MRS in Epilepsy

Speaker

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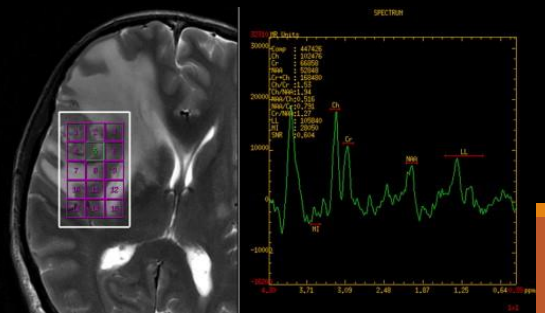
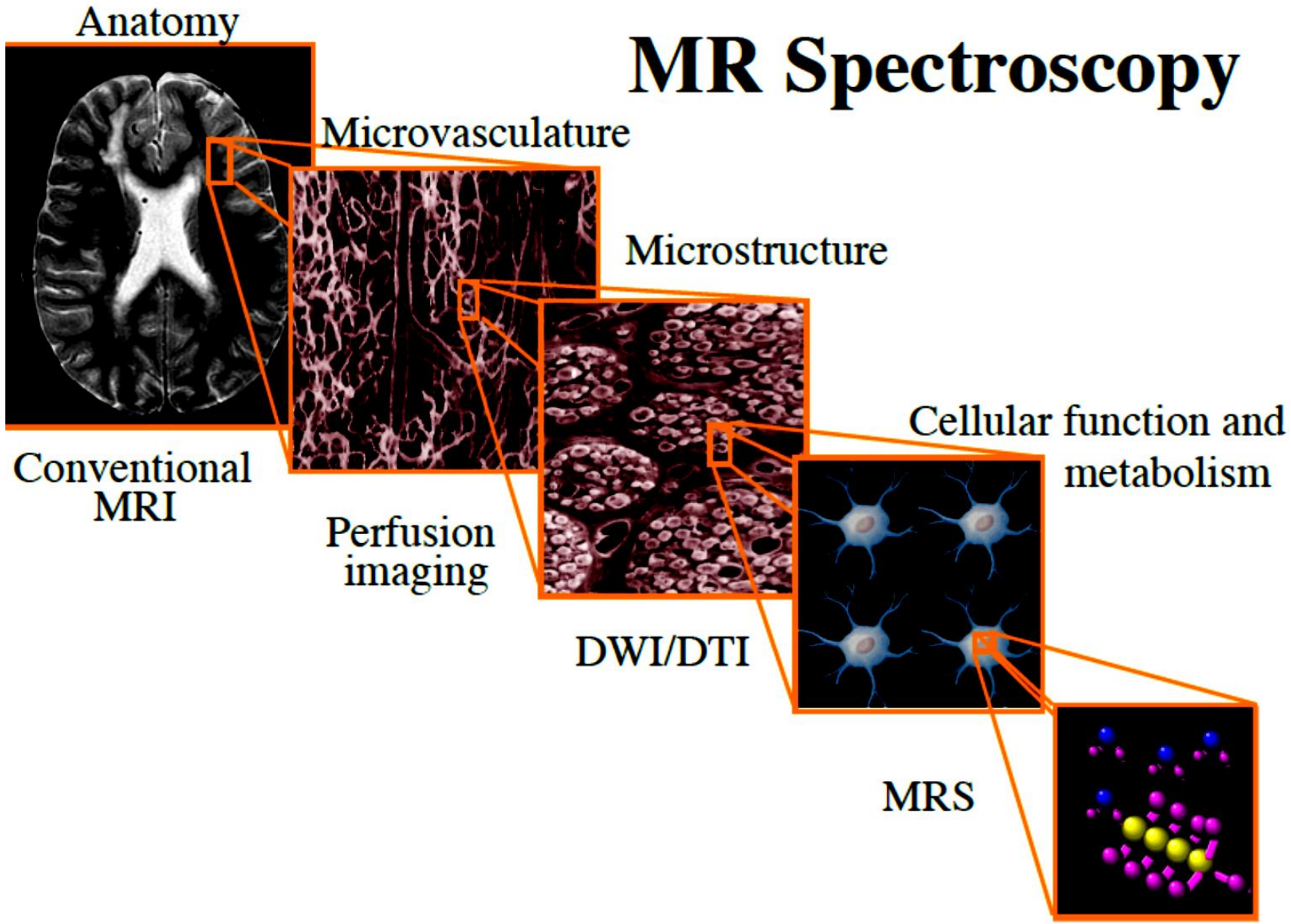


MR Spectroscopy



MRS

Magnetic resonance spectroscopy (MRS) allows the non-invasive measurement of selected biological compounds in vivo.

