

Basic Characteristics of Glutamates and Umami Sensing in the Oral Cavity and Gut

The Representation of Umami Taste in the Taste Cortex^{1,2}

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ABSTRACT To investigate the neural encoding of glutamate (umami) taste in the primate, recordings were made from taste-responsive neurons in the cortical taste areas in macaques. Most of the neurons were in the orbitofrontal cortex (secondary) taste area. First, it was shown that there is a representation of the taste of glutamate that is separate from the representation of the other prototypical tastants, sweet (glucose), salt (NaCl), bitter (quinine) and sour (HCl). Second, it was shown that single neurons that had their best responses to sodium glutamate also had good responses to glutamic acid. Third, it was shown that the responses of these neurons to the nucleotide umami tastant inosine 5'-monophosphate were more correlated with their responses to monosodium glutamate than to any prototypical tastant. Fourth, concentration-response curves showed that concentrations of monosodium glutamate as low as 0.001 mol/L were just above threshold for some of these neurons. Fifth, some neurons in the orbitofrontal region which responded to monosodium glutamate and other food tastes, decreased their responses after feeding with monosodium glutamate to behavioral satiety, revealing a mechanism of satiety. In some cases, this reduction was sensory-specific. Sixth, it was shown in psychophysical experiments in humans that the flavor of umami is strongest with a combination of corresponding taste and olfactory stimuli (e.g., monosodium glutamate and garlic odor). The hypothesis is proposed that part of the way in which glutamate works as a flavor enhancer is by acting in combination with corresponding food odors. The appropriate associations between the odor and the glutamate taste may be learned at least in part by olfactory to taste association learning in the primate orbitofrontal cortex. *J. Nutr.* 130: 960S–965S, 2000.

KEY WORDS: • taste cortex • orbitofrontal cortex • insular cortex • glutamate • umami • primates
• nucleotide • olfaction

To understand how appetite and food intake are controlled by the human brain, and how disorders in appetite and feeding develop, the underlying neural mechanisms are being analyzed in primates (Rolls 1994 and 1999). A reason for performing these experiments with primates is that the primate taste system may be organized anatomically in a manner different from that of nonprimates (Beckstead et al. 1980, Norgren and Leonard 1973, Norgren 1984, Rolls 1989 and 1995). For example, unlike rodents, macaques have no subcortical set of pathways from the brainstem; instead, there exists an obligatory relay from the nucleus of the solitary tract via the taste thalamus to the taste cortex.

In the orbitofrontal cortex of primates, there is a region of

secondary taste cortex in which neurons are activated by the taste of food (Baylis et al. 1994, Rolls et al. 1990, Rolls 1989, 1995 and 1997). These orbitofrontal taste neurons can be tuned quite finely to gustatory stimuli (Rolls et al. 1990). 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 (Rolls et al. 1989). These neurons show effects of sensory-specific satiety, an important mechanism in the control of feeding (Rolls 1989, 1994, 1995 and 1997, Rolls et al. 1989, Rolls and Rolls 1997). This region is implicated in the control of feeding because it is the first part of the taste system of primates in which neuronal responses to the taste of food occur when hunger exists, but not after satiation (Rolls et al. 1989, Rolls 1989, 1995 and 1997).

The orbitofrontal cortex also contains neurons with multimodal representations, for example, neurons that respond to olfactory and taste stimuli, or to visual and taste stimuli (Rolls 1989, 1995 and 1997, Rolls and Baylis 1994). A neuronal representation of flavor appears to be formed in the orbitofrontal cortex. Approximately 40% of the olfactory neurons in the orbitofrontal cortex have activity that depends on the association of the olfactory input with a taste reward, in that some categorize odors depending on whether they are associated with glucose or saline in an olfactory discrimination task (Critchley and Rolls 1996a, Rolls et al. 1996b). Moreover,

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these olfactory responses may be modified during the reversal of this olfactory discrimination task (Rolls et al. 1996a). The responses of some of these orbitofrontal cortex olfactory and visual neurons are also modulated by hunger and contribute to sensory-specific satiety (Critchley and Rolls 1996b, see also Rolls and Rolls 1997).

