Functional neuroimaging of umami taste: what makes umami pleasant?[1–4]

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ABSTRACT

The cortical processing of umami shows what makes it pleasant and appetitive. The pleasantness of umami reflects and is correlated with processing in the secondary taste cortex in the orbitofrontal cortex and tertiary taste cortex in the anterior cingulate cortex, whereas processing in the primary (insular) taste cortex reflects physical properties such as intensity. However, glutamate presented alone as a taste stimulus is not highly pleasant and does not act synergistically with other tastes (sweet, salt, bitter, and sour). When glutamate is given in combination with a consonant, savory odor (vegetable), the resulting flavor, formed by a convergence of the taste and olfactory pathways in the orbitofrontal cortex, can be much more pleasant. This pleasantness is shown by much greater activation of the medial orbitofrontal cortex and pregenual cingulate cortex than the sum of the activations by the taste and olfactory components presented separately. Furthermore, activations in these brain regions were correlated with the pleasantness and fullness of the flavor and with the consonance of the taste and olfactory components. The concept is proposed that umami can be thought of as a rich and delicious flavor that is produced by a combination of glutamate taste and a consonant savory odor. Glutamate is thus a flavor enhancer because of the way that it can combine supralinearly with consonant odors in cortical areas in which the taste and olfactory pathways converge far beyond the receptors. Cognitive and attentional modulation of the orbitofrontal cortex also contributes to the pleasantness and appetitive value of umami.   *Am J Clin Nutr* 2009;90(suppl):804S–13S.

INTRODUCTION

The taste referred to by the Japanese word *umami* has come to be recognized as a "fifth taste" (1, 2) (after sweet, salt, bitter, and sour; umami captures what is sometimes described as the taste of protein). In fact, multidimensional scaling methods in humans (3) have shown that the taste of glutamate [as its sodium salt monosodium glutamate (MSG)] cannot be reduced to any of the other 4 basic tastes. Specific taste receptors for glutamate have been found (4–6). Umami taste is found in a diversity of foods rich in glutamate such as fish, meat, milk, tomatoes, and some vegetables and is enhanced by some ribonucleotides (including inosine and guanosine nucleotides) (7, 8), which are present in meat and some fish (9). The mixture of these components underlies the rich taste characteristic of many cuisines.

In this review, I summarize discoveries on how umami taste is represented by the exquisitely tuned neurons found in the macaque taste cortical areas and then build on these studies to examine the representation of umami taste in the human brain. An underlying theme is what makes umami taste pleasant. Part of the importance of understanding this is that umami is a key sensory indicator of foods that contain proteins and thus a key sign of foods that help to maintain a nutritionally appropriate diet.

NEURONAL RECORDINGS IN MACAQUES

To understand how appetite and food intake are controlled by the human brain, and disorders in appetite and feeding, the neural mechanisms involved have been investigated in primates as well as humans (10–13). A reason for performing some of these experiments with primates is that the primate taste system may be organized anatomically and physiologically differently from the taste system of nonprimates (14–16). For example, unlike rodents, there is in macaques no subcortical set of pathways from the brainstem, and instead there is an obligatory relay from the nucleus of the solitary tract by the taste thalamus to the taste cortex (14, 15). This makes the primate taste system easier to analyze and more like that of humans, in that taste processing proceeds to the primary taste cortex and then to other areas (*see* **Figure 1**), whereas in rodents there are outputs from a brainstem pontine taste area to subcortical systems. In addition, feeding to satiety reduces taste neuron responsiveness in the secondary (orbitofrontal) taste cortex but not in the primary (insular) taste cortex, whereas satiety effects on taste processing are found even in the nucleus of the solitary tract of rodents (15), making the rodent taste system much more complex to analyze.

