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BRAIN RESEARCH

Research Report

Projections from the anteroventral part of the medial amygdaloid nucleus in the rat

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ABSTRACT

The medial amygdaloid nucleus (Me) integrates pheromonal and olfactory information with gonadal hormone cues, being implicated in social behaviors. It is divided cytoarchitectonically in an anterodorsal, anteroventral (MeAV), posterodorsal and posteroventral part, whose projections are well characterized, except for those of the tiny MeAV. Here, MeAV efferents were examined in the rat with the anterograde *Phaseolus vulgaris* leucoagglutinin (PHA-L) and retrograde Fluoro-Gold (FG) tracers and compared with those of other Me parts. The present PHA-L observations show that the MeAV projects profusely to itself, but its projections to other Me parts are modest. In conjunction with FG experiments, they suggest that the MeAV innervates robustly a restricted set of structures it shares with the anterodorsal and/or posteroventral Me. Its major targets are the core of the ventromedial hypothalamic nucleus (especially the dorsomedial and central parts), reached mainly via the stria terminalis, and the amygdalostriatal transition area. In addition, the MeAV innervates substantially the lateral and posterior basomedial amygdaloid nuclei and the intraamygdaloid bed nucleus of the stria terminalis. In contrast to other Me parts, it provides only modest inputs to the main and accessory olfactory systems, medial bed nucleus of the stria terminalis and reproductive hypothalamic nuclei. This anatomical framework suggests that the MeAV may play a role in orienting responses to chemosensory cues and defensive behaviors elicited by the odor of predators.

1. Introduction

The medial amygdaloid nucleus (Me) integrates chemosensory signals from the vomeronasal and main olfactory systems with gonadal steroid hormone cues (Canteras et al., 1995; Gomez and Newman, 1992; McDonald, 1998; Pro-Sistiaga et al., 2007; Swanson and Petrovich, 1998) and is thought to play a key role in social behaviors (Choi et al., 2005; Kollack-Walker and Newman, 1995; Newman, 1999), including social learning and memory (Luiten et al., 1985), as well as in innate anti-predatory defensive responses (Canteras et al., 2001; Dielenberg et al., 2001; Martinez et al., 2011).

The Me is divided cytoarchitectonically in an anterodorsal (MeAD), anteroventral (MeAV), posterodorsal (MePD) and posteroventral part (MePV) (Paxinos and Watson, 2007). This parceling is also supported by the selective expression of members of the conserved family of LIM homeodomain genes (Choi et al., 2005). In particular, the Lhx5 gene occupies a well-demarcated region, which corresponds roughly to the MeAV. Other neurochemical attributes further differentiate the MeAV from the rest of Me, such as a high density of glutamatergic (Poulin et al., 2008) and nitric oxide producing neurons (McDonald et al., 1993) allied to a virtual absence of gamma amino butyric acid (GABA)ergic neurons (Poulin et al., 2008).

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The major features of Me connectivity have long been established and differences between the anterior Me, primarily dependent on chemosensory inputs, and the MePD, heavily interconnected with gonadal steroid-responsive brain regions, are widely acknowledged (Canteras et al., 1995; Coolen and Wood, 1998; Gomez and Newman, 1992). Canteras et al. (1995), in a comprehensive study in the rat using the sensitive *Phaseolus vulgaris* leucoagglutinin (PHA-L) anterograde tracer, described in detail the projections arising from the MeAD, MePV and MePD, but the projections of the MeAV, due to the small size of this division, were not thoroughly examined. They noted however, that injections encompassing the MeAV and MeAD produced a dense terminal field in the core region of the ventromedial hypothalamic nucleus (dorsomedial and central divisions), whereas injections restricted to the MeAD labeled primarily the shell region. In consonance with Canteras et al. (1995), Choi et al. (2005) reported in mice that MeAV neurons are retrogradely labeled after injections into hypothalamic nuclei (the anterior nucleus and dorsomedial part of the ventromedial nucleus) associated with defensive behavior (Canteras et al., 2001; Swanson, 2000).

In the present study, MeAV projections will be documented based on the analysis of a case with an injection of PHA-L virtually confined to the MeAV and control cases in which injections of the retrograde tracer Fluro-Gold (FG) were placed in major terminal fields of the Me.

