Activation of NPY receptors suppresses excitatory synaptic transmission in a taste-feeding network in the lower brain stem

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Chen Z, Travers SP, Travers JB. Activation of NPY receptors suppresses excitatory synaptic transmission in a taste-feeding network in the lower brain stem. Am J Physiol Regul Integr Comp Physiol 302: R1401–R1410, 2012. First published April 18, 2012; doi:10.1152/ajpregu.00536.2011.—Consummatory responses to taste stimuli are modulated by visceral signals processed in the caudal nucleus of the solitary tract (cNST) and ventrolateral medulla. On the basis of decerebrate preparations, this modulation can occur through local brain stem pathways. Among the large number of neuropeptides and neuromodulators implicated in these visceral pathways is neuropeptide Y (NPY), which is oftentimes colocalized in catecholaminergic neurons themselves implicated in glucoprivic-induced feeding and satiety. In addition to the cNST and ventrolateral medulla, noradrenergic and NPY receptors are found in circumscribed regions of the medullary reticular formation rich in preomotor neurons. To test the hypothesis that NPY may act as a neuromodulator on preomotor neurons, we recorded the effects of bath application of NPY and specific Y1 and Y2 agonists on currents elicited from electrical stimulation of the rostral (taste) NST in prehypoglossal neurons in a brain stem slice preparation. A high proportion of NST-driven responses were suppressed by NPY, as well as Y1 and Y2 agonists. On the basis of paired pulse ratios and changes in membrane resistance, we concluded that Y1 receptors influence these neurons both presynaptically and postsynaptically and that Y2 receptors have a presynaptic locus. To test the hypothesis that NPY may act in concert with norepinephrine (NE), we examined neurons showing suppressed responses in the presence of a Y2 agonist and demonstrated a greater degree of suppression to a Y2 agonist/NE cocktail. These suppressive effects on preomotor neurons may reflect a satiety pathway originating from A2 neurons in the caudal brain stem.

CIRCUITS CONTROLLING THE CONSUMMATORY behaviors of ingestive oromotor; ingestion; reticular formation; norepinephrine

input from brain stem orosensory and viscerosensory nuclei, including the rostral (gustatory) nucleus of the solitary tract (rNST), caudal (visceral) NST (cNST), the parabrachial nucleus, and ventrolateral medulla (8, 28, 34, 54, 64). Results from decerebrate preparations in which visceral signals, such as gastric load (49) and glucoprivation (15, 21), modify the amount of a palatable (sweet) stimulus that is consumed, suggest that these local pathways exert a potent influence over this consummatory circuitry (reviewed in Refs. 24, 45, 46). Although some amino acid-mediated excitatory and inhibitory inputs to IRt/PCRt preomotor neurons have been identified from the rostral (gustatory) nucleus of the solitary tract (41), little is known of the neurochemical identity of other local modulatory influences on these neurons. Indirect influences on IRt/PCRt premotor neurons, however, can be inferred from brain stem/fourth ventricle infusions of neuromodulators that impact feeding behavior. Brain stem infusions of opioids (32, 34), ghrelin (20), catecholamines (53), and neuropeptide Y (12, 13, 53), all modulate ingestive behavior, and some or all of these responses may involve circuits complete within the brain stem.

The present study was undertaken to begin to identify neuromodulators that modify the influence of rNST (gustatory) stimulation on prehypoglossal neurons in the IRt/PCRt. We focused on agonists for receptors for the neuropeptide Y (NPY) family of peptides, in particular, Y1 and Y2 receptors, because they are well represented in the IRt/PCRt (33, 51) and because the brain stem contains sources for their endogenous ligands; i.e., NPY in the cNST and ventrolateral medulla, and PYY in the medial RF (19, 23, 26, 39, 48). Our results, indeed, demonstrate that activation of these receptors has a marked influence on rNST-driven responses in IRt/PCRt prehypoglossal neurons. Both Y1 and Y2 agonists cause presynaptic inhibition, and Y1 has an additional postsynaptic inhibitory effect on these responses. Because a large proportion of NPY-positive neurons in the lower brain stem colocalize with catecholamines, we also examined whether norepinephrine (NE) also modulated neurons affected by NPY. In neurons inhibited by a Y2 agonist, NE had a further suppressive effect. These inhibitory results on presumably excitatory preomotor neurons are not easily related to the orexigenic effects of fourth ventricle NPY infusions but could be explanatory for a satiety pathway originating from A2 neurons that colocalize NPY and NE.