In the orbitofrontal cortex of primates, there is a region of secondary taste cortex [which receives from the primary taste cortex in the insula and adjoining frontal operculum (17–20)] in which neurons are activated by the taste of food (12, 21) (*see* Figure 1). These orbitofrontal cortex taste neurons can be tuned quite finely to gustatory stimuli (21). Moreover, their activity is related to food reward, in that those that respond to the taste of food do so only if the monkey is hungry (22). These neurons
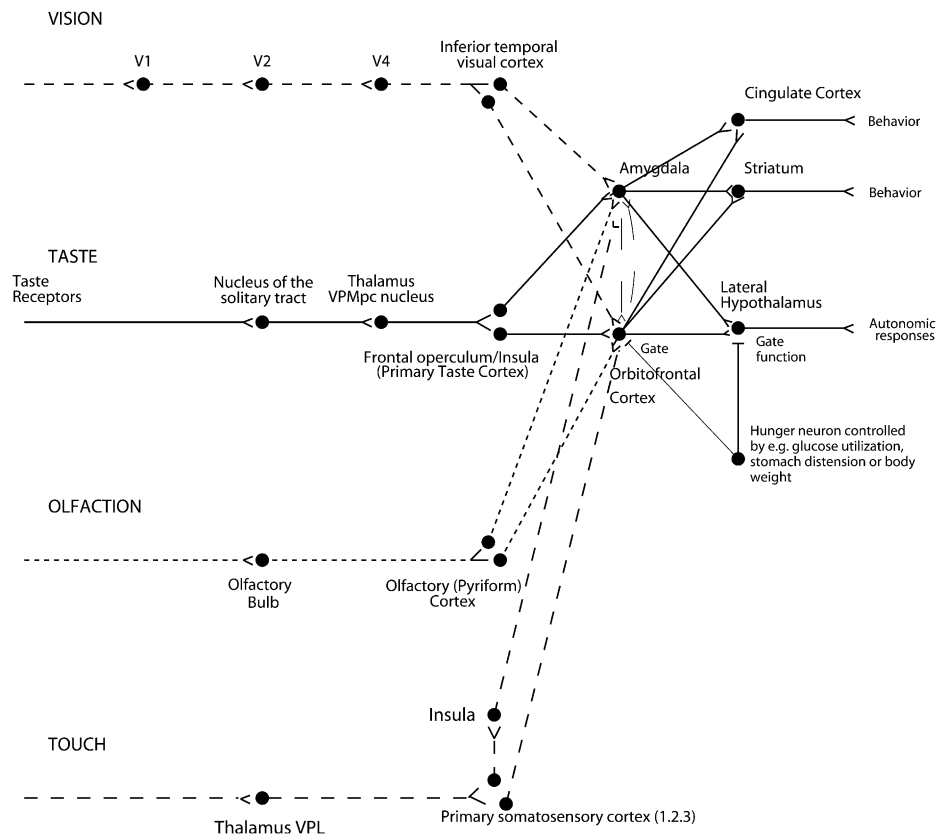
FIGURE 1. Schematic diagram of the taste and olfactory pathways in primates, including humans, showing how they converge with each other and with the visual and somatosensory pathways. The unimodal inputs enter from the left (each with its own line style), and the ends of the mainly unimodal processing provide a cortical representation of what stimulus is present, and its intensity, in the column with the inferior temporal visual cortex, the primary taste cortex, the pyriform (primary) olfactory cortex, and the primary somatosensory cortex and insula. The pathways converge to form multimodal representations in the orbitofrontal cortex and amygdala. (The insular taste cortex does contain bimodal taste and oral somatosensory/temperature-responsive neurons.) Hunger, reflecting factors such as gastric distension, gut stimulation by food, and satiety hormones, acting probably through the hypothalamus, modulates the responsiveness of the representations in the orbitofrontal cortex of the taste, smell, texture, and sight of food (indicated by the gate function), and the orbitofrontal cortex is where the palatability, pleasantness, and reward value of food is represented. Behavioral and autonomic responses to food are produced by stages of processing beyond the orbitofrontal cortex and amygdala, including the pathways shown on the right. VPMpc, ventralposteromedial thalamic nucleus; V1, V2, and V4, visual cortical areas; VPL, ventral posterolateral nucleus of the thalamus.

show effects of sensory-specific satiety, an important mechanism in the control of feeding that has important implications for the control of appetite and food intake (10, 11, 22–24). The orbitofrontal cortex is implicated in the control of feeding, for it is the first part of the taste system of primates in which neuronal responses to the taste of food occur while hungry but not after satiation (11, 22, 23, 25, 26).

Neurons specifically tuned to glutamate

To investigate whether umami taste operates through information channels in the primate taste system which are separable from those for the "prototypical" tastes sweet, salt, bitter, and sour, Baylis and Rolls (27) made recordings from 190 taste responsive neurons in the primary taste cortex and adjoining orbitofrontal cortex taste area in alert macaques. Single neurons were found that were tuned to respond best to MSG (umami taste), just as other cells were found with best responses to glucose (sweet), sodium chloride (salty), hydrogen chloride (sour), and quinine hydrogen chloride (bitter). Across the population of neurons, the responsiveness to glutamate was poorly correlated with the responsiveness to sodium chloride, so that the

representation of glutamate was clearly different from that of sodium chloride. Furthermore, the representation of glutamate was shown to be approximately as different from each of the other 4 tastants as they are from each other, as shown by multidimensional scaling and cluster analysis. Baylis and Rolls (27) concluded that in primate taste cortical areas, glutamate, which produces umami taste in humans, is approximately as well represented as are the tastes produced by glucose (sweet), sodium chloride (salty), hydrogen chloride (sour), and quinine hydrogen chloride (bitter).

Neurons that respond to the taste of MSG also respond to the taste of glutamic acid

To examine further the role of the glutamate ion in umami taste representation, Rolls et al (28) performed a neurophysiologic investigation in which glutamic acid was used, and recordings were made from neurons in the macaque orbitofrontal cortex. All solutions were made in distilled water. It was found that some of the neurons had large responses to the taste of 0.05 mol glutamic acid/L and that the cells that responded to glutamic acid also typically responded to MSG and did not necessarily have large

responses to 0.01 mol hydrogen chloride/L. (The pH of the glutamic acid was 2.1.) The correlation between the responses of this population of neurons to MSG and glutamic acid was 0.75, and this similarity was greater than most other correlations between other taste stimuli. This strengthens the evidence that umami taste is represented in the primate brain separately from the representations of the other tastants.

Neurons that respond to the taste of MSG also respond to the taste of inosine monophosphate

Given that inosine 5′-monophosphate (IMP) in the mouth can produce umami taste in humans and can synergize with MSG, its neurophysiologic effects in primates have been investigated (28). The set of tastants 1.0 mol glucose/L, 0.1 mol NaCl/L, 0.01 mol HCl/L, 0.001 mol quinine hydrogen chloride/L, 0.1 mol MSG/L, and 0.0001 mol IMP/L was tested in random sequence, as described above. This is a low concentration of IMP, but it was chosen because it was found in our preliminary studies to be effective in producing neuronal responses in macaques. This concentration is just below the human detection threshold for IMP alone (7), but it is a concentration that appears to be able to affect the human taste system, in that in humans this is in the concentration range that has a synergistic effect with MSG. It was shown that primate orbitofrontal cortex neurons had responses to concentrations as low as 0.0001 mol IMP/L and that typically the cells that responded to IMP also responded to MSG, and indeed across the population of cells, IMP produced responses that were much more similar to MSG than to any of the other tastants (28).