The orbitofrontal cortex is thus a region that is involved in taste, olfactory and flavor information processing in nonhuman primates. Using functional magnetic resonance imaging, we have also demonstrated the existence of corresponding taste and olfactory regions in the human orbitofrontal cortex (Francis et al. 1999, Rolls et al. 1997).

An important food taste that appears to be different from that produced by sweet, salt, bitter or sour is the taste of protein. At least part of this taste is captured by the Japanese word umami, which is a taste common to a diversity of food sources including fish, meats, mushrooms, cheese and some vegetables including tomatoes. Within these food sources, it is the synergistic combination of glutamates and 5'-nucleotides that creates the umami taste (Ikeda 1909, Yamaguchi 1967, Yamaguchi and Kimizuka 1979). Monosodium L-glutamate (MSG), GMP and inosine 5'-monophosphate (IMP) are examples of umami stimuli.

Umami does not act by enhancing the tastes of sweetness, saltiness, bitterness or sourness in foods, but instead may be a flavor in its own right, at least in humans. For example, Yamaguchi (1967) found that the presence of MSG or IMP did not lower the thresholds for the prototypical tastes (produced by sucrose, NaCl, quinine sulfate and tartaric acid), suggesting that umami did not improve the detection sensitivity for the four basic taste qualities. Also, the detection thresholds for MSG were not lowered in the presence of the prototypical taste stimuli. This suggests that the receptor sites for umami substances are different from those for other prototypical stimuli (Yamaguchi and Kimizuka 1979). (A synergistic effect was found when IMP was added to MSG in that the detection threshold for MSG was dramatically lowered.) Yamaguchi and Kimizuka (1979) tested the "singularity" of umami by presenting human subjects with 21 taste stimuli including single and mixture solutions of MSG and sucrose, NaCl, tartaric acid and quinine sulfate. The subjects sorted the stimuli on the basis of taste quality similarity. These scores were placed into a similarity matrix and analyzed using multidimensional scaling procedures. The results revealed that, within a three-dimensional tetrahedron, the four prototypical stimuli were located at the vertices of a tetrahedron. The mixtures, containing two, three or four prototypical stimuli, were located on the edges or surfaces of the tetrahedron. However, MSG was located outside of the tetrahedron, implying that the taste of umami is qualitatively different from the four prototypical stimuli used. In spite of this perceptual distinctiveness, traditional taste-quality descriptors are frequently used in describing the quality evoked by monosodium glutamate, particularly saltiness (O'Mahoney and Ishii 1987, Zwillinger and Halpern 1991).

Neurons responsive to the taste of monosodium glutamate

These findings raise the question whether umami taste operates in the primate taste system through information channels that are separable from those for the "prototypical" tastes, sweet, salt, bitter and sour. To investigate the neural encoding of glutamate in the primate, Baylis and Rolls (1991) 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 monosodium glutamate (umami

taste), just as other cells were found with best responses to glucose (sweet), sodium chloride (salty), HCl (sour) and quinine HCl (bitter). Examples of single neurons tuned to glutamate taste are shown in **Figure 1**.

Across the population of neurons recorded by Rolls and Baylis (1994), the responsiveness to glutamate was poorly correlated with the responsiveness to NaCl; thus the representation of glutamate was clearly different from that of NaCl. Further, the representation of glutamate was shown to be approximately as different from each of the other four tastants as they are from each other, as shown by multidimensional scaling and cluster analysis. Moreover, it was found that glutamate is approximately as well represented in terms of mean evoked neural activity and the number of cells with best responses to it as the other four stimuli, i.e., glucose, NaCl, HCl and quinine. Baylis and Rolls (1991) 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), NaCl (salty), HCl (sour) and quinine HCl (bitter).

Glutamic acid

These studies indicated that a separate mechanism from that for other tastes operates for the neurophysiological processing and for the perception of umami. However, the role played by the sodium cation in the MSG molecule remains an interesting issue; the degree to which this contributes to umami taste quality has not been clarified completely. We therefore performed a neurophysiological investigation in which glutamic acid was used; its effects on a population of neurons in the orbitofrontal cortex were compared with those of the prototypical tastants as well as monosodium glutamate (Rolls et al. 1996c). It was possible to complete the testing for 70 taste-responsive cells. It was found that some of the cells had large responses to 0.05 mol/L glutamic acid. The cells that responded to glutamic acid also typically responded to MSG and did not necessarily have large responses to 0.01 mol/L HCl. (The pH of the glutamic acid was 2.1.)

