BOLD signal changes of imaginary walking before and after lumbar puncture in NPH-patients

E. Küstermann[1], M. Ebke[2], K. Dolge[3], D. Leibfritz[4], and M. Herrmann[5]

[1]ZKW & CAI, University of Bremen, Bremen, Bremen, Germany, [2]Neurology, Stroke Unit, Klinikum Bremen-Mitte, Bremen, Germany, [3]Jacobs Center on Lifelong Learning and Institutional Development, Jacobs University, Bremen, Germany, [4]Organic Chemistry, Instr. Analytics, University of Bremen, Bremen, Germany, [5]Department of Neuropsychology and Behavioral Neurobiology, University of Bremen, Bremen, Germany

Introduction: In normal pressure hydrocephalus (NPH) little is known about the specific pathophysiological disturbances in movement disorders as well as in cognitive functions and bladder disturbance. However, it is established that lumbar puncture (LP) with removal of ca. 50 ml cerebrospinal fluid (CSF) could treat patient with the diagnosis of NPH successfully. Different hypotheses about the etiology of the disease consider (i) a reduced resorption of CSF in cerebrum leading to penetration of CSF into the frontal and parietal lobe inducing gait disturbances or (ii) a decreased cerebral blood flow (CBF) induced by CSF being pressed into white matter leading to a CBF reduction near the ventricles. PET-based CBF measurements revealed diminished CBF rates in Basal Ganglia, Thalamus and frontal areas [1-3]. CBF changes correlating with disease severity were reported for frontal medial areas [3]. In order to investigate the effects of the diagnostic LP on gait performance, the brain activity of NPH patients during imagined walking was investigated with fMRI before and after LP. In order to explore neuronal correlates of brain activity and gait, subjects were asked to perform imaginary walking tasks after a short training outside the magnet. Similar tasks investigating imaginary walking were reported recently [4-6].

Methods: Functional MRI scanning was performed on 14 subjects (m/w = 5/9, mean age = 71.4 ± 5.7years) with 11 measurements conducted before and 15 after LP. Immediately before MR scanning, subjects were asked to walk with closed eyes (i) freely and (ii) guided by a hand of a supporter for about forty meters. Subjects were instructed via headphones to perform the following tasks: (A) move the right foot; (B) imagine moving the right foot; (C) imagine walking freely and (D) imagine guided walking as trained just before. Task and rest duration was 15 seconds. During one run (11min duration), each task was repeated five times. Subjects were requested to perform two runs. A T1-weighted structural 3D-data set (MPRAGE, 1x1x1mm spatial resolution) was acquired in between both fMRI runs. Imaging was performed at 3 Tesla on a Siemens head scanner (Allegra; Siemens, Erlangen/D) with a conventional EPI-sequence covering the whole brain (TE/TR = 30/2600 ms, 64x64 matrix, 45 slices, 3x3x3mm spatial resolution). Data were preprocessed (motion correction, time slicing, normalization to custom derived NPH-template in register with the standard MNI-template, 8 mm spatial smoothing) and analyzed with SPM5 [7] with a fixed effect analysis for each subject. Artefacts due to head movements were removed by interpolation using the ArtRepair toolbox [8,9]. Statistical maps of brain activation before and after LP were calculated for both imaginary walking conditions (C+D) together. Differences between pre- and post LP status were assessed by an interaction analysis.

Results: After LP, all tested patients improved their gait performance. FMRI reveals positive BOLD signals upon imaginary walking tasks which are similar to those recently published [4-6]. As shown in figure 1, upon imagination of walking – indicated by light blue bars in time course graphs -, task specific positive BOLD responses were found in the Brodmann area BA40 (#1), the precentral region (#2), the SMA, the cerebellum, and the basal ganglia (#3) on both hemispheres with almost identical signal time courses. Differences between fMRI-detectable activation patterns during imaginary walking were found at lower significance levels of p<0.005 (not corrected). In figure 2, *black* areas represent regions in which the BOLD signal prior to LP has a larger amplitude than afterwards (#1: left precuneus; #2 right parietal lobe / angular gyrus; #3: right middle temporal gyrus; #4 fronto-polar, BA10/11). Averaged time courses of areas #1-3 exhibit similarities: Prior to LP (red trace), the BOLD signal increases upon task execution, whereby after LP (green trace) the time courses become negative with a pronounced time lag. In the fronto-orbital region #4 the BOLD signal also increases pre- and decreases post-LP but without noticeable time lags. The opposite is observed in the regions around the Rolandic Operculum (#5 in figure 2, *gray* areas): here, the BOLD signal becomes larger after diagnostic LP.