MRI: Signal versus time

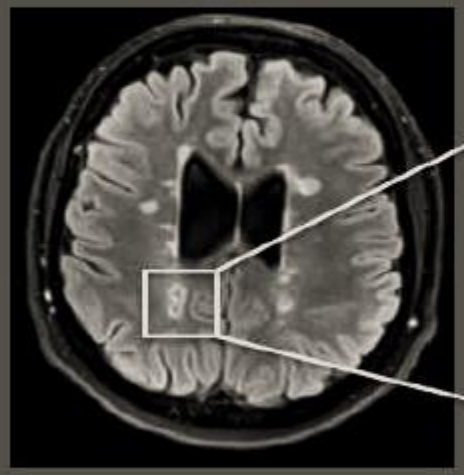
(anatomic changes)

MRS: signal versus frequency

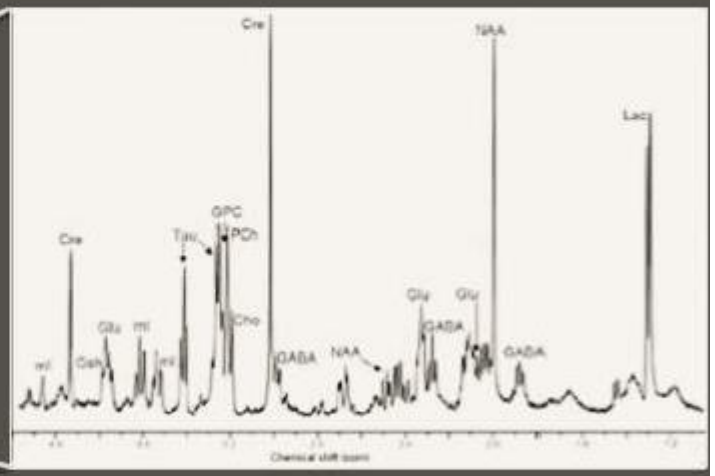
(biochemical and metabolic changes)