Satiety

Feeding to satiety decreases the responses of orbitofrontal taste cortex neurons to a food with which a monkey has been fed to satiety (22, 23). Such a modulation of taste responses by hunger has not been found in the primary taste cortex. Moreover, the reduction in neuronal responsiveness in the secondary taste cortex is at least partly specific to the food with which the monkey has been fed to satiety. This is thus a sensory-specific reduction in responsiveness (11). We investigated whether satiety induced by feeding with MSG solution would affect the responses of orbitofrontal cortex cells responsive to the taste of monosodium glutamate, and, if so, whether the response would be sensory specific. A modulation of responsiveness by hunger would implicate the neurons in a system involved in motivational responses to food. A demonstration of sensory-specific satiety would add further evidence for a separate neural mechanism for the perception of umami taste.

Cells, which responded to the taste of MSG or which responded to the sight of food (29), were tested before, during, and after feeding a monkey with 0.1 mol MSG/L until behavioral satiety was achieved. Rolls et al (28) performed experiments studying the effect of satiety on taste responses to glutamate on 5 neurons. It was found that at least some of these neurons showed a smaller response to the taste of glutamate after it was fed to satiety but remained responsive to other tastes. Thus, the reward value and pleasantness of umami taste is represented in the orbitofrontal cortex (30, 31).

These and many related investigations have provided a fundamental basis at the neuronal level for understanding the taste, olfactory, oral texture, oral temperature, and visual processing involved in the sensory analysis of foods, in making the reward value explicit in the representation as shown by the effects of feeding to satiety, and in thus playing an important role in appetite and the control of food intake (10–12, 16, 32, 33). We now turn to investigations in humans that used functional neuroimaging to build on this fundamental understanding.

REPRESENTATION OF UMAMI TASTE IN THE HUMAN CORTEX

de Araujo et al (34) investigated whether cortical areas previously shown to be activated by taste in humans with the use of functional magnetic resonance imaging (fMRI) (35, 36) were activated by the taste of umami and whether activation in particular areas reflected the synergism between MSG and IMP. A feature of our taste investigations with fMRI is that a tasteless control solution (25 mmol KCl/L + 2.5 mmol NaHCO$_3$/L) is used to compare with the response produced by the taste stimuli. By using this contrast, effects because of taste can be measured, because the tasteless solution controls for somatosensory effects of the solution, as well as for the movement required to swallow the solution at the end of each taste delivery period. Cortical responses to umami stimuli were investigated in 10 subjects by delivering solutions consisting of either glucose (1 mol/L, as a localizer), MSG (0.05 mol/L), IMP (0.005 mol/L), or MSG + IMP (mixed with the same concentrations) (34). The experimental protocol in this and our other studies consisted of an event-related interleaved design. At the beginning of a random variable period of 12–20 s, 1 of the 4 stimuli was delivered in 0.75-mL aliquots to the subject's mouth; swallowing was cued after 10 s, and then a tasteless control solution was administered at the beginning of the next period. This was followed by one of the other stimuli determined by a pseudo-random sequence. This was repeated for 12 cycles. The data were obtained with the 3T fMRI scanner at Oxford, with acquisition details used to minimize distortion and dropout (34, 37).

The effects of umami taste as produced by the prototypical stimulus 0.05 mol/LMSG on cortical activation in the group analysis are shown in **Figure 2**, row 3; the activations produced by IMP (0.005 mol/L) are shown in Figure 2, row 2; and the activations produced by the sweet tastant 1 mol/L glucose are shown in Figure 2, row 1. For all stimuli, activation of the insular-opercular taste cortex, which is the putative human primary taste cortex, and the orbitofrontal cortex were found. The activation produced by IMP shows that umami, even when the solution administered contains no sodium ions, activates these areas of the cerebral cortex. To analyze whether there are areas of overlap of the activations produced by the umami stimuli and the glucose used as a prototypical taste stimulus, Figure 2, row 5, shows the conjunction across stimulus conditions and subjects (38) of the effects produced by MSG, IMP, MSG + IMP, and glucose. These results (34) provided evidence that when MSG and IMP, umami tastants, are placed in the mouth, cortical areas known to be activated by other taste stimuli are activated.

