fMRS of visual cortex at 3T with periodic averaging of a block design paradigm

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Target Audience: MR spectroscopists, neuroscientists, researchers interested in functional magnetic resonance spectroscopy (fMRS).

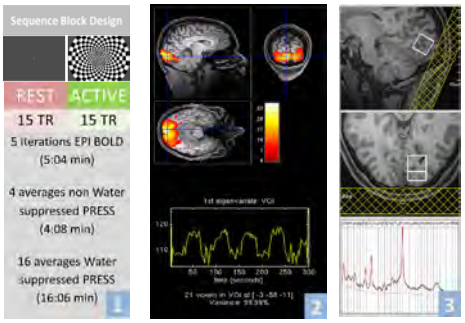
Purpose: In recent years, several studies have been performed with the aim of characterizing the relationship between neuronal activation and energy or neurotransmitter metabolism. Dynamic changes of metabolite concentrations in the human brain were already shown in response to visual, motor or auditory stimulation.[1-5] All of those studies relied on the use of prolonged stimulation periods, in the order of a few minutes. Here, we seek to introduce a novel sequence design for high-temporal-resolution fMRI and fMRS data sampling across the activity evolution of the stimulation paradigm. This approach allows to increase the time resolution up to a single TR, which would in turn exclude the regulation of astrocytes from the observed response, given their slower response (seconds or tens of seconds) compared to neuronal-neuronal communication (milliseconds).[6,7] We acquire both metabolites and water references with a paradigm such that the effect of blood-oxygenation level dependent (BOLD) is canceled out in the signals of the metabolites, which makes linewidth corrections during metabolic quantification unnecessary.

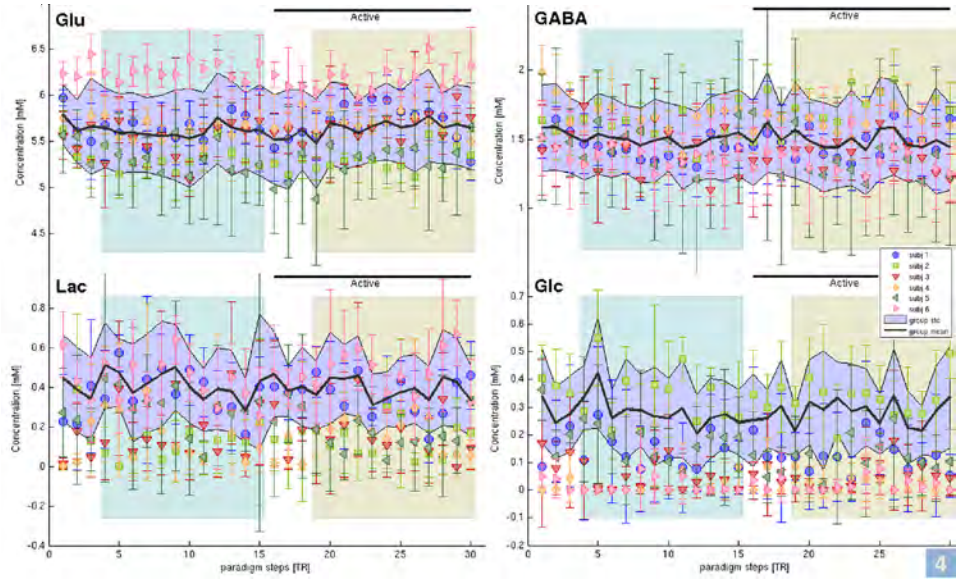
Methods: Six healthy volunteers (3 men and 3 women, aged 24 - 31 years) participated in the fMRS study. The recruiting criterion was based on the possibility of placing a well shimmed 8 mL-voxel in the visual cortex. Scans were performed on a 3T whole-body system (TIM Trio Siemens Healthcare, Erlangen, Germany) using a 32-channel receive coil. The stimulus consisted on a full-field radial 25.5% grey/black flickering checkerboard (**Fig. 1**). A block design alternating 15 TR rest (R) and 15 TR visual activation (A) was used for fMRI and fMRS (TR = 2 sec), with 5 repetitions for T2* echo-planar imaging (EPI) and 4/16 averages for unsuppressed/suppressed water spectra, respectively (PRESS, TE = 30 ms). First- and second-order shims were adjusted using FAST(EST)MAP.[9,10] A standard SPM8 processing scheme was employed to obtain the BOLD activation map, including realignment, slice-time correction and spatial smoothing using an 8-mm full-width-half-maximum Gaussian kernel. Localization of the voxel for fMRS was done by co-registration the thresholded BOLD activation map to the MPRAGE anatomical image (**Fig. 2**, top: Z-score overlaid on T1w, bottom: BOLD response). Spectra quantification was performed using LCModel[8] (**Fig. 3**, top: VOI, bottom: typical fit). The BOLD effect was canceled out by means of non-suppressed water spectra used as a water reference and taken from the same TR along the block design for each individual spectrum (**Fig. 1**). Intra subject (n = 4) and group (n = 4×6 = 24) mean and standard deviation (SD) of each metabolite's concentration were calculated. Mean values and SDs of the Cramér–Rao Lower Bounds (CRLB) of all data points for each metabolite were calculated as well. For glutamate, CRLB were 7.1 ±0.9 %SD, therefore a threshold of 20%SD was taken for the group average. CRLB for GABA were 24.1 ±9.7 %SD and a threshold of 50%SD was applied for the group average. For lactate and glucose, whose CRLB were 105.6 ±75.2 %SD and 128.4 ±78.8%SD respectively, no filter was applied.

