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Research report

Overlap and interdigitation of cortical and thalamic afferents to dorsocentral striatum in the rat

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Abstract

Dorsocentral striatum (DCS) is an associative region necessary for directed attention in rats. DCS is defined as the main region in which axons from ipsilateral medial agranular cortex (AGm) terminate within the striatum. In this double-labeling study, we placed a green axonal tracer in area AGm and a red one in an additional brain region. We examined the spatial relationship between terminals from area AGm and other portions of the cortical–basal ganglia–thalamic–cortical network involved in directed attention and its dysfunction, hemispatial neglect, in the rat. These include lateral agranular cortex (AGl), posterior parietal cortex (PPC), ventrolateral orbital cortex (VLO), and secondary visual cortex (Oc2M). One important finding is the presence of a dense focus of labeled axons within DCS after injections in cortical area PPC or Oc2M. In these foci, axons from PPC or Oc2M extensively overlap and interdigitate with axons from cortical area AGm. Additionally, retrograde labeling of striatal neurons, along with double anterograde labeling, suggests that axons from cortical area AGm and AGl cross and possibly make contact with the dendritic processes of single medium spiny neurons. Axons from thalamic nucleus LP were observed to form a dense band dorsal to DCS which is similar to that seen following PPC injections, and a significant number of LP axons were also observed within DCS. Projections from thalamic nucleus VL are present in the dense dorsolateral AGm band that abuts the external capsule, are densest in the dorsolateral striatum, and were not observed in DCS. These results extend previous findings that DCS receives input from diverse cortical areas and thalamic nuclei which are themselves interconnected.

Theme: Motor systems and sensorimotor integration
Topic: Basal ganglia

Keywords: Rat; Hemispatial neglect; Anterograde; Corticostriatal; Thalamostriatal

1. Introduction

Using a rodent model of hemispatial neglect [19,20,21,33,38–41], our group has determined that the medial agranular cortex (AGm or Fr2 [28]), a multimodal association premotor cortex with diverse cortical connections [30], and posterior parietal cortex (PPC) are components of a cortical–basal ganglia–thalamic–cortical network mediating directed attention in the rat [5]. The dorsocentral striatum (DCS), defined anatomically as the central striatal terminal field of projections originating from cortical area AGm, is critical for normal directed attention. Destruction of DCS results in chronic neglect which does not recover or respond to

Abbreviations: AC, anterior cingulate cortex; AGl, lateral agranular cortex; AGm, medial agranular cortex; cg, cingulum bundle; DCS, dorsocentral portion of the dorsal striatum; Fr1, frontal cortex, area 1; Fr2, frontal cortex, area 2; LD, laterodorsal thalamic nucleus; LP, lateral posterior thalamic nucleus; LO, lateral orbital cortex; lv, lateral ventricle; Oc2M, occipital cortex, area 2, medial part; PPC, posterior parietal cortex; PPCl, posterior parietal cortex (lateral portion); PPCm, posterior parietal cortex (medial portion); VO, ventral orbital cortex; VL, ventrolateral thalamic nucleus; VLO, ventrolateral orbital cortex

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dopamine agonists [29,38–40]. For these reasons, region DCS has become the focus of work on the cortical–basal ganglia–thalamic–cortical network mediating directed attention in the rat.

In previous anterograde and retrograde studies, we demonstrated that the cortical regions AGm, PPC, ventrolateral orbital cortex (VLO), and secondary visual cortex (Oc2M) all send projections to each other and to DCS [4,5,29,33]. Projections from each of these areas form a dense primary projection field in the dorsal striatum and an additional diffuse pattern of labeling in or near DCS. This pattern of labeling in the rat striatum has been described by many authors [1,2,15,25,33,43], and suggests the presence of at least two systems of corticostriatal projections terminating in the rat striatum, termed "discrete" and "diffuse" [43]. The same diffuse region of corticostriatal labeling was also described in the monkey [10,11], and may therefore be an innate property of corticostriatal organization. We have previously published a thorough examination of the band/diffuse pattern of labeling in the rat network for directed attention [33].