Given the evidence that IMP (or its guanosine equivalent) and MSG can show synergism psychophysically (8), it was of considerable interest that de Araujo et al (34) found that the left
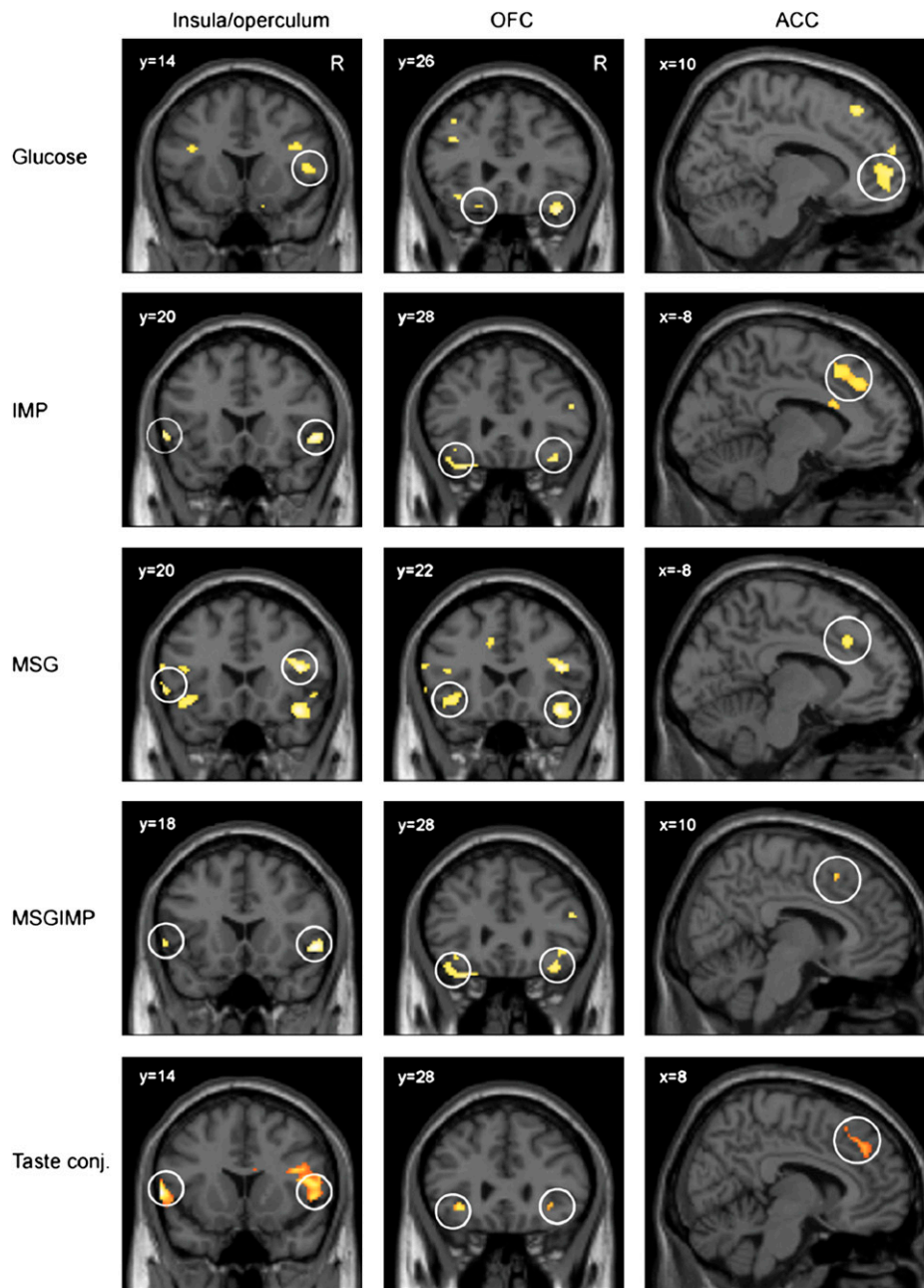
FIGURE 2. Activations produced in the rostral insula-operculum, the orbitofrontal cortex (OFC), and the anterior cingulate cortex (ACC) by the tastants glucose (1 mol/L), inosine 5′-monophosphate (IMP; 0.005 mol/L), and monosodium glutamate (MSG; 0.05 mol/L) and by a combination of the MSG and IMP (MSGIMP) or the conjunction of all tastants (Taste conj.). Reproduced with permission from reference 34.

anterior lateral orbitofrontal cortex ($x = -44$, $y = 34$, $z = -18$) showed supralinear additivity for the MSG + IMP combination; ie, significantly more activation was observed by the MSG + IMP combination than by the sum of the effects of MSG alone and IMP alone, as shown in Figure 2. The actual interaction between MSG and IMP may be expressed in part in the taste receptors themselves, or there may be somewhat different receptors for the different umami tastants (4–6), but in any case the results of the study by De Araujo et al (34) show that there is a part of the human anterior orbitofrontal cortex in which supralinear additivity shows up very strongly in the statistical analysis. Because this part of the human orbitofrontal cortex statistically reflects supraadditive effects between umami tastants evident in the BOLD (blood oxygenation level dependent) signal, makes it likely that activity in this part of the orbitofrontal cortex is especially relevant to the perceived sensation of umami taste and to the behavioral preferences for umami taste. The special role of this part of the human cerebral cortex in the taste of umami could arise because it is able to provide a nonlinear amplification of the MSG and IMP inputs already combined in the taste receptors, or it could be that this part of the cortex is able to combine information from partly separate umami channels to produce the large response to the combination of MSG and IMP. This will be an interesting issue for future investigation.

UMAMI: A DELICIOUS FLAVOR FORMED BY CONVERGENCE OF TASTE AND OLFACTORY PATHWAYS IN THE HUMAN BRAIN

Glutamate does not act synergistically with other tastes (sweet, salt, bitter, and sour) (3). Moreover, when glutamate is presented alone as a taste stimulus, it is not highly pleasant (39). The question then arises of how glutamate contributes to the delicious and pleasant quality of some foods.

McCabe and Rolls (40) were able to show that when glutamate is given in combination with a consonant, savory odor (vegetable), the resulting flavor can be much more pleasant. We then investigated the brain mechanisms that underlie this effect. (Flavor is defined as a combination of taste and smell.) For the combination of smell and taste to be effective, the taste and olfactory signals must be brought together. From studies in nonhuman primates it is known that the primary taste cortex in the anterior insula contains neurons that respond to the taste and texture of what is in the mouth but not its smell (41). Both the primary taste cortex and the pyriform (olfactory) cortex project forward into the orbitofrontal cortex, and it is here that bimodal taste and olfactory neurons are found (29). These flavor-responsive neurons are built by olfactory-to-taste association learning (42, 43). Olfactory areas have been identified in the pyriform cortex and the orbitofrontal cortex (44, 45). Studies of where taste and smell are brought together in the human brain have started (46–48), and indeed it has been shown that there are areas in the orbitofrontal cortex and adjoining agranular (far anterior) insula that can be activated by both sucrose taste and strawberry odor (49).

