

# Emerging Metabolic Imaging and Spectroscopic Methods to Study Neurodegenerative Diseases

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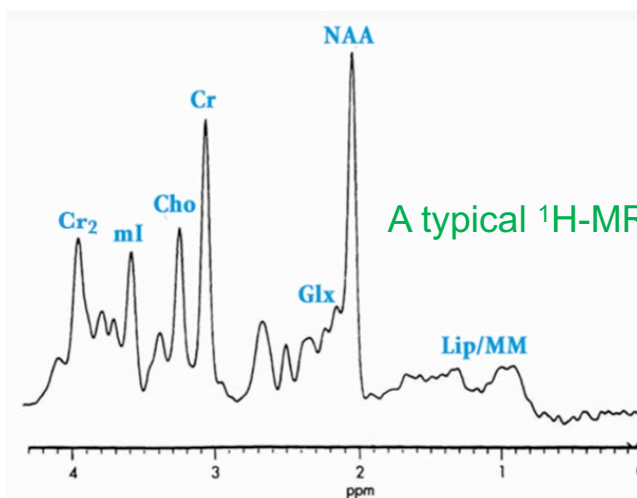
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## Proton MR Spectroscopy: a Promising Tool

- Proton magnetic resonance spectroscopy ( $^1\text{H}$ -MRS) allows non-invasive assessment of metabolic landscape of a biological tissue



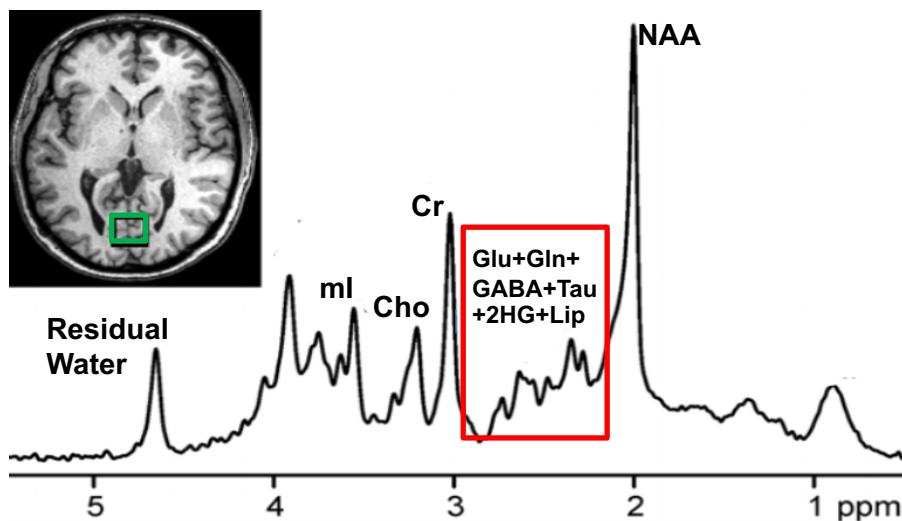
A typical  $^1\text{H}$ -MRS from Normal Brain



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## Proton MR Spectroscopy: Limitations

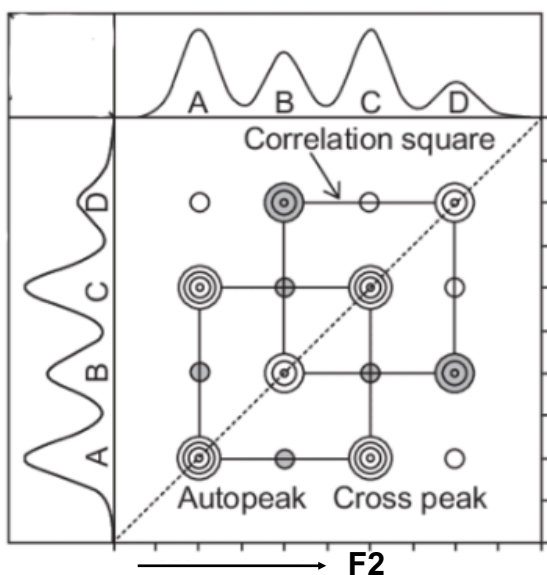
- Generally, proton MR spectroscopy is constrained by poor spectral resolution



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## Two-dimensional Correlation Spectroscopy (2D-COSY)

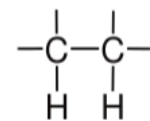


Two Types of Peaks on 2D-COSY Spectrum

**Auto-peak/Diagonal Peak:-**  
indicates that protons are not J-coupled with neighboring protons

**Cross-peak/Off diagonal peak:-**  
indicates spin-spin couplings between two protons up to three bonds apart (vicinal coupling)

In -Phase doublet

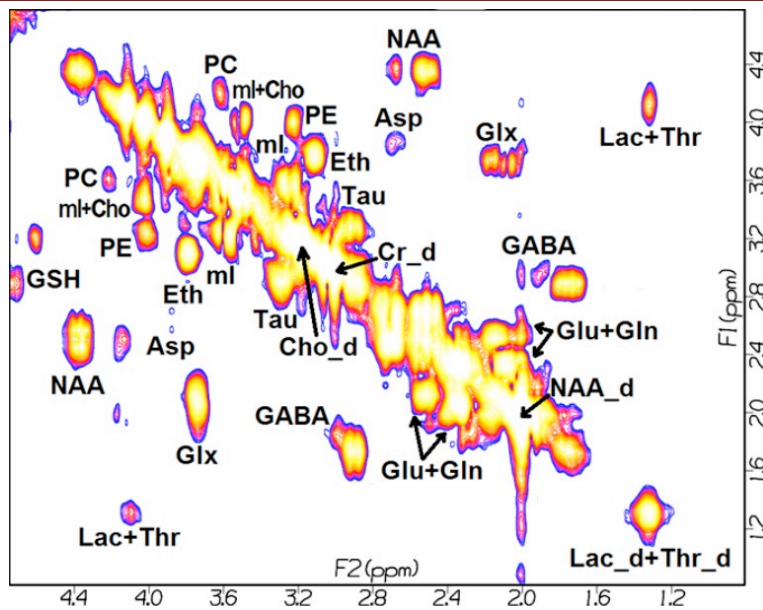


Vicinal Protons

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## 2D-Corelation Spectroscopy from Normal Brain on 7T



