^{1}H-MRS with Visual Stimulation in the study of Brain Bioenergetics and Glu-Gln dynamics in 3T

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Target audience

Scientists and physicians interested in detection and quantification of human brain metabolites (including Lac, Glu and Gln) using a dynamic experiment with visual stimulation in a 3 T clinical scanner.

Purpose

The uncoupling between local blood flow and metabolic rate of oxygen consumption in the brain during increased neuronal activity suggests that other energetic pathways, rather than oxidative metabolism, should supply the additional energetic demand [1]. Proton Magnetic Resonance spectroscopy (^{1}H-MRS) allows the non-invasive study of metabolic pathways and physiologic changes in the *in vivo* human brain. The acquisition of MRS data with simultaneous visual stimulation makes feasible the quantification of local metabolic changes. Over the last decade several studies suggested that lactate increases with visual stimulation [2-4]. However, due to highly variable reports, this finding remains controversial. In this study we evaluate metabolic changes in the visual cortex induced by photic stimulation in healthy young subjects using ^{1}H-MRS in 3T.

Methods

^{1}H-MRS data were obtained from 21 healthy young subjects (16 males, age 21 to 30 years) using a 3T scanner (Achieva, Philips). The study was approved by the Ethics Review Boards of the institution and all subjects gave written consent. A PRESS sequence (TE/TR=144/1500 ms, NSA=16, 3200 Hz bandwidth, 1024 complex data points) was used for data acquisition from a volume of interest of 20x35x26 mm³ located in the visual cortex. For lactate detection, selection gradients order was AP/RL/FH and saturation slabs were positioned in the basis and posterior region of the head to avoid spectra contamination with lipids and macromolecules (MM). The stimulation paradigm consisted of 3 blocks (*off→on→off*) with duration of 6.75 min each (15 spectra/block, total duration of 20.25 min). The visual stimulus consisted of a radial black-white checkerboard flickering at 8Hz, which was shown to the subjects using the ESys fMRI system (Invivo). Spectra were processed using LCModel without considering relaxation effects. Metabolites quantification relied on one representative spectrum from each block, which was created by the sum of 15 spectra acquired during each time period. A moving average (5 spectra sliding offset) was performed to evaluate correlation between metabolites over time. Paired Student's t tests were performed to statistically infer differences between blocks.

Results

Minimal contamination with lipids and MM were achieved using AP/RL/FH order for selection gradients and saturation slabs in the basis and posterior region of the head. Mean SNR of 63 spectra representative from each block was 36±6.7, which allowed the quantification of N-Acetylaspartate (NAA), Choline (Cho), Creatine (Cr), Glutamate (Glu), Glutamine (Gln), Inositol (Ins) and Lactate (Lac). The mean *on/off* area ratio from Lac for all subjects was 1.41 (non-significant). Analysis of Glu showed an 8% increase (p=0.005) during stimulation in comparison to baseline and 10.5% decrease (p=0.001) in recovery relative to stimulation. Our data also showed a Gln increase of 9.4% (p=0.03) during recovery relative to stimulation (Figure 1). Other quantified metabolites showed no statistically significant change during stimulation.

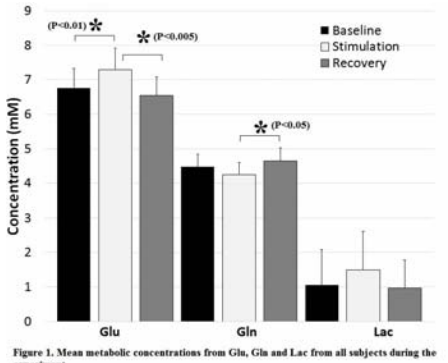

Figure 1. Mean metabolic concentrations from Glu, Gln and Lac from all subjects during the experiment

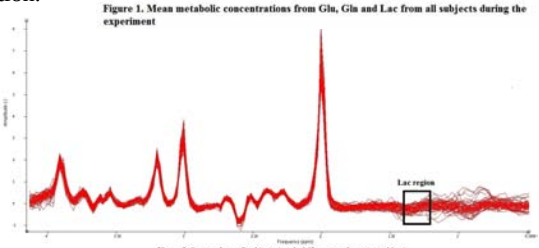

Figure 2. Spectra from all subjects (total of 63 spectra, 3 spectra/subject)

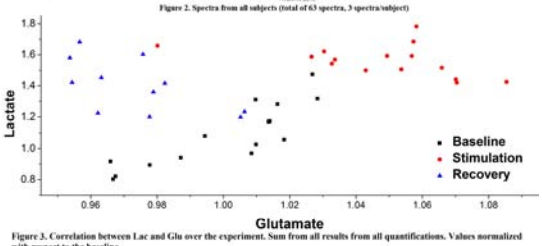

Figure 3. Correlation between Lac and Glu over the experiment. Sum from all results from all quantifications. Values normalized with respect to the baseline.

Discussion

Despite the efforts to eliminate lipids and MM in the region of 1.3 ppm, some subjects showed residual contamination (Figure 2), which may have led to increased variability in lactate quantification. Correlation between Lac and Glu (Figure 3) shows raised Lac levels with increasing Glu, although Lac has a slower return to baseline. Recent reports of Lac and Glu findings in 7 T [2-4] estimate a mean Lac/Glu increase ratio ranging from 5.1 to 7.6, which was also observed here, possibly due to coupling between Lac and Glu during increased neuronal activity. Higher concentrations of Glu during stimulation suggest increased synaptic activity as a consequence of enhanced neuronal activity [2]. A significant decrease in Gln during stimulation wasn't detected, however the posterior increase in recovery compared to stimulation may result from the neurotransmitter cycling process (Figure 4). For the best of our knowledge, this is the first report of Glu/Gln changes in dynamic studies under 3 T, thus demonstrating its feasibility.

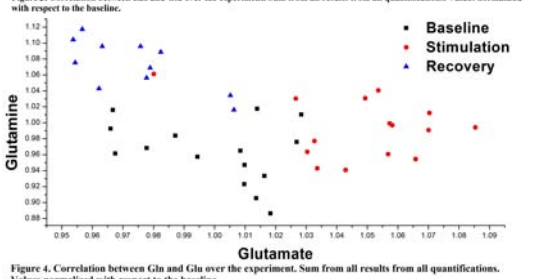

Figure 4. Correlation between Gln and Glu over the experiment. Sum from all results from all quantifications. Values normalized with respect to the baseline.

Conclusion

^{1}H-MRS allowed the quantification of 7 metabolites and detection of metabolic changes from Glu and Gln under 3 T. Detected Lac showed no statistical significant change during stimulation, however the correlation between Lac and Glu suggests a coupling between both metabolites during increased neuronal activity. Glu-Gln dynamics caused by stimulation was measured, indicating increased synaptic activity due to increased neuronal activity. Further studies using different stimulation paradigms would be required to evaluate temporal evolution of metabolic changes described in this study.

References

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