Flexible and dynamic representations of gustatory information

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Despite its high biological relevance in the regulation of eating behavior, little is known about the mechanisms of human taste perception. Here, I review recent findings on human taste processing and discuss the main factors that have hindered human taste research from progressing at the pace of the other sensory modalities. I mention methodological hurdles that have impeded much-needed neuroscientific applications in general and electrophysiological studies in particular. I argue that the current foci – on animal models on one hand, and neuroimaging in humans on the other – should be adjusted to include human electrophysiology because this approach could capture dynamically changing aspects of neuronal responses that remain uncharted territory in gustation.

Introduction

Taste is a gateway to nutrient sensing, driving adaptive behavior to support a sufficient and balanced nutrient supply, and likewise to avoid potential toxins, which makes it indisputably crucial to maintain our physical and mental wellbeing. Understanding how taste informa- tion is processed is pertinent to tackling its disturbances and associated health effects including malnutrition and obesity — both major global health concerns. Although taste has fascinated scholars over centuries, the most fundamental question of how the human gustatory sys- tem encodes and conveys taste information from the sensory organ to the brain remains largely unanswered [1]. An inevitable and impactful consequence of this knowledge gap is that it hinders further research on gustatory perception and cognition, and it impedes the development of robust theories. Here, I review recent findings on human taste processing and discuss what I consider the main factors that are holding back the field and most recent advances that have the potential to take taste research in new directions.

The taste pathway

Unravelling the gustatory projections from tongue to cortex has challenged researchers for decades. In rodents, the understanding of the roles played by different relays along the gustatory neuroaxis has significantly progressed during the past decades, partly owing to technological advances in neuroimaging. Yet, researchers are still to find consensus on the basic mechanisms underlying taste processing in animal models [1]. Taste signaling (Figure 1) begins with the detection of chemicals and their concentrations by taste receptor cells in the oral cavity [2]. It is then transmitted via bilateral branches of cranial nerves innervating one side of the tongue (hemi-tongue). In rodents, afferent fibers are routed through nerve-specific ganglia and project ipsilaterally to the gustatory nucleus of the solitary tract (NTS) and para- brachial nucleus of the pons (Pbn) from where they propagate to the ventroposterior medial nucleus of the thalamus (VPM) [cf. 1]. In primates, ascending fibers are thought to be routed to the primary taste area within the insula and then further to the orbitofrontal cortex [3, cf. 4]. Perhaps surprisingly to scholars from the other senses, even the exact location of the primary taste area is still controversial (see Primary taste cortex). Human neuroimaging [cf. 5] and lesion studies [cf. 6] have yielded inconsistent results in this respect.

Although taste is typically experienced across the entire mouth, psychophysical experiments [7] suggest a lateralization of taste processing. Based on our understanding of the other senses, one can assume numerous possible models of taste information flow; the most intuitive would assume ipsilateral or contralateral ascension with complete or partial crossing of fibers (models 1 and 2 in Figure 2a), ipsilateral ascension with a crossing of fibers at the cortical level (model 3) or a hybrid model with ipsilateral and contralateral ascension (model 4) [8–11]. The apparent incompatibility can be attributed to small sample sizes, heterogeneous lesions, and different methodological approaches, and it only further illustrates the urgency to unravel the human taste-processing pathway. Past studies have, however, equipped us with a pool of putative taste relays waiting to be studied in humans (see Figure 2b). The discovery of functional lateralization and hemispheric dominance, for example for language, has revolutionized cognitive neurosciences and our under- standing of how the human mind works. A detailed understanding of the gustatory pathway would provide a pertinent addition to this body of evidence and support diagnosis and prediction of functional deficits in brain injury.

Localizing taste

In humans, past research has been constrained by methodological challenges. The delivery of liquids with millisecond- precision to a defined area on the tongue is one such challenge but obligatory for achieving the high temporal resolution needed to assess functional pathways. Also, liquids evoke a touch sensation, thereby rendering the study of taste independent of somatosensation particularly difficult. These, and other, factors contribute to a notoriously poor signal-to-noise ratio of taste-evoked responses, complicating detection and analysis. Electrophysiological (i.e. magnetoencephalography/ electroencephalography, MEG/ EEG) studies are, consequently, scarce as these are less forgiving of poor temporal stimulus control than hemodynamic measures (e.g. functional magnetic resonance imaging, fMRI). However, there is no doubt that the high temporal resolution offered by electrophysiological measures is essential for capturing the dynamics of gustatory responses.

