006	***N* = 67, *p* = 0.004***	***N* = 70, *p* = 0.010***	*N* = 71, *p* = 0.351
Cho	**−0.26 (−0.24)**	−0.09 (−0.06)	−0.14 (−0.11)	0.00 (0.04)
	***N* = 73, *p* = 0.029**	*N* = 68, *p* = 0.486	*N* = 71, *p* = 0.228	*N* = 72, *p* = 0.968
GABA	−0.11 (−0.02)	−0.13 (−0.06)	−0.21 (−0.12)	−0.04 (0.03)
	N = 75, *p* = 0.336	*N* = 70, *p* = 0.281	*N* = 73 *p* = 0.080	*N* = 74, *p* = 0.770
NAA	−0.11 (−0.10)	−0.08 (−0.07)	−0.13 (−0.12)	0.16 (0.16)
	N = 72, *p* = 0.350	*N* = 67, *p* = 0.507	*N* = 70, *p* = 0.298	*N* = 72, *p* = 0.190

Partial correlations removing the linear effects of age at time of testing and gray matter volume are shown in parenthesis. *P* values are shown for zero-order correlations only. Significant effects are indicated in bold.

*Indicates significance after correction for multiple comparisons.

RESULTS



igure 2. Relationship between metabolites and reading ability. Scatterplot of correlations between (***a***) Glu and Reading Composite scores, and (***b***) Cho and Reading Composite scores. Rea
ıeeting criteria for TD readers are shown in dark gray squares, RD readers are shown in black triangles, and readers that did not meet either group criteria are shown in light gray circles. Bar gra
resent (***c***) Glu and (***d***) Cho mean levels in TD and RD readers. Error bars represent SEM. Metabolites levels are expressed as ratios to Cr.

Discussion

- Neurochemistry in **typically** and **atypically** developing children → **neurocircuits** that come to support skilled reading are still developing.
- Relationship between **children's reading skills** and the major excitatory and inhibitory neurotransmitters, **Glu** and **GABA**
- **Cho** and **Glu** concentrations were inversely correlated with reading and related linguistic measures
- **Glu** → reading and reading-related deficits could have potential implications for neural oscillatory processing deficit accounts