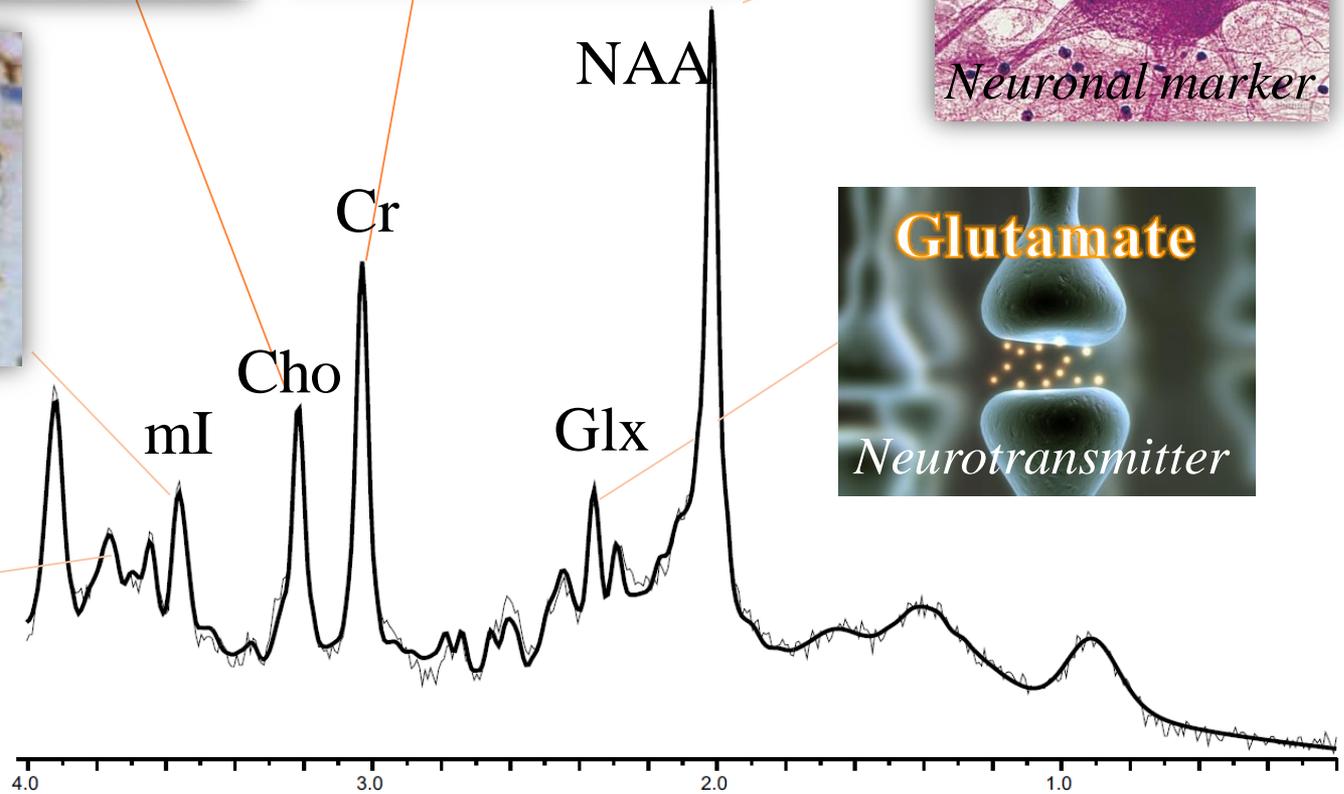
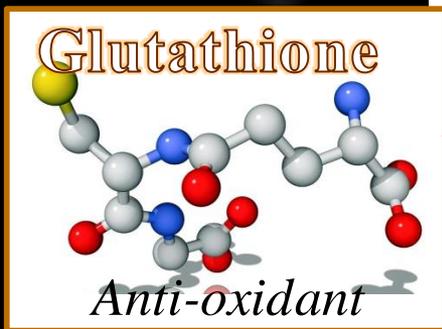
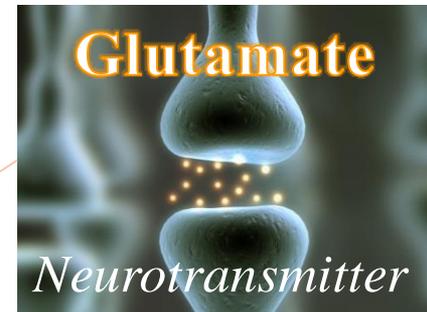
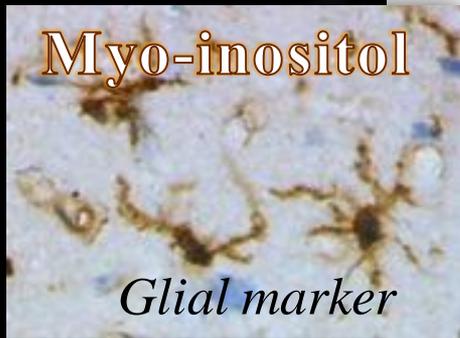
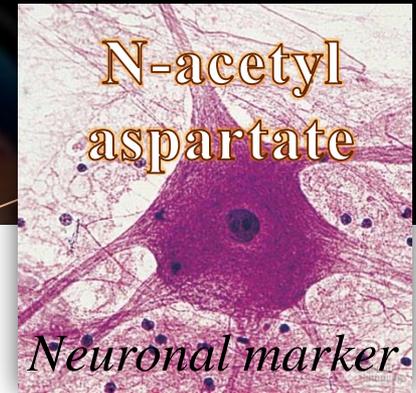
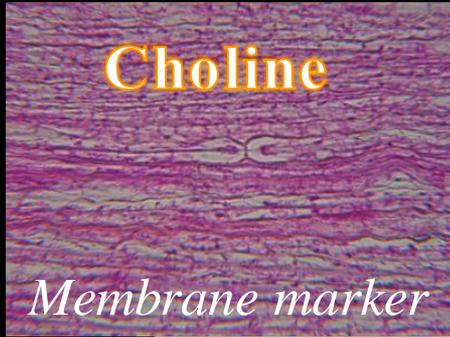