To test how similarly the whole population of 70 cells responded to the two umami tastants, MSG and glutamic acid, compared with other stimuli, we computed the correlations of the responses of all 70 cells to each pair of stimuli out of monosodium glutamate (M), glutamic acid (GLA), glucose (G), sodium chloride (N), acid (H) and quinine (Q). The Pearson correlation coefficients are shown in **Table 1**. It can be seen from Table 1 that the correlation between the responses of this population of neurons to M and GLA was 0.75; this similarity was greater than most other correlations between stimuli shown in Table 1 and was higher than the correlation of glutamic acid with any other stimulus. (The other somewhat high correlation of glutamic acid with another tastant was 0.71 with HCl, a finding consistent with the fact that both are acidic, and that some neurons in the population reflect the acidity of tastants.)

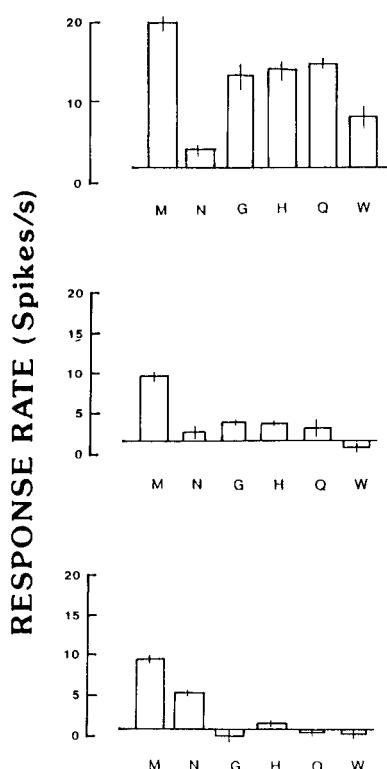
In summary, glutamic acid produced responses in this population of neurons that were more similar to those produced by MSG than to those produced by any other tastant. This finding strengthens the evidence that umami taste is represented in the primate brain separately from the representations of the other tastants.

Inosine monophosphate

Although IMP in the mouth can produce umami taste in humans and can synergize with MSG, its neurophysiological

MSG-BEST CELLS

PRIMARY TASTE CORTEX



SECONDARY TASTE CORTEX

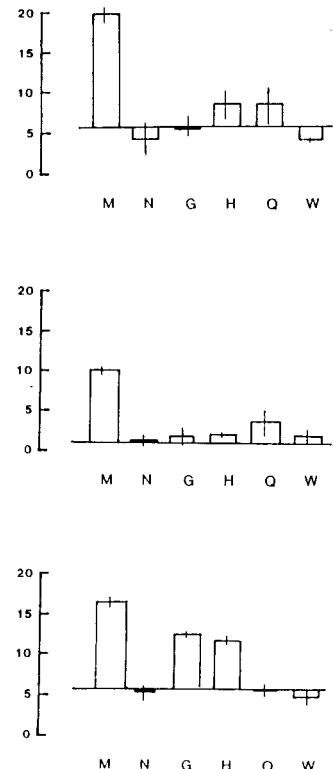


FIGURE 1 Examples of the responses of three cells in the primary taste cortex and of three cells in the secondary taste cortex to monosodium glutamate and other taste stimuli. The firing rate is shown in spikes/s, relative to the spontaneous baseline firing rate. The means and the standard errors of the responses calculated over 4–6 presentations of each tastant in random sequence are shown. The set of tastants was as follows: 1.0 mol/L glucose (G), 0.1 mol/L NaCl (N), 0.01 mol/L HCl (H), 0.001 mol/L quinine-HCl (Q), distilled water (W) and 0.1 mol/L monosodium glutamate (M).

effects in primates have been investigated only recently (Rolls et al. 1996c).

The set of tastants, 1.0 mol/L glucose (G), 0.1 mol/L NaCl (N), 0.01 mol/L HCl (H), 0.001 mol/L QHCl (Q), 0.1 mol/L MSG (M), and 0.0001 mol/L IMP, was tested in random sequence, as described above. This concentration of IMP is small, but was chosen because it was found in our preliminary studies to be effective in producing neuronal responses in macaques; it is just below the human detection threshold for IMP alone (Yamaguchi 1967) but is a concentration that appears to affect the human taste system, in that it produces a taste synergism with MSG.

