FMRI of hippocampal deep brain stimulation in the rodent brain

N. Van Den Berge[1], I. Dauwe[2], P. van Mierlo[1], K. Vonck[2], C. Vanhove[1], R. Van Holen[1]

[1] Medical Image and Signal Processing Group, Ghent University-iMinds Medical IT department, Ghent, Belgium
[2]Laboratory for Clinical and Experimental Neurophysiology, Neurobiology and Neuropsychology, Ghent University Hospital, Ghent, Belgium

Background: Deep Brain Stimulation (DBS) is a promising treatment for neurological and psychiatric disorders. However, the underlying mechanism of action of DBS remains unknown. The effect of DBS has been studied primarily by direct neural recording studies, which lack the ability to elucidate DBS related responses on a whole-brain scale. Functional Magnetic Resonance Imaging (fMRI) reflects changes in neural activity throughout the entire brain volume and may thus reveal neuroanatomical connectivity of the targeted structure in vivo. In order to visualize the whole-brain blood oxygen level dependent (BOLD) responses to DBS, we have developed an MR-compatible electrode and an acquisition protocol for simultaneous DBS and BOLD fMRI. With this study, we aimed to demonstrate that DBS during fMRI is a valuable technique to investigate the whole-brain effect of DBS.

Methods: Three adult male Sprague-Dawley rats were stereotactically implanted with a custom-made MR-compatible PtIr DBS-electrode in the right hippocampus. Electrical on-and-off Poisson distributed stimulation was applied (amplitude 75mA, pulse duration 100µs, frequency 130Hz) using a block-design paradigm (20s on/40s off). MR images were acquired on a Pharmascan 7T (Bruker) using a rat brain volume coil. Rats were sedated with medetomidine during all fMRI acquisitions. Each fMRI run consisted of 150 repetitions with TR=2s, TE=20ms. Data were processed by means of independent component analysis. Clusters were accepted as significant if p-values were 0.05 or less after correction for multiple comparisons. Each resultant statistical map was co-registered onto a structural MR image for anatomical correlation.

Results: Hippocampal DBS evokes a bilateral BOLD response in hippocampal and thalamic substructures, as shown in fig. 1. Activation not only occurs near the electrode, but also contralateral to the electrode. Results were consistent among rats.

Conclusions: Our data indicate that real-time hippocampal DBS evokes a bilateral BOLD response in hippocampal and thalamic substructures. We demonstrated that simultaneous DBS and fMRI can be used to explore the whole-brain effect of modulating neural circuitry, making this technique potentially powerful for exploration of cerebral changes of DBS in animal models of neurological or psychiatric disorders.

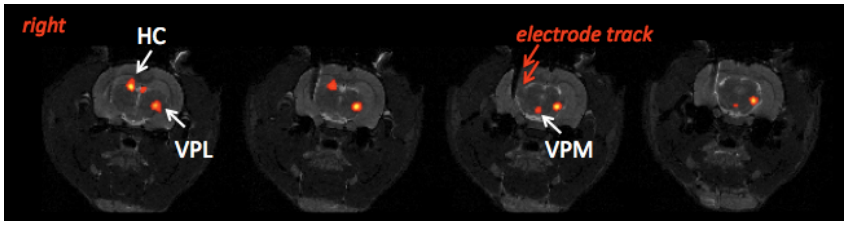

Figure 1. Findings of one rat in whole-brain BOLD fMRI during hippocampal DBS.The statistical map is thresholded at $p<0.05$. Activation occurs in hippocampal (HC) and thalamic (VPM/VPL) structures.