Previously, we identified the thalamic nuclei with which the cortical components of the rat network for directed attention are each reciprocally interconnected [29]. Because of the known functional and anatomical relationships between cortical areas and thalamic nuclei in the network [22,29–32], it is important to understand the topography of their striatal projections and the spatial relationship of these projections with respect to DCS. More detailed examination of the relationship between the convergent terminal fields of these key regions will provide a better basis to understand how their inputs interact to influence the activity of neurons in the DCS. Cortical–basal ganglia–thalamic–cortical networks have also been proposed as mediators of directed attention in primates. Similar to the rat network, the primate networks involve regions of prefrontal cortex and posterior parietal cortex, as well as associated regions of the basal ganglia and thalamic nuclei [24,26,36].

Our interest in these specific cortical areas extends to the more general question of whether multiple cortical areas terminate on or near the dendrites of individual striatal medium spiny neurons. This hypothesis has been proposed previously [44] and is supported by both electrophysiological and anatomical data [6,9,27], although it remains untested in a multi-labeling experiment at the light microscopic level. If it exists, this pattern of connectivity would support the hypothesis that the rat striatum, and potentially individual medium spiny neurons, plays a key role in integrating multimodal input from diverse cortical areas, and that the rat DCS is a center for convergence of diverse corticostriatal inputs related to directed attention. Our previous findings support these hypotheses. In a recent report, we found that many cortical areas project to region DCS, but none more consistently than AGm, PPC, and Oc2M [4]. Subsequently, we demonstrated that axons from cortical areas AGm and PPC exhibit both overlap and interdigitation in the rat DCS, using an anterograde tracer placed in individual cortical areas, as well as in two double-labeled cases [33]. The data from our previous papers regarding the spatial arrangement of corticostriatal projections are summarized in Fig. 1.

In the current multiple-labeling study, we directly tested the hypothesis that projections from cortical areas AGl (Fr1 [28]), PPC, and VLO, as well as thalamic nuclei VL and LP, overlap and/or interdigitate with projections from cortical area AGm in the striatal region DCS. Further, we sought to demonstrate whether neurons from anatomically non-adjacent cortical areas form terminals on or near the dendrites of the same individual medium spiny neurons in the rat striatum.

2. Materials and methods

All animal procedures were conducted according to institutional protocols that meet or exceed NIH and Society for Neuroscience guidelines. Animals were anesthetized with ketamine/xylazine (90 mg/kg:10 mg/kg). Upon cessation of tail pinch and eyeblink responses, animals were placed in a small animal stereotaxic device and a holes were drilled in the skull at the selected location. The dura was then incised, exposing the brain surface. All rats received one injection of a 10,000-mw dextran conjugated to a green-fluorescing molecule (100 nl of a 10% AlexaFluor 488 solution [15] in phosphate buffer; Molecular Probes) in area AGm using procedures derived from our previous work [4,30,31,33]. Additionally, each rat received an injection of a red fluorescing molecule conjugated to a 10,000-mw dextran (100 nl of a 10% FluoroRuby [34] or MicroRuby [23] solution in phosphate buffer; Molecular Probes, Inc.) in one of the following regions: cortical area AGl (case DCS 193), PPC (case DCS 178), VLO (case DCS 147), or

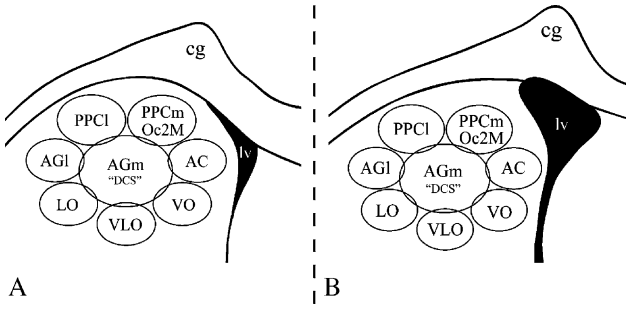

Fig. 1. Schematic representation of corticostriatal terminal fields at levels near: (A) the level of the genu and (B) the level of the septal nuclei. This figure was constructed from previously published data [30]. Corticostriatal terminal fields from many cortical areas project in a topographical way to the dorsal striatum and partially overlap and interdigitate with the terminal field of cortical area AGm. The striatal region containing the terminal field of cortical area AGm in a given brain is referred to as DCS.