McCabe and Rolls (40) used a set of stimuli designed to allow umami taste (produced by 0.1 mol MSG/L and 0.005 mol IMP/L) to be tested alone or in combination with a complementary, savory odor, for which vegetable odor (supplied by Firmenich SA) was used. This allowed effects of the combination (MSGV in **Table 1**) to be compared with the effects of the gustatory (MSG in Table 1) or odor (tIV) components delivered separately. To provide an anchor and comparison stimulus for whether the taste and olfactory components were consonant, the umami taste was also presented in combination with a dissonant odor, rum. The stimuli were delivered intraorally made up in a tasteless solution. A further part of the design was to take psychophysical ratings of pleasantness, consonance, and fullness of flavor made on every trial by the subjects during the fMRI experiments, so that the subjective effects of the stimuli in terms of their pleasantness could be correlated with the BOLD signals measured on every trial.

The ratings of pleasantness, consonance, and fullness of flavor are shown in **Figure 3**. The combination of MSG and vegetable odor was rated as significantly more pleasant than MSG alone ($P < 0.015$, paired t test). The combination of MSG and vegetable odor was rated as more pleasant than the combination of sodium chloride and vegetable odor as shown in Figure 3, and it was shown in a 2-factor analysis of variance that the increase of pleasantness was greater when vegetable was added to MSG than when vegetable was added to sodium chloride [which actually produced a decrease in pleasantness, as shown in Figure 3] [interaction in a within-subjects 2-factor analysis of variance, $F(1,11) = 22.05$, $P < 0.001$]. Similar interaction effects of adding vegetable to MSG when compared with the effect of adding vegetable to sodium chloride were found for consonance [$F(1,11) = 12.03$, $P < 0.005$], and for fullness of flavor [$F(1,11) = 5.92$, $P < 0.03$].

A main focus of the investigation by McCabe and Rolls (39) was on whether the combination of MSG taste with a consonant odor, vegetable, might produce selective activations of some brain regions. To test this, a contrast of the effects of the mixture of MSG and vegetable (MSGV) is shown in **Figure 4**, with the sum of the activations to MSG and vegetable presented separately. This contrast thus is of supralinear additivity, used as an indicator of an interaction between the taste and olfactory components. This shows a highly significant effect in the medial orbitofrontal cortex centered at [(-6, 52, -14) $Z = 3.96$; fully corrected $P = 0.002$], which extends up into the pregenual cingulate cortex. In addition, a part of the ventral striatum-olfactory tubercle, which receives inputs from the orbitofrontal cortex, showed significant supralinear activation. It was notable that there was no evidence of this supralinearity in the taste insula or in the agranular insula. Supralinear effects were much less (and significantly less) evident for sodium chloride and vegetable odor. Furthermore, activations in these brain regions were correlated with the pleasantness and fullness of the flavor and with the consonance of the taste and olfactory components (40).

I thus propose that glutamate acts by the nonlinear effects it can produce when combined with a consonant odor in multimodal cortical taste-olfactory convergence regions. I propose the concept that umami can be thought of as a rich and delicious flavor that is produced by a combination of glutamate taste and a consonant savory odor. Glutamate is thus a flavor enhancer because of the way that it can combine supralinearly with consonant odors in cortical areas where the taste and olfactory pathways converge far beyond the receptors and where the pleasantness of flavor is represented.

TABLE 1
Stimuli and abbreviations used in the investigation by McCabe and Rolls (40) of pleasant umami flavor produced by a convergence of monosodium glutamate (MSG) taste and a consonant savory odor

Abbreviation	Compounds administered
MSG	0.1 mol MSG/L + 0.005 mol inosine 5′monophosphate/L
MSGV	0.1 mol MSG/L + 0.005 mol inosine 5′monophosphate/L + 0.4% vegetable odor
NaCl	0.1 mol NaCl/L
NaClV	0.1 mol NaCl/L + 0.4% vegetable odor
MSGR	0.1 mol MSG/L + 0.005 mol inosine 5′monophosphate/L + 2% rum odor
Tl	25 mmol KCl/L + 2.5 mmol NaHCO₃/L (tasteless control)
tIV	25 mmol KCl/L + 2.5 mmol NaHCO₃/L + 0.4% vegetable odor