Discussion: The brain activity upon imaginary walking - as shown in figure 1 - is in good agreement with the current picture of cerebral movement control and literature [4-6]. However, the explanation of the effects of LP on brain activity upon imaginary walking is not straightforward. In the fronto-polar cortex, changes of the BOLD signal may reflect the involvement of this region in decision making [10] or planning [11]. Furthermore, the frontal cortex and the precuneus have been described as parts of the default mode network [12] which might illuminate the neuronal basis of gait improvement after diagnostic LP. A closer inspection of the BOLD time courses reveals large standard deviations reflecting the signal variability due to (i) individual task performance and (ii) hemodynamic response as well as (iii) larger head movements as compared to the usual young healthy subjects of fMRI studies. Thus, more subtle effects of interest are probably hidden by measurement errors and individual variability. Howsoever, the benefit of this exploratory study is to generate hypotheses for an independent follow-up study with an improved experimental design.

References: [1] Owler, JCBFM 24:579. [2] Okamoto, Neurol.Res. 29:830. [3] Klinge, Clin.Neurol.Neurosurg110:369. [4] Jahn, NeuroImage 22:1722. [5] Malouin, HBM19:47. [6] Iseki, NeuroImage 41:1021. [7] SPM: http://www.fil.ion.ucl.ac.uk/spm. [8] ArtRepair: http://spnl.stanford.edu.tools/ArtRepair.htm. [9] Mazaika, HBM conference 2007. [10] Kringelbach, Nat.Rev.Neurosci. 6:691-702. [11] Dreher, PloS ONE 3:e3227. [12] Sridharan, PNAS 105:12569.
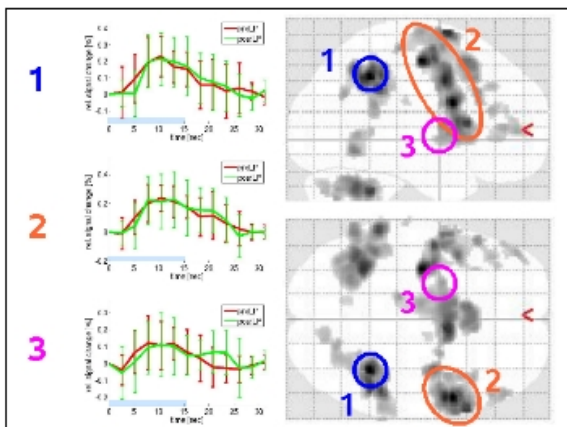
Figure 1: Positive BOLD signals of imaginary walking (pre- + post-LP, tasks C+D) at p<0.00001 (uncorr.).
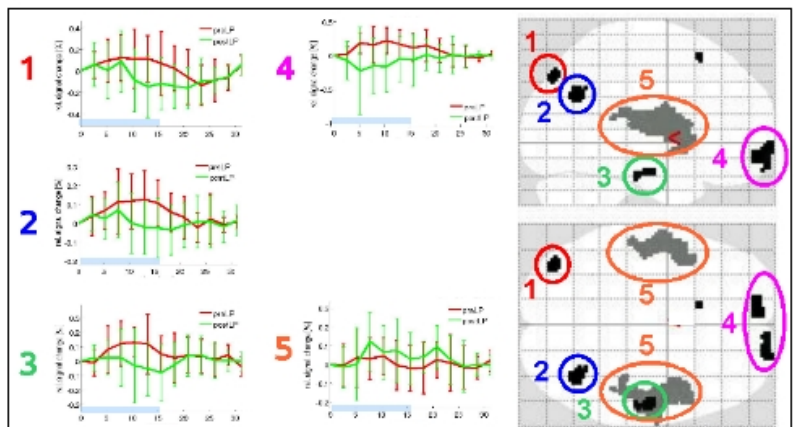
Figure 2: Different BOLD signals at pre- and post-LP status of imaginary walking (tasks C+D) at p<0.01 (uncorr.). *Black*: pre > post, *Gray*: post > preLP.

Both figures: Time courses: averaged signals, error =standard deviation.   *Red* =preLP, *Green*=postLP.   Light blue bars represents task duration.