SPECIAL ISSUE

CONTRIBUTIONS OF THALAMIC NUCLEI TO DECLARATIVE MEMORY FUNCTIONING

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ABSTRACT

In spite of the acknowledged role that the thalamus plays in declarative memory, details about the precise memory processes it is involved in and which are the structures of the thalamus that contribute to these processes remain unknown. An overview is presented of human clinical and animal experimental findings showing the involvement of the thalamus, at the level of white matter tracts and separate nuclei, in aspects of memory functioning. The region in the thalamus that contributes to declarative memory is the anterior and medial division, containing the anterior nuclei, the medial dorsal nucleus and the intralaminar and midline nuclei. A lesion to the anterior nuclei or their afferent white matter tract, the mammillothalamic tract, results in deficits of encoding of new stimuli. Lesions to the medial dorsal nucleus affect executive processes pertaining to declarative memory, such as the use of memory strategies for retrieval; damage to the intralaminar and midline nuclei results in decreased arousal and thus affects the declarative memory process. Based on anatomical and functional data, a theory is proposed of how the thalamus might play a role at different levels of declarative memory functioning. Firstly, the anterior and mediodorsal nucleus are involved in processing the contents of the stimuli for storage and recall. The anterior nuclei influence the selection of material to be stored and remembered, whereas the mediodorsal nucleus is involved in the coordination and selection of the strategies used to retrieve material. Secondly, the intralaminar and midline nuclei and specifically the lateral and ventral components, maintain a necessary state of the cortical regions involved in the ongoing memory processes. The two types of function subserved by these groups of thalamic nuclei, focussing on contents vs. state, need to work in parallel to mediate and allow memory functioning, respectively.

Key words: thalamus, diencephalon, memory, limbic, frontal, executive, thalamocortical

INTRODUCTION

It is commonly appreciated that declarative memory can only be sustained by integrated circuits that encompass areas of the brain that are widely distant and of different structure (Mishkin, 1982; Zola-Morgan and Squire, 1993; Parker and Gaffan, 1997; Milner et al., 1998). An integral part of different circuits underlying memory processes, is the thalamus (Aggleton and Brown, 1999). Issues that remain, however, concern: 1) which thalamic structures are involved in human memory; 2) whether these thalamic structures are involved in some aspects of

memory, or in all, and; 3) whether separate structures of the thalamus each play a different role in the various memory processes or whether they act in concert.

Evidence for thalamic involvement in memory is derived amongst others from patients with infarctions, haemorrhages, mechanical injury or tumours interfering with the integrity of the thalamus. Studies like these have shown a role for the thalamus in the various cognitive functions related to memory: the formation of new memories (Squire et al., 1989; Graff-Radford et al., 1990; Bentivoglio et al., 1997), attention to stimuli and events (Bogousslavsky et al., 1988; Rousseaux, 1994) and the use of memory strategies, part of the so-called fronto-executive functions (Sandson et al., 1991; Van Der Werf et al., 1999). A role in memory, furthermore, has been suggested based on the finding that in patients with alcoholic Korsakoff's syndrome, the lesions are mainly found in the thalamus (Squire, 1981; Victor et al., 1989; Kopelman, 1995; Mayes et al., 1997; Visser et al., 1999). The evidence for involvement of the thalamus in human memory is, however, often circumstantial and inconclusive due to the inherent variability of clinical studies.

Over the years, we have been actively involved in the study of memory functions, using a variety of experimental approaches both in experimental animals and in humans. These include neuropsychological assessments of human cognitive function in normal, elderly and demented patients, the analysis of behavioural experiments in animals and anatomical and electrophysiological studies of the cortico-hippocampal, prefrontal and thalamic systems and their respective interactions (e.g. Dolleman-Van Der Weel and Witter, 1995; Dolleman-Van Der Weel et al., 1997; Groenewegen and Uylings, 2000; Jolles, 1986; Jolles et al., 1995; Tisserand et al., 2000; Uylings and Van Eden, 1990; Uylings et al., 2000; Van Boxtel et al., 2000; Witter et al., 1989). A recent emphasis has been on the the contributions of thalamic structures in cognitive processes (Van Der Werf, 2000, 2001; Van Der Werf et al., 1998, 1999, 2000, 2002; Visser et al., 1999; Witter and Van Der Werf, 1999).

It is the aim of the present manuscript to describe the involvement of separate structures in the thalamus in different cognitive processes related to memory. We have restricted our focus to declarative memory, i.e. the memory for facts and events (or semantic and episodic memory). It should be noted, however, that the thalamus is involved in many different aspects of memory and other kinds of cognitive functioning that fall outside the scope of this paper. We will present an overview of findings from studies in healthy subjects, from clinical investigations and animal experimental studies. Based on these data, we will present our hypothesis of 'focussing', as the central aspect of the thalamic contribution to declarative memory.

The Place of the Thalamus in Brain Circuitry

The concept of diaschisis

The thalamus, located in a central position in the brain, regulates the flow of information from the brainstem and sensory organs *en route* to other areas, both