BRAIN RESEARCH 1598 (2015) 97–113

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Brain Research

Research Report

# Hypothalamic, feeding/arousal-related peptidergic projections to the paraventricular thalamic nucleus in the rat

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ARTICLE INFO

*Article history:*
Accepted 11 December 2014
Available online 19 December 2014

*Keywords:*
Neuropeptide Y (NPY)
Cocaine- and amphetamine-regulated transcript (CART)
Melanin-concentrating hormone (MCH)
Orexin (ORX)
Paraventricular thalamic nucleus (PVT)
Nucleus accumbens shell (NAcSh)

ABSTRACT

Based on the importance of paraventricular thalamic nucleus (PVT) as a relay station of energy balance, arousal, and food reward, we aimed in the present study to determine projection patterns of neuropeptide Y (NPY), cocaine- and amphetamine-regulated transcript (CART), melanin-concentrating hormone (MCH), and orexin (ORX)-ergic fibers to the PVT. First, the distribution of peptidergic axon terminals within the PVT was examined. NPY and CART terminals were confined within the boundary of the thalamic nucleus, exhibiting almost identical distribution. MCH terminals were rarely observed. In contrast, ORX terminals were as extensive as NPY/CART terminals, but spread into the peri-PVT region. Second, neuronal origin of feeding/arousal-related peptides projecting to the PVT was investigated. NPY neurons were observed in the medial subdivision of the arcuate nucleus (Arc), whereas CART cells were in the lateral Arc as well as other hypothalamic regions including the paraventricular hypothalamic nucleus, lateral hypothalamus (LH), dorsal hypothalamic area, and zona incerta. Both NPY- and CART-fiber projections to the PVT were bilateral; ipsilateral proportion was 54.0%±3.6% ($n$=6) for NPY and 57.1%±2.5% ($n$=6) for CART. The total number of CART neurons projecting to the PVT exceeded that of NPY cells; the ratio of labeled CART neurons to NPY cells was 2.4±0.2 ($n$=6). In contrast, ORX-ergic fiber projection to the PVT exhibited a slight ipsilateral dominance (62.7%±1.6%, $n$=6), with majority of labeled cells located in the LH medial to the fornix (72.2% ±2.3%, $n$=6). Third, based on heavy projection from the PVT to the nucleus accumbens shell (NAcSh), the convergence of NPY and CART terminals on a single PVT neuron was identified; the proportion of labeled PVT neurons that received converging NPY/CART terminals compared with the total PVT neurons projecting to the NAcSh was 2.7%±0.6% ($n$=3). Finally, PVT cells receiving NPY, CART, or ORX terminals provided divergent axon collaterals to NAcSh and medial prefrontal cortex. The present observations provided the anatomical evidence that the PVT might play an essential role in the integration of antagonistically-acting, feeding/arousal-related peptidergic inputs on their way to the cortical reward circuit.



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http://dx.doi.org/10.1016/j.brainres.2014.12.029
0006-8993/

## 1. Introduction

The paraventricular thalamic nucleus (PVT), developmentally originated from the epithalamus, is distinct from other midline/intralaminar thalamic nuclei in its neural connections and physiological roles (Groenewegen and Berendse, 1994; Pinault, 2004). The thalamic nucleus is unique in that it receives extensive, hypothalamic feeding/arousal-related inputs. Remarkably high density of orexin (ORX)-ergic inputs from the lateral hypothalamus (LH) terminate in the nucleus, implying its role in arousal, anxiety, and food reward (Kelley