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Hellekant, Göran, Vicktoria Danilova, and Yuzo Ninomiya.
Primate sense of taste: behavioral and single chorda tympani and glossopharyngeal nerve fiber recordings in the rhesus monkey, *Macaca mulatta*. J. Neurophysiol. 77: 978–993, 1997. The responses of 51 chorda tympani proper (CT) and 33 glossopharyngeal (NG) neural taste units from the rhesus monkey (*Macaca mulatta*) were recorded during stimulation of either the anterior (CT) or posterior (NG) part of the tongue with 26 stimuli that taste salty, umami, sour, bitter, and sweet to humans. In the CT, hierarchical cluster analysis separated four major clusters. The N and S clusters were most populous, followed by the H cluster and a small Q cluster. NaCl, monosodium glutamate (MSG), and MSG with guanosine 5'-monophosphate were the best stimuli in the N cluster. Amiloride suppressed responses to NaCl. KCl did not stimulate fibers from this cluster. S cluster fibers were characterized by strong responses to all sweeteners. The H cluster responded best to acids but also to some of the sweeteners such as xylitol, fructose, and sucrose. Q fibers responded well to quinine hydrochloride (QHCl) and caffeine, but not to denatonium benzoate. In the NG, hierarchical cluster analysis separated three major clusters. Q fibers formed the largest cluster. QHCl, caffeine, and sucrose octa-acetate but not denatonium benzoate elicited very strong responses in these fibers. S fibers formed a second cluster. Although most of the sweeteners stimulated the S fibers, their responses were not so pronounced as in CT S fibers. The small M cluster was formed by fibers that responded best to MSG. They also responded to NaCl and acids. Two bottle preference tests showed a positive relationship between a sweetener’s ability to stimulate the taste fibers and the animals’ consumption. Thus the most-liked sweeteners stimulated the S fibers with NaCl best, whereas less-liked sweeteners such as d-phenylalanine elicited a response in Q fibers and sodium cyclamate stimulated N fibers. The results show that both CT and NG taste fibers of *M. mulatta* group according to the human concepts of taste qualities.

**INTRODUCTION**

It is evident that our growing knowledge of taste differences between species necessitates a more cautious choice of animal model in our attempts to understand the human sense of taste. Many of these species differences reflect phylogenetic relationships.

In primates, influence of the phylogeny has been repeatedly documented with regard to the taste of sweeteners and the effects of sweet taste modifiers (cf. Glaser et al. 1978; Hellekant 1975; Hellekant and van der Wel 1989). In nonprimates, species differences affect not only the taste of sweeteners, but also the taste of other compounds. It is evident, for example, that the threshold for a rejection of denatonium benzoate is higher in rodents than in humans (Whitney et al. 1990). Tannins are integral parts of the food for several lemuriform primates, whereas their aversive taste to foods of the rhesus monkey (*Macaca mulatta*) was In salty taste, the varying species effect of amiloride on two of 51 chorda tympani ... to NaCl serves as an example (e.g., Ninomiya and Funakoshi 1988; Tonosaki and Funakoshi 1989).

The effects of phylogenetic differences are not limited to the taste of compounds representing the four taste qualities. They also affect other compounds. Ethanol may serve as one example; recordings from the human taste nerve, the chorda tympani proper (CT), give a response that is quite different from that in the CT of cats, dogs, and rats (Diamant et al. 1965; Hellekant 1965a,b). From this follows that the closer the phylogenetic relationship is between the animal model and humans the more applicable are the data acquired. For these reasons nonhuman primates such as the rhesus monkey (*Macaca mulatta*) can be assumed to offer a better model than, for example, dogs, but knowledge is still needed of the similarities and dissimilarities of the sense of taste of *M. mulatta* with the human sense of taste.

The response in CT taste fibers of macaques has been recorded earlier. The most notable studies are by Sato et al. (1975) and Brouwer et al. (1983), although the early study by Gordon et al. (1959) should not be forgotten. However, only one study of the other taste nerve of the tongue, the glossopharyngeal nerve (NG), has been published (Farbman and Hellekant 1989). In this study we present recordings of the taste response from both the CT and NG of rhesus monkeys and relate them with behavioral observations. The closeness between chimpanzee and human is then used to assess the usefulness of the rhesus as the animal model for humans by comparing the sense of taste of rhesus and chimpanzee. We thus attempt to assess the validity of the rhesus model for the human sense of taste by comparing the data here with data from our earlier studies in chimpanzee (Hellekant and Ninomiya 1991, 1994a,b; Hellekant et al. 1985, 1996, 1997; Ninomiya and Hellekant 1991).

**METHODS**

**Electrophysiology**

**ANIMALS.** Twenty rhesus monkeys (*M. mulatta*) of both sexes were used for electrophysiological recordings. Their weights ranged from 3.4 to 7.6 kg.
SURGERY. Anesthesia was initiated with ketamine (50 mg im). The monkey was then intubated and the anesthesia maintained with halothane (0.7–1.0%). Fluid losses were replaced with 5% dextrose and lactated Ringer solution. Body temperature, heart rate, and respiratory rate were continuously monitored.

