Metabolite concentration changes during visual stimulation using functional Magnetic Resonance Spectroscopy (fMRS) on a clinical 7T scanner

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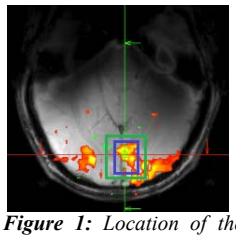

Figure 1: *Location of the voxel (blue) and the shim volume (green)*

Introduction: Functional MR Spectroscopy (fMRS) allows direct measurement of metabolic changes during neuronal activation through continuous acquisition of MR spectra, and thus can provide insight into brain metabolism. Over the last decade, previous studies suggested that lactate increases with visual stimulation, the magnitude of which, however, remains controversial. ^{1}H MR spectroscopy is a low sensitivity method which presents significant challenges for the study of low concentrated metabolites with small concentration changes (within 0.2µmol/g). A recent quantification of metabolite changes during visual stimulation was achieved with inter-subject averaging to increase sensitivity using the STEAM sequence which acquires only half of the signal intensity from a voxel [1, references therein]. The aim of the present study was to use the spin echo based sequence SPECIAL (SPin Echo full Intensity Acquired Localized Sequence) combined with the advantages of increased sensitivity and spectral resolution at 7T [2-3], to investigate the temporal concentration changes of metabolites during neuronal activation in vivo.

Materials and Methods: Six healthy subjects (4 women, 2 men aged 20 to 28 years) gave informed consent according to the procedure approved by the local ethics committee. A shielded quadrature transmit/receive surface RF coil (R=6cm) was used to acquire data in the occipital lobe using a 7T Siemens scanner. At the beginning of the study a brief checkerboard fMRI experiment, covering the entire visual field (frequency 9Hz, 10s ON, 20s OFF, TA=2.5min) was used to place the acquisition voxel for the subsequent fMRS scans in an area of high visual activation (fig. 1). First and second order shims were adjusted using FASTMAP. For fMRS, each subject was exposed to the same visual stimulation consisting of five alternate periods of 5min of rest and visual stimulation (25min total). A red cross was positioned in the center of the screen and rotated every 30s to maintain attention. During the experiment, ^{1}H MRS was continuously acquired using the SPECIAL sequence (TR/TE=5000/6ms, BW=4000Hz, vector size=2048 pts, VOI=20*22*20mm^3, 300 scans) [2-3] employing VAPOR water and outer volume suppression [4]. The unsuppressed water signal was measured at the end of the experiment (nt = 8 scans). The individual MR spectra were frequency and phase corrected using Matlab. Metabolites were quantified using LC Model [6] with a basis set of simulated spectra of 21 metabolites (only metabolites with CRLB<30% were used, metabolite concentrations are expressed in µmol/g). For the inter-subject analysis, the spectra were summed over the 6 subjects in blocks of 24 spectra (4 scans for each subject) and a moving average (sliding offset = 4scans) was performed for the plot of concentration time courses.

Results and Discussion: Shimming resulted in typical water linewidths of 12.5-13.5 Hz. The SNR for a single spectrum of 2 scans was between 30 and 40 (mean SNR=33). The location of the voxel and the placement of OVS bands were carefully set to minimize lipid contamination (fig 2a). The use of the SPECIAL sequence with OVS bands ensures a reliable quantification of the Lac concentration (fig. 2.a). The region at 1.3ppm was devoid of any apparent variations. Averaging 24 spectra allowed quantification of 18 metabolites with CRLB less than 30%, in particular, Lac and Asp with CRLB below 25%, and Glu below 5%. The BOLD effect increases T_2^* and thus induced a line-narrowing on the spectra during activation [5] which

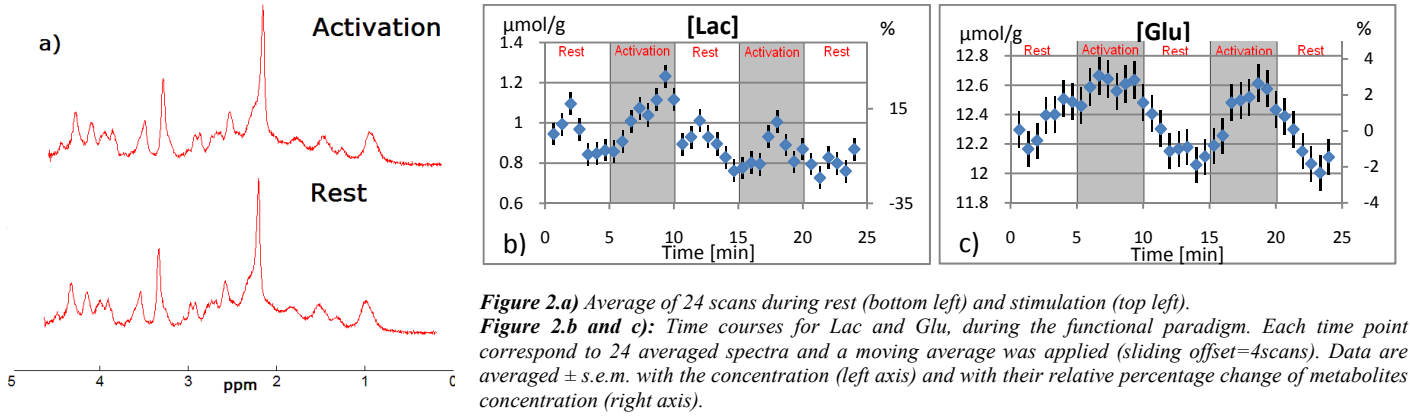

Figure 2.a) *Average of 24 scans during rest (bottom left) and stimulation (top left).*
Figure 2.b and c): *Time courses for Lac and Glu, during the functional paradigm. Each time point correspond to 24 averaged spectra and a moving average was applied (sliding offset=4scans). Data are averaged ± s.e.m. with the concentration (left axis) and with their relative percentage change of metabolites concentration (right axis).*

could be observed in the time course of the creatine peak height. An average increase of 2% between rest and activation confirmed the position of the voxel in the activated area. The time courses of Lac and Glu were measured by combining the data of the 6 subjects with a time resolution of 20s. The time courses from six subjects are plotted (fig. 2.b-c) with a moving average (sliding offset=4). Inter-subject analysis revealed an increase of [Lac] of 25±9% ($p<0.05$) and [Glu] of 4±1% ($p<0.02$) in the visual cortex during the second part of the activation. A decrease of Asp of 9%±3.5% ($p<0.05$) has also been measured. A trend for Glc decreasing during activation was further observed. The use of the SPECIAL sequence at 7T yielded an increased SNR compared to STEAM providing a twofold time resolution for the time courses of different metabolites concentration compared to the previous study performed on twelve subjects and further support the notion of predominant oxidative metabolism during activation. By increasing the number of subjects a detailed study on the dynamics of amino acid changes should be feasible. The magnitude and sign of [Lac] and [Glu] changes are in agreement with a previous study [1] though at a reduced number of subjects.

References and Acknowledgements: [1] S. Mangia, JCBFM, 27:1055-1063, 2007 [2] V. Mlynarik *et al.*, MRM, 56:965-970, 2006 [3] R. Mekle *et al*, MRM, 61(6):1279-85, 2009 [4] I. Tkac *et al,*AMR, 29(1):139-157,2005 [5] Zhu X-H *et al*, MRM, 2001:46 [6] S. Provencher, MRM, 30, 1993.
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