# Lecture #16
# Clinical $^{1}$H Spectroscopy

- Neurospectroscopy in clinical practice and research
- Body applications
- References
  - P. Barker, et al., Clinical MR Spectroscopy Techniques and Applications, Cambridge University Press, 2009, Online ISBN: 9780511770647.
  - C. Stagg and D. Rothman, Magnetic Resonance Spectroscopy: Tools for Neuroscience Research and Emerging Clinical Applications, Academic Press, 20013, ISBN-13: 978-0124016880.

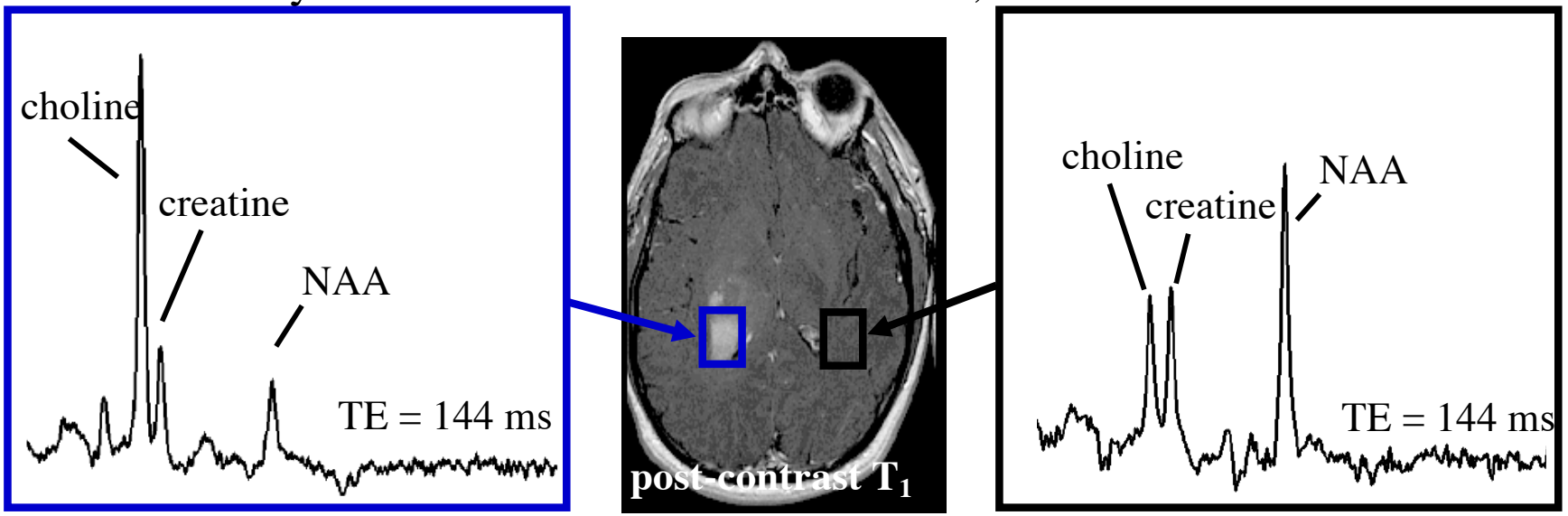
# Brain Tumors – Key Points*

- Multimodal imaging providing improved diagnostic and prognostic accuracy, fundamental in disease monitoring and assessing response to therapy.
- $^{1}$H-MRSI provides a valuable clinical tool depicting metabolic changes reflective of cellular density, anaplasia, and mitotic index.
- Cho is elevated in all tumor types due to altered membrane metabolism, and shows correlation with cellular density and indices of cell proliferation. NAA decreases with tumor infiltration and substitution of normal neural and glial cells. The Cho/NAA ratio is a useful parameter particularly in most primary brain tumors, with a higher ratio correlating with higher cell density and generally associated with a poor prognosis.
- While $^{1}$H-MRS can show different metabolic patterns in different tumor types, it is not used as a primary diagnostic tool.
- Increasing Cho/NAA and Cho/Cr ratios in serial exams of a primary astrocytoma are suggestive of transformation to a higher grade and can be useful in monitoring disease progression or response to therapy.
- $^{1}$H-MRSI may provide guidance for targeted biopsy, surgery, or therapy.

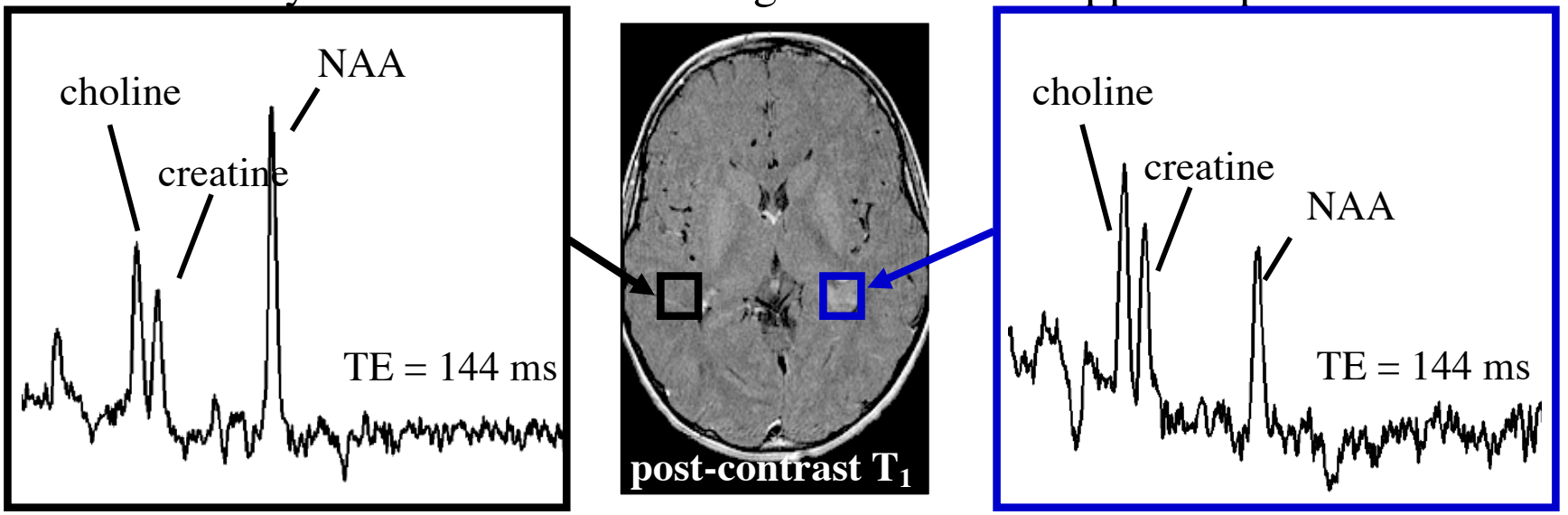
*Barker, et al.

# Tumor vs non-Tumor

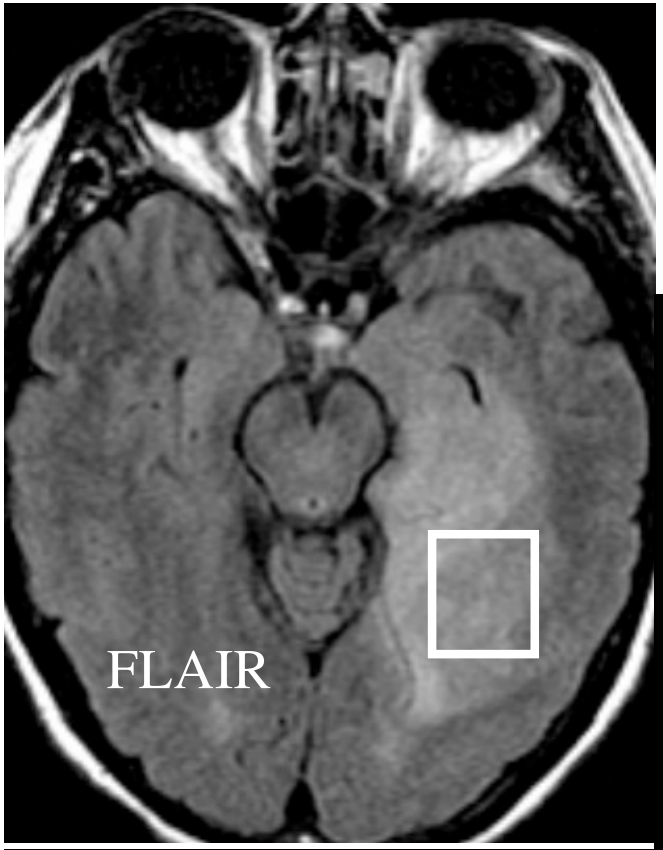
52 y.o male: MRI #1 - rule out stroke, MRI #2 - tumor?

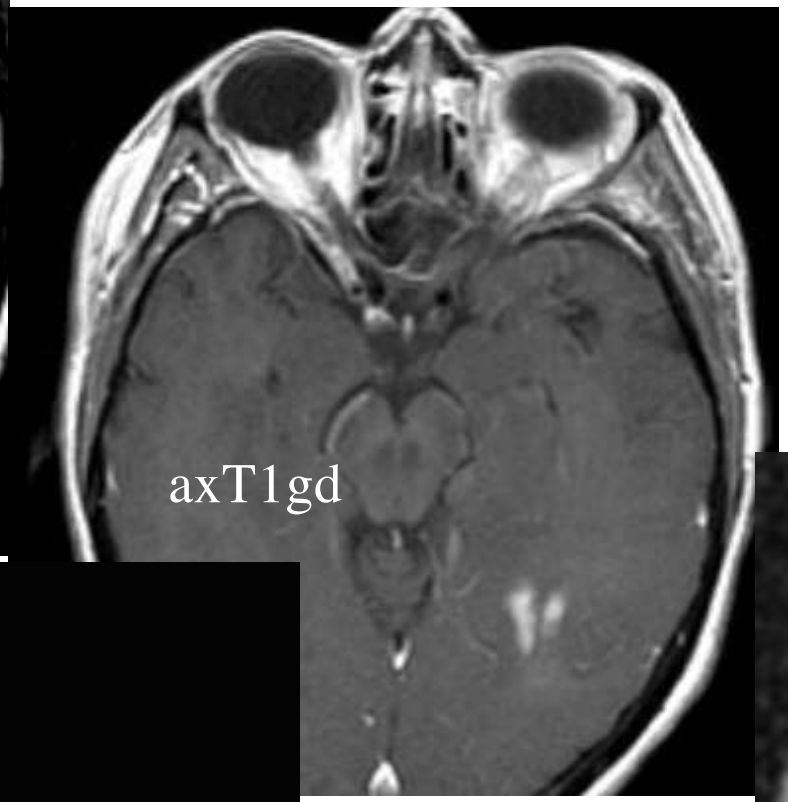


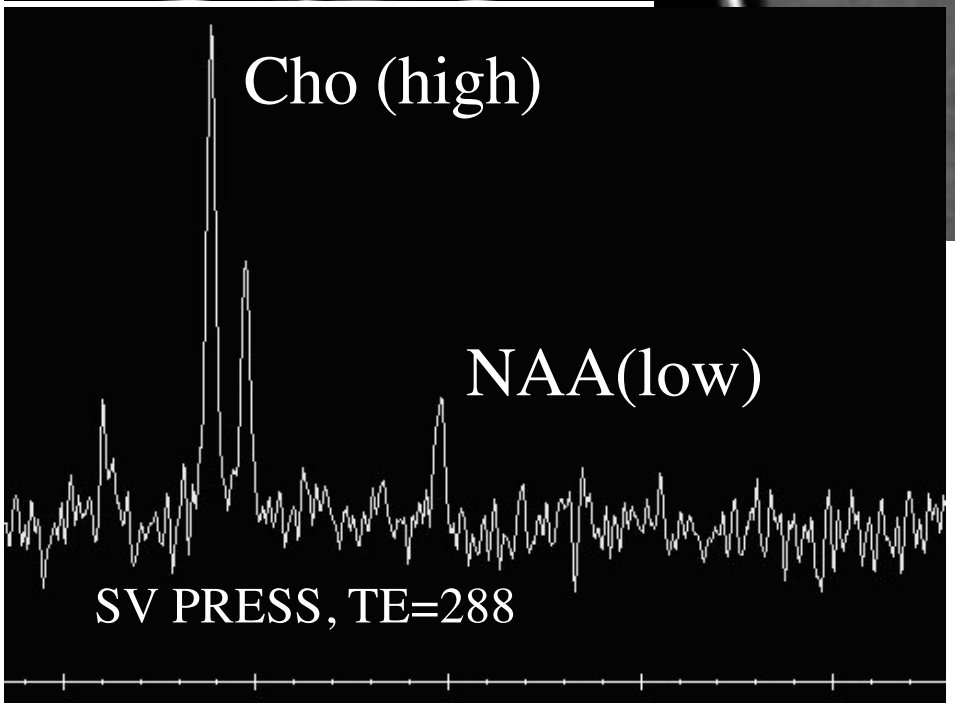

9 y.o male: non-enhancing lesion in left hippocampus



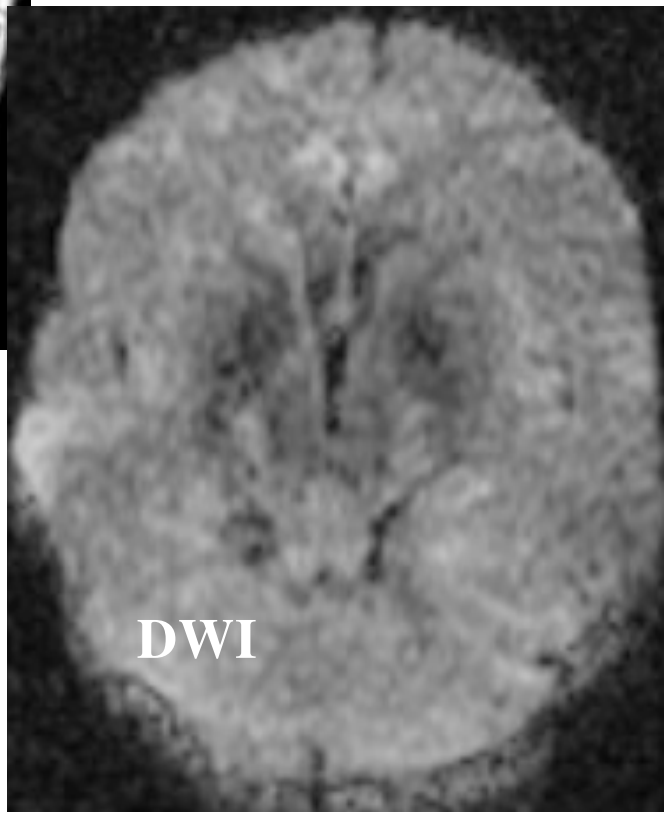
**68 F who reports fairly abrupt onset of a visual field defect. Pt is referred for MR to r/o PCA stroke**

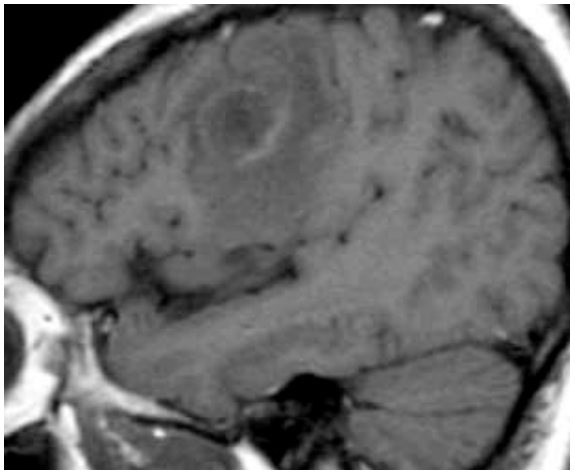


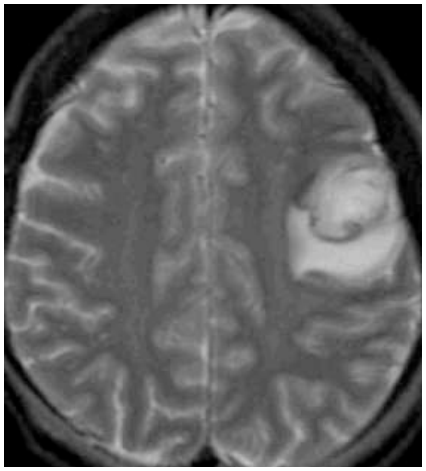



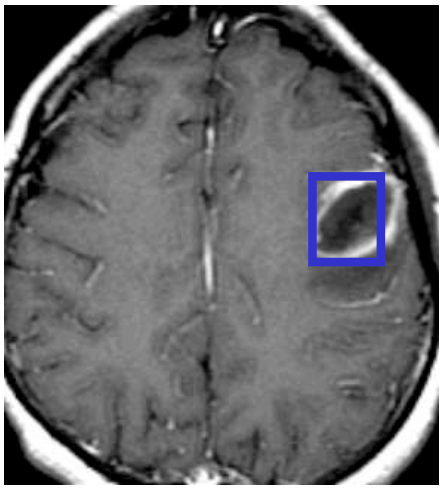

**Dx=GBM**

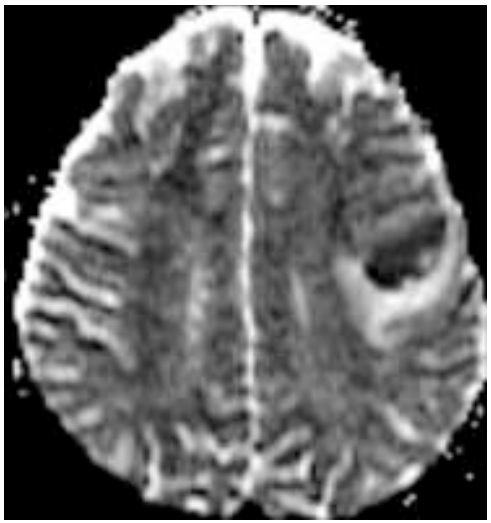


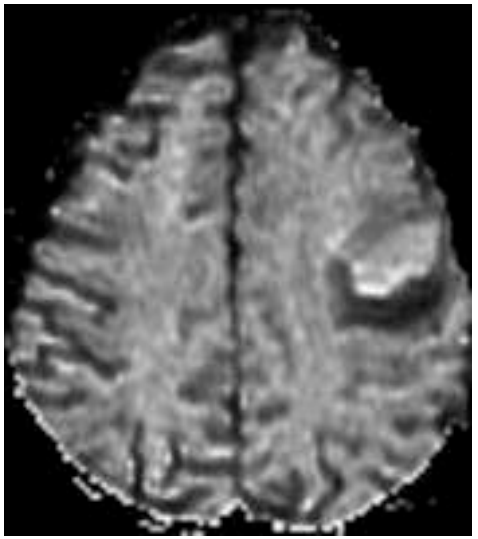


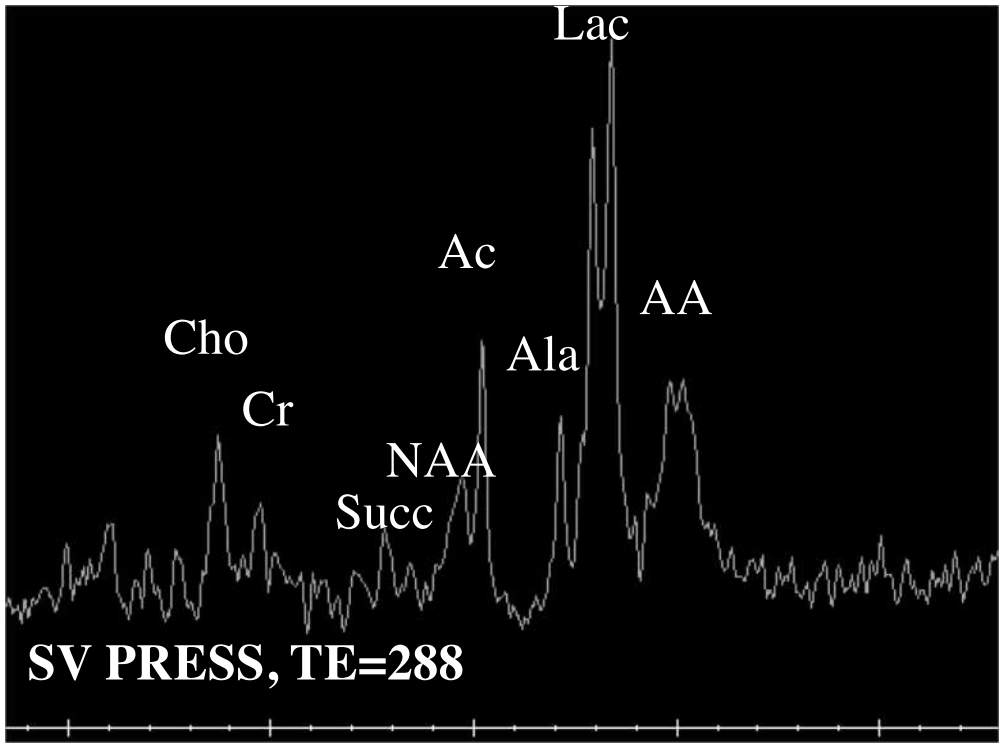
**44 F with acute onset aphasia, clinical ddx includes demyelination, abscess, glioma and met**