MRI vs. MRS

T2w FLAIR MRI in Multiple Sclerosis Patient



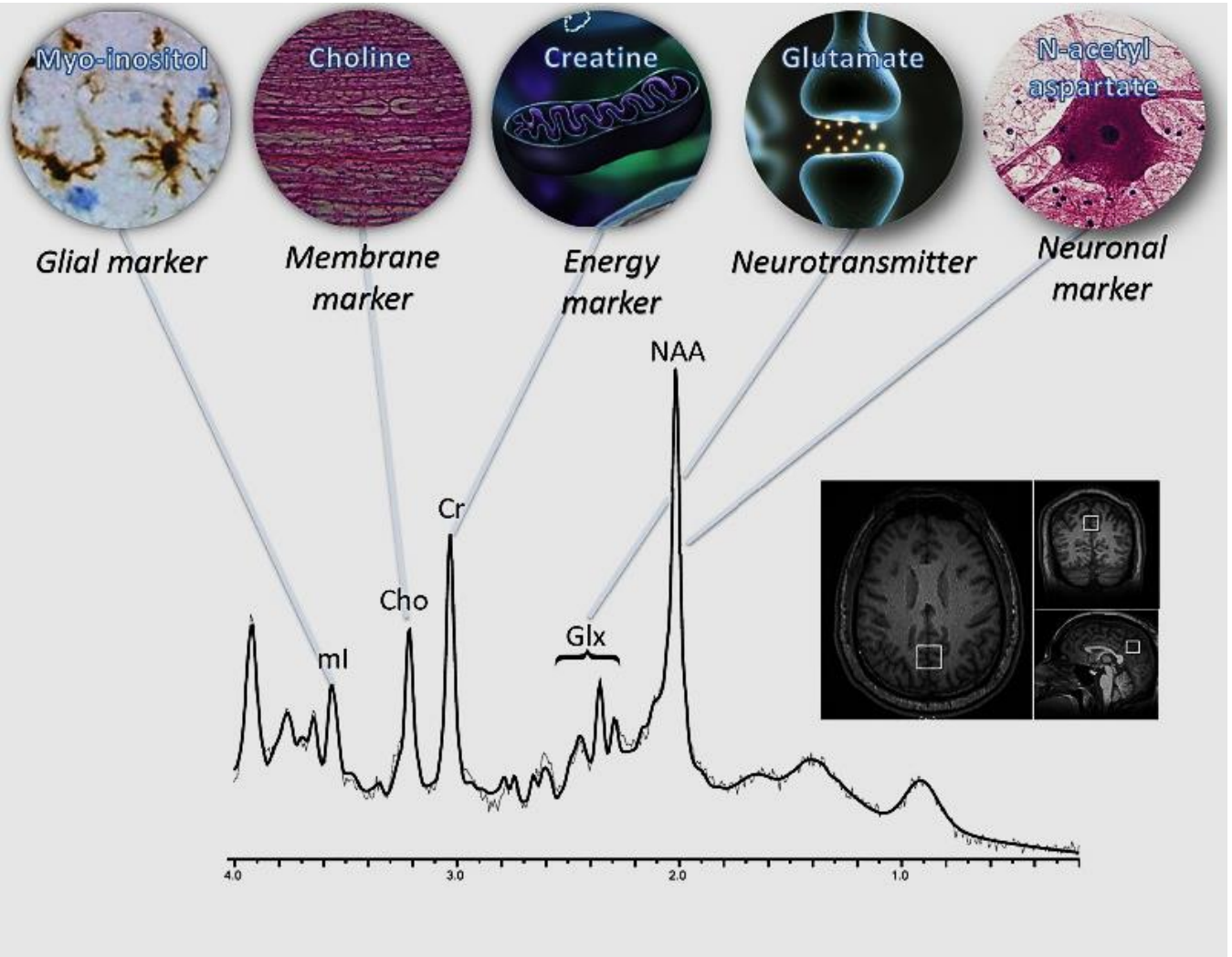
Spectroscopy



Imaging signal comes from water protons

Spectroscopy signal comes from protons in other environments

Some common MRS metabolites that are assessed as biomarkers

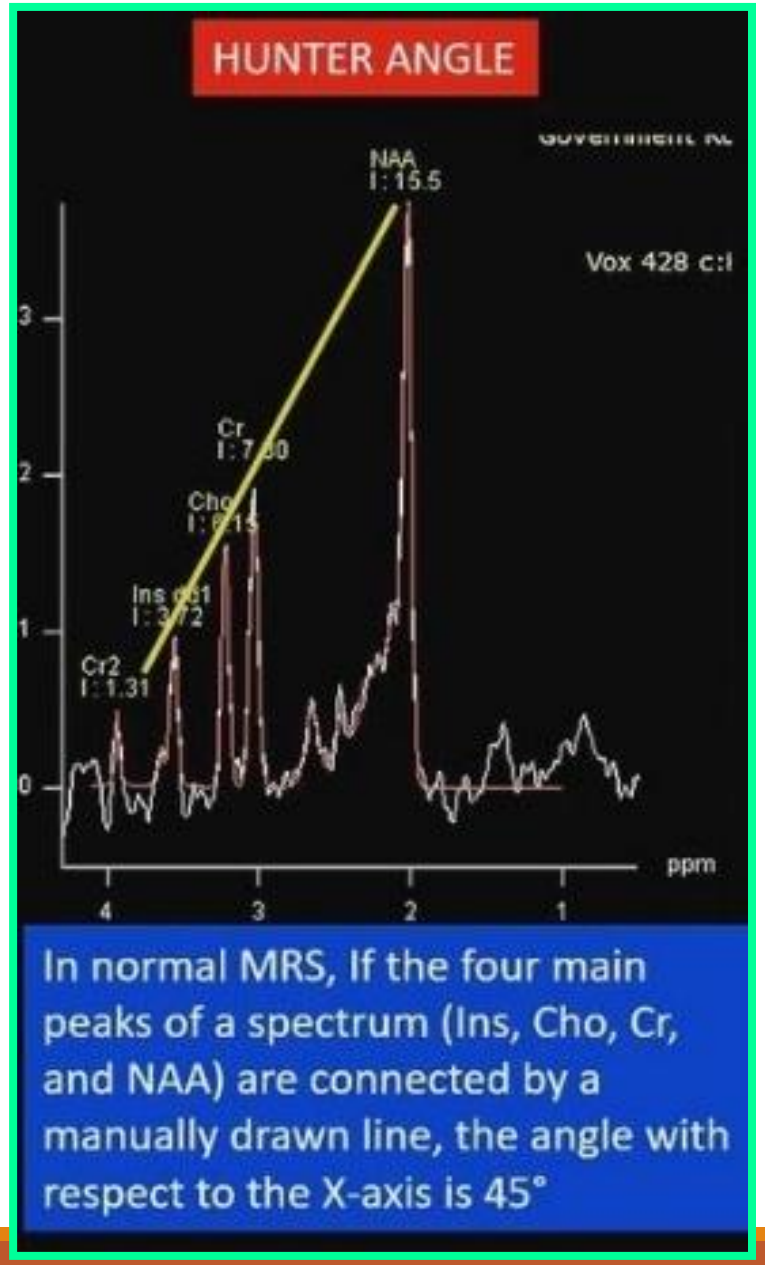


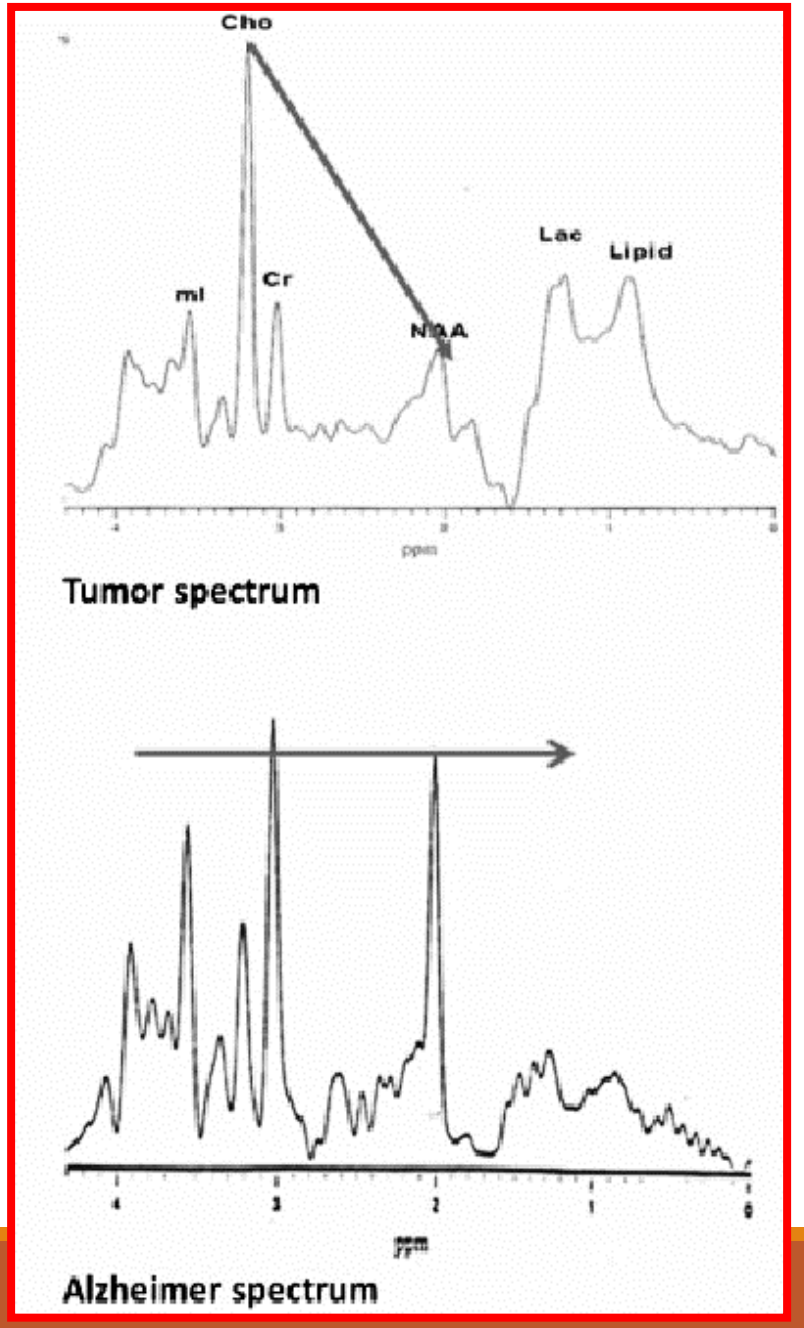
