Combined Rather than Separate Pathways for Hedonic and Sensory Aspects of Taste in Fly Larvae?

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ABSTRACT

In mammals, the hedonic aspects (good versus bad) and sensory aspects (i.e., the molecular quality) of taste are associated with different brain regions. Anatomical data argue against such a separation in the primary taste center of Drosophila larvae. Is only one aspect of taste represented or do both co-exist at the same location? I present evidence for a hedonic representation in the larval taste center and review anatomical and behavioral data which support the co-existence of a sensory representation of taste with a hedonic representation.

The brain collects two types of information from taste stimuli: the hedonic aspect (Is it good or bad?) and the sensory aspect (What kind of molecule is it?). While the hedonic information commands ingestion or rejection of food, molecular information is thought to be essential for modifying responses to food through learning, In mammals, these two features are represented in different brain areas: while taste afferents project in the entire nucleus of the solitary tract, the dendrites of second order neurons are restricted to its medial or lateral part, depending on whether they deal with the hedonic or the sensory aspect of taste, respectively.[1]

Is there a hedonic and sensory aspect of taste representation in the fly brain? Recent reports support the idea for a hedonic circuitry in Drosophila, both in adults and larvae. A sensory aspect of taste in flies has not been extensively studied, but there are some hints in the literature that flies may also have a sensory representation. However, our recent neuroanatomical studies suggest different organizational principles of hedonic and sensory information in the taste center of Drosophila larvae than in mammals.

The taste system of the larva comprises the gustatory receptor neurons (GRNs), located at the periphery, and their target interneurons in a region behind the brain proper, called suboesophageal ganglion (SOG). GRNs are located on the tip of the larval head as well as internally, along the pharynx. In the first of two articles,[2] we studied the targets of GRNs, making use of Gal4 lines driven by the promoters of gustatory receptor genes. We distinguished two main primary gustatory target regions in the SOG (Fig. 1A and B): a median area associated exclusively with projections from internal taste organs and a lateral area, which receives gustatory input from both internal and external organs. Within these areas, GRN afferents do not appear to segregate further (but see below). The second article[3] presents the anatomy of each of the 20 neurons expressing the hugin neuropeptide, which were shown to be involved in feeding behavior.[4] Arborizations of these neurons, presumably of dendritic nature, are close to taste projections or even overlap with them. They are either restricted to a median area or cover the whole lateral area of the SOG (Fig. 1C), reminiscent of the terminal arborizations of taste afferents. Hence, while these neurons may be able to distinguish between ingested and non-ingested tastants, it is not known whether they can distinguish between other aspects of taste.

Spatially separate pathways for the hedonic and sensory aspects of taste are not evident in the larva. This is suggested by our observation that dendrites of *hugin* neurons cover each of the two areas—median or lateral—entirely. In other words, these putative second-order taste neurons receive information from many types of external or internal GRNs (Fig. 2). Do both hedonic and sensory representations coexist at the same brain location, or is there just a single type of taste representation?

Recent reports strongly support the idea for a hedonic taste circuitry in adult flies.[5] Using a genetic approach, the promoters of the caffeine receptor Gr66a[6] and of the trehalose (a sugar) receptor Gr5a[7] were used to drive the expression of Gal4 in two
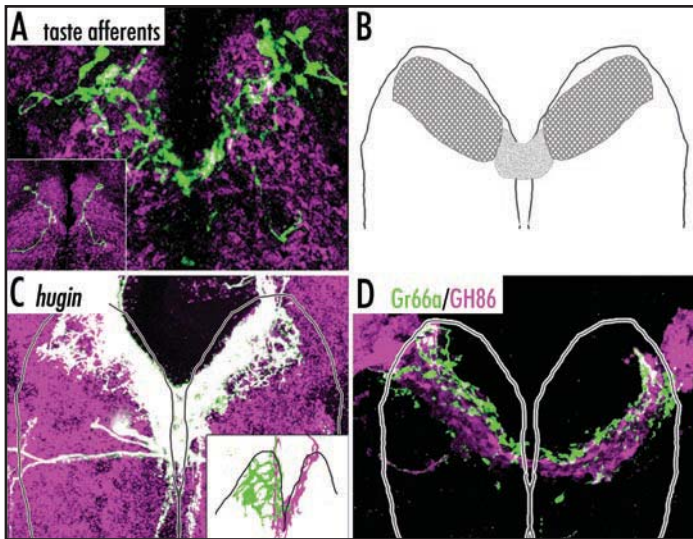
Figure 1. General organization of taste centers in the SOG of Drosophila larvae. Black lines indicate the neuropile border as visualized with an antibody against anti-acetylcholine transferase (magenta staining in A and C). (A) Terminal projections of taste afferents from both external and internal taste organs labeled by the Gr66a-GFP driver line, and from external organs only labeled by the Gr28be-Gal4 driver line (inset). (B) Proposed organization of the primary taste center in the larva. A medial area is associated with taste input from internal organs and is covered by the arborizations of three types of *hugin* neurons, whereas a lateral area receives mixed taste input from internal and external organs and is covered by the arborizations of another type of *hugin* cells. (C) Arborization pattern of the 20 *hugin* cells in the SOG. Inset: montage of the extension of two *hugin* neurons projecting respectively to the medial (magenta) and to the lateral SOG neuropile (green). (D) The projections labelled by the GH86 enhancer trap line (appetitive and aversive) are slightly more posterior than those of GR66a-GFP (aversive), especially in the medial area.

different populations of taste receptor cells.[8,9] Indeed, these two sets of neurons were shown to target different areas of the SOG.[10,11] Interestingly, the projections of water responsive cells overlap with those of sugar responsive cells,[12] arguing in favor of a hedonic representation of taste in the adult SOG. In addition, transgenic expression of a capsaicin receptor in either Gr66a-Gal4- or Gr5a-Gal4-labelled neurons changes the behavior of flies from indifferent to repulsive or attractive, respectively, when stimulating with capsaicin.[13] These data nicely correlate activity in different parts of the SOG with repulsion and attraction.