METHODS

Retrograde tracing. To record from identified prehypoglossal neurons, a retrograde tracer was injected into the hypoglossal nucleus (mXII) (41). Briefly, under deep anesthesia with a combination of ketamine and xylazine (90/30 mg/kg ip), Sprague-Dawley rat pups (P7–P10) were placed in a stereotaxic frame and held in place with

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mouse ear cups. After opening the caudal medulla at the level of the area postrema, injections of rhodamine-labeled fluorescent microspheres (Invitrogen: 0.04 μm diameter, 50 to 100 nl) were made into the mXII 0.2 mm rostral to obex and 0.2 mm lateral to the midline. The depth was predetermined by observing microstimulation-induced lingual movements through a micropipette (tip diameter 20–40 μm) filled with 0.9% saline. The surgical wound was gently packed with gelfoam, and the skin was joined with wound clips. Pups were returned to their home cage and survived for 12–48 h to allow retrograde transport of the fluorescent tracer. All experimental protocols were approved by the Ohio State University Institutional Animal Care and Use Committee in accordance with guidelines from the National Institutes of Health.

Slice preparation. Slices containing prehypoglossal neurons were obtained as reported previously (41, 62). Rat pups were decapitated under deep anesthesia (33% urethane, 10 ml/kg). The brain stem was quickly extracted and placed in an ice-cold, oxygenated (95% O2–5% CO2) normal Kreb’s solution containing (in mM): 110 choline, 25 NaHCO3, 3 KCl, 7 MgSO4, 1.5 NaH2PO4, 10 d-glucose, and 0.5 CaCl2. The brain was blocked ~1 mm caudal to obex and rostrally at the level of the incoming VIIth nerve and glued to a ceramic block with cyanoacrylate glue for sectioning in the coronal plane on a Vibratome 1000 (Vibratome, St. Louis, MO). Coronal slices of the brain stem were cut with a sapphire knife at 350 μm and transferred to an incubation chamber containing an oxygenated normal Kreb’s solution (in mM): 124 NaCl, 25 NaHCO3, 3 KCl, 1 MgSO4, 1.5 NaH2PO4, 10 d-glucose, and 1.5 CaCl2. Sections used for recording included those from the level where NST starts to separate from the solitary tract (rNST) produces inward current during electrical stimulation of the rNST were typically recorded under voltage clamp near the resting membrane potential using Clampfit 9.2 software (Molecular Devices, Union City, CA). Reported values were not corrected for a junction potential of ~12 mV. In a subset of experiments, changes in spontaneous firing frequency were monitored in current clamp.

Drug application. All drugs were kept as a concentrated stock solution stored at −20°C and diluted to their final concentration immediately before application. The following drugs were used: NPY (0.1–5 μM; Sigma, St. Louis, MO), a potent Y2 agonist (5, 6); D-arg-25-NPY (0.01–0.5 μM; American Peptide, Sunnyvale, CA) a Y1 agonist (22); BIIE 0246 (1 μM), a Y2 antagonist (17) and BIBO 3304 (1 μM; Tocris, Ellisville, MO), a Y1 antagonist, (17, 63), and NE (2-100 μM; Sigma-Aldrich). To test the pharmacological effects on the evoked postsynaptic currents, membrane resistance, 40 mV action potential amplitude, and stable resting membrane potential more negative than −40 mV. Action potential properties and membrane resistance were determined under current clamp with a series of current steps: −0.2 to 0.2 nA in 0.05 nA steps. Resting membrane potential and membrane resistance were monitored periodically throughout the recordings. Responses to electrical stimulation of the rNST were typically recorded under voltage clamp near the resting membrane potential using Clampfit 9.2 software (Molecular Devices, Union City, CA). Reported values were not corrected for a junction potential of ~12 mV. In a subset of experiments, changes in spontaneous firing frequency were monitored in current clamp.

Fig. 1. A: Stimulation of the rostral (gustatory) nucleus of the solitary tract (rNST) produces inward current during baseline condition (black). Suppression of rNST-evoked inward current following bath application of NPY (red: 0.5 μM) followed by return to baseline during washout (blue). B: dose-dependent effect of NPY on both excitatory (solid) and inhibitory (dashed) responses. C: in a larger population of neurons, 0.5 μM NPY reduces excitatory current by nearly 60%.
brane resistance, and spontaneous firing frequency, drugs were applied for 1 to 10 min following a minimum of 5 min of baseline recording. Following drug application, the normal Krebs solution was reapplied. Neurons that did not show at least a partial recovery were excluded from statistical analyses.