Gray matter has more creatine

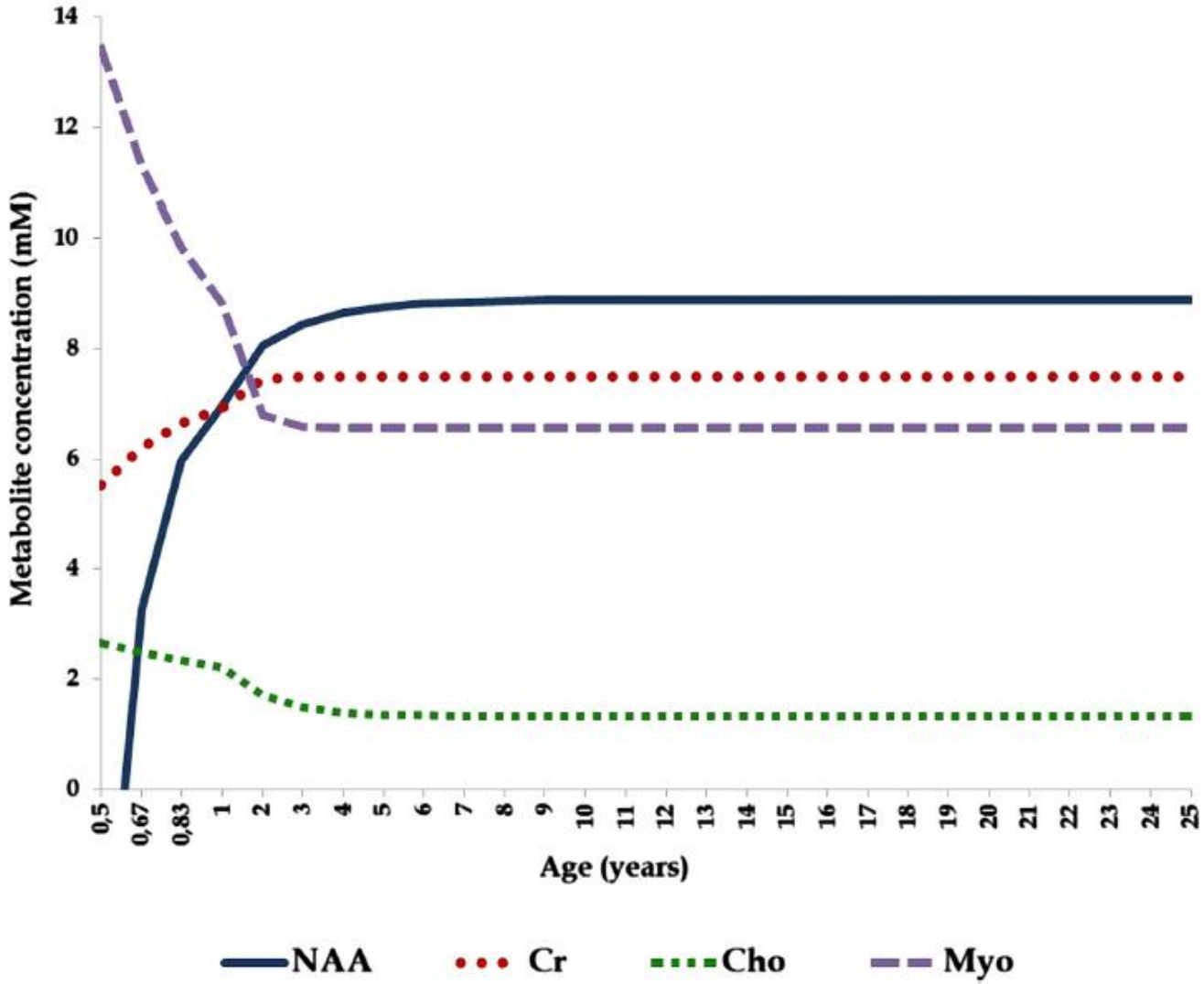
Standard range of MRS metabolites

ppm	Metabolite	Properties
0.9-1.4	Lipids	Products of brain destruction
1.3	Lactate	Product of anaerobic glycolysis
2.0	NAA	Neuronal marker
2.2-2.4	Glutamine/GABA	Neurotransmitters
3.0	Creatine	Energy metabolism
3.2	Choline	Cell membrane marker
3.5	*myo*-inositol	Glial cell marker, osmolyte hormone receptor mechanisms

- **NAA** is considered as a **good** metabolite (as it represents neuronal health)
- **Choline** is considered as a **bad** metabolite (as it is seen in tumors) and
- **Lipid lactate** doublet as an **ugly** metabolite (as it is seen in necrotic tumors).