2. Results

2.1. *Anterograde tracing experiments*

2.1.1. *Injection sites*

A total of 14 cases with PHA-L injections in the Me were examined, 4 of them (516, 517, 564 and 565) extracted from a library of cases. One injection (case 565; Figs. 1 and 2) is almost confined to the tiny MeAV, two were located in the MeAD (cases 516 and 517; Fig. 2), one (case 564) involved both the MeAD and MeAV, and six (cases 758, 765, 788, 790, 791 and 798; Fig. 2) were primarily in the MePV. The remaining injections encompassed to a variable extent the MeAD, MePV and/or MePD.

2.1.2. *Case 565*

This case had an injection in the MeAV with only a few PHA-L labeled neurons in the MeAD (Figs. 1 and 2A). Efferents issued from the MeAV are almost exclusively ipsilateral and innervate substantially a restricted set of structures, their main target being the core region of the ventromedial hypothalamic nucleus (Fig. 3).

Many labeled fibers with closely spaced varicosities were seen in the MeAV (Fig. 4A) and a light to moderately dense terminal labeling was observed in the other divisions of the Me, being more pronounced in the MePV (Figs. 3E–H, 4B). A group of fibers extending caudally from the injection site innervates very substantially the amygdalostriatal transition area (Figs. 3F–H, 5A) and moderately, the lateral amygdaloid nucleus (mainly the ventrolateral division, but also the ventromedial division), posterior basomedial amygdaloid nucleus and intraamygdaloid part of the bed nucleus of the stria terminalis (BST; Figs. 3G–J, 5). Varicose fibers could also be traced into the posterior part of the capsular division of the central nucleus, which otherwise is sparingly labeled (Figs. 3E–G). A modest terminal labeling was noted in the posterolateral and posteromedial cortical nuclei, becoming more expressive caudally (Figs. 3G–K). The basolateral nucleus is free of labeling, except for some varicose axons in the lateral part of the posterior division (Fig. 3G). The anterior amygdaloid area and anterior basomedial amygdaloid nucleus are traversed by unbranched fibers with occasional bouton-like swellings, interpreted as fibers-of-passage (Figs. 3E and F).

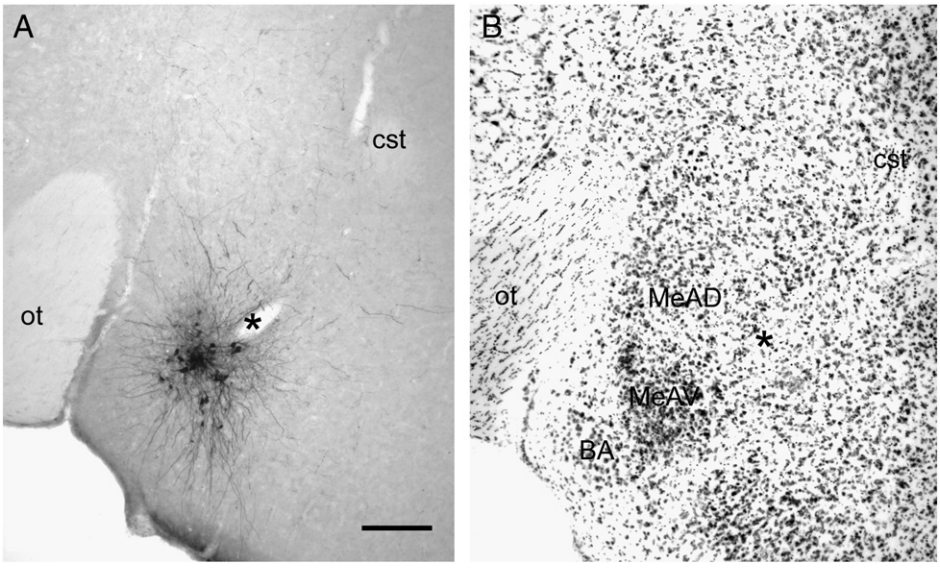

Fig. 1 – Brightfield photomicrographs showing a PHA-L injection site in the anteroventral part of the medial amygdaloid nucleus (MeAV; case 565) and the adjacent Nissl-stained section. *Indicates the same blood vessel. BA, bed nucleus of the accessory olfactory tract; cst, stria terminalis, commissural component; MeAD, medial amygdaloid nucleus, anterodorsal part; ot, optic tract. Scale bar = 200 μm.