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## 2D-COSY of Phantom on 3T and 7T: SNR and Reproducibility

Name	Pk	3T brain phantom (N = 27)				7T brain phantom (N = 30)				7T/3T Gain
		SNR	/Cr 3.0	SD	CV	SNR	/Cr 3.0	SD	CV	
Lac	d	5.6	0.08	0.01	11.2	19.6	0.13	0.01	6.6	3.5
Lac	C	2.0	0.03	0.01	24.4	6.5	0.09	0.01	6.4	3.2
NAA	d	107.5	1.63	0.13	8.0	240.7	1.57	0.06	4.0	2.2
NAA	C	3.7	0.06	0.01	15.0	13.3	0.09	0.01	6.2	3.6
Glu	C	19.3	0.29	0.05	17.0	45.5	0.61	0.09	14.4	2.4
Gln	C	9.8	0.15	0.01	7.9	24.1	0.33	0.07	20.0	2.5
GABA	C	3.8	0.06	0.01	24.3	8.6	0.11	0.02	15.6	2.3
Cr 3.0	d	66.3	1.00	0.00	0.0	153.5	1.00	0.00	0.0	2.3
Cr 3.9	d	54.3	0.82	0.06	7.9	117.1	0.76	0.04	4.9	2.2
Cho	d	62.0	0.94	0.08	8.1	119.0	0.78	0.02	2.5	1.9
Tau	C	6.2	0.10	0.01	15.6	24.1	0.32	0.04	11.1	3.9
ml	d	25.0	0.38	0.04	9.7	79.4	0.52	0.02	3.0	3.2
ml	C	6.7	0.10	0.01	12.7	24.8	0.33	0.04	13.3	3.7
Glx	C	7.3	0.11	0.01	8.2	16.9	0.23	0.03	14.9	2.3
Asp	C	1.9	0.03	0.01	23.6	3.3	0.03	0.00	12.5	1.8
Eth	C	7.8	0.12	0.01	9.2	23.5	0.31	0.02	7.2	3.0
GPE/PE	C	4.3	0.07	0.01	13.2	16.2	0.21	0.01	6.9	3.7
ml+Cho	C	4.3	0.07	0.01	11.6	9.5	0.12	0.01	10.9	2.2
GPC/PC	C	2.7	0.04	0.01	26.6	5.9	0.08	0.01	12.0	2.2
GSH	C	7.7	0.12	0.14	119.3	3.7	0.02	0.00	12.1	0.5

\*The 7T/3T column at right shows the ratio of SNR at 7T compared to 3T.

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Verma G, et al. J Magn Reson Imaging. 2014;40:1319-27.

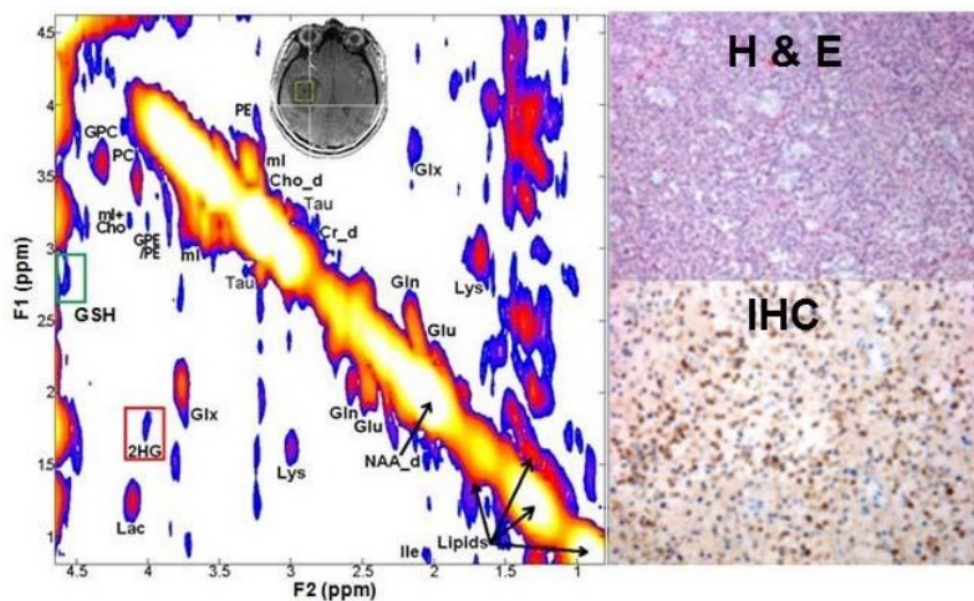
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## 2D-COSY of Healthy Volunteers on 7T: a Reproducibility Study

