MAYO CLINIC

Transient Global Amnesia

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Abstract

Transient global amnesia (TGA) is a clinical syndrome characterized by the sudden onset of anterograde amnesia (the inability to encode new memories), accompanied by repetitive questioning, sometimes with a retrograde component, lasting up to 24 hours, without compromise of other neurologic functions. Herein, we review current knowledge on the epidemiology, pathophysiology, clinical diagnosis, and prognosis of TGA. For this review, we conducted a literature search of PubMed, with no date limitations, using the following search terms (or combinations of them): *transient global amnesia, etiology, pathophysiology, venous hypertension, migraine, magnetic resonance imaging, computed tomography, electroencephalography, prognosis,* and *outcome*. We also reviewed the bibliography cited in the retrieved articles. Transient global amnesia is a clinical diagnosis, and recognition of its characteristic features can avoid unnecessary testing. Several pathophysiologic mechanisms have been proposed (venous insufficiency, arterial ischemia, and migrainous or epileptic phenomena), but none of them has been proved to consistently explain cases of TGA. Brain imaging may be considered and electroencephalography is recommended when episodes are brief and recurrent, but otherwise no investigations are necessary in most cases. Data on long-term prognosis are limited, but available information suggests that the relapse rate is low, the risk of stroke and seizures is not considerably increased, and cognitive outcome is generally good.

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Transient global amnesia (TGA) was initially described in 1956 by Bender,[1] and at the same time but independently by Courjon and Guyotat,[2] as a syndrome characterized by sudden and temporary memory loss. Yet, it was not until 1964 that it gained recognition as we know it today, when Fisher and Adams[3] described the syndrome as TGA. Initially referred to as a heterogeneous clinical syndrome, the approach to the condition was refined by the diagnostic criteria proposed by Caplan[4] and consolidated by Hodges and Warlow[5,6] in 1990. Since the first description of the disorder, a lot has been published about its clinical characteristics, and several hypotheses regarding its pathogenesis have been proposed. Yet, the cause and mechanisms of TGA remain unclear.

Several reviews on TGA have been published,[7-12] but they have all been addressed to neurologists. However, TGA can be encountered by internists, emergency department physicians, and family medicine practitioners. We aim to synthetize current knowledge and to propose a practical approach to this condition that can be useful for daily practice. Herein, we also review the epidemiology, pathophysiology, diagnostic criteria, differential diagnosis, and expected long-term outcome of TGA.

The content of this review is based on a literature search of PubMed, with no date limitations, using the following search terms (or combinations of them): *transient global amnesia, etiology, pathophysiology, venous hypertension, migraine, magnetic resonance imaging, computed tomography, electroencephalography, prognosis,* and *outcome*. We also reviewed the bibliographies cited in the retrieved articles. The studies referenced in this article were selected based on study quality and clinical relevance.

BASIC CONCEPTS ON MEMORY

Memory is the brain function that allows us to encode, store, and retrieve information. It can be divided into 3 different types: immediate or working memory, short-term memory, and long-term memory.[13] Immediate memory refers to the information that can be retained for a short period of time without active involvement of the memory pathways. It can be simply tested by asking the patient to repeat a 7-digit number. This type of memory can be affected by attention or language impairment or by a lesion to the superior frontal neocortex. Short-term memory (also called episodic memory) implies the ability to encode, store, and retrieve information after minutes or hours; this is the type of memory that requires normal functioning of the hippo-

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campus and parahippocampal areas located in the medial temporal lobe. It can be tested at the bedside by asking the patient about his or her activities earlier in the day. Long-term or remote memory relates to long-known information (where we were born, which school we attended); it includes semantic memory, which enables us to have a general knowledge of concepts, facts, and meanings (eg, definitions of words), and it is supposed to rest in multiple cortical regions, including the visual association cortex, temporal cortex, and other cortical structures according to the type of memory involved.