The method of dissecting the right CT was recently described (Hellekant and Roberts 1995). Briefly, an incision was made along the mandibular angle between the rostral lobes of the parotid gland and the mandibular bone. Then the tissue attached to the mandibular angle was dissected through and the caudomedial side of the pterygoid muscle was followed down to its origin at the pterygoid plate of the skull to the CT.

The method of dissecting the right lingual branch of the NG was also recently described (Hellekant and Roberts 1995). The incision was made ventral to the mandibular angle, ventral to the rostral lobes of the parotid gland to reach the nerve dorsal and medial to the much larger hypoglossal nerve. The NG distinguishes itself with a very typical meandering course caudal to the hyoid bone. For single-fiber recording it was not necessary to cut either the CT or NG. Instead, single fibers were dissected off fine strands of the nerves. The method left a major part of the nerve trunk intact.

At the end of the experiment, deeper structures were sutured with absorbable suture as needed. The skin was closed with nylon sutures that were removed after 7–10 days.

STIMULATION Table 1 presents the compounds and their concentrations for both series of experiments. The compounds were chosen to represent the human taste qualities. Their concentrations were influenced by our results from chimpanzees, especially with regard to the sweeteners, but we also tried to maintain a continuity with other earlier studies. Generally we attempted to use the same array of stimuli for both nerves. However, there were a few exceptions, as shown in Table 1. The structure of super-aspartame, which incorporates aspartame and suosan into a single molecule, has been given in Hellekant and Walters (1991). Structural formulas for three guanidine analogues are shown in Fig. 1.

All compounds except quinine hydrochloride (QHCl), which for solubility reasons was dissolved in distilled water, were dissolved in artificial saliva (Table 2).

STIMULATION The tastants were delivered to the tongue with an open flow system (Taste-O-Matic) controlled by a computer (Hellekant and Roberts 1995). It delivered the solutions at given intervals, over a preset time, under conditions of constant flow and temperature (33°C). Two periods of taste stimulation were used, 5 and 8 s. During the CT experiments the flow was directed over the fungiform papillae. To ensure that the foliate and vallate taste buds were stimulated in the NG experiments the tongue was stretched. Between stimulations the tongue was rinsed for 55–52 s with artificial saliva.

RECORDING TECHNIQUE Single-nerve impulses from the CT or NG were recorded with a PAR 113 amplifier, monitored over a loudspeaker and on an oscilloscope, and fed into a recorder (Gould ES 1000). An impulse amplitude analyzer with a window with adjustable upper and lower levels was used to discriminate between nerve impulses. These levels could be set so that when a nerve impulse exceeded the lower but not the upper level it triggered an impulse.

TABLE 1. List of solutions used in electrophysiological and behavioral experiments

