Alcohol transport and MRS visibility in the brain

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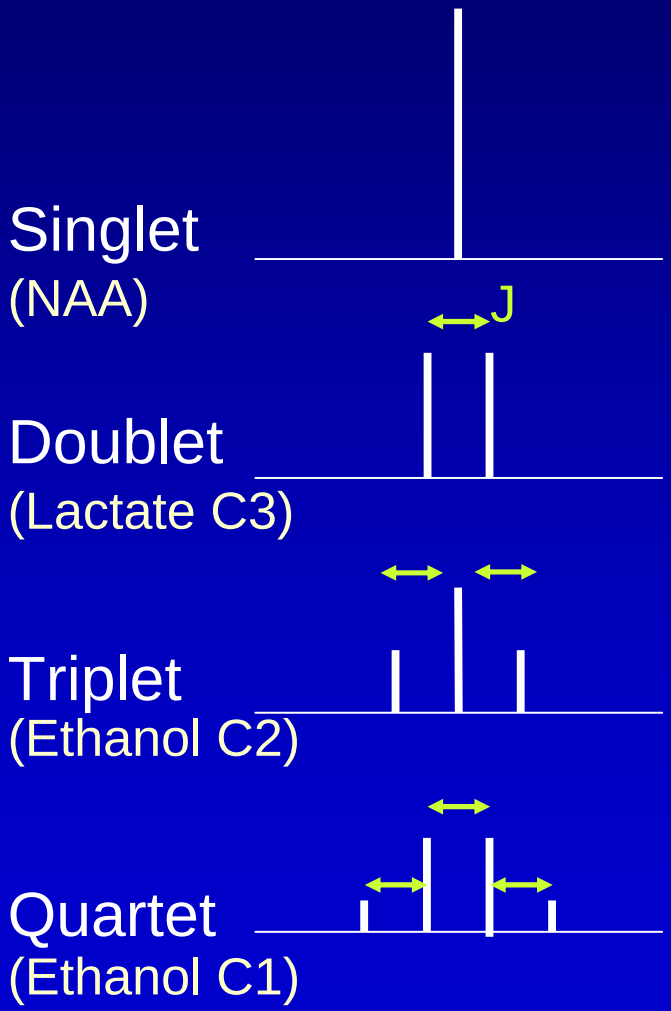
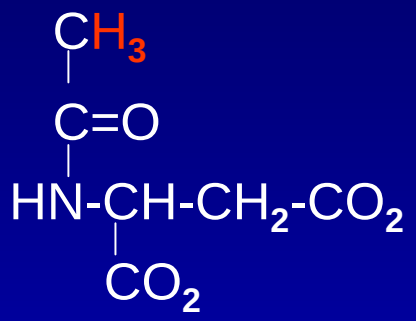
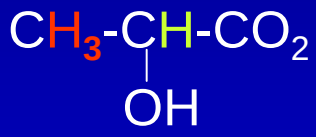
NMR Studies of Alcohol Visibility and Tolerance

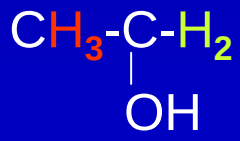
- Alcohol use shows acute tolerance (more impaired on ascending limb of uptake/clearance curves).
- Chronic abusers show tolerance (at higher blood/brain levels less impaired than moderate users).
- Initially hypothesized that alcohol acts by disrupting membranes.
- NMR studies (1985 - 1998) report :
  - Rose, Moxon, Mendelson, Chiu, Kaufman 20-30% visible
  - Spielman (40-70%), Meyerhoff (50-70), Petroff (100%) visible
  - Acute tolerance shows increased visibility at long TE (Kaufman)
  - Chronic tolerance shows increased visibility at short TE (Chiu)
- Decreased visibility believed to be alcohol interacting with membranes and transmembrane proteins

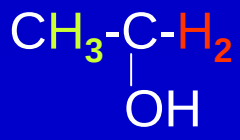
J-Coupling


Singlet
(NAA)
J
Doublet
(Lactate C3)
Triplet
(Ethanol C2)
Quartet
(Ethanol C1)

