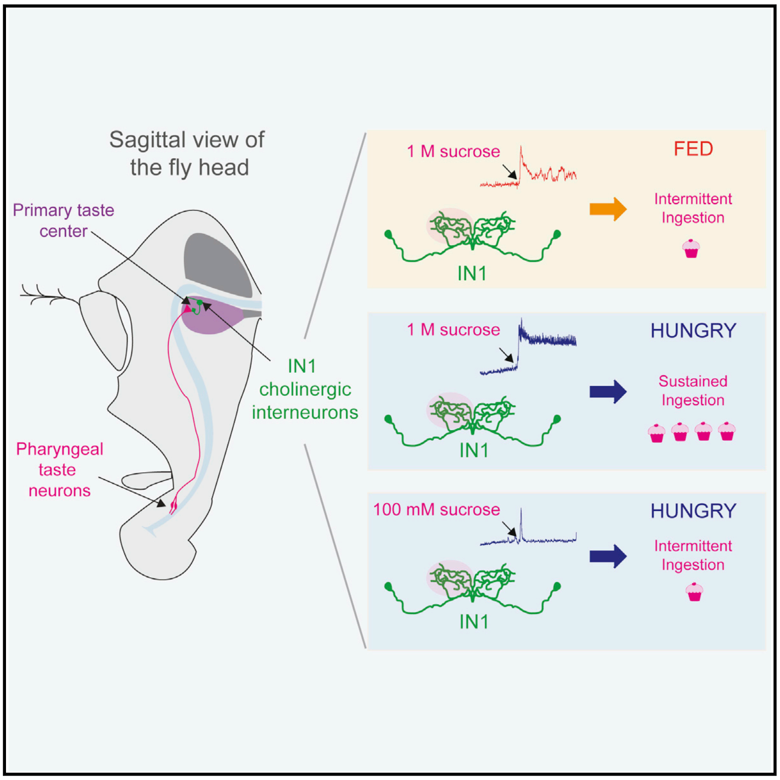
Cell

Article

A Taste Circuit that Regulates Ingestion by Integrating Food and Hunger Signals

Graphical Abstract



Authors

Nilay Yapici, Raphael Cohn, Christian Schusterreiter, Vanessa Ruta, Leslie B. Vosshall

Correspondence

leslie.vosshall@rockefeller.edu

In Brief

A neural circuit that connects sweet taste neurons in the pharynx with local interneurons in the primary taste center allows flies to regulate their ingestion of food by integrating information about hunger state and food quality.

Highlights

- Expresso system measures single fly ingestion in real time at nanoliter resolution
- Flies regulate ingestion by integrating hunger state and food quality
- IN1 interneurons receive input from pharyngeal taste neurons and regulate ingestion
- IN1 neurons respond to sucrose ingestion in a hunger-state-dependent manner

Yapici et al., 2016, Cell *165*, 715–729
April 21, 2016
http://dx.doi.org/10.1016/j.cell.2016.02.061

Article

Cell

A Taste Circuit that Regulates Ingestion by Integrating Food and Hunger Signals

Nilay Yapici,[1] Raphael Cohn,[2] Christian Schusterreiter,[3,4] Vanessa Ruta,[2,5] and Leslie B. Vosshall[1,5,6,*]
[1]Laboratory of Neurogenetics and Behavior, The Rockefeller University, New York, NY 10065, USA
[2]Laboratory of Neurophysiology and Behavior, The Rockefeller University, New York, NY 10065, USA
[3]Department of Computer Science, University of Oxford, Oxford OX1 3QD, UK
[4]Ticomo Research GmbH, 6300 Zug, Switzerland
[5]Kavli Neural Systems Institute, New York, NY 10065, USA
[6]Howard Hughes Medical Institute, New York, NY 10065, USA
*Correspondence: leslie.vosshall@rockefeller.edu
http://dx.doi.org/10.1016/j.cell.2016.02.061