<table>
<thead>
<tr>
<th>CT Series</th>
<th>NG Series</th>
<th>TBP Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl (0.07 M)</td>
<td>NaCl (0.1 M)</td>
<td></td>
</tr>
<tr>
<td>NaCl (0.07 M) + Amiloride (0.5 mM)</td>
<td>KCl (0.1 M)</td>
<td></td>
</tr>
<tr>
<td>NaCl (0.07 M) + Novobiocin (1 mM)</td>
<td>MSG (70 mM)</td>
<td></td>
</tr>
<tr>
<td>KCl (0.1 M)</td>
<td>KCl (0.1 M)</td>
<td></td>
</tr>
<tr>
<td>MSG (70 mM)</td>
<td>MSG (70 mM)</td>
<td></td>
</tr>
<tr>
<td>MSG (70 mM) + GMP (0.3 mM)</td>
<td>Citric acid (40 mM)</td>
<td></td>
</tr>
<tr>
<td>Citric acid (40 mM)</td>
<td>Aspartic acid (50 mM)</td>
<td></td>
</tr>
<tr>
<td>HCl (10 mM)</td>
<td>HCl (10 mM)</td>
<td></td>
</tr>
<tr>
<td>Quinine HCl (5 mM)</td>
<td>Quinine HCl (5 mM)</td>
<td></td>
</tr>
<tr>
<td>Caffeine (0.1 M)</td>
<td>Caffeine (0.1 M)</td>
<td></td>
</tr>
<tr>
<td>Denatonium benzolate (0.01 mM)</td>
<td>Denatonium benzolate (0.1 mM)</td>
<td></td>
</tr>
<tr>
<td>Sucrose (0.3 M)</td>
<td>Sucrose (0.3 M)</td>
<td></td>
</tr>
<tr>
<td>Fructose (0.3 M)</td>
<td>Fructose (0.3 M)</td>
<td></td>
</tr>
<tr>
<td>Aspartame (5 mM)</td>
<td>Aspartame (5 mM)</td>
<td></td>
</tr>
<tr>
<td>Alitame (0.3 mM)</td>
<td>Alitame (0.3 mM)</td>
<td></td>
</tr>
<tr>
<td>Super-aspartame (0.1 mM)</td>
<td>Super-aspartame (0.1 mM)</td>
<td></td>
</tr>
<tr>
<td>Acesulfame-K (3.5 mM)</td>
<td>Acesulfame-K (3.5 mM)</td>
<td></td>
</tr>
<tr>
<td>Saccharin-Na (1.6 mM)</td>
<td>Saccharin-Na (1.6 mM)</td>
<td></td>
</tr>
<tr>
<td>Cyclamate-Na (10 mM)</td>
<td>Cyclamate-Na (10 mM)</td>
<td></td>
</tr>
<tr>
<td>Stevioside (0.87 mM)</td>
<td>Stevioside (0.87 mM)</td>
<td></td>
</tr>
<tr>
<td>Xylitol (0.8 M)</td>
<td>Xylitol (0.8 M)</td>
<td></td>
</tr>
<tr>
<td>d-Tryptophan (0.03 M)</td>
<td>d-Tryptophan (0.03 M)</td>
<td></td>
</tr>
<tr>
<td>d-Phenylalanine (0.1 M)</td>
<td>d-Phenylalanine (0.1 M)</td>
<td></td>
</tr>
<tr>
<td>d-Glucose (0.3 M)</td>
<td>d-Glucose (0.3 M)</td>
<td></td>
</tr>
<tr>
<td>l-Glucose (0.3 M)</td>
<td>l-Glucose (0.3 M)</td>
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<tr>
<td>Galactose (0.3 M)</td>
<td>Galactose (0.3 M)</td>
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</tr>
<tr>
<td>Dulcin (1.6 mM)</td>
<td>Dulcin (1.6 mM)</td>
<td></td>
</tr>
<tr>
<td>SC-45647 (0.04 mM)</td>
<td>SC-45647 (0.04 mM)</td>
<td></td>
</tr>
<tr>
<td>NC-00174 (0.03 mM)</td>
<td>NC-00174 (0.03 mM)</td>
<td></td>
</tr>
<tr>
<td>NC-00351 (0.03 mM)</td>
<td>NC-00351 (0.03 mM)</td>
<td></td>
</tr>
<tr>
<td>Brazzein (0.3%)</td>
<td>Brazzein (0.3%)</td>
<td></td>
</tr>
</tbody>
</table>

CT, chorda tympani proper; NG, glossopharyngeal nerve; TBP, 2-bottle preference; MSG, monosodium glutamate; GMP, guanosine 5'-monophosphate.
BEHAVIORAL EXPERIMENTS. Two-bottle preference tests were carried through with 16 animals (10 males and 6 females) housed individually. The animals had uninterrupted water access. The experiments were preceded by a training period. Different animals were used for the electrophysiology.

Table 1, third column, lists the compounds used in the behavioral experiments. They were dissolved in distilled water. One bottle contained 30 ml of the test solution and the other 30 ml of distilled water. The bottles were left on the cages until one bottle was emptied or for at most 15 min. Each solution was tested twice with changed position of the bottles. Only one sweetener was tested each day.

The preference ratio was calculated as consumption of sweetener divided by the total volume consumed. The results were averaged. A preference ratio > 0.5 was chosen as the criterion for preference. A two-tailed t-test was used to compare mean preference ratios with 0.5. To compare preferences between all sweeteners, the results were first assessed with the use of analysis of variance. Then Student-Newman-Keuls test was used to make all pairwise comparisons. P < 0.01 was chosen as significance level.

RESULTS

Single-fiber response in the CT

Figure 2 shows an example of the nerve impulses recorded from single CT taste fiber (RH95D19H). Here we present only a part of the recordings from this unit. However, it is evident that NaCl, the acids, and to some extent sodium cyclamate gave a response. Some of these features will be discussed later.

Figure 3 gives an overview of the responses in all 51 CT fibers with the use of a topographical method in which the area of the circles represents impulse activity over the first 5 s of stimulation. The legend to Fig. 3 relates the area of the circles with the nerve responses. Open circles indicate a suppression of the nerve activity during a stimulation. The legend to Fig. 3 relates the area of the circles with the nerve responses. Open circles indicate a suppression of the nerve activity during a stimulation. The stimuli are arranged along the X-axis in the order of salt, umami compounds, acids, bitter compounds, and sweet compounds. The fibers are ordered along the Y-axis in groups, starting with the fibers responding best to NaCl, followed by the fibers mainly stimulated by citric acid, QHCl, and finally sucrose.

The average spontaneous activity was 16.4 ± 1.5 (SE) impulses measured over 5 s before stimulations.

Hierarchical cluster analysis

The responses of 47 of these CT fibers to 25 stimuli were included in the hierarchical cluster analysis. Because four fibers were tested with only five stimuli, we did not include them in the analysis. The result is represented as a dendrogram.

