Examination of the GABA-BOLD relationship in multiple brain regions

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Background: Using inter-individual differences, it has previously been shown that measured GABA+ levels are is inversely correlated with task-related BOLD activity in individual, regional studies.[1-6]

Objective: To determine whether the correlations between measured GABA+ and BOLD activation generalize to multiple brain regions and corresponding relevant tasks. A range of cognitive processing tasks and regions were chosen, from lower, primary sensory processing to higher-order cognitive tasks.

Methods: GABA+ and BOLD data were collected at 3T (Philips Acheiva, 32-channel head coil) in 18 participants across two sessions. GABA+-edited MEGA PRESS data were acquired in the occipital cortex (OCC), auditory cortex (AUD), sensorimotor cortex (SM), frontal eye fields (FEF) and dorsolateral prefrontal cortex (DLPFC). Acquisition parameters included: 14 ms editing pulses applied at 1.9 ppm in the ON condition and at 7.46 in the OFF condition, TR/TE = 2s/68 ms, 320 averages with ON-OFF editing pulses alternating every 2 averages, 16-step phase cycle and VAPOR water suppression. All MRS voxels were 3×3×3 cm^3 except for the AUD voxel, which was 4×3×2 cm^3. GABA+ data were processed using the 'Gannet'[7] program and expressed relative to the brain water signal. Five runs of BOLD weighted fMRI data were acquired with a gradient-echo EPI acquisition; TR/TE = 2.5s/30 ms, 144 repetitions, 3×3×3 mm^3 voxels and were processed with a standard pipeline using 'FSL'[8] including motion correction, slice-timing correction, skull-stripping, smoothing (6mm Gaussian kernel) registration and a general linear model analysis. The tasks performed during BOLD-fMRI, for regional activation corresponding to the GABA+ measurements, were: appearance of a visual grating in the lower left quadrant, auditory white noise, sequential finger tapping, eye movement/tracking and a 2-back working memory task. All tasks stimulus duration was 2s with a jittered 10s ISI except for the working memory task which was a 30s block design. One session included GABA+-edited MRS of the OCC, AUD and SM and the corresponding BOLD tasks and the second session included GABA+-edited MRS of the FEF and DLPFC with the eye tracking and working memory task. The order of the sessions was randomized. The primary analysis correlated the BOLD peak activation localized within the MRS voxel and the water-referenced GABA+ (quantified in institutional units). The threshold for significance was set to p=0.01 to correct for multiple comparisons. Secondary analyses included examining GABA+ referenced to creatine and BOLD activation averaged across anatomical masks, significant activation maps and the entire MRS-voxel.

Results: No correlations between measured GABA+ and BOLD activation were detected in either the primary or secondary analyses.

Discussion: The measures applied are surrogates for the underlying characteristics of interest; BOLD is a surrogate for neural activation and GABA+ measurements reflects total GABA+ rather than specific GABA+ inhibitory neurotransmitter. While this study was not a strict replication of previous studies, BOLD and GABA+ acquisitions and analyses were consistent with previous work.

Surprisingly, we did not detect any correlations between regional GABA+ measurements and BOLD activation for a relevant task. The lack of observed correlation compared with previous work may indicate the original correlations are not as strong as originally observed or there are unidentified system complexities or confounds. These results reinforce the need to interpret correlative imaging studies with caution.

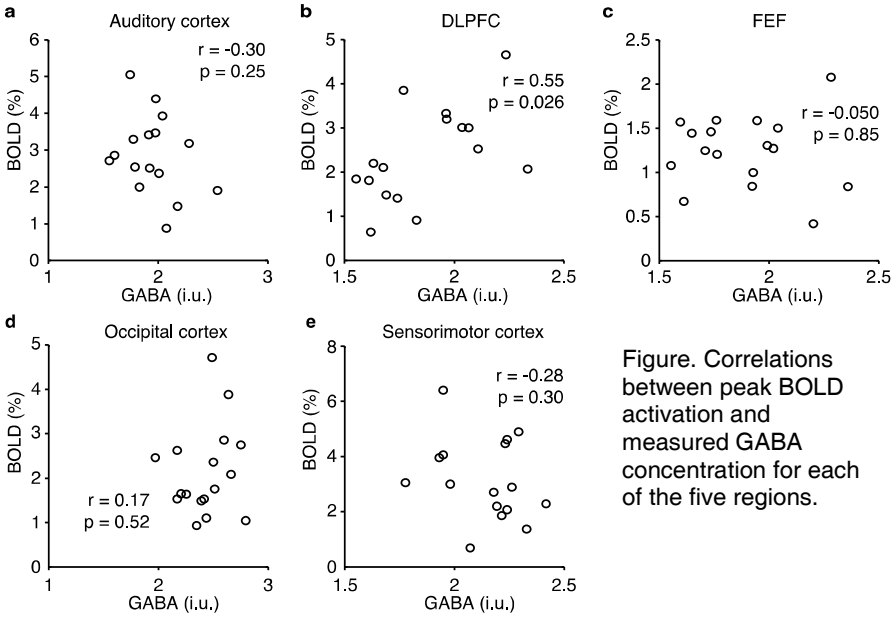

Figure. Correlations between peak BOLD activation and measured GABA concentration for each of the five regions.

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