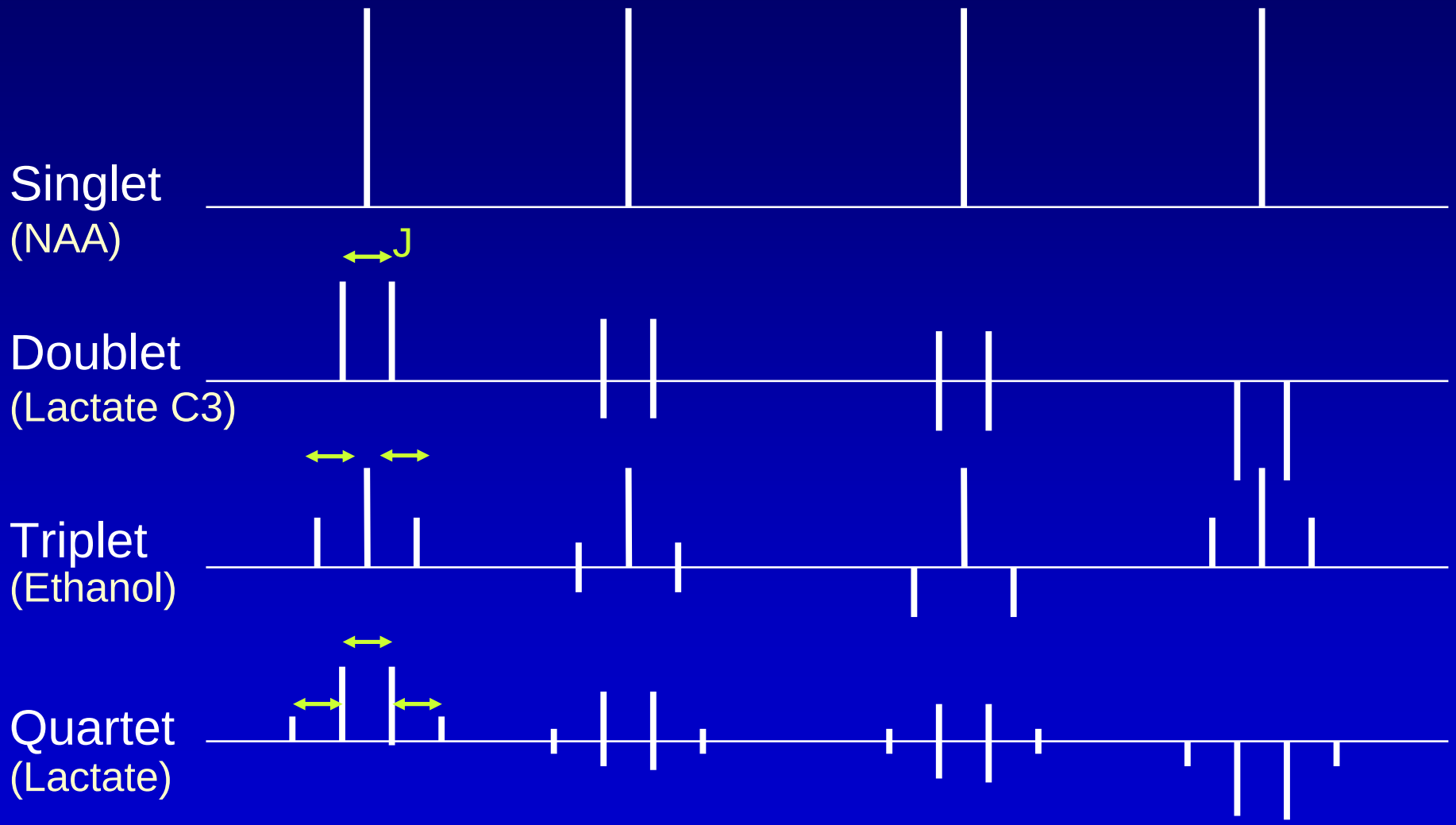

CH3
C=O
HN-CH-CH2-CO2
CO2


CH3-CH-CO2
OH


CH3-C-H2
OH


CH3-C-H2
OH

J-Modulation



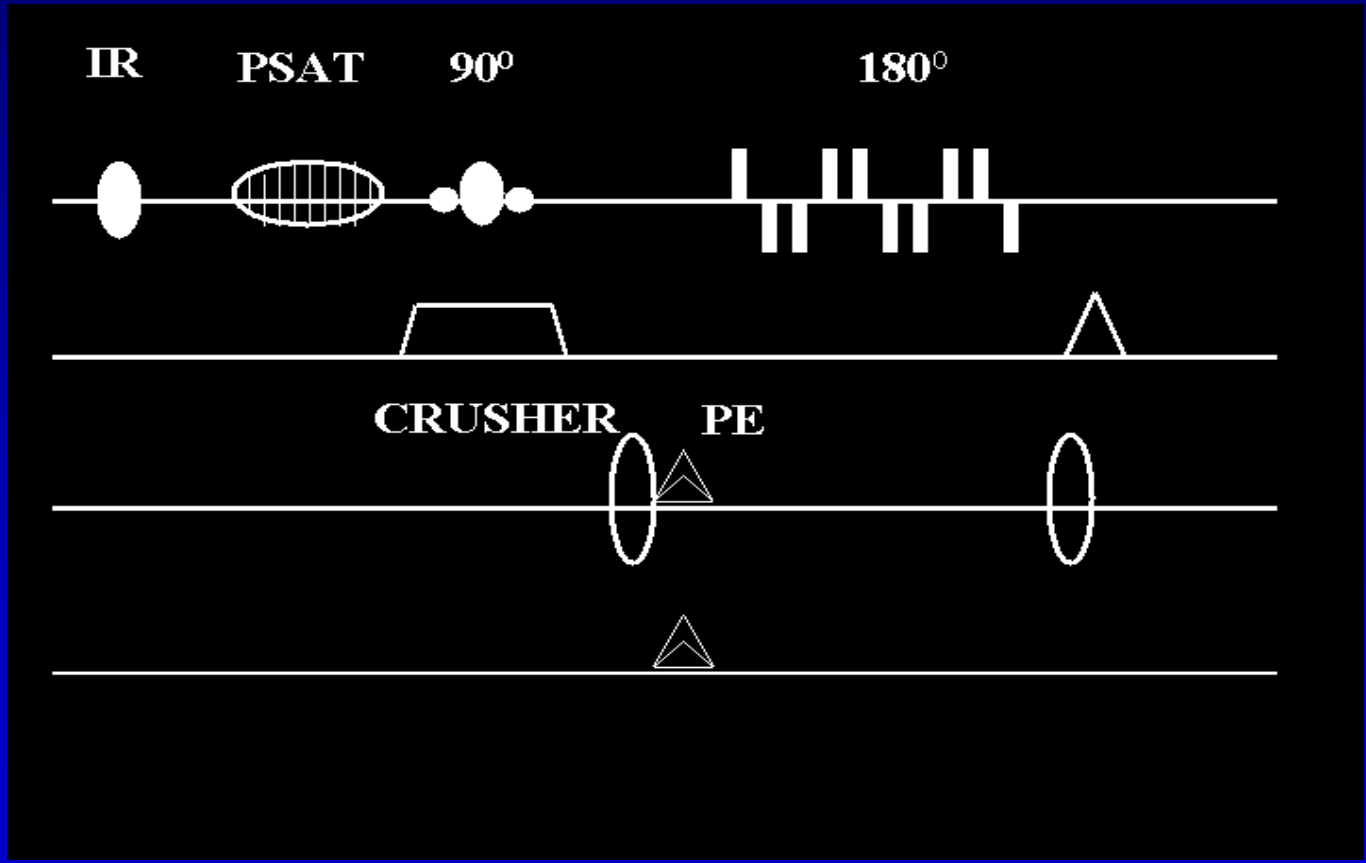
NMR Studies of Alcohol Visibility and Tolerance

- Previous work was methodologically limited
  - J-modulation of alcohol resonance not accounted for.
  - Data was acquired at long TE, differential T2 losses.
  - Choice of internal reference was incorrect (7 v. 10 mM).
  - Correct for partitioning of alcohol to GM,WM,CSF and blood.