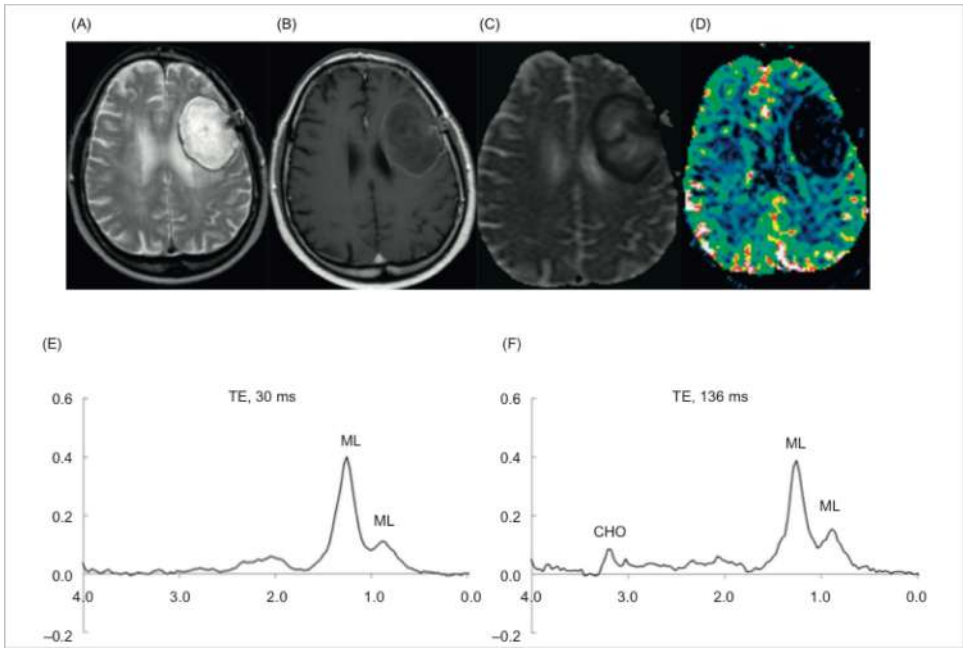


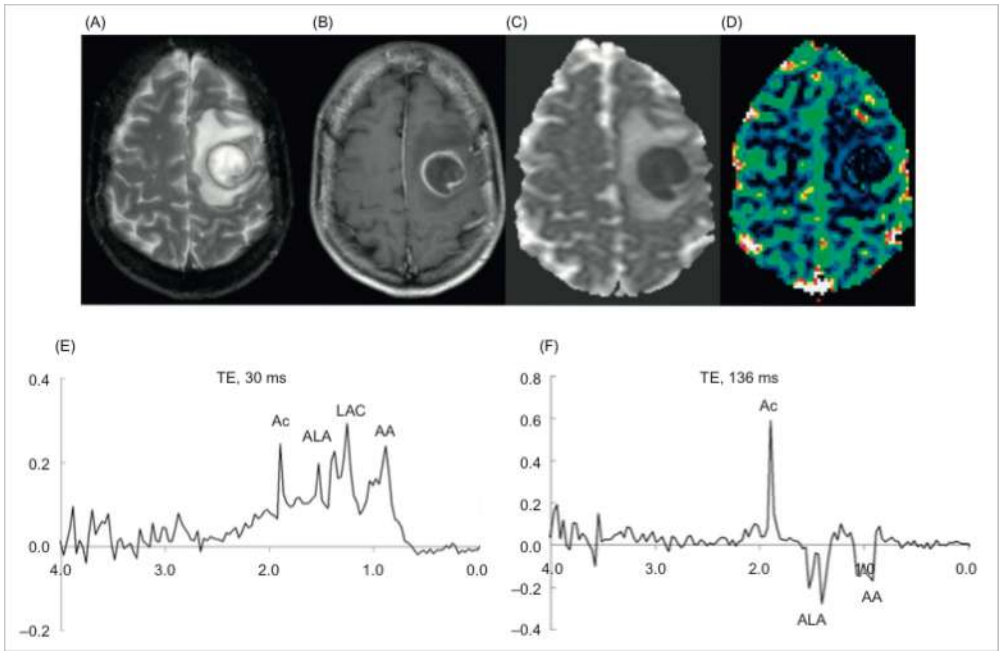





**Dx: *Strep viridans* abscess**

# Diagnosis?



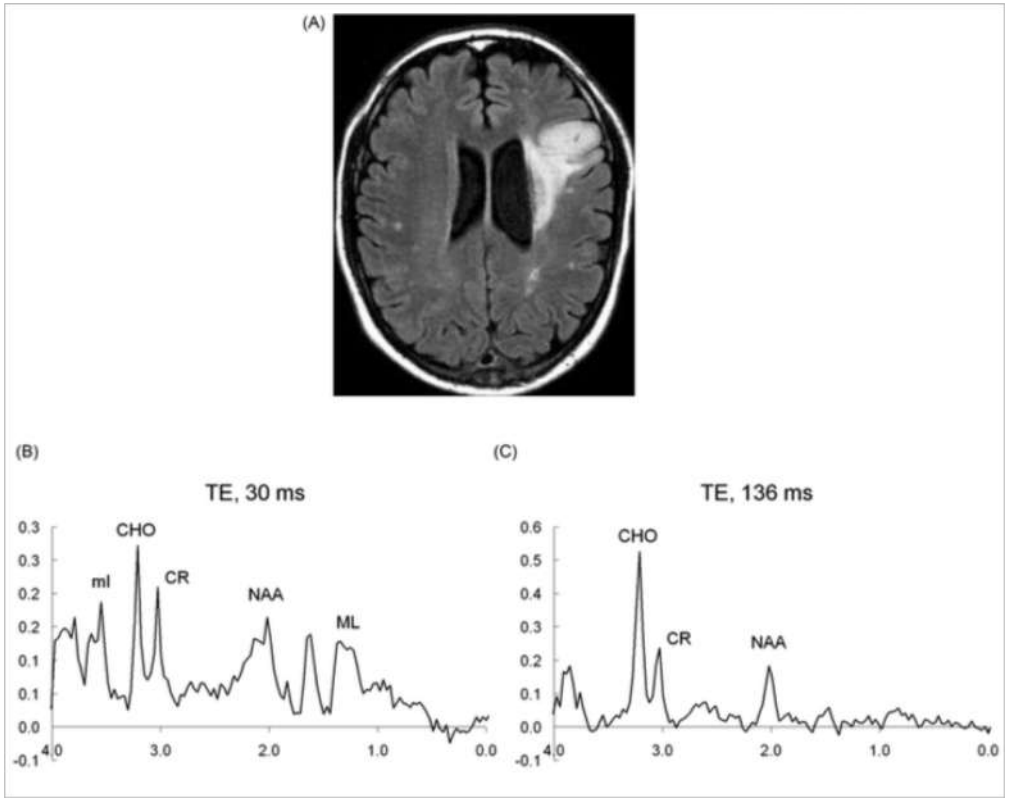




Necrotic mass

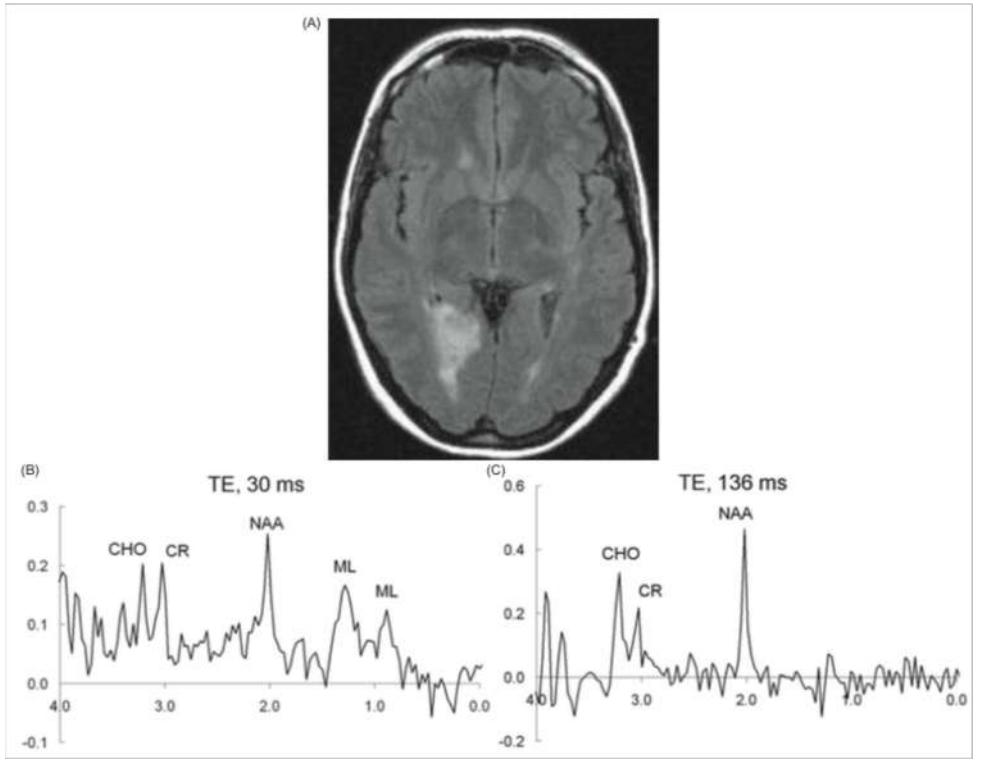
Abscess with bacterial metabolism

Stagg and Rothman

# Tumor vs non-Tumor



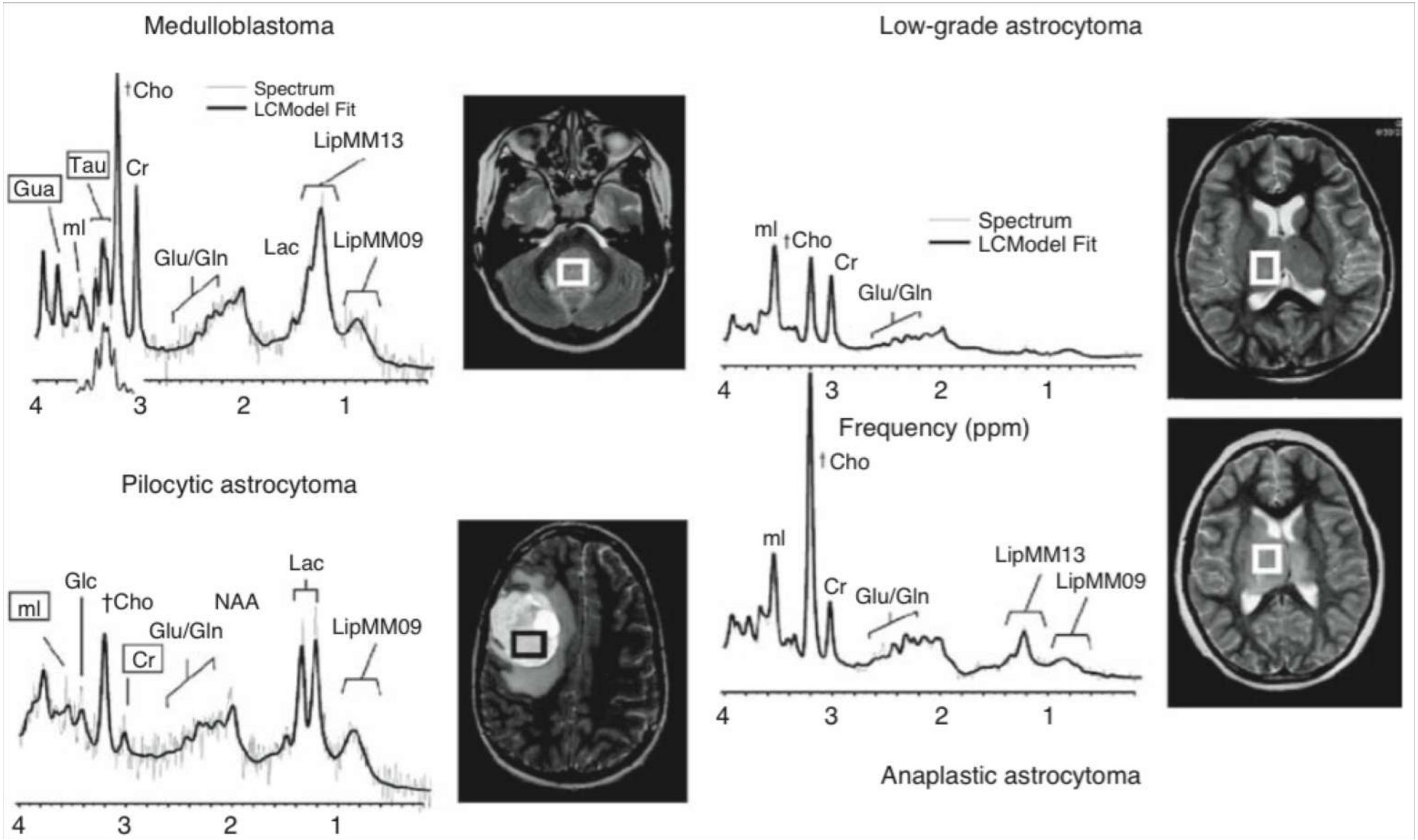

Diagnosis: olioastrocytoma grade II




Multiple sclerosis diagnosed at follow-up

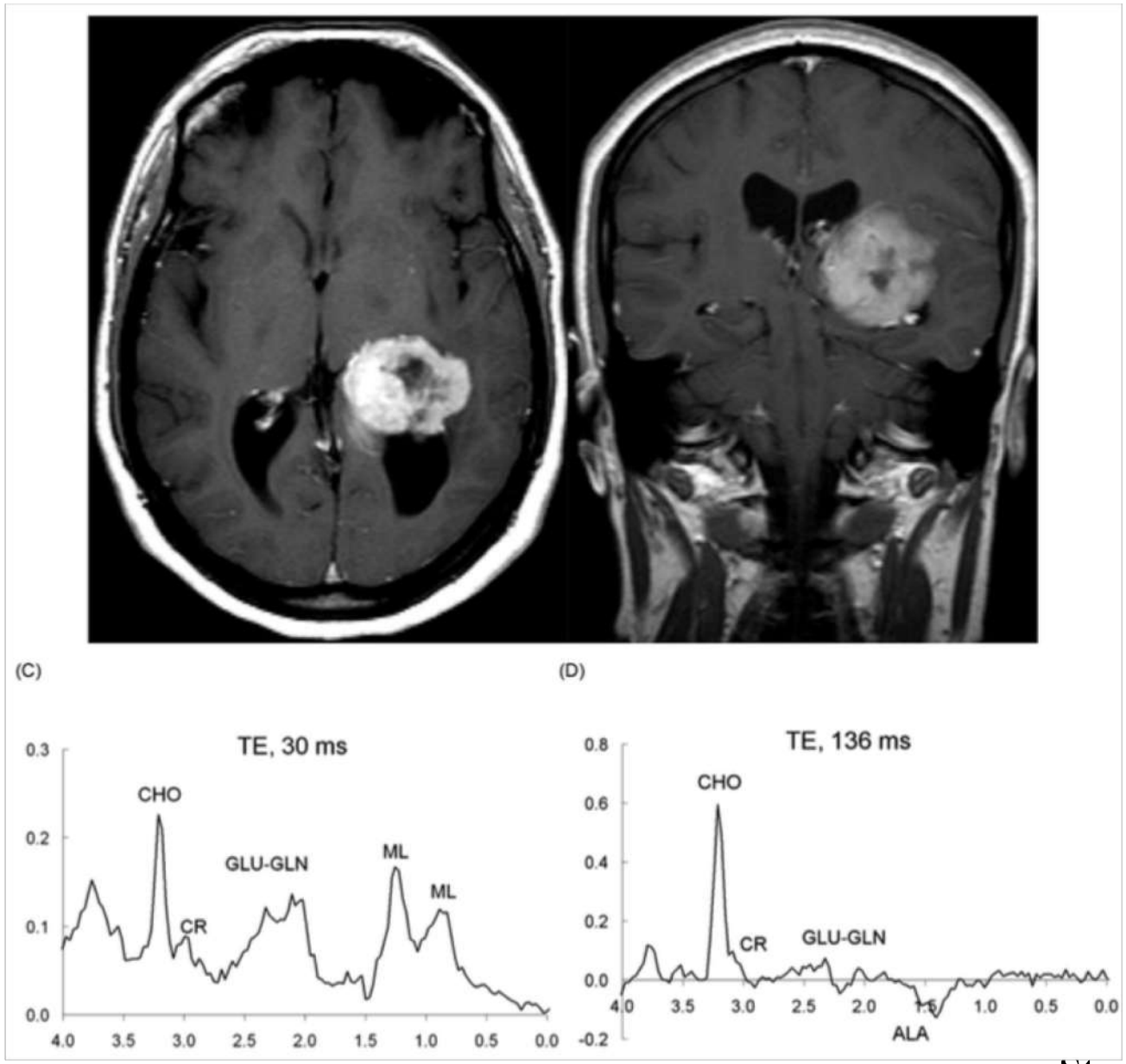
Stagg and Rothman

# Pediatric Brain Tumors



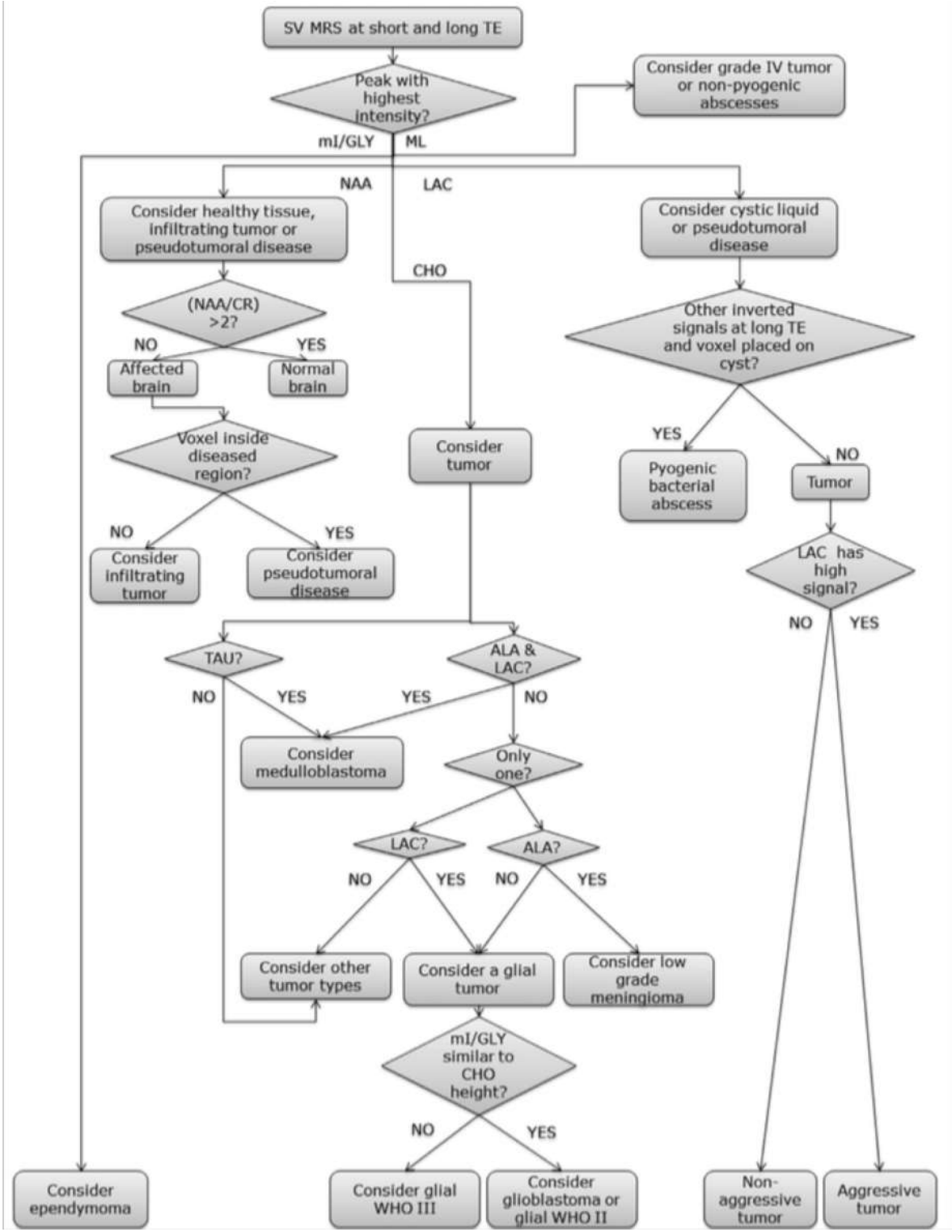

Barker, et al.

# Meningioma




Stagg and Rothman

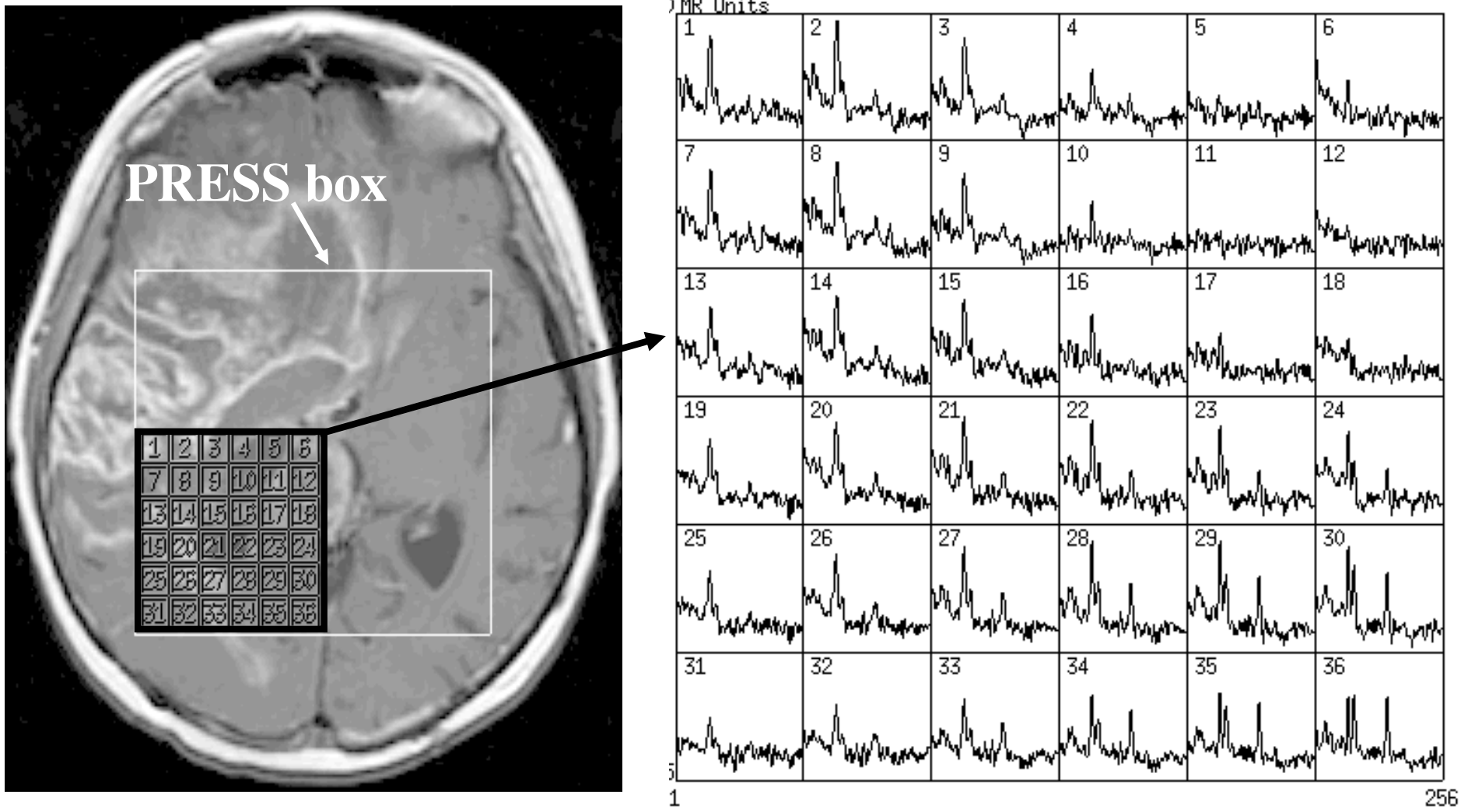
# $^{1}$H MRS brain tumor flow chart



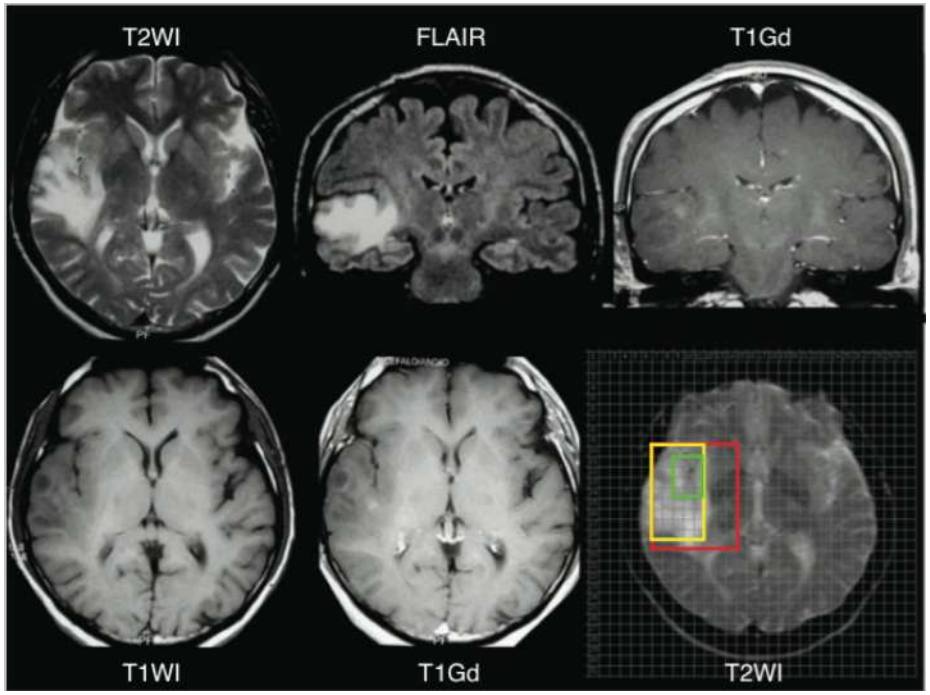

Stagg and Rothman

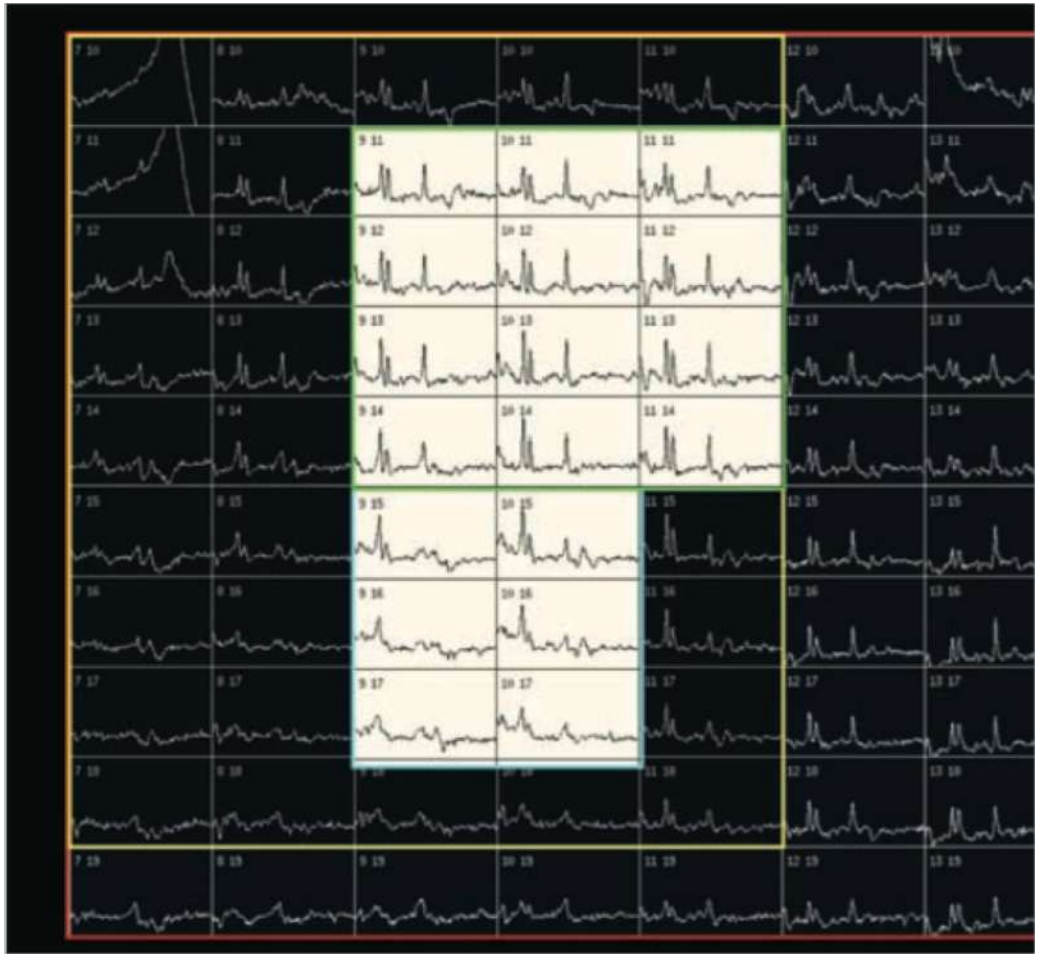
# PRESS $^{1}$H MRSI

Typical clinical parameters: TR/TE=1500/144 ms, 16x16 matrix, 1.5 cm slice, 24 cm FOV, 3.4 cc voxels, 6-8 min acquisition, 3T.