Name	Pk	Intrasubject (N = 7)			Intersubject (N = 6)		
		Mean	SD	CV	Mean	SD	CV
Lac	C	0.02	0.00	11.3	0.01	0.00	16.0
NAA	d	1.45	0.13	8.9	1.37	0.20	14.3
NAA	C	0.05	0.00	4.6	0.05	0.01	12.1
Ile	C	0.05	0.01	15.0	0.05	0.01	21.2
Glu	C	0.29	0.04	13.1	0.23	0.04	18.2
Gln	C	0.23	0.01	3.9	0.20	0.02	9.3
Lys	C	0.11	0.02	13.5	0.10	0.01	6.6
GABA	C	0.10	0.02	21.6	0.07	0.01	16.6
Cho	d	0.69	0.05	7.5	0.64	0.03	4.3
Tau	C	0.10	0.02	21.7	0.09	0.02	22.9
ml	d	0.35	0.02	6.1	0.28	0.02	5.8
ml	C	0.24	0.02	9.3	0.24	0.06	24.8
Cr	d	0.89	0.08	9.5	0.79	0.09	11.1
Glx	C	0.21	0.01	5.6	0.17	0.02	10.5
Asp	C	0.05	0.00	8.5	0.05	0.01	22.7
Eth	C	0.08	0.01	16.6	0.08	0.02	26.3
GPE/PE	C	0.06	0.00	5.7	0.04	0.01	25.0
ml+Cho	C	0.06	0.01	13.4	0.05	0.01	24.0
GPC/PC	C	0.04	0.01	19.2	0.04	0.01	24.4
GSH	C	0.03	0.01	20.2	0.03	0.01	21.8

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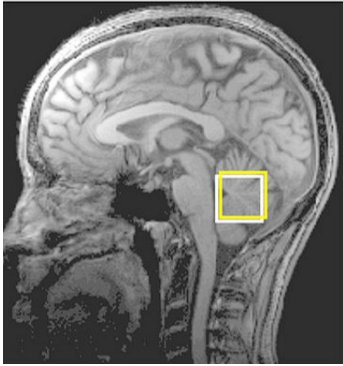
## IDH Mutant Grade-III, Anaplastic Astrocytoma



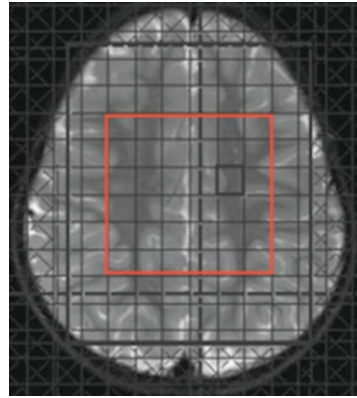
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## Proton MR Spectroscopy: Limitations

- Widely-used single-voxel or single-slice two-dimensional  $^1\text{H}$ -MRS methods constrained by limited spatial coverage