COGNITIVE MODULATION OF AFFECTIVE RESPONSES TO THE TASTE AND FLAVOR OF UMAMI

We have just seen how an important factor in the pleasantness of umami is the combination of glutamate taste with a consonant odor. Another factor that is important in making umami pleasant is the cognitive label or description attached to the taste of glutamate or the flavor of umami, as shown in an investigation by Grabenhorst et al (50). The taste stimulus, consisting of 0.1 mol MSG/L with 0.005 mol IMP/L, which produced the taste of
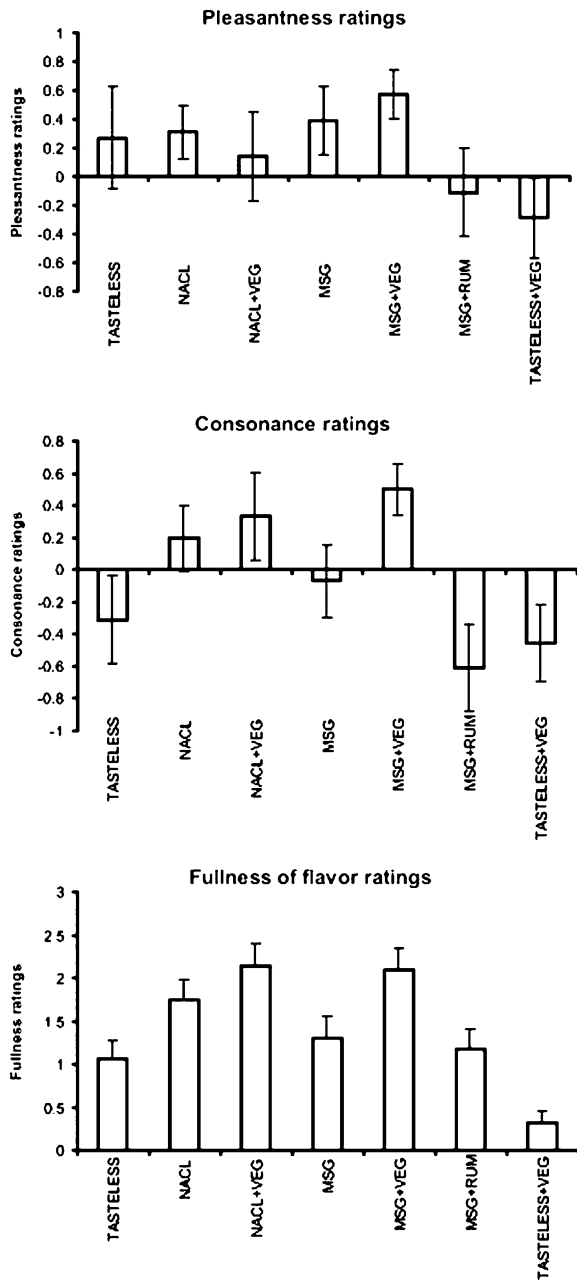
Pleasantness ratings

Consonance ratings

Fullness of flavor ratings

FIGURE 3. Mean (±SEM) ratings of pleasantness, consonance, and fullness of flavor in the investigation of pleasant umami flavor produced by a convergence of monosodium glutamate (MSG) taste and a consonant savory odor. Summary of statistical analyses is as follows. The pleasantness ratings were significantly different between the stimuli (one-factor within-subjects ANOVA, $F[6,66] = 2.49$, $P = 0.031$), as were the consonance ($F[6,66] = 5.71$, $P < 0.00003$) and fullness of flavor ratings ($F[6,66] = 21.24$, $P < 0.001$). The combination of MSG and vegetable (VEG) odor was rated as more pleasant than MSG alone (paired t test, $P < 0.015$ in a planned comparison). The combination of MSG and vegetable odor was rated as more pleasant than the combination of NaCl (NACL) and vegetable odor as shown, and it was shown in a 2-factor ANOVA that the increase of pleasantness was greater when vegetable was added to MSG than when vegetable was added to NaCl (which actually produced a decrease in pleasantness, as shown) (interaction in a within-subjects 2-factor ANOVA, $F[1,11] = 22.05$, $P < 0.001$). Reproduced with permission from reference 40.

umami, was labeled by a visual stimulus on different trials as "rich and delicious taste" (MSGrich) or "MSG" (MSGbasic). Similarly, the flavor stimulus, produced by a combination of the

Supralinearity: MSGV > (MSG + V) p=0.002
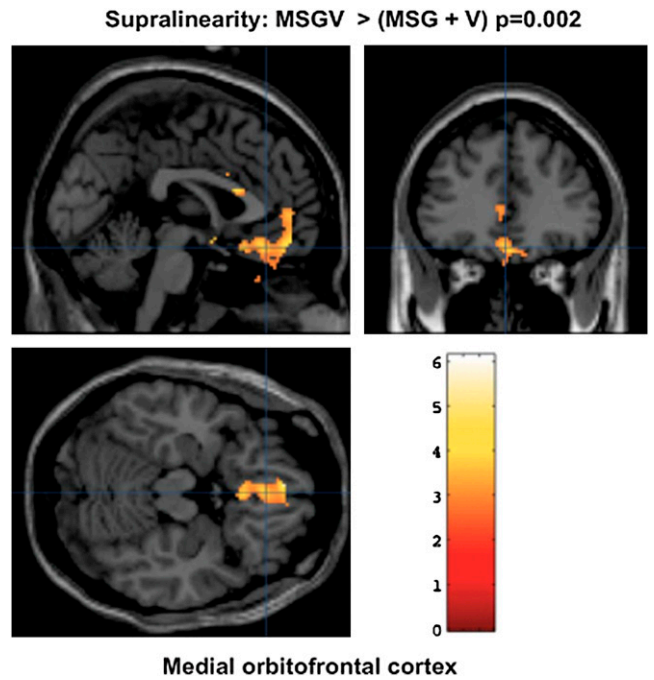

Medial orbitofrontal cortex

FIGURE 4. Supralinear additivity between monosodium glutamate (MSG) and vegetable (V) odor. A contrast of the activations produced by the mixture of MSG and vegetable (MSGV), with the sum of the activations to MSG and vegetable presented separately. This contrast shows a highly significant effect in the medial orbitofrontal cortex centered at $(-6, 52, -14)$ fully corrected $P = 0.002$, with the activation extending up into the pregenual cingulate cortex. The colored bar shows the statistical significance of the effects in terms of t values as provided in the statistical parametric map by SPM (Statistical Parametric Mapping, Wellcome Trust Centre for Neuroimaging, London, United Kingdom). Reproduced with permission from reference 40.

same taste stimulus and vegetable odor, was labeled on different trials as "rich and delicious flavor" (MSGVrich) or "boiled vegetable water" (MSGVbasic). The subjects were not informed at the start of the experiment about exactly what taste or flavor stimuli were being delivered into the mouth. That the MSG was rated as significantly more pleasant when labeled as a rich and delicious taste than when labeled MSG ($P = 0.002$) is shown in **Figure 5**. Similarly, the MSGV was rated as significantly more pleasant when labeled "rich and delicious flavor" than when labeled "boiled vegetable water" ($P = 0.003$). In contrast, the labels did not produce significant differences in the intensity ratings for the MSG.