# Measuring Changes in Brain Chemistry after Repetitive Brain Trauma using MR Spectroscopy

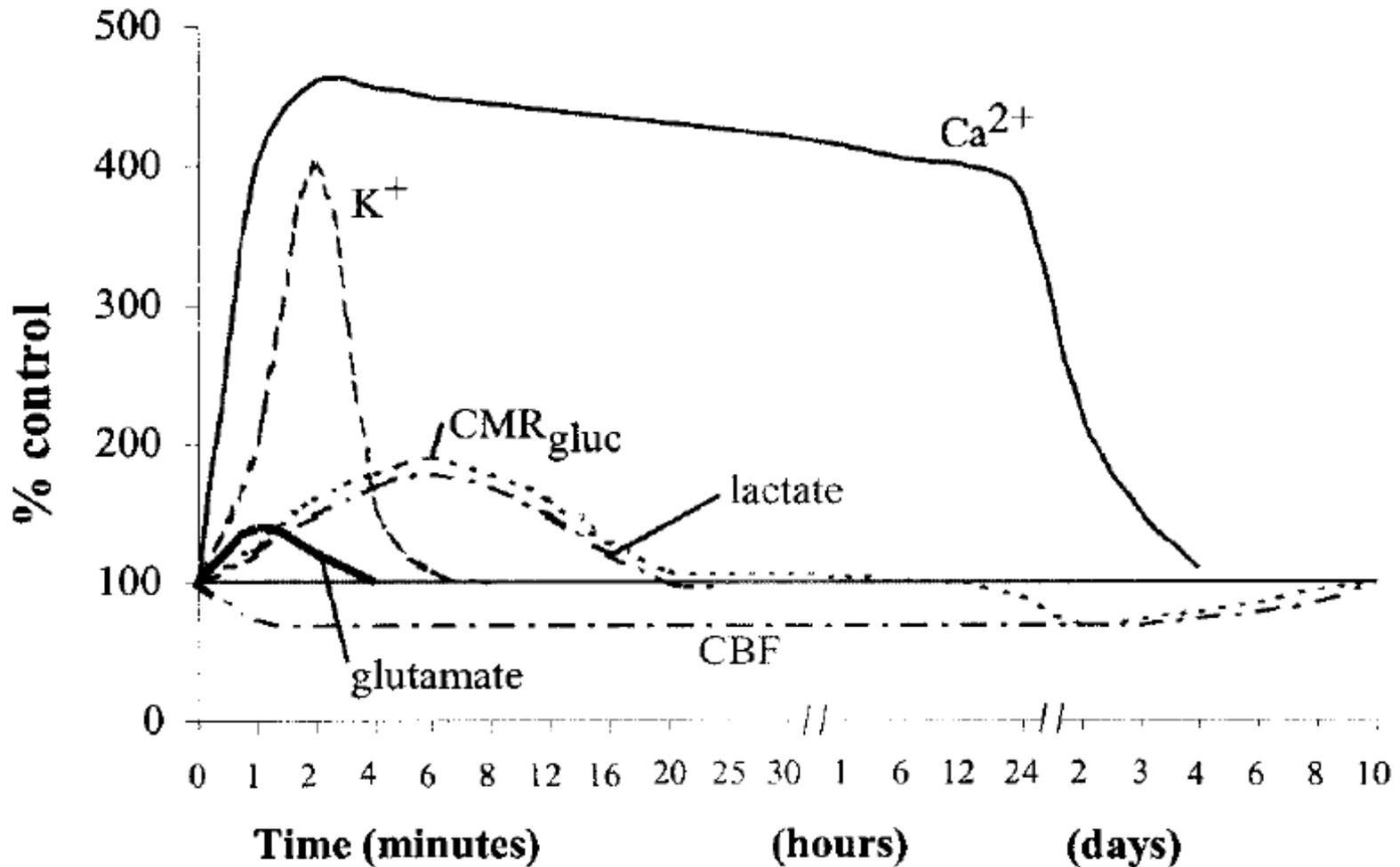


Alexander P. Lin, PhD  
Center for Clinical Spectroscopy  
Brigham and Women's Hospital  
Harvard Medical School

# MR Spectroscopy: The Virtual Biopsy



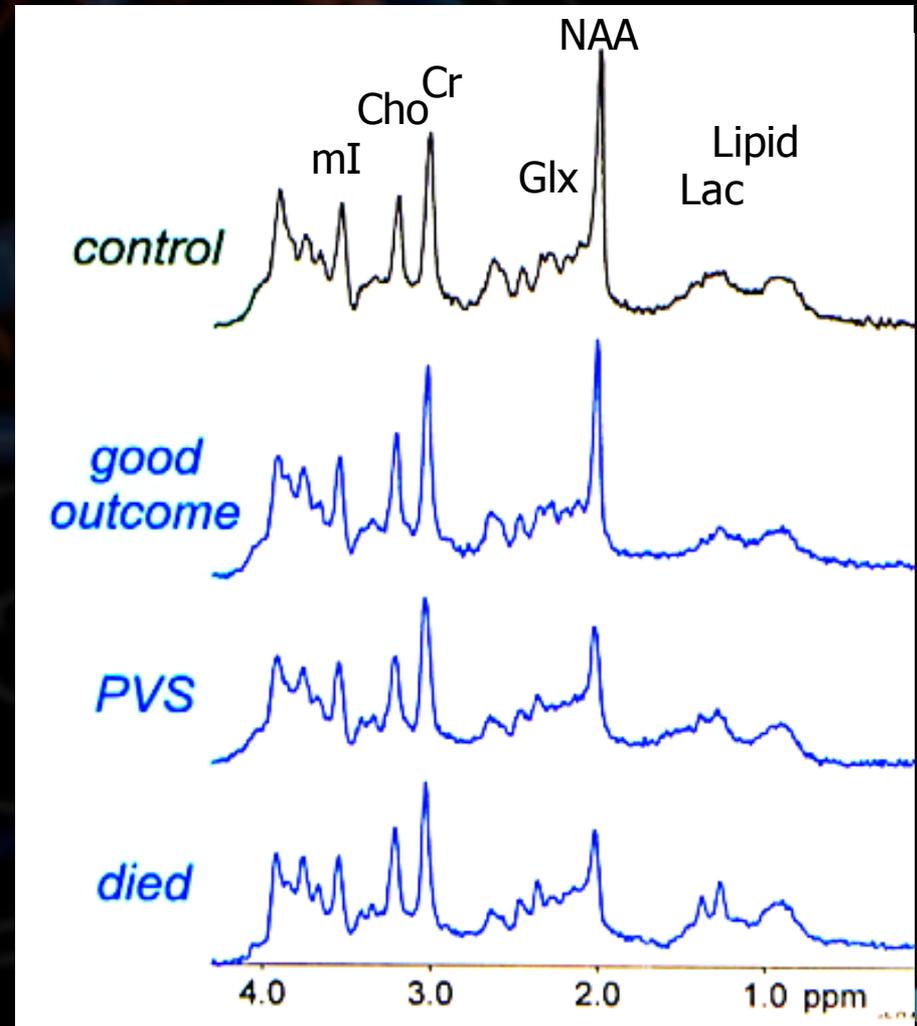
# Neurometabolic Cascade of Concussion



From Hovda et al J Neurotrauma 1995

# MR Spectroscopy of Severe Head Injury

- Acute changes:  
optimal time: 4 days  
after injury
- Progressive changes:
  - Decreased NAA
  - Increased Glx
  - Increased lactate