Primary taste cortex

Most previous work has favored haemodynamic measures and exploited its advantageous spatial resolution to localize gustatory areas. Recent meta-analyses highlighted activation in several cortical areas including the anterior insula and frontal operculum, mid-dorsal insula and Rolandic opercu- lum, posterior insula and parietal operculum, but also the postcentral gyrus [5,12]. Of these, the mid-dorsal insula is likely the human primary gustatory cortex based on fMRI [13,14], EEG [15], and direct electrical stimulation [16] studies. The mid-dorsal insula of the human is anatomically close to gustatory thalamic projection fields in the anterior and middle insula of the macaque monkey [17]. It should be noted, however, that others have proposed the posterior insula as primary gustatory cortex [18]. Unlike the primary visual cortex, the primary gustatory cortex (like the entire insula) is best viewed as a multimodal integration hub owing to its many afferent connections to other brain areas associ- ated with internal and external sensations, emotions, and motivation and because only a small fraction of neurons in the insula is taste-specific [19]. While this may complicate strictly unimodal investigations, it does reflect on the multisensory nature of taste processing, which is naturally linked with somatosensation (i.e. touch, texture, temperature), olfaction, and interoception (i.e. sense of the internal state of the body) as these (and other) sensations are an integral part of the eating experience [20].

Taste features

For any sensory system, an important research question is how its pertinent stimulus features, such as contrast, color, and size in vision, or frequency, pitch, and loudness in audition, are neuronally represented. Taste is often characterized in terms of qualities (e.g. sour or sweet), intensity (i.e. chemical concentration), and hedonics (i.e. pleasantness), although more features certainly exist [cf. 21]. Behaviorally, these dimensions are not independent: for example, sweet is more pleasant than bitter irrespec- tive of their concentration (quality-hedonics link) and the pleasantness of sour decreases with increasing concentration (intensity-hedonics link). However, most previous neuroimaging studies have investigated taste quality [22,23], intensity [24], and hedonics [25] in isolation, thereby overlooking their relations — with only a few exceptions [26,27]. Human neuroimaging studies have, accordingly, identified somewhat inconsistent 'hot spots' for taste, intensity, and affective value – with some spatial overlap but also spatially separate areas – as neuroanatomical correlates of these features [5,12]. Taste hedonics – the emotional dimension of taste – has been associated with activation in the amygdala (which is implicated in the control of emotions and hedonic tone [28], and orbitofrontal cortex. Taste identification and intensity have been predominantly localized to segregated areas within the insula [see Ref. 12]. Together these findings have supported the view of a functional modularity within the taste network, where physical dimensions (taste identity and intensity) are processed in taste-specific, sensory areas, whereas the psychological, evaluative dimension (preference and aversion) is processed in the 'emotional brain' [5,12]. Expanding this vista, a recent neuroimaging study proposed a novel role of the amygdala in human taste intensity perception via an inhibitory gain to the thalamus [29]. Electrophysiological recordings in rats revealed that this gain is dynamic and contains both excitatory (early) and inhibitory (late) outputs [30].

Dynamic coding

The combination of neuroimaging techniques that overlook the dynamic nature of neuronal responses together with the focus on the localization of taste function has promoted a static, modular view of the human gustatory system, where different taste features are represented in different brain areas [24]. I challenge this view because neuronal responses are highly dynamic, changing within milliseconds. Thus, temporal dynamics, rather than being viewed as a nuisance for measurements, may rightfully be considered an integral and informative parameter of gustatory coding [31]. It is hence important to consider that taste perception unfolds in time: it requires more than an instantaneous gustatory 'snapshot' and it is more dynamic than the sustained activation of certain 'hot spots', as depicted by fMRI. Rather, the dynamic nature of gustatory perception is best illustrated by time-resolved measures such as MEG/EEG, which have revealed a chain of microstates [32] that each reflect different aspects of the taste experience [cf. 33] and that are generated by different sources within the brain [34–36] (see Figure 2c for an illustration of the principle of dynamic responses). Dynamic electrophysiological response patterns carry the information needed to decode different tastes [15,37,38] and they revealed that taste sensory and hedonic computations operate on different time scales [39,40,41] in humans and in rats.

Linking brain activity with behavior

In contrast to animals, human subjects offer the unique opportunity to examine the links between the chemical, neuronal, and psychological spaces of taste processing [cf. 14]. Chemical space includes parameters such as identity and concentration of the taste stimulus, neuro- nal space reflects activation of the neural circuits at different levels in the taste axis, and psychological space describes perceptions such as 'sweet' and behaviors associated with taste. Distances within and between spaces can be used to formalize their (dis) similarity. A full account of gustatory perception should,

hence, consider all three spaces. Unravelling their inter- relations, however, requires subjects who can report on their perceptual experiences in ways that exceed what can be assessed with simple approach and avoidance behavior observable in animal models. In human sub- jects, taste-evoked neural response patterns carry the information to successfully predict taste perception and taste-related behavior [15,39,42].