# Metabolic and histopathologic heterogeneity in low-grade astrocytoma

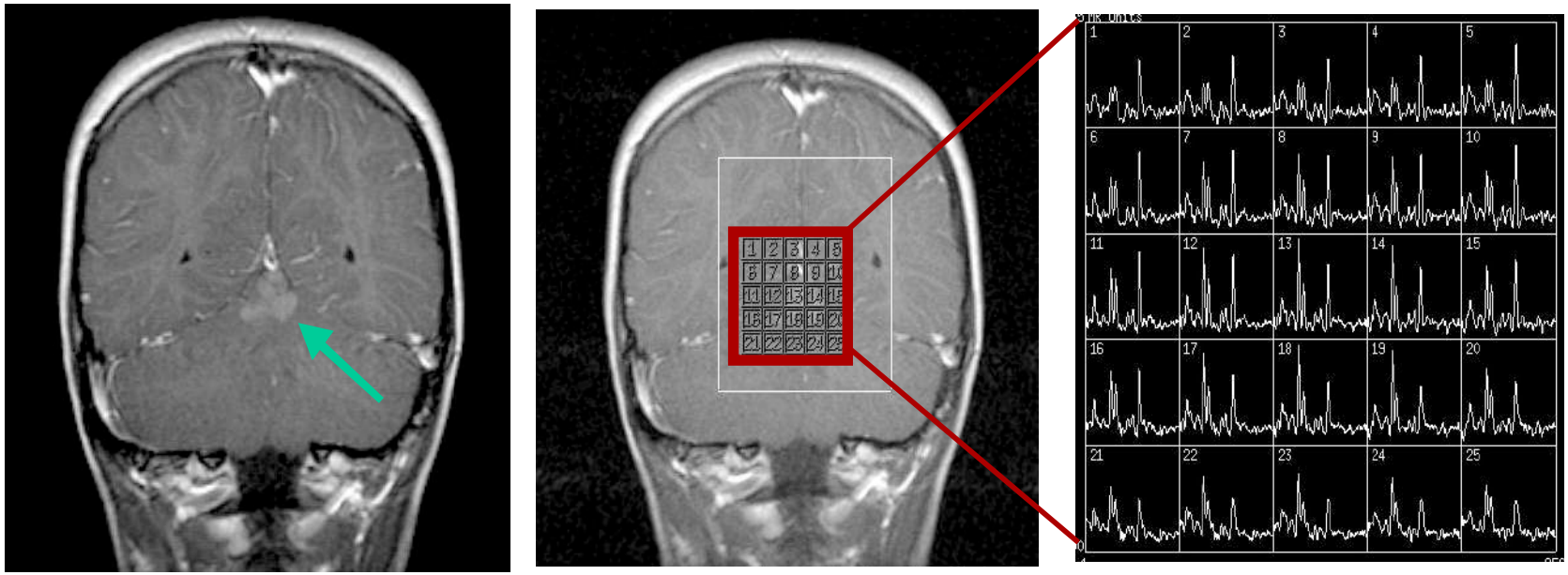


MRSI (PRESS: TR/TE = 1200/ 135 ms; 24 × 24 matrix; FOV = 200 × 200 × 15 mm3)

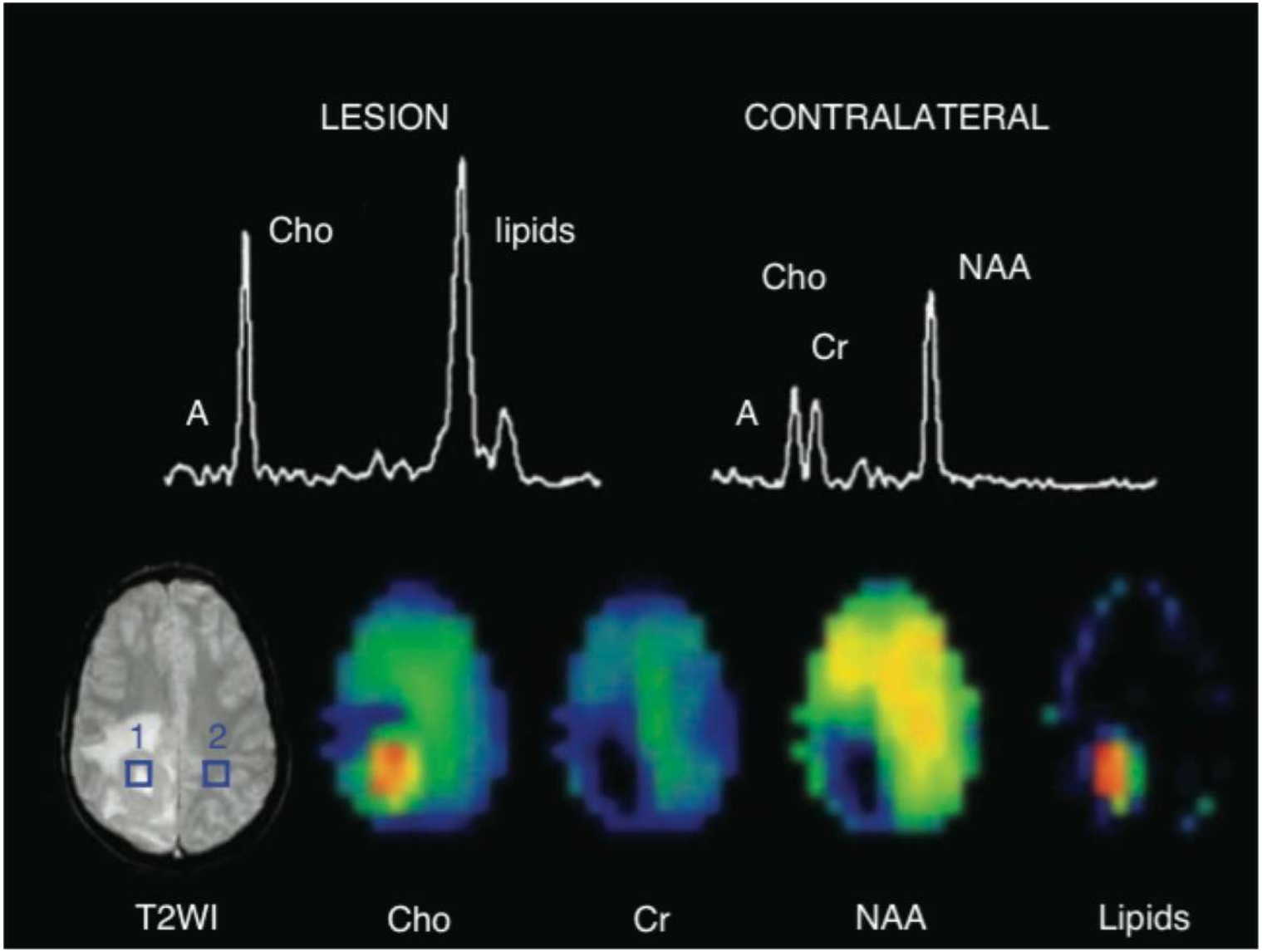
Stagg and Rothman

# Pediatric brain lesion




MRSI used for early diagnosis of 7 year old with small asymptomatic tumor (medulloblastoma). Note, very high choline in lesion.

# Lymphoma

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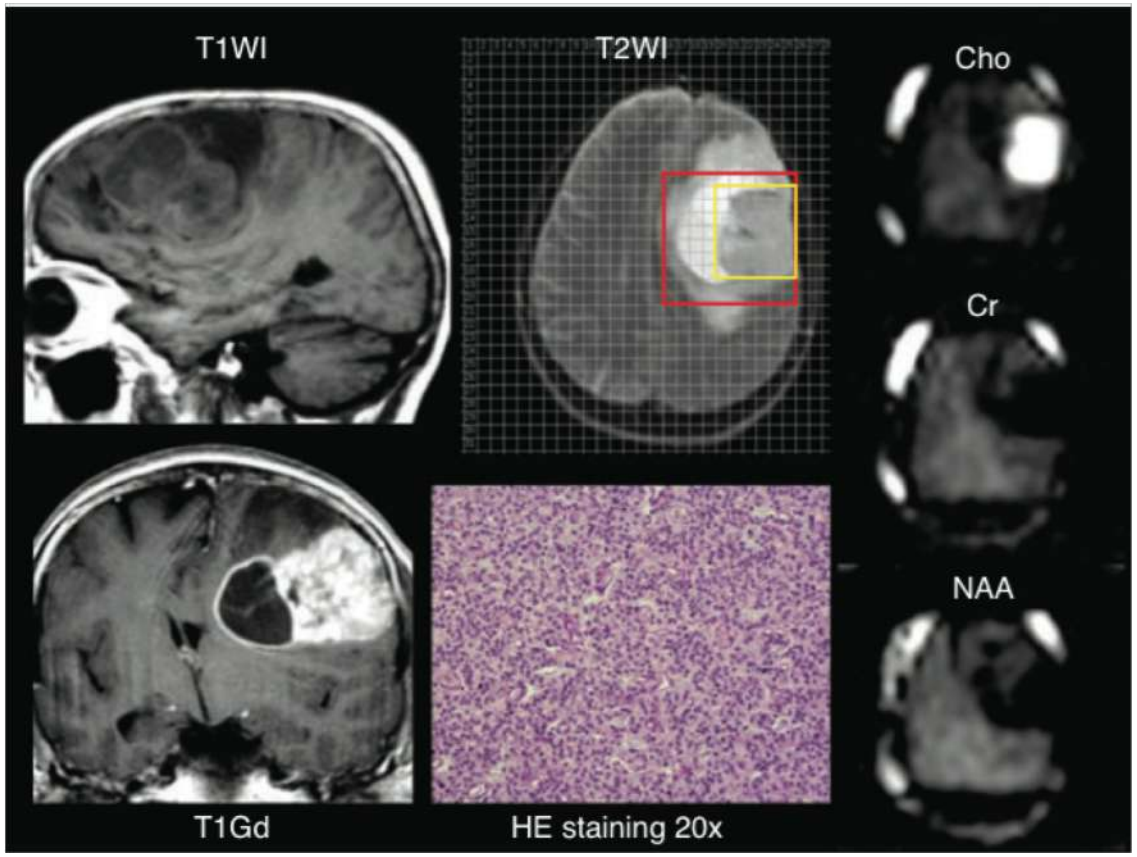
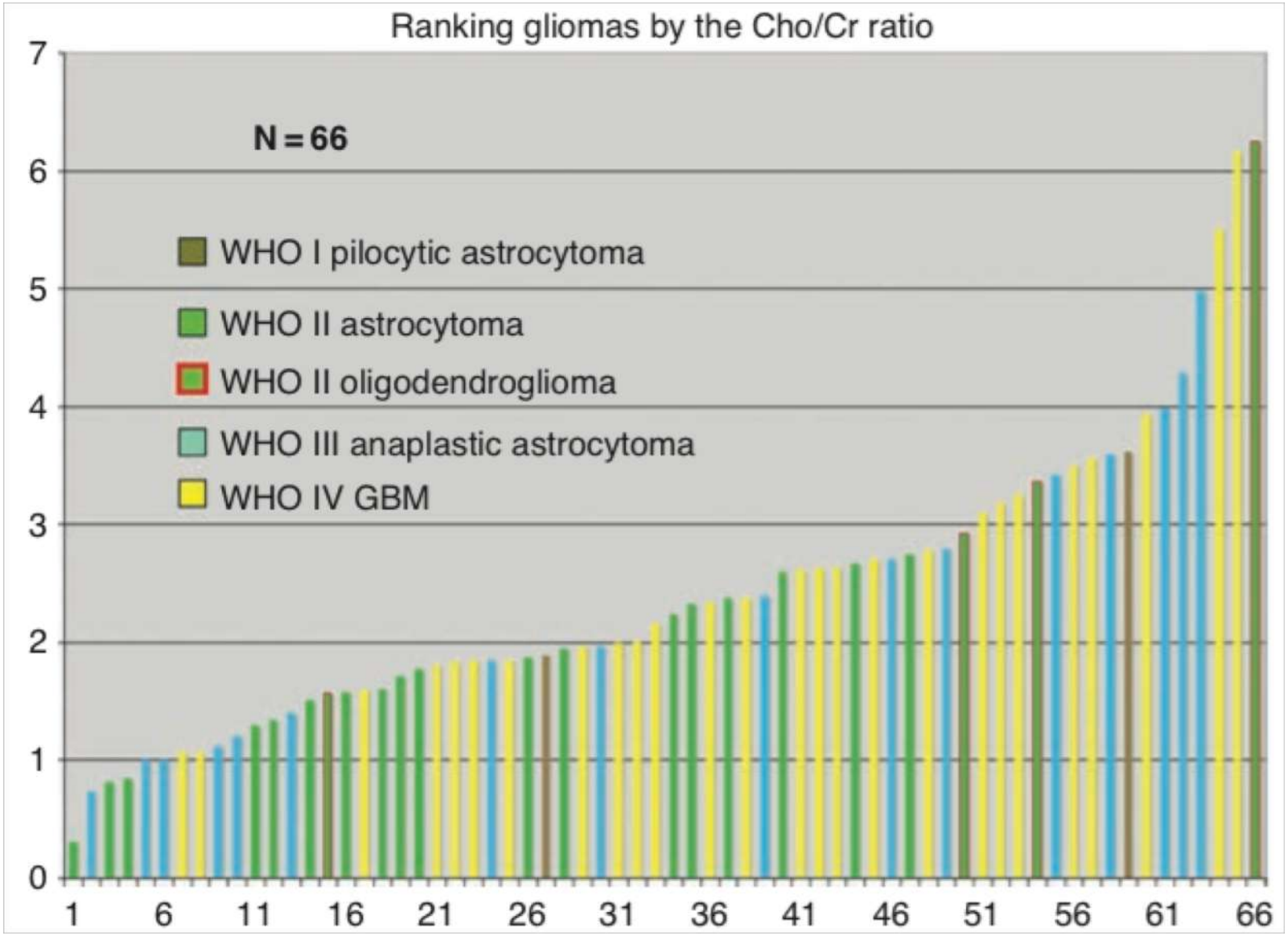
# High choline in an oligodendroglioma




Surprisingly at histopathology the diagnosis of low-grade oligodendroglioma was made. The very high Cho signal is likely related to the very high cellular density that was demonstrated on the HE-stained histologic slide. The rate of mitosis and anaplasia was very low in this oligodendroglioma.

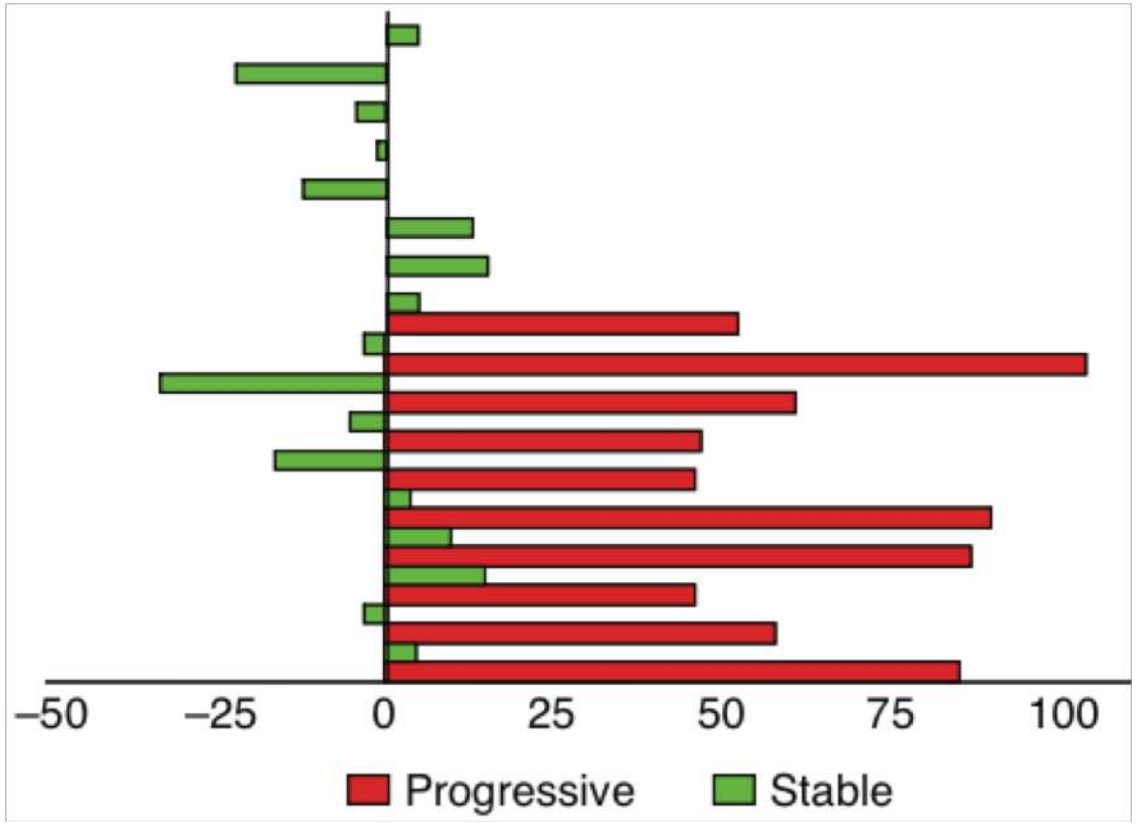
Barker et al.

# Tumor Grading




Barker, et al.

# Tumor Grading and Disease Progression

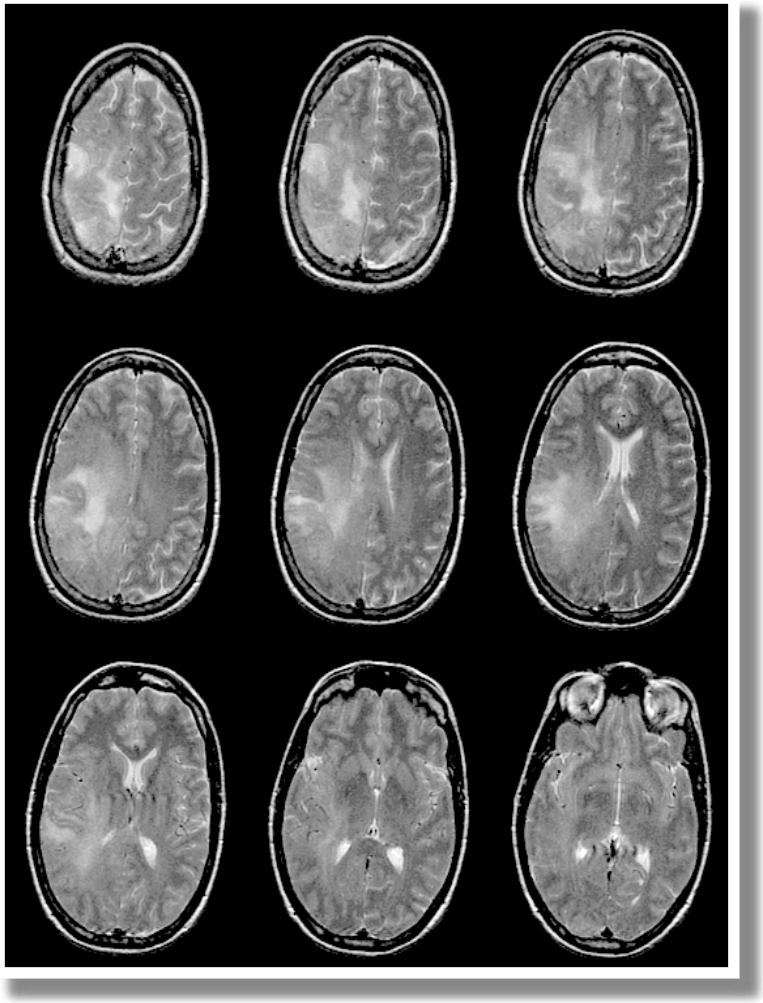



Choline changes between consecutive studies in progressive (**red**) versus stable (**green**) brain tumor patients