A hedonic representation seems to exist in larvae as well, although the situation is less clear, because none of the available Gr5a-Gal4 lines shows expression at this developmental stage. However, using a Gal4 line, GH86, that labels a large subset of taste receptor neurons (including sugar-responsive cells[14] but excluding Gr66a-Gal4 positive cells), we followed the same approach as in the adult, i.e., expressing the capsaicin receptor.[2] Since stimulating GH86 larvae in such experiments with capsaicin drives indifferent behavior, we propose that the neurons labeled by GH86 belong to two populations of cells, responding to attractive and aversive stimuli, respectively. Interestingly, the GH86-labelled taste neurons project more posteriorly in the SOG than the Gr66a expressing neurons, which drive aversive behavior in the capsaicin experiment (Fig. 1D). Therefore, we suggest that sensory neurons responding to aversive stimuli may project more anteriorly than those responding to attractive cues.
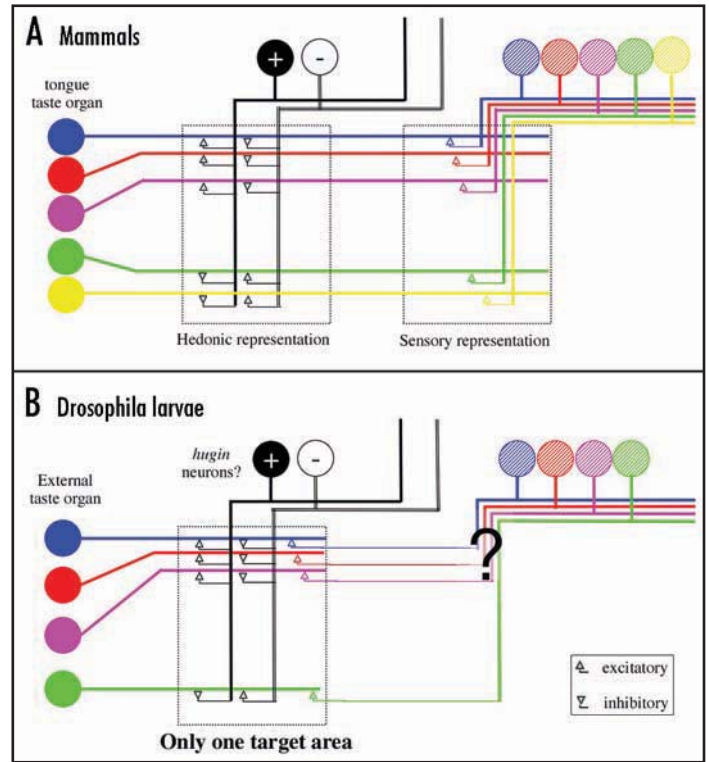

Figure 2. Highly simplified model of the organization of the primary taste center in mammals and in the fly larva. Only the part dealing with input from external organs is represented. Three different neurons responding to appetitive tastants and one responding to aversive tastants (green) are drawn. Second order neurons coding the hedonic representation get input from different categories of afferents, while those coding the sensory aspect have more restricted dendritic trees. (A) In mammals, the two types of second order neurons target different brain regions. (B) In Drosophila larvae, only one area appears to exist; it is covered by *hugin* neurons which may be second-order neurons coding the hedonic representation of taste. We postulate the existence of another type of second-order neurons, which would be intermingled anatomically with the hedonic representation.

Consequently, *hugin* neurons, judged by their extensive dendritic arbors and their putative role in feeding, are likely to be involved in computing the sum of gustatory inputs.

Whereas a hedonic representation of the primary taste center is obvious for adults and likely for larvae, the literature nearly ignored the issue of a sensory representation. This is surprising, because various data support the presence of sophisticated taste specificities in the periphery, especially in adults. For instance, from the four functional types of taste neurons identified by electrophysiological recording, three respond selectively to the attractive stimuli sugar, water, or salt at low concentration, whereas the fourth, responding to high salt concentrations as well as to bitter ligands, appears to be composed of different subpopulations of cells with diverse sensitivity profiles.[15] Furthermore, both in adults[10,11] and in larvae,[2] different gustatory receptor Gal4 lines label subpopulations of bitter-responding cells, reflecting probably the expression of different gustatory receptors. Accordingly, different sensory neurons likely express different combinations of receptors, which result in different response profiles. Thus, both electrophysiological and molecular approaches suggest that taste neurons show some selectivity to different tastants within a hedonic category.

It seems quite unlikely that taste specificity information provided by primary taste neurons is lost in the central nervous system. We rather propose that a molecular representation overlaps with the hedonic representation. Yet uncharacterized types of second-order taste neurons in adults and larvae, connected to subsets of afferents may be involved in the perception of specific molecular features of tastants (Fig. 2). This would allow animals to distinguish qualitatively between different tastants within the same hedonic category, and thus to learn avoiding specific food components.[1] In this context, it is interesting to note that in honeybees certain neurons connecting the SOG to the mushroom bodies, a center for learning, seem to establish spatially restricted dendritic trees.[16]

In conclusion, spatially separated pathways for hedonic and molecular aspects of taste are very unlikely in the primary taste center of Drosophila larvae. However, these two pathways may be intermingled anatomically, driving different types of second-order taste neurons (Fig. 2). Identifying the major types of such neurons, recording their response profiles and developing new behavioral paradigms for testing taste discriminative abilities will certainly shed light on this issue.

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