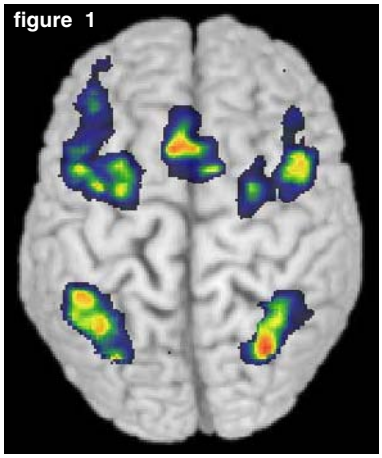
Working memory related differences in brain activation measured with functional Magnetic Resonance Imaging (fMRI) in patients 1 month after minor head injury compared to healthy controls.

M. Smits[1], D. W. Dippel[2], P. A. Wielopolski[1], G. C. Houston[3], P. J. Koudstaal[2], M. M. Hunink[4], and A. van der Lugt[1]

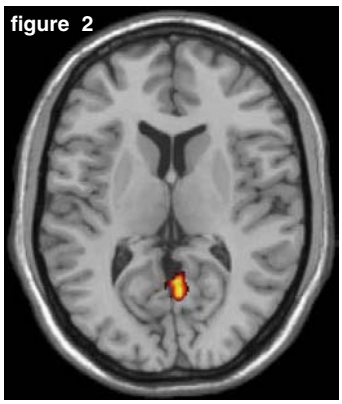
[1]Radiology, Erasmus MC, Rotterdam, Zuid-Holland, Netherlands, [2]Neurology, Erasmus MC, Rotterdam, Zuid-Holland, Netherlands, [3]GE Healthcare, 's Hertogenbosch, Brabant, Netherlands, [4]Radiology and Epidemiology & Biostatistics, Erasmus MC, Rotterdam, Zuid-Holland, Netherlands

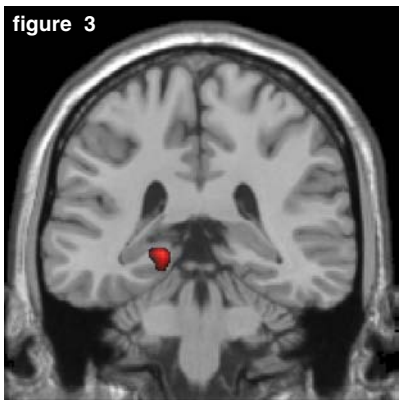
purpose Postconcussive symptoms, such fatigue, headache and cognitive complaints, are common after minor head injury (MHI), while conventional imaging and neuropsychological tests are often normal. It has been suggested that postconcussion syndrome is caused by brain damage, undetectable by conventional imaging techniques, affecting cognitive function (McAllister et al. Neurology 1999; 53:1300-1308; Audoin et al. Hum Brain Mapp 2003;20:51-58). Neural plasticity compensating for these abnormalities may explain why subjects with cognitive complaints have normal performance on neuropsychological tests, but could be detected with functional MRI (fMRI) as an increase of neural activity. Purpose of this study was to compare working memory related fMRI-activation of MHI patients, with and without postconcussive symptoms, and healthy controls.

materials and methods Subjects were prospectively recruited between December 2005 and November 2006. 22 Patients 1 month after MHI and 11 healthy controls (matched for age, gender and educational level) were scanned on a 3T MRI scanner (GE Healthcare, US). For anatomical reference, a high-resolution 3D IR-FSPGR T1-weighted image was acquired (acquisition time 4:57 mins). For functional imaging, a T2*w GE-EPI sequence was used (TR/TE 2500/30 ms; acquisition time 6:30 mins). An n-back task was presented auditorily, using a parametric blocked design with different levels of working memory load: 0-back, 1-back and 2-back (in order of increasing load). The task was performed twice by each subject. Postconcussive symptoms were evaluated with the Rivermead questionnaire (Ingebrigtsen et al. J Neurol 1998;245:609-612). Statistical analysis of fMRI data was performed using SPM2 (Wellcome dept, London, UK). Single subject analysis consisted of realignment, coregistration, normalization and smoothing (6x6x6 mm^3 3D Gaussian kernel). Activation maps were created using the general linear model, and contrasting the each of the conditions with the condition(s) of a lower working memory load (e.g. 1-back>0-back). Single subject contrast maps were then used for random effects group analysis.



results Subjects' age ranged from 18-45 years, 20 subjects were male. 12 (55%) MHI patients had postconcussive symptoms (Rivermead scores 8-46). In all subjects combined, significant ($p<0.001$), bilateral activation was seen in the prefrontal cortex (Brodmann area (BA) 9,13,45,47), precuneus, superior parietal lobule (BA 7,19,40) and left middle frontal gyrus (BA 6) for the 2-back versus 0-back comparison (**figure 1**). In patients with postconcussive symptoms compared to controls and to asymptomatic patients, significant ($p<0.001$) activation was seen in the posterior cingulate gyrus (BA 23,31; **figure 2**), the isthmus (BA 29,30) and the parahippocampal gyrus (BA 27; **figure 3**).





conclusion Patients with postconcussive symptoms 1 month after MHI have shown to recruit additional brain regions to perform a working memory task, when compared to healthy controls and to asymptomatic MHI patients. These areas are functionally related to memory processing, and have been implicated in other cognitive disorders, such as minor cognitive deficit (Yetkin et al. Eur Radiol 2006;16:193-206).The observed differences in activation patterns may reflect injury-related changes, compensating for brain damage, that is thus far undetectable with conventional structural imaging techniques.