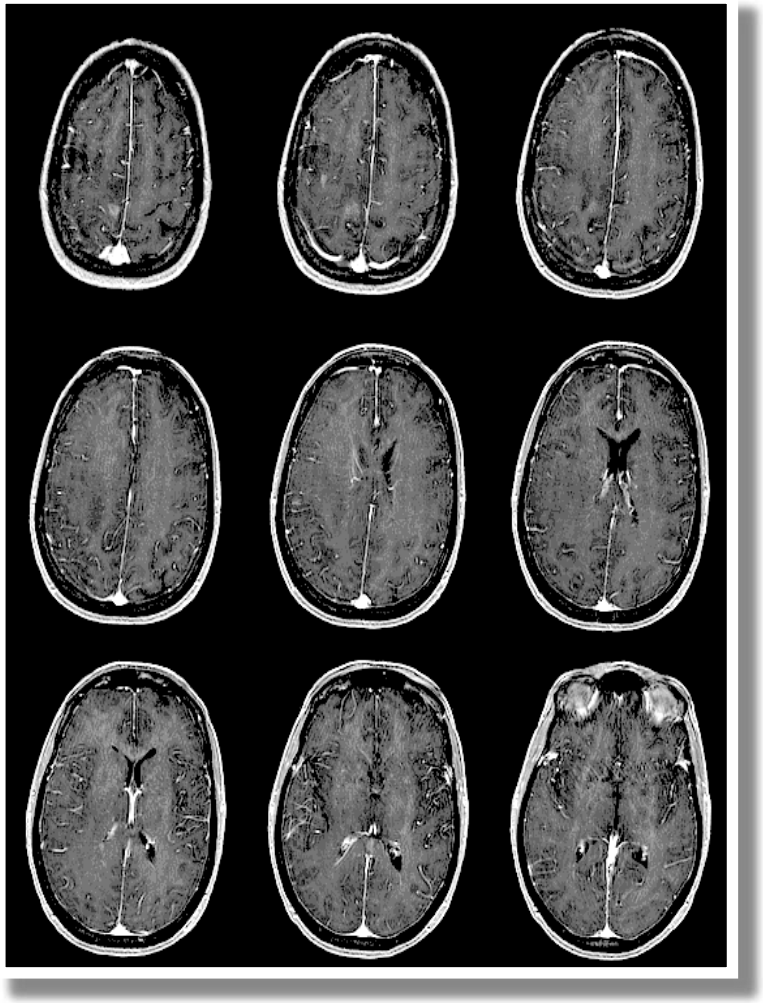
Stagg and Rothman

# MRS-Aided Biopsy

## 42 y.o. male with non-enhancing glioma



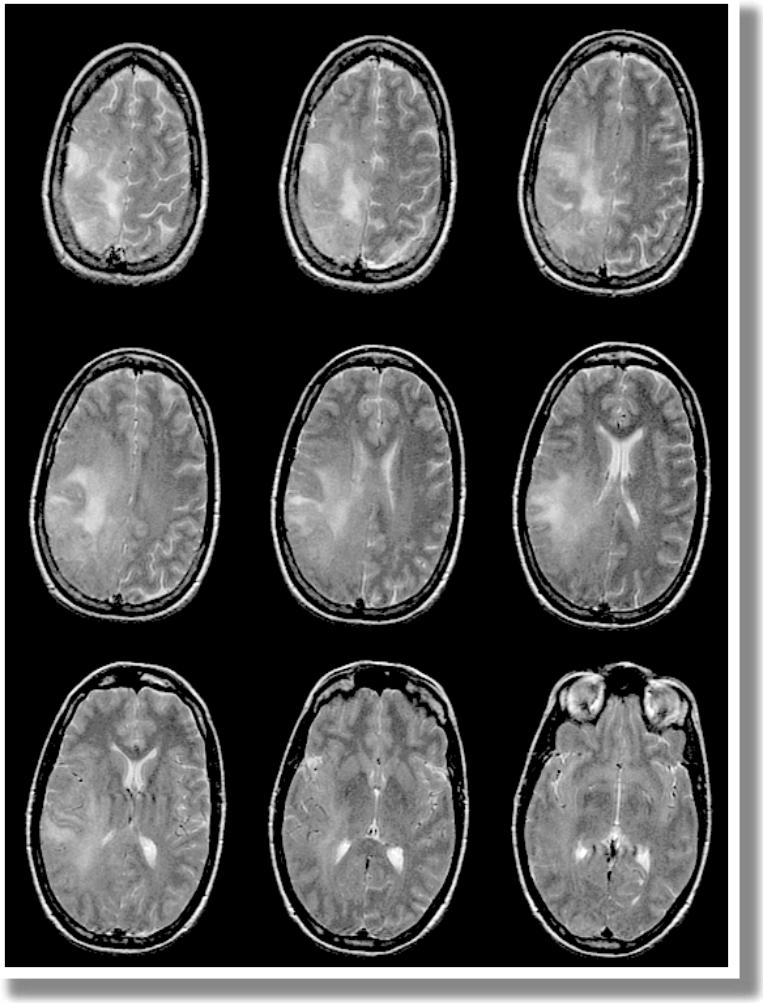
$T_2$-weighted FSE



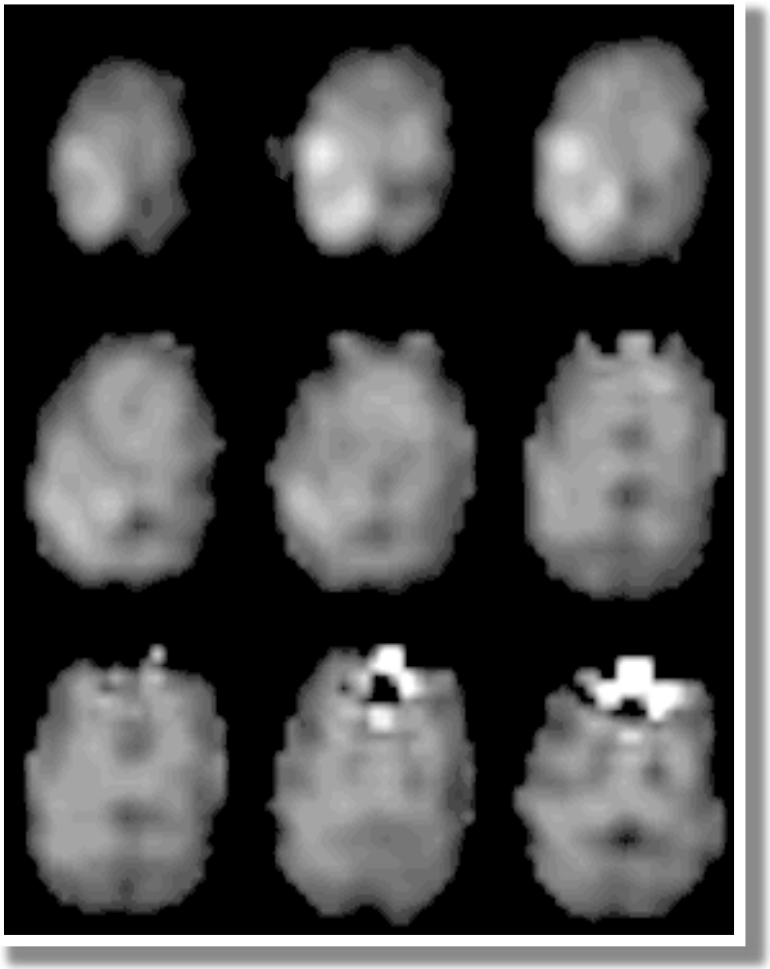
Post-contrast GRE

# MRS-Aided Biopsy

## 42 y.o. male with non-enhancing glioma

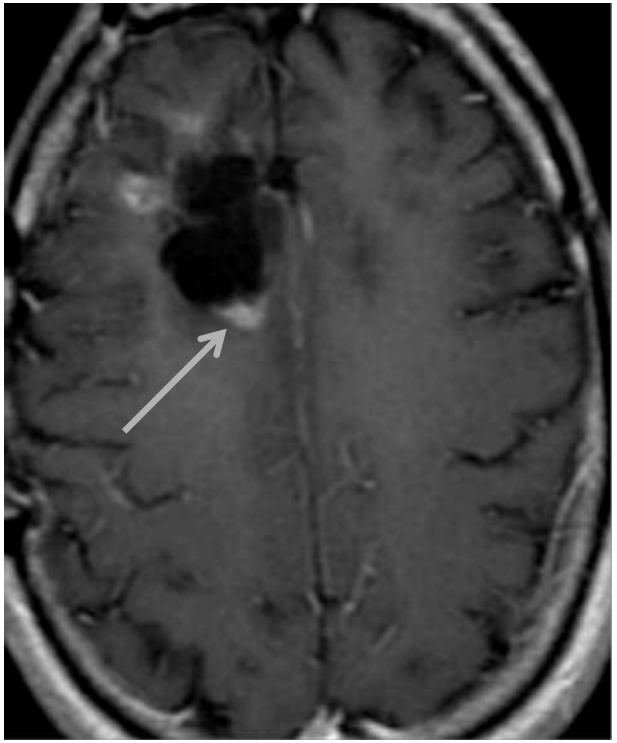


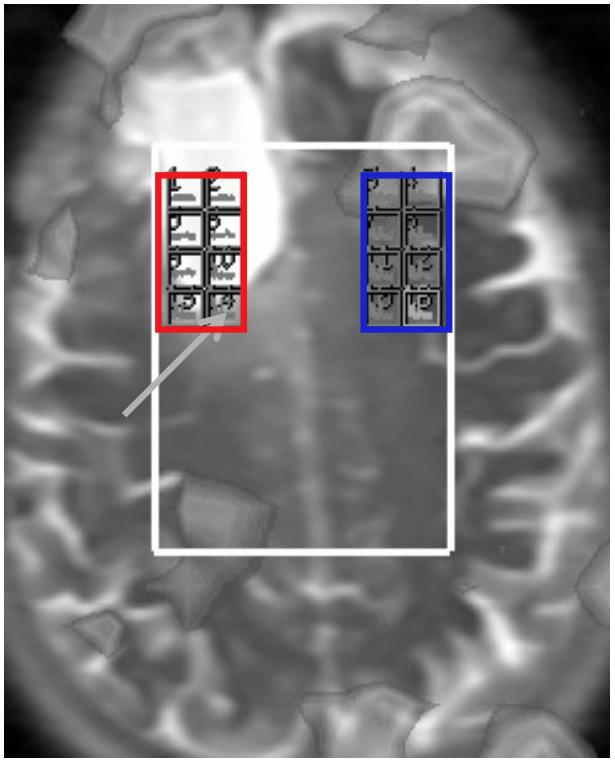
$T_2$-weighted FSE

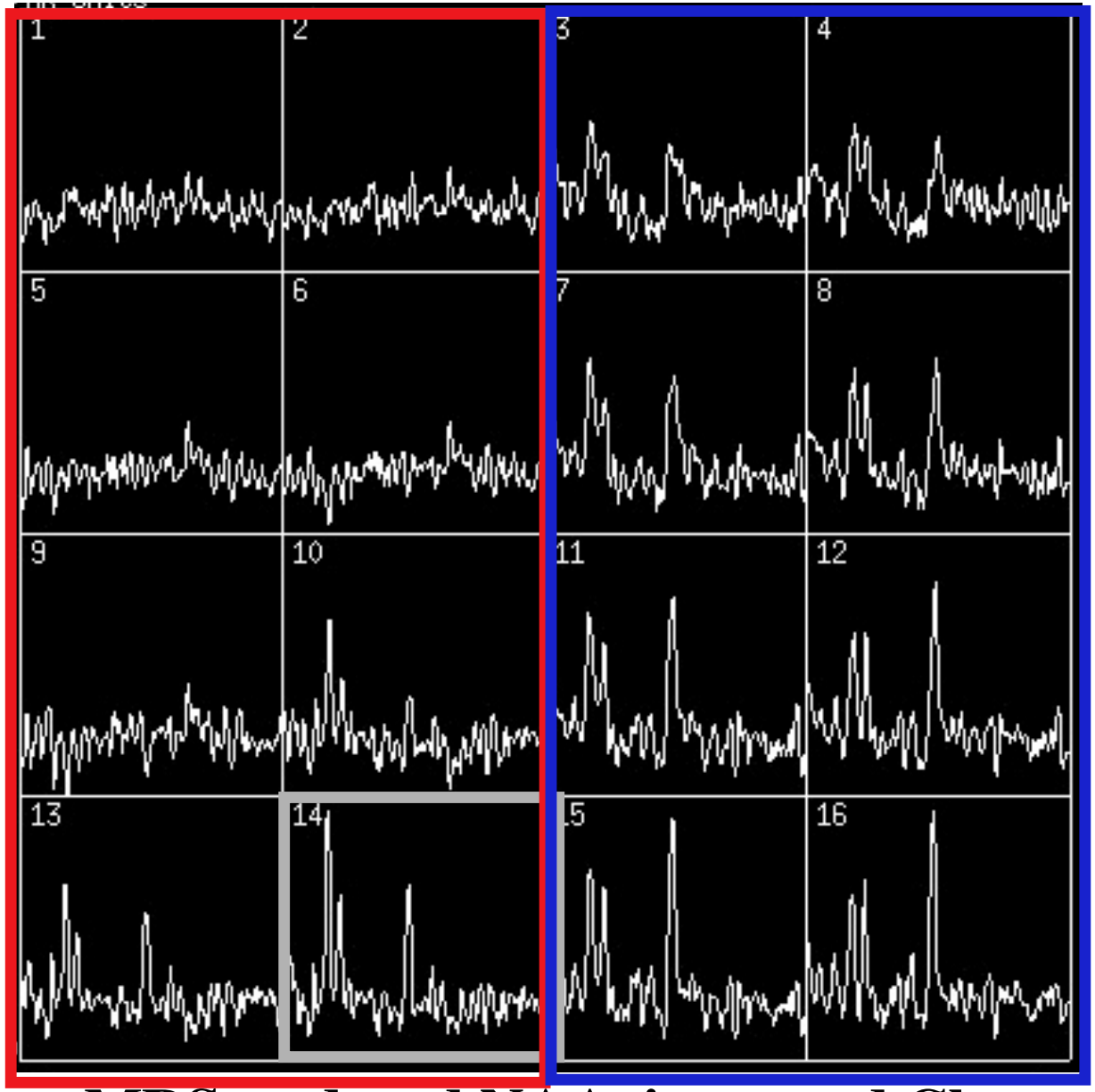


Choline

# 51 M s/p surgery and XRT for anasplastic astrocytoma, now with new area of enhancement

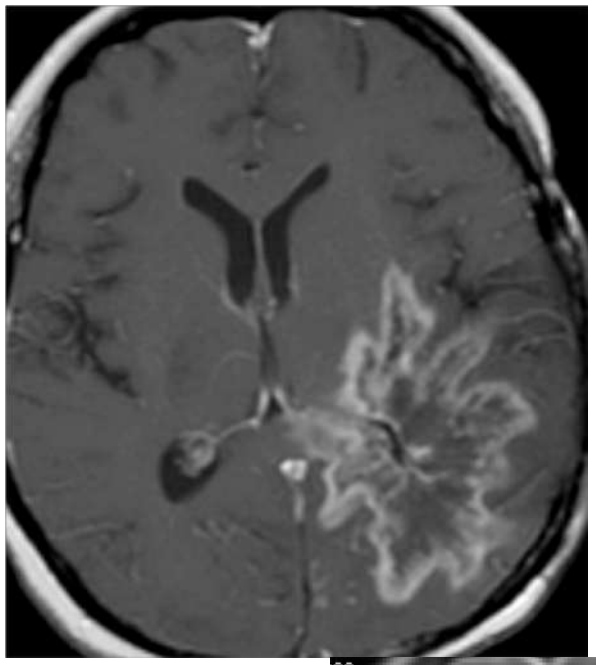


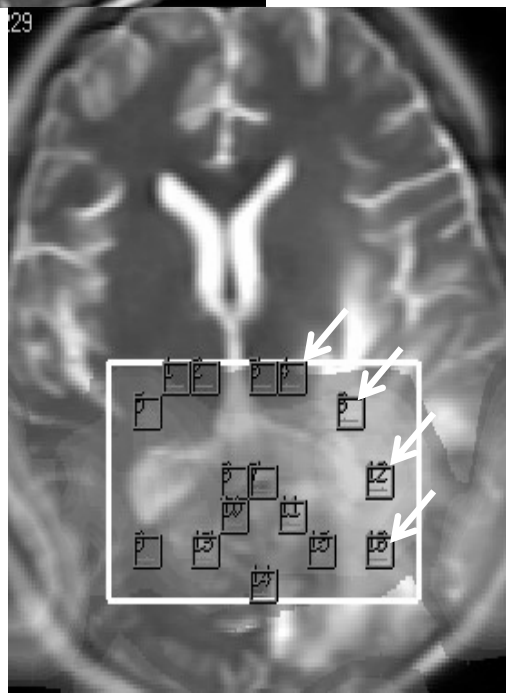


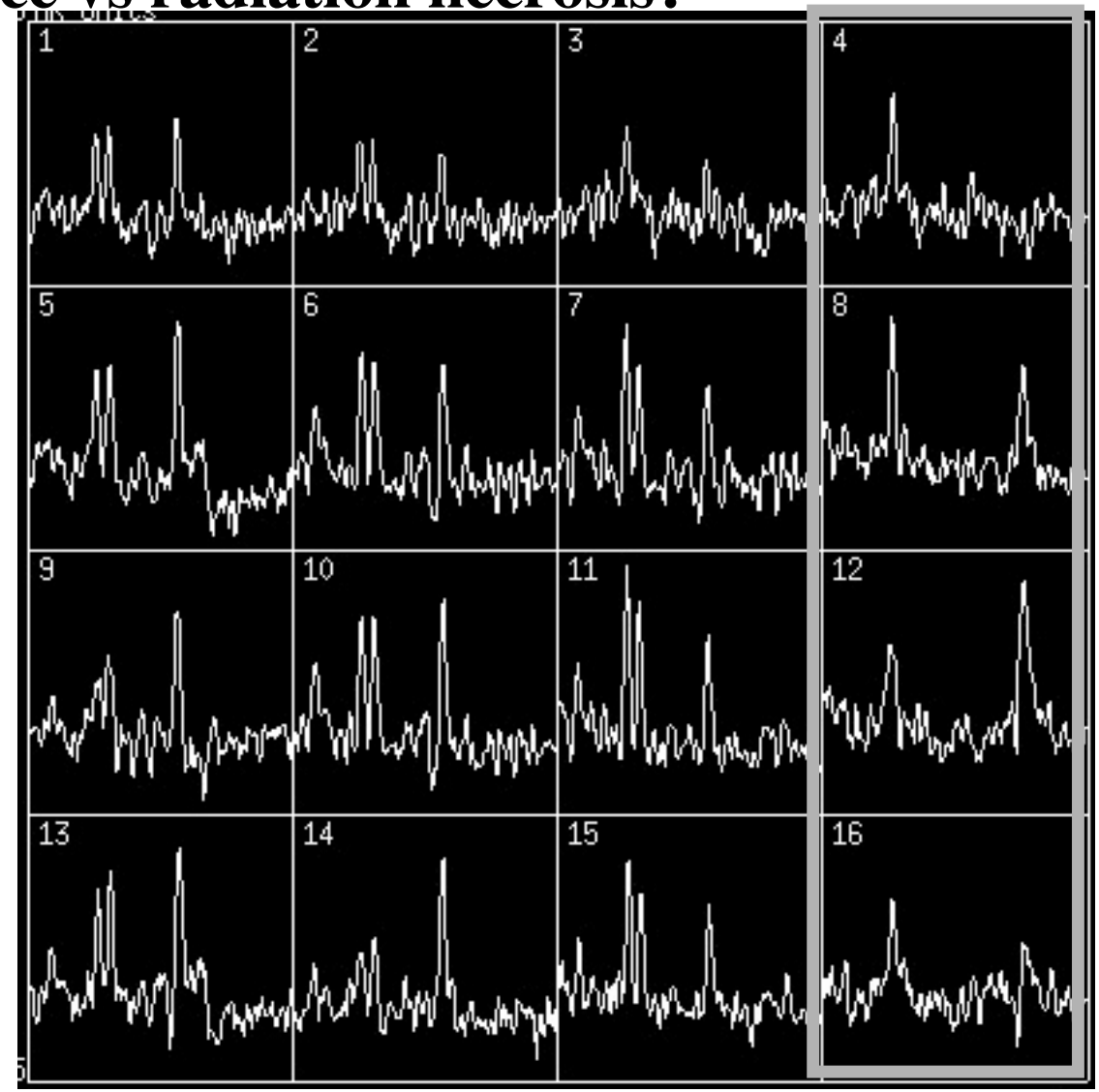



**MRS: reduced NAA, increased Cho c/w normal. Dx: tumor recurrence**

# 34 F previously rx'd with surgery and high dose XRT for GBM
# Tumor recurrence vs radiation necrosis?

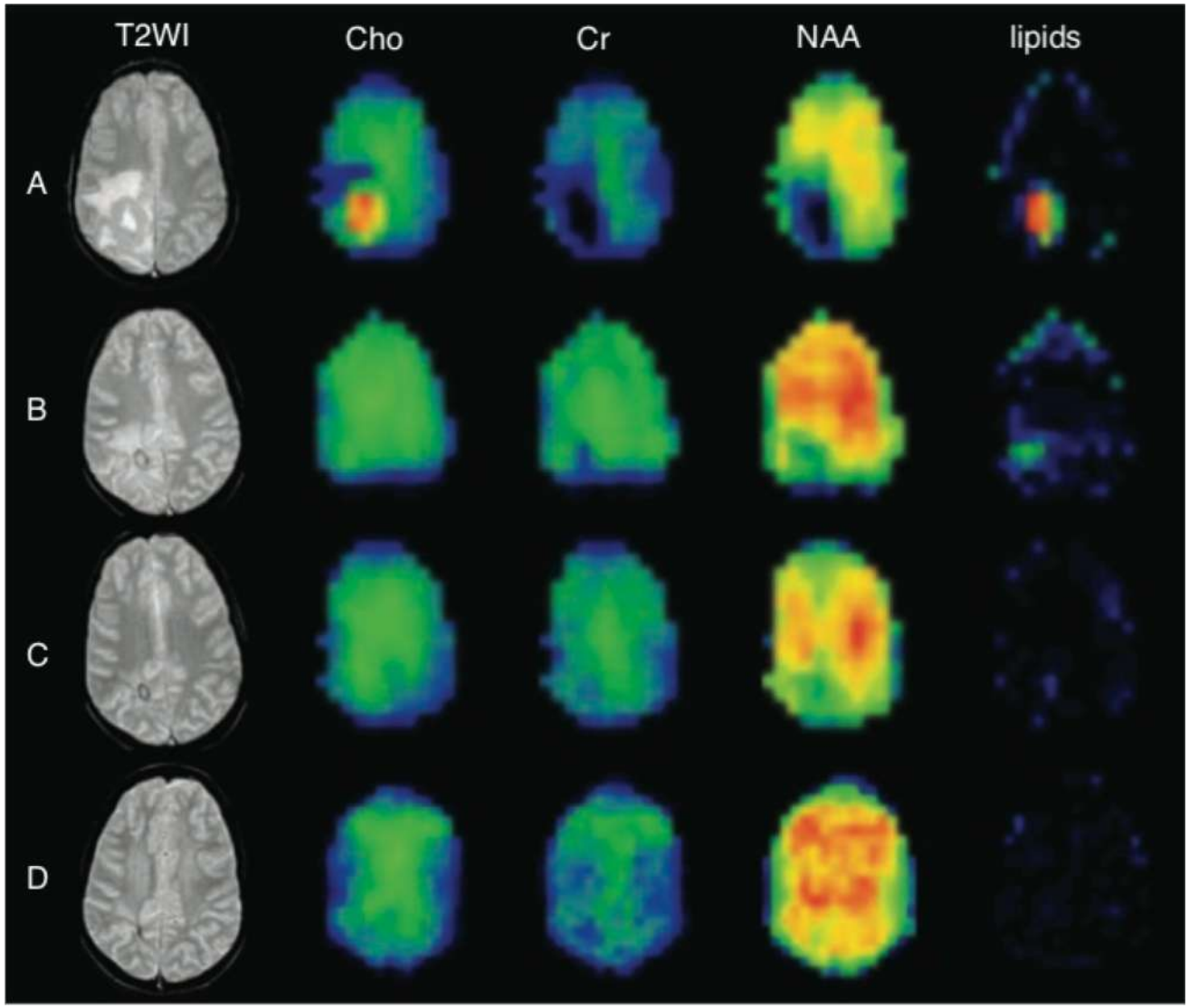







**Cho can transiently increase after XRT, but these findings are worrisome for tumor recurrence.**

# Response to therapy in lymphoma




$^{1}$H-MRSI maps of Cho, Cr, NAA, and lipids from a serial exams in a patient with non-Hodgkin lymphoma (A) before, (B) 17 days and (C) 28 days after initiation of radiation therapy, and (D) at 33-month follow-up.

Barker, et al.

# Metabolic Disorders - Key Points*

- MR spectroscopy is a valuable tool to direct biochemistry work-up of patients with inborn errors of metabolism, with MRSI the best method to study the heterogeneous anatomic distribution of metabolic diseases.
- The interpretation of MR spectra and MR images together increases diagnostic accuracy.
- Abnormal MR spectral peaks are diagnostic of a few hereditary metabolic disorders.
- Lactate is elevated in about half of patients with mitochondrial disorders, in most patients with leukoencephalopathies with demyelination or rarefaction of white matter, and in few with organic acidopathies targeting the subcortical gray matter nuclei.
- MRS may be useful to monitor response to therapy when available.

*Barker, et al.

# Succinate Dehydrogenase Deficiency

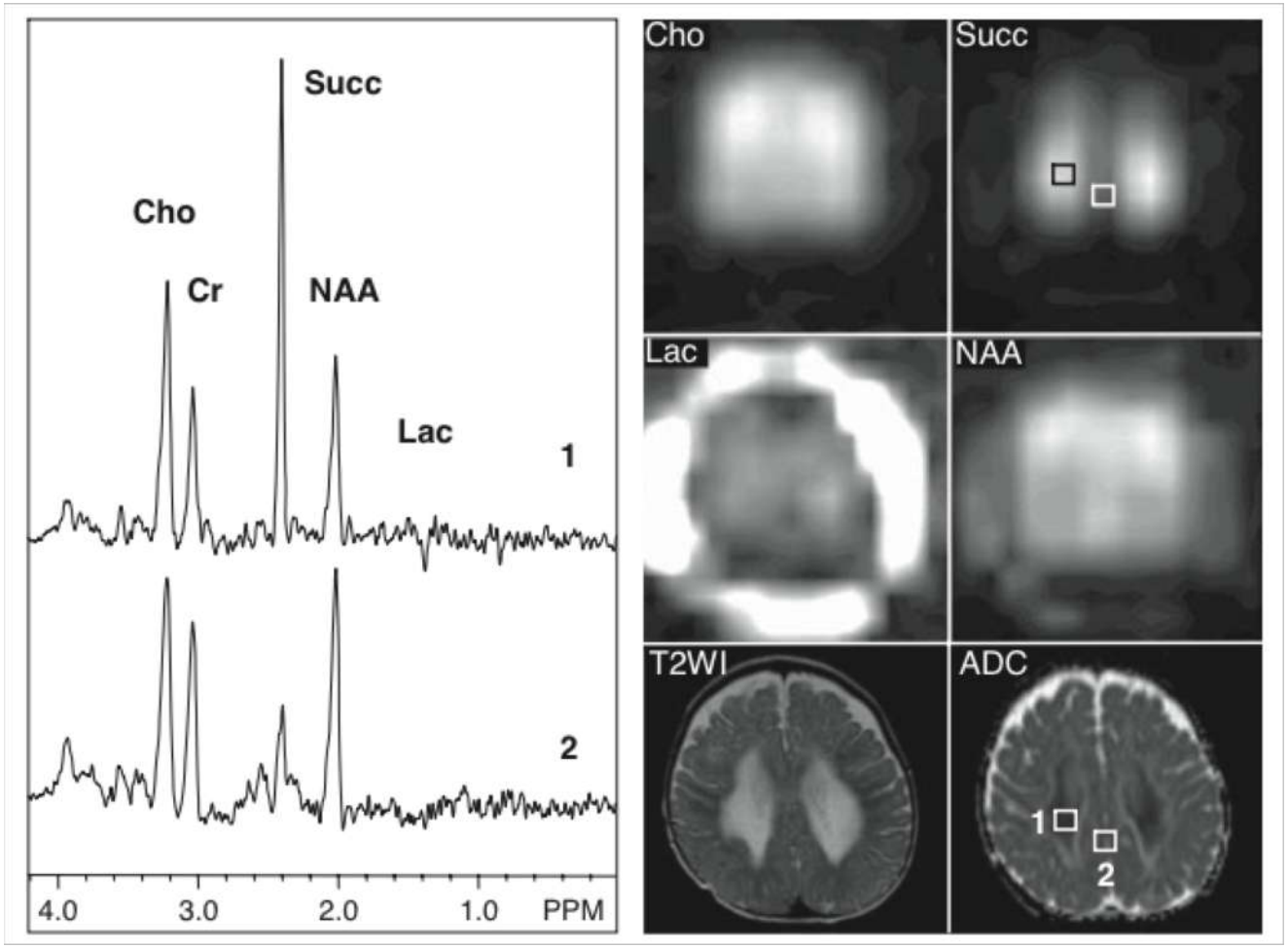



**Figure 11.2**. A 12-month-old boy with 3 month history of arrest of psychomotor development and tetraparesis. He was diagnosed with mitochondrial encephalopathy due to succinate dehydrogenase deficiency (SDH). MRSI (PRESS: TR/TE = 1200/135 ms; 24 × 24 matrix; FOV = 200 × 200 × 15 mm3) was acquired at the level of the centrum semiovale. Cho, succinate (Succ), lactate (Lac) and NAA maps with two selected spectra are illustrated.

The white matter spectrum from the right centrum semiovale (1) showed an abnormally elevated succinate peak at 2.42 ppm, associated with moderate NAA and mild Cr signal losses. Lactate was mildly elevated in white matter voxels. The gray matter spectrum from the adjacent parasagittal parietal cortex showed only minimal succinate accumulation and mild NAA signal loss. The Succ map elegantly demonstrates accumulation selectively in white matter, confirming that the metabolic defect targets white matter and spares gray matter. In the Lac map the bright signal around the brain arises from the lipid signal in the scalp.

On the $T_2$-weighted MR images at the level of the centrum semiovale, note the signal hyperintensity in the deep white matter with relative sparing of the subcortical white matter. On the ADC map diffusivity is reduced in the deep periventricular white matter; it was reduced also in the corpus callosum and corticospinal tracts (images not shown).

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# Mitochondrial Encephalopathy

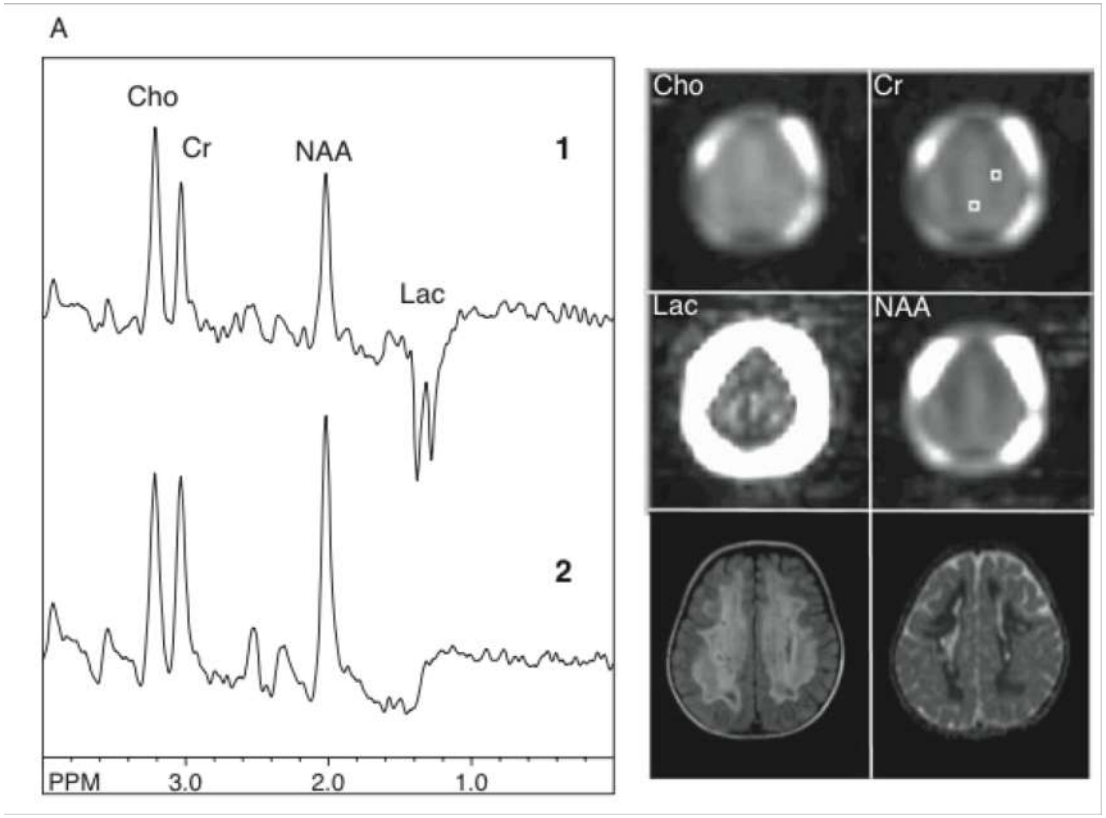
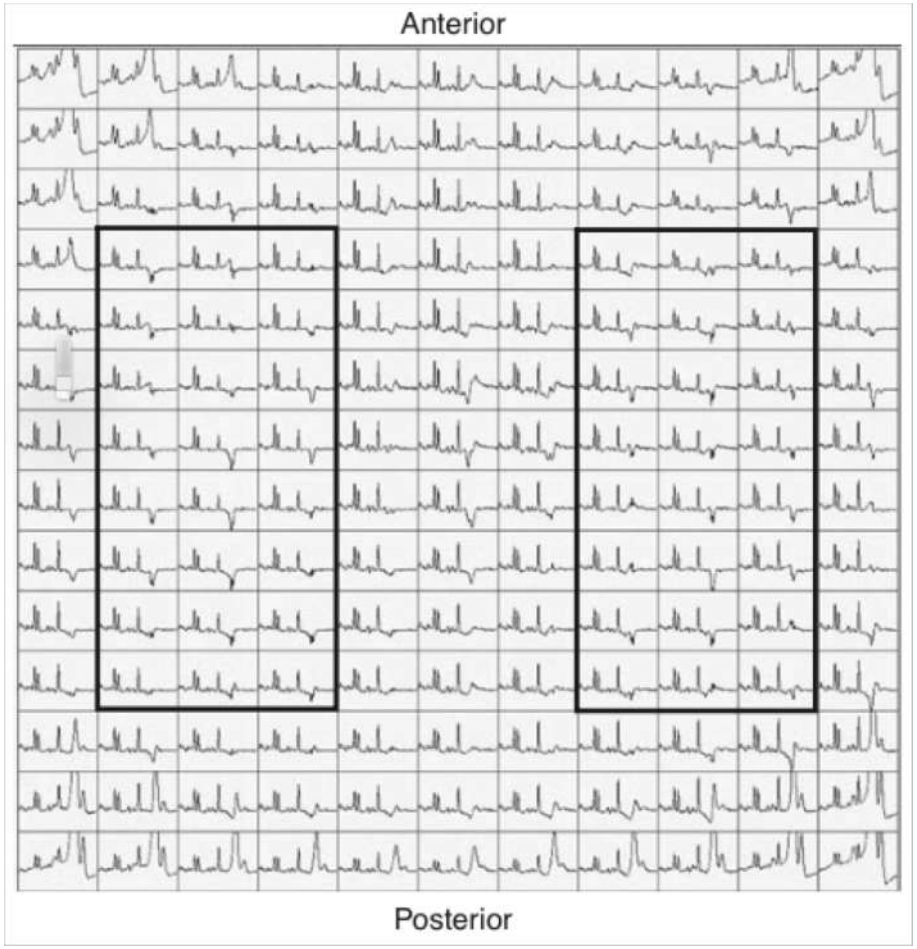