**Data analysis.** All data were expressed as means ± SE. The amplitudes of the rNST-evoked excitatory postsynaptic currents (EPSCs) were measured following the first response to a paired pulse stimulation or following a single pulse before and after drug application. The paired pulse ratio was computed as the amplitude of the 2nd EPSC divided by the 1st EPSC. Membrane resistance was calculated as the slope of the membrane voltage against the amount of current injected. Mean spontaneous firing frequency (SFF) was measured in current clamp before and after drug application. Mean control SFF was calculated from the number of spikes occurring during a 5-min interval prior to drug perfusion; mean drug SFF was calculated as the number of spikes occurring during a 1–3-min period following drug application. Paired t-tests or repeated-measures ANOVA were used to assess drug effects (P < 0.05 criteria).

**RESULTS**

The effects of bath application of NPY, d-arg-25-NPY (Y1 agonist), and NPY3–36 (Y2 agonist) on NST stimulation-induced EPSCs were studied in a total of 125 mXII-projecting IRt/PCRt neurons. NPY suppressed rNST-evoked excitatory and inhibitory responses in a dose-dependent fashion in the subset of neurons tested with multiple concentrations (Fig. 1B). Separate repeated-measures ANOVA were performed for excitatory (P < 0.013, n = 3) and inhibitory (P < 0.033, n = 3) responses. In a larger population of neurons tested at a concentration of 0.5 μM (n = 7), the mean peak excitatory response was suppressed by nearly 60% (paired t-test: P < 0.008). To more fully determine the type and location of the receptors mediating this suppression, we examined paired pulse ratios and changes in membrane resistance to bath application of specific Y1 and Y2 agonists.

Following bath application of the Y1 receptor agonist d-arg-25-NPY (0.01–0.5 μM) or the Y2 agonist NPY3–36 (0.01–1.0 μM), there was a dose-dependent reduction in the peak amplitude of the NST-evoked EPSCs (Figs. 2A and Fig. 3A). At 0.5 μM, d-arg-25-NPY significantly suppressed the peak excitatory current from 59.8 pA to 33.1 pA (−44.7%) followed by recovery during washout to 53.8 pA (Fig. 2B). The difference between the control and drug conditions was statistically significant (P < 0.001, paired t-test, n = 18). At 0.5 μM, NPY3–36 significantly suppressed the peak excitatory current from 63.5 pA to 32 pA (−49.6%) followed by recovery during washout to 55.4 pA (Fig. 3B). The difference between the control and drug condition was also significant (P < 0.025, n = 11). Both Y1 (n = 1) and Y2 (n = 2) agonists also suppressed rNST-evoked inhibitory currents, but the small number of inhibitory responses precluded any statistical treatment.

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**Fig. 2.** A: mean suppression of rNST-evoked inward current by Y1 receptor agonist d-arg-25-NPY at 3 concentrations. B: suppression at 0.5 μM is statistically significant (paired t-test). The suppression recovered almost completely with washout. C: example of the increase in the paired-pulse ratio. D: average increase in paired-pulse ratio was statistically significant for the 12 out of 18 neurons that showed suppression with d-arg-25-NPY.
For both NPY agonists, there was a significant increase in the paired pulse ratio. For the 12 (out of 18) neurons showing some degree of suppression to D-arg-25-NPY, the mean paired-pulse ratio increased from 0.99 during control to 1.4 following drug application (P < 0.004, paired t-test) (Fig. 2D). NPY3–36 increased the paired pulse ratio from 1.1 to 1.7 for the 9 neurons (out of 11) showing response suppression (P < 0.029) (Fig. 3D). These results imply a presynaptic inhibition of the excitatory synaptic transmission by Y1 and Y2 receptors.

Furthermore, the inhibitory effects of D-arg-25-NPY or NPY3–36 on the NTS-evoked EPSCs were abolished by the NPY Y1-selective antagonist BIBO3304 (1 μM, Fig. 4, A and B) or Y2-selective antagonist BIIE0246 (1 μM, n = 4, Fig. 4, C and D).