It was possible to complete the testing for 18 cells (Rolls et al. 1996c). It was found that some of the cells had responses to concentrations as low as 0.0001 mol/L of IMP; typically, the cells that responded to IMP also responded to MSG.

Across this set of 18 cells, the correlations between IMP and the other stimuli calculated from the response profiles are shown in Table 2. The results show that across the population of cells, IMP produced responses that were much more similar to M than to any of the other tastants (Pearson correlation coefficient = 0.80).

These findings (Rolls et al. 1996c) provided further evidence that the representation of umami taste is separate from that of other tastants, in that IMP and MSG produced similar activations of the orbitofrontal cortex taste neurons. They may potentiate each other in humans. Though we did not find this synergism neurophysiologically in the macaque, this result may be related to the fact that even very low concentrations of IMP (0.0001 mol/L) produced quite large neuronal responses in macaques. In any case, macaques are also quite sensitive to the taste of MSG, with

TABLE 1

Correlation coefficients between the profiles of responses generated by each stimulus across the population of 70 cells¹

	G	N	H	Q	W	M	GLA
G	—						
N	0.43	—					
H	0.46	0.70	—				
Q	0.35	0.61	0.66	—			
W	0.47	0.72	0.79	0.66	—		
M	0.60	0.69	0.73	0.57	0.65	—	
GLA	0.34	0.62	0.71	0.61	0.62	0.75	—

¹ G, glucose; N, NaCl; H, HCl; Q, quinine-HCl; W, distilled water; M, monosodium glutamate; GLA, glutamic acid.

TABLE 2

Correlation coefficients between the profiles of activity of 18 cells generated between inosine 5'-monophosphate (IMP) and each of the other stimuli¹

	G	N	H	Q	M	W
IMP	0.15	0.55	0.32	0.44	0.80	0.37

¹ G, glucose; N, NaCl; H, HCl; Q, quinine-HCl; M, monosodium glutamate; W, water.

neurophysiological effects apparent with concentrations as low as 0.001 mol/L (Rolls et al. 1996c).

Satiety

It has been shown that feeding to satiety decreases the responses of orbitofrontal taste cortex neurons to a food with which a monkey has been fed to satiety (Rolls et al. 1989). Such a modulation of taste responses by hunger has not been found in the primary taste cortex (Rolls et al. 1988, Yaxley et al. 1988). 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. Thus, this is a sensory-specific reduction in responsiveness (Rolls et al. 1989). We investigated whether satiety induced by feeding with MSG solution would affect the responses of orbitofrontal cortex cells 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 that responded to the taste of MSG or to the sight of food (see Rolls and Baylis 1994, Thorpe et al. 1983) were tested before, during and after feeding a monkey 0.1 mol/L MSG until behavioral satiation was achieved. Satiety was induced by feeding the monkey 0.1 mol/L MSG rapidly while recording the behavioral acceptance as a function of volume consumed. The responses of cells were measured at varying stages in the delivery of the satiating solution and after the monkey was sated.

It was possible to perform experiments studying the effect of satiety on taste responses to glutamate on five neurons (Rolls et al. 1996c). The responses of one of these neurons during feeding to satiety are shown in Figure 2. The response to the taste of glutamate decreased from a value of 19.5 spikes/s when the monkey was hungry to a value of 9.1 spikes/s when the monkey was sated. A similar reduction was not found for the other tastants, and indeed the response to the taste of glucose increased (see Fig. 2). There was a significant interaction between the responses to the different tastants and feeding to satiety (two-way ANOVA, $P < 0.01$, $F(1,46) = 9.8$). In two of the other four taste neurons also tested in this way, there was a generalized decrease in the response to MSG and to the other tastants. A larger volume of satiating fluid was used in both cases (125 and 200 mL), and this may account for the non-sensory-specific modulation of responsiveness in these cells.

Satiety experiments using MSG were also performed on three cells responsive to the sight of food. The response to the sight of an MSG-containing syringe was decreased after satiety in two of the three food-responsive visual neurons. In one case, this was a sensory-specific effect in which the response to the

MSG-containing syringe was significantly decreased ($P < 0.02$) (to the level of the spontaneous activity) during behavioral satiation, whereas the cell remained unchanged in its responses to foods such as banana, or a syringe containing blackcurrant juice (Rolls et al. 1996a).

