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Research Report

Injections of muscimol into the paraventricular thalamic nucleus, but not mediodorsal thalamic nuclei, induce feeding in rats

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ABSTRACT

The paraventricular thalamic nucleus (PVT) is a component of the midline thalamic group that is interconnected with several brain regions known to play important roles in the control of food intake, including the lateral hypothalamus and nucleus accumbens shell, suggesting that the PVT itself may be involved in mediating feeding behavior. In the current study, we examined whether inhibition of cells in the PVT with the $GABA_A$ agonist muscimol could alter food intake in non-deprived rats. To control for possible spread of the drug, we also observed food intake after injections of muscimol into the overlying ventricle or laterally adjacent mediodorsal thalamic nuclei (MD). We found that muscimol injections into the central PVT dose-dependently increased food intake. In contrast, intra-MD injections of muscimol resulted in a potent dose-dependent suppression of food intake, while those into the overlying ventricle had no effect. These results support the proposal that the PVT is a component of the neural circuitry controlling feeding behavior.

1. Introduction

The investigation of diencephalic control of food intake has largely centered on the hypothalamus, but evidence is available which suggests that the paraventricular nucleus of the thalamus (PVT) may also play a role. This nucleus projects heavily to the shell region of nucleus accumbens, a structure which is able to exert a powerful influence on feeding behavior (Stratford, 2007), as well as to a number of feeding related sites in the medial hypothalamus (Kiss et al., 2011; Moga et al., 1995). Conversely, the PVT receives inputs from a number of sites known to be involved in the control of food intake including the nucleus of the solitary tract, the parabrachial nucleus, the lateral hypothalamus and several medial hypothalamic nuclei (Brog et al., 1993; Chen and Su, 1990; Christie et al., 1987; Cornwall and Phillipson, 1988; Groenewegen et al., 1982; Ruggiero et al., 1998). The possibility that these connections may be involved in ingestive behavior is reinforced by findings that many of them contain substances which have been shown to influence food intake; for example, projections to the PVT from the nucleus of the solitary tract contain glucagon-like peptide 1 (GLP-1) (Llewellyn-Smith et al., 2011), those from the arcuate and dorsomedial hypothalamic nuclei contain cocaine and amphetamine regulated transcript peptide (CART) and cholecystokinin (CCK), respectively (Kirouac et al., 2006; Otake,

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2005), and those from the lateral hypothalamic region contain orexin (Kirouac et al., 2005). Although the transmitters involved have not been identified, it has also been shown that dorsomedial hypothalamic projections to the PVT originate from cells expressing receptors for the adipocyte hormone leptin (Gautron et al., 2010). Additionally, the PVT contains high levels of neuropeptide Y (NPY) and its receptors as well as the MC-4 melanocortin receptor (Freedman and Cassell, 1994; Gelez et al., 2010; Nichol et al., 1999).

Although these neuroanatomical and neurochemical data certainly suggest a role for the PVT in controlling food intake, functional data are far more limited, but still suggestive. Fos expression within the PVT has been shown to be altered both by ingestive behavior and by the administration of glucoprivic agents (Horn and Friedman, 1998; Nakahara et al., 2004; Warne et al., 2007). Additionally, lesions of the PVT have been reported to increase food intake and weight gain in rats (Bhatnagar and Dallman, 1999), although a similar effect was not obtained in hamsters (Purvis and Duncan, 1997).

Given the fragmentary nature of the experimental evidence linking the PVT to food intake, we, in the current study, investigated the effects of acute inhibition of PVT neurons with the $GABA_A$ receptor agonist muscimol on short-term feeding behavior in satiated rats. As controls for spread of the drug, we also evaluated the effects of muscimol injections aimed at the laterally adjacent mediodorsal thalamic nucleus (MD) and the overlying ventricle. The results of these studies support the view that the PVT is able to influence ingestive behavior.

2. Results

2.1. *Experiment 1: Response to muscimol injections into the PVT and third ventricle*

Three animals were excluded for inappropriate placements, and, in the remaining 13 subjects histological analysis revealed that the ventral tip of each cannula track terminated within the boundaries of the PVT (Fig. 1, round symbols; Fig. 2a). In the three animals in which Fluoro-Gold injections were made dorsal to the PVT, diffusion of the dye into the third ventricle and cerebral aqueduct could be observed through a fluorescence microscope.

