Neurochemical and BOLD Responses in Activated Blob and Interblob Neuronal Populations Measured in the Human Visual Cortex at 7T

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Introduction. Two neuronal populations with substantially different content of cytochrome-oxidase (CO) have been reported in the primate striate cortex.[1] The CO rich "blob" neuronal population is selectively activated by chromatic visual stimuli (CHROM), whereas the neighboring "interblob" CO-poor population is activated by achromatic (ACHROM) stimuli.[1] Different CO content suggests distinct level of oxidative neuronal metabolism between blob and interblob. For instance, delayed increase of oxygen consumption was ascribed to stimulation of interblob regions by achromatic stimulus in a PET study.[2] On the other hand, the same aerobic response to CHROM and ACHROM stimulations was suggested in a recent study, where BOLD and cerebral blood flow (CBF) changes were equally correlated under either stimulation.[3] In the current study we compared neurochemical and fMRI-BOLD responses to CHROM and ACHROM stimuli that were designed to specifically activate either 'blob' or 'interblob' neurons. With the aim to exploit different metabolic properties of these two neuronal populations during activation, we used functional spectroscopy (fMRS) at 7T.[4]

Methods. The fMRS/fMRI experiments were conducted using a 7T/90cm Agilent magnet interfaced to Siemens console. Data were acquired from 12 subjects, scanned twice (24 sessions in total). Radial checkerboards, either black and white (ACHROM) or red and green (CHROM) were utilized as stimulation. Checkerboards rotated and simultaneously expanded/contracted at a frequency of 2 Hz. The contrast of ACHROM stimulation was adjusted during preliminary acquisitions to achieve roughly the same BOLD response during CHROM and ACHROM stimulation (Fig. 1a). The luminance of colors in CHROM checkerboard was matched on a subject-by-subject basis in a separate perceptive flickering experiment before each scan.[3] fMRI paradigm consisted of 7.5 s STIM and 20 s REST periods repeated 6 times. Metabolite spectra were acquired with semi-LASER (TR = 5 s, TE = 26 ms) during 25 min-long fMRS paradigm (REST-STIM-REST-STIM-REST, the first REST lasted 2.7 min, the following blocks 5.3 min each). The STIM conditions alternated CHROM and ACHROM stimuli, the order of which was randomized between sessions and among subjects. The line-width of the spectra acquired during STIM and consequent REST was matched using the line-width change measured on creatine peaks at 3ppm as described previously.[4] The resulting spectra corrected for the line-broadening effect of BOLD were then quantified with LCModel. The concentration differences between STIM and following REST were calculated for CHROM and ACHROM separately and averaged across session #1 and session #2 per each subject. Finally, the average BOLD-fMRI amplitude of CHROM and ACHROM stimuli were obtained from the same voxel used for spectroscopy.

Results and Discussion. The functional concentration changes of lactate (Lac), glutamate (Glu), and aspartate (Asp) were highly significant for both CHROM and ACHROM stimuli (Fig. 2) and were in excellent agreement with previous findings.[4,5] On average concentration changes in µmol/g (mean ± SEM) were: Δ[Glu] = 0.26 ± 0.03 and 0.32 ± 0.06, Δ[Lac] = 0.23 ± 0.03 and 0.19 ± 0.06, Δ[Asp] = -0.19 ± 0.03 and -0.19 ± 0.04 for CHROM and ACHROM, respectively. In addition, we observed a small increase of glutamine (Gln) during ACHROM stimulation (Δ[Gln] = 0.05 ± 0.02, p = 0.04). Glucose could be reliably quantified in 9 out of 12 subjects and did not reach statistical significance for CHROM stimuli. In order to confirm the neurochemical changes obtained with LCModel, we also calculated group difference spectra between rest and CHROM or ACHROM conditions (Fig. 1b) using spectra from all sessions. Average amplitude of the fMRI-BOLD signal was 2.7% ± 0.3% and 2.9% ± 0.3% (mean ± SEM) for CHROM and ACHROM, respectively, without statistical difference between conditions. Importantly, also neurochemical changes measured in the same voxel were not different between stimuli. These observations are consistent with previous findings which have demonstrated equal aerobic response to CHROM and ACHROM stimuli.[3] Finally, we observed a strong correlation between Δ[Glu] and fMRI-BOLD (Fig 3) responses (R=0.63 and p=0.001), that confirms our previous findings[4] and further supports that Glu might be considered as a probe of increased neuronal oxidative metabolism.

Conclusions: Despite different functional metabolisms might be expected between selectively activated CO-rich and CO-poor neuronal populations, our data provide no indication of such a discrepancy, thus suggesting universal nature of the neuronal metabolic response in the human visual cortex. Our findings also indicate that metabolic response is presumably not hampered by insufficient aerobic capacity.

References : [1] Tootell et al. *J Neurosci* 1988; 8**:** 1569 **[2]** Mintun et al. *Neuroimage* 2002; 16**:** 531 **[3]** Leontiev et al. *Neuroimage* 2013; 68**:** 221 [**4**] Bednarik et al. ISMRM 2014 [**5**] Mangia et al. *JCBFM* 2007; 27: 1055.

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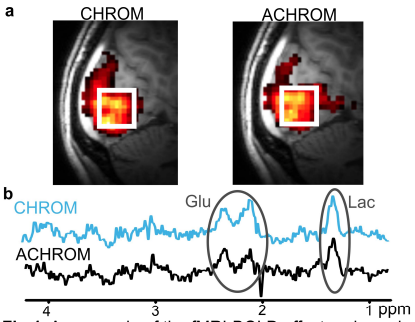

Fig 1. An example of the fMRI-BOLD effect and voxel position in one subject **(a)**. Difference spectra represent metabolic response to CHROM and ACHROM stimuli in group of 12 subjects **(b).**

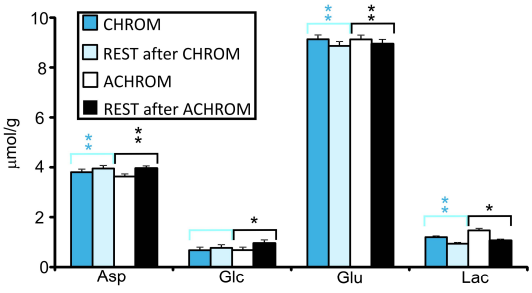

Fig 2. Concentrations during fMRS paradigm averaged across session and subjects (∗∗ p < 0.005, ∗p < 0.01, paired two-tailed t-test). Error bars = SEM.

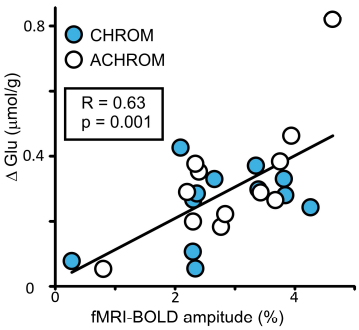

Fig.3. Correlation between the fMRI-BOLD effect and Δ[Glu] measured during CHROM and ACHROM stimulation.