Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com

Hippocampus and epilepsy

Hippocampal modifications in transient global amnesia

Modifications hippocampiques dans l'ictus amnésique idiopathique

P. Quinette [a,b,c,d], J.M. Constans [e], M. Hainselin [a,b,c,d,f], B. Desgranges [a,b,c,d], F. Eustache [a,b,c,d,*], F. Viader [a,b,c,d,g]

[a] U1077, Inserm, 5, avenue de la Côte-de-Nacre, CS 30001, 14033 Caen Cedex 9, France
[b] UMR-S1077, University of Caen - Basse-Normandie, esplanade de la Paix, 14032 Caen Cedex 5, France
[c] UMR-S1077, École Pratique des Hautes Études, 5, avenue de la Côte-de-Nacre, 14032 Caen Cedex 5, France
[d] U1077, Caen University Hospital, 5, avenue de la Côte-de-Nacre, 14033 Caen Cedex 9, France
[e] Radiology and Medical Imaging Department, Amiens University Hospital, place Victor-Pauchet, 80054 Amiens Cedex 1, France
[f] CRPCPO, EA 7273, University of Picardie Jules Verne, chemin du Thil, 80000 Amiens, France
[g] Neurology Department, Caen University Hospital, avenue de la Côte-de-Nacre, 14033 Caen Cedex 9, France

INFO ARTICLE

Article history:
Received 22 December 2014
Accepted 28 January 2015
Available online 11 March 2015

Keywords:
Amnesia
Hippocampus
Diffusion magnetic resonance imaging
Spectroscopy

Mots clés :
Amnésie
Hippocampe
Imagerie par résonance magnétique de diffusion
Spectroscopie

ABSTRACT

Transient global amnesia (TGA) is an acute and transient syndrome with a remarkably stereotypical set of signs and symptoms. It is characterized by the abrupt onset (no forewarning) of massive episodic memory impairment, both anterograde and retrograde. Ever since it was first described, TGA has fascinated neurologists and other memory experts, and in recent years, there has been a surge of neuroimaging studies seeking to pin down the brain dysfunction responsible for it. Several pathophysiological hypotheses have been put forward, including the short-lived suggestion of an epileptic mechanism. All the available data indicate that the brain modifications are reversible, and that the mechanism behind TGA is of a functional nature. However, while diffusion-weighted imaging studies have clearly identified the hippocampus and, more specifically, the CA1 area, as the locus of brain modifications associated with TGA, researchers have yet to determine whether the origin of the mechanism is vascular or neurochemical. Spectroscopy may provide a means of settling this issue once and for all.

* *Corresponding author at:* Inserm, EPHE, Université de Caen/Basse-Normandie, Unité de recherche U1077, GIP Cyceron, boulevard Henri-Becquerel, BP 5229, 14074 Caen Cedex 05, France.
E-mail address: francis.eustache@inserm.fr (F. Eustache).

http://dx.doi.org/10.1016/j.neurol.2015.01.003
0035-3787/

RÉSUMÉ

L'ictus amnésique idiopathique est un syndrome amnésique aigu et transitoire dont la sémiologie est remarquablement stéréotypée : il se caractérise par la survenue soudaine et sans signe avant-coureur d'une atteinte massive de la mémoire épisodique (amnésie antérograde et rétrograde). Depuis ses premières descriptions, l'IA a suscité l'intérêt de tous les neurologues et autres spécialistes de la mémoire, mais ces dernières années ont vu l'émergence de nombreux travaux en neuro-imagerie dont l'objectif principal concerne la localisation et la nature du dysfonctionnement cérébral responsable de l'IA. Plusieurs hypothèses physiopathologiques ont été proposées, parmi lesquelles un mécanisme épileptique très rapidement écarté. Si les études en IRM de diffusion ont clairement établi l'hippocampe, et plus particulièrement le champ CA1, comme le siège des modifications cérébrales associées à l'épisode, l'origine vasculaire ou neurochimique du mécanisme reste débattue. La spectroscopie pourrait être une méthode pertinente pour apporter des arguments en faveur de l'une ou l'autre des hypothèses. Enfin, l'ensemble des données s'accorde sur la nature réversible des altérations cérébrales et confirme le caractère fonctionnel du mécanisme en jeu dans l'ictus amnésique idiopathique.

1. Introduction

It was in two studies published back in 1956 – one French [1], the other American [2] – that transient global amnesia (TGA) was described for the first time. Its low reported incidence in the general population, ranging from five to 11 cases per 100,000 per year, means that it is seldom encountered, although its true incidence is certainly somewhat higher, as the episodes are extremely short-lived and not always detected in A&E departments. The signs and symptoms of this amnesic syndrome are remarkably stereotypical. Of sudden onset, TGA generally occurs in individuals aged around 60 years, who display massive anterograde amnesia and a more variable degree of retrograde amnesia, but no disturbance of identity. The clinical picture includes temporal, and sometimes spatial, disorientation, and iterative questioning is almost always present. Apart from the transient memory impairment, there are no discernible neurological disturbances. Four to 6 hours later on average, the episode slowly starts to ebb, leaving behind lacunar amnesia for the episode and the period immediately preceding it. TGA is generally an isolated syndrome, and repeat episodes are rare. It has been shown to be benign, even if three cases of primary progressive aphasia have been described in individuals who had each had a recurrent attack of TGA [3]. A suggested link with Alzheimer's disease so far remains unproven [4].

The turning point in the history of this syndrome came in 1990, when Hodges and Warlow [5] established strict diagnostic criteria. We therefore have a clear framework to work within, and where patients' symptoms do not meet the TGA criteria, physicians need to look for a different diagnosis. Even so, despite the many advances that have been made over more than two decades, TGA still holds many unsolved mysteries.

The neuropsychology of TGA has been the subject of extensive investigations, mainly focusing on patients' memory capacity in the acute phase. As tests have confirmed the strictly episodic nature of the amnesia, TGA is now regarded as a pure model of episodic memory, offering neuropsychologists a unique opportunity to explore human memory systems. Of particular interest are the handful of studies that have used brain imaging to identify the pathophysiological mechanisms and brain regions implicated in this syndrome.

2. Pathophysiological hypotheses

Given the episodic nature of the amnesia, the fact that it is an isolated occurrence, and the topography of the anomalies that are regularly observed in magnetic resonance imaging (MRI) investigations, most contemporary authors are agreed that TGA's underlying dysfunction lies in the hippocampus (see Section 3 ''Neuroimaging'' below). However, the precise mechanism behind this dysfunction is still largely an enigma, and several hypotheses have been advanced to resolve it.

2.1. *Epileptic mechanism*

Within a decade of the first observations being made, researchers had raised the possibility of an epileptic mechanism [6]. However, despite reports of electroencephalography (EEG) anomalies, several studies have established a clear difference between TGA and episodes of epileptic amnesia, which are even more fleeting, and tend to be repeated at close intervals [7,8]. Epileptic amnesia is therefore a differential diagnosis, and not a mechanism or aetiology of TGA [7,9]. One of Hodges and Warlow's criteria for TGA is precisely the absence of epileptic disorders.

2.2. *Vascular mechanisms*

The abrupt onset of TGA has fuelled the hypothesis of a vascular problem, and anomalies picked up in diffusion-weighted imaging (DWI) tend to support this. In a series of 28 patients, Winbeck et al. [10] found that these anomalies were correlated with more pronounced carotid atheroma, and suggested that some TGA attacks could have an underlying