*From Ross et al AJNR 1997*

# MRS Predictive of Outcome

TABLE 4. RESULTS OF LOGISTIC REGRESSION ANALYSES TO PREDICT SHORT- AND LONG-TERM NEUROLOGIC OUTCOME

Variables used	Prediction of dichotomized GOS outcome at 1 month					Prediction of dichotomized GOS outcome at 6–12 months				
	Accuracy	%FP	%FN	$\chi^2$	p	Accuracy	%FP	%FN	$\chi^2$	p
Admission GCS	60%	100	0	5.2	0.39	77%	0	100	12.4	0.02
Field GCS	60%	100	0	4.3	0.50	76%	0	100	4.3	0.50
Motor GCS	62%	47	32	2.9	0.58	67%	13	100	13.3	0.01
SSEP <sup>a</sup>	69%	7	46	—	—	83%	19	11	—	—
Age	60%	100	0	11.6	0.11	76%	0	100	18.7	0.02
Pupil reactivity	62%	94	0	2.6	0.11	76%	0	100	—	—
Age + pupil + M-GCS	67%	47	24	14.2	0.08	67%	13	100	16.9	0.03
O-Glx	67%	47	20	7.7	0.36	89%	0	50	12.1	0.10
Best early MRS levels	82%	31	9	6.7	0.57	89%	4	37	28.3	<0.001
Best early MRS ratios	78%	38	13	14.7	0.06	94%	4	12	11.0	0.14
Best MRS levels + field GCS	73%	35	21	5.9	0.65	91%	0	37	32.9	<0.001
Best MRS ratios + motor GCS	73%	31	25	6.7	0.56	97%	0	12	15.5	0.03
Best MRS levels + SSEP	75%	15	32	10.1	0.26	88%	8	25	4.6	0.80
Best MRS ratios + SSEP	81%	8	26	4.4	0.82	91%	4	25	3.3	0.92

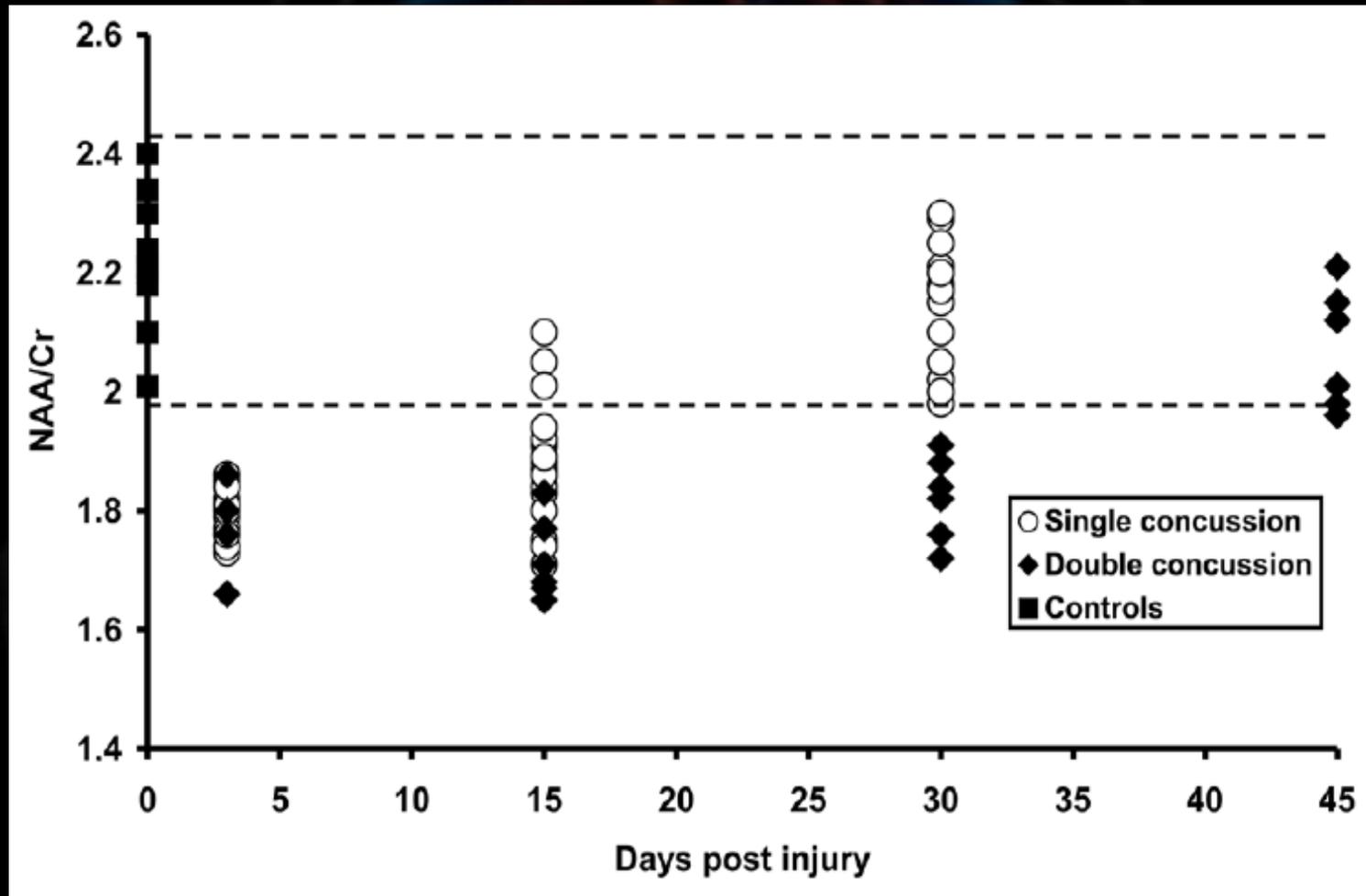
$\chi^2$ , Hosmer-Lemeshow Goodness-of-Fit test; FP, false positives; FN, false negatives; M-GCS, best motor GCS in first 24 h; SSEP, somatosensory evoked potentials.

Best early MRS levels used to predict 1-month outcome = PWM Glx and OGM Cho and used to predict 6-month outcome = PWM Cho and OGM Glx; Best early MRS ratios used to predict 1-month outcome = PWM Glx/Cr and PWM NAA/Cr and used to predict 6-month outcome = PWM Cho/Cr, NAA/Cho, and OGM Glx/Cr.

<sup>a</sup>Data for SSEPs were acquired in 39 of 42 patients.

From Shutter et al J Neurotrauma 2004

# MRS in Acute Sports-Related Mild Head Injury



From Vagnozzi et al J Neurosurg 2008



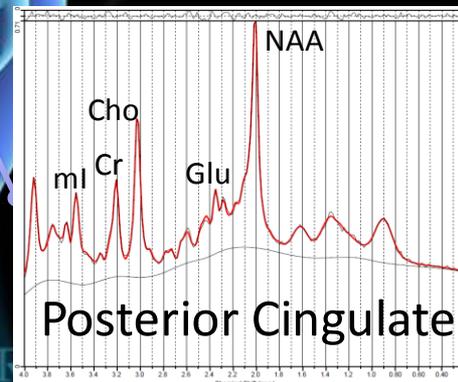
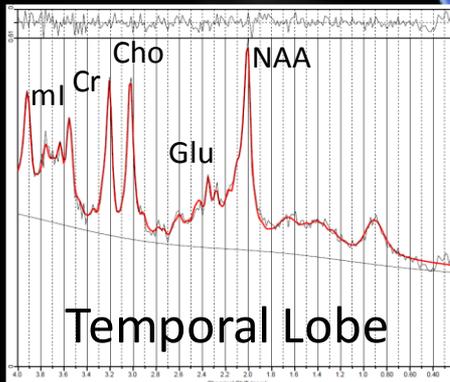
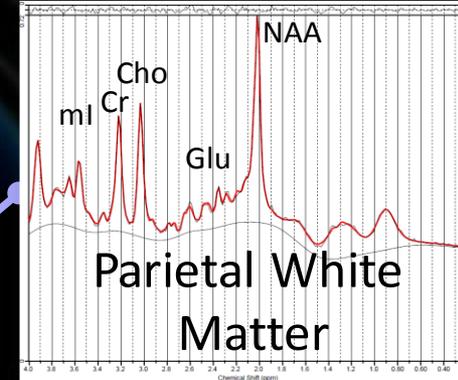
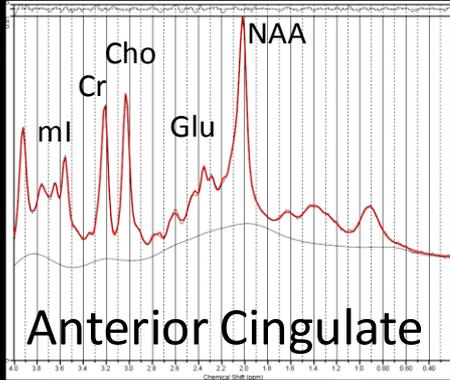
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# Aims