SUMMARY

Ingestion is a highly regulated behavior that integrates taste and hunger cues to balance food intake with metabolic needs. To study the dynamics of ingestion in the vinegar fly *Drosophila melanogaster*, we developed Expresso, an automated feeding assay that measures individual meal-bouts with high temporal resolution at nanoliter scale. Flies showed discrete, temporally precise ingestion that was regulated by hunger state and sucrose concentration. We identify 12 cholinergic local interneurons (IN1, for "ingestion neurons") necessary for this behavior. Sucrose ingestion caused a rapid and persistent increase in IN1 interneuron activity in fasted flies that decreased proportionally in response to subsequent feeding bouts. Sucrose responses of IN1 interneurons in fed flies were significantly smaller and lacked persistent activity. We propose that IN1 neurons monitor ingestion by connecting sugar-sensitive taste neurons in the pharynx to neural circuits that control the drive to ingest. Similar mechanisms for monitoring and regulating ingestion may exist in vertebrates.

INTRODUCTION

All animals must simultaneously integrate external sensory stimuli with internal state to control behavioral decisions (Davis, 1979; Tinbergen, 1951). One behavior under strict neural and metabolic control is eating, which is regulated both by peripheral sensory detection of food and by internally generated states of hunger and satiety (Brobeck et al., 1943; Burton et al., 1976; Hoebel and Teitelbaum, 1962; Kennedy, 1953; Mayer, 1953; Raubenheimer and Simpson, 1997; Read et al., 1994). Perturbations in these homeostatic systems can lead to obesity and associated health problems (Morton et al., 2014). In both vertebrates and insects, the optimization of food intake requires tight regulation of behaviors responsive to food quality and hunger state. Once food is ingested, it takes several minutes for enteric nutrient sensing to regulate subsequent eating behavior, which may be too slow to control the amount of food ingested (Dus et al., 2015; Miyamoto et al., 2012; Zukerman et al., 2011). The biology of ingestion is poorly understood.

Mechanisms of peripheral taste processing and the regulation of the hunger state have been studied intensively in vertebrates. Taste receptors in the mouth and cortical regions in the brain that respond to taste qualities have been identified (de Araujo and Simon, 2009; Barretto et al., 2015; Chandrashekar et al., 2010; Chen et al., 2011; Huang et al., 2006; Mueller et al., 2005; Nelson et al., 2001; Zhao et al., 2003). The activation of sweet cells promotes food acceptance in hungry animals, while the activation of bitter cells stimulates food avoidance (Mueller et al., 2005; Zhao et al., 2003). Neurons in the hypothalamic neuroendocrine circuits express proopiomelanocortin (POMC), agouti-related peptide (AgRP), and melanocortin receptor (MC4R) and orchestrate ingestion in response to the hunger state of the animal (Aponte et al., 2011; Atasoy et al., 2012; Carter et al., 2013; Fan et al., 1997).

The mechanisms controlling taste and food intake in insects are remarkably similar to those in vertebrates. *Drosophila* flies detect and evaluate food using taste cells located in the periphery (Stocker, 1994). The insect equivalent of the vertebrate tongue is the labellum on the proboscis. This structure is decorated with taste sensilla that house gustatory neurons, which express gustatory receptors (GRs) that respond to sweet or bitter tastants (Chyb et al., 2003; Clyne et al., 2000; Dahanukar et al., 2001, 2007; Scott et al., 2001; Weiss et al., 2011). Stimulation of sweet taste neurons in the labellum and legs triggers extension of the proboscis in fasted flies, followed by initiation of food intake (Dethier, 1976; Dethier et al., 1956). Upon ingestion, food comes in contact with taste neurons located in the pharynx (Stocker, 1994). The function of these pharyngeal taste neurons is poorly understood, but a subset has been shown to regulate sugar ingestion (LeDue et al., 2015).

Taste neuron afferents from the mouthparts and pharynx target distinct regions of the subesophageal zone (Ito et al., 2014), the taste center of the fly brain (Marella et al., 2006). This is a densely innervated brain structure housing projection neurons, interneurons, and motor neurons that are required for taste acceptance, along with motor circuits that regulate ingestion (Flood et al., 2013; Gordon and Scott, 2009; Kain and