For example, the more similar EEG response patterns are between any two tastes, the more likely participants are to confuse these tastes, thereby displaying a neuronal-phenomenological mapping [15]. This is surprising as one could expect that the chemical identity solely deter- mines associated neuronal processes and with that also the resulting percept. Instead, perception mirrors the 'errors' in neuronal processing. The time point at which EEG response patterns were informative, varied with participants' behavioral goal such that discriminative information was available earlier when the task required a quick response (i.e. pressing of a button), and later when subjects were allowed to respond more slowly [42]. More- over, the latency of neural information predicted participants' response times at the single trial level, suggesting that the speed of neuronal processing determines the speed of perceptual decision-making [39]. Successful regulation of nutrient uptake and rejection of harmful substances is likely to demand more than the mere detection of a taste. A taste also needs to be identified and differentiated from other tastes to elicit the appropriate behavior. Accordingly, mere detection of a taste stimulus is faster than the identification and discrimination between tastes, yet the hedonic value is assessed in parallel [41] and may facilitate taste identification [39].

Future considerations

Most of the (neuro)physiological understanding of mammalian taste processing comes from rodents, and to a much lesser extent from monkeys [43–45]. In contrast to vision, human cognitive gustatory neuroscience relies on an incomplete understanding of the anatomical and physiological organisation of the system. Given these starting conditions, it must be acknowledged that the successful transfer from animal models to humans hinges on the similarities between the species. For example, while there are many similarities, important differences also exist, for example, in the effects of agonists for taste receptor cells for certain taste stimuli [46]. Also, taste- specific fibers ascend through the parabrachial nucleus on their way to the gustatory thalamus in rodents, but not in monkeys [47], raising the question as to whether the parabrachial nucleus has any role in human taste processing [48]. Commonalities, on the other hand, are evident particularly in central coding mechanisms, particularly those considering the dynamic nature of neuronal activity [30,38,41,43].

Understanding the function of central taste relays in the coding of the main dimensions of taste requires an experimental approach that appreciates the multivariate link between different taste features. A change in perspective is, thus, obligatory to understand the nature of taste perception. This is now possible, owing to recent methodological [15,49,50] but also conceptual [37,39,42] advances, which enable us to overcome the limitations of past approaches. Specifically, precision gustometry [15,50,51], with its meticulous temporal, spatial, thermal, and sensory control, is obligatory for electrophysiological recordings and has already begun to push boundaries and let us already discover thus far unknown mechanisms of neural taste coding. These advances will continue to open up new avenues to characterize taste information flow and function.

Conflict of interest statement

Nothing declared.