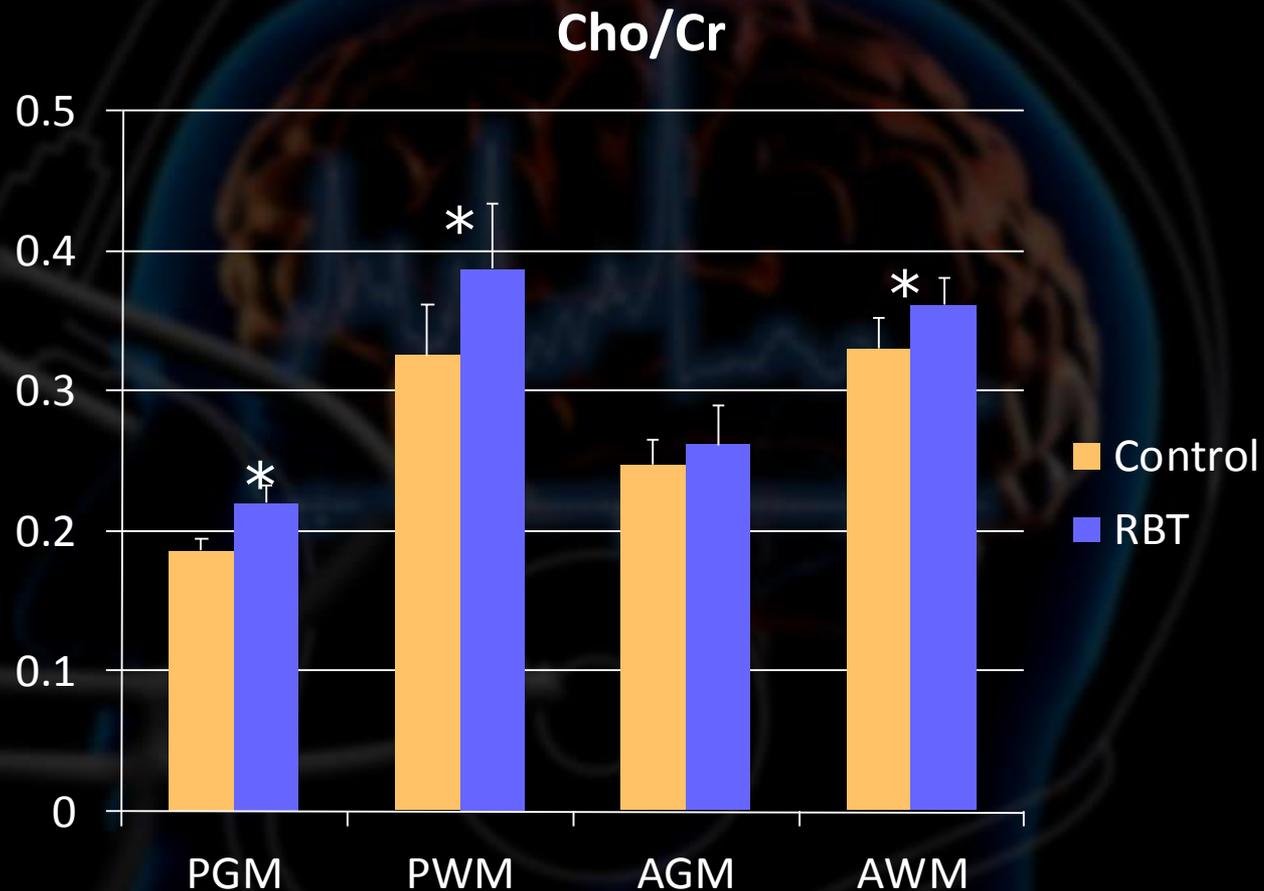
- Diagnosis for CTE **in life** is needed
- Identify biomarkers for repetitive head injury using **advanced MR spectroscopy** methods
- Measure brain chemistry in retired professional athletes with history of multiple concussions **and CTE-related complaints**



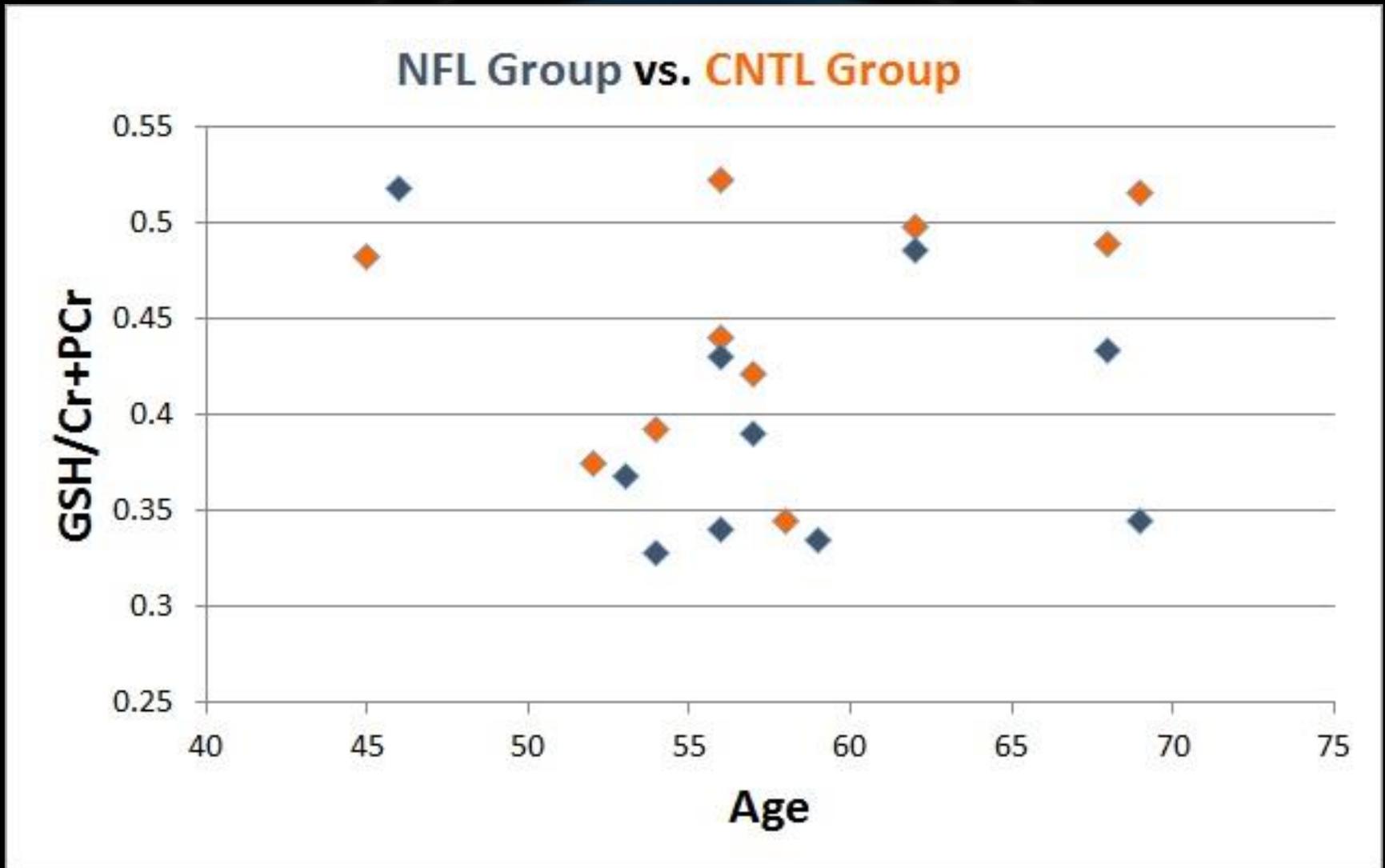
# Regional Metabolite Profiles in Chronic Sports-Related Concussion