Umami flavor produced by a combination of taste and olfactory inputs

Taste and olfactory inputs converge onto single neurons in the primate orbitofrontal cortex (Rolls and Baylis 1994). This convergence likely produces the flavor, which can be defined as the sensation produced by a combination of taste and olfactory stimuli. It is suggested here that this convergence may underlie at least in part how the taste of MSG or IMP can produce the flavor of umami. In particular, the hypothesis suggested is that umami flavor can be produced especially when MSG or IMP facilitate the effect produced by an appropriate olfactory input.

The fact that the taste of glutamate and the smell of a savory food can activate the same orbitofrontal cortex neuron is documented in Figure 3. This neuron responded well to both the taste of 0.1 mol/L MSG (M) and to the odor of salmon or onion (Rolls and Baylis 1994). This type of convergence onto different orbitofrontal cortex neurons was found in a number of cases (Critchley and Rolls 1996a, Rolls and Baylis 1994). Such corresponding olfactory and taste responses are likely to be built in the brain at least in part by olfactory to taste association learning, as demonstrated by Rolls et al. (1996a).

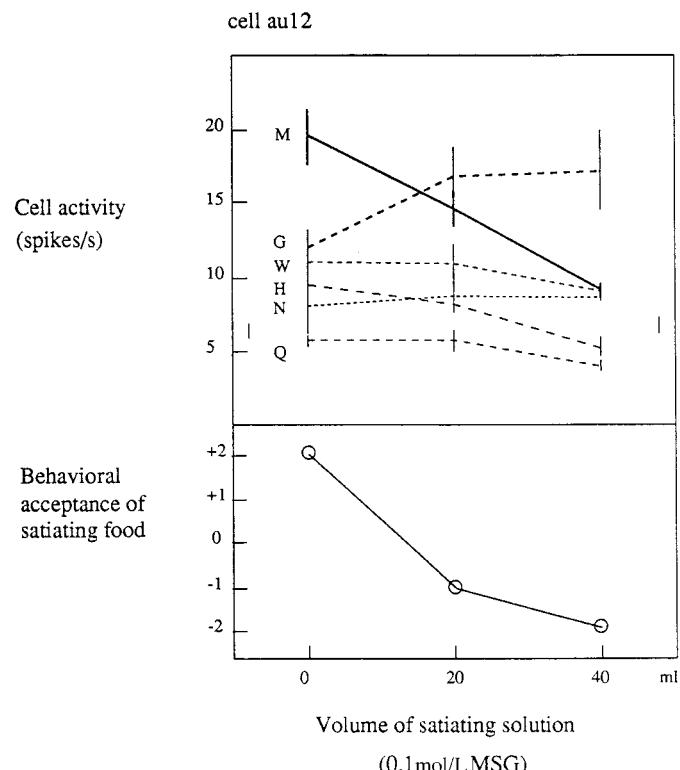


FIGURE 2 The effect of satiation induced with 0.1 mol/L monosodium glutamate on the response of a cell to the following tastes: glucose, G, (1.0 mol/L); NaCl, N, (0.1 mol/L); HCl, H, (0.01 mol/L); quinine-HCl, Q, (0.001 mol/L); distilled water, W; and monosodium glutamate, M, (0.1 mol/L). The behavioral acceptance of the satiating fluid is illustrated below the neuronal response. The scale runs from keen, avid acceptance (+2), through neutral (0) to firm rejection (-2).

FIGURE 3 The responses of a bimodal neuron recorded in the caudolateral orbitofrontal cortex: G, 1 mol/L glucose; N, 0.1 mol/L NaCl; H, 0.01 mol/L HCl; Q, 0.001 mol/L quinine-HCl; M, 0.1 mol/L monosodium glutamate; Bj, 20% blackcurrant juice; Tom, tomato juice; B, banana odor; Cl, clove oil odor; On, onion odor; Or, orange odor; S, salmon odor; C, control (no odor). The mean responses \pm SEM are shown. The neuron responded best to the tastes of NaCl and monosodium glutamate and to the odors of onion and salmon.

