

No evidence of acute or predisposing structural abnormalities in patients with transient global amnesia (TGA): a Tract Based Spatial statistics (TBSS) study

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Introduction: Transient global amnesia (TGA) is a neurological disorder characterized by a sudden onset of antero- and retrograde amnesia, and a complete recovery from this cognitive disturbance within 24 hours. The underlying etiology is unknown, but cortical spreading depression, ischemic stroke, and venous congestion have been suggested as possible pathomechanisms. Until today, MRI has only detected small punctuate lesions in the lateral aspect of the hippocampal formation on diffusion-weighted imaging (DWI) in the subacute phase of TGA [1]. We sought to elucidate a possible underlying more extensive disturbance of the hippocampal network in a prospective explorative approach using diffusion tensor imaging (DTI) and tract-based spatial statistics which have already been used in patients with hippocampal sclerosis [2] demonstrating loss of structural integrity in perihippocampal and limbic areas.

Methods: Diffusion tensor imaging (DTI) data (TR/TE 9200/95 ms, 128x128 matrix, 54 slices of 2.5 mm thickness, $b=0/900$ s/mm² in 30 diffusion directions) were acquired on a 3T MRI scanner (Siemens Trio) in 10 subjects with clinically identified TGA and proven typical DWI lesion in the hippocampal formation, and processed in the TBSS framework (www.fmrib.ox.ac.uk/fsl) [3]. Fractional anisotropy (FA) and mean diffusivity (MD) maps were created and registered into standard space. A mean FA skeleton representation was generated and a voxelwise statistics was performed comparing TGA patients with healthy control subjects matched for age, sex and extent of chronic white matter lesions on FLAIR images. Furthermore, all patients underwent a standardized diagnostic protocol including a detailed physical and neurological examination, a comprehensive neuropsychological assessment battery as well as Doppler and duplex sonography of the extracranial vessels, transcranial Doppler sonography, EEG, and laboratory tests.

Results: There were 9 women and 1 man in the study population; the mean age was 66 years (minimum 58 years, maximum 77 years). Two of these patients had a history of TGA 5 and 15 years earlier, respectively. All patients reported an emotional trigger before onset of the TGA episode. Neurological examination, ultrasound studies, and EEG were normal in all patients. Persisting mild cognitive deficits could be demonstrated in the subacute phase after the end of the episode in all patients. On DWI, all patients had single (six patients) or multiple (four patients) focal hyperintensities in the lateral hippocampus. The latter were always located bilaterally; there were six lesions in the right hemisphere and nine lesions in the left hemisphere (see Figure 1). Regarding the extent of chronic white matter lesions, six patients had no white matter lesions (Fazekas grade 0) and four patients had mild white matter lesion load (Fazekas grade 1). Tract-based spatial statistics revealed no significant differences in FA and MD values ($p<0.05$) between TGA patients and healthy controls (see Figure 2).

Conclusion: This work demonstrates that there is no preexisting lesion burden or structural tissue damage in TGA patients. While in patients with hippocampal sclerosis extensive network changes have been demonstrated with DTI [2], tract-based spatial statistics display no disturbed hippocampal network integrity in TGA patients in the subacute phase despite persisting mild memory disturbances. This finding suggests a transient functional perturbation than an impaired structural integrity of hippocampal and/or mesiotemporal memory circuits in TGA patients.

References:

1. Sedlaczek O et al. Detection of delayed focal MR changes in the lateral hippocampus in transient global amnesia. *Neurology* 2004; 62:2165-2170.
2. Focke NK et al. Voxel-based diffusion tensor imaging in patients with mesial temporal lobe epilepsy and hippocampal sclerosis. *Neuroimage* 2008; 40:728-737.
3. Smith SM et al. Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. *Neuroimage* 2006; 31:1487-1505.

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Figure 1. Schematic drawing of focal DWI lesions located in the hippocampus in 10 patients with transient global amnesia (each color represents a specific patient).

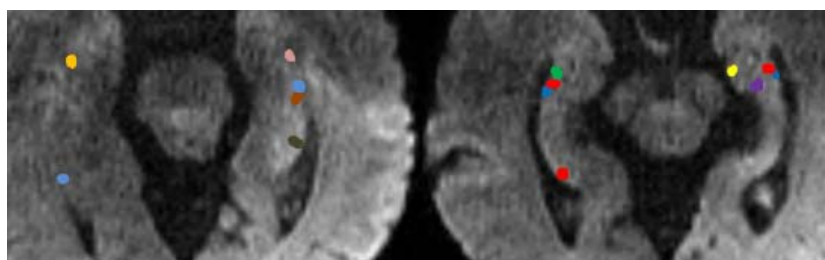


Figure 2. Axial images demonstrating skeletal voxels without significantly ($p<0.05$) reduced FA values in patients with TGA compared to healthy controls. The background image is the MNI152 standard space T1 template; the slice localizations are in the MNI152 coordinate system.