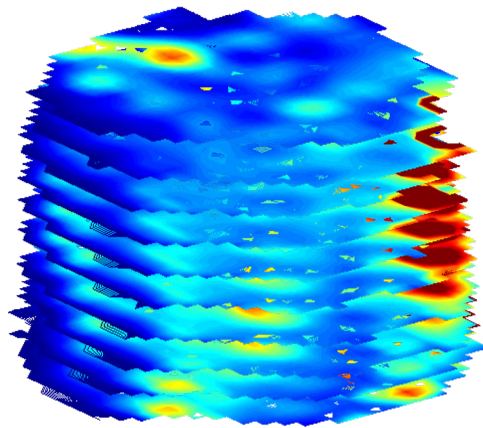


Single Voxel

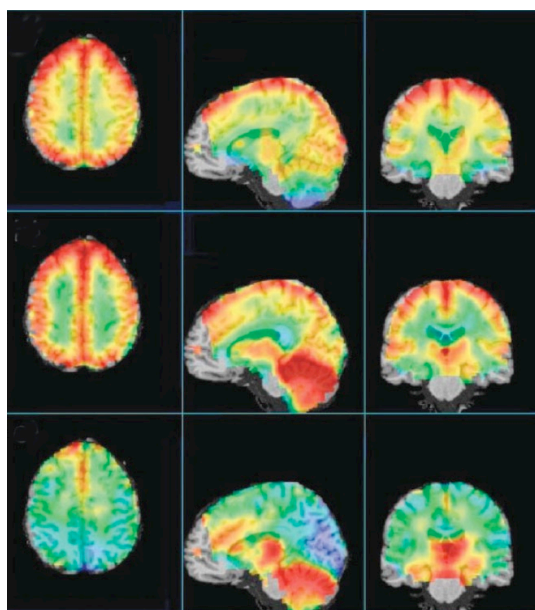


Single slice multivoxel

## Whole Brain Spectroscopic Imaging: Metabolite Maps



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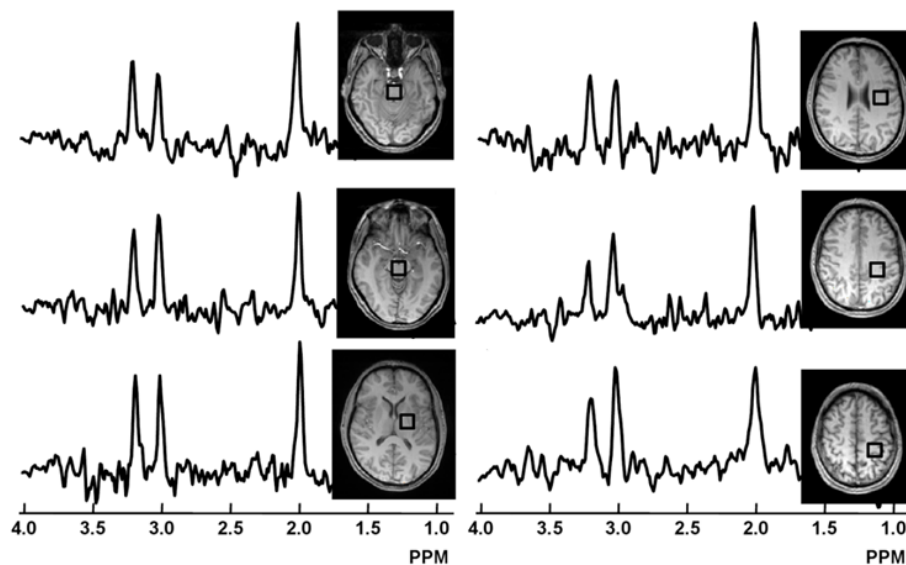