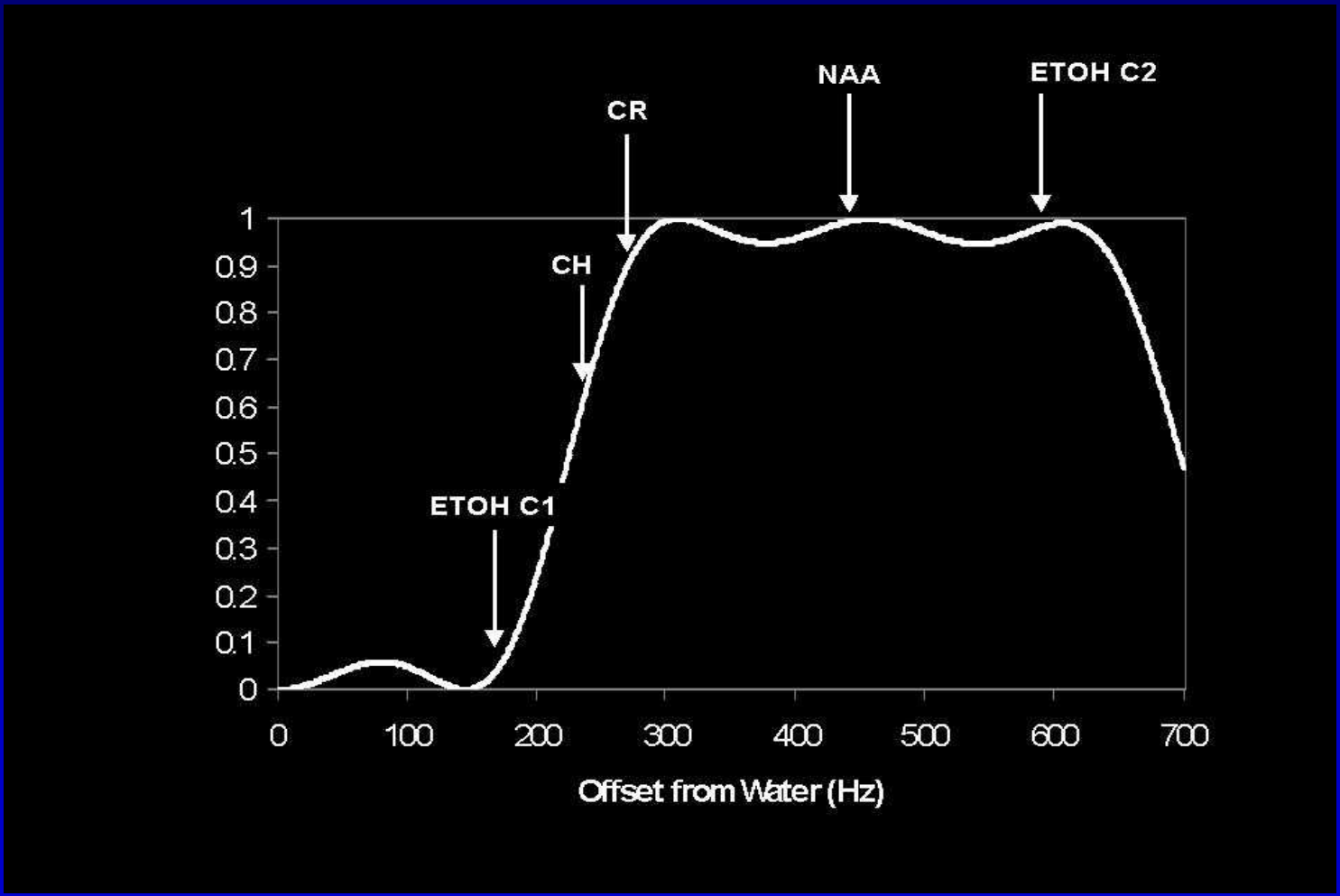
Pulse Sequence

- Eliminate/Reduce J-modulation by use of semi-selective refocusing pulses
- Minimize TE by use of short echo and inversion recovery sequence to minimize lipid contamination and macromolecule contamination
- Use 10.2mM NAA reference and correct for CSF inclusion
- Correct for fraction of water in GM (85%), WM (70%), CSF (100%) and Blood (80%).

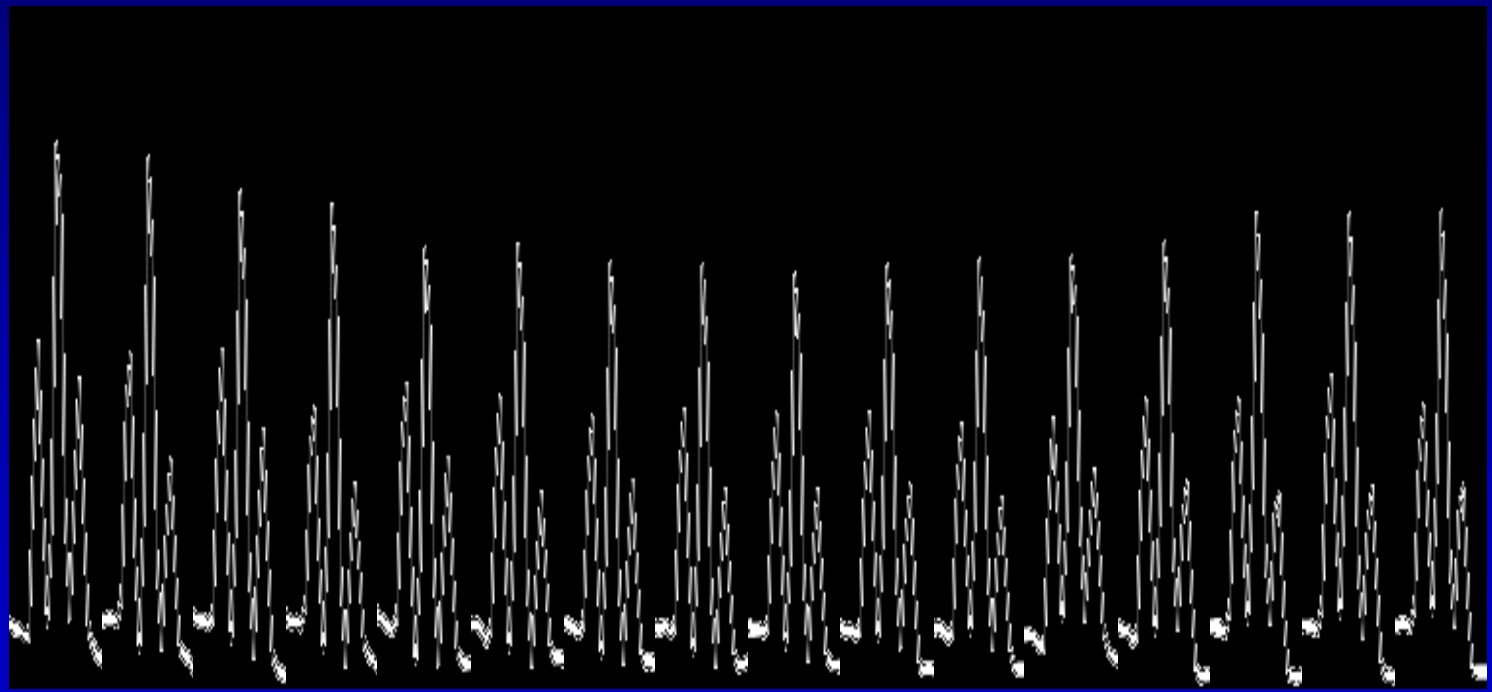
Pulse Sequence



Semi-selective Profile



J-Modulation



24 40 56 72 88 104 120 136 152 168 184 200 216 232 248 264

Protocol

- Place subject in magnet, select plane along cingulate gyrus
- Acquire scouts, quantitative T1 images and baseline image spectroscopic image (16x16) TE= 24ms
- Subject drinks 0.5g/kg etoh in 355ml sugar/caffeine free beverage
- Acquire spectroscopic images (16x16) 8.5 min
- Collect venous blood samples in 10min intervals
- Acquire data for 90min post drinking