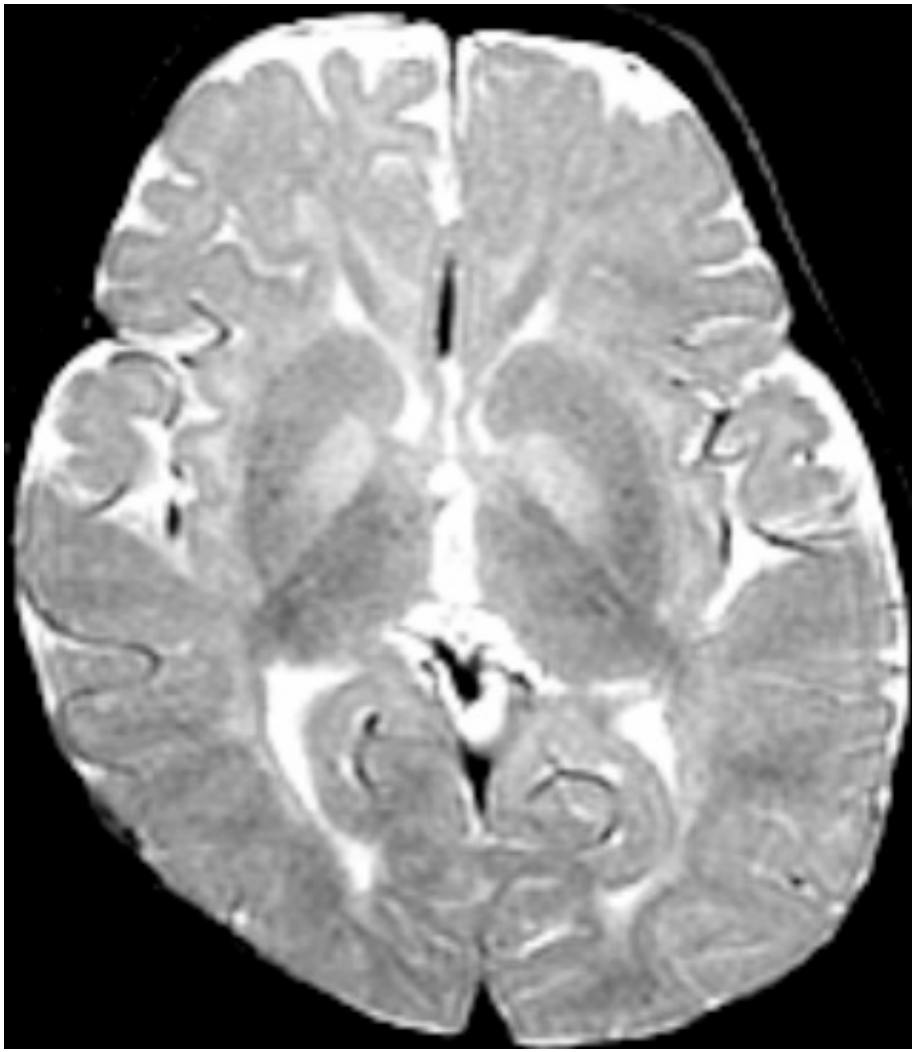

**Figure 11.6**. 16-month-old girl who presented with ataxia and severe developmental delay. She was diagnosed with mitochondrial encephalopathy due to complex I respiratory chain defect:

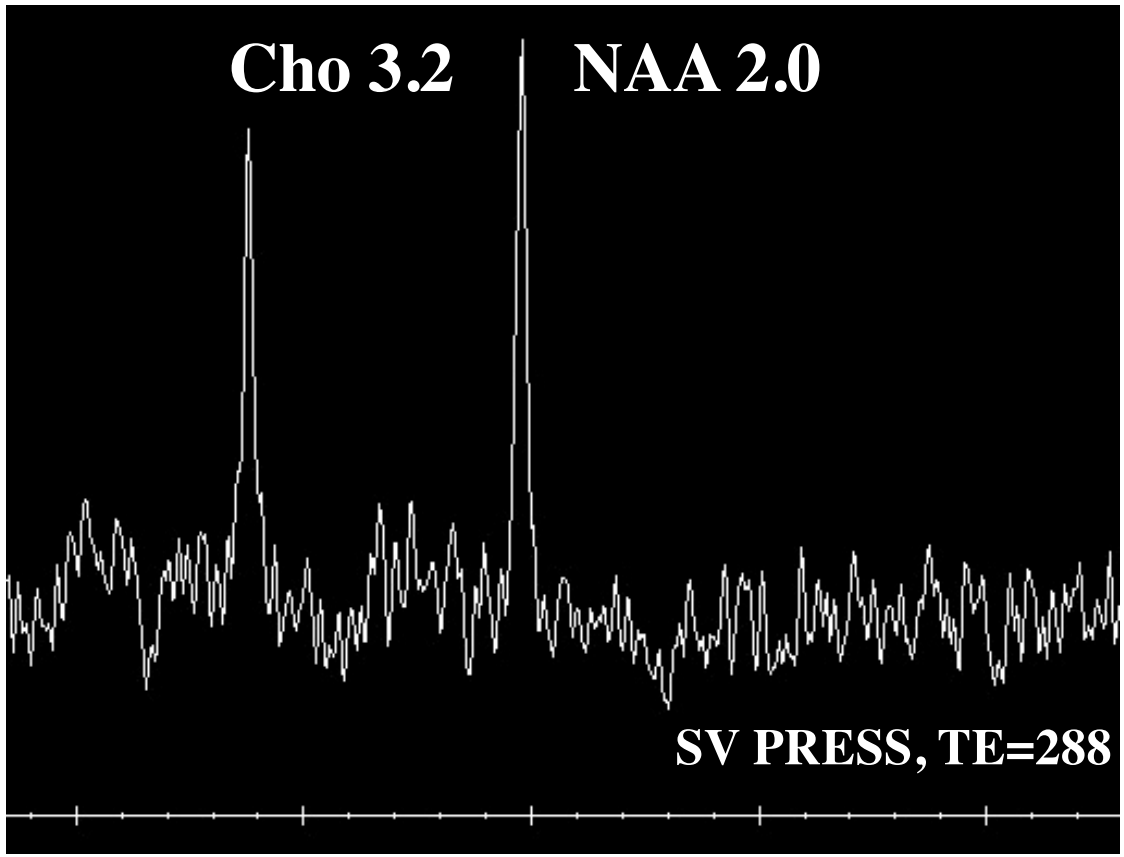



Multivoxel display shows extensive elevation of lactate in the white matter of the centrum semiovale, whereas in the gray matter there is no Lac accumulation and Cho, Cr, and NAA have normal signal intensities.

Barker, et al.

# 13 mo F with hypotonia and developmental delay

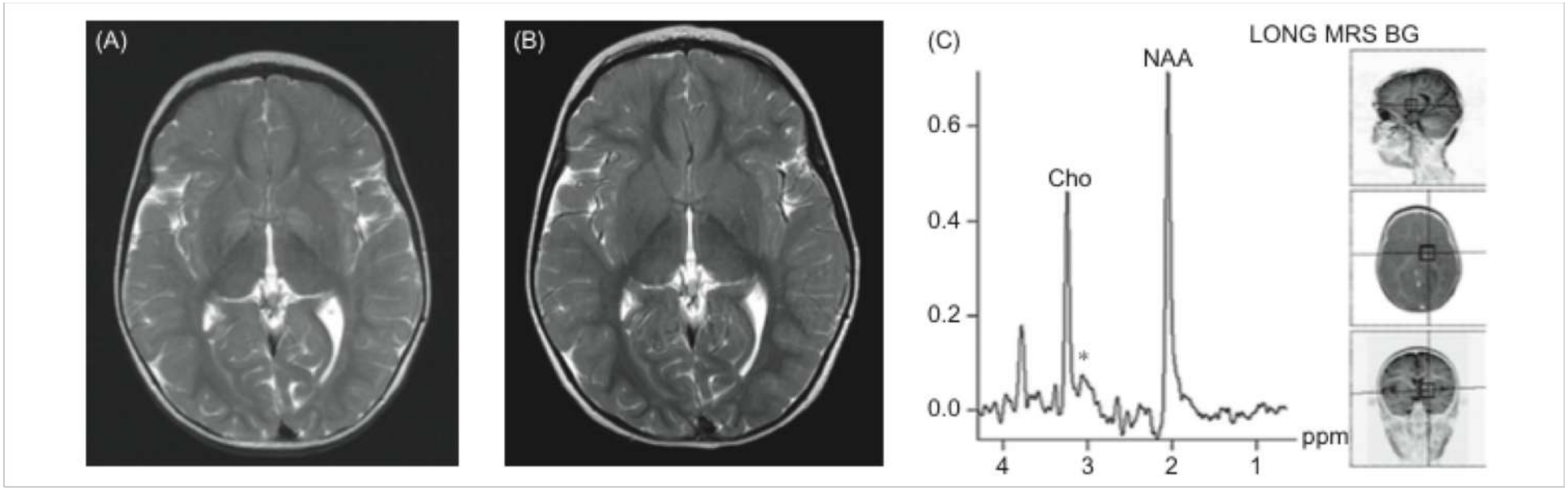


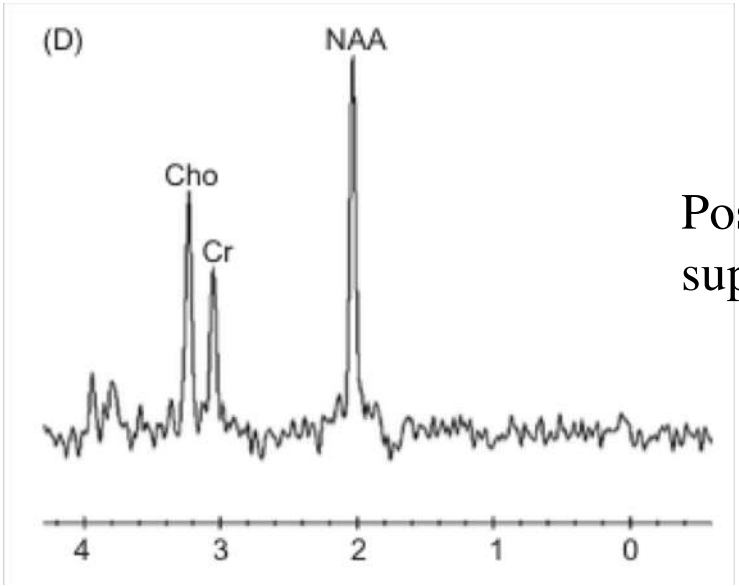



Absence of Cr peak at 3.0 ppm

Dx: creatine deficiency (guanidinoacetate methyltransferase [GAMT] deficiency).

# Creatine deficiency: Treatment Response

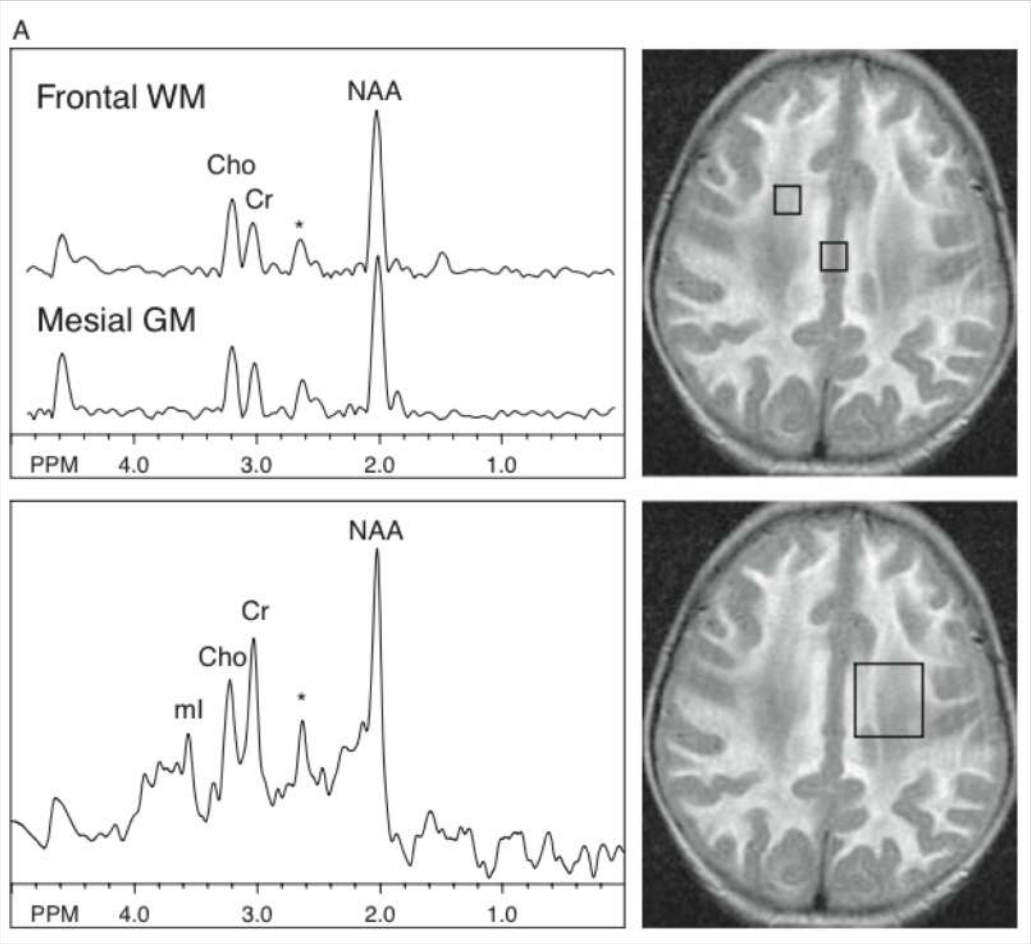



Post dietary supplementation

Barker, et al.

# Cystathionine B-Synthase deficiency



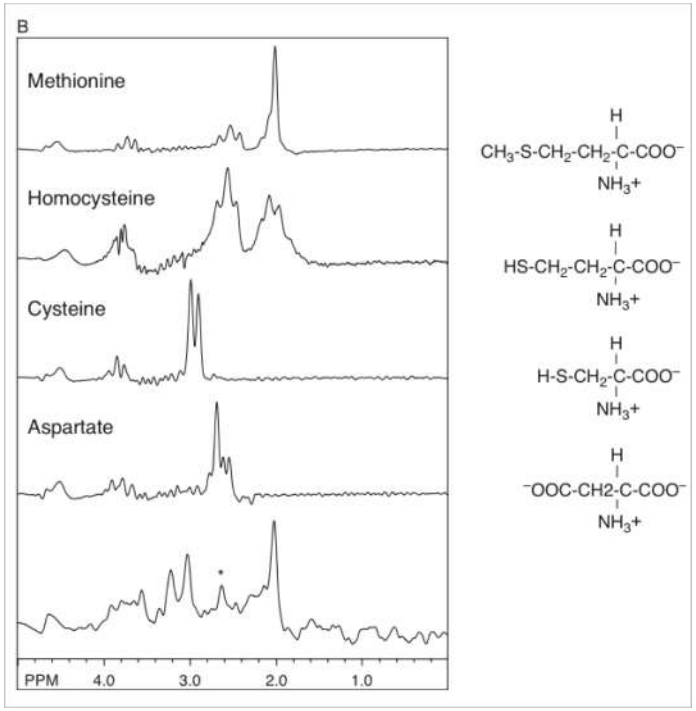




**Figure 11.8A.** Ten-year-old female with Cystathionine B-Synthase (CBS) deficiency, hyperhomocysteinemia, and elevated plasma methionine levels. $T_2$-MRI at presentation shows global elevation of white matter signal intensity, while selected spectra from gray and white matter (MRSI, TR/TE 2300/270 ms, top row) show near-normal metabolite levels, suggesting vasogenic edema rather than demyelination or axonal loss. Short TE white matter spectrum (bottom row) also shows near-normal metabolite levels. (*) indicates unknown resonance at approximately 2.6 ppm, possibly due to homocysteine.

Barker, et al.

# Alexander Disease

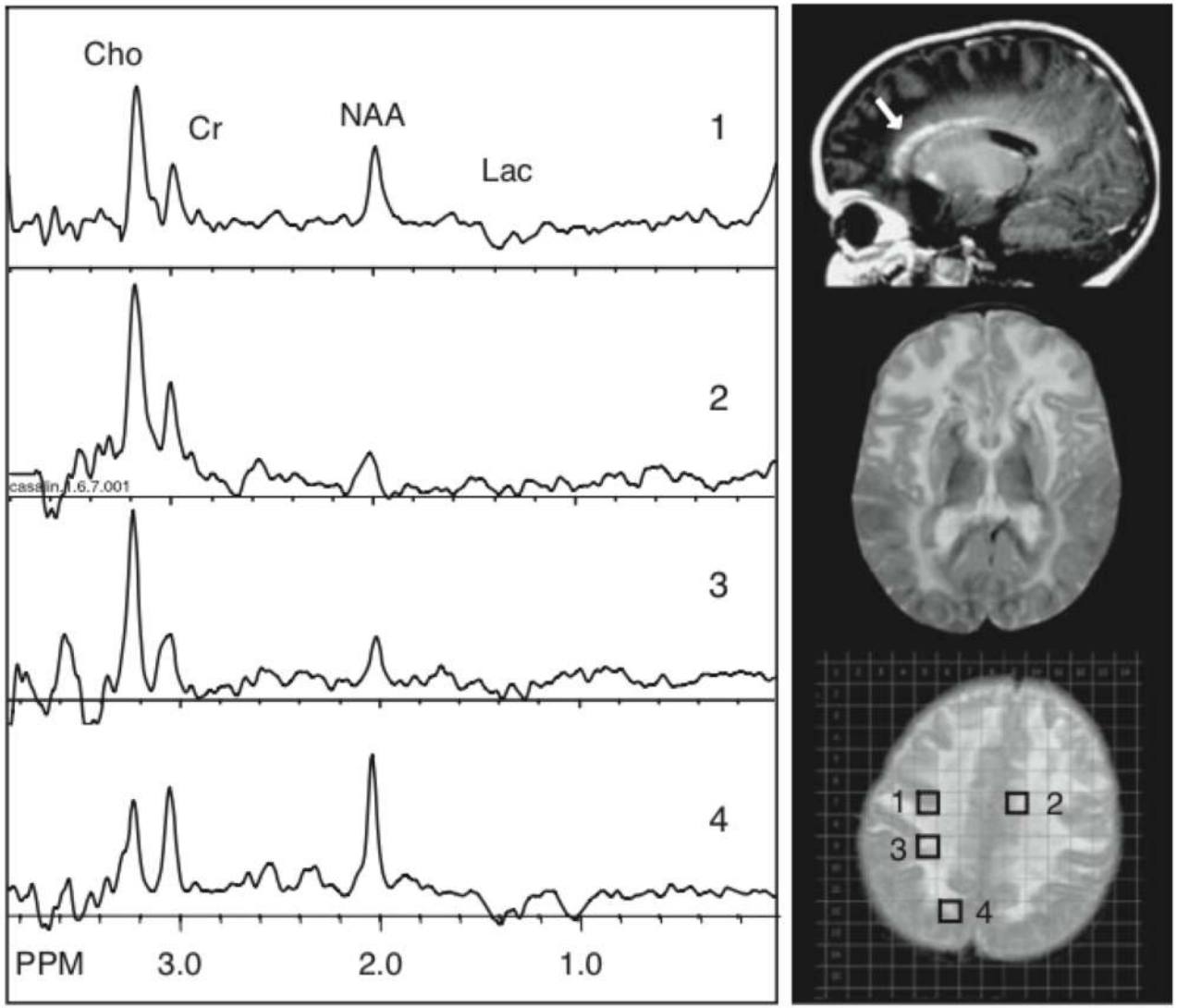


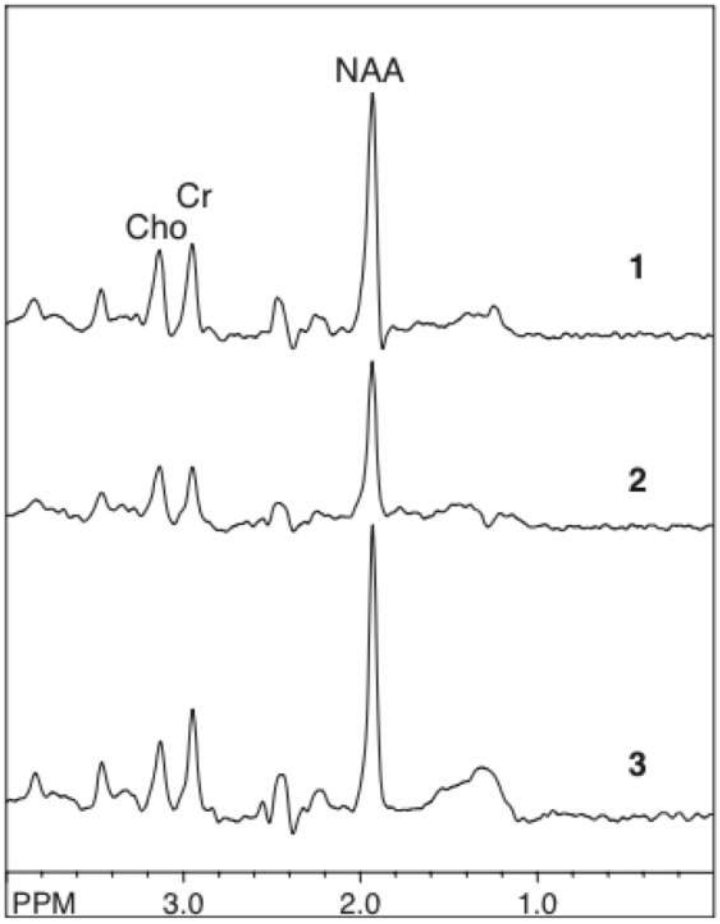

**Figure 11.14.** Two-year-old girl with severe developmental delay and macrocephaly since the first year of life, muscle hypotonia, dysphagia, and cerebellar ataxia. She was diagnosed with **Alexander disease**.

MRSI (PRESS: TR/TE = 1500/135 ms; $32 \times 32$ matrix; FOV = $160 \times 160 \times 20\,mm^3$) was acquired at the level of the centrum semiovale. The location of four selected spectra is overlaid on the $T_2$-weighted MR image.

Note increased Cho with decreased NAA and Cr in the spectra from the right and left centrum semiovale (1, 2, 3). Minimal lactate elevation is also detected (1), while the gray matter spectrum (4) is normal. Swelling with diffuse signal hyperintensity throughout the white matter, in the basal ganglia, and subependymal regions is illustrated in the axial $T_2$-weighted MR images. Note "enhancement" of the periventricular rim (arrow) after i.v. gadolinium administration in the sagittal $T_1$-weighted MR image, which is a very suggestive finding of infantile AD.

Barker, et al.

# Canavan's Disease



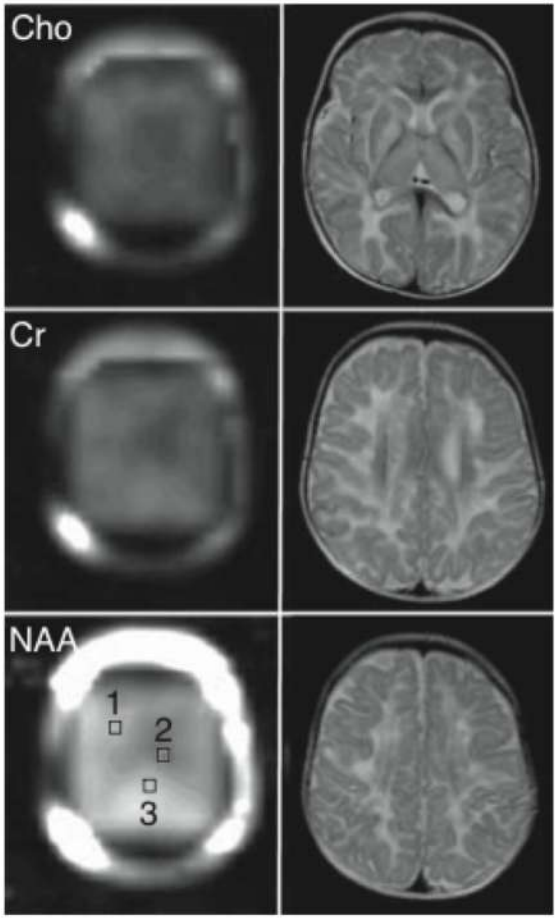




**Figure 11.3.** Ten-month-old girl presenting with hypotonia with poor head control, mild spasticity, and macrocephaly, diagnosed with **Canavan disease**.

MRSI (PRESS: TR/TE = 1200/135 ms; 24 × 24 matrix; FOV = 200 × 200 × 15 $mm^3$) was acquired at the level of the lateral ventricles. Cho, Cr, and NAA maps with three selected spectra are illustrated.