<table>
<thead>
<tr>
<th>Salt</th>
<th>Concentration, mM</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl</td>
<td>4</td>
<td>230 mg/l</td>
</tr>
<tr>
<td>KCl</td>
<td>10</td>
<td>746 mg/l</td>
</tr>
<tr>
<td>NaHCO₃</td>
<td>6</td>
<td>504 mg/l</td>
</tr>
<tr>
<td>KHCO₃</td>
<td>6</td>
<td>588 mg/l</td>
</tr>
<tr>
<td>HCl</td>
<td>3.6</td>
<td>6 ml</td>
</tr>
<tr>
<td>CaCl₂</td>
<td>0.5</td>
<td>55.5 mg/l</td>
</tr>
<tr>
<td>MgCl₂</td>
<td>0.5</td>
<td>47.5 mg/l</td>
</tr>
<tr>
<td>K₂HPO₄</td>
<td>0.24</td>
<td>42 mg/l</td>
</tr>
<tr>
<td>KH₂PO₄</td>
<td>0.24</td>
<td>33.3 mg/l</td>
</tr>
</tbody>
</table>
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Figure 2. Recordings from the chorda tympani proper (CT) NaCl-best filament RH95D19H during stimulation with NaCl, NaCl with amiloride, KCl, citric acid, aspartic acid, sodium cyclamate, sucrose, saccharin, potassium acesulfame (ace-K), aspartame (APM), alitame, and quinine hydrochloride (QHCl). Onset and offset of stimuli are shown as changes in bar code.

Average response profiles

Figure 5 shows the average response profiles of these four clusters. The stimuli are listed along the X-axis, whereas the average impulse activity measured over 5 s is plotted along the Y-axis. The vertical lines illustrate the SE of these averages. In the following we present each cluster.

N cluster

As shown in Fig. 4, this cluster included 19 units and was the largest one. NaCl elicited the strongest response in 15 of these fibers. There were four monosodium glutamate (MSG)/acid-best fibers, judged by the stimulus that elicited the largest responses. Fibers RH92M12B and RH92M12C were not subjected to cluster analysis, but we included them among the NaCl-best fibers in Figs. 3 and 5A because among the four basic stimuli, NaCl elicited the largest response in these fibers.

Figure 5A shows that the N cluster was characterized by strong responses to NaCl and MSG alone or mixed with guanosine 5'-monophosphate. Amiloride suppressed the response to NaCl (Figs. 2, 3, and 5A). Novobiocin, which has been reported to enhance the salt response in some species (cf. Feigin et al. 1994), had no effect here. Interestingly, KCl elicited no response in these fibers, whereas citric and aspartic acid evoked a moderate response (Figs. 2, 3, and 5A). These fibers did not respond to bitter compounds, and of the sweeteners only sodium cyclamate and xylitol elicited some response in these fibers (Figs. 2, 3, and 5A).

H cluster

Figure 5B shows the average response profile of eight units. Citric and aspartic acids elicited the best responses in these fibers. Generally the sweeteners did not stimulate fibers of this cluster. The exceptions were the carbohydrates and xylitol. Xylitol evoked ~70–80% of the response to citric acid. In fiber RH92U23D, xylitol elicited the strongest response among all stimuli. As can be seen in Fig. 5B, the fibers of this cluster did not respond to salty and bitter compounds.

Q cluster

Figure 5C presents the average response profile for the Q cluster. This cluster consisted of four QHCl-best fibers. Fiber RH92U24K was not subject to cluster analysis, but we included it among the QHCl-best fibers in Figs. 3 and 5C because QHCl elicited the largest response in this fiber. Figure 5C shows that these fibers responded well to QHCl and caffeine but not to 0.01 mM denatonium benzoate. Considering the fact that amiloride tastes bitter to humans, it is interesting that NaCl with amiloride and KCl with amiloride elicited a response in these Q fibers. They also responded to saccharin, xylitol, D-phenylalanine, D-tryptophane, and carbohydrates.

S cluster

The S fiber cluster was the second largest and consisted of 16 fibers. One fiber (RH92M12D) was not subject to cluster analysis, but we included it in Fig. 5D because among the four basic stimuli sucrose elicited the best response in this fiber. Figure 5D shows that these fibers responded to every sweet stimulus. These included 0.3 M D- and L-glucose; 0.3 M galactose; 1.6 mM dulcin; three guanidine deriv-
atives (0.04 mM SC-45647, 0.03 mM NC-00174, and 0.03 mM NC-00351); brazzein; and monellin. The S fibers quite often responded to aspartic acid and, to a lesser extent, MSG and citric acid, but not to salts and bitter compounds (Fig. 5D).

Multidimensional scaling

On the basis of a correlation matrix of the stimuli, we performed multidimensional scaling. The spatial representation of the similarities among 25 stimuli is shown in Fig. 6. The stress value is 0.047. All sweeteners formed a tight group separate from the other stimuli. Another compact group included NaCl alone or mixed with novobioin and the umami compounds. Then caffeine and QHCl stayed very close but denatonium benzoate was positioned separately. KCl and mixtures of salts with amiloride were located most closely to the bitter compounds. It is interesting and corroborates Fig. 5C that the addition of amiloride moved NaCl into the bitter group. Less evident, perhaps, is the grouping of cyclamate among salty compounds, but, as shown in Fig. 5A,
it gave a response in N cluster fibers too. Citric and aspartic acid were located close to each other, with HCl somewhat distant.