We further studied the site of inhibition by measuring membrane resistance. Perfusion of D-arg-25-NPY (0.5 μM) reduced the membrane resistance by 10.9% (P < 0.001, n = 4) (Fig. 5A); bath application of NPY3–36 (0.5 μM) had no significant effect (P = 0.38) (Fig. 5B). These results indicate that D-arg-25-NPY, but not NPY3–36, also exerts a postsynaptic effect in the inhibition of IRt/PCRt neurons to rNST stimulation. The reduction in membrane resistance following D-arg-25-NPY (0.5 μM) was blocked by the Y1-selective antagonist BIBO3304 (1 μM, n = 4; data not shown). These findings suggest that Y1 but not Y2 receptors exist in IRt/PCRt neurons. The inhibitory effect of both NPY agonists was also apparent from a reduction in mean spontaneous firing under current clamp. Application of D-arg-25-NPY (0.5 μM) reduced the spontaneous firing frequency by 60% (P < 0.004, n = 10), NPY3–36 reduced activity by 42% (P < 0.002, n = 11) (Fig. 6).

To determine whether NE was effective in RF neurons responsive to an NPY agonist, we first determined that bath application of NE produced a dose-dependent decrease in rNST-induced excitatory responses from RF neurons (Fig. 7). A concentration of 2 μM NE significantly reduced rNST-induced excitatory responses by 42% from 91.2 pA to 52.67 pA (P = 0.012). This dose was also effective in suppressing the one inhibitory response that we recorded. We then tested the effects of 2 μM NE on rNST-evoked responses in prehypoglossal RF neurons that showed at least a 10% reduction to NPY3–36 (Fig. 8). These neurons showed a further significant decrease in the rNST-evoked response compared with neurons that only received NPY3–36 (ANOVA: trial × group interaction: P = 0.035). The additional suppression in the evoked response to NE preceded by NPY3–36 was comparable to the reduction observed by NE alone. Specifically, the reduction seen between trial 8 (66% of baseline) and trial 10 (38% of baseline) represents a 42% reduction comparable to the mean reduction observed to 2 μM NE given by itself (Fig. 7).

**Histology.** Of 125 neurons identified as prehypoglossal and located in the reticular formation subjacent to the nucleus of
the solitary tract, 26 were reconstructed (Fig. 9). We targeted neurons to be subjacent to the rostral NST; however, a small proportion of them were located at an intermediate level, where the NST abuts the fourth ventricle (Fig. 9). Most of the neurons were large multipolar neurons, oftentimes, with processes extending dorsal toward or into the rNST. Neurons suppressed by Y1 and Y2 receptor agonists were intermingled with nonresponsive neurons.

DISCUSSION

We can conclude from our study that Y1 receptors influence prehypoglossal neurons both presynaptically and postsynaptically and that Y2 receptors also have a presynaptic locus. Although the source of the endogenous ligand for these receptors remains unknown, the brain stem is rich in neurons expressing NPY, as well as PYY, albeit to a much lesser extent. Both of these neuromodulators are associated with homeostatic energy regulation, suggesting that IRt/PCRt preromotor neurons are themselves a site of integration.

Location of cells. Neurons in this study were located immediately ventral to the rNST. Compared with the location of prehypoglossal neurons described in anatomical studies (e.g., 14, 58), it is clear that our study primarily sampled the dorsal-most extent of this population, in a region similar to those reported in two previous studies (41, 62). The region immediately ventral to the rNST has the densest population of prehypoglossal neurons, as well as the densest terminal field of afferent fibers emanating from the rNST (1, 54, 55, 59). Hence, it offers the greatest likelihood for sampling rNST/prehypoglossal interactions. Save for a modest propensity for prehypoglossal neurons innervating lingual retractor motoneurons to be somewhat dorsal compared with lingual protrudor premo
toneneurons (16), a spatial specialization of IRt/PCRt premo
toneneurons has not been reported. Thus, it seems reasonable to hypothesize that the results of the present study could be extended to more ventral populations.

Presynaptic vs. postsynaptic inhibition. Excitatory input from rNST stimulation produces an inward current via non-NMDA glutamate receptors (41). In the present study, bath application of the Y1 agonist d-arg-25-NPY reduced the rNST-evoked inward current and suppressed spontaneous action potentials. Both of these effects were blocked by the specific Y1 receptor antagonist BIBO3304. An increase in the paired-pulse ratio and a decrease in membrane resistance following d-arg-25-NPY indicated both a presynaptic and postsynaptic location for Y1 receptors. Although Y1 receptors have not
been specifically localized to prehypoglossal neurons in the
IRt/PCRt, Y1 receptor-like immunoreactivity is well repre-
sented in this general region (33). A postsynaptic location for
Y1 receptors with inhibitory effects is present in other central
neurons, including orexin-containing neurons in the lateral
hypothalamus (22), as well as brain stem neurons. For exam-
ple, Y1 agonists postsynaptically suppressed excitatory cur-
rents in dorsal motor nucleus (DMN) neurons in response to
cNST stimulation (6).