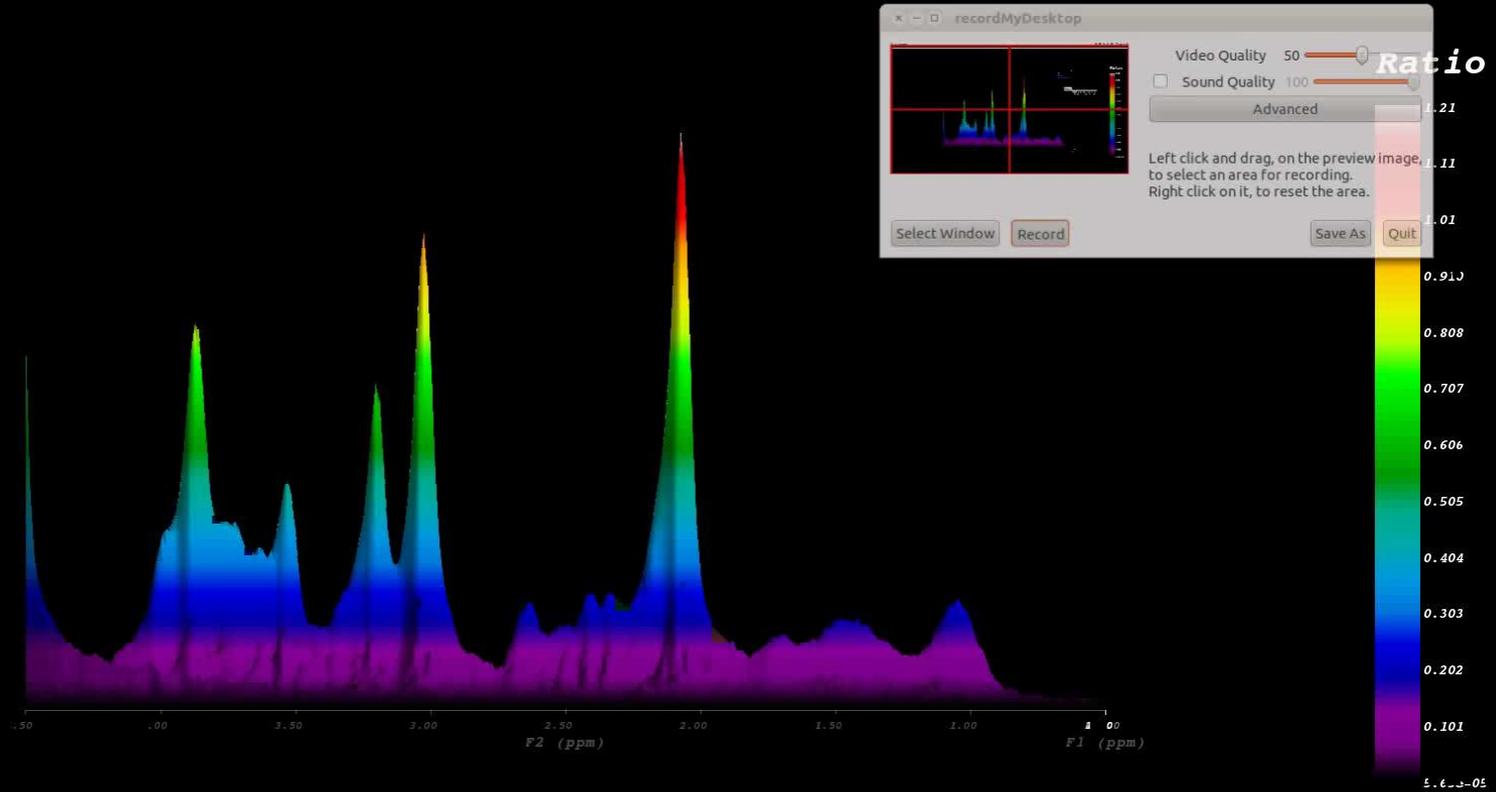
# Significant Metabolite Changes

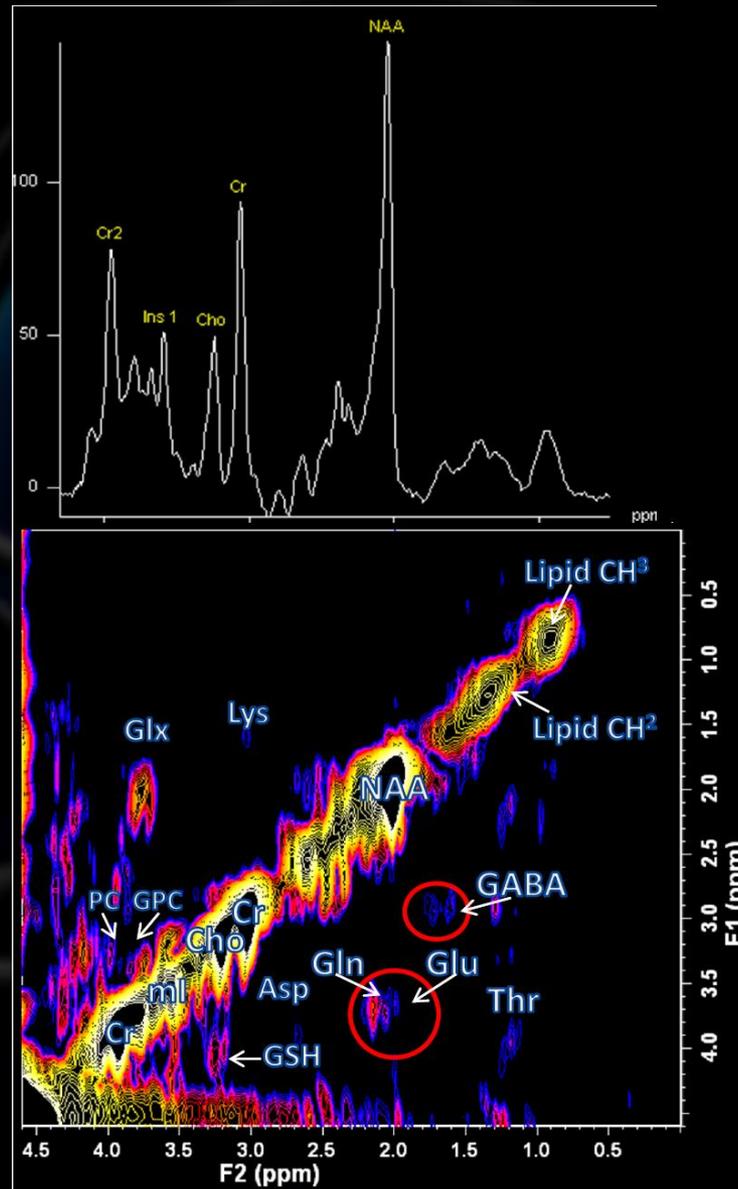


# Glutathione



# 2D MRS



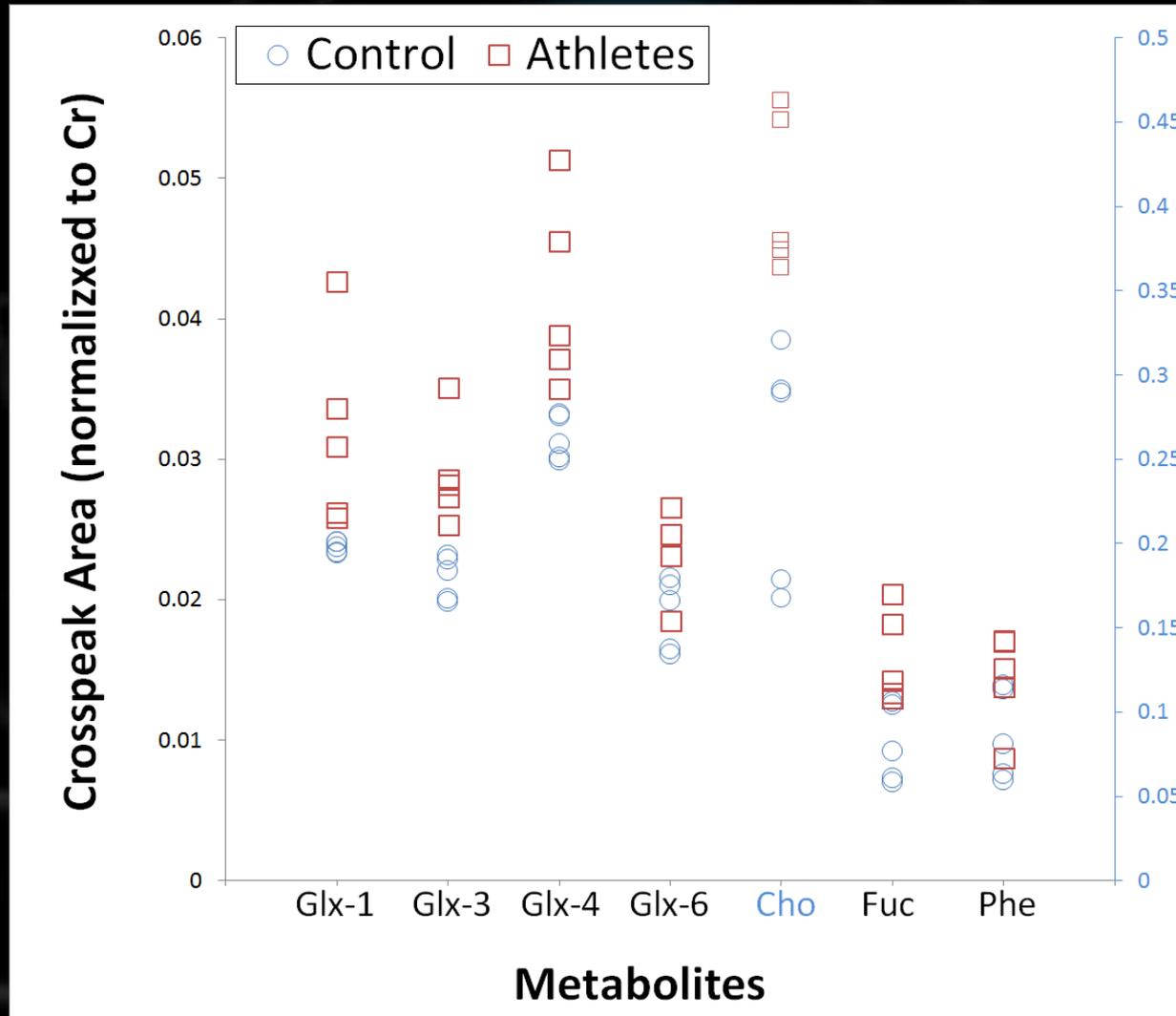


*From Lin and Bluml. MR Spectroscopy of Pediatric Brain Disorders. Eds Bluml and Panagrahy, Springer 2012*



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# 2D MRS: Significant Changes