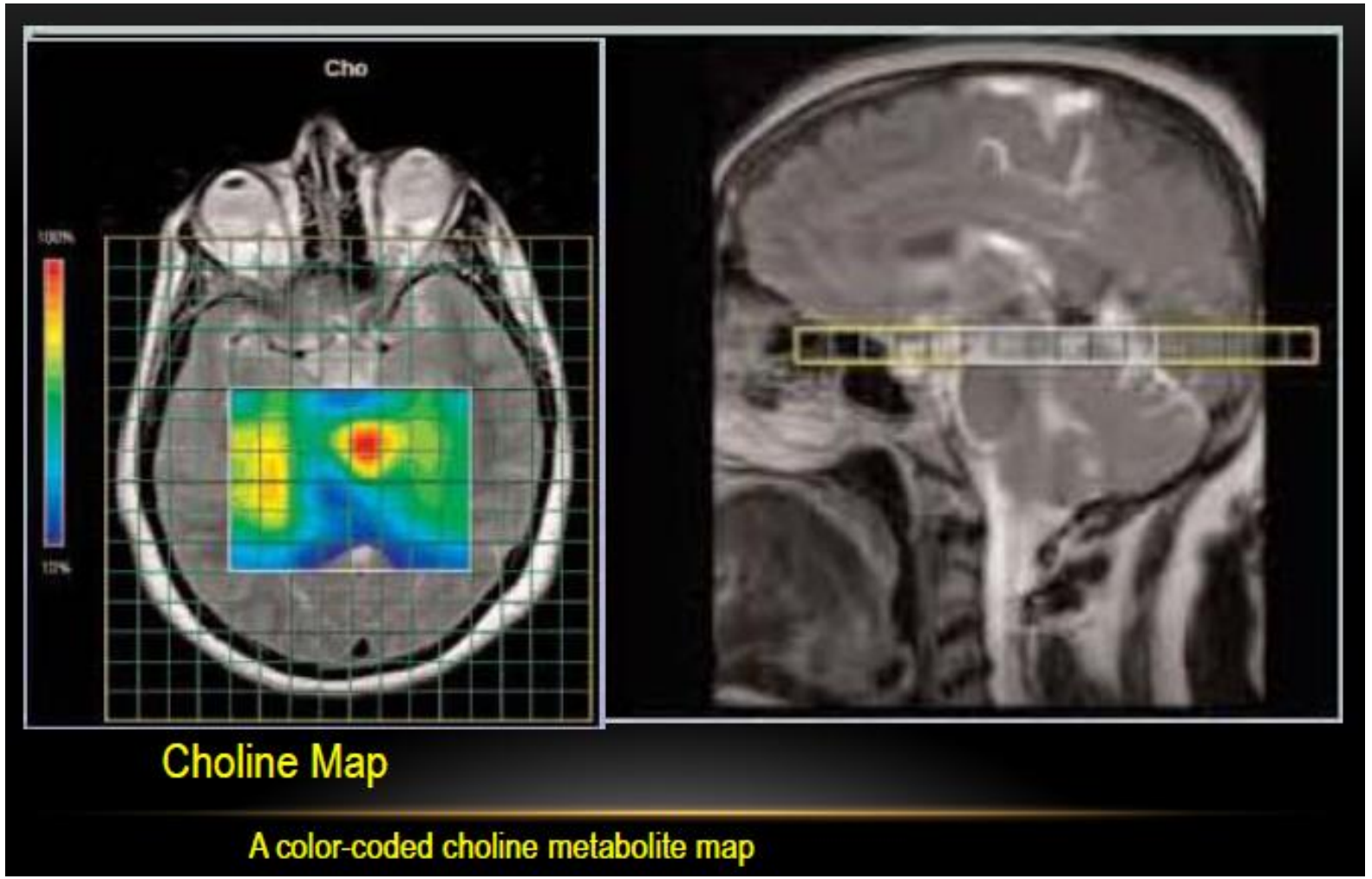

HUNTER ANGLE
NAA
I : 15.5
Vox 428 c:l
Cr
Cho
Cr2
I : 1.31
ppm
4
3
2
1
In normal MRS, If the four main peaks of a spectrum (Ins, Cho, Cr, and NAA) are connected by a manually drawn line, the angle with respect to the X-axis is 45°


Cho
mI
Cr
NAA
Lac
Lipid
ppm
Tumor spectrum
Alzheimer spectrum



Kries graph in developmental MRS

Single voxel vs. Multivoxel Spectroscopy (MVS)



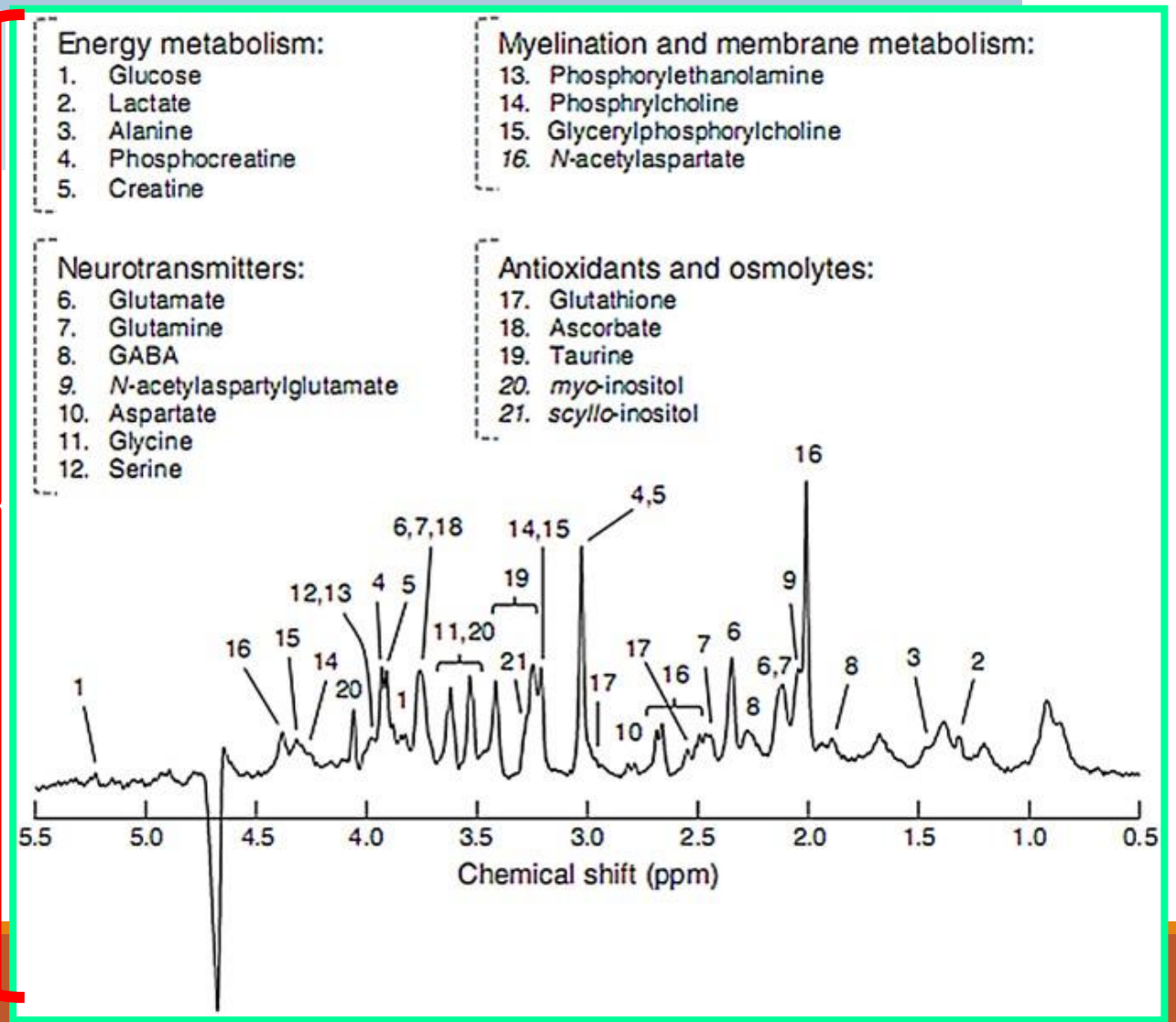
The neurochemical profile detected by ^{1}H MRS in the brain