Time Course Brain ETOH

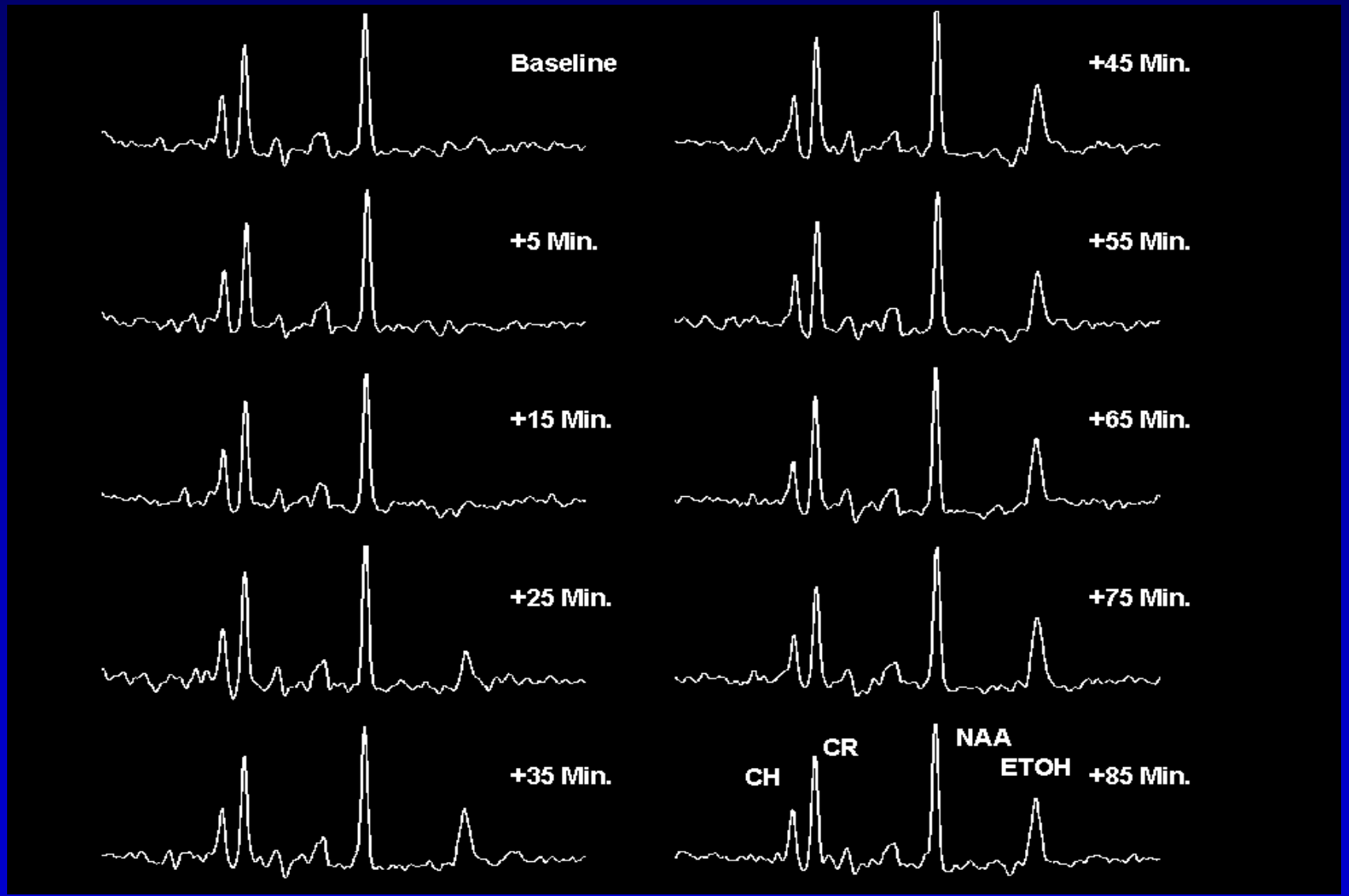
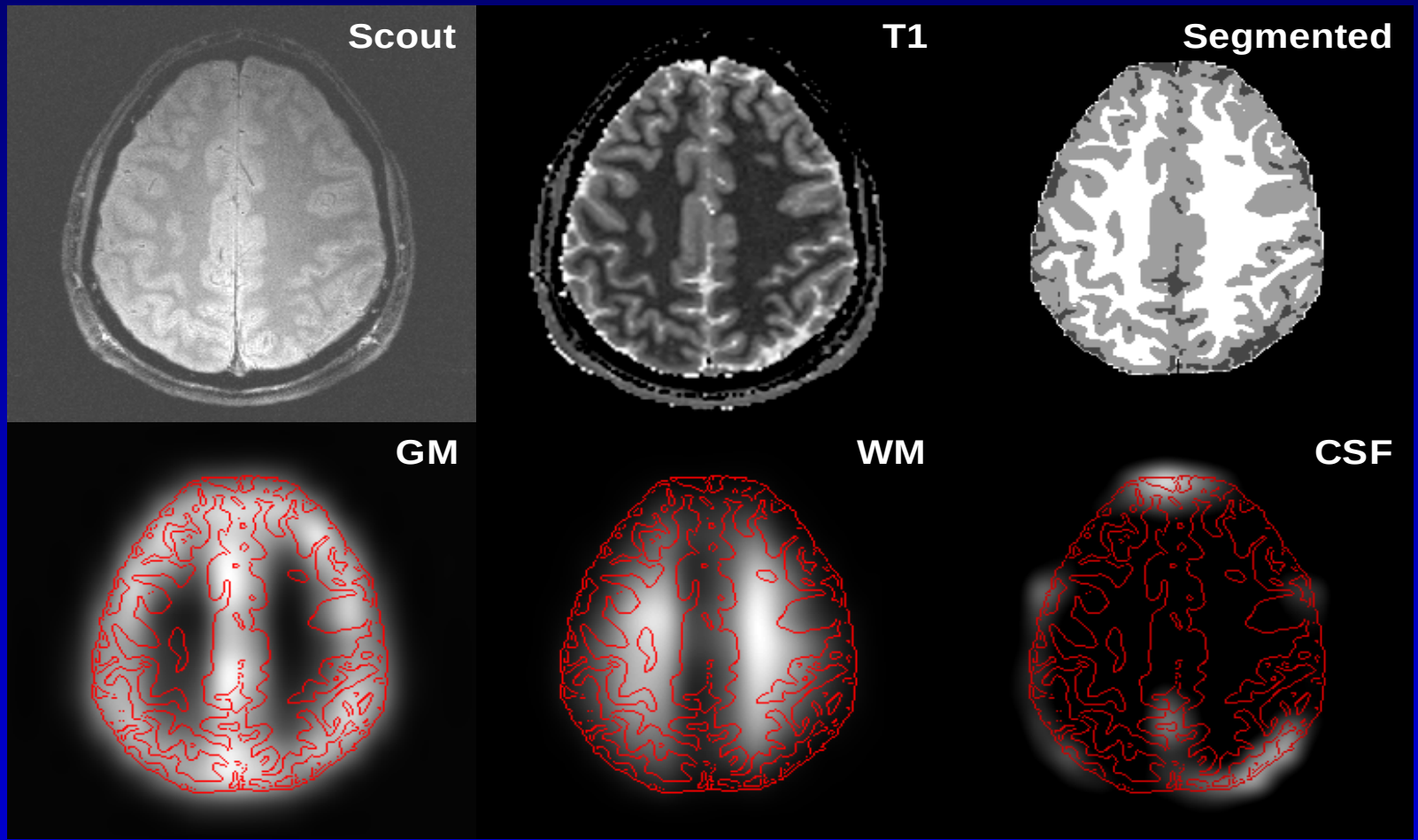
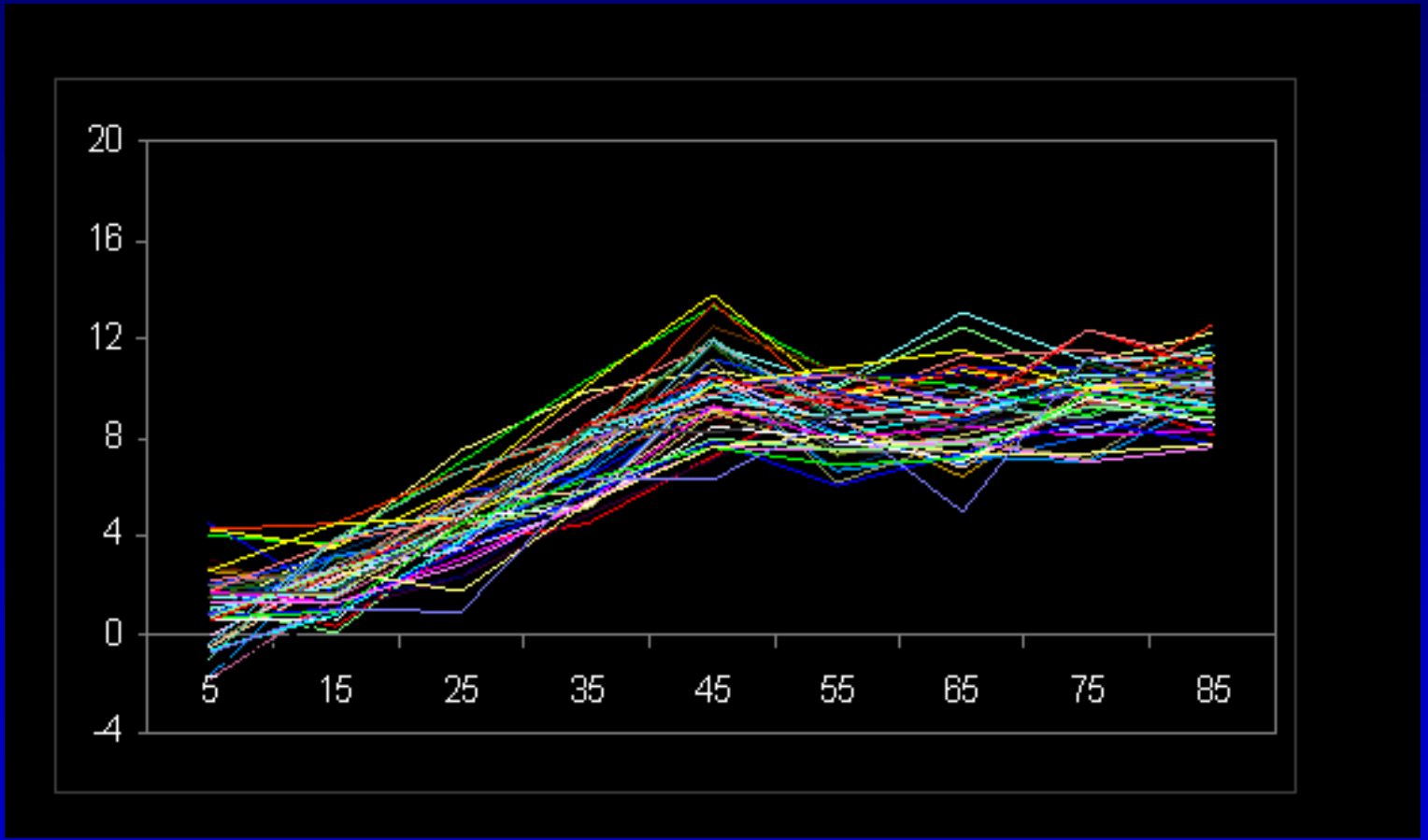