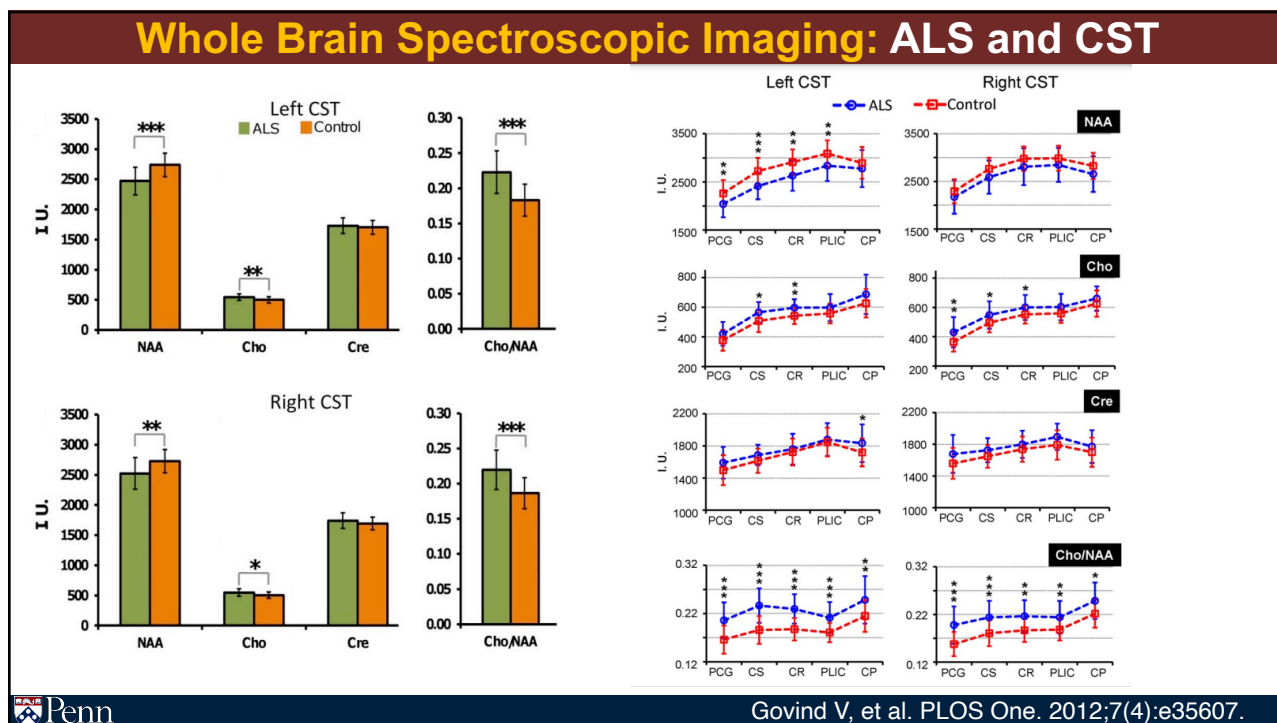
**N-acetylaspartate (NAA)**

**Creatine**

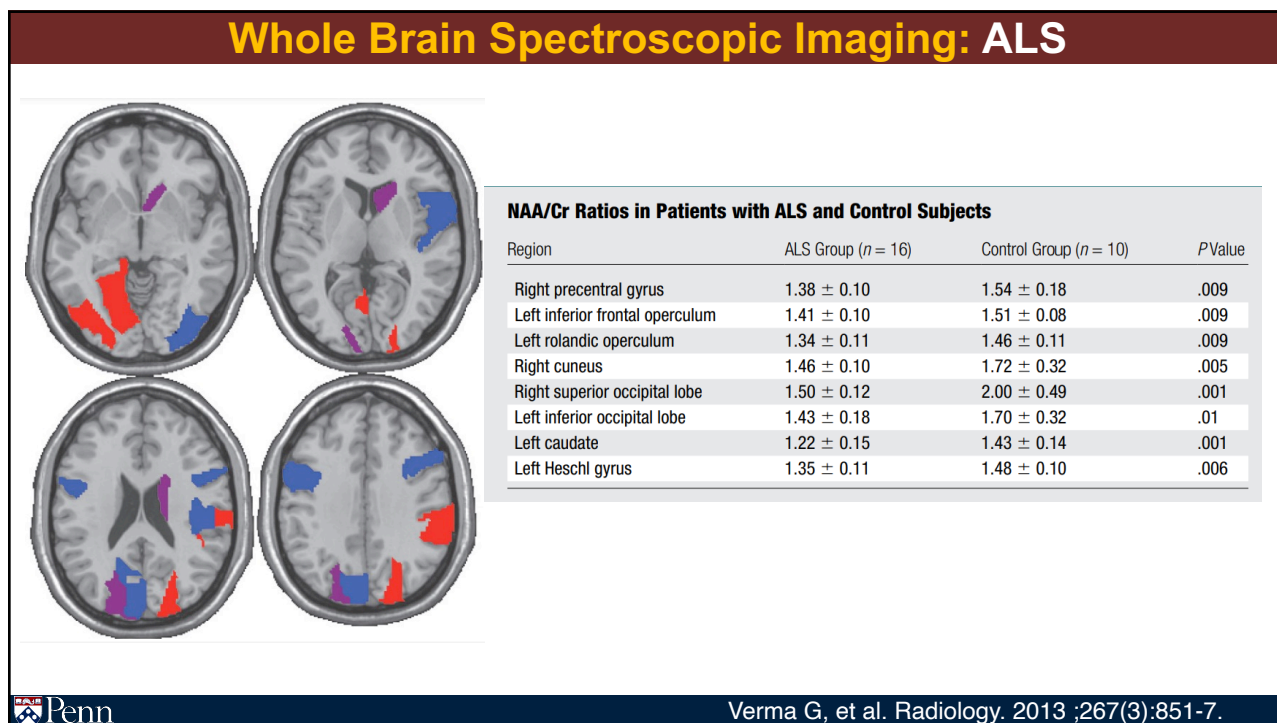
**Choline**

## Whole Brain Spectroscopic Imaging: ALS and CST

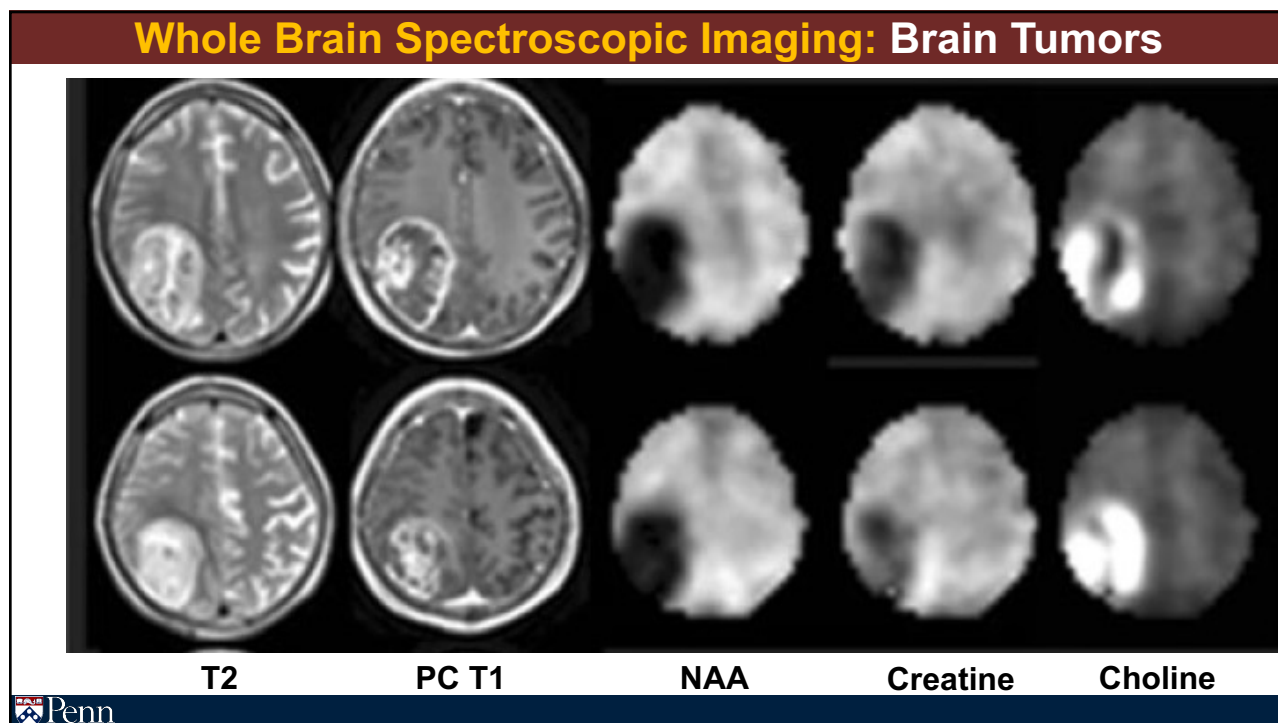




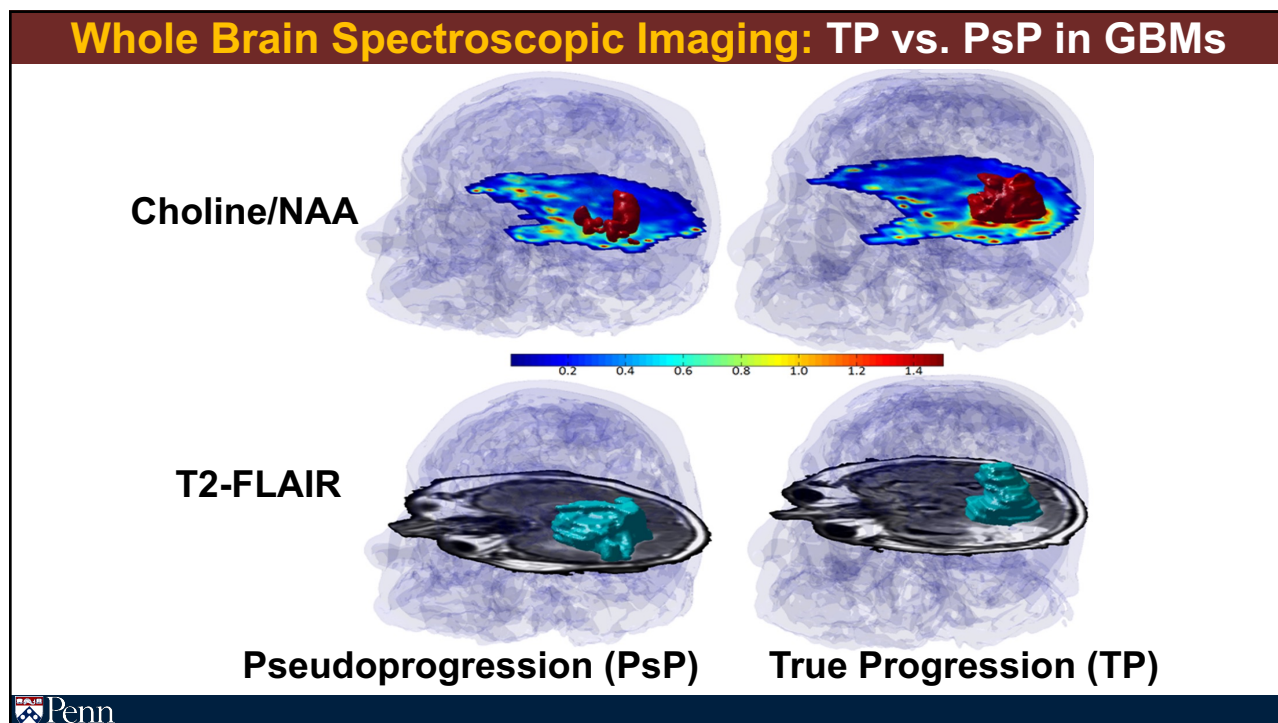