**Single-fiber response in the NG**

Figure 7 shows as an example nerve impulses recorded from the single NG fiber RH94Y23D. Here we present only a part of the recordings from this unit. As can be seen from the responses shown, it responded to stimulation with QHCl and caffeine, and displayed some response to KCl, sucrose, and D-phenylalanine. It was characterized as a QHCl-best fiber.

Figure 8 gives an overview of the responses in all 33 NG fibers. The results were plotted in the same way as in Fig. 3. Figure 8 shows that the fibers responding to bitter compounds constituted the largest group.

The average spontaneous activity was $8.6 \pm 1.3$ (SE) impulses measured over 5 s before stimulations.

**Hierarchical cluster analysis**

The responses of all NG fibers to 20 stimuli were subjected to hierarchical cluster analysis. The result is represented as a dendrogram in Fig. 9. The analysis resulted in three major clusters: M, Q, and S clusters. The identity num-

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**FIG. 4.** Hierarchical cluster analysis of the response profiles for 47 CT fibers. Intercluster similarity was measured with the use of the Pearson correlation coefficient and cluster analysis proceeded according to the average linkage method. Fiber number and response category on the basis of its response to the 4 basic solutions are listed on the left. N, H, Q, and S: NaCl-, citric acid-, QHCl-, and sucrose-best fibers, respectively.
ber of the fiber and response category on the basis of its best response to the four basic solutions are listed on the left side of the dendrogram. Figure 10 shows the average response profiles of these three clusters. In the following we present each cluster of fibers.

**M cluster**

The average response profile of the M cluster in Fig. 10A shows that MSG elicited the largest response, and NaCl, citric acid, and aspartic acid elicited a substantial response in these fibers, whereas the bitter compounds and the sweeteners did not stimulate. The M cluster included three NaCl-best and two citric acid-best fibers according to their responses to the four basic stimuli.

**Q cluster**

The cluster analysis in Fig. 9 confirmed that the fibers mainly responding to bitter compounds constituted the
largest group in the NG (20 fibers of a total of 33 single fibers). We added sucrose octa-acetate (SOA), a compound bitter to humans, to our array of stimuli for the NG recordings. The data in Fig. 10B indicate that SOA stimulated these fibers as well as QHCl and caffeine did. The lack of a response to denatonium benzoate corroborates our findings in the CT. The finding that NaCl with amiloride elicited a larger response in the Q cluster than in the M cluster corroborates the effects of NaCl with amiloride on the CT. The Q cluster did not respond to NaCl, acids, or sweeteners, but sucrose, fructose, xylitol, and D-phenylalanine elicited some response.

**S cluster**

S fibers constituted the second largest, but considerably smaller, group of eight fibers in the NG (Fig. 9). They...
did not respond to stimulation with salts, acids, and bitter solutions. Despite the fact that sweeteners were their best stimuli, their response to these was small and inconsistent (Fig. 10C). Further, aspartame and sodium cyclamate elicited small responses, whereas some of the other sweeteners, such as stevioside, did not elicit any response in these fibers.

**Multidimensional scaling**

Figure 11 shows the results of multidimensional scaling for 18 stimuli. The separation of the tastants in space is less evident than for the CT data. Dimension 2 separated a group consisting of citric and aspartic acid, NaCl, sodium cyclamate, and MSG. Dimension 1 suggested a group of sweeteners in the background of the left side and a group of bitter compounds in the foreground. Because SOA and denatonium benzoate were not used in all fibers, they were not included in the analysis.

**Comparison of CT and NG fibers**

Figure 12 presents the distribution of the different types of single taste fibers in the CT and NG according to their best response to one of the four basic stimuli. In the CT the two largest groups were the NaCl- and sucrose-best fibers. In the NG there were few NaCl-best fibers. However, the response to NaCl in the NaCl-best fibers of the CT (124.4 ± 17.3 impulses per 5 s) did not differ (tailed t-test, \( P > 0.1 \)) from the response in the NaCl-best fibers of the NG (97.1 ± 85.5 impulses per 5 s).

The percentage sucrose-best fibers was about the same in the NG as in the CT. But the response to sucrose in the NG sucrose-best fibers (56.5 ± 11.8 impulses per 5 s) was significantly smaller (2-tailed t-test, \( P < 0.01 \)) than in the CT (119.4 ± 13.8 impulses per 5 s). This difference in responses is indicated by the asterisk in Fig. 12.