Image Segmentation



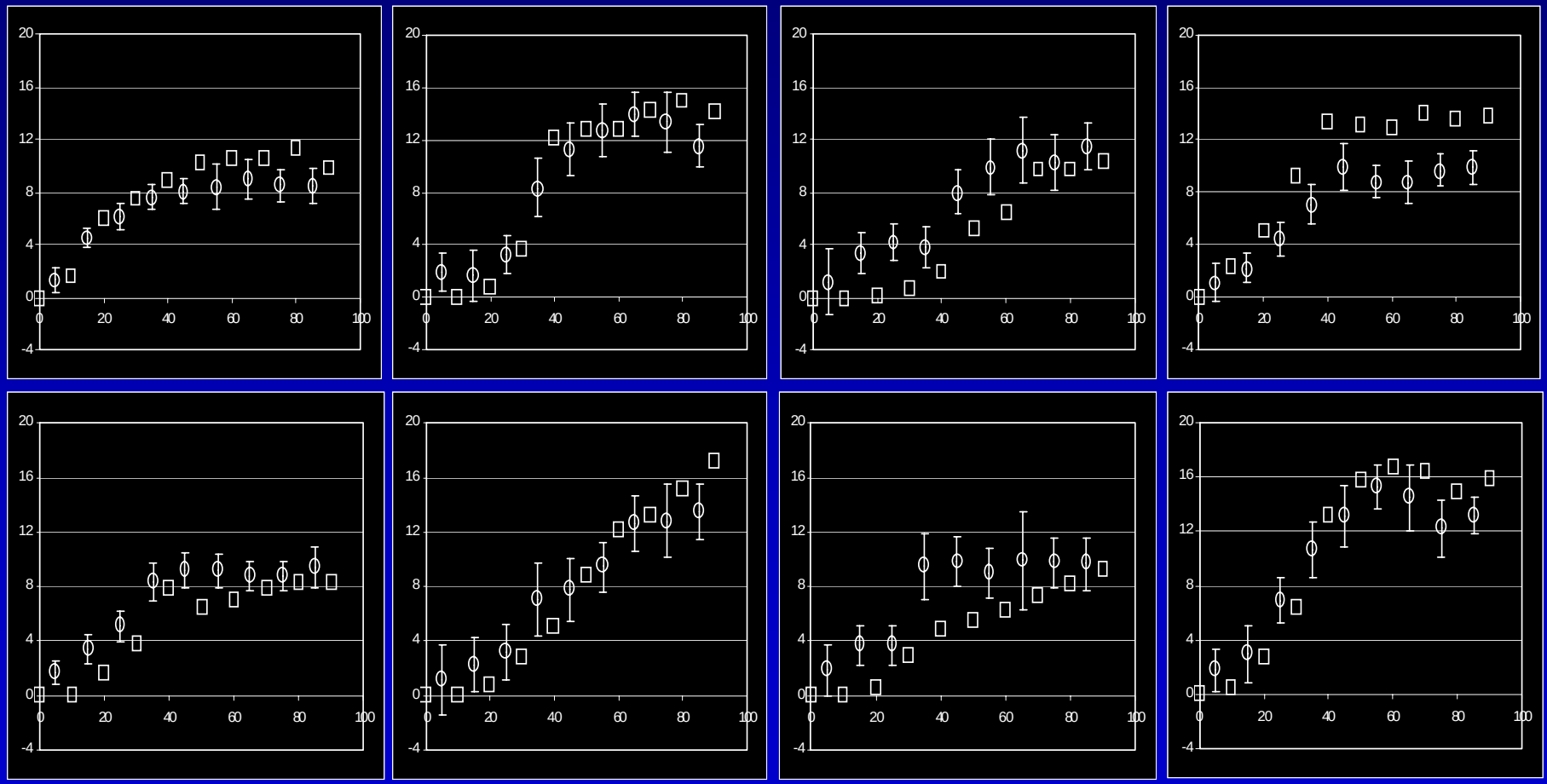
Time Course Brain ETOH



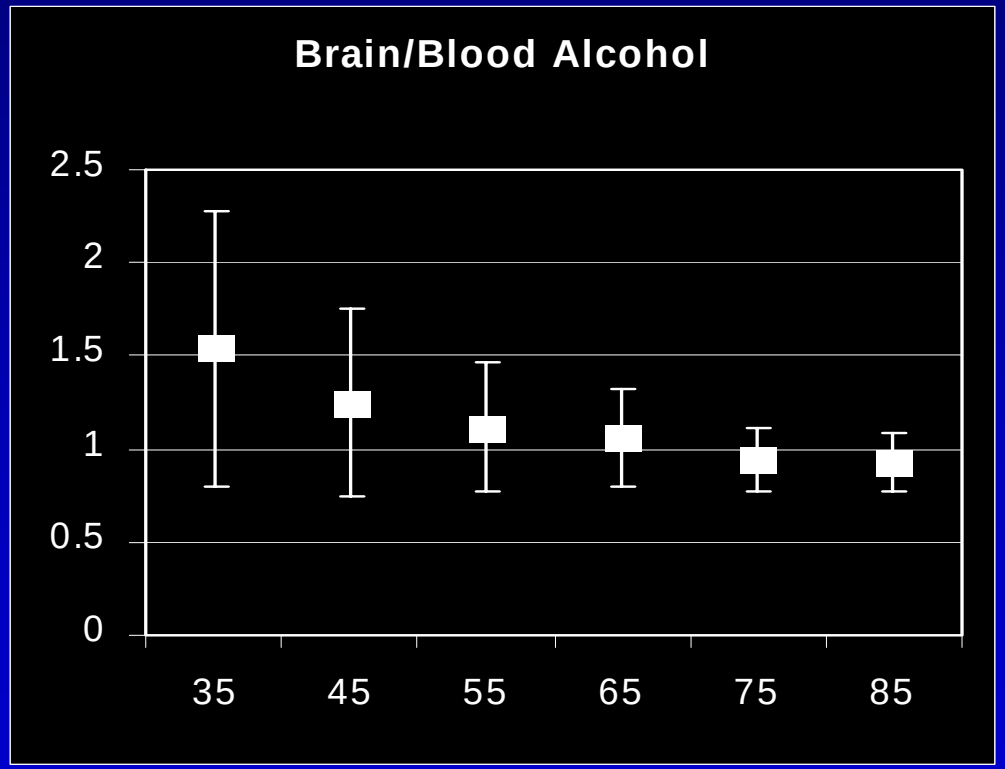
Data Analysis

- Fit ^{1}H spectra using singlet gaussians for CH,CR,NAA and triplet gaussian for ETOH (A_{naa},A_{etoh}).
- Reference ETOH area to NAA area 10.2mM.
- Correct ETOH area for 10% loss due to residual J-modulation 1.1)
- Correct for tissue composition
  - $[ETOH] = [NAA_{ref}]* 1.1 * A_{etoh}/A_{naa} *X_{water}$
  - $[NAA]_{ref} = 10.2/(X_{gm}+X_{wm})$
  - $X_{water} = 1/(1.0*X_{csf} + 0.85*X_{gm} + 0.70*X_{wm})$

Brain Ethanol Time Course



Brain/Blood ETOH Time Course (n=8)



Conclusions

- The visibility of brain ethanol is approximately 100%.