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Figures

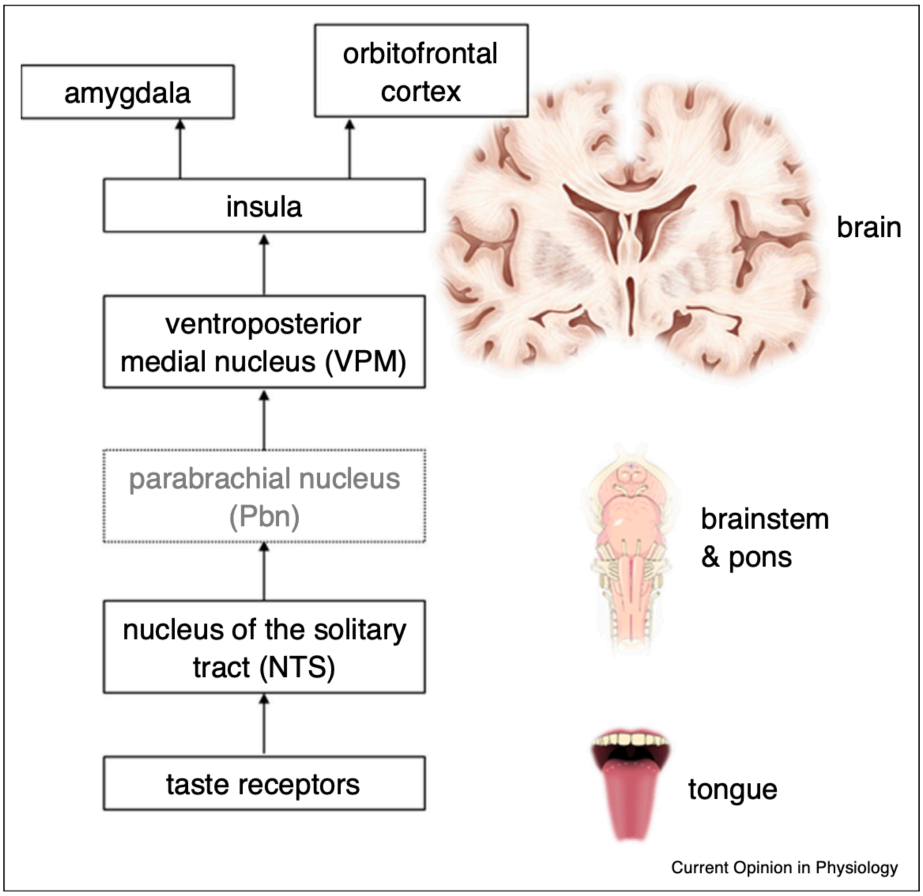

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Figure 1. Schematic diagram of the human gustatory pathway. The role of the Pbn in the primate brain is unclear — it is included to facilitate the comparison with the rodent pathway. Recurrent connections are disregarded.

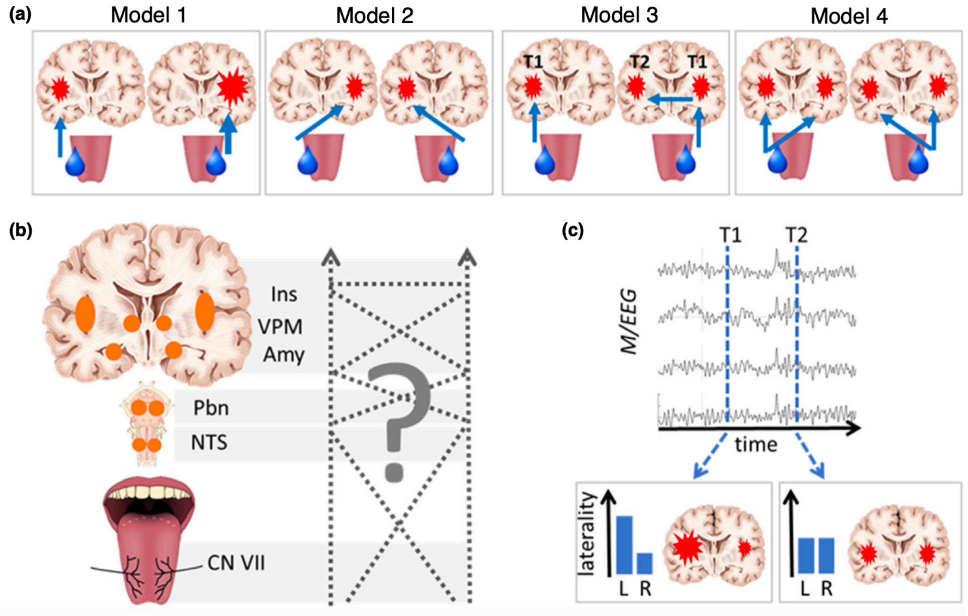

Figure 2. Simplified models of taste information flow illustrate the ascent from the left and right hemitongue to cortex.
(a) Model 1 (ipsilateral ascension): ipsilateral cortex activation with right dominance. Model 2 (contralateral ascension): only contralateral activity in the cortex. Model 3 (dynamic): initial ipsilateral cortex activation for single-side stimulation (T1), followed by bilateral cortex activation (T2). This model is an example for dynamic, hemispheric information exchange. Model 4 (ipsilateral and contralateral ascension): bilateral cortical activity for stimulation of either side of the tongue. The models make no predictions as to where (anatomical level) or when information crosses hemispheres. (b) Putative anatomical levels of taste processing: cranial nerve VII on the tongue, nucleus tractus solitarius (NTS) in the brain stem, parabrachial nucleus (Pbn) in the pons, ventroposterior medial nucleus of the thalamus (VPM), amygdala (Amy), and insular cortex (Ins) in either hemisphere. In primates, it is unclear where the Pbn is part of the taste pathway. Taste information could be transmitted to higher levels with or without complete or partial crossing of fiber at each or between levels. (c) Schematic example of a dynamic change in hemispheric dominance over time in M/EEG (magnetoencephalogram/electroencephalogram) recordings: from stronger activation in the left cortex at T1 to equal activation of both hemispheres at T2. Plots below the time course show the strength of lateralization formalized as laterality index for the right (R) and left (L) hemisphere.