Note abnormal marked elevation of the NAA peak in the right centrum semiovale (spectrum 1) and in the parasagittal parietal lobe (spectrum 3). The elevation of NAA is milder in the left corona radiata where less signal hyperintensity is seen on the $T_2$-weighted MR images (right column).

Barker, et al.

# Traumatic Brain Injury - Key Points*

- TBI is a major cause of morbidity in young adults and children.
- Low levels of NAA and, if seen, increased lactate, in the early stage of injury are prognostic of poor outcome with other common abnormalities being increased levels of choline, myo-inositol, and Glx.
- Metabolic abnormalities are observed with MRS in regions of the brain with normal appearance in conventional MRI.
- MRI and MRS are difficult to perform in acutely ill TBI patients: MRS may be more feasible in mild TBI patients for the purpose of predicting long-term cognitive deficits.
- The role of MRS in guiding TBI therapy is unknown, and the comparative value of MRS compared to other advanced imaging modalities remains to be determined.

*Barker, et al.

# TBI

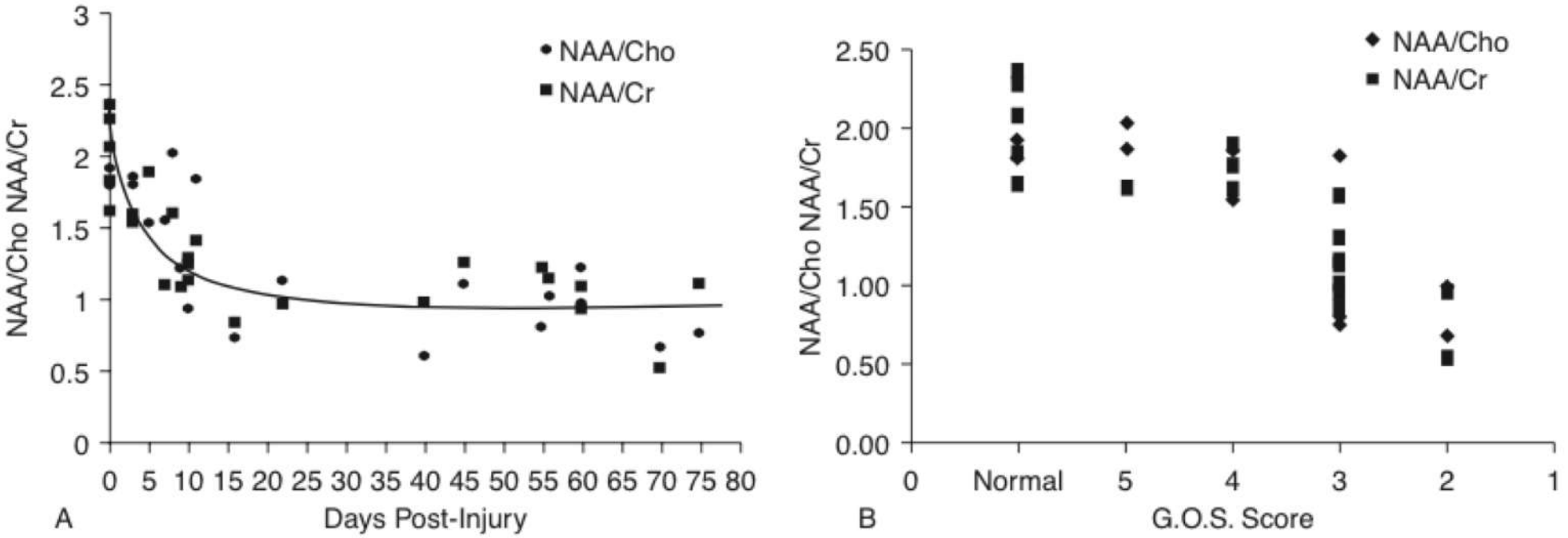



**Figure 10.9.** (A) Graph showing the time course of NAA/Cho and NAA/Cr decline in patients with head injuries who had poor outcomes. The NAA reduction was gradual and non-linear, reaching its lowest point at about 10 days and showing no recovery up to 60 days. (B) Scatter plot demonstrating the association between NAA reduction and 6-month outcome (Glasgow Outcome Score, GOS). Patients with good outcomes exhibited mean ratios >1.50. Conversely, those with poor outcomes were characterized by ratios <1.50, identifying a possible threshold of irreversible neurochemical damage. Note that the metabolite ratios in patients with GOS scores indicating good recovery or moderate disability are not significantly different from those of healthy volunteers. The metabolite ratios of patients with poor outcomes at 6 months were significantly lower than controls ($p < 0.01$). (Adapted with permission from [114].)

Barker, et al.[32]

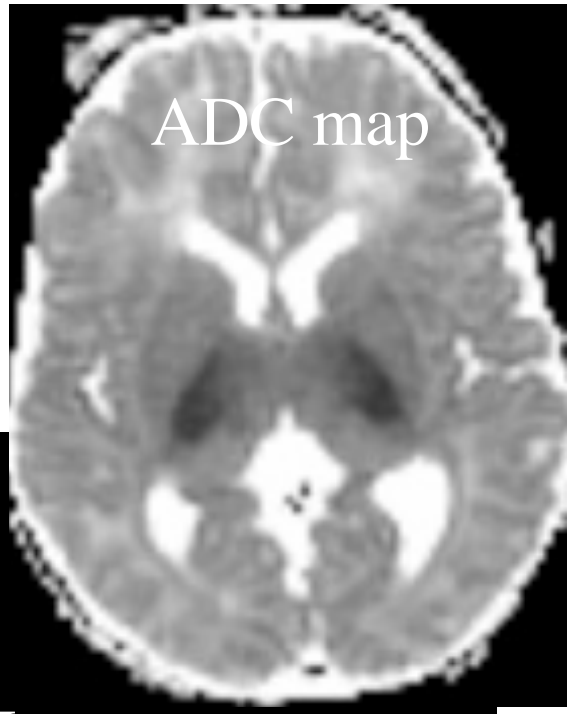
# Stroke and Hypoxic Ischemic Encephalopathy – Key Points*

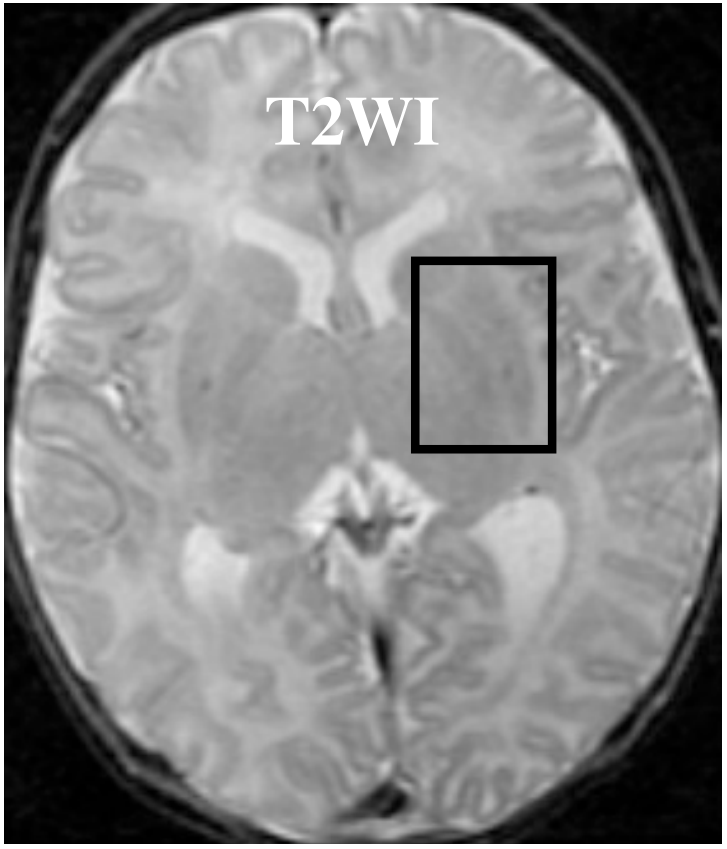
- MRS is highly sensitive to metabolic changes associated with hypoxic or ischemic injury to the brain.
- Lactate is elevated during acute hypoxia or ischemia, and may also increase during "secondary" energy failure after reperfusion.
- NAA decreases with prolonged hypoxia or ischemia.
- In $^{31}P$ MRS, high-energy phosphates decrease, inorganic phosphate increases, and pH decreases during acute hypoxia and ischemia.
- Both $^{1}H$ and $^{31}P$ MRS offer prognostic information in HIE, which may be complementary to, and sometimes easier to interpret than, conventional or diffusion-weighted MRI in the neonatal brain.
- DWI may be better for evaluating small HIE lesions than MRS.

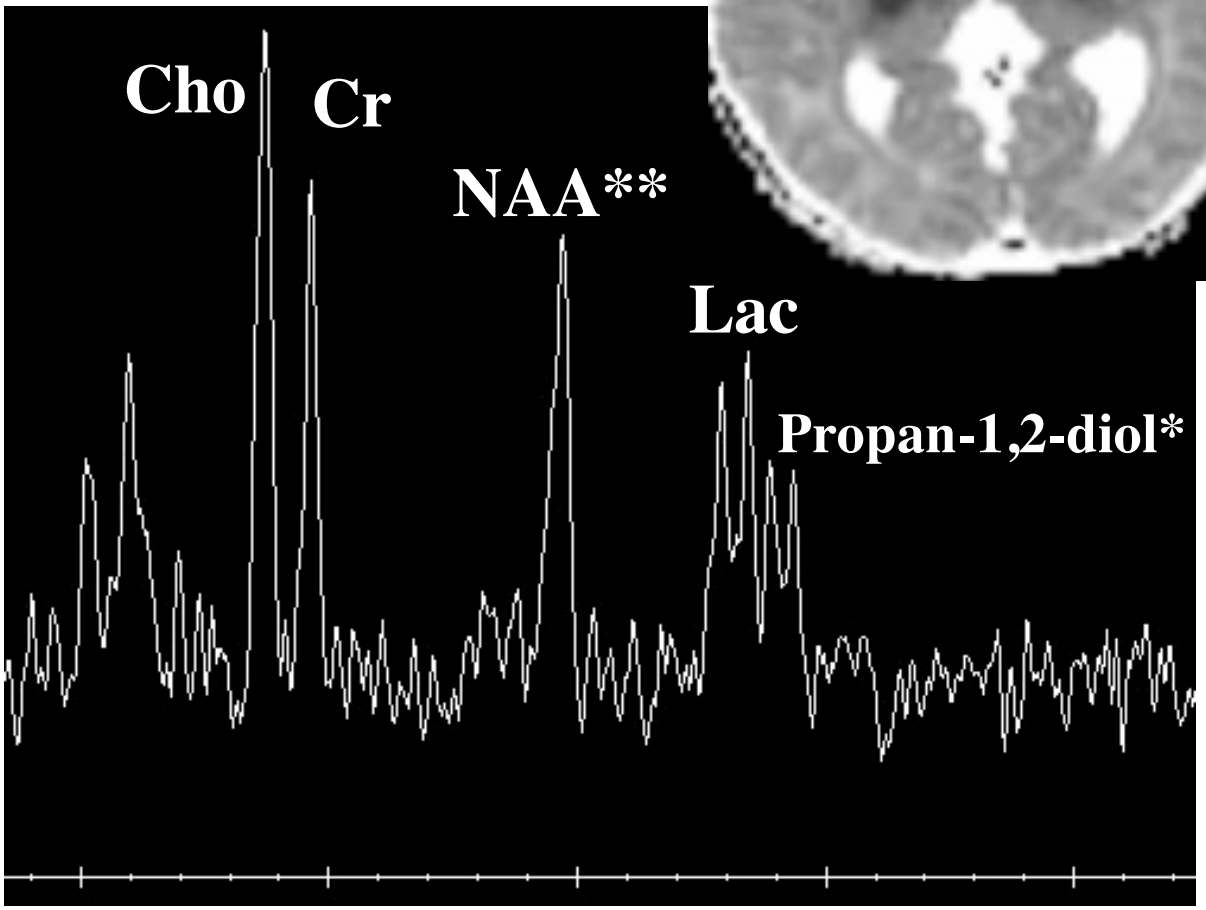
*Barker, et al.

**18 hr old term infant s/p 30 min arrest**

**Dx: anoxic injury**




***injection solvent for anticonvulsants, center 1.1 ppm**
****note the relatively low NAA in the term neonate**

# Neonatal Encephalopathy

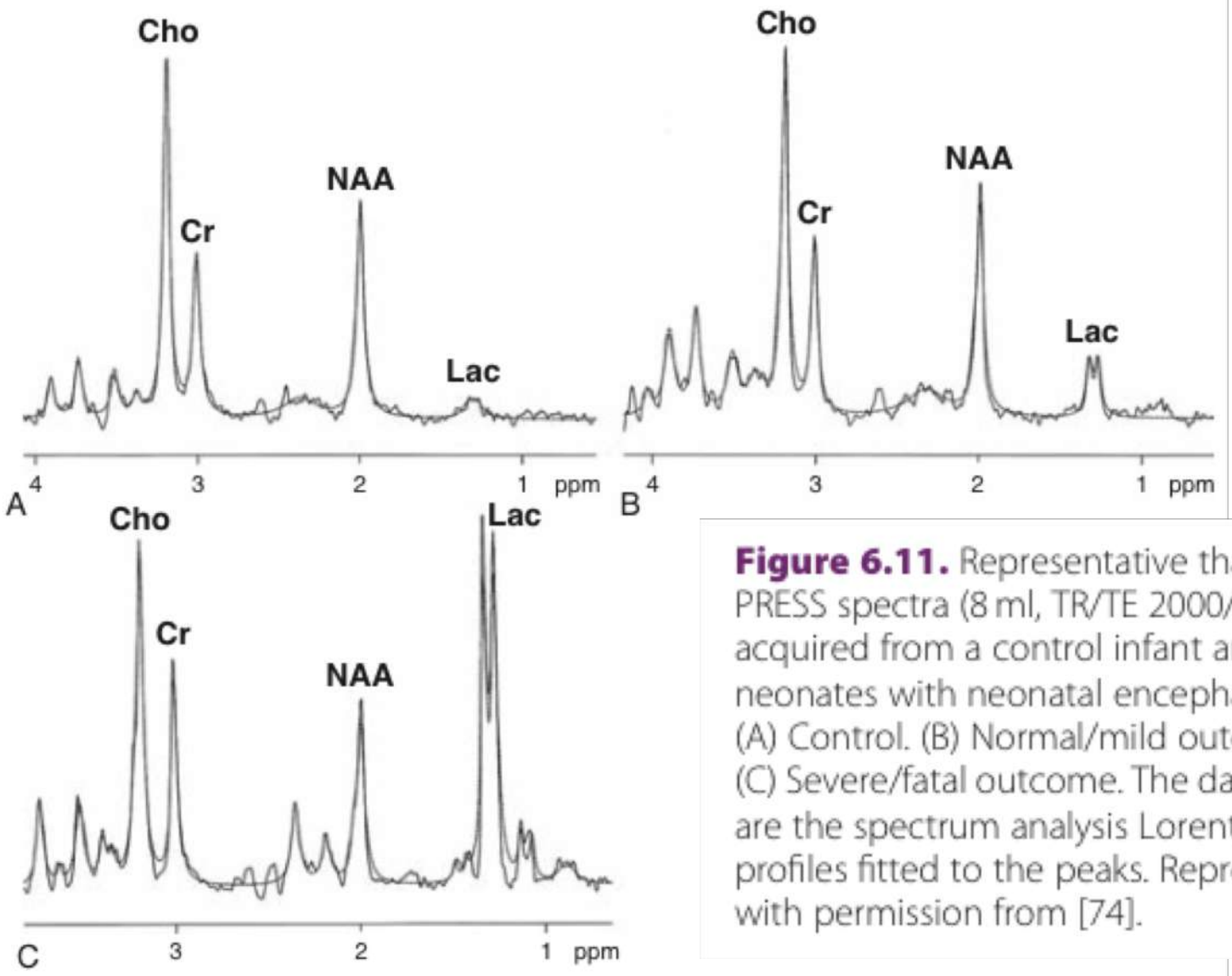
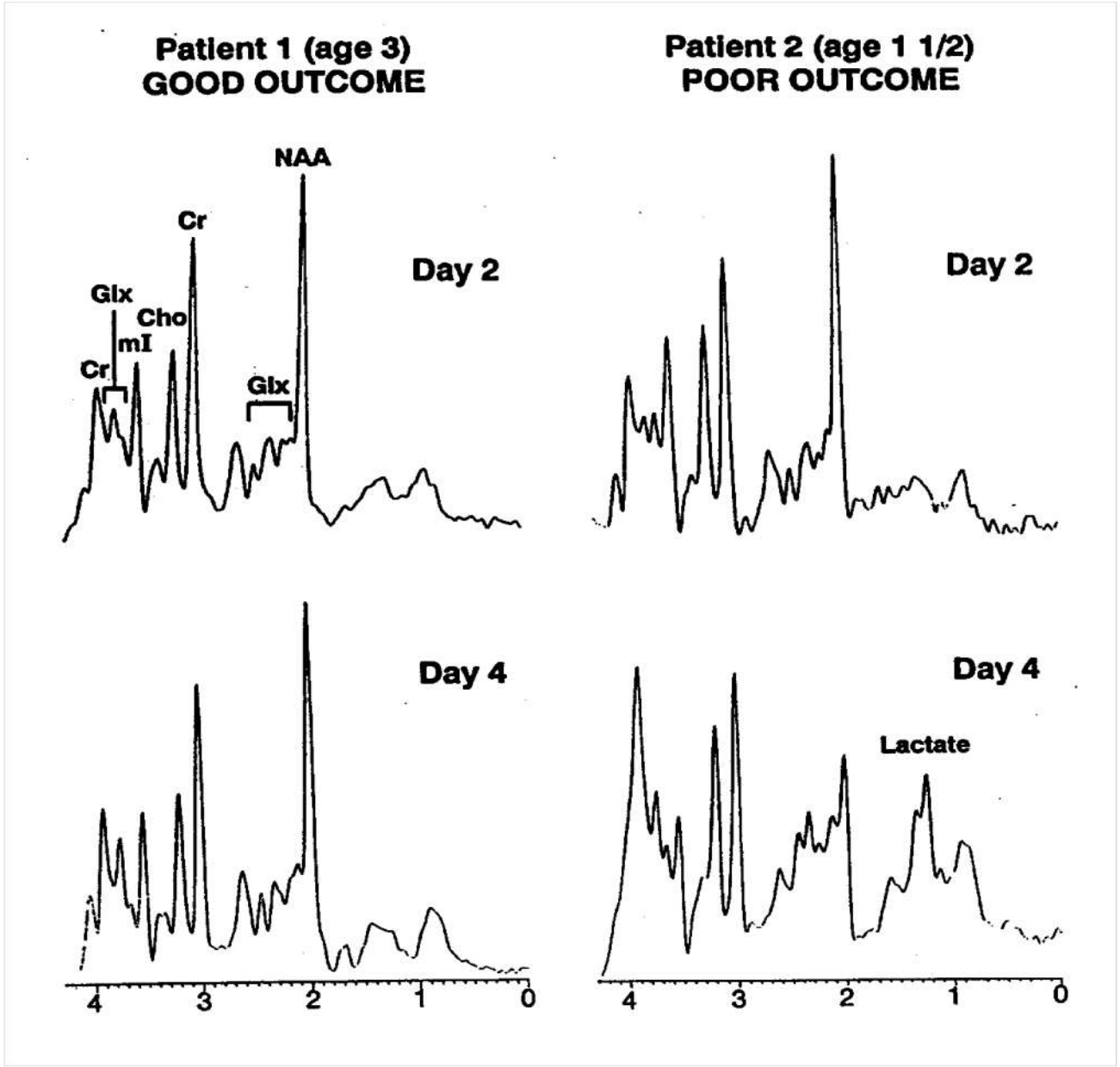



**Figure 6.11.** Representative thalamic PRESS spectra (8 ml, TR/TE 2000/270 ms) acquired from a control infant and 2 neonates with neonatal encephalopathy. (A) Control. (B) Normal/mild outcome. (C) Severe/fatal outcome. The dashed lines are the spectrum analysis Lorentzian profiles fitted to the peaks. Reproduced with permission from [74].

Barker, et al.

# Acute CNS Injury: Near Drowning




Moats, et al.
JCAT,
19:480, 1995

# Hepatic Encephalopathy

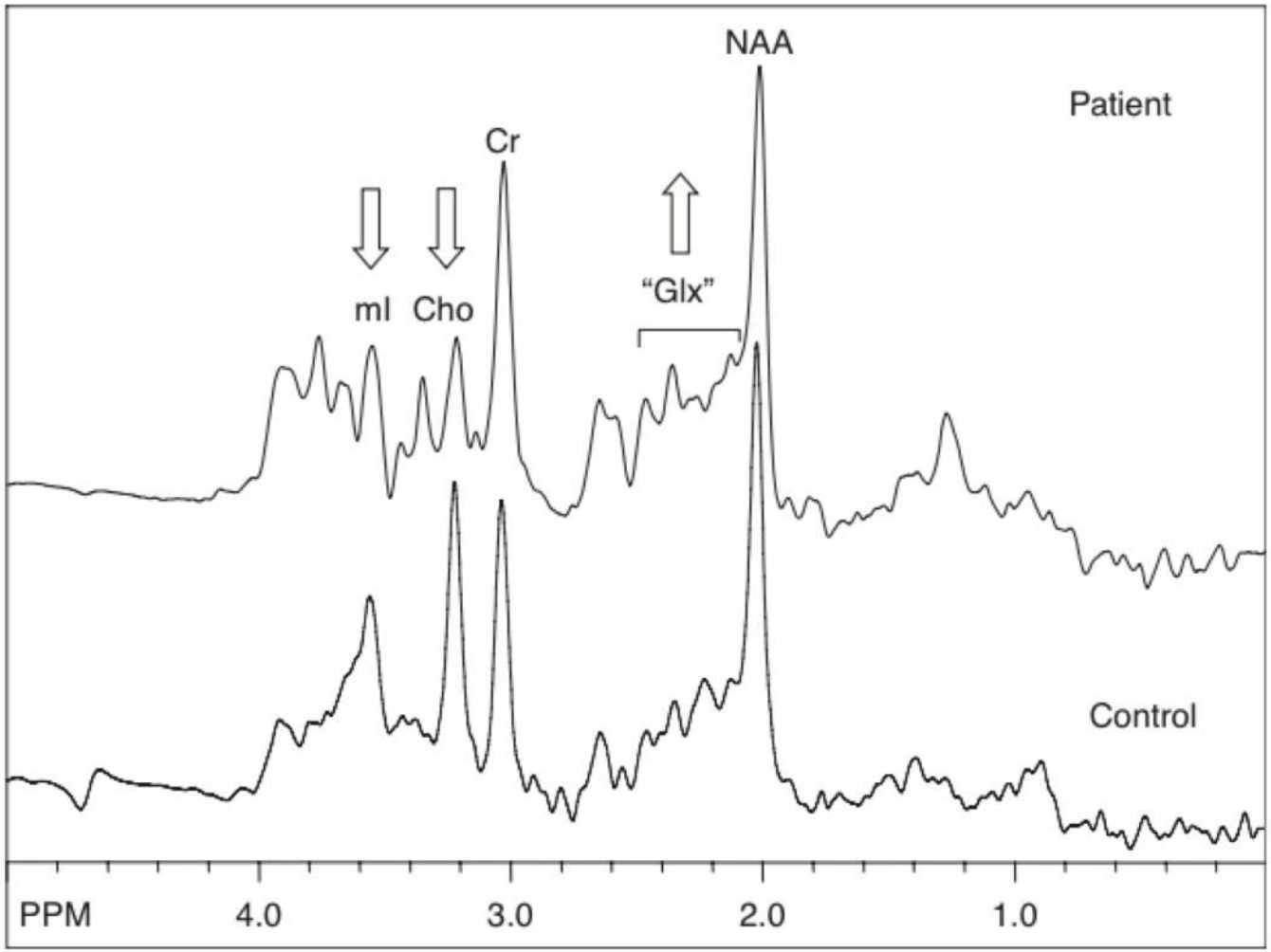



**Figure 11.7. Hepatic encephalopathy**. Example of single-voxel PRESS spectra from parietal white matter (short echo time, TE 35 msec) from a 2-year-child with liver failure and an age-matched control subject. Note the increased signal from Glx (due to increased glutamine) and decreased Cho in the patient. There is also a small decrease in *myo*-inositol.

Barker, et al.

# Brain Development – Key Points*

- Substantial regional variations in proton brain spectra exist; differences between gray and white matter, anterior–posterior gradients, and differences between the supra- and infra-tentorial brain are common.
- Spectra change rapidly over the first few years of life; at birth, NAA is low, and choline and myo-inositol are high. By about 4 years of age, spectra from most regions have a more "adult-like" appearance.
- In normal development, only subtle age-related changes are found between the ages of 4 and 20 years.
- In normal aging, only subtle age-related changes are found. A recent meta-analysis indicated the most common findings are mildly increased choline and creatine in frontal brain regions of elderly subjects (> 68 years), and stable or slightly decreasing (parietal regions only) NAA.

*Barker, et al.