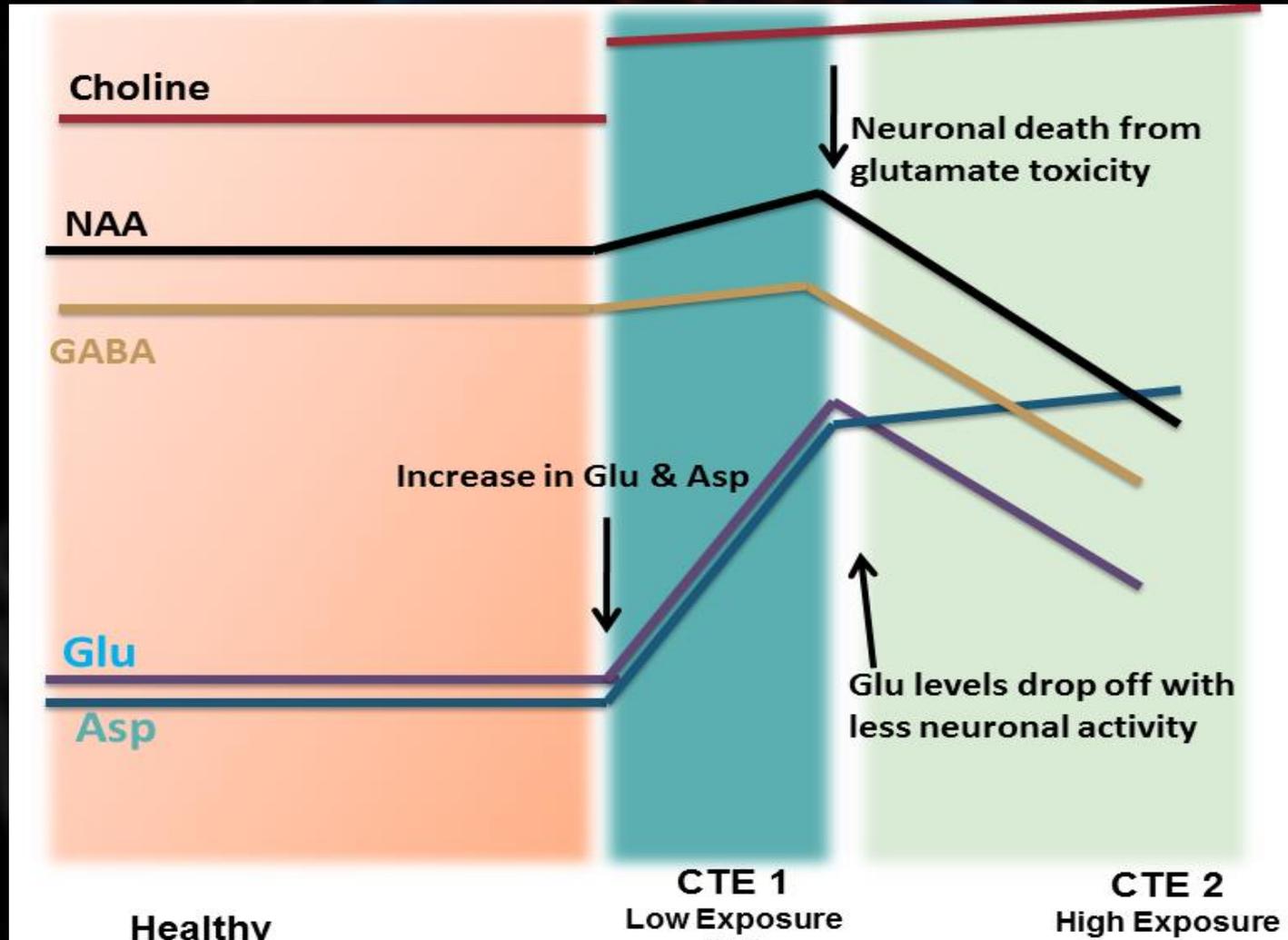


*Lin et al Alz Res Therapy 2015*



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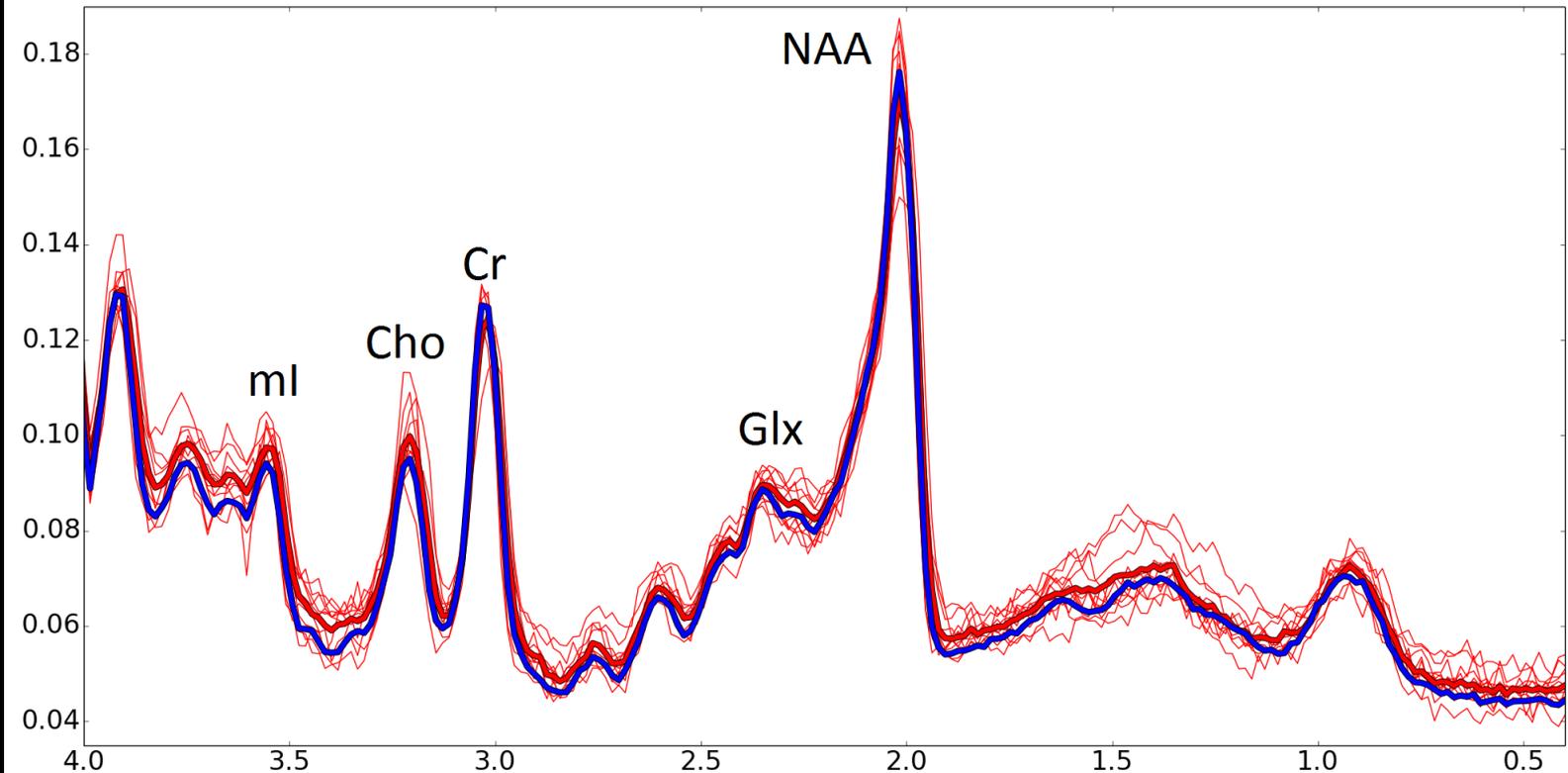
# Potential Treatment Targets



