Correlation Between MEG Gamma Phase Locking and 1H-MRS Determined Temporal Lobe GABA in Subjects With Schizophrenia and Normal Controls
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INTRODUCTION
Magnetoencephalography (MEG) recordings of neural oscillations of the gamma band (~40 Hz) phase locking factor (PLF) yield a number that measures how well the response coincides with the stimulus in time. Numerically, values range from near zero for random phase trials to one for completely synchronized trials1. Previous studies have suggested MEG determined auditory evoked gamma band phase locking may index neocortical GABAergic inhibitory interneuronal activity. Last year, we reported preliminary results showing correlation between the PLF and levels of MRS–measured GABA in normal control subjects2. We have now added studies on schizophrenics as well as expanded the control group. The results show marked differences in the correlations between the two groups.

METHODS
MRS determined temporal lobe GABA levels and MEG evoked phase locking were determined in 9 schizophrenics (7 males, mean age = 46) and 15 normal adult subjects (9 males, mean age = 34) in good physical health using techniques described last year. Briefly, MRS GABA levels were determined for both left and right temporal lobes via J-editing subtraction techniques and a MEGA-PRESS sequence3. The GABA peak area obtained from the difference spectrum was divided by the area of the creatine peak in the edit-off spectra to produce the GABA/Cr ratio. MEG auditory gamma band responses were produced using 500 ms duration 60 db HL 1 kHz sine waves amplitude modulated by 40 Hz sine waves. Stimuli were repeated every 3.5 seconds for 200 or more trials at each ear (monaural presentation) using foam insert earpieces. Magnetic evoked fields were recorded in the supine position using a whole head neuromagnetometer (Magnes 3600 WH) while subjects watched a silent video. Details of recording and data analytic methods have been previously described4.

RESULTS
Plots of the PLF versus GABA/Cr ratio for left and right temporal cortex are shown below. The control results (in gray) show a highly significant positive correlation between the transient gamma (40 Hz) PLF and the GABA/Cr in both right (p=.03, r= 0.5) and left (p=0.005, r= .64) auditory cortex. The schizophrenics (in black) show a non-significant positive correlation (p=.15, r= 0.39) on the right side but a significant, negative correlation on the left side (p=0.006, r= -0.79). Interestingly, there were no significant differences in the overall measured GABA levels between the controls and schizophrenics. Results from short-echo time PRESS spectra (also performed) show no significant differences in creatine levels between groups.

DISCUSSION
The schizophrenic group shows no correlations between GABA/Cr and PLF in the right hemisphere, but a strong negative correlation compared to the positive correlation of the normal controls in the left hemisphere. These results suggest that it is not overall reduced levels of temporal lobe GABA in schizophrenics, but rather reduced utilization in some way (perhaps due to reduced pyramidal cell somal volume5, or dendritic spine density6, or a reduction in GABA reuptake7), that lead to the impaired auditory phase-locking capability in the schizophrenics. The equivalence of creatine levels as shown by single voxel short-echo time PRESS spectra (also performed) show no significant differences in creatine levels between groups.

REFERENCES:

SUPPORT Work supported by USPHS 1 RC1 MH 088623 and NIH/NCRR Colorado CTSI Grant Number 5 UL1 RR025780. The abstract contents are the authors’ sole responsibility and do not necessarily represent official NIH views.