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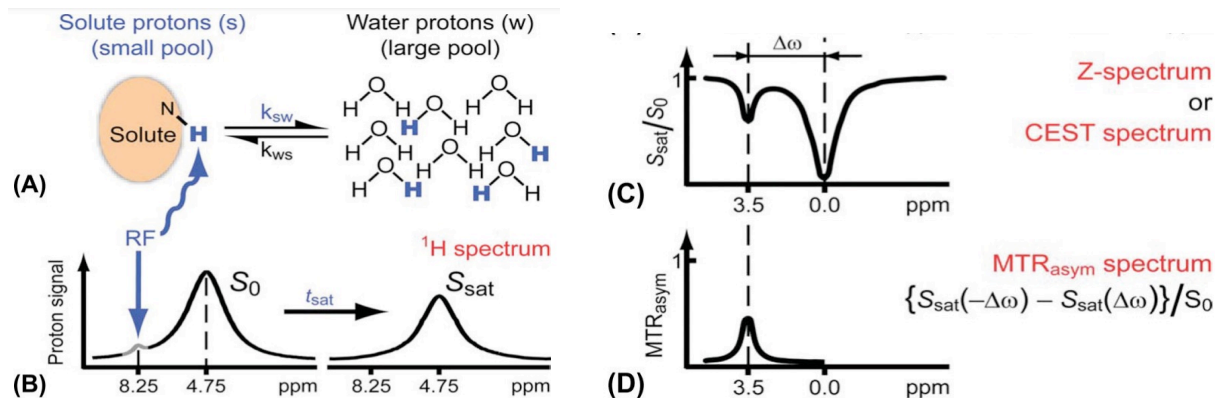
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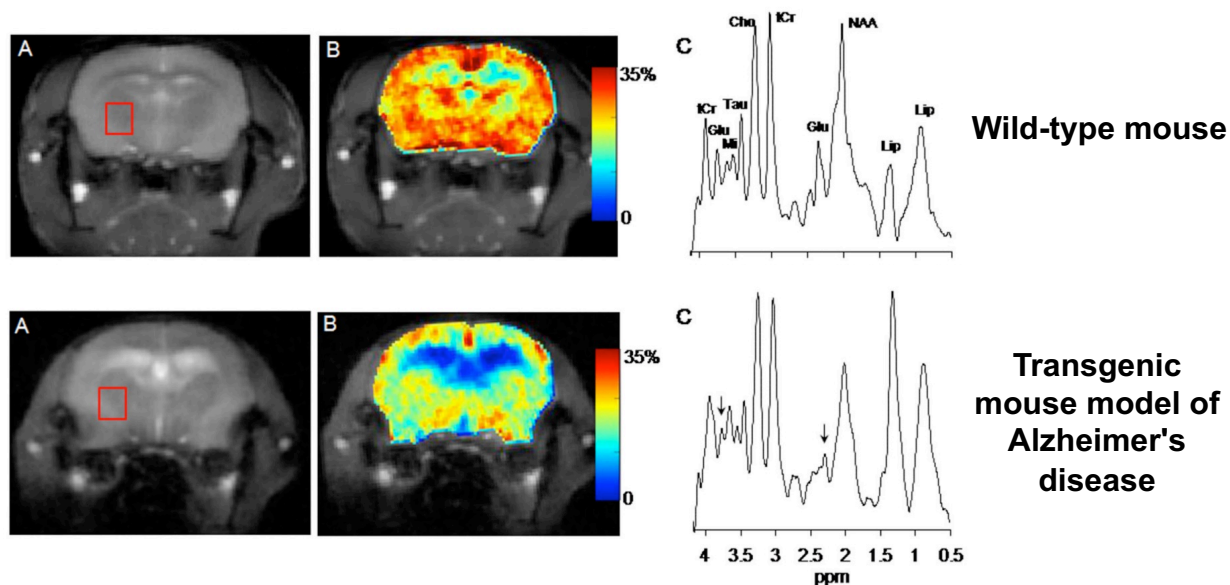
## Chemical Exchange Saturation Transfer- Basic Principle



