Dynamics of lactate concentration and BOLD effect upon repeated identical visual stimuli

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Introduction

In a previous study conducted with functional proton MRS at 7 T in humans [1], lactate concentration [Lac] was found to reach a new steady-state level (higher by 0.2 μmol/g) within the first minute of prolonged visual stimulations. During the second repetition of a 5-min long stimulus, [Lac] was observed to increase slightly less than during the first presentation of the stimulus, however the difference didn't reach statistical significance. The aim of the present work was to further investigate the time-course of [Lac] using the same experimental settings as previously, but with increased number of shorter (2-min long) visual stimulation periods. In order to gain additional insights into the neural mechanisms of adaptation, the [Lac] time-course was compared to the BOLD time-course acquired during the same functional paradigm.

Methods

Twelve healthy volunteers were examined on a 7T/90 cm magnet (Magnex Scientific, UK), interfaced to Varian INOVA console. Ultra-short echo-time STEAM (TE = 6 ms, TR = 5 s) [2] was used to acquire data from the primary visual cortex during the visual stimulation paradigm. A radial red/black flickering (8 Hz) checkerboard, which covered the entire visual field, was turned on and off every 2 min during a 32-min paradigm. All single scan data from each subject were pooled together and then frequency and phase corrected. FIDs were summed between subjects (4 scans per subject), which resulted in spectra of 48 scans and 20 s time resolution. Spectra were analyzed by LCModel with simulated basis set [3]. BOLD-based activation maps were obtained from some subjects during the same protocol applied for functional MRS (GE-EPI, 16 sagittal slices, TE = 22 ms, spatial resolution = 2.5 x 2.5 x 2.5 mm^3, TR = 5 s). The BOLD effect was evaluated also on metabolites, by plotting the time-course of the signal height of the strong singlet of the methyl group of total creatine (Cr) at 3.03 ppm [1,4].

Results and discussion

The spectral quality achieved in this study (Fig. 1) guaranteed reliable quantification of [Lac] (Cramer–Rao lower bounds below 10 %). Periodic increases in [Lac] by ~0.2 μmol/g between resting and stimulation periods were observed only in the first half of the paradigm, but were attenuated later on, to gradually disappear in the noise (Fig. 2A). On the contrary, the BOLD response (as revealed by the height of total Cr signal and by the fMRI signal, Fig. 2B-C) was persistent upon all repeated stimuli. This discrepancy between [Lac] and BOLD time-courses indicates that the [Lac] changes and the BOLD effect are sensitive to different aspects of neuronal activation. Measurements of intra-cortical electrical activity and BOLD fMRI conducted in monkeys lead to the conclusion that the BOLD contrast reflects mostly the "perisynaptic" activity (input plus intra-cortical processing) rather than the spiking activity [5]; on the other hand, energetic demands (monitored here by [Lac] [1]) have been reported to be correlated to neurotransmission rates [6]. Based on the above considerations, the findings of the present study might suggest a differential adaptation of cortical output that is not reflected at the level of the global excitation-inhibition activity of the cortical canonical circuits.

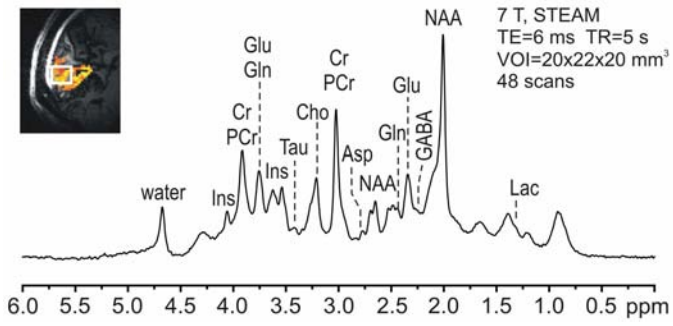

Fig. 1: Example of *in vivo* proton NMR spectra, obtained by summing 4 scans from each subject. Inset: sagittal image (turboflash) with superimposed fMRI data and localization of the VOI.

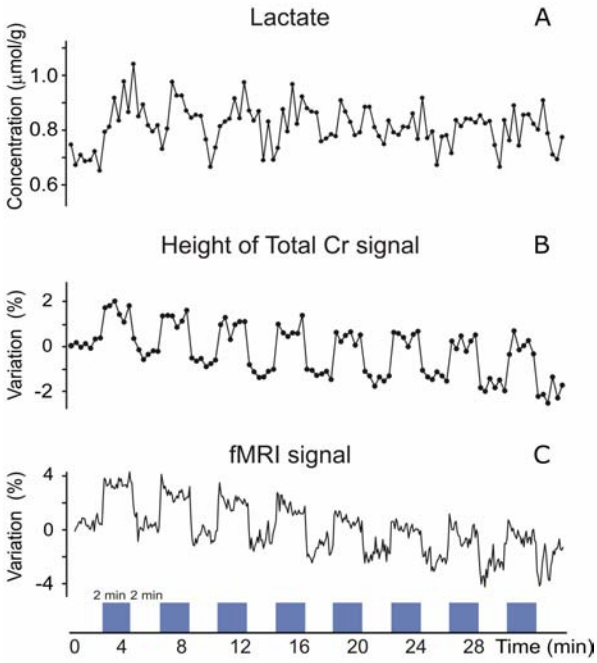

Fig. 2: Time-courses of [Lac] (A), peak height of total Cr at 3.03 ppm (B), and fMRI signal (C) acquired during the functional paradigm from the same VOI in the primary visual cortex.

References: [1] Mangia et al., JCBFM advance online publication, 11 October 2006 doi:10.1038/sj.jcbfm.9600401 [2] Tkac et al., App Magn Reson 29:139 (2005); [3] Provencher, MRM 90:672 (1993) [4] Zhu and Chen, MRM 46:841 (2001) [5] Logothetis et al., Nature 412:150 (2001) [6] Sibson et al., PNAS 95:316 (1998)
Acknowledgments: NIH P41RR08079, NS38672, BTRR P41 008079, Keck Foundation and Mind Institute.