To investigate how taste and olfactory stimuli related to umami flavor combine, we (Rolls, Hernadi and Browning, unpublished data) performed a psychophysical experiment in humans. The subjects rated the intensity of the flavor of umami using a visual analog rating scale. This was a 100-mm line marked "very weak" at one end and "very intense" at the other end (see e.g., Rolls and Rolls 1997). The values obtained from a rating were thus in the range from 0 to 100, obtained by measurement of the distance along the line marked by the subject as representing the intensity of the umami flavor. The taste part of the stimuli consisted of MSG in concentrations of 0.005, 0.01 and 0.05 mol/L, as well as distilled water. To each of these solutions was added 0, 1, 5 or 10 ppm (μ L/L) of methyl furyl disulfide ($C_{10}H_{10}S_2$; Firmenich, Geneva, Switzerland), which has a garlic/meaty/savory odor and was dissolved in the solution. On each trial, the subject was given (in random sequence and with no knowledge of which sample was selected for that trial) one of the 16 samples to rate for the intensity of umami flavor. The subject placed 0.5 mL of the sample in the mouth and rated the intensity while the substance was in the mouth. After the rating, the sample was expectorated into a sink, and the mouth was rinsed with 15 mL of water, which was also expectorated. There was then a

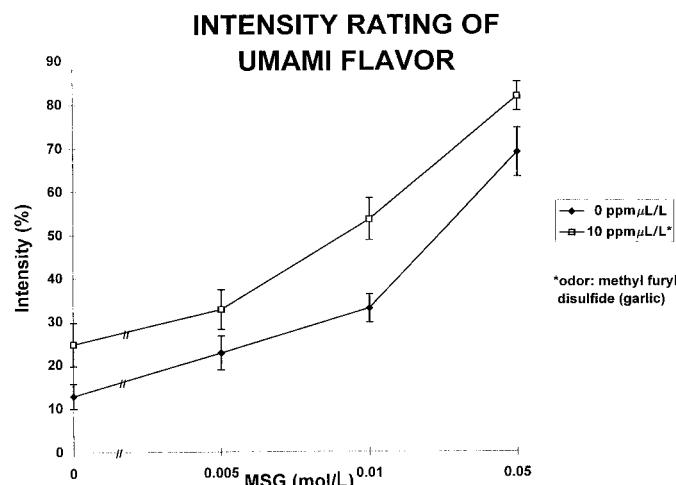
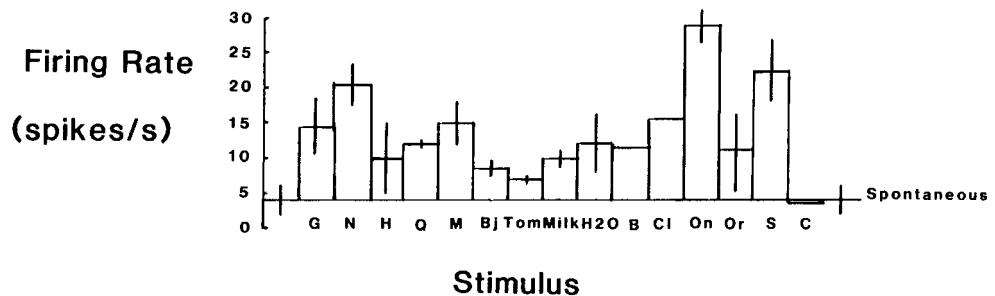


FIGURE 4 The intensity of the flavor of umami produced by combinations of the tastant monosodium glutamate in concentrations of 0.005 mol/L, 0.01 mol/L and 0.05 mol/L, and 0 or 10 μ L/L of methyl furyl disulfide, which has the odor of garlic and was dissolved in the solution. The ratings were made by four experienced human subjects. The means \pm SEM of the ratings made using a 100-mm visual analog rating scale are shown.

Cell 084.1 Bimodal Taste/olfaction



waiting time to produce a constant intersample interval of 45 s. After a practice session, new sequences were repeated until the subject had provided three ratings of each sample.

The results of this experiment on four experienced subjects are shown in Figure 4. For clarity, the results with no odor and with 10 μ L/L methyl furyl disulfide are shown on the graph. It can be seen that there is an approximately additive effect of the 10 μ L/L methyl furyl disulfide odor and the MSG in producing the flavor of umami. A two-way ANOVA showed highly significant effects of both MSG ($F_{3,176} = 119, P \ll 0.001$) and methyl furyl disulfide ($F_{3,176} = 11.3, P < 0.001$), and no significant interaction term ($P = 0.3$).