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## Glutamate-CEST: Mouse Model of Alzheimer's Disease

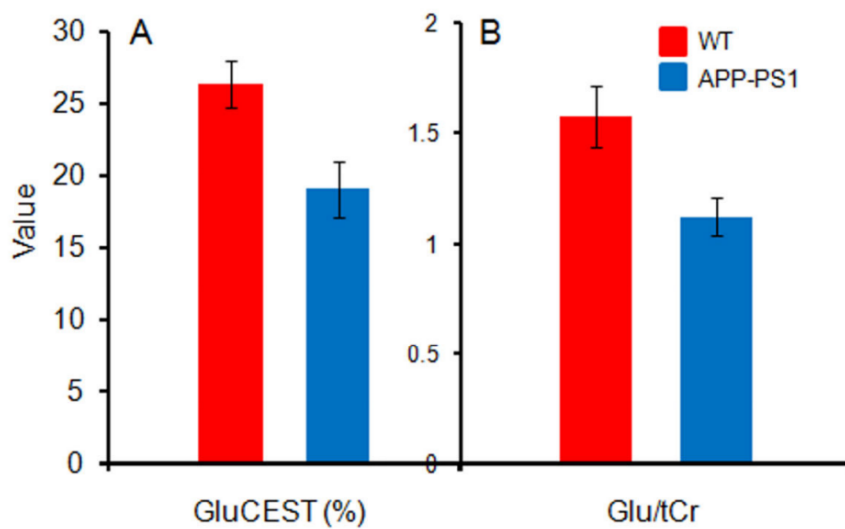


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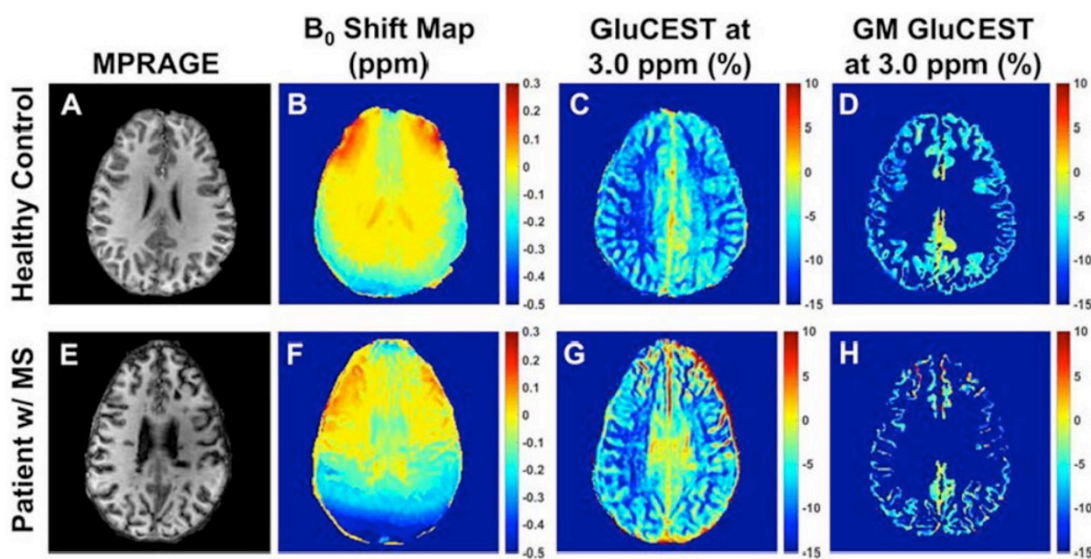
Haris M, et al. NMR Biomed. 2013; 26; 386-91.