- Previous studies of brain alcohol which minimized ETOH J-modulation (Spielman, Meyerhoff) used long echo times.
- T2 of ethanol may be shorter than that used in previous calculations
  - Rose 330ms T2
  - Spielman 350ms T2
  - Meyerhoff 200ms T2
- All previous T2 measurements made with 3 time point with shortest time of 136ms.
- Increased visibility reported by Kaufman in long TE data may be due to a change in T2.

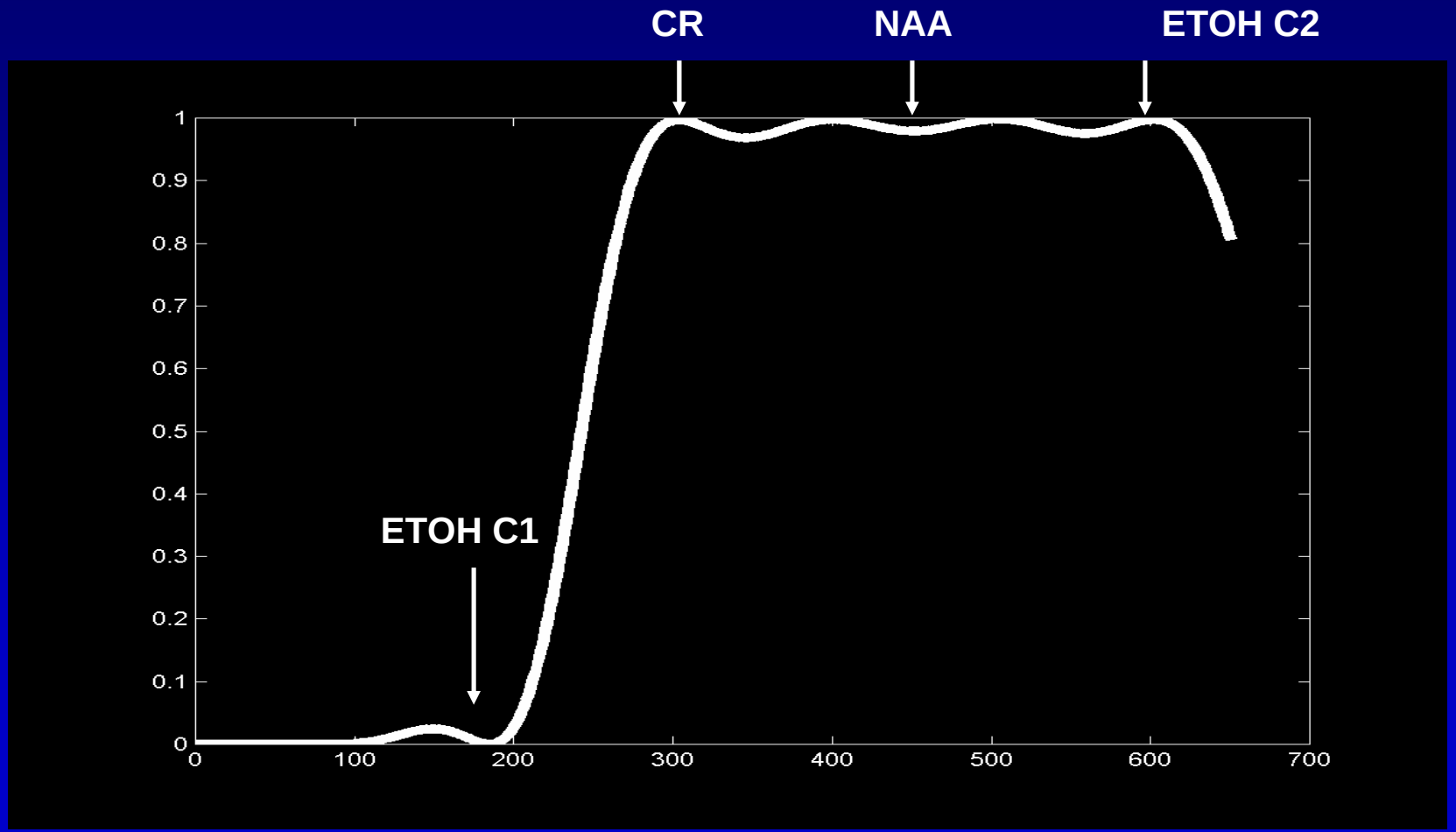
T2 Measurements of Brain Alcohol

- Need to acquire as many time point as feasible
- Need to acquire first echo time as short as possible
- Need to completely eliminate J-modulation
- Assess GM,WM and CSF differences

