Functional spectroscopy: A new experimental method in exploring the Glutamate-Glutamine cycle in the human brain

K. Specht[1], R. Grüner[1,2], R. Barndon[2], H. K. van Wageningen[1], L. Ersland[2], K. Hugdahl[1,3]

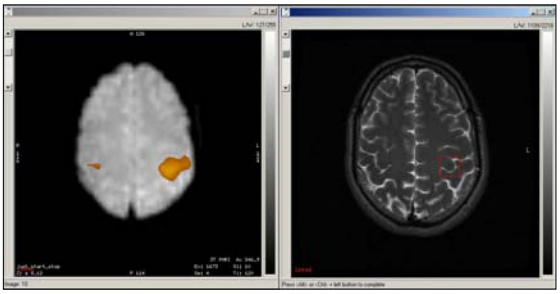
[1]Department of Biological and Medical Psychology, University of Bergen, Bergen, Norway, [2]Radiological Department, Haukeland University Hospital, Bergen, Norway, [3]Section for Psychiatry, University of Bergen, Bergen, Norway

Introduction

In this study, we were especially interested to test whether it is possible to detect changes in the concentration of the neurotransmitter Glutamate within the sensory-motor system during an active task. Using spectroscopy for exploring brain-functions is not a new method by its own, but mainly the visual system was explored so far, and only changes in Lactate were reported. Less was done with respect to the neurotransmitter, which are important for forwarding an action potential from an axon to the next neuronal.

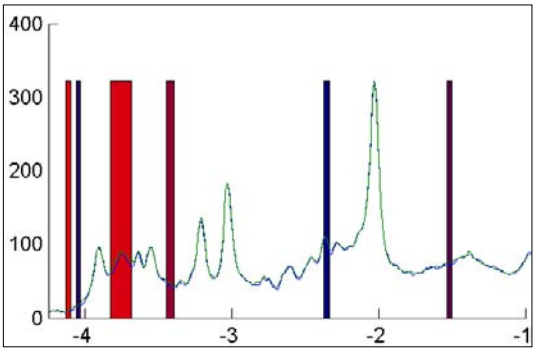
Method

We explored 20 healthy subjects with this new functional-spectroscopy protocol on a 3T GE-Signa MRI scanner. Prior to the spectroscopy, each subject underwent an fMRI examination, in which a finger-opposition task was performed. The real-time activation maps obtained at the scanner were used to guide the positioning of a 20x20mm voxel for the spectroscopy on a T2-weighted dataset, acquired in the same orientation as the fMRI (upper figure).



We used a single-voxel spectroscopy measurement (PRESS, TR 1500ms, 8 averages) with a short echo-time of TE 35ms in order to be sensitive enough to small changes in the concentration of the neurotransmitter Glutamate and Glutamine. The shimming-procedure was optimized to get a line-width less than 8 Hz and a water suppression level of at least 96%.

Two spectroscopy acquisitions were performed: 1) An activation condition, in which the subject performed the same task as during the fMRI; 2) A control condition, in which no task was performed. The order of these two conditions was randomized and the shimming parameters were kept constant. In additional five subjects this procedure was repeated while acquiring the spectroscopy data in the occipital lobe, where no changes were expected.



The spectroscopy data were analysed using own software. In order to increase the SNR, all data were smoothed. For the statistical comparisons, a paired t-test was performed, comparing the Activation and Rest conditions over the 20 subjects. A significance threshold of $p<0.05$ was used, and only changes extending over at least three adjacent data-points (0.023ppm) were considered. The areas of significant changes were overlaid onto the mean spectra, with colours indicating the significance (blue=low, red = high; lower figure).

Results & Discussion

All subjects showed significant activations of the sensory-motor system during the fMRI task, which enabled us to place the voxel for the spectroscopy in the centre of the detected activation. The statistical comparisons demonstrated significant differences close to the peaks for Glutamate, the combined Glutamate/Glutamine (Glx) peak, Glucose, and Lactate (see Table & lower Figure). By contrast, the same comparison for the occipital lobe revealed no significant differences between motor activation and rest. Interestingly, all the metabolites whos concentrations changed during activation, belong to the Glutamate-Glutamine cycle. This cycle is responsible for the continuity of neuronal activations through the recycling process of released Glutamate and reuptake of this neurotransmitter into the axon. This Glutamate-Glutamine cycle needs Glucose for its process and releases lactate, as well. In summary, functional spectroscopy might be a useful tool for exploring activation-related changes in the concentration of neurotransmitter and metabolites was observed in humans.

	theory	**func-spec-data**
Glutamte	2,380	**2,360**
Glx	3,780	**3,775**
Glucose	3,430	**3,416**
Lactate	1,330	**1,520**
	4,1000	**4,114 & 4.039**