Internal Jugular Vein Valve Incompetence in Transient Global Amnesia
More Circumstantial Evidence or the Proof Solving the Mystery?
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See related article, pages 67–71.

Transient global amnesia (TGA) was generally believed to have a psychogenic, epileptic, or thromboembolic etiology until the frequent comorbidity with migraine and the common accompanying symptoms (headache and dizziness) pointed toward cortical spreading depression as a pathogenic suspect.1,2

More recently, based on evidence that Valsalva-like activities may represent the precipitating factors in most TGA patients, cerebral venous congestion leading to venous ischemia was hypothesized as a possible pathophysiologic mechanism.3 Corroborating this hypothesis, the prevalence of internal jugular vein (IJV) valve incompetence, as assessed by ultrasound, was found to be more prevalent in patients with TGA than in controls.4–8 In all of these studies, IJV valve incompetence was detected in 97 of 131 patients (74%) and in 65 of 191 controls (34%).

In this issue of Stroke, Cejas and coauthors9 confirmed these findings in a larger population, reporting IJV valve insufficiency in 113 patients with TGA (79.5%) and in 10 controls (25%). Apparently, this could solve the TGA mystery: physical activities associated with Valsalva-like maneuvers would increase venous return and cerebral venous pressure, leading to ischemia. This hypoperfusion would affect mainly mediobasal temporal regions, as the watershed area between the upper and lower hippocampal arteries is thought to be particularly hypoxia-susceptible (the so-called sector of Sommer).10

In line with this theory, magnetic resonance imaging (MRI) studies reported a variable percentage of hippocampal abnormalities displaying restricted diffusion in patients with TGA who lacked vascular risk factors, large-artery stenoses or small-vessel disease, and underlying sources of cardioembolism.11–13 Indeed, MRI diffusion restriction is not a specific finding, as it is also observed in ischemic depolarization and cortical spreading depression. Can venous ischemia and cortical spreading depression represent 2 not-mutually exclusive mechanisms?

Control subjects with IJV valve insufficiency may be symptoms-free until they encounter precipitating events, but because a quarter of patients with TGA had competent IJV valves, venous congestion cannot represent the only determinant of TGA. In addition, unless IJV valve insufficiency is transitory, one would expect a higher TGA recurrence rate than is usually observed.13 Could cortical spreading depression be the pathogenetic factor in that 25% of patients without IJV valve incompetence?

A psychogenic origin of TGA had been proposed for a long time on the basis of epidemiologic studies describing emotional distress as a precipitating event and a phobic personality in patients with TGA.14 Strong emotions may excite the hippocampal neurons to trigger a glutamate release, which in turn may trigger the spreading depression.1 In addition, some authors have proposed that emotional and phobogenic events might lead to an involuntary Valsalva maneuver or to a hyperventilation-induced vasoconstriction,15 the latter indirectly worsening the hemodynamic changes due to venous congestion.

Cejas and colleagues investigated the presence of triggering factors preceding TGA in 79 of the 142 enrolled patients. Half of these subjects reported sustained activities possibly associated with a Valsalva maneuver; among them, 12 patients had experienced an intense emotional state. The prevalence of IJV valve incompetence did not differ between patients with or without precipitating events. This finding suggests that both the Valsalva maneuver and IJV valve incompetence alone may be sufficient to precipitate TGA and that, more relevantly, there is a subgroup of patients (~9%) who do not present with either precipitating factors or IJV valve incompetence. Again, it could be hypothesized that different pathogenic pathways subtend the TGA phenomenon. From a clinical point of view, the findings of Cejas and colleagues support an IJV valve competence evaluation as part of the TGA diagnostic work-up. However, the evidence available so far cannot yet justify the preclusion of other more expensive diagnostic examinations.
Further clinical questions remain unsolved. Although more recent MRI studies cast doubt on an arterial ischemic pathogenesis of TGA, a more consistent vascular profile was previously observed in patients with TGA with diffusion-restricted MRI lesions compared with those without. Should these patients be considered at higher risk of future vascular events? Which therapeutic approach would be more appropriate?

In summary, the evidence of a high prevalence of IJV valve incompetence in patients with TGA provides an important basis for understanding TGA pathophysiology, but the mystery remains partly unresolved. Investigating the case of TGA, we have definitely identified the suspects, but we still have to prove them guilty.

Disclosures

None.

References


Key Words: carotid ultrasound cerebrovascular disease transient global amnesia
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Stroke. 2010;41:1-2; originally published online November 19, 2009; doi: 10.1161/STROKEAHA.109.569582

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