At high magnetic field [7 T and above], a neurochemical profile of more than 20 metabolites can be determined under normal physiological conditions

^{1}H MRS can detect all compounds existing in a concentration above 0.5 µmol/g (Ref: Duarte)

Duarte JM, Lei H, Mlynárik V, Gruetter R. The neurochemical profile quantified by in vivo 1H NMR spectroscopy. Neuroimage. 2012 Jun 1;61(2):342-62.

1) **These metabolites categorized into four types:**
2) **neurotransmitters,**
3) **energy metabolism,**
4) **myelination and membrane metabolism,**
5) **antioxidants and osmolytes**



1H-MRS is important in the management of intracranial lesions. This important role has been identified in the following areas:

1) Diagnosis without neurosurgery.
2) Guiding neurosurgery procedures.
3) Provide an assessment of response to treatment.
4) Diagnosis of recurrence or progression of the disease.

EPILEPSY

TEMPORAL LOBE EPILEPSY: MESIAL TEMPORAL SCLEROSIS

IF MRI NEGATIVE

TO EVALUATE THE OTHER APPARENT NORMAL HIPPOCAMPAL HEAD

TO PREDICT OUTCOME OF SURGERY

LOW NAA/CR AND NAA/CHO

HIGH LAC IN POST-ICTAL PHASE FOR 6 HOURS

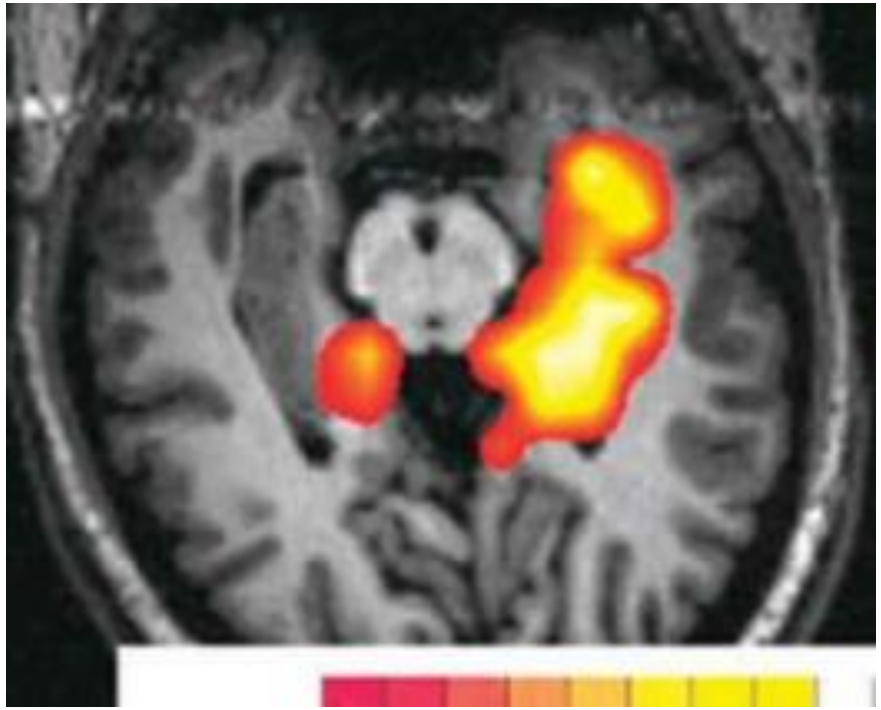
What is being measured?

- The first study of 1H-MRS in epilepsy was done in the early 90s.
- professor Hugg (1993) initially demonstrated a significant asymmetry of NAA left/right metabolite ratios (decrease in NAA in the affected temporal lobe of TLE patients).

- Kuzniecky (1998) investigated the validity of 1H-MRS in lateralizing the pathologic area in 30 consecutive preoperative TLE patients with mesial temporal lobe sclerosis on MRI. Volumetry technique correctly duagnosed in 93% of patients while 1H-MRS did so in 97%.

- 1H-MRS was sensitive in detecting bilateral dysfunction and has high concordance to the degree of bilateral EEG findings in patients with TLE.

MRSI statistical map showing the bilateral but dominant left hippocampal abnormalities in NAA/Cr.



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Original article

Role of magnetic resonance spectroscopy (MRS) in nonlesional temporal lobe epilepsy

Abdel Aziz Kamal Aun [a], Amr Ahmed Mostafa [a]

Between April 2011 and December 2013, a total of 30 patients having partial seizures with or without secondary generalization.
All patients included in the study had clinical history, seizure symptoms, inter-ictal EEG, and neuroimaging findings that were consistent with “non-lesional epilepsy of temporal lobe origin”.