Pulse Sequence

- Acquire 16 TE values 30-280ms, exponential sampling
- Improved refocusing pulse, completely eliminates J-modulation
- Acquire 8x8 CSI 16.2x16.2 FOV
- Acquire quantitative T1 images for image segmentation

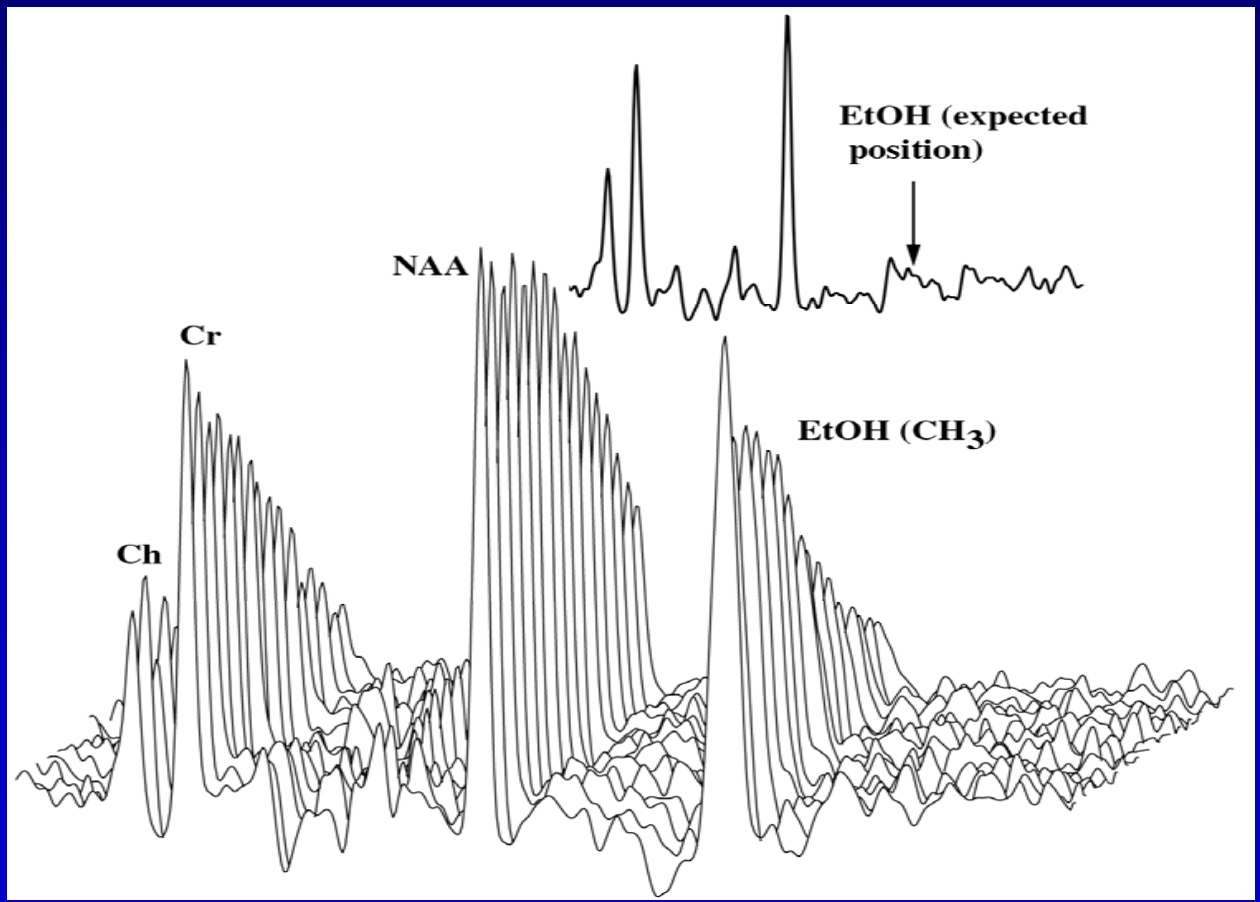
Frequency Dependence



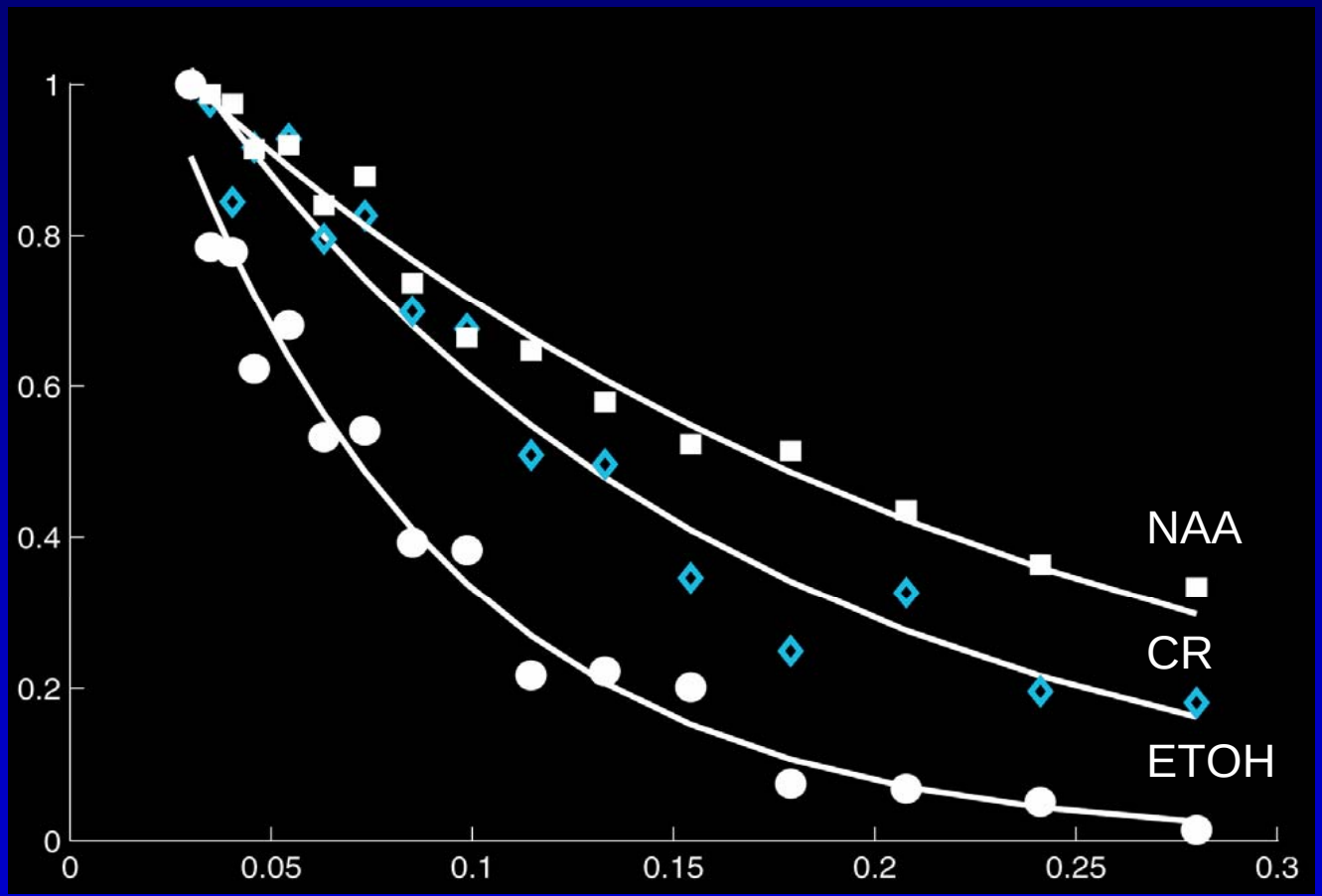
Protocol

- Position subject, select cingulate gyrus
- Acquire scout, and quantitative T1 images for image segmentation
- Subject drinks 0.75g/kg in 355 ml of sugar/caffeine free beverage 3-7minutes
- Acquire 16x16 spectroscopic images for 60 minutes along with blood samples (10 min. intervals)
- Acquire 8x8 16TE SI to measure T2 (34 min duration)
- Acquire final 16x16 SI

T2 Measurement



T2 Measurement



T2 Measurement

Subj	CR	NAA	ETOH
1	157±19	232±19	96±13
2	139±16	216±25	75±7
3	141±11	226±23	86±7
4	143±14	213±15	76±6
5	142±16	204±10	81±7
Pool	**144±15**	**218±17**	**83±8**

T2 Measurement