In the NG the QHCl-best fibers were more populous than in the CT, but their responses to QHCl did not differ significantly (NG: 116.5 ± 15.8 impulses per 5 s; CT: 173.8 ± 52.5 impulses per 5 s). Although the percentage of citric-acid-best fibers was higher in CT than in NG, their responses to citric acid did not differ significantly (CT: 98.1 ± 14.5 impulses per 5 s; NG: 62.4 ± 34.1 impulses per 5 s).
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FIG. 9. Hierarchical cluster analysis of the response profiles for 33 NG single fibers. Intercluster similarity was measured with the use of the Pearson correlation coefficient and cluster analysis proceeded according to the average linkage method. Fiber number and response category on the basis of its response to the 4 standard solutions are listed on the left.

**Breadth of tuning**

Table 3 shows the breadth of tuning ($H$) for each group of fibers in both nerves. The $H$ value varied between 0.37 and 0.81, with the lowest for the QHCl-best fibers in both CT and NG fibers. This means that the QHCl-best fibers were the most specific in both nerves.

**Behavioral experiments**

Figure 13 presents the results of the two-bottle preference experiments with the sweeteners listed in Table 1. For all solutions, which are sweet to humans, the mean preference ratios were significantly larger than the chance level (0.5). Summarizing pairwise comparisons, the preference ratios for cyclamate and D-phenylalanine were significantly lower than for other sweeteners. The preference ratio for NC-00351 was lower than ratios for super-aspartame and sucrose.

**Discussion**

In the CT the hierarchical cluster analysis separated four major clusters. The N and S clusters were most populous, followed by the H cluster and a small Q cluster. In the N cluster, NaCl and MSG were the best stimuli. Amiloride always suppressed the response to NaCl, whereas KCl did not stimulate fibers from this cluster. All sweeteners stimulated the S cluster fibers. The H cluster fibers were characterized by strong responses to acids. Xylitol and carbohydrates elicited a response in some of these fibers. Q fibers responded well to QHCl and caffeine, but not to denatonium benzoate.

In the NG the analysis separated three major clusters.
The Q cluster was the largest. QHCl, caffeine, and SOA but not denatonium benzoate elicited very strong responses in these fibers. Sucrose-best fibers formed a second S cluster. Although most of the sweeteners stimulated these fibers, the responses were not so pronounced as in CT S cluster. The smallest cluster was formed by fibers that responded best to MSG. They also responded to NaCl and acids.

We first discuss the taste fibers of the NG, then compare CT results with data from other studies on CT and cortex, and finally examine the similarity between the sense of taste in rhesus monkey with that of human and chimpanzee, in an attempt to decide to what extent the rhesus monkey can serve as the animal model in taste.

**Taste fibers in the NG**

There is to our knowledge no single-fiber study published from the NG of a macaque, although there is an earlier study, which presented summated recordings (Farbman and Hellekant 1989). This prevents direct comparisons of fiber distribution, etc. However, the parallel
is evident between our finding of a large group of QHCl-best fibers in the NG and the reports of human taste sensitivity to bitterness, prevalently from the back of the tongue (Hänig 1901; cf. Pfaffmann et al. 1971), especially if we compare it with the many sweet-best and salt-best fibers found in the CT of the rhesus monkey and the sensitivity to salt and sweet reported as being most prominent on the front of the human tongue.

Taste fibers in the CT

In contrast, there are some studies from the CT nerve of macaques. Zotterman, who was the first to publish taste fiber recordings (Zotterman 1935), was also one of the authors of the first study of the CT of M. mulatta (Gordon et al. 1959). That study concluded that “certain gustatory fibers responded very specifically to one class of substances only e.g. to salt, acid, or to QHCl.” Also noted was the link between compounds within the same taste quality: “fibers responding to sucrose almost always responded to saccharin as well.”

After miraculin, acids taste sweet to humans (e.g., Kurihara et al. 1969) and the summated CT response to acids is enhanced in macaques (Diamant et al. 1972; Hellekant 1977; Hellekant et al. 1974, 1976). In 1983, we published a single-fiber study of the CT of M. mulatta (Brouwer et al. 1983) based on these earlier findings. The study showed that after miraculin, sucrose-best fibers responded to acids as if the acids had become sweeteners.

In this context it is interesting that one puzzling observation in the study by Brouwer et al. (1983) may be explained by observations here. We used sucrose and citric acid to distinguish and classify the sucrose-best and acid-best fiber types and found an overlap between these stimuli. This corroborates Fig. 5B here, which shows that sucrose stimulates to some extent fibers in our H cluster. Judged by the responses to fructose, D-glucose, and L-glucose, probably carbohydrates, in general, stimulate these H fibers. Consequently carbohydrates are less suited for distinguishing between acid-best and sweet-best fibers. One of the high-potency sweeteners, e.g., aspartame, would have been a better choice than sucrose because, as shown in Fig. 5B, aspartame did not stimulate the H cluster. This corroborates a recent study in chimpanzee that shows that high-potency
sweeteners stimulate sucrose-best fibers more selectively than sucrose and other carbohydrates (Hellekant et al. 1997).