Sensitivity and specificity of the MRS for the detection of mesial TLE: 65% and 83% respectively.

Meta-Analysis > Adv Clin Exp Med. 2023 Feb;32(2):163-173. doi: 10.17219/acem/152943.

A meta-analysis to investigate the role of magnetic resonance spectroscopy in the detection of temporal lobe epilepsy

Xiangxiang Cui [1], Dan Zhong [1], Jinou Zheng [1]

Results: A total of 16 studies published between 2000 and 2022 were included, which encompassed a total of 645 patients. We obtained a high sensitivity of 84.8%, which shows a high efficiency of MRS, and a pooled OR value of 0.37 (95% confidence interval (95% CI): 0.14-0.97) with a tau2 value of 2.63, $\chi 2$ value of 84.99, degrees of freedom (df) value of 15, I2 value of 82%, Z-value of 2.03, and $p < 0.05$. The pooled RR was 0.82 (95% CI: 0.69-0.97) with a tau2 value of 0.10, $\chi 2$ value of 122.11, df of 15, I2 value of 88%, Z-value of 2.25, and $p < 0.05$. These results were statistically significant for a low risk of publication bias.

Comparison between EEG, [1] HMRS and MRI for lateralization of the side of the lesions

		Group 1 (n = 20)	Group 2 (n = 12)	Group 3 (n = 8)
EEG lateralization *N* (%)	**Lateralized**	20(50%)	-	-
	Strictly lateralized	15		
	Lateralized with side Predominance	5		
	Non lateralized	-	12(30%)	-
	Normal EEG	-	-	8(20%)
[1]HMRS lateralization *N* (%)	**Lateralized**	19(95%)	9(75%)	5(62.5%)
	Strictly lateralized	16		
	Lateralized with side Predominance	3		
	Non lateralized	-	3(25%)	2(25%)
	Normal MRS	1(5%)	-	1(12.5%)
MRI lateralization *N* (%)	Lateralized	11(55%)	9(75%)	3(37.5%)
	Non lateralized	4(20%)	-	2(25%)

Azab, S.F., Sherief, L.M., Saleh, S.H., Elshafeiy, M.M., Siam, A.G., Elsaeed, W.F., Arafa, M.A., Bendary, E.A., Sherbiny, H.S., Elbehedy, R.M. and Aziz, K.A., 2015. Childhood temporal lobe epilepsy: correlation between electroencephalography and magnetic resonance spectroscopy: a case–control study. *Italian journal of pediatrics*, *41*(1), pp.1-7.

Multi-voxel magnetic resonance spectroscopy at 3T in patients with idiopathic generalised epilepsy

M.T. Doelken [a], A. Mennecke [a], A. Stadlbauer [c], L. Kecskeméti [a b], B.S. Kasper [b], T. Struffert [a], A. Doerfler [a], H. Stefan [b], Thilo Hammen [a]

[a] Department of Neuroradiology, University of Erlangen-Nuremberg, Schwabachanlage 6, 91054 Erlangen, Germany

1) generalised tonic–clonic seizures (GTCS) patients versus healthy controls have significant decrease of NAA in the cortex of the central region and Cingulum and the thalami.
2) Glx was elevated broadly in both hemispheres, in particular in central region, cingulum, insular cortex and left putamen.

Conclusion:

1) In patients with >2 tonic–clonic seizures in the last 12 months a trend towards higher Glx and lower NAA levels was observed.
2) altered metabolism of basal ganglia-central regions in patients with GTCS, in particular the major role of relay in seizure generation.

Overview of in-vivo imaging biomarkers for epilepsy

Imaging Modality	Epilepsy Models	Potential Biomarker
T1, T2-weighted MRI	Post-SE, kindling, LFPI-TBI	T2-weighted signal hyperintensity for edema, gliosis, cell loss, BBB impairment
Contrast-enhanced MRI	Post-SE	Gadolinium, iron oxide, and magnesium enhanced signal change for mossy fiber, BBB breakdown, CBV and CBF changes
Diffusion MRI	Post-SE, kindling, LFPI-TBI	Changes in FA, perfusion, and diffusion for edema, axonal injury, and connectivity changes
Functional MRI	Post-SE, kindling, LFPI-TBI	Changes in BOLD signal for alterations in brain network connectivity and activity
MRS	Post-SE, kindling	Changes in NAA, mIns, GABA-A, glutamate, and glutamine, and glutathione for neuronal death and dysfunction
PET-FDG	Post-SE, kindling, LFPI-TBI, SRS	Changes in glucose metabolism for brain activation, metabolic alterations, and neuronal loss
PET-TSPO	Post-SE, SRS	Changes in TSPO for neuroinflammation
PET Radiotracers	Post-SE, kindling, SRS	PET radiotracers for neurotransmitter density, drug resistance, and BBB integrity

SE, status epilepticus; TBI, traumatic brain injury; LFPI, lateral fluid-percussion injury; FA, fatty acid; SRS, spontaneous recurrent seizures; FDG, fluorodeoxyglucose; TSPO, 18-kDa translocator protein.