The findings of this psychophysical experiment suggest that one way in which MSG and the 5'-nucleotide tastants work is in combination with appropriate, savory odorants, to produce a full umami flavor.

DISCUSSION

The neurophysiological experiments reviewed here provide evidence that there is a neural system involved in representing protein (or umami) taste, by showing that the representation of MSG is different from that of other prototypical tastants, sweet, salt, bitter and sour, and by showing that the neurons in this system respond not only to MSG, but also to other umami taste stimuli such as glutamic acid and IMP. In other investigations, gustatory responses of single neurons selective to MSG have also been reported from the primary taste cortex and lateral hypothalamic areas of macaques (Oomura et al. 1991, Plata-Salaman et al. 1992). Given the role of the orbitofrontal cortex in food selection and the control of motivational behavior to food (Baylis and Gaffan 1991, Rolls et al. 1989, Rolls 1989, 1995 and 1999), the independent encoding of motivationally and ethologically significant foods such as the taste of umami becomes more important than earlier in the taste system (cf. Plata-Salaman et al. 1992). The clear separation of the representation of umami from other tastants in the secondary orbitofrontal cortex would enable processes such as sensory-specific satiety to remain specific to individual foods, thereby allowing a finer control of nutrient intake.

The results of the psychophysical experiment described here suggest that part of the way in which MSG is effective is that in combination with appropriate odorants, it produces a full umami flavor.

LITERATURE CITED

- Baylis, L. & Gaffan, D. (1991) Amygdectomy and ventromedial prefrontal ablation produce similar deficits in food choice and in simple object discrimination learning for an unseen reward. *Exp. Brain Res.* 86: 617-622.

