A multimodal study, combining functional MRI, ASL perfusion, MR spectroscopy, and dynamic causal modelling

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Introduction

In the recent years, an increasing number of studies is including magnetic resonance spectroscopy (MRS) in their functional magnetic resonance imaging (fMRI) study protocols. In particular, the influence of the excitatory neurotransmitter glutamate (Glu) or the combined concentration of glutamate and glutamine (Glx) on higher cognitive functions is of interest.

In continuation of earlier studies, the here presented study combines not only fMRI with MRS, but takes also behavioural measures (response rate) as well as arterial spin labelling (ASL) perfusion measures into account. Thus, the data were analysed with a standard general linear model approach and dynamic causal modelling (DCM), which allows inferring on effective connectivity within a given network of nodes. Using a simple motor task, we setup a DCM model, containing the three most relevant nodes, i.e. the left motor cortex, left supplementary motor area (SMA), and the right cerebellum for testing the hypothesis, that the inter-subject variability of the additionally acquired parameter (ASL, MRS) are reflected in the individual variation of the connection strength in the DCM model.

Method

Fifteen healthy, right-handed subjects were investigated on a 3T GE-Signa MRI scanner. During the fMRI task, which was a simple motor task, subjects were asked to regularly press with their right index finger a response button with their preferred speed. These data were recorded and used as estimates for the individual response rate.

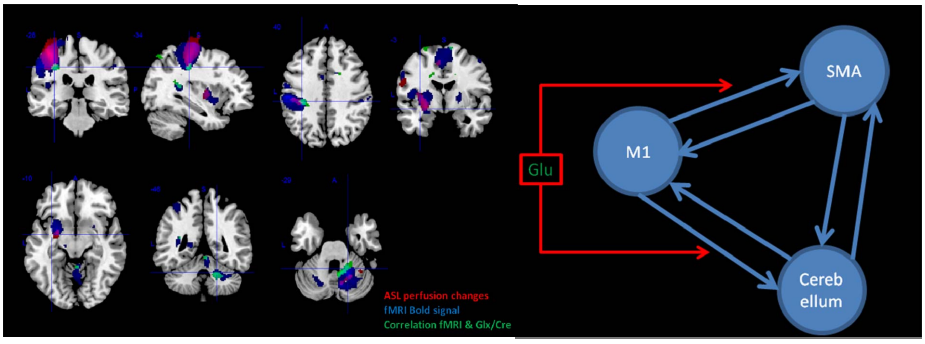
The fMRI data were analysed directly on the scanner, using the real-time option, implemented on the scanner. The thus obtained activation map was used for positioning the voxel for the MRS examination within the motor cortex. A single-voxel spectroscopy measurement was used with a short echo-time of TE 35ms. The shimming-procedure was optimized for getting a line-width less than 8 Hz and a water suppression level of at least 96%. Two spectroscopy acquisitions were performed, while the shimming parameters were kept constant. During one acquisition, subjects performed the same task as during the fMRI, while no was performed in the other session.

Similarly, there were two 3D ASL perfusion measurements, one with and one without the motor task. The order of the tasks during the MRS and ASL measurements were randomized across subjects.

The analysis of the MRS data was performed using LCModel, while all other analyses were conducted using SPM8. For the DCM analysis, the three nodes were connected with bi-directional connection

Results

The results are demonstrating for both, the fMRI as well as the ASL data, overlapping activations within the left motor cortex, SMA, putamen, as well as right cerebellum. In addition, using the individual difference in Glx/Cre between the ON and OFF MRS session, correlations were found between the MRS data and the fMRI data in particular within the left motor cortex and the right cerebellum (See Figure), after correcting for the influence of the BOLD effect on MRS resolution. Using a ROI approach, perfusion changes in the motor cortex and SMA correlated with the total concentration of Glu. In addition, the response rate correlated with the fMRI activations within the left motor cortex as well as anterior cingulated cortex.



Comparing the DCM connection strength with results from the spectroscopy, no significant correlation was detected. However, there were reasonable strong correlations between the total Glu concentration and the connection between motor cortex and SMA as well as cerebellum (both r=0.47).

Discussion

As expected, there were significant changes in the BOLD signal as well as regional perfusion in response to the motor task. In addition, the speed of the task performance correlated with the activations in relevant areas. Although no direct relationship between the DCM parameter and neurotransmitter concentration was found, the strength of the correlation suggests that they are not complete independent, but may be coupled in a non-linear relationship. Larger sample sizes and in particular the inclusion of GABA measurement in the post-hoc analysis of DCM results may help uncovering the underlying mechanisms a greater details.