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BRAIN RESEARCH

Review

Ascending projections from the caudal visceral nucleus of the solitary tract to brain regions involved in food intake and energy expenditure

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ABSTRACT

Metabolic homeostasis reflects the complex output of endocrine, autonomic, and behavioral control circuits that extend throughout the central nervous system. Brain regions that control food intake and energy expenditure are privy to continuous visceral sensory feedback signals that presumably modulate appetite, satiety, digestion, and metabolism. Sensory signals from the gastrointestinal tract and associated digestive viscera are delivered to the brain primarily by vagal afferents that terminate centrally within the caudal nucleus of the solitary tract (NST), with signals subsequently relayed to higher brain regions by parallel noradrenergic and peptidergic projection pathways arising within the NST. This article begins with an overview of these ascending pathways identified in adult rats using a standard anterograde tracer microinjected into the caudal visceral sensory region of the NST, and also by immunocytochemical localization of glucagon-like peptide-1. NST projection targets identified by these two approaches are compared to the distribution of neurons that become infected after inoculating the ventral stomach wall with a neurotropic virus that transneuronally infects synaptically-linked chains of neurons in the anterograde (i.e., ascending sensory) direction. Although the focus of this article is the anatomical organization of axonal projections from the caudal visceral NST to the hypothalamus and limbic forebrain, discussion is included regarding the hypothesized role of these projections in modulating behavioral arousal and coordinating endocrine and behavioral (i.e., hypophagic) responses to stress.

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1. Introduction

Metabolic homeostasis reflects the complex output of endocrine, autonomic, and behavioral control circuits that extend throughout the central nervous system (CNS). Brain regions that control energy intake and expenditure are privy to continuous interoceptive feedback from the body that can modulate appetite, satiety, digestion, and metabolism. Interoceptive signals from the gastrointestinal tract and associated digestive viscera are delivered to the brain primarily by vagal afferents that terminate centrally within the medullary dorsal vagal complex (DVC), comprising the dorsal motor nucleus of the vagus (DMV), nucleus of the solitary tract (NST), and area postrema (AP) (Rinaman, 2003a). In addition to vagal inputs from gastrointestinal and other thoracic and abdominal viscera, DVC neurons receive direct and indirect interoceptive signals from olfactory, glossopharyngeal, trigeminal, facial, and spinal afferent systems. A strong topography is evident in the terminal arborizations of primary visceral afferents, with inputs from the gut terminating within the caudal medial NST (Altschuler et al., 1989; Shapiro and Miselis, 1985). In

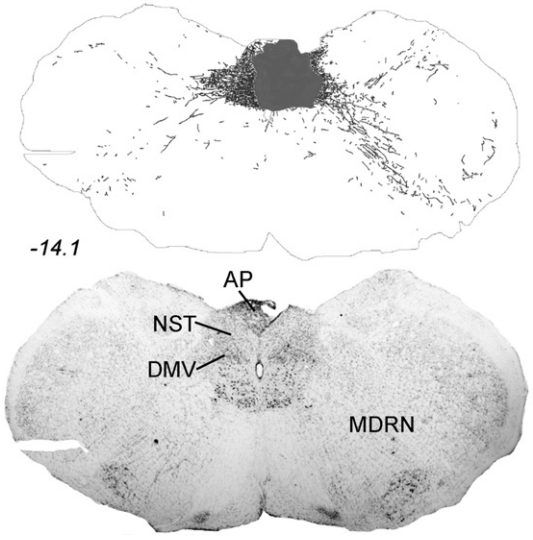

Fig. 1 – Iontophoretic PhAL injection site within the caudal DVC in an adult male Sprague–Dawley rat. The dark gray shaded area in the upper panel depicts the region of the tracer injection site, which contained PhAL immunoperoxidase labeling that was too dense to accurately draw. See Fig. 2 for immunofluorescence labeling of PhAL-concentrating neurons in an adjacent tissue section. Labeled fibers throughout the rest of the section in the upper panel (and in Figs. 3–10) arise from PhAL-concentrating neurons located within the injection site. The lower panel is a nearby Nissl-stained tissue section from the same rat. The approximate rostro-caudal level of each section (relative to bregma, in mm) is indicated, based on a standard rat brain atlas (Swanson, 2004). See Table 1 for abbreviations.

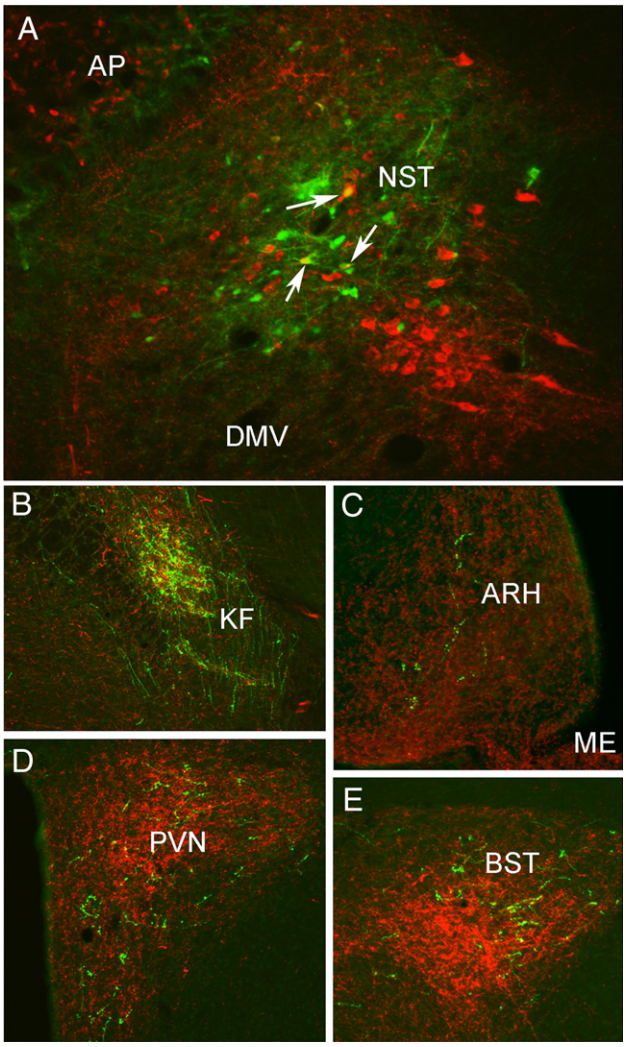

Fig. 2 – Dual immunofluorescent localization of PhAL (green) and the noradrenergic synthetic enzyme, DbH (red). A: Individual NST neurons concentrating PhAL (green) within the iontophoretic tracer injection site (see Fig. 1). A subset of these PhAL-positive neurons are DbH-positive (arrows point out 3 examples). B: PhAL-labeled fibers within the KF subregion of the lateral parabrachial nucleus. C: PhAL-labeled fibers within the hypothalamic ARH. D: PhAL-labeled fibers within the PVN. E: PhAL-labeled fibers within the BST. Note that each photomicrograph depicts PhAL and DbH immunofluorescent labeling photographed at only one focal plane through the section. See Table 1 for abbreviations.