A simplified memory circuit includes the hippocampus on each side projecting to the septal areas via the fornix, then to the mammillary bodies, and subsequently to the anterior nucleus of the thalamus; from there it projects to the cingulate gyrus of the frontal lobe and back to the hippocampus, thus completing the Papez circuit, crucial for short-term memory (Figure 1). Amnesia is caused by the disruption of these pathways. Specific memory impairments are determined by the site of involvement. Affection of the hippocampus will produce anterograde amnesia, characterized by the inability to lay down new information.

ARTICLE HIGHLIGHTS

- Transient global amnesia is a condition that can be encountered by internists, emergency department physicians, family medicine practitioners, and, ultimately, neurologists. Its correct diagnosis relies on recognition of the disease, which can prevent unnecessary testing.
- We propose a diagnostic algorithm for patients with sudden-onset anterograde amnesia and present the diagnostic criteria for transient global amnesia.
- Episodes are self-limited, and spontaneous improvement is noted within 24 hours of onset.
- Available data to date indicate that long-term outcome is generally good in terms of relapse rate and risk of stroke and seizures. Information regarding long-term cognitive outcome is scarce but suggests that these patients are not at higher risk for cognitive impairment.

EPIDEMIOLOGIC PROFILE

Transient global amnesia affects predominantly middle-aged or elderly patients. Its annual incidence has been reported to be 3.4 to 10.4 per 100,000 people.[6,14-16] If we narrow it to the population older than 50 years, the incidence increases to 23.5 per 100,000 per year.[17] It is more common in individuals with migraine.[18,19]

CLINICAL PRESENTATION AND DIAGNOSTIC CRITERIA

Transient global amnesia is a clinical syndrome characterized by the sudden onset of anterograde amnesia, accompanied by repetitive questioning, sometimes with a retrograde component, lasting up to 24 hours, and without compromise of other neurologic functions. Typically, TGA is encountered in patients aged 50 to 70 years who are brought to medical attention because they are noticed to have acutely lost the ability to understand their situation and grasp their surroundings. Patients repeatedly ask questions, such as "Why are we here?" "What time is it?" or "How did I get here?" The answers are immediately forgotten owing to their inability to encode new information. Other neurologic functions are preserved, including procedural memory. Thus, these patients can perform previously learned activities (eg, driving) without impairment. These episodes are sometimes preceded by a precipitating event, such as an activity associated with a Valsalva maneuver, emotional stress, immersion in cold or hot water, sexual intercourse, or pain.

Patients having an episode of TGA are characteristically not well aware of their problem,

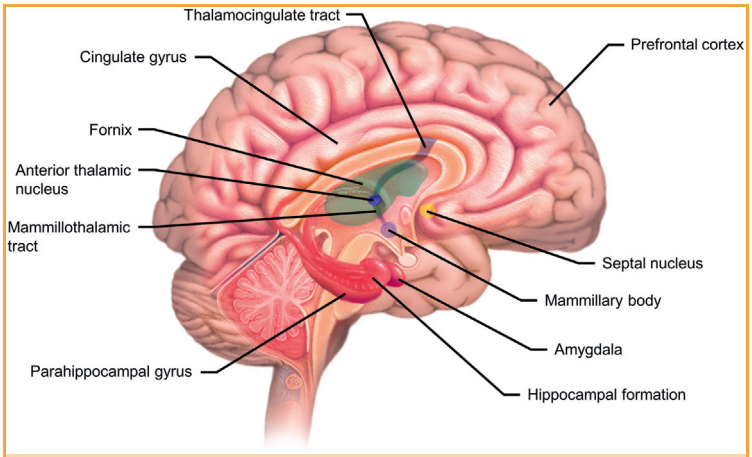

FIGURE 1. The Papez circuit of short-term memory. The hippocampus on each side projects to the septal areas via the fornix, then to the mammillary bodies, the anterior nucleus of the thalamus, the cingulate gyrus of the frontal lobe, and back to the hippocampus.