Resting neurotransmitter levels correlate with peak EEG gamma frequency and power

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Introduction: Alterations in the excitation-inhibition balance maintained by glutamatergic and GABAergic neurotransmission are thought to underly a number of neuropsychiatric disorders including epilepsy[1] and schizophrenia[2]. The balance of neuronal excitation and inhibition is also thought to determine the peak frequency of cerebral electrical oscillations in the gamma (30-100 Hz) band.[3] Resting GABA concentrations have been observed to correlate with the peak gamma frequency during visual stimulation,[4] but the relationship between neurotransmitter levels and oscillations in electrical activity at rest has not yet been explored. The purpose of this study was to explore potential interactions between GABA, glutamate, and peak EEG gamma frequency and power at rest. Based on the positive correlation previously reported between resting GABA levels and the peak gamma frequency during visual stimulation, we hypothesized that GABA would be positively correlated to gamma frequency.

Methods: The subject group consisted of fourteen healthy volunteers (7 female, mean age 29 years) with no history of neurological or psychiatric illness. MR imaging and spectroscopy studies were performed with a 3T GE HD.xt TwinSpeed MRI scanner (GE Healthcare, Milwaukee, WI, USA), using an 8-channel receive-only head coil. Four consecutive resting single-voxel MEGA-edited ^{1}H MR PRESS spectra were acquired from a 2.5x3x4 cm^3 voxel of interest in the left DLPFC with TE/TR = 68/1800 ms and 320 averages (160 pairs). Water-scaled metabolite concentrations were derived using LCModel.[5] Resting-state EEG data were acquired outside the MRI scanner (in a separate measurement session) from 60 scalp electrodes during an eyes closed rest condition. Data were sampled at 500 Hz, and bandpass filtered from 0.1 to 250 Hz. EEG processing was performed using BrainVision Analyzer (Brain Products, Munich, Germany). The Global Spectral Power (GSP) was calculated as the root mean square across all Fast Fourier-transformed (Hanning window: 10%, zero padded, resolution 0.25 Hz) scalp channels. The individual peak power and corresponding peak frequency were calculated within the lower (30-48 Hz) and upper (53-70 Hz) gamma bands, and the peak power was then log-transformed. Correlations between GABA and glutamate (Glu) and between neurotransmitter levels and peak gamma power and frequency were examined with a nonparametric Spearman's rho correlation analysis. The statistical analysis was performed with SPSS version 14.0 (SPSS inc. Chicago, Illinois, USA).

Results: A significant positive correlation was observed between the glutamate and GABA concentrations across the subject group (Spearman's rho=0.75, $p<0.01$, 2-tailed). No significant correlations were evident between GABA and the peak gamma frequency or power, but glutamate was inversely correlated to the peak gamma frequency in the 53-70 Hz range, as well as the peak gamma power (Spearman's rho=0.6, $p<0.05$, 2-tailed).

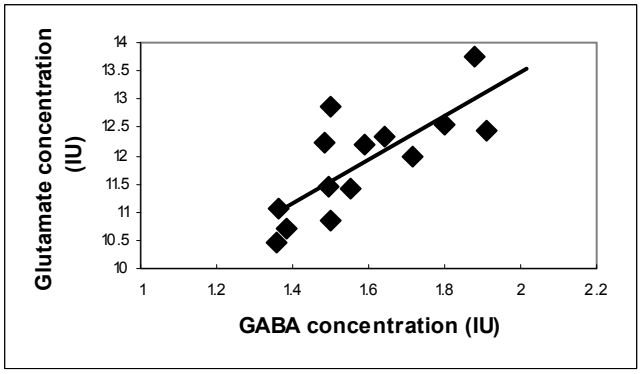

Figure 1. Inter-correlation between GABA and glutamate concentrations in the left DLPFC (rho=.75, $p<0.01$)

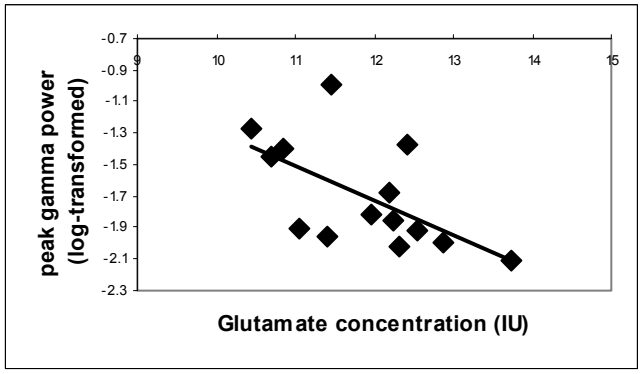

Figure 2. Correlation between resting DLPFC glutamate concentration and peak gamma power (rho = .6, $p<0.05$)

Discussion: The strong positive correlation seen between GABA and glutamate highlights the inter-dependence of excitatory and inhibitory neurotransmitter concentrations. The lack of a significant association between GABA and the peak gamma frequency may be due to insufficient statistical power, or it may be related to changes in the gamma frequency peak with a visual task, since the correlation reported previously between GABA and the peak gamma frequency was observed during visual stimulation.[4] Future studies will be necessary to further elucidate the link between gamma frequency and GABA both at rest and during stimulation. However, the correlation between glutamate and gamma frequency and power provides support for recent theories that the peak gamma frequency depends on the balance of excitation and inhibition between glutamatergic cells and GABAergic interneurons.

References: [1]Helms et al. *JNNP* 2006; 77:489-494, [2]Stone et al. *J Psychopharmacol* 2007; 21:440-452, [3]Brunel & Wang. *J Neurophysiol* 2003; 90:415–430, [4]Muthukumaraswamy et al. *PNAS* 2009; 106:8356–8361, [5]Provencher S. *MRM* 1993; 30:672-679