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Long-term memory deficits in temporal lobe epilepsy

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ABSTRACT

Memory complaints and deficits are common in patients with epilepsy, especially temporal lobe epilepsy (TLE), where memory-related brain structures are directly involved in the epileptic process. In recent years, substantial progress has been made in delineating memory impairment in TLE, challenging the traditional neuropsychological approach of the disorder. In particular, several lines of evidence have suggested that, beyond the apparent deficit demonstrable by standardized neuropsychological evaluations, TLE may also negatively interact with long-term memory, producing considerable loss of information of the patient's autobiographical history and an inability to maintain newly acquired information over a period of time. These observations have led to the development of innovative assessment techniques, and prompted a new domain of investigation focused on the relationships between interictal epileptiform activities and the integrity of anatomo-functional systems. The present paper reviews the available evidence for long-term memory deficits in TLE with respect to remote and very long-term memory, and discusses their putative pathophysiological mechanisms and the developing potential strategies to improve memory functioning.

1. Introduction

Memory complaints and deficits are commonly seen in patients with epilepsy, especially temporal lobe epilepsy (TLE), where memory-related brain structures are directly involved by seizures. Numerous studies and reviews have delineated the clinical neuropsychology of TLE, particularly with respect to lateralization of seizures within the classic visual/verbal memory framework and in comparisons of pre- and post-surgery memory performance, in attempts to reliably predict postsurgical outcomes [1]. The material-specific model

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of memory relies on the idea that, in right-handers, the left temporal lobe sustains verbal memories, while the right temporal lobe sustains non-verbal memories (for a recent review, see Willment and Golby [2]). However, over the years, neuropsychological and neuroimaging studies have progressively challenged this model. For instance, non-verbal deficits have been less consistently associated with right TLE than verbal memory has been with left TLE, and aberrant lateralization of activation patterns have been demonstrated during material-specific memory tasks in functional neuroimaging studies.

In recent years, additional issues challenging the traditional neuropsychological approach to TLE have emerged. First, the severity of memory complaints has not been consistently captured by standardized neuropsychological assessment, with many TLE patients performing at average levels or above [3]. Standardized memory tests typically assess the ability to retain new information over relatively short (from 20 min to 1 h) delays [4], whereas several lines of evidence suggest that TLE may also interfere with long-term consolidation, with successfully memorized information after short delays progressively fading over periods of days or weeks. Second, paralleling the progress in our understanding of declarative memory organization, the possibility that TLE memory deficits might be analyzed beyond the scope of the verbal/visual dichotomy has been raised [5], leading to the development of complementary assessment paradigms (for reviews, see Bell and Giovagnoli [6] and Butler and Zeman [7]). Finally, characterization of memory impairment in seizure-free patients has stimulated the development of a new area of research, focusing on the relationships between interictal activities and functional deficits.

Thus, the present report reviews all the available evidence on long-term memory deficits in TLE and discusses some of their putative pathophysiological mechanisms, along with potential strategies aimed at optimalizing memory functioning.

2. Remote memory in TLE

Remote memory deficits can have a considerable impact on psychological well-being and may represent one of the main complaints of TLE sufferers [8]. However, while the ability to acquire new information (anterograde memory) has been investigated in detail in TLE, relatively few studies have focused on remote memory, which is multifaceted, comprising memories encoded in the relatively distant past [7,9], with episodic and semantic components. Episodic memory is typically autobiographical, involving the recollection of personally experienced events through ''mental time travel'' (or ''autonoetic awareness'') [10]. Semantic memory enables the recollection of declarative facts, and includes personal (for example, what schools were attended) and public (such as facts about famous people) knowledge.

In a review of the literature, Butler and Zeman [7] gathered 18 case reports and 13 group studies reporting pronounced retrograde memory impairment in the context of epilepsy. As emphasized by the authors, the study of remote memory poses several methodological challenges [7], and the magnitude of the deficits has proved to be variable. Overall, however, almost all studies have demonstrated remote memory deficits in TLE patients involving, to various extents, episodic memory, personal semantics and public knowledge. Some studies revealed impairment of autobiographical memory throughout the entire lifetime [11,12], whereas others reported a circumscribed deficit limited to the past 5 years [13]. Such reduced vividness of autobiographical recollection has also been associated with loss of temporally specific details [14]. Viskontas et al. [11] found autobiographical memory deficits but with intact personal semantics, whereas others have reported additional impairment for public events [15,16] or a disproportionate loss of public semantics compared with autobiographical memory [17–19]. Recent studies have also demonstrated evidence of general semantic knowledge disorders in TLE patients (for a review, see Jaimes-Bautista et al. [20]).

Transient epileptic amnesia (TEA) is a late-onset, treatment-responsive form of TLE in which approximately two-thirds of patients spontaneously complain of autobiographical memory impairment [21,22] (for a review, see Butler and Zeman [7]). In the typical form of TEA, the main manifestation of seizures consists of acute amnesia episodes usually lasting < 1 h, during which other cognitive functions remain intact. In these cases, several lines of clinical, electrophysiological and neuroimaging evidence point towards a seizure focus originating in the medial temporal lobes (MTLs), particularly within the hippocampal formation [7,23,24]. Despite successful resolution of seizures, most patients complain of persistent autobiographical memory loss; case and group studies of TEA have indicated normal [5,24] or mildly impaired personal semantic memory [22,25], but marked episodic autobiographical memory loss [5,22,24,26–29]. Despite knowing substantial information about their past, patients are typically unable to recollect the specific contextual details that characterize each life event. While subtle deficits of public semantic memory have been highlighted in some reports [25], general semantic knowledge is largely preserved overall [5,24,27].

Some studies have attempted to identify the potential factors interacting with retrograde memory in epilepsy [11,12,16,30–32]. Several variables have been examined, such as demographics and epilepsy characteristics, the antiepileptic drugs (AEDs) used and psychosocial factors, but no correlation between epilepsy characteristics and autobiographical memory performance has conclusively been determined. Correlations with non-personal semantics (remote memory for public events and general knowledge) have suggested the negative effects of persistent post-operative seizures [31], yet no effects from duration of epilepsy [16,31] and seizure frequency [16]. In addition, contradictory findings have been reported regarding the impact of the lifetime number of generalized tonic-clonic seizures [30–32], age at epilepsy onset [12,16,31,32] and duration of epilepsy [31]. Several factors may account for these inconsistencies, including the difficulty of accurately estimating seizure frequency, an emphasis on patients with medically intractable seizures, and the possible contribution of other confounding factors such as mood status and general intelligence.