

Research Report

Topography in the projections of lateral posterior thalamus with cingulate and medial agranular cortex in relation to circuitry for directed attention and neglect

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ABSTRACT

In the rat, the lateral posterior thalamic nucleus (LP) has reciprocal connections with areas of the cortex and the striatum involved in directed attention and its dysfunctional counterpart, contralateral neglect. It has also been shown that the medial portion of the mediorostral part of LP (mLPMR) is of special interest because it has connections with the dorsocentral striatum, a key node in this circuitry. In the present study we used neuroanatomical tracers to map the specific connections and topography of LP with the anterior cingulate cortex (ACC) and medial agranular cortex (AGm). We primarily used Alexa Fluor conjugates of the retrograde tracer cholera toxin subunit B, and injected two different colored conjugates into ACC and AGm in the same animal in order to directly compare the differential topography of the thalamocortical connections of mLPMR. The bidirectional tracer, dextran amine, was also used to examine anterograde corticothalamic projections of AGm and ACC. We found that mLPMR consists of two distinct groups of neurons, with the more dorsal group projecting to ACC and the more ventral group projecting to AGm. This is mirrored by a similar corticothalamic topography. These findings suggest that the ventral mLPMR is specifically associated with AGm and dorsocentral striatum, while dorsal mLPMR is associated with ACC. They also suggest that ACC may play a role in the circuitry for directed attention and contralateral neglect, as it is known to do in humans.

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Abbreviations: 3kDA, 3000 MW dextran amine; ACC, anterior cingulate cortex; AD, anterodorsal thalamic nucleus; AF, Alexa Fluor; AGl, lateral agranular cortex; AGm, medial agranular cortex; AM, anteromedial thalamic nucleus; AP, anterior–posterior coordinate; AV, anteroventral thalamic nucleus; cDCS, dorsocentral striatum, central part; CL, centrolateral thalamic nucleus; CTB, cholera toxin subunit B; DCS, dorsocentral striatum; HL, hindlimb cortex; LDDM, lateral dorsal thalamic nucleus, dorsomedial part; LP, lateral posterior thalamic nucleus; LPLR, lateral posterior thalamic nucleus, laterorostral part; LPMR, lateral posterior thalamic nucleus, mediorostral part; MD, mediodorsal thalamic nucleus; MDl, mediodorsal thalamic nucleus, lateral part; nucleus, lateral posterior thalamic nucleus; MDl, mediodorsal thalamic nucleus, lateral part; Cortex, area 2, nedial portion of the lateral posterior thalamic nucleus; PC, paracentral thalamic nucleus; PL, prelimbic cortex; PPC, posterior parietal cortex; RSa, retrosplenial granular cortex; S1, primary somatosensory cortex; VM, ventromedial thalamic nucleus; VP, ventral posterior thalamic nucleus

1. Introduction

The rat lateral posterior thalamic nucleus (LP) has connections with associative regions of cerebral cortex (Reep et al., 1990, 1994; Sefton et al., 2004; Sukekawa, 1988) and with superior colliculus (McHaffie et al., 2005; Sefton et al., 2004; Taylor et al., 1986), suggesting that it participates in multimodal integration and behavior. More specifically, the connections of LP indicate that it may play a key role in the circuitry for directed attention, and its dysfunctional counterpart, contralateral neglect. Recent studies from our group have indicated that the connections of LP are complex and topographic (Chandler et al., 1992; Kamishina et al., 2006, 2008).

LP has reciprocal connections with medial agranular cortex (AGm) and posterior parietal cortex (PPC). Unilateral lesions of either AGm or PPC produce contralateral neglect of visual, auditory and tactile stimuli, as do knife cuts that disconnect the corticocortical axons linking AGm and PPC (Reep et al., 2004). Additionally, LP projects to the dorsocentral striatum (DCS), which is the site of corticostriatal projections from AGm and PPC (Kamishina et al., 2008; Reep et al., 2003). DCS is a key node in the network subserving directed attention and it is necessary for recovery from neglect (Van Vleet et al., 2003a). Therefore, a detailed understanding of the connections of LP is of particular interest due to its central role in the network of brain regions implicated behaviorally in directed attention and neglect.

The central region of DCS (cDCS) receives LP input from only the far medial portion of mediorostral LP (mLPMR) (Kamishina et al., 2008). Furthermore, we have found that mLPMR has reciprocal connections with AGm (Kamishina et al., 2006), and AGm projects to cDCS (Kamishina et al., 2008; Reep et al., 2003). Thus, there is a complete thalamic–corticalstriatal loop linking mLPMR, AGm, and cDCS. Cortical area PPC has reciprocal connections with central LPMR, which projects to the dorsal periphery of DCS (Kamishina et al., 2006, 2008; Reep et al., 2003). The dorsal periphery of DCS is a target of input from PPC (Kamishina et al., 2008). Therefore, a second thalamic-cortical-striatal loop links central LPMR, PPC, and dorsal peripheral DCS.

Of particular interest is the specific topography within LPMR, since this area serves as an important relay node in the circuitry due to its connections to cortical areas AGm and PPC, and to DCS. Our group has discovered that there is very little overlap in the populations of neurons projecting from LPMR to AGm and PPC. Double injections of retrograde tracers into AGm and PPC revealed no double-labeled neurons in LPMR, and virtually complete segregation of the these neighboring cell populations (Kamishina et al., 2006). The neurons projecting to AGm are located in the ventral portion of mLPMR (Kamishina et al., 2006), and retrograde transport after tracer injections in cDCS produces neuron labeling in the same region (Cheatwood et al., 2003). The dorsal portion of mLPMR was labeled in cases where the injection site in AGm encroached upon the medially adjacent anterior cingulate cortex (ACC). Fig. 1 gives an overview of the location of ACC compared to other areas of the cortex.

Given the role of this circuitry in multimodal processing and neglect, the purpose of the present study was to use retrograde tracers to test the hypothesis that dorsal mLPMR projects to ACC, whereas ventral mLPMR projects to AGm, with no overlap between these neuronal populations. We used the newly available Alexa Fluor (AF) conjugates of cholera toxin subunit B (CTB). Thereby, we wished to ascertain a more complete picture of the connectivity of mLPMR, and its potential role in circuitry related to directed attention, neglect, and processing of multimodal information.

2. Results

Although we focused our analysis on the labeling only within LPMR and nearby nuclei, other labeling was also seen in many other nuclei as previously reported by other studies for this pathway. Fig. 1 indicates the anterior–posterior (AP) range from bregma of cortical injection sites made in this study.



Fig. 1 – Dorsal view of the left hemisphere of the rat cortex. The horizontal dashed line represents the dorsal midline. The unfolded medial wall appears above this line. The vertical dashed lines indicate the AP range of injection sites used in this study. For abbreviations, see list.

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