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 trials[1]. 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 subjects[2]. 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.

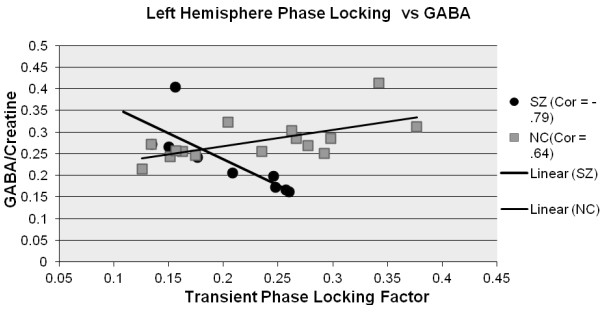
METHODS

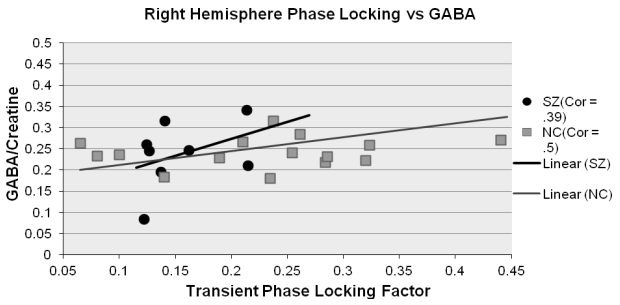
MRS determined temporal lobe GABA levels and MEG evoked phase locking were determined in 9 schizophrenics (7 males, mean age = 46) and 15 normal adult subjects (9 males, mean age = 34) in good physical health using techniques described last year. Briefly, MRS GABA levels were determined for both left and right temporal lobes via J-editing subtraction techniques and a MEGA-PRESS sequence[3]. 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 described[4].

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=0.15, 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 volume[5], or dendritic spine density[6], or a reduction in GABA reuptake[7]), 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 between both groups shows that this is not an artifactual result due to differing levels of creatine.

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