Results: After shimming, the water linewidth was 7.43 ± 0.55 Hz. After computing the group average of each metabolite (**Fig. 4**, mean and SD were calculated for R and A conditions, excluding the data points from the first three TRs of each condition), a slight concentration increase of glutamate (R: 5.60 ± 0.06 mM, A: 5.65 ± 0.07 mM), and decrease of GABA (R: 1.50 ± 0.04 mM, A: 1.49 ±0.06 mM) and of lactate (R: 0.42 ± 0.07 mM, A: 0.39 ±0.05 mM) were observed, whereas glucose concentration remained unchanged.

Discussion: Despite the large variation, a slight increase of the glutamate concentration (not significant) was observed during activation, consistent with previous studies.[3,4] In addition, the absence of a significant increase in lactate concentration could suggest that it serves as an energy source during the relatively short activation, whereas for more prolonged activations (over 2 min) an increase of the lactate concentration has been reported.[1,3,4]

Conclusion: This approach provides the advantage of direct comparability with BOLD EPI and offers the benefit of canceling the BOLD effect for the metabolic quantification. This methodology could be improved using shorter TE sequences (e.g. 6 ms with SPECIAL), [11] at higher magnetic fields (7T), [1-5] and with motion corrected sequences, which would increase SNR and reduce the variability. Additionally, further improvements of the sequence could be considered in order to mitigate possible non-perfectly spoiled spurious signals, imperfect phase-cycling, or B_0 drift.





References and Acknowledgments: [1] Mangia, S. JCBFM, 2007 [2] Lin, Y. JCBFM, 2012 [3] Schaller, B. Neurosci Res, 2013 [4] Schaller, B. NeuroImage, 2014 [5] Schaller, B. ISMRM 2014, [6] Perea, G. Trends Neurosci., 2009 [7] DiNuzzo, M. J Neurophysiol, 2011 [8] Provencher, S.W. MRM, 1993 [9] Gruetter, R. MRM, 1993 [10] Gruetter, R. & Tkac, I. MRM, 2000 [11] Mlynarik V, MRM. 2006. Funding by EU MC-ITN "TRANSACT" and "HiMR" and by Helmholtz Alliance "ICEMED".