A study in *M. fascicularis* by Sato et al. (1975), later reanalyzed in Sato et al. 1994, is of particular interest here. Sato et al. concluded that the CT fibers could be classified into four categories, depending on their best sensitivity to one of the four basic stimuli. Sucrose-best, NaCl-best, and QHCl-best fibers were rather specifically sensitive to sucrose, NaCl, and QHCl, respectively, whereas acid-best fibers also responded relatively well to a series of salts in addition to 0.01 M HCl. Interestingly, all NaCl-best fibers in the study by Sato et al. and in this one show the same lack of a response to KCl.

In agreement with our CT observations, the bitter sensitive group in the study by Sato et al. was the smallest, ~16% of the total fibers. Saccharin produced a good response in sucrose-best fibers, but the bitter-sensitive fibers also responded to saccharin, more to 0.3 M than to 0.01 M. Considering the increased bitter taste with increasing concentration of saccharin, this is interesting and fits the conclusion below.

Because there was some discrepancy in breadth of tuning between the data of Sato et al. (1994) and ours, we recalculated breadth of tuning in our study with the use of HCl instead of citric acid. As shown in Table 4, we arrive at virtually the same average. Only the order between fiber groups is somewhat different.

Further, Sato et al. found that macaque monkey taste fibers are more narrowly tuned to one of the four basic taste stimuli than CT fibers of rats, hamsters, and squirrel monkeys (cf. Sato et al. 1994), which is in agreement with this study. They concluded, in agreement with our conclusions here, ‘‘that in the monkey CT each of the four classes of fibers predominantly contributes to mediate gustatory information for sweet, salty, sour and bitter stimuli.’’

**Cortical studies**

Similar ranges of taste stimuli have been employed in macaques earlier. There are, as a matter of fact, more recordings from cortical neurons than from peripheral neurons in macaques, although from a different species, *M. fascicularis*. Many studies originate from the laboratories of Rolls and Scott, who in a number of studies have presented data from the primary taste area in awake animals (Baylis and Rolls 1991; Plata-Salaman et al. 1992, 1993, 1995; Scott et al. 1991, 1994). It is therefore of interest to relate taste responses in the CT and NG with some of these findings from the cortical taste area.

The cortical results gave a large, well-delineated S cluster and N cluster (Plata-Salaman et al. 1993; Scott et al. 1994) and less delineated H and Q clusters (Plata-Salaman et al. 1993, 1995). This agrees better with our findings in CT fibers than with the large Q cluster and low-level response to sweeteners in the NG. The most likely explanation is that when working with an awake monkey the tasteants will mainly stimulate the anterior tongue. Consequently the results of, for example, cluster analyses of the responses in cortical neurons conform better with the results from the CT than from the NG.

Cortical neurons seem to be less specific. Thus the highest mean value for breadth of tuning of CT and NG fibers is 0.54, which is lower than the lowest mean value obtained for cortical taste neurons, 0.59 (Plata-Salaman et al. 1993). This suggests that cortical taste neurons are more generalist than the peripheral ones. Considering their integrative role in taste, this is not unexpected. The important point is that all the way through the taste system a relationship between human taste qualities and neuron identity is maintained in macaques.

Baylis and Rolls (1991) identified an umami group of cortical neurons. Here we obtained as good a response to MSG as to NaCl in the N fibers of the CT (Fig. 5). As a matter of fact, in four fibers MSG elicited the largest response. Our cluster analysis of the fibers in the NG separated a group that predominantly responded to MSG. Two conclusions can be drawn. One is that MSG is a powerful taste stimulus to macaques. This agrees with and supports the results of Baylis and Rolls, who concluded that ‘‘glutamate, which produces umami taste in humans, is approximately as well represented as are the tastes produced by: glucose, NaCl, HCl and QHCl.’’ On the other hand, our cluster analysis did not indicate that MSG was handled as a separate taste quality, which seems to be the conclusion reached by Baylis and Rolls (1991).

**Validity of the macaque model**

How good a model is *M. mulatta* for the study of the human sense of taste? One answer to this question can be obtained by comparing the results here with human psychophysical observations. The parallel is evident between the human taste sensitivity to bitter taste, reported as being predominantly from the back of the tongue, and the large number of QHCl-best fibers in the rhesus NG mediating taste from the back of the tongue. However, this feature is also found in other species (Frank 1991; Hanamori et al. 1988), although this seems not to be the case in all species (e.g., Hård af Segerstad and Hellekant 1989). Similarly, the larger number of salt-best fibers and the more intense responses to sweet in the CT are in agreement with the higher sensitivity to sweet and salt stimuli from the CT tongue area in humans (Collings 1974; Hång 1901).