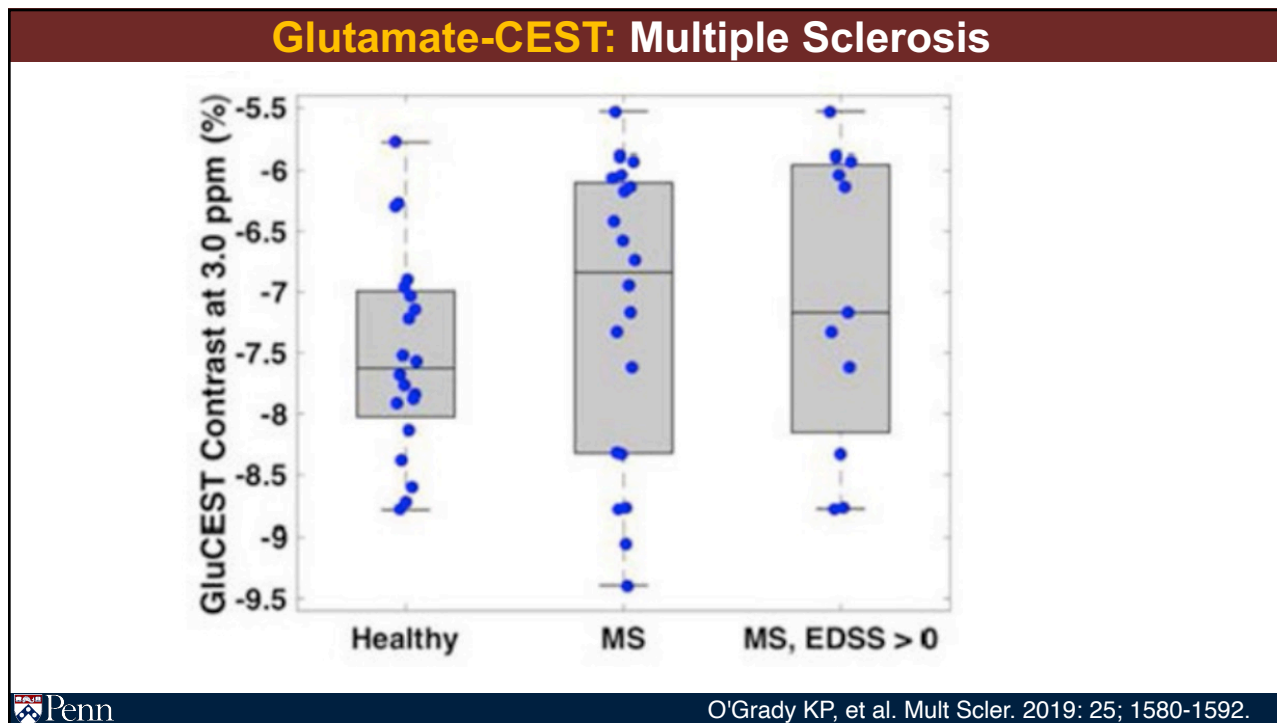
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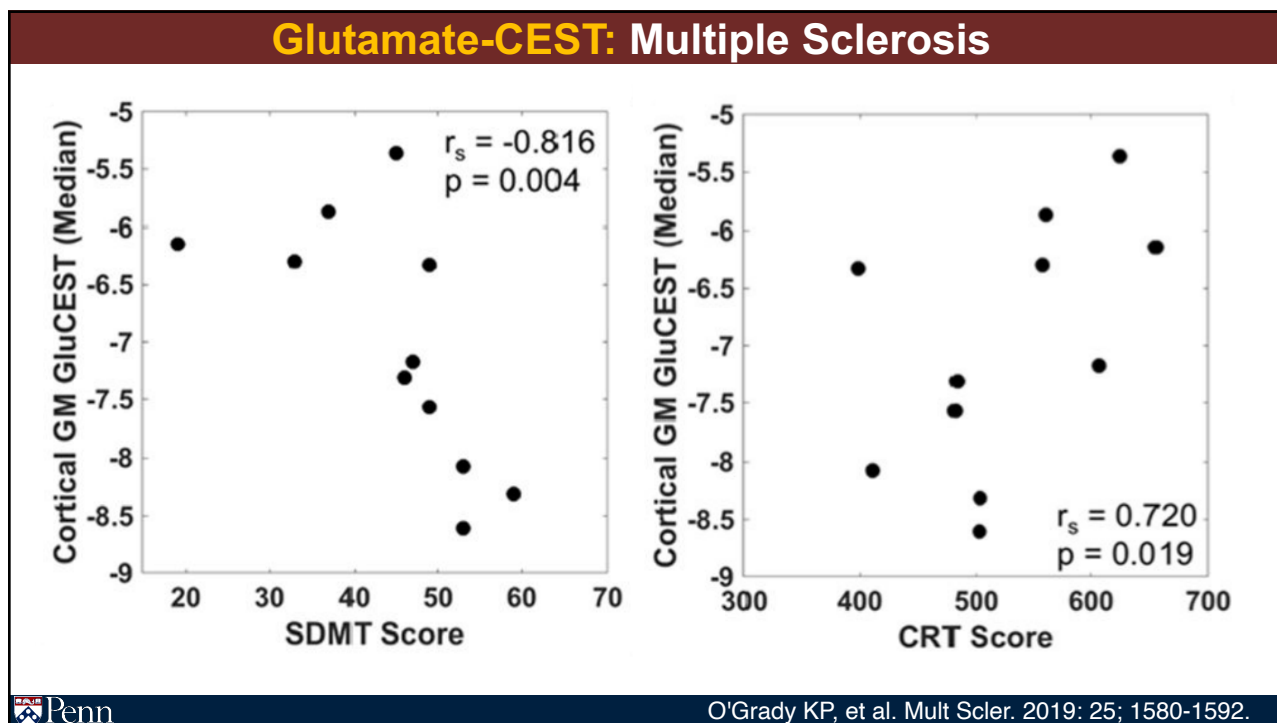


## Glutamate-CEST: Multiple Sclerosis





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## Acknowledgements



**Laurie Loevner, MD**  
Neuroradiology, UPenn  
(Section Chief)



**Suyash Mohan, MD, PDCC**  
Neuroradiology, UPenn



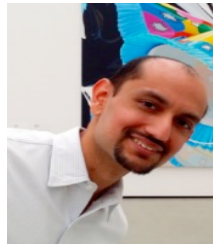
**Harish Poptani, PhD**  
University of Liverpool



**Ravindra Reddy, PhD**  
Radiology, UPenn



**Mohammad Haris, PhD**  
Radiology, UPenn



**Gaurav Verma, PhD**  
Icahn School of Medicine at Mount Sinai



**Andrew A. Maudsley, PhD**  
University of Miami



## Thank You!