Y2 receptor-mediated inhibition appeared to be presynap-
tic to IRt/PCRt prehypoglossal neurons, and Y2R immuno-
reactivity appears not only well represented in the lower brain stem
(18, 42) but is clearly concentrated in the IRt/PCRt compared
with either the more lateral or medial RF (see Fig. 3I in Ref.
51). Similar Y2-mediated presynaptic inhibition of glutamate-
geric input was also observed in orexin neurons in the lateral
hypothalamus (22), as well as in DMN neurons in response to
cNST stimulation (4).

Possible sources of endogenous ligand. The endogenous
ligand(s) for Y1 and Y2 receptors is(are) most likely of brain
stem origin, as NPY neurons in the hypothalamus do not
appear to project to the brain stem reticular formation (2).
Neurons expressing NPY, however, are found in both the
caudal NST and ventral medulla, oftentimes colocalized with
catecholamines (19, 26, 39, 48), and there is extensive overlap
of Y1, Y2, and A2α adrenergic receptors in the IRt/PCRt where
we did our recordings (see Fig. 4E in Ref. 47) (33, 51). The
results of the present study demonstrating that NE acts in a
parallel fashion to a Y2 agonist in suppressing rNST-induced
responses is consistent with brain stem CA/NPY neurons as a
(single) source for these ligands. In addition to NPY, PYY is
also an endogenous ligand for Y1 and Y2 receptors and has

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**Fig. 5.** A: d-arg-25-NPY reduces the net change of the membrane potential induced by a series of depolarizing pulses. B: significant reduction in membrane resistance following application of Y1 agonist (n = 28). C: NPY 3–36 has no discernible effect on the potential change induced by depolarizing pulses. D: no significant change in membrane resistance following application of NPY 3–36.

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**Fig. 6.** A: reduction in spontaneous activity following infusion with Y1 agonist d-arg-25-NPY is accompanied by lowered resting membrane potential. B: significant reduction in spontaneous activity (paired t-test) following infusion with Y1 agonist returns to near normal following washout. C: significant reduction in spontaneous activity (paired t-test) following infusion with Y2 agonist returns to near normal following washout. Decrease in spontaneous activity was not associated with a change in resting membrane potential (not shown).

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been localized to neurons in the medial RF (3, 23, 44). PYY-immunoreactive fibers are evident in the medullary RF, including the IRt/PCRt.

Functional significance. NPY is a potent orexigenic peptide (52). In addition to its role in promoting food intake via hypothalamic pathways (reviewed in Ref. 65), there is growing evidence that NPY endogenous to the lower brain stem promotes food intake as well. Thus, infusions of NPY into the 4th ventricle lead to increased food consumption, similar to that observed following third ventricular infusions (12, 13, 53) Likewise, glucoprivation-induced feeding appears to depend on intact brain stem catecholamine-containing NPY neurons (CA/NPY) (35, 36, 46) and glucoprivation-induced feeding can be elicited in decerebrate preparations (15, 21). Thus, a parsimonious argument might simply hold that brain stem CA/NPY neurons augment food intake by direct action on preoromotor neurons. However, there are important unresolved issues with this chain of reasoning.

First, the majority of CA/NPY neurons implicated in glucoprivically induced feeding are in the ventral medulla, somewhat removed from the fourth ventricle (reviewed in Ref. 46). Although C1 neurons, many of which contain NPY (19, 48), traverse the preoromotor RF substrate en route to the cNST (8), it is not known whether this projection specifically includes C1 neurons colocalizing NPY, nor is it known if this pathway actually terminates on preoromotor neurons. Indeed, even if this were the case, it is difficult to envision how the inhibitory effects that we observed would produce an orexigenic effect. Activation of Y1 receptors is typically associated with a profound increase in food intake (e.g., 30). Thus, inhibition of (primarily) excitatory inputs from the rNST to prehypoglossal neurons, which are also primarily excitatory, runs counter to the expected increase in evoked activity that one might expect if activation of Y1 receptors were orexigenic. Interestingly, however, this paradoxical effect parallels the influence of NPY on lateral hypothalamic neurons (22), where it was observed that Y1 agonists postsynaptically inhibit identified hypocretin/orixin neurons. On the face of it, this suppression would also be unexpected if effects were related to feeding, as hypothalamic NPY and orexin/hypocretin both increase feeding. Indeed, the authors discuss NPY’s inhibition of orexin/hypocretin neurons in the context of arousal as an alternative to feeding mechanisms. Similarly, we cannot rule out a potential role for NPY’s effect on preoromotor neurons that is not directly related to food intake.