The contrast of MSGVrich compared with MSGVbasic showed significant effects in the medial orbitofrontal cortex, in that this region was activated more strongly when the flavor stimulus was labeled "rich and delicious flavor" than when it was labeled "boiled vegetable water" (at $-8, 28, -20$; **Figure 6**A; the BOLD signal for the 2 conditions is shown in Figure 6B, and the peaks were significantly different as shown in Figure 6C). Thus, the word labels influenced the activations produced by the umami flavor in this area. Moreover, activations in the medial orbitofrontal cortex reflected the pleasantness of the stimuli, as shown by a correlation with the subjective pleasantness ratings of the stimuli (MSGVrich, MSGVbasic, MSGrich, and MSGbasic) (*see* Figure 6D, which shows the BOLD signal as a function of the ratings). Thus, in the orbitofrontal cortex the activations to taste and flavor were modulated by the word
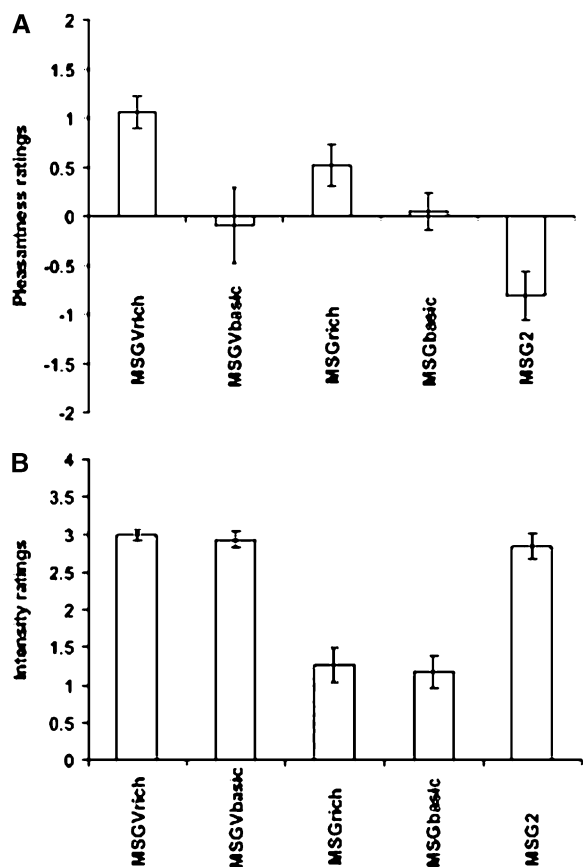
FIGURE 5. Mean (±SEM) ratings of pleasantness (A) and intensity (B) for the taste and flavor stimuli. The taste stimulus monosodium glutamate (MSG) was rated as significantly more pleasant when labeled "rich and delicious taste" than when labeled "MSG." [A within-subjects ANOVA ($F(4,11) = 10.2$, $P < 0.001$) followed by a post hoc least square difference (LSD) test showed $P = 0.002$.] Similarly, the flavor stimulus MSG with vegetable (MSGV) was rated as significantly more pleasant when labeled "rich and delicious flavor" than when labeled "boiled vegetable water" (post hoc LSD test, $P = 0.003$). In contrast to the effects on the pleasantness ratings, the labels did not produce significant differences in the intensity ratings for the taste and flavor stimuli. (The participants rated the pleasantness and the intensity of the taste or flavor on every trial by using a button box and visually presented rating scale.) These findings provide clear evidence that these cognitive labels were modulating the perceived pleasantness, but not the intensity, of the taste and flavor. The more concentrated taste stimulus MSG2 was rated as significantly less pleasant and more intense than the identically labeled taste stimulus MSGbasic. In this case the labels were identical (MSG), and this provides evidence that the perceived taste reflected also the properties of the stimuli (low compared with high concentration). Reproduced with permission from reference 50.

labels, and the cognitive modulation was of activations that were related to the pleasantness of these stimuli. Affect-related activations to glutamate taste were modulated in a region that receives from the orbitofrontal cortex, the pregenual cingulate cortex, and to glutamate taste and umami flavor in another region that receives from the orbitofrontal cortex, the ventral striatum. In a related study, we showed that the effects of top-down cognitive labels presented alone on these areas was relatively weak and that large effects were found when they interacted with incoming stimuli (51). The mechanism can thus be understood as a top-down biased competition influence similar to that involved in top-down attention (52–55). Affect-related cognitive modulations were not found in the insular (primary)

taste cortex, where the intensity but not the pleasantness of the taste was represented. Grabenhorst et al (50) concluded that top-down language-level cognitive effects reach far down into the earliest cortical areas that represent the appetitive value of taste and flavor. This is an important way in which cognition influences the neural mechanisms that control the pleasantness of glutamate taste and umami flavor and thus appetite.

ATTENTIONAL INFLUENCES ON THE PROCESSING OF UMAMI STIMULI

How does attention influence umami processing? Grabenhorst and Rolls (56) have shown that when paying attention to the pleasantness of an umami taste or flavor (because one has been instructed at the start of the trial to rate the pleasantness of the stimulus), processing in brain regions such as the orbitofrontal cortex is enhanced. When paying attention to the intensity of umami taste or flavor (because one has been instructed at the start of the trial to rate the intensity of the stimulus), processing in brain regions such as the insular primary taste cortex was enhanced. Moreover, the subjective pleasantness of umami taste was correlated with taste-related activations in the orbitofrontal cortex, whereas the subjective intensity of umami taste is correlated with activations in the primary taste cortex (56). Thus, depending on the context in which tastes are presented and whether affect is relevant, the brain responds to a taste differently. This differential biasing of brain regions engaged in processing a sensory stimulus, depending on whether the cognitive demand is for affect-related or for more sensory-related processing, may be an important aspect of cognition and attention. It has many implications for understanding and investigating psychophysically and neurally the effects not only of taste but also of other sensory stimuli, including odor (57). It shows that when evaluating umami stimuli, the attentional set brought to bear, of paying attention to the physical properties of the stimuli, such as their intensity, or the affective value of the stimuli, such as their pleasantness, can be very important and that brain systems are even differentially engaged by these 2 types of tasks.