# Brain Development

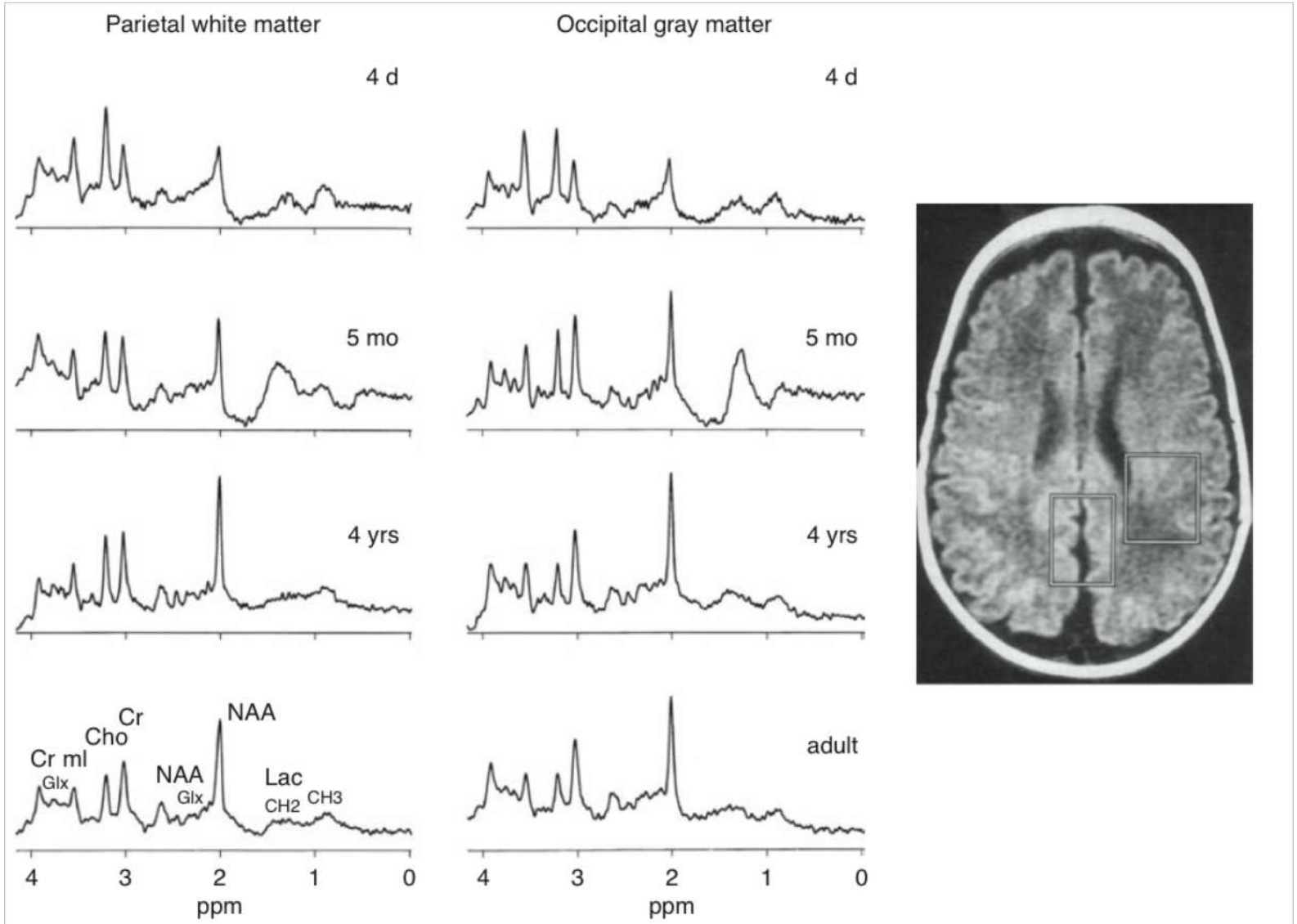
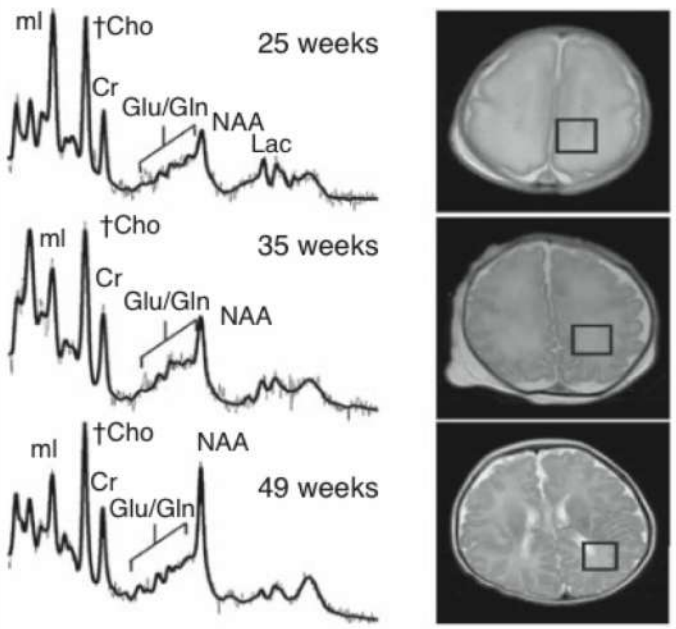
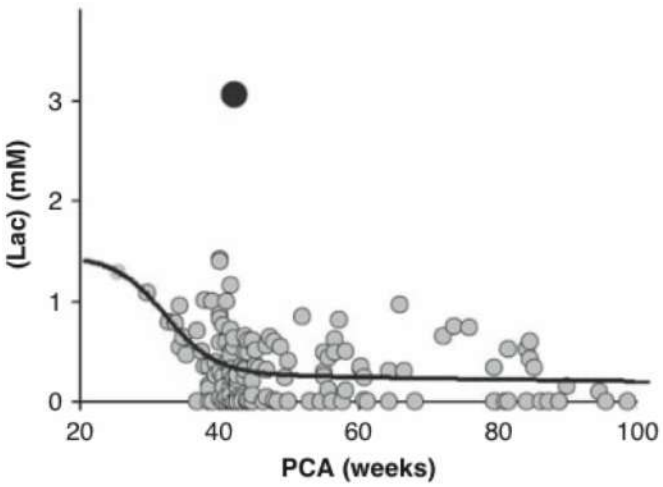


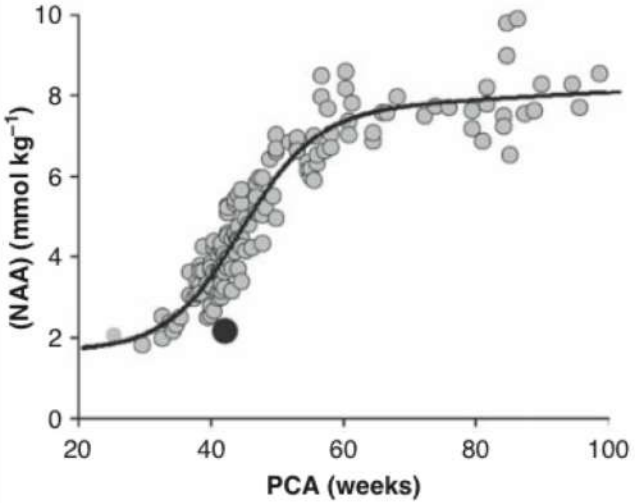

**Figure 4.8.** Age-related variations in MRS – the normal developing brain. At birth, spectra of both gray and white matter show low signals from NAA and elevated levels of Cho and mI. As the brain develops, NAA increases and Ch and mI decrease so that by about 4 years of age (in these locations) the spectra are essentially indistinguishable from those in young adults. Reproduced with permission from [17]. Spectra recorded at 1.5 T.

Barker, et al.

# Brain Development



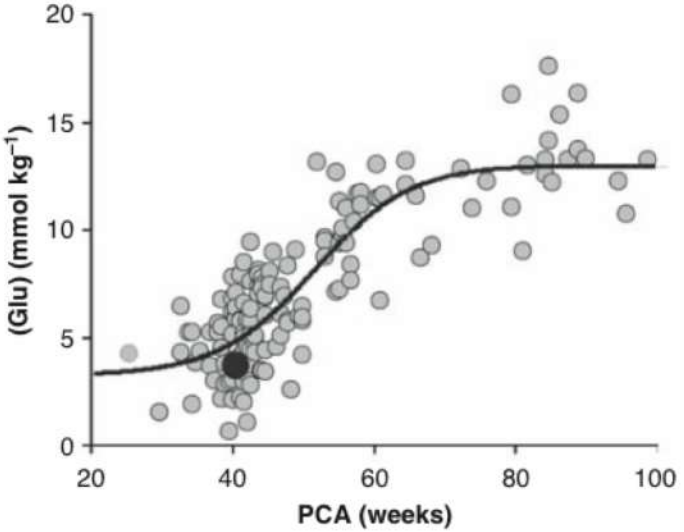




**Figure 6.7.** Representative short echo time single voxel spectra from neonates of 25, 35, and 49 weeks gestational age. Of note is the decrease of ml and increase in NAA with age. A small lactate peak is also clearly visible in the younger neonates. Normative curves showing evolution of NAA, lactate (Lac) and glutamine (Glu) with gestational age from 20 to 100 weeks are shown. The black dots represent NAA, Lac, and Glu values from one infant with methyl malonic aciduria (MMA), clearly showing the deviation from the normal age-related metabolic pattern (elevated Lac, low NAA). Reproduced with permission from [63].

Barker, et al.

# Neurodegenerative Disorders- Key Points*

- Despite the relatively common occurrence of neurodegenerative diseases, MRS is lightly used likely due lack of sensitivity and overlap of spectral findings.
- MRS usually shows decreased levels of NAA in dementia.
- Dementias associated with gliosis (e.g. Alzheimer's) also have increased myo-inositol (mI), and mI/NAA ratios may be helpful in the differential diagnosis of different dementias (Alzheimer, vascular, frontotemporal, Lewy body).
- Parkinson's disease does not seem to be associated with any metabolic disorders, and metabolic changes in Huntington's disease are unclear.
- Prion diseases are characterized by decreased NAA levels.
- In amyotrophic lateral sclerosis (ALS), NAA decreases may be helpful in establishing a diagnosis.

*Barker, et al.

# Neurodegenerative Disorders

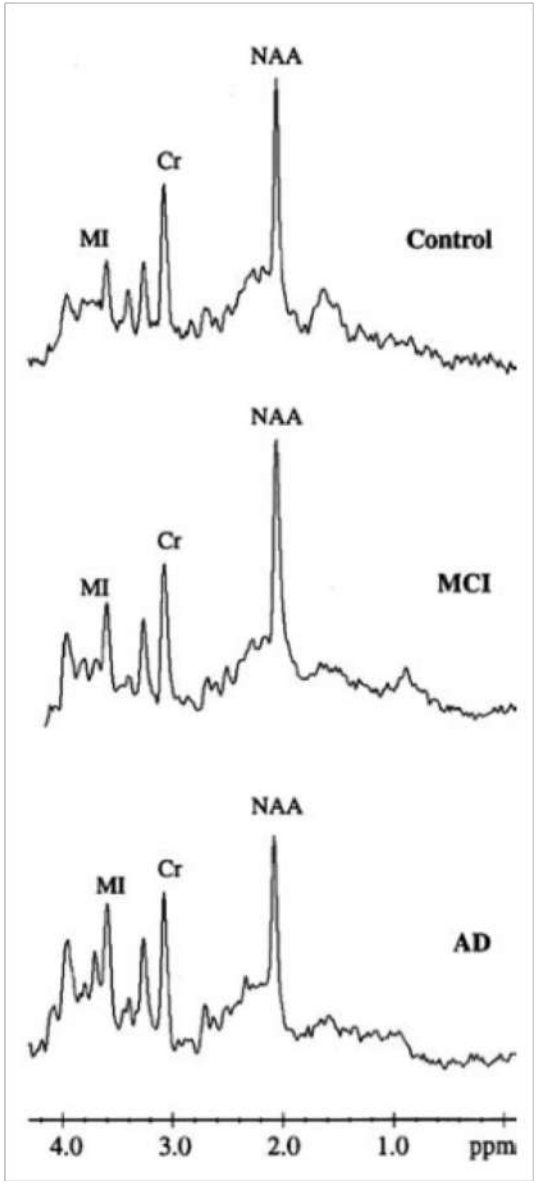



**Figure 9.2.** Examples of proton spectra obtained from the posterior cingulate VOI with a TE of 30 ms in a control subject (top), in a patient with MCI (middle), and in a patient with AD (bottom). NAA/Cr ratio is lower in the patient with AD than both the patient with MCI and the control subject. ml/Cr ratios are higher in patients with MCI and AD than the control subject. The ml/Cr ratio is also higher in the patient with AD than the patient with MCI. [Adapted from Kantarci *et al.*, *Neuroimag Clin N Am* 2003; **13**: 197–209, figure 3, with permission.]

Barker, et al.

# Research Topics on some key brain metabolites…

| | | |
|---|---|---|
| γ-amino-butyrate (GABA) | Metabolic/functional activity | May increase or decrease depending on the cell types responsible: decreased by mainstream inhibitory activity |
| | | Increased by some benzodiazepines |
| | | Marker for gamma synchrony |
| | | Marker for tonic inhibition |
| Glucose | Glucose use | Blood glucose levels |
| | Glucose transport | Transporter expression |
| | Supply and demand | Blood glucose concentration and metabolic activity |
| Glutamate | Metabolic activity | Increases with increased metabolic activity |
| | | May be marker for addiction |
| Glutamine | Metabolic activity | Correlates strongly with glutamate |
| | | Hyperammonaemia |
| Glutathione (GSH) | Increased oxidative stress | Preconditioning, stress levels |

Rae, Neurochem Res, 2014

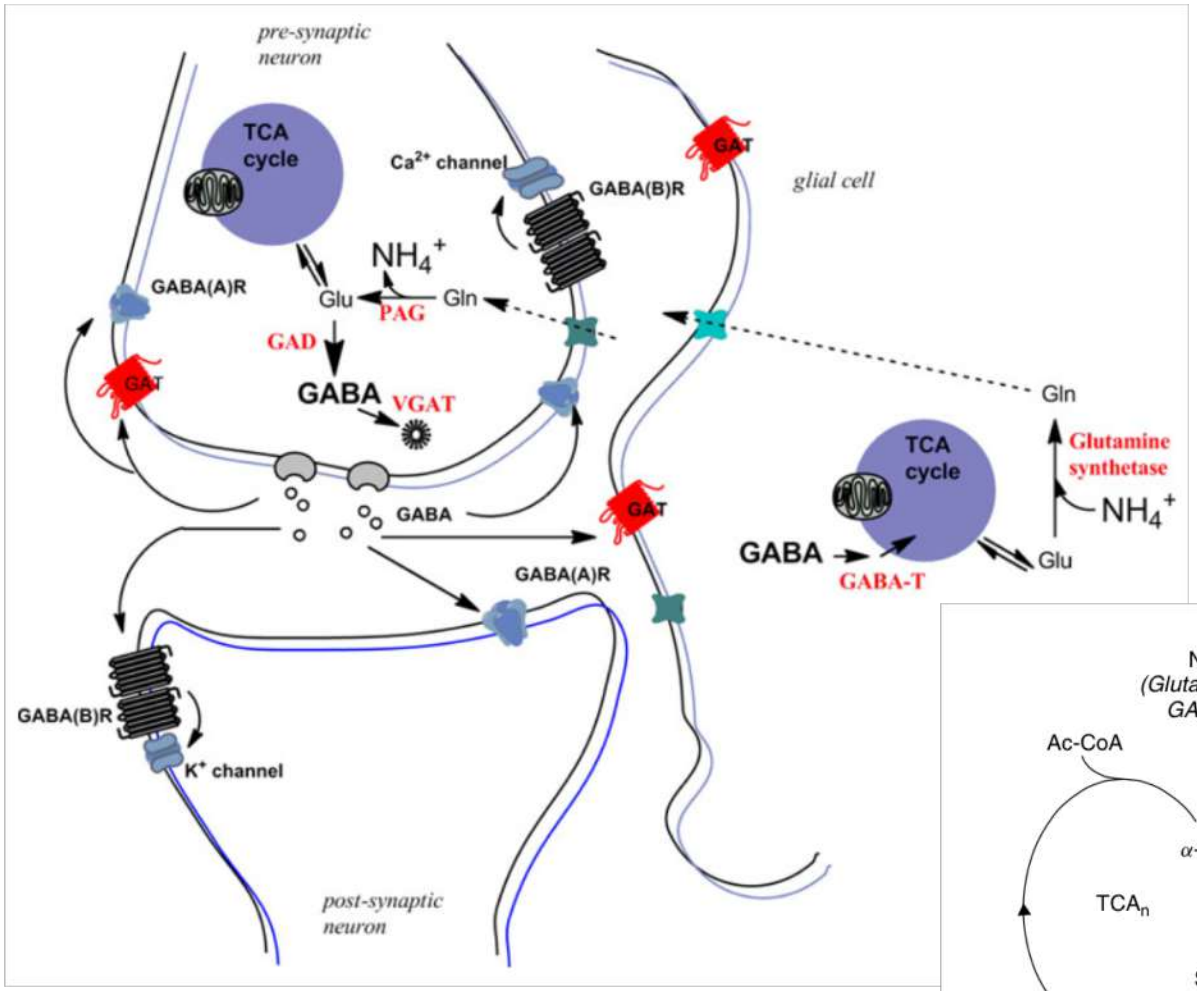
# E/I Imbalance

An imbalance between excitatory and inhibitory processes is a leading hypothesis for the neuropathological changes underlying autism spectrum disorder (ASD)

Review – Model of autism: increase ratio of excitation/inhibition in key neural systems
J. L. Rubenstein and M. M. Merzenich
*Genes, Brain and Behavior* (2003) 2: 255-267

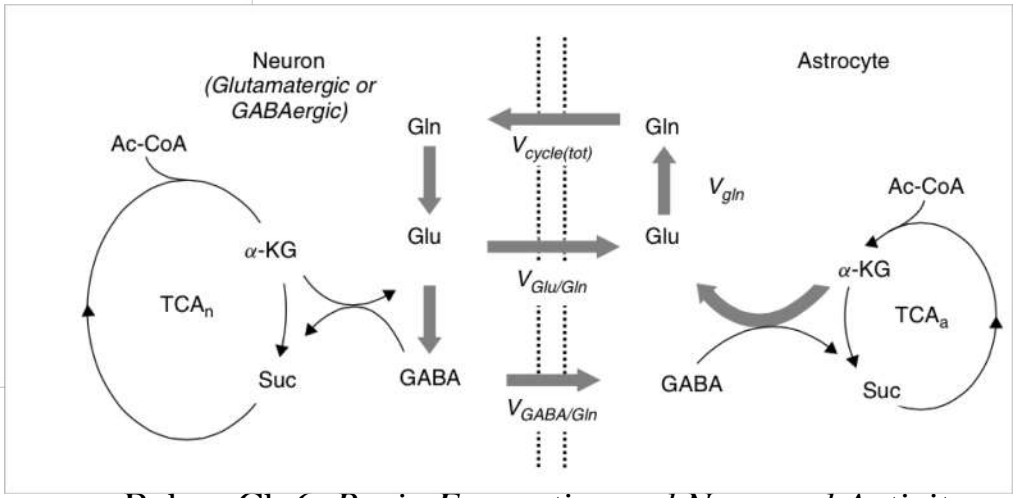
**Abstract** Autism is a severe neurobehavioral syndrome, arising largely as an inherited disorder, which can arise from several diseases. Despite recent advances in identifying some genes that can cause autism, its underlying neurological mechanisms are uncertain. Autism is best conceptualized by considering the neural systems that may be defective in autistic individuals. Recent advances in understanding neural systems that process sensory information, various types of memories and social and emotional behaviors are reviewed and compared with known abnormalities in autism. Then, specific genetic abnormalities that are linked with autism are examined. Synthesis of this information leads to a model that postulates that some forms of autism are caused by an increased ratio of excitation/ inhibition in sensory, mnemonic, social and emotional systems. The model further postulates that the increased ratio of excitation/inhibition can be caused by combinatorial effects of genetic and environmental variables that impinge upon a given neural system. Furthermore, the model suggests potential therapeutic interventions.

# A GABAergic Synapse




Rae, Neurochem Res, 2014

**Modeling and fluxes**




Behar, Ch 6, *Brain Energetics and Neuronal Activity,* Rothman and Shulman, 2004 John Wiley & Sons, Ltd

Neuroscience and Biobehavioral Reviews 36 (2012) 2044–2055

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journal homepage: www.elsevier.com/locate/neubiorev

Review

# GABA system dysfunction in autism and related disorders: From synapse to symptoms

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Inhibitory interneurons

ABSTRACT

Autism spectrum disorders (ASDs) are neurodevelopmental syndromes characterised by repetitive behaviours and restricted interests, impairments in social behaviour and relations, and in language and communication. These symptoms are also observed in a number of developmental disorders of known origin, including Fragile X Syndrome, Rett Syndrome, and Foetal Anticonvulsant Syndrome. While these conditions have diverse etiologies, and poorly understood pathologies, emerging evidence suggests that they may all be linked to dysfunction in particular aspects of GABAergic inhibitory signalling in the brain. We review evidence from genetics, molecular neurobiology and systems neuroscience relating to the role of GABA in these conditions. We conclude by discussing how these deficits may relate to the specific symptoms observed.

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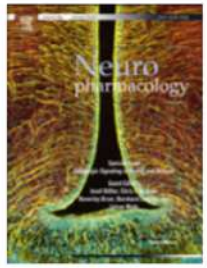

Review

# Insights into $GABA_A$ergic system deficits in fragile X syndrome lead to clinical trials

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Fragile X syndrome
$GABA_A$ receptor
Targeted treatment
Gaboxadol
Ganaxolone

ABSTRACT

An increasing number of studies implicate the $GABA_A$ergic system in the pathophysiology of the fragile X syndrome, a frequent cause of intellectual disability and autism. Animal models have proven invaluable in unravelling the molecular mechanisms underlying the disorder. Multiple defects in this inhibitory system have been identified in *Fmr1* knockout mice, including altered expression of various components, aberrant $GABA_A$ receptor-mediated signalling, altered GABA concentrations and anatomical defects in GABAergic neurons. Aberrations compatible with those described in the mouse model were detected in *dfmr1* deficient *Drosophila melanogaster*, a validated fly model for the fragile X syndrome. Treatment with drugs that ameliorate the $GABA_A$ergic deficiency in both animal models have demonstrated that the $GABA_A$ receptor is a promising target for the treatment of fragile X patients. Based on these preclinical studies, clinical trials in patients have been initiated.

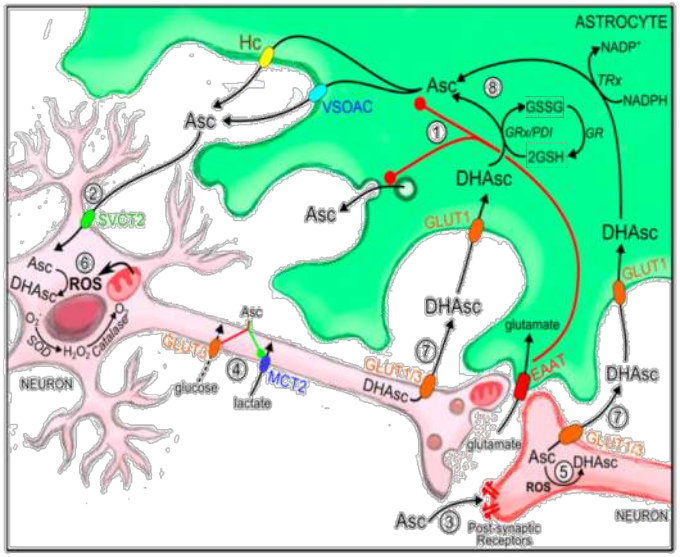
This article is part of the Special Issue entitled 'GABAergic Signaling in Health and Disease'.

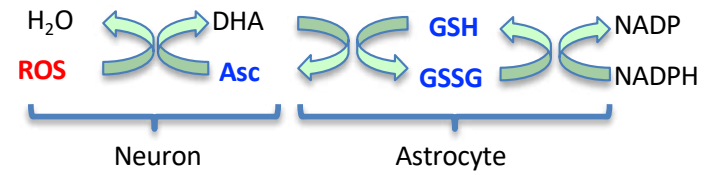
# TBI and Oxidative Stress

- The effects of oxidative stress, elevated reactive oxygen species, following TBI, have been studied in both animals and humans.
- Whereas primary brain injury lesions are related to the site of impact, secondary brain injury results from physiological changes caused by oxidative stress and inflammatory responses occurring after the primary insult.
- Clinical studies (some highlights)
  - A pediatric study of antioxidant reserve and oxidative injury in clinical TBI found "Progressive compromise of antioxidant defenses and … These markers could be used to monitor antioxidant strategies in clinical trials". (Bayir, et al, Pediatric Res, 2002)
  - "Quantifying biomarkers of oxidative stress and antioxidant status of serum correlate with trauma severity and may be used to predict outcomes after TBI. Higher serum GSH levels on admission are associated with better outcome." (Wang, et al, World Neurosurgery, 2016)
  - A prospective study of moderate to severe TBI patients found "Recovery after TBI was dependent on the resolution of oxidative stress imbalance". (Muballe, et al, J Neurosurg, 2018)

# Oxidative Stress in the Brain

The antioxidants Ascorbate (Asc) and glutathione (GSH) are the brain's primary defense against oxidative stress via a linked neuron-astrocyte cycling process.

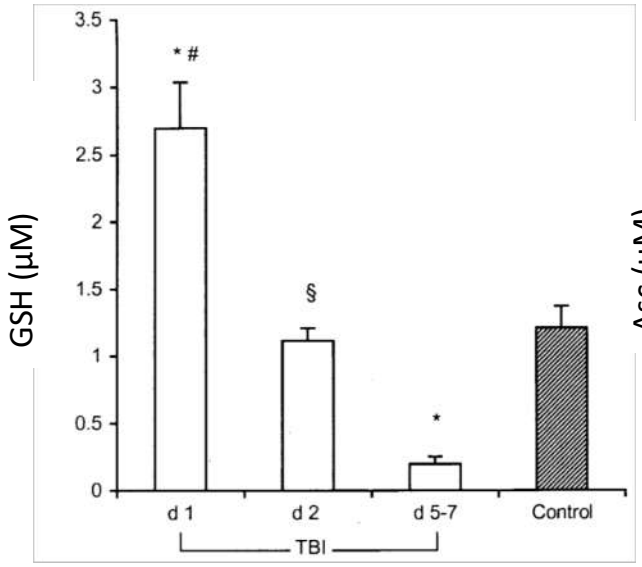


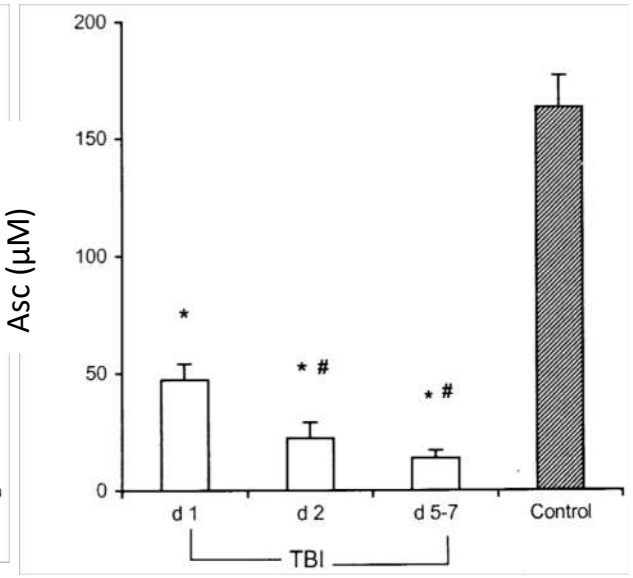

$^1$H MRS detectable

Convarrubias-Pinto, et al. " Old Things New View: Ascorbic Acid Protects the Brain in Neurodegenerative Disorders", Int. J. Mol. Sci. 2015, 16, 28194–28217.