- Baylis, L. L. & Rolls, E. T. (1991) Responses of neurons in the primate taste cortex to glutamate. *Physiol. Behav.* 49: 973-979.
- Baylis, L. L., Rolls, E. T. & Baylis, G. C. (1994) Afferent connections of the orbitofrontal cortex taste area of the primate. *Neuroscience* 64: 801-812.
- Beckstead, R. M., Morse, J. R. & Norgren, R. (1980) The nucleus of the solitary tract in the monkey: projections to the thalamus and brainstem nuclei. *J. Comp. Neurol.* 190: 259-282.
- Critchley, H. D. & Rolls, E. T. (1996a) Olfactory neuronal responses in the primate orbitofrontal cortex: analysis in an olfactory discrimination task. *J. Neurophysiol.* 75: 1659-1672.
- Critchley, H. D. & Rolls, E. T. (1996b) Hunger and satiety modify the responses of olfactory and visual neurons in the primate orbitofrontal cortex. *J. Neurophysiol.* 75: 1673-1686.
- Francis, S., Rolls, E. T., Bowtell, R., McGlone, F., O'Doherty, J., Browning, A., Clare, S. & Smith, E. (1999) The representation of pleasant touch in the brain and its relationship with taste and olfactory areas. *NeuroReport* 10: 453-459.
- Ikeda, K. (1909) On a new seasoning. *J. Tokyo Chem. Soc.* 30: 820-836.
- Norgren, R. (1984) Central neural mechanisms of taste. In: *Handbook of Physiology—The Nervous System III, Sensory Processes 1* (Darien-Smith, I., ed.), (Brookhart, J. & Mountcastle, V. B., section eds.), pp. 1987-1128. American Physiological Society, Washington, DC.
- Norgren, R. & Leonard, C.M. (1973) Ascending central gustatory pathways. *J. Comp. Neurol.* 150: 217-238.
- O'Mahoney, M. & Ishii, R. (1987) The umami taste concept: implication for the dogma of four basic tastes. In: *Umami: A Basic Taste* (Kawamura, Y. & Kare, M. R., eds.), pp. 365-385. Marcel Dekker, New York, NY.
- Oomura, Y., Nishino, H., Karadi, Z., Auo, S. & Scott, T. R. (1991) Taste and olfactory modulation of feeding related neurons in the behaving monkey. *Physiol. Behav.* 49: 943-950.
- Plata-Salaman, C. R., Scott, T. R. & Smith-Swintosky, V. L. (1992) Gustatory coding in the monkey: L-amino acids. *J. Neurophysiol.* 67: 1552-1561.
- Rolls, E. T. (1989) Information processing in the taste system of primates. *J. Exp. Biol.* 146: 141-164.
- Rolls, E. T. (1994) Neural processing related to feeding in primates. In: *Appetite: Neural and Behavioural Bases* (Legg, C. R. & Booth, D. A., eds.), pp. 11-53. Oxford University Press, Oxford, England.
- Rolls, E. T. (1995) Central taste anatomy and neurophysiology. In: *Handbook of Olfaction and Gustation* (Doty, R. L., ed.), pp. 549-573. Marcel Dekker, New York, NY.
- Rolls, E. T. (1997) Taste and olfactory processing in the brain. *Crit. Rev. Neurobiol.* 11: 263-287.
- Rolls, E. T. (1999) *The Brain and Emotion*. Oxford University Press, Oxford, England.
- Rolls, E. T. & Baylis, L. L. (1994) Gustatory, olfactory and visual convergence within the primate orbitofrontal cortex. *J. Neurosci.* 14: 5437-5452.
- Rolls, E. T., Critchley, H., Mason, R. & Wakeman, E. A. (1996a) Orbitofrontal cortex neurons: role in olfactory and visual association learning. *J. Neurophysiol.* 75: 1970-1981.
- Rolls, E. T., Critchley, H. D. & Treves, A. (1996b) The representation of olfactory information in the primate orbitofrontal cortex. *J. Neurophysiol.* 75: 1982-1996.
- Rolls, E. T., Critchley, H., Wakeman, E. A. & Mason, R. (1996c) Responses of neurons in the primate taste cortex to the glutamate ion and to inosine 5'-monophosphate. *Physiol. Behav.* 59: 991-1000.
- Rolls, E. T., Francis, S., Bowtell, R., Browning, D., Clare, S., Smith, E. & McGlone, F. (1997) Taste and olfactory activation of the orbitofrontal cortex. *NeuroImage* 5: S199.
- Rolls, E. T. & Rolls, J. H. (1997) Olfactory sensory-specific satiety in humans. *Physiol. Behav.* 61: 461-473.
- Rolls, E. T., Scott, T. R., Sienkiewicz, J. Z. & Yaxley, S. (1988) The responsiveness of neurons in the frontal opercular gustatory cortex of the macaque monkey is independent of hunger. *J. Physiol.* 397: 1-12.
- Rolls, E. T., Sienkiewicz, Z. J. & Yaxley, S. (1989) Hunger modulates the responses to gustatory stimuli of single neurons in the caudolateral orbitofrontal cortex of the macaque monkey. *Eur. J. Neurosci.* 1: 53-60.
- Rolls, E. T., Yaxley, S. & Sienkiewicz, Z. J. (1990) Gustatory responses of single neurons in the orbitofrontal cortex of the macaque monkey. *J. Neurophysiol.* 64: 1055-1066.
- Thorpe, S. J., Rolls, E. T. & Maddison, S. (1983) Neuronal activity in the orbitofrontal cortex of the behaving monkey. *Exp. Brain Res.* 49: 93-115.
- Yamaguchi, S. (1967) The synergistic taste effect of monosodium glutamate and disodium 5'-inosinate. *J. Food Sci.* 32: 473-478.
- Yamaguchi, S. & Kimizuka, A. (1979) Psychometric studies on the taste of monosodium glutamate. In: *Glutamic Acid: Advances in Biochemistry and Physiology* (Filer, L. J., Garattini, S., Kare, M. R., Reynolds, A. R. & Wurtman, R. J., eds.), pp. 35-54. Raven Press, New York, NY.
- Yaxley, S., Rolls, E. T. & Sienkiewicz, Z. J. (1988) The responsiveness of neurons in the insular gustatory cortex of the macaque monkey is independent of hunger. *Physiol. Behav.* 42: 223-229.
- Zwillinger, S. A. & Halpern, B. P. (1991) Time-quality tracking of monosodium glutamate, sodium saccharin and a citric acid-saccharin mixture. *Physiol. Behav.* 49: 855-862.