Study	CR	NAA	ETOH
4.1T GM	140±16	227±27	
4.1T WM	141±18	233±27	
4.1T GM	149±10	232±15	
4.1T WM	143±8	228±26	
4.0T	142±13	184±24	
4.0T	**144±15**	**218±17**	**83±8**
1.5T	240	450	

ETOH T2 as a function of Tissue Type

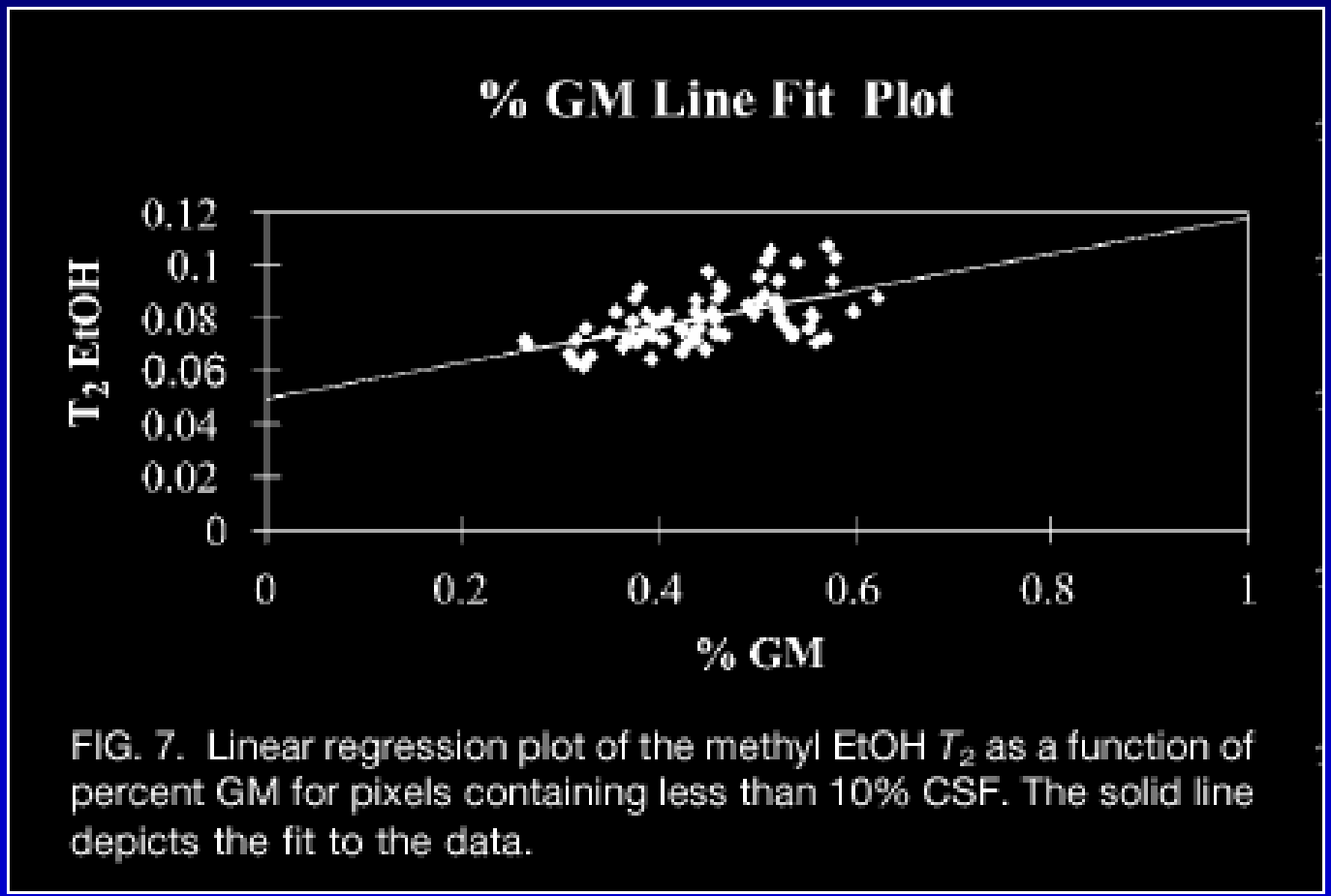


FIG. 7. Linear regression plot of the methyl EtOH T_2 as a function of percent GM for pixels containing less than 10% CSF. The solid line depicts the fit to the data.

Conclusions

- Brain ethanol T2 is 83±8ms significantly shorter than previously measured at 1.5T.
- T2 of brain ethanol is significantly shorter than NAA and CR, suggesting additional mechanisms of relaxation (membrane/protein interactions).
- Preliminary regression analysis suggests WM T2 < GM T2 < CSF T2 (57±17, 110±20, and 200-300ms).
- Projecting to 1.5T suggests brain ethanol T2 would be 154ms, consistent with Meyerhoff (200ms).

Acknowledgement

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