Letters to the Editor

The recent publication of Baracchini et al entitled “Jugular Veins in Transient Global Amnesia: Innocent Bystanders” in Stroke reports extra- and transcranial high-resolution venous echo-color Doppler sonography findings in patients who have had an episode of transient global amnesia (TGA). The main finding of the authors is the absence of any intracranial venous hemodynamic alteration in these patients as compared with control subjects. They suggest that future research should be aimed at the assessment of intracranial venous hemodynamics during the acute stage of TGA.

The cause of TGA has been a matter of longstanding debate among researchers. Although the nature of the memory deficit occurring in TGA and the finding of a dot-like lesion on diffusion-weighted MRI actually link the disorder to the hippocampus, the exact etiology of TGA and the involvement of the observed hippocampal lesion remain uncertain. In search of an answer, several possible causes (ischemia, migraine, epileptic seizures, or, more recently, a disturbance of venous hemodynamics) have been hypothesized. However, to date there is no scientific proof of any of these mechanisms.

It is therefore legitimate to think outside of these boxes and consider a completely different hypothesis, namely the role of stress. Indeed, physical, emotional, or behavioral stress has been reported as a precipitating event in up to 89% of TGA cases. Activation of the hypothalamus–pituitary–adrenal axis during accidental or experimentally induced stress is known to lead to an elevation of glucocorticoid hormone levels. High glucocorticoid levels in turn have been shown to increase neuronal vulnerability in the hippocampus, to induce a decrease in regional cerebral blood flow in the mesial temporal lobe, and to have a negative effect on cognition and memory. In a previous study focusing on the neuropsychological characterization of TGA, we found that memory disturbance was indeed associated with a selective effect on specific, hippocampus-related recognition memory subprocesses, which are more pronounced in patients with TGA who show visible hippocampal lesions on diffusion-weighted imaging than those who do not. A recent experimental study demonstrated that cell death in the hippocampus caused by moderate ischemia was dramatically amplified in rats that experienced stressful episodes before the ischemic event. The animals also displayed a pronounced increase in corticosterone levels and hippocampus-related learning and memory deficits. These findings indicate that prior stress sensitizes hippocampal neurons to the damaging effects of hypoperfusion. However, to date no study has addressed the possible role of cortisol or stress-induced individual cortisol responses in patients with TGA.

In line with the assumption that TGA is a disorder caused by the stress-related transient inhibition of memory formation in the hippocampus, we propose that patients with TGA exhibit increased reactivity to stress and that changes in brain activation patterns during memory formation and retrieval are a pathophysiological correlate of TGA. To test these hypotheses, we are currently performing a study in cooperation with the Central Institute of Mental Health in Mannheim (Institute of Neuropsychology and Clinical Psychology) funded by the German Research Foundation (DFG) that is intended to determine the effect of experimental exposure to stress on cortisol levels and on hippocampal activation patterns using functional MRI in patients with TGA.

Disclosures

None.

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