EARLY COMPENSATORY CHANGES WITHIN THE MEMORY NETWORK OF MULTIPLE SCLEROSIS PATIENTS

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Introduction: Cognitive decline, most notably memory impairment, is highly prevalent in MS. As the hippocampus is crucial to memory processing (both encoding and consolidation), this study set out to specifically investigate possible changes in hippocampal activation patterns in MS, with the hypothesis that changes in brain function (as measured with fMRI) precede cognitive impairment.

Methods: Functional MRI (echo planar imaging, TR 2220ms, TE 60ms, 25 slices) and 3D-T1 images (TR 2700ms, TE 5ms) of 34 MS patients (9 males, 25 females; mean age: 47.1 ± 8.7 years) and 15 healthy controls (4 males, 11 females; mean age 46.3 ± 9.5 years) were acquired on a 1.5T scanner (Siemens Sonata). Out of 34 MS patients, 24 patients were cognitively preserved (CP) and 10 cognitively impaired (CI) based on the neuropsychological examination (which involved tests for visuospatial memory, verbal memory, working memory, speed of information processing).
A declarative memory encoding paradigm was used for the fMRI measurements, in which 50 different landscape images were presented to the subjects, intermixed with control images. To ensure sufficient attention, subjects were asked to decide whether the images were 'tropical' or 'non-tropical' by pressing a button. During the retrieval phase, 100 landscape images were shown, 50 of which were novel and 50 of which were already shown in the encoding phase. Subjects had to indicate whether they had or had not seen the pictures before. Image analysis was performed using FSL's FEAT (FMRIB, Oxford, UK) where correctly remembered items were contrasted with control images.

Results: CP MS patients showed increased activation in the lateral parietal occipital area (see figure 1). No brain areas with reduced activation in response to the encoding task were found in this group. When comparing CI patients to HC, the opposite was found (see figure 2): there were no brain areas showing increased activation, however several brain areas showed reduced brain activation. The reduced brain activation was found in the right hippocampus, the right and left parahippocampal gyrus, and several areas in the occipital lobe.

Conclusions: In the CP patients increased brain activation was seen in the right parietal-occipital junction, which is part of the dorsal stream of the memory network (selectively involved in spatial vision). The increased activation of the dorsal stream in response to correctly encoded items might be necessary to preserve normal cognitive function (functional reorganization), and might be present due to decreased activation in other brain areas (hippocampal areas) which we could not yet measure. Interestingly, CI patients showed a reduction of activation in the (para)hippocampal areas as well as brain areas associated with the ventral stream of the memory network (selectively involved in object vision). No increased brain activation patterns were observed in this group. Since these patients have measurable cognitive deficits, and there are no compensatory brain areas active, our results indicate that functional reorganization is an early and finite phenomenon in MS.

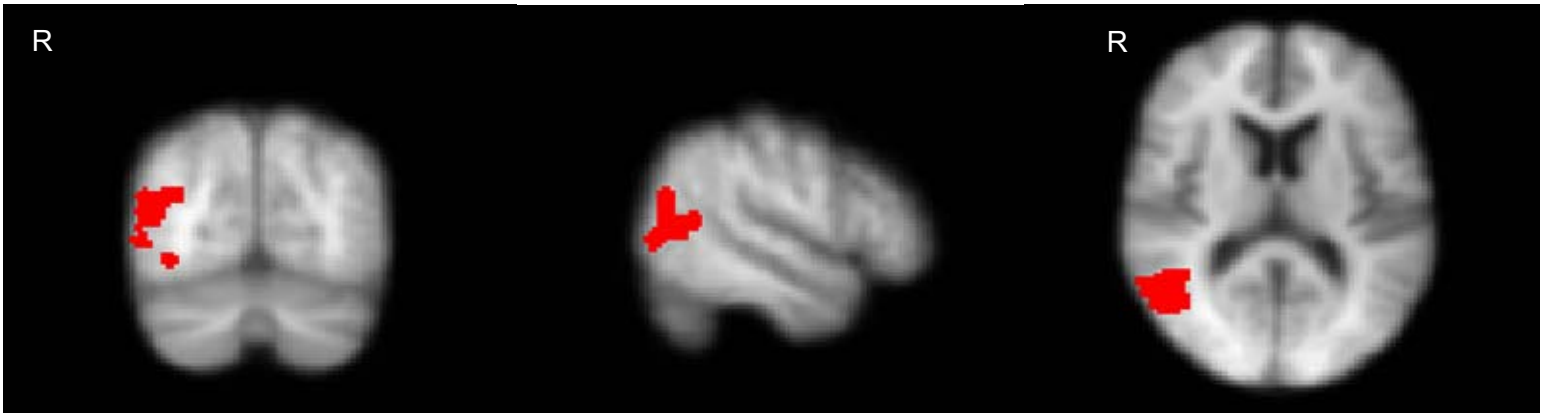

Figure 1. Increased brain activation patterns (as indicated in red) in CP patients compared to healthy controls. The area that is more active in CP patients is located in the right parietal-occipital junction and is assumed to be part of the dorsal stream of the memory network (cluster correction, Z=2.0, p=0.05).

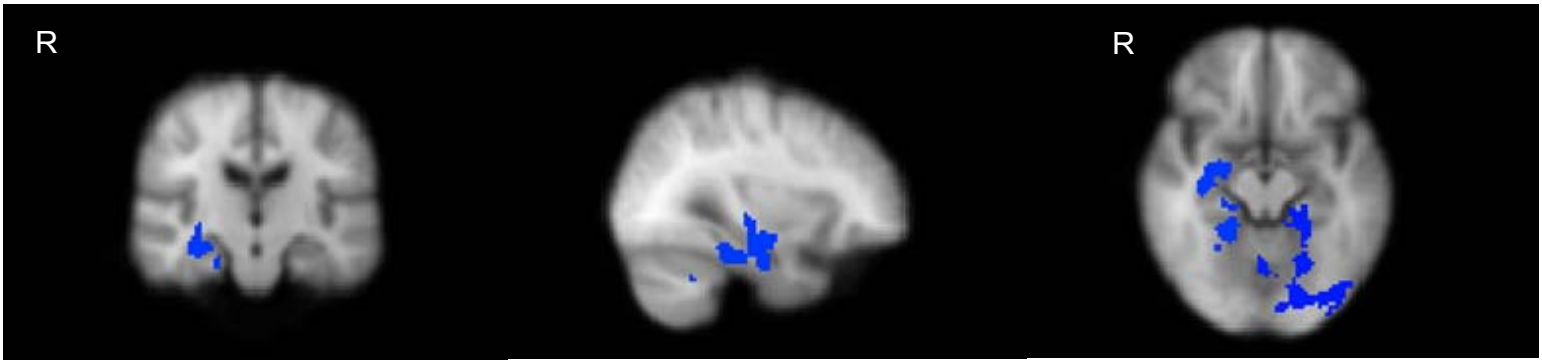

Figure 2. Decreased brain activation patterns (as indicated in blue) in CI patients compared to healthy controls. The brain areas that show decreased activation are the right hippocampus and right and left parahippocampal areas as well as some areas located in the occipital lobe that are assumed to be part of the ventral stream of the memory network (cluster correction, Z=2.0, p=0.05).

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