# Subconcussive Head Injury



# Heading Changes Brain Chemistry

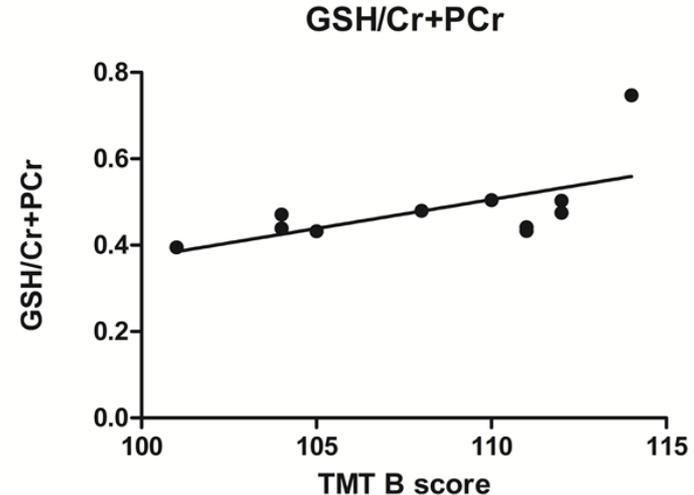
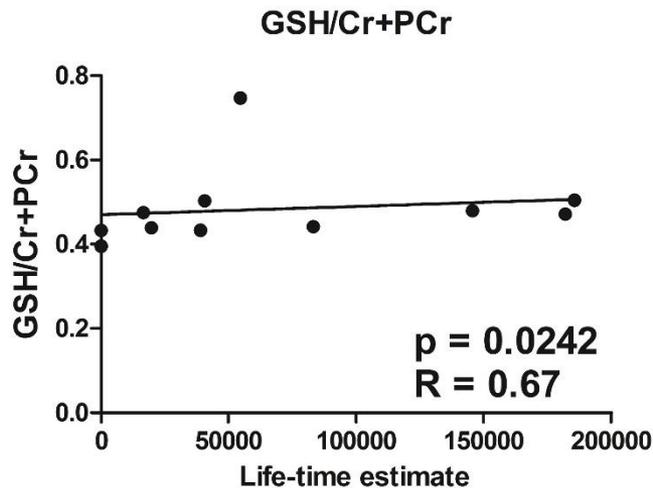
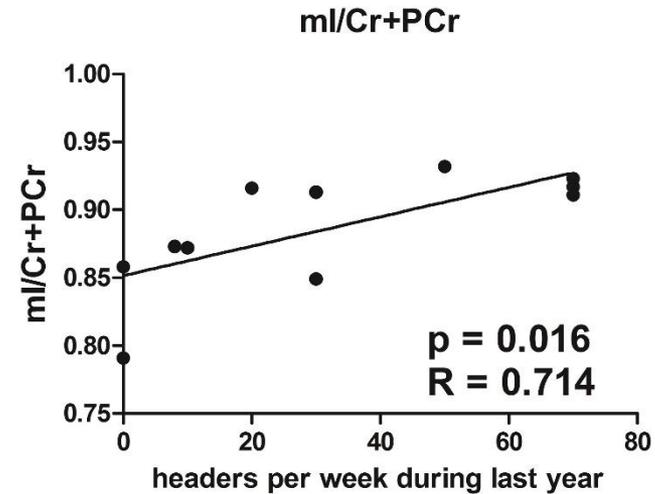
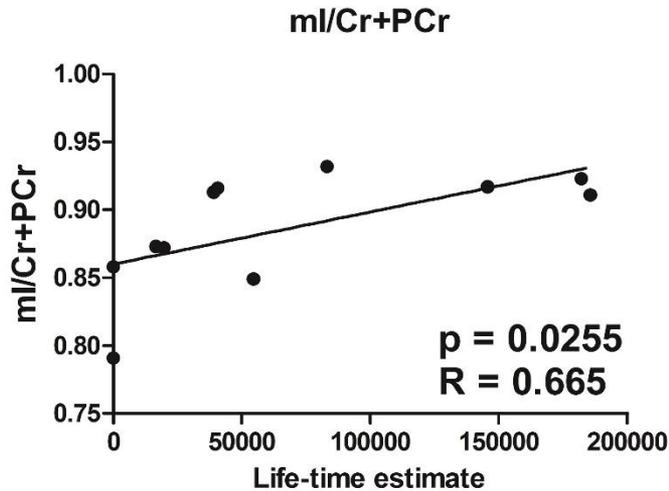


*Koerte\*, Lin\* et al. J Neurotrauma 2015*

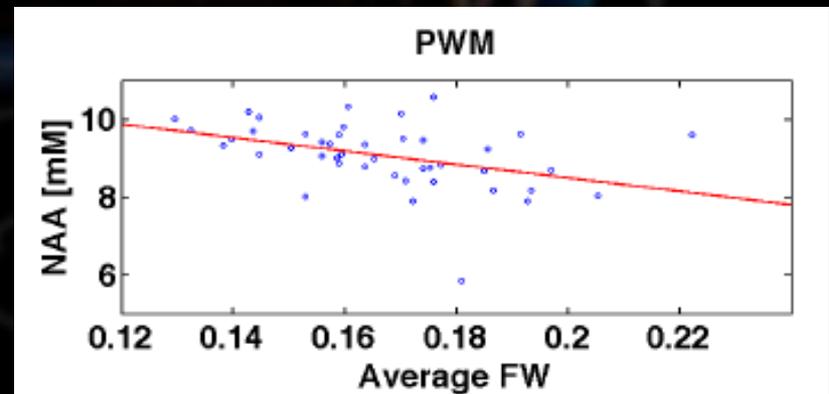
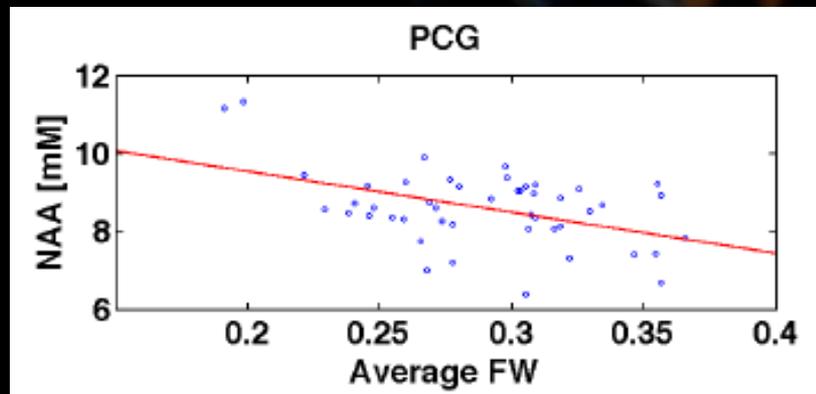
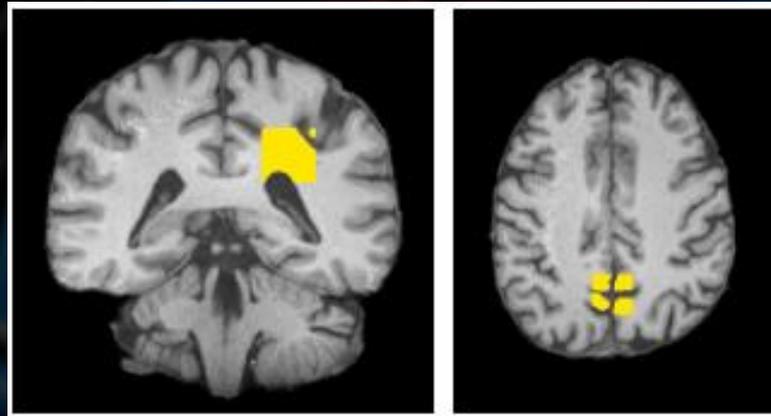


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# Correlation with Number of Headings



# Multimodal Imaging



*Pasternak et al ISMRM 2014*



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- Josh Ladner



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- Boston University Center for Study of Traumatic Encephalopathy

- **Dr. Robert Stern**



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