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What happens to the pontine processing?: Repercussions of interspecies differences in pontine taste representation for tasting and feeding

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Abstract

In rodents there is an important gustatory relay in the pontine parabrachial nucleus (PbN) upon which much centrifugal modulation occurs to guide complex feeding behaviors. From the PbN two separate projections arise, one which synapses in the parvocellular medial tip of the ventroposteromedial nucleus of the thalamus, which in turn sends axons to taste cortex. This pathway is thought to be largely sensory in nature. A second pathway projects widely to the ventral forebrain areas including hypothalamus, and amygdala and is thought to be largely affective in nature. Recent support for this dissociation comes from Hajnal and Norgren who found that lesions of the pons but not the thalamus disrupted dopamine overflow in the accumbens during sucrose licking. Remarkably, the pontine taste relay does not appear to exist in human and nonhuman primates, or if it does exist, its role is much reduced. The aim of this symposium is to outline the role of the PbN in sensory and affective processing of taste in rodents and to speculate upon the implications of interspecies differences for tasting and feeding in primates. The specific aim of the introductory comments will be to provide an overview of evidence for these interspecies differences to set the stage for the remaining papers.

Keywords

Corticalization of function; comparative physiology; comparative anatomy; ingestive behavior; brainstem; obesity; reward; appetitive behavior

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In rodents taste information is conveyed by cranial nerves 7, 9 and 10 to the nucleus of the solitary tract (NTS) ^{1–3} (Figure 1). The majority of NTS taste neurons responding to stimulation of the taste receptors of the anterior tongue project to the ipsilateral medial aspect of the pontine parabrachial nucleus (PbN)⁴. The remainder project to adjacent regions of the medulla ^{2, 4–6}, whose role in taste processing remains largely unknown. From the PbN the gustatory pathway bifurcates into two pathways; 1) a ventral “affective” projection to the hypothalamus, central gray, ventral striatum, bed nucleus of the stria terminalis and amygdala and 2) a dorsal “sensory” pathway, which first synapses in the thalamus and then the agranular and dysgranular

insular gustatory cortex^{1, 3, 7–9}. These regions, in turn, project back to the PbN to sculpt the gustatory code and guide complex feeding behaviors^{1, 8, 10–14}. Relevant to the current discussion, it is notable that the source of centrifugal input to the PbN and NTS differ¹³, and stimulation of forebrain results in inhibition on PbN and excitation in NTS¹⁵. This suggests that the NTS and PbN play unique roles in tasting and feeding in the rodent.

In the primate taste information is also carried to the NTS by cranial nerves 7, 9, and 10¹⁶ (Figure 1). However, there is now strong evidence to indicate that the PbN gustatory relay is absent in the human and the nonhuman primate. First, second-order gustatory projections that arise from rostral NTS appear not to synapse in the PbN and instead join the central tegmental tract and project directly to the taste thalamus^{17, 18}. Parenthetically, although there are afferent projections from NTS to the PbN, these projections arise from the caudal viscerosensory NTS, not the rostral gustatory NTS¹⁷. Second, despite several attempts, no one has successfully isolated taste responses in the monkey PbN (Ralph Norgren, personal communication; Tom Pritchard, personal communication and see¹). Third, in monkeys the projection arising from the PbN does not terminate in the region of ventral basal thalamus that contains gustatory-responsive neurons¹⁸. In addition, Pritchard, Hamilton and Norgren note that the projections from PbN to the hypothalamus are neither as intense nor as widespread as in the rat, and that monkeys lack a projection from the PbN to the frontal and insular cortex. Fourth, although there are occasional clinical reports of taste deficits following pontine damage in humans^{19, 20}, the only experimental study of coding in this area clearly shows that the rostral NTS but not the PbN responds to taste stimulation²¹. In this study Topolovec and colleagues used functional magnetic resonance imaging, optimizing signal acquisition for maximal sensitivity over the brainstem, to investigate visceromotor and taste representation in the brainstem. Subjects engaged in a series of tasks that influenced sympathetic tone including isometric hand grip (increases heart rate), inspiration (leads to drop in blood pressure), and the Valsalva maneuver (increases blood pressure). They also engaged in tongue contraction and sampling a sweet taste. The PbN responded during the hand grip, Valsalva maneuver, and inspiration tasks but not during tongue contraction, which elicited response confined to the hypoglossal nucleus, or to taste, which elicited response primary in the NTS. Thus it would seem that in humans, as in monkeys, tasting and feeding occur without the input of the PbN gustatory relay.

The functional significance of these dramatic interspecies differences remains unknown. Are taste, food reward, and homeostatic control functionally similar in rodents and primates with different anatomy representing these functions? Is it the case that the NTS takes over the function of the PbN in primates or conversely, that this coding is transferred to the thalamus or even the insula? An altogether different possibility is that the PbN processing may not “transfer” to a higher or lower order taste relay, but actually disappear altogether, leading to fundamental differences in the function of taste coding and feeding. One obvious difference, which has been recognized²² is that the level at which taste information is integrated with affective and homeostatic signals differs between the species. In rodents taste information is sent directly to the reward and homeostatic centers (e.g. nucleus accumbens, amygdala and hypothalamus), whereas in primates it must first be relayed through the thalamus and insula before reaching reward and homeostatic centers. Thus it is likely that the way taste sensations influence feeding behavior, and conversely, the way feeding and homeostatic signals influence taste, is going to be fundamentally different in rodents and primates. This opens up the possibility that in primates, but not rodents, taste sensations influence feeding behavior irrespective of homeostatic state. The advantage might be that the double fudge sundae keeps on tasting great. However, the disadvantage might also be that the double fudge sundae keeps on tasting great.

Given the gravity of the recent obesity epidemic^{23, 24}, the likelihood that individual differences in food reward put some at risk for developing obesity in the presence of high energy dense

foods²⁵, and the tremendous advances being made in understanding how homeostatic signals interact with reward signals in the rodent brainstem^{26–28}, it seems imperative that we take time now to address these profound interspecies differences so that we can best know how to incorporate and use findings from rodent work to inform studies in primates, and to ultimately understand ingestive behavior in humans.

With this in mind the goal of this symposium is first to review what is known about the role of the rodent PbN in taste and feeding. Collectively, the presentations by Takashi Yamamoto, Patricia Di Lorenzo, Andras Hajnal and Ivan de Araujo will portray the rodent PbN, not as a simple relay, but rather as an important processing center for taste quality coding^{29–33} and a site where there is significant potential for sensory signals to be integrated with affective, homeostatic and other corticofugal inputs to guide complex feeding behaviors^{12, 13, 29, 30, 34–43}. A key question that remains is to determine whether sensory, homeostatic, and reward signals interact at the level of single cells (or circuits) within the PbN, and if so, how? The symposium will conclude with Tom Scott, who will review the primate gustatory system, highlight the known interspecies differences in hedonic coding of taste, and end with speculation on further repercussions of the interspecies differences.

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Figure 1.

Schematic depicting the gustatory pathway in rodents (dotted line representing tracks and black circles representing synapses) and in human and nonhuman primates (solid grey line representing tracks and grey circles representing synapses). Note that the primary distinction is that there is no synapse in the PbN (Pontine Parabrachial Nucleus) in primates. As such, gustatory information must first travel to the cortex (GC) before reaching the amygdala (Amyg) and hypothalamus (Hypothal). rNST = rostral Nucleus of the Solitary Tract; VPMpc = Ventroposteromedial Nucleus of the Thalamus (parvocellular division).