GABA and Gamma: GABA MRS correlates with Gamma Oscillations recorded with MEG in Visual and Motor Cortex

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Introduction: Animal and non-invasive human pharmacological studies demonstrate a relationship between cortical neural oscillations and the inhibitory neurotransmitter γ-Amino butyric acid (GABA)[1]. The present study compared visual and motor cortex gamma oscillatory activity (~40 to 90 Hz), detected with magnetoencephalography (MEG), with each subject's level of GABA in visual and motor areas, detected with magnetic resonance spectroscopy (MRS).

Materials and Methods: Eight healthy adult control subjects participated (3F, 22-45 years). Each subject underwent MEG with visual and motor paradigms designed to elicit gamma oscillations in primary sensory cortex. MEG data was recorded using a 275-channel biomagnetometer (VSM Medtech). To identify motor cortex gamma activity, participants made button responses using their right-index finger in response to a change in the color of a visually presented fixation cross. Peri-movement gamma activity was estimated by localizing contralateral motor cortex using a differential beamformer, and then source waveforms from the peak event-related desynchronization (ERD) location (15-30Hz) were used to estimate peri-movement gamma-band power (65-90Hz). For visual cortex, a small grating stimuli was displayed in the lower-left quadrant of the visual field, and subjects responded via a button press when the grating disappeared. Similar to motor gamma activity, visual gamma activity was assessed from the beamformer localized source waveform. In a separate exam, single voxel (30x30x30mm) GABA MRS was obtained using the MEGAPRESS spectral editing sequence[2], with TE=68ms at 3T (acquisition time < 13'). MRS voxels were placed based on anatomic consideration, centered on the "hand-knob" of the left central sulcus for motor areas, and in calcarine cortex for visual areas. Local high-order shimming allowed FWHM line-widths <10Hz for the unsuppressed water peak. After Fourier transformation, phase correction was applied to the un-subtracted spectra (on the Cr resonance) and propagated to the subtracted spectrum. The integral under the GABA resonance (at 3ppm) was obtained by spectral peak-fitting using a Gaussian resonance. A reference phantom of 50mM GABA was placed in the head coil with the subject and was also interrogated (using a 14x14x30mm voxel). GABA levels were estimated as the ratio of the cortical GABA integral to that of the phantom, and also with respect to an internal cortical reference NAA resonance at 2ppm. Associations were tested using linear regression in SPSS 16.0.

Results: GABA levels (whether quantified with respect to internal NAA or to the 50mM phantom) were clearly resolved and measured in all subjects in visual (e.g. Fig 1 left) and motor regions of interest (ROIs). A negative association of GABA level with age was observed for visual and motor cortex (r=-0.76, $p<0.05$; r=-0.88, $p<0.01$, Fig. 2). Similarly gamma-band activity (e.g. Fig. 1 right) was determined in all subjects (with the exception of visual cortex in a single subject). The center frequency of gamma oscillations also showed a negative association with age for both primary sensory cortices (r= -0.53; r= -0.59). Furthermore, GABA levels and gamma frequency were positively associated in both primary sensory cortices (r=0.52; r=0.69, $p=0.056$, Fig. 3).

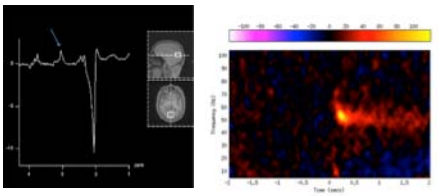

Fig. 1 (left) edited spectrum showing GABA resonance (arrow), obtained from occipital cortex voxel; (right) time-frequency spectrogram from MEG detected visual cortex activity during visual gating task. Peak gamma activity is identified by hottest color.

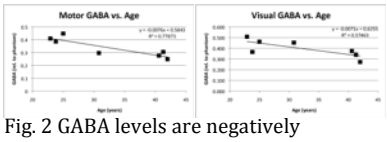

Fig. 2 GABA levels are negatively associated with age in both motor (left, $p<0.01$) and visual (right, $p<0.05$) cortex.

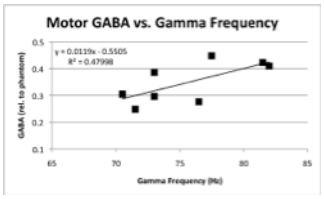

Fig. 3 positive association ($p=0.056$) between GABA levels and peak gamma-band frequency in motor cortex.

Discussion: GABA levels and gamma band activity can be resolved and localized to motor and visual cortices. Both decline with increasing age. Furthermore, GABA levels correlate positively with gamma frequency for each cortical ROI. This suggests a multimodal neurobiological probe of brain function at the neurotransmitter and electrophysiological level. Present findings also provide support for a role of GABA in the generation and modulation of endogenous rhythmic brain activity.

1. Muthukumaraswamy, S., Edden, R., Jones, D., Swettenham, J., Singh, K. *Proc. Nat. Acad Sci USA* **106(20):**8356-61 (2009)
2. Mescher, M., Tannus, A., Johnson, M.O. and Garwood, M. *J Magn Reson A* **123 (2)**: 226-229 (1996)