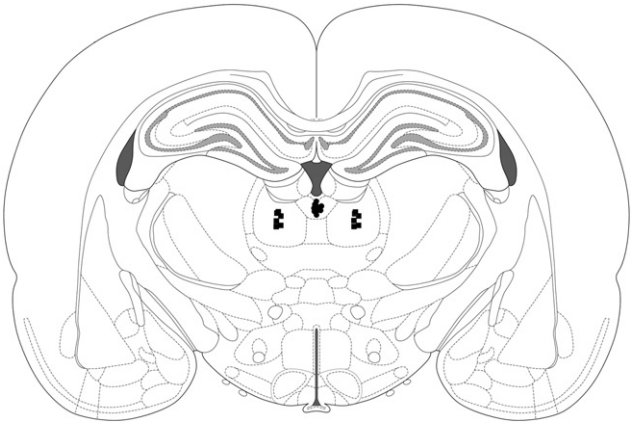

Fig. 1 – Schematic illustration of the location of paraventricular thalamic (circles) and mediodorsal thalamic (squares) injection sites in the current study. Section modified from (Paxinos and Watson, 2007), Plate 60.

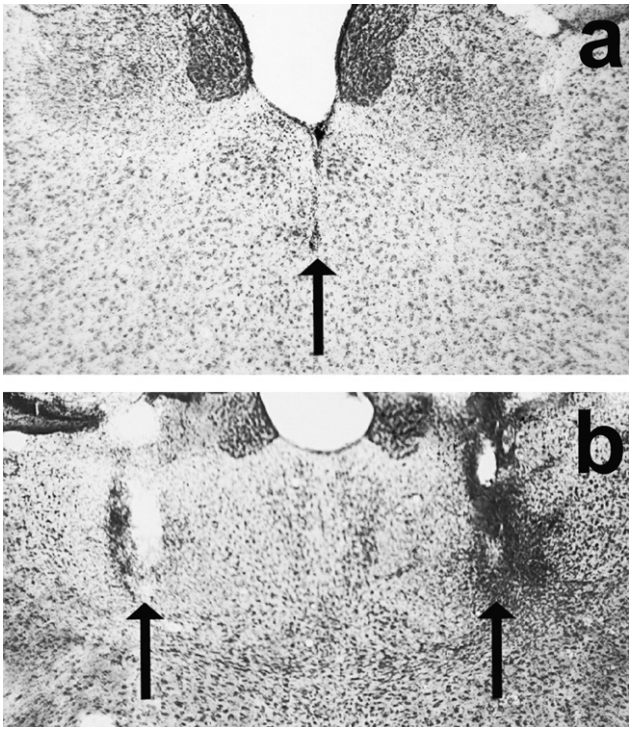

Fig. 2 – Photomicrographs of coronal sections of the rat brain showing infusion cannula tracks terminating in the (a) PVT and (b) MD.

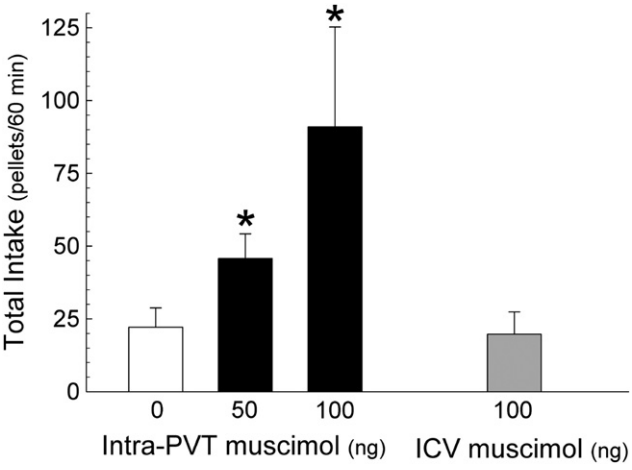

Fig. 3 – Mean (+SEM) food intake after muscimol injections into the PVT or the overlying ventricle. Intra-PVT muscimol dose-dependently increased food intake while intraventricular injections had no effect. $^*=p<0.001$ vs. saline injection.

As can be seen in Fig. 3, injections of muscimol into the PVT induced a pronounced increase in food intake ($F_{(2,12)}=21.5$; $p<0.001$). Post hoc comparisons showed that food intake was increased by both the 50 ng and 100 ng doses