It is well known that rhesus monkeys have a sweet tooth. We used this in the two-bottle preference tests. As shown in Fig. 13, all the tasteants, which have been described as being sweet to humans, were liked. The low liking for D-phenylalanine and sodium cyclamate parallels observations in humans, who rate them as less attractive than, e.g., sucrose (Schiffman et al. 1979). For evident reasons it is impossible
TABLE 4. Breadth of tuning of CT single fibers

<table>
<thead>
<tr>
<th></th>
<th>NaCl-Best Fibers</th>
<th>HCl-Best Fibers</th>
<th>QHCl-Best Fibers</th>
<th>Sucrose-Best Fibers</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study</td>
<td>0.23</td>
<td>0.45</td>
<td>0.32</td>
<td>0.42</td>
<td>0.36</td>
</tr>
<tr>
<td>Sato et al. (1994)</td>
<td>0.35</td>
<td>0.63</td>
<td>0.37</td>
<td>0.28</td>
<td>0.38</td>
</tr>
</tbody>
</table>

For abbreviations, see Tables 1 and 3.

Further, the human response to acids and QHCl, especially in children (Steiner 1994), parallels that of rhesus monkeys. Our earlier two-bottle preference study (Brouwer et al. 1983) shows that acids are rejected by rhesus monkeys. As in humans, the rejection can be overcome by addition of sucrose or by application of miraculin (Brouwer et al. 1983). QHCl is strongly disliked by rhesus monkeys. The rejection can also be overcome with sweeteners (Hellekant 1980). The parallel with human experiences, especially with children, is evident.

With regard to the possibility of direct comparisons between this study and human taste nerve recordings, there are few recordings from human taste nerves and none from single taste fibers (Diamant et al. 1963, 1972; Oakley 1985; Zotterman 1971). This limits comparisons between nerve responses in humans and macaques.

Comparison with chimpanzee

As mentioned earlier, we are publishing a series of studies in chimpanzees. These show a strong similarity between the sense of taste in chimpanzees and humans (Hellekant and Ninomiya 1991, 1994a,b; Hellekant et al. 1985, 1996, 1997; Ninomiya and Hellekant 1991). This is not unexpected, considering that the chimpanzee is phylogenetically closer to humans than any other species (cf. Begun 1992; Miyamoto et al. 1987; Pilbeam 1984) and shows strong similarities in food choices (cf. Nowak 1991). Thus it seems that a comparison between the characteristics of the CT nerve of chimpanzee and rhesus monkey could yield data applicable to the question on how good a model the rhesus monkey is.

It seems to us that the most important difference is in the way gustmamic acids affect sweet taste. In humans (Bartoshuk et al. 1969) and chimpanzees (Hellekant et al. 1985, 1996, 1997), gymnemic acids abolish sweet taste in general, whereas they have no effects on the taste of sweeteners in macaques (Hellekant et al. 1974). Here we observe five considerably smaller differences between chimpanzee and rhesus monkey.

1) Acids never stimulated S fibers in the chimpanzee; here they elicited some response in S fibers.
2) The sensitivity to denatonium benzoate is higher in the chimpanzee CT, where 0.001 mM elicited a response, compared with the 0.01 and 0.1 mM used here with almost no effect. The monkey seems to share less sensitivity to denatonium benzoate with some other species, e.g., mice (Whitney et al. 1990). However, when a small response occurred it was only observed in Q fiber.
3) Here, we found one group of NaCl-best fibers that did not respond to KCl and whose response to NaCl was generally suppressed by amiloride. In chimpanzee we identified three fiber groups within the N cluster: fibers responding best to NaCl but not to KCl, fibers responding best to both NaCl and KCl, and fibers responding best to MSG (Hellekant et al. 1997). Only the first group shared features with the NaCl-best group in rhesus.
4) The effects of umami compounds (MSG, guanosine 5’-monophosphate) were different. In the chimpanzee these compounds stimulated, in addition to fibers of the M cluster, some sucrose-best fibers. Here they stimulated mostly fibers of the N cluster. This may indicate that to the rhesus monkey the taste of MSG does not carry any sweet qualities.
5) Finally, the CT fibers of rhesus monkey were more broadly tuned than the CT fibers of chimpanzee (mean value of entropy for all fibers: 0.53 vs. 0.3). However, these differences are only minor, not major as when a compound with an intense sweet taste to humans has no taste at all to an animal species (e.g., Glaser et al. 1978).

To summarize, the taste fibers of M. mulatta cluster in both CT and NG according to the human concepts of taste qualities. The finding of a strong representation of QHCl-
best fibers from the back of the tongue, and of NaCl- and sucrose-best fibers from the front of the tongue, although not unique among mammals, corresponds with the human distribution of mostly bitter taste on the back and sweet/salty from the front. The fiber pattern of the CT of the rhesus monkey mirrors that of the chimpanzee and its behavioral response to tastants parallels the psychophysical and electrophysiological observations in humans well enough to support the conclusion that the rhesus monkey, from most points of view, can serve as a relevant animal model of the human sense of taste. We conclude that the sense of taste in macaques is quite similar to that of humans and different from that of commonly used nonprimate species. This conclusion forms the basis for and may in some cases necessitate the use of higher primates as models for the human taste of both “standard” tastants, such as bitter or sweet compounds, and compounds with an enigmatic taste, such as ethanol.

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