Nor is this paradox resolved by the recognition that Y1 receptors also bind PYY. Like NPY, PYY induces an orexigenic response when infused into the fourth ventricle (13). Although it is likely that PYY-positive neurons, located in nucleus gigantocellularis of the medullary RF project to the IRt/PCr (3, 23, 44), these PYY-positive neurons are in close association with melanin-concentrating hormone and orexin/positive fibers, orexigenic peptides originating from the hypothalamus.

Unlike Y1 receptor activation, however, Y2 receptor activation is associated with suppressing food intake, at least in some studies (e.g., 27, 42). Because A2 neurons are strongly implicated in satiety mechanisms (reviewed in Ref. 45), including those that survive decerebration (25), an alternative hypothesis to an orexigenic (excitatory) role for NPY on prehypoglossal neurons could involve the colocalization of NPY in a subset of A2 neurons (19, 48). In that case, the inhibition of preoromotor neurons observed in the present study could represent a brain stem satiety pathway originating from A2 neurons in the cNST, in which the release of NPY and/or NE suppresses excitatory

Fig. 7. Response of prehypoglossal neurons to stimulation of the rostral nucleus of the solitary tract in the presence of norepinephrine (0 to 100 μM). The absolute value of the inhibitory current from one neuron is plotted.

Fig. 8. A: prehypoglossal neuron that showed suppression of the amplitude of the rostral solitary nucleus stimulation-induced excitatory postsynaptic currents (EPSC) in the presence of NPY3–36, showed a further reduction following application of norepinephrine (black; baseline; red: 0.5 μM NPY3–36; blue: 0.5 μM NPY3–36 + 0.2 μM norepinephrine; green: washout). B: this reduction was significant across a population of NPY3–36 cells showing at least a mean 10% reduction following NPY3–36 (black line: n = 6) compared with similar neurons continuing to receive only NPY3–36 (red line: n = 5). Interestingly, in four neurons not showing the 10% reduction following NPY3–36 (blue line), there was no NE effect; these neurons were excluded from the ANOVA.
Fig. 9. Location of 26 neurons. Neurons with significant reductions (range: 29–100% suppression) following Y1 agonist (solid red), significant reductions (range: 22–100%) following Y2 agonist (solid blue), nonsignificant changes (range: 0–3%) to Y1 agonist (open red), nonsignificant changes (range: 0–3%) to Y2 agonist (open blue). Gi, nucleus gigantocellularis; IRt, intermediate subdivision of the reticular formation; mXII, hypoglossal nucleus; PCRt, parvocellular reticular formation; rNST, rostral nucleus of the solitary tract.
input from the rNST. The observation that NE acts in parallel with NPY agonists supports such a pathway, although it remains to be determined whether such effects actually originate from A2 neurons.

**Perspectives and Significance**

Considerable progress has been made in identifying neural and hormonal pathways that signal metabolic need or surfeit. Ultimately, these signals must influence neurons that control the actual behavior of feeding and a number of studies suggest that the IRt/PCRt is a critical region of the medullary reticular formation for the coordination and expression of oromotor consummatory behavior. The present paper demonstrates that activation of specific receptors for NPY or NE, neuropeptides with powerful effects on feeding behavior, also modulate the activity of oromotor neurons that control lingual movements. This study emphasizes the integrative capacity of brainstem circuits and suggests that these neuropeptides are likely to be but one of many in the hindbrain that modulates control of consummatory behavior.

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**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the authors.

**AUTHOR CONTRIBUTIONS**

Author contributions: Z.C., S.P.T., and J.B.T. conception and design of research; Z.C. performed experiments; Z.C. and J.B.T. analyzed data; Z.C., S.P.T., and J.B.T. drafted manuscript; Z.C., S.P.T., and J.B.T. edited and revised manuscript; Z.C., S.P.T., and J.B.T. approved final version of manuscript.

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