CONCLUSIONS

In this research, we have seen that, at the neuronal level, there are separate neuronal representations of glutamate taste from other taste stimuli in the primary taste cortex and in the orbitofrontal cortex; that some single neurons combine glutamate taste with olfactory, oral texture, oral temperature, and visual stimuli; and that the reward value of glutamate taste is represented by neurons in the orbitofrontal cortex. We have seen that in humans glutamate activates the primary (insular), secondary (orbitofrontal), and pregenual cingulate (tertiary) taste cortices (*see* Figure 1), and that the pleasantness of umami is produced by a combination of glutamate taste with consonant odor inputs in areas far beyond the umami taste receptor, the orbitofrontal and pregenual cingulate cortices. We have also seen that cognitive effects reach down into the first part of the taste and flavor system at which the pleasantness or affective value is made explicit in the representation, the orbitofrontal cortex, to influence the pleasantness of the taste and flavor of umami. We have also seen how whether attention is being paid to the physical properties of umami, or its affective value, even has
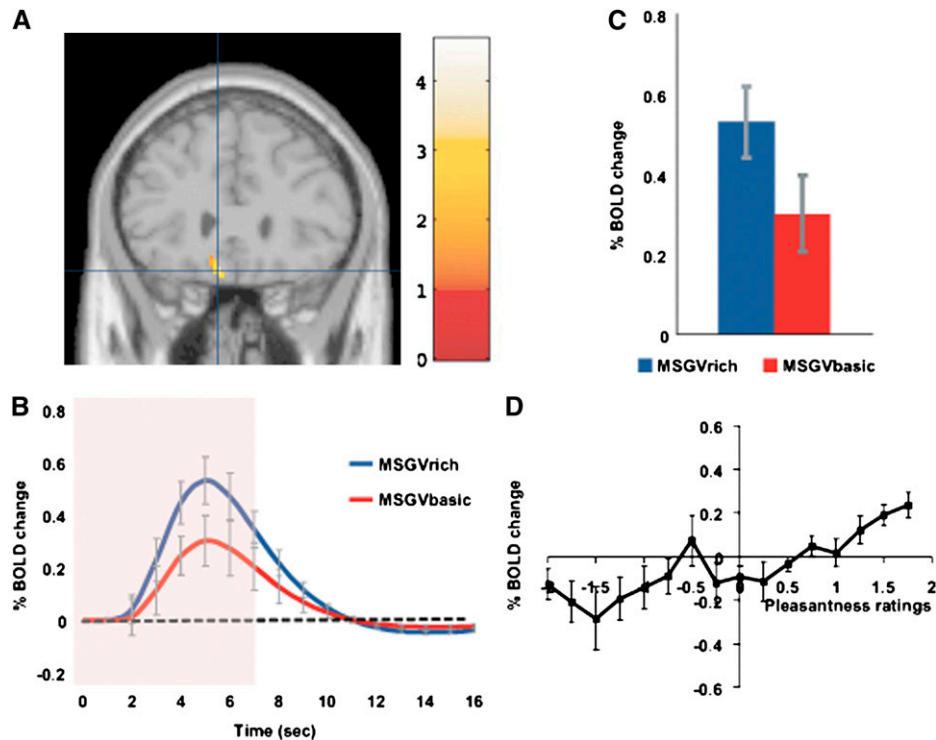
FIGURE 6. A: The medial orbitofrontal cortex was more strongly activated when the flavor stimulus [monosodium glutamate [MSG] with vegetable (V)] was labeled "rich and delicious flavor" (MSGVrich) than when it was labeled "boiled vegetable water" (MSGVbasic) (-8, 28, -20). B: The time course of the BOLD (blood oxygenation level dependent) signals for the 2 conditions. C: Across-subjects mean ($\pm$SEM) percentage changes in BOLD signals. The peak values of the BOLD signal for the site shown in panel A were significantly different ($t = 3.06$, df $= 11$, $P = 0.01$) when the flavor stimulus was labeled "rich and delicious flavor" (MSGVrich) than when it was labeled "boiled vegetable water" (MSGVbasic). D: Across-subjects mean ($\pm$SEM) percentage changes for the BOLD signal in the medial orbitofrontal cortex were correlated with the subjective pleasantness ratings of taste and flavor ($r = 0.86$, $P < 0.001$). Reproduced with permission from reference 50.

top-down modulatory effects on different cortical processing systems activated by umami. Overall, we have an understanding of how important cortical processing is to umami flavor, and this in turn helps us to understand how umami works to promote a rich delicious flavor in food. This in turn has important implications for understanding the use of umami flavor to promote good nutrition. (Other articles in this supplement to the Journal include references 58–86.)

I have worked on some of the investigations described here with I de Araujo, GC Baylis, LL Baylis, A Bilderbeck, HD Critchley, F Grabenhorst, M Kadohisa, M Kringelbach, C Margot, C McCabe, J O'Doherty, BA Parris, TR Scott, MI Velazco, and JV Verhagen, and their collaboration is sincerely acknowledged.

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