Available online at www.sciencedirect.com
ScienceDirect
Neurobiology of Learning and Memory 90 (2008) 71–80
Neurobiology of Learning and Memory
www.elsevier.com/locate/ynlme

Anterior but not intralaminar thalamic nuclei support allocentric spatial memory

Mathieu Wolff [a], Sheree J. Gibb [a], Jean-Christophe Cassel [b], John C. Dalrymple-Alford [a,*]

[a] Van der Veer Institute for Parkinson's and Brain Research, Department of Psychology, University of Canterbury, Private Bag 4800, Christchurch 8020, New Zealand
[b] Laboratoire d'Imagerie et de Neurosciences Cognitives, UMR 7191, Université Louis Pasteur, Strasbourg, France

Received 14 October 2007; revised 28 December 2007; accepted 8 January 2008
Available online 4 March 2008

Abstract

Medial thalamic damage is a common cause of severe memory disruption in humans. Both the anterior thalamic nuclei (ATN) and the intralaminar thalamic nuclei (ILN) have been suggested as primary sites of diencephalic injury underlying learning and memory deficits, but their respective roles have yet to be resolved. The present study explicitly compared two spatial memory tasks in male PVGc hooded rats with selective neurotoxic lesions to either (1) the ATN or (2) the rostral ILN (and adjacent lateral mediodorsal thalamic nuclei; ILN/LT lesions). As predicted, the ATN group, but not the ILN/LT group, exhibited clear deficits in the Morris water maze task for the initial acquisition of a fixed hidden platform and its reversal to a new position. The second task examined acquisition of egocentric spatial reference memory for a left or right body turn, using any three arms in an 8-arm water maze on any given trial; contrary to predictions, both lesion groups performed as well as the Sham group. The lack of deficits in ILN/LT rats on this second task contrasted with previous findings reporting a detrimental effect of ILN/LT lesions on egocentric working memory. The clear dissociation between the influence of ATN and ILN/LT lesions with respect to allocentric spatial reference memory in the Morris maze emphasizes that caution is required when interpreting the effects of non-ATN thalamic lesions on spatial memory when the lesions encroach substantial areas of the adjacent ATN region.

Keywords: Anterior thalamic nuclei; Intralaminar thalamic nuclei; Allocentric spatial memory; Egocentric spatial memory; Water maze; Rat

1. Introduction

Medial thalamic injury is a common cause of severe memory disruption in humans (Kopelman, 2002; Van der Werf, Witter, Uylings, & Jolles, 2000; Van der Werf et al., 2003). The critical thalamic regions that contribute to diencephalic amnesia are, however, unclear as non-specific brain damage often occurs in clinical cases. Separate lines of evidence in rat lesion models have focussed on the anterior thalamic nuclei (ATN) or the adjacent intralaminar thalamic nuclei (ILN) as two key regions that are likely to cause memory impairment after injury (Aggleton & Brown, 1999, 2006; Aggleton & Pearce, 2001; Mair, 1994; Mair, Burk, & Porter, 2003). Unfortunately, the interpretation of many of these experimental studies is confounded by the potential influence of overlap in lesion extent or the use of conventional lesions that disrupt the complex fiber pathways that traverse this region. The present study explicitly addressed this problem by providing a direct comparison between the effects of highly selective neurotoxic lesions to the ATN and the ILN in rats using behavioral tasks that compared different spatial abilities.

Previous studies that examined lesions targeted at either the ATN or ILN provide some indications as to the comparative learning and memory processes that are

* Corresponding author. Fax: +64 3 364 2181.
E-mail address: john.dalrymple-alford@canterbury.ac.nz (J.C. Dalrymple-Alford).

1074-7427/$ - see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.nlm.2008.01.007

disrupted by injury to these regions. The view that the ILN play a significant role in learning and memory is supported by delay-independent memory deficits in rats with ILN lesions when tested in a variety of matching and non-matching to sample tasks, including object, auditory, olfactory, retractable-lever and maze-arm stimuli (Bailey & Mair, 2005; Burk & Mair, 1998; Harrison & Mair, 1996; Young, Stevens, Converse, & Mair, 1996; Zhang, Burk, Glode, & Mair, 1998). Damage to the ATN is most commonly associated with allocentric spatial memory impairment (Byatt & Dalrymple-Alford, 1996; Celerier, Ognard, Decorte, & Beracochea, 2000; Mitchell & Dalrymple-Alford, 2005; Moran & Dalrymple-Alford, 2003; van Groen, Kadish, & Wyss, 2002; Warburton & Aggleton, 1999; Warburton, Baird, & Aggleton, 1997), which may reflect an interdependency between the ATN and the hippocampal system (Warburton, Baird, Morgan, Muir, & Aggleton, 2000, 2001). Such findings support the hypothesis that the ATN and the hippocampus constitute essential components of an extended system underlying episodic memory (Aggleton & Brown, 1999; Aggleton & Pearce, 2001), which is consistent with recent studies on clinical cases that emphasize the deleterious effect of ATN damage in diencephalic amnesia (Caulo et al., 2005; Gold & Squire, 2006; Harding, Halliday, Caine, & Kril, 2000). A severe impairment in allocentric spatial memory in the Morris water maze has also been reported in rats with ILN lesions (Mair, Burk, & Porter, 1998; Savage, Castillo, & Langlais, 1998), but it is unclear whether encroachment of these ILN lesions to the adjacent ATN can account for these results (Mair et al., 2003). In a similar vein, there is mixed evidence whether the extension to adjacent thalamic structures also contributes to spatial memory impairments found after large ATN lesions (Warburton & Aggleton, 1999; Warburton, Morgan, Baird, Muir, & Aggleton, 1999; Warburton et al., 1997).