## Pediatric TBI




Days post injury



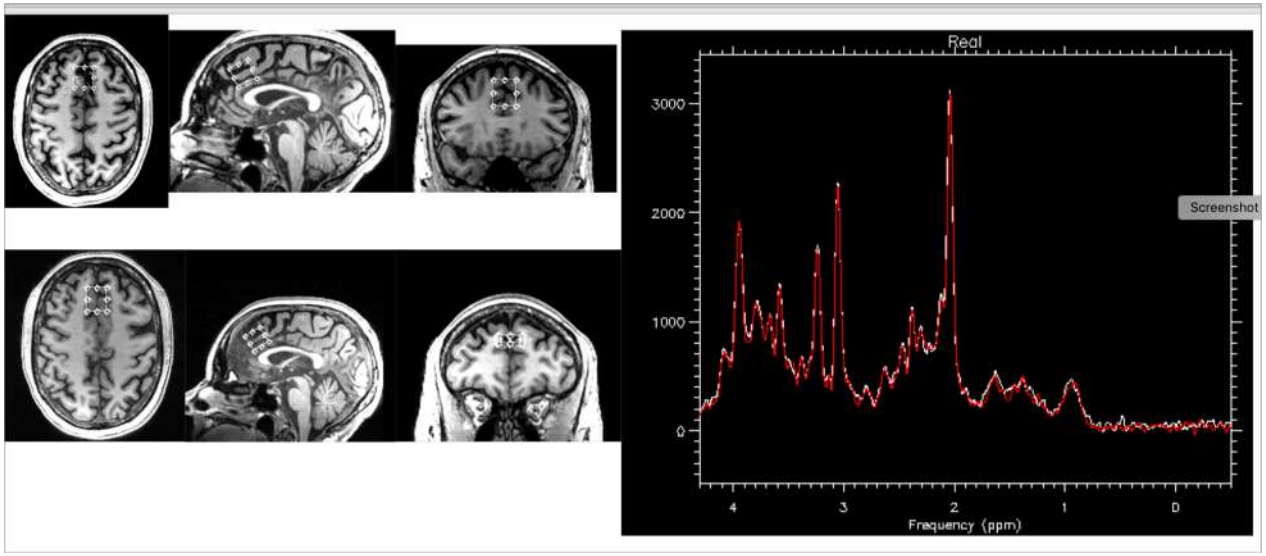

Days post injury

Bayir, et al., Assessment of Antioxidant Reserves and Oxidative Stress in Cerebrospinal Fluid after Severe Traumatic Brain Injury in Infants and Children, Pediatric Research, 2002

87 cerebrospinal fluid samples from 11 infants and children with severe TBI (Glasgow Coma Scale score ≤ 8) and 8 controls

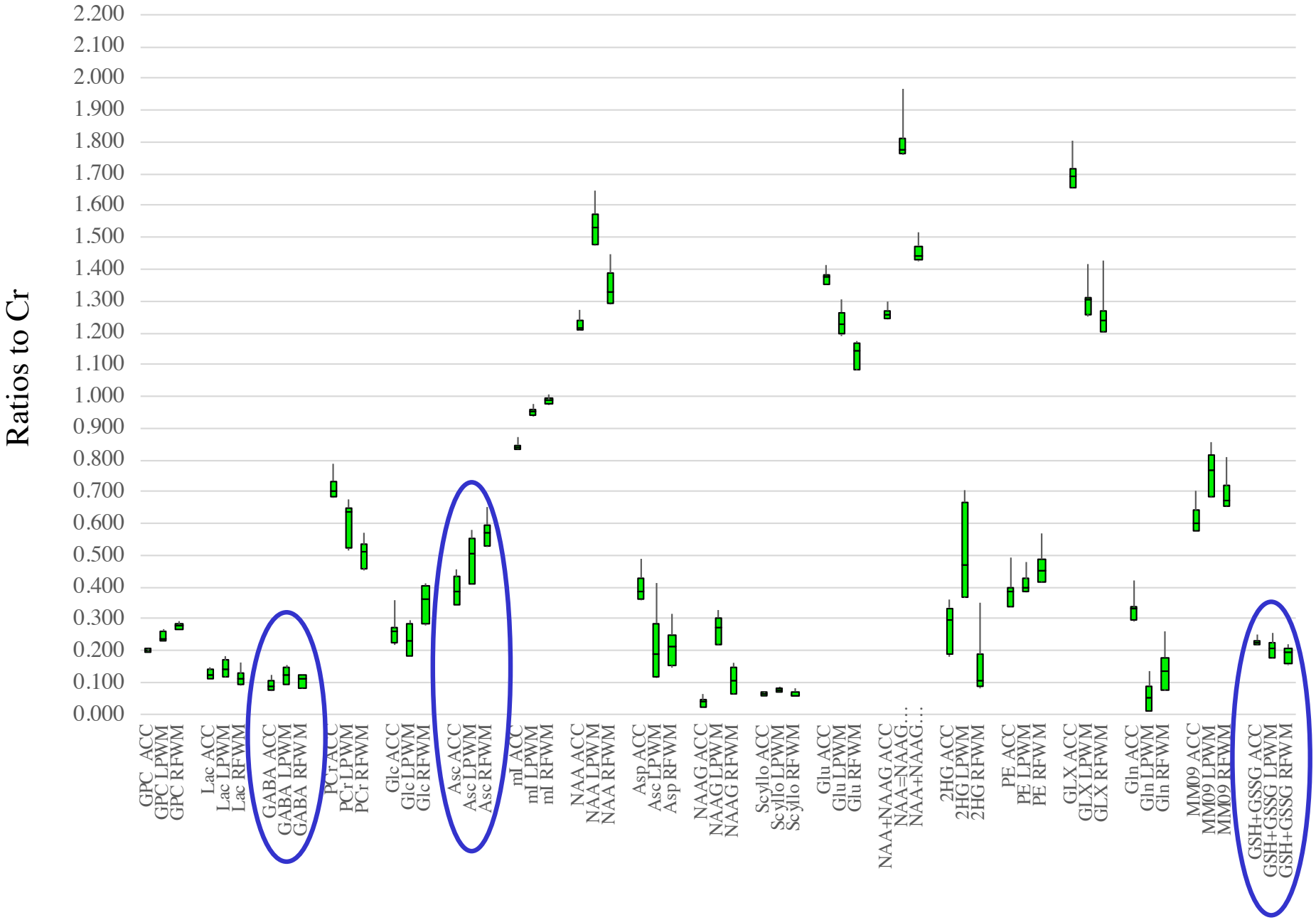
# Our Recent $^{1}$H-MRS Findings

- We have modified a standard short-TE single-voxel PRESS acquisition
  - Narrowband water suppression
  - Improved quantification using measured rather than simulated metabolic basis spectra.
- Now confident that we can robustly measure GSH and Asc (and probably GABA also)




Example: ACC, 18 x 18 x 18 mm3 voxel, TE/TR=35/2000 ms, 64 Avg, 2:56 min total scan time, with excellent repeatability.

# Repeatability Study



# Prostate Cancer – Key Points*

- High incidence; a leading causes of death in men.
- The sensitivity and specificity of diagnosing prostate cancer with conventional imaging methods (ultrasound, MRI) is relatively low.
- The normal prostate contains high levels of citrate (Cit) which can be detected in the proton spectrum at 2.6 ppm. Other compounds detectable in vivo include creatine, choline, spermine, and lipids.
- Citrate is a strongly coupled mutiple at 1.5 and 3.0 T. For optimum detection, careful attention to pulse sequence parameters (TR, TE) is required. TE 120 ms is commonly used at 1.5 T, and TE 75–100 ms at 3 T.
- Multiple studies have reported that prostate cancer is associated with decreased levels of citrate and increased levels of Cho, compared to both normal prostate and also benign prostatic hyperplasia (BPH).
- MRS and MRSI of the prostate is technically challenging: water- and lipid-suppressed 3D- MRSI is the method of choice for most prostate spectroscopy studies.
- Some studies report that adding MRSI to conventional MRI increases sensitivity and specificity of prostate cancer diagnosis.
- MRSI is traditionally performed with an endorectal surface coil, but acceptable quality data may be obtained at 3 T with external phased-array coils which are more comfortable for patients.

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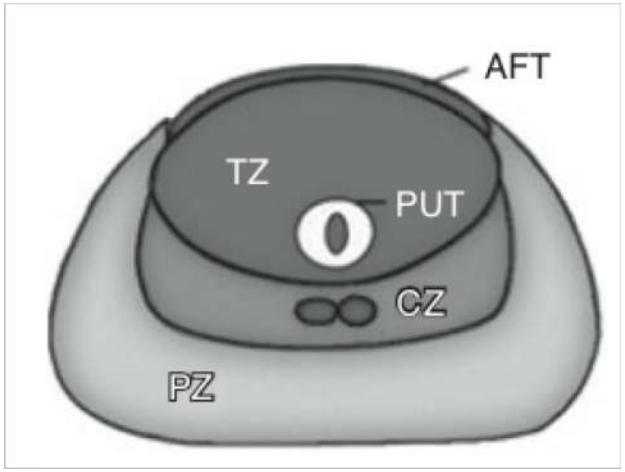
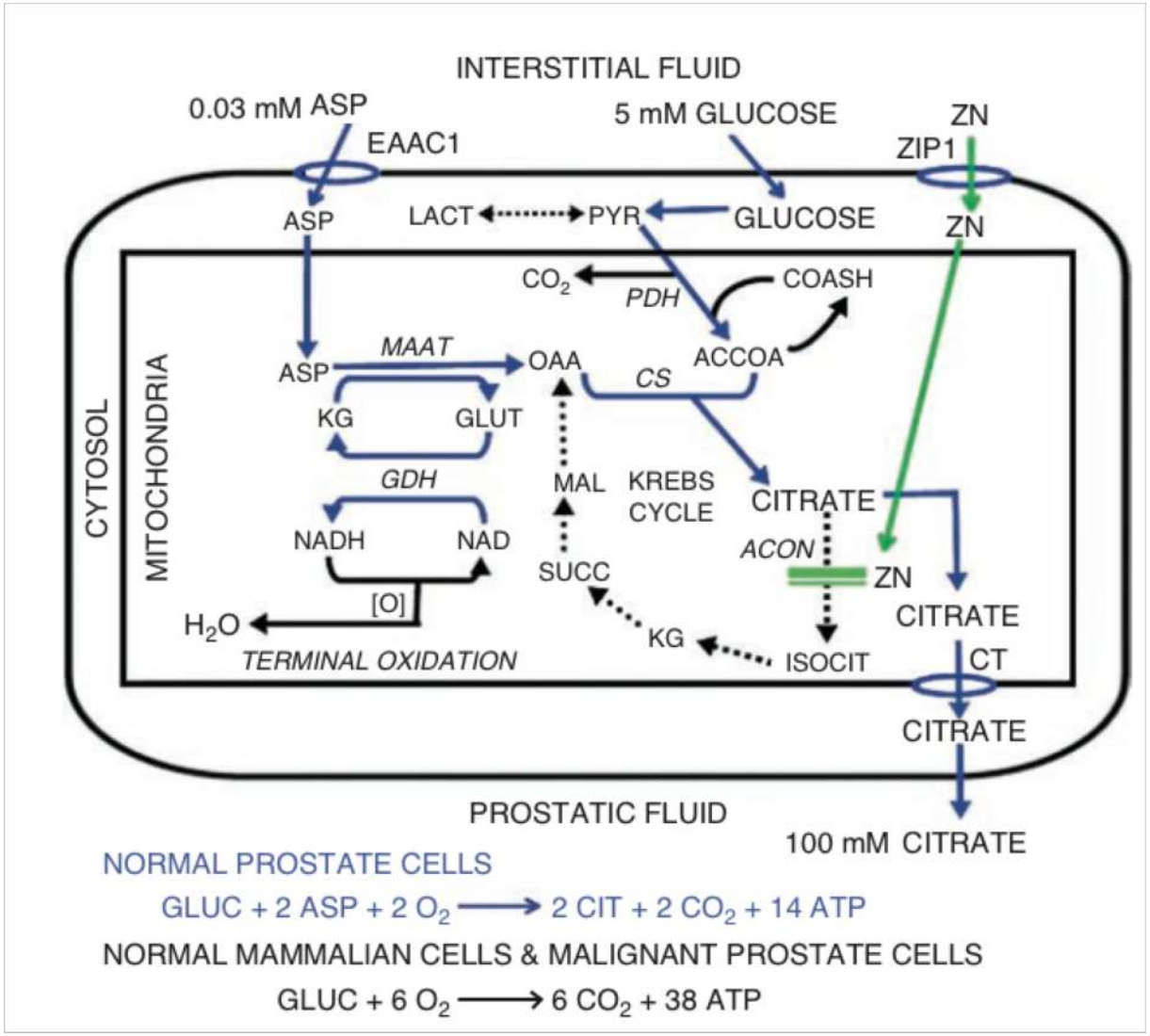
# Prostate Anatomy and Metabolism




Prostate gland in the axial plane. PZ, peripheral zone; CZ, central zone; TZ, transitional zone; U, urethra; AFT, anterior fibromuscular tissue; UT, periurethral tisue; ED, ejaculatory duct; NVB, neurovascular bundle; SV, seminal vesicles; B, bladder; P, prostate.

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# Prostate Cancer: $^{1}$H MRS Exam

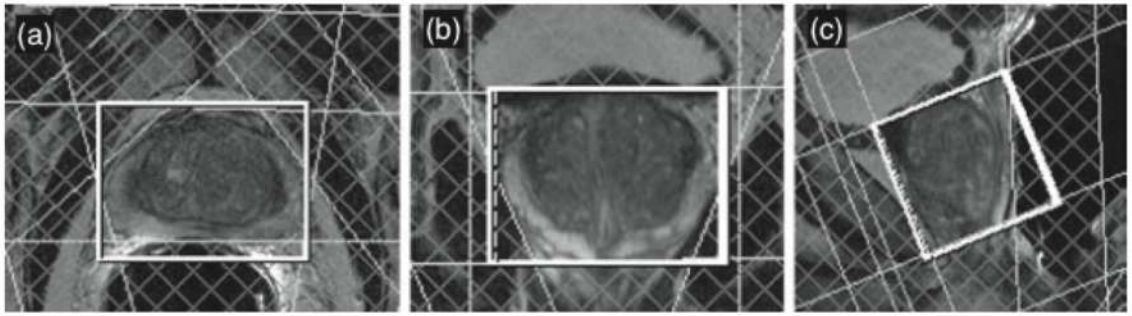


**Figure 12.5.** Multiple spatial saturation pulses are used in the (a) axial, (b) coronal, and (c) sagittal plane to conform to the shape of the prostate to minimize off-resonance artifacts in the resultant spectra. The white rectangular box shows the bounding box for the prostate and the hashed lines represent the saturation slabs that are used to shape the prostate.

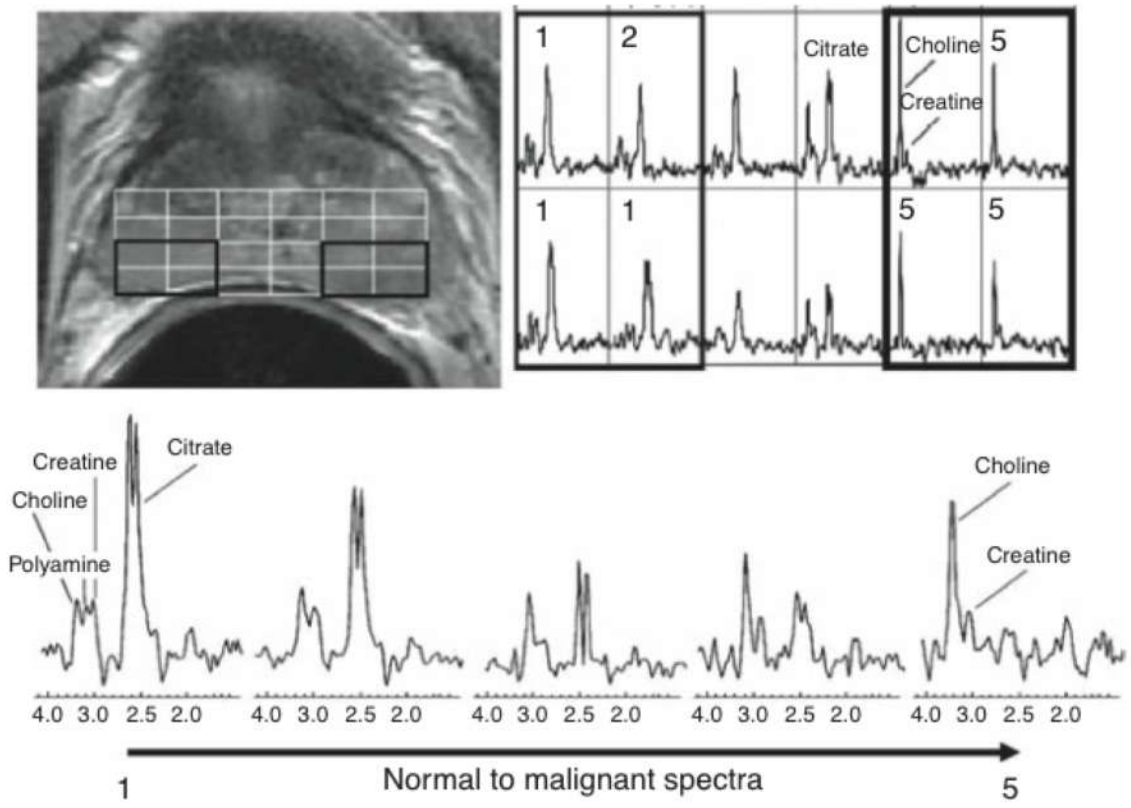


**Figure 12.6.** Scoring methodology employed by the University of San Francisco researchers for the interpretation of the prostate spectra that takes into consideration the role of polyamines. A score of 1 is considered normal prostate tissue, whereas a score of 5 indicates malignant prostate tissue whose [Cho+Cr]/Cit ratio is greater than four standard deviations from the normal ratio of $0.22 \pm 0.13$. From [74], with permission.

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# Prostate Cancer: Treatment Response

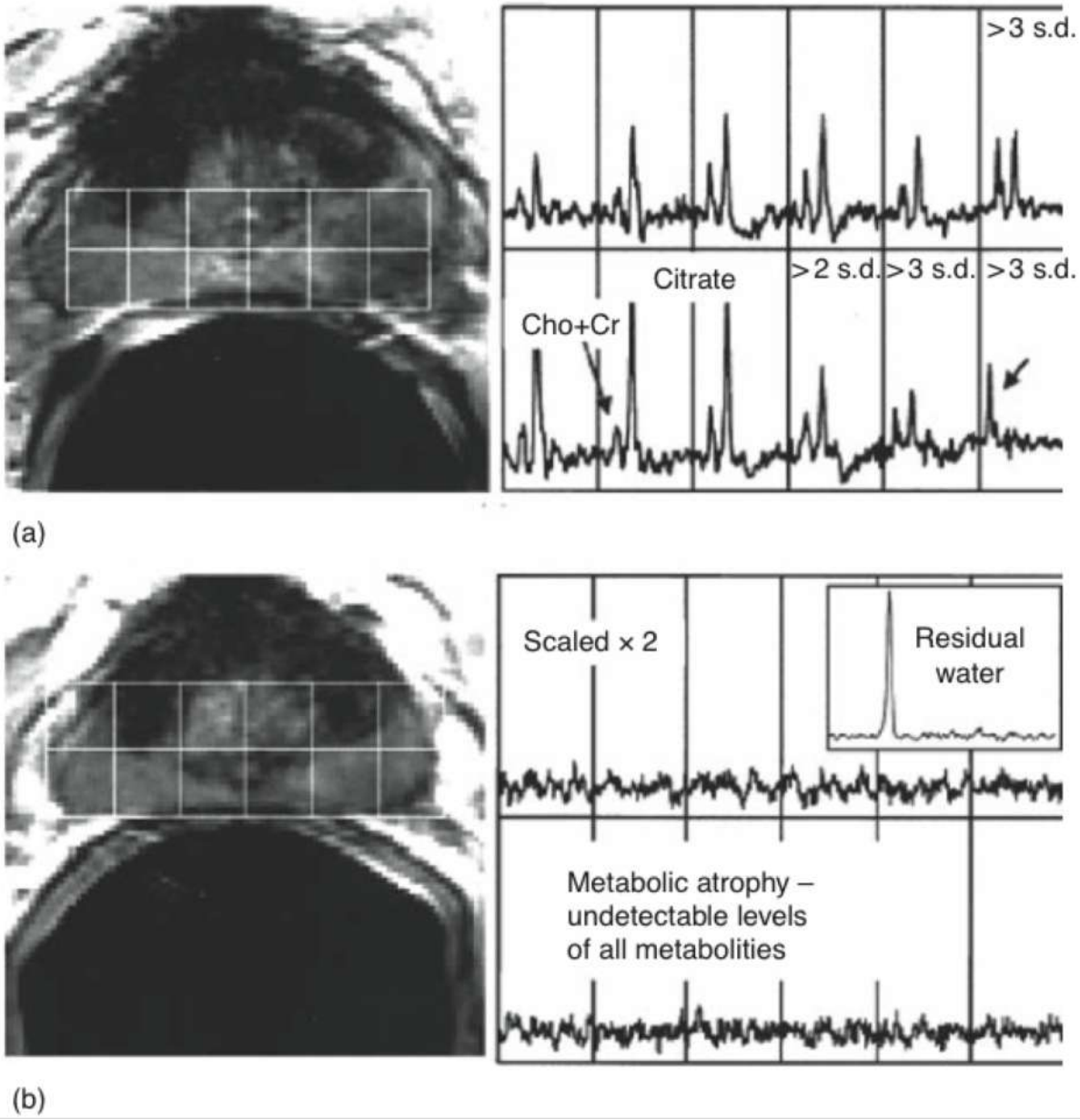


**Figure 12.4.** Metabolite concentrations (a) before and (b) ~3 years after external beam radiation therapy. Note the increase in (Cho+Cr)/Cit ratio in the left peripheral zone. Complete metabolic atrophy is seen after radiation therapy which may be mistaken for failed exam. The quality of the exam can be confirmed by verifying the linewidth of the residual water peak which confirms metabolic atrophy. From [67], with permission.

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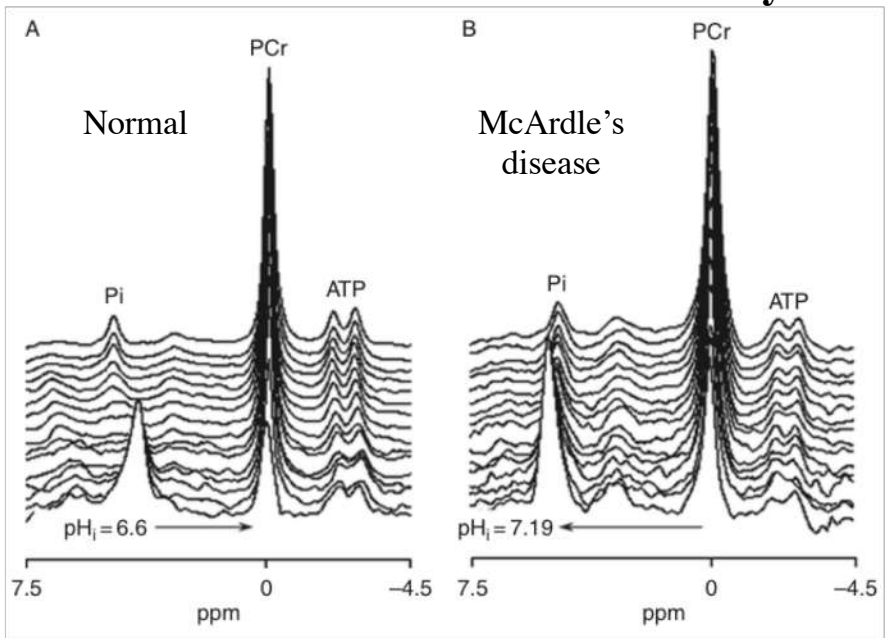
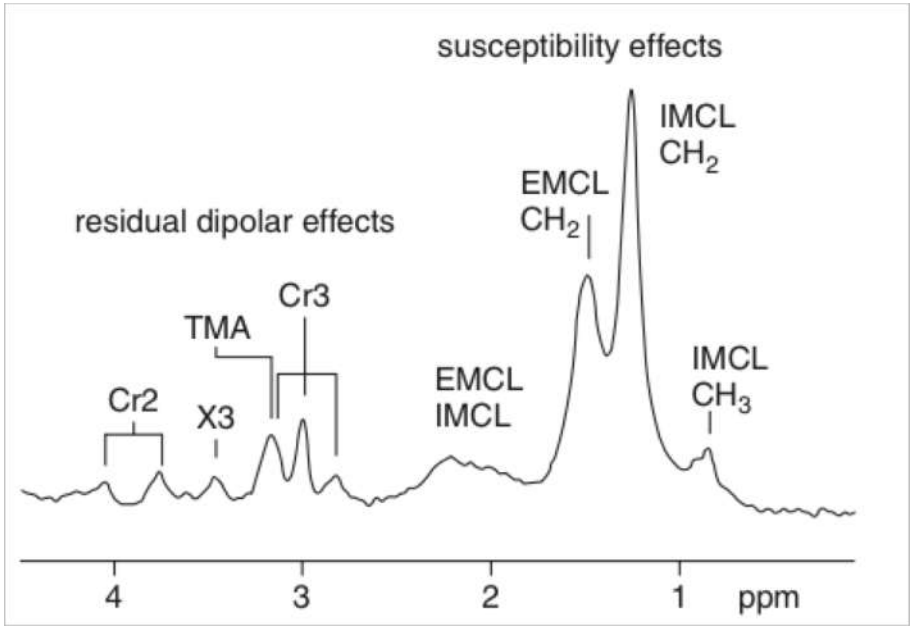
# MSK – Key Points*

- $^{31}$P-MRS detects metabolites central to energy metabolism and is valuable in monitoring therapeutic response in a number of neuromuscular disorders.
- $^{1}$H-MRS of muscle has a limited clinical role, but is used as a research tool to assess intramyocellular lipid, e.g insulin resistance and type 2 diabetes mellitus.

**$^{31}$P-MRS: Exercise and Recovery**




**$^{1}$H-MRS: anterior tibialis**

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# Next Lecture:
# Current Research Topics in $^{13}C$ MRS