Recent studies have begun to focus on more selective, subtotal lesions to the ATN and the ILN. For example, Mair and his colleagues have shown that ATN lesions induce a delay-dependent impairment when varying arms in a radial maze are used for a non-matching to sample task (Mair et al., 2003), whereas restricted ILN lesions have no effect (Bailey & Mair, 2005). Our laboratory has explicitly contrasted rats with selective ATN and ILN lesions that have as minimal overlap as possible from one region to the next. As these ILN lesions included the adjacent lateral region of the mediodorsal (MD) thalamic nucleus, we have previously labeled these "lateral thalamic" (LT) lesions. This lateral MD region is impossible to avoid when making neurotoxic ILN lesions, but all the nuclei in this ILN/LT region have overlapping prefrontal and striatal connections (Berendse & Groenewegen, 1991; Mitchell & Dalrymple-Alford, 2005; Van der Werf, Witter, & Groenewegen, 2002). We found that ATN lesions severely impaired preoperatively-trained working and reference memory in a radial-arm maze, whereas rats with ILN rats exhibited only a very mild and transient working memory deficit (Mitchell & Dalrymple-Alford, 2005). A second study revealed a double dissociation in which only ATN lesions impaired the post-operative acquisition of spatial working memory in a radial-arm maze, whereas only ILN lesions produced a deficit on a preoperatively acquired response-related (egocentric) working memory task in a cross maze (Mitchell & Dalrymple-Alford, 2006). However, both ATN and ILN lesions produced severe impairments when the rats were required to learn arbitrary associations between an odor and a place (Gibb, Wolff, & Dalrymple-Alford, 2006), an ability that also requires the functional integrity of the hippocampus (Gilbert & Kesner, 2002). Together with uncertainty in terms of their effects on acquisition of spatial memory in the water maze, the latter finding suggests that the ATN and the ILN may sometimes produce similar impairments on learning and memory tasks and that both perhaps mediate some aspects of hippocampal-dependent learning.

A direct examination of the involvement of these two thalamic regions on spatial memory that does or does not require the hippocampus is therefore warranted. Hippocampal system functions are believed to support allocentric spatial memory but not egocentric spatial processing, whereas the reverse is generally true of the dorsal striatum (Cook & Kesner, 1988; DeCoteau & Kesner, 2000; Kesner, Bolland, & Dakis, 1993; McDonald & White, 1993, 1994; Morris, Schenk, Tweedie, & Jarrard, 1990; Packard & Teather, 1998). It is particularly interesting that one perspective that has emerged from the recent thalamic lesion literature is that ILN lesions, but not ATN lesions, impair egocentric spatial working memory tasks (Bailey & Mair, 2005; Mair et al., 1998, 2003; Mitchell & Dalrymple-Alford, 2006), which is consistent with the above-mentioned fact that some of the prominent connections of the ILN/LT region are with the dorsal striatum and dorsal prefrontal cortex (Van der Werf et al., 2002). If ILN/LT lesions impair functions associated with the dorsal striatum, then these thalamic lesions should also disrupt other egocentric spatial memory and response-related learning tasks that have been shown to be sensitive to caudate lesions. A severe impairment with dorsal caudate lesions has been reported when rats were trained on a left/right discrimination task in a Y-maze, especially when distal spatial cues are minimized (Mitchell & Hall, 1987, 1988). As ATN damage appears to influence hippocampal-dependent, allocentric spatial memory, but does not appear to disrupt egocentric (response-related) spatial reference memory (Aggleton, Hunt, Nagle, & Neave, 1996; Warburton et al., 1997), we tested the prediction that selective ATN and ILN lesions would produce a double dissociation across spatial memory in the Morris water maze and a water adaptation of left/right discrimination in a Y-maze. The use of two swimming tasks ensured that the basic motivational and motor requirements remained the same while the spatial memory demands differed across the two tasks.