Discrimination between the Tastes of Sucrose and Monosodium Glutamate in Rats

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Abstract

Conditioned taste aversion studies have demonstrated that rats conditioned to avoid monosodium glutamate (MSG) with amiloride added to reduce the intensity of the sodium component of MSG taste, will generalize an aversion for MSG to sucrose and vice versa. This suggests that taste transduction for sodium, sucrose and MSG may intersect at some point. Generalization of conditioned taste aversion indicates that two substances share similar taste features, but it does not reveal the extent of their differences. In this study, we tested how well rats can discriminate sucrose and MSG under a variety of conditions. Water-deprived rats were trained on a combination of water reinforcement and shock avoidance to discriminate between MSG and sucrose, both with and without amiloride, and with and without equimolar NaCl in all solutions. In the absence of amiloride, rats reliably distinguished between MSG and sucrose down to 10 mM solutions. However, they could correctly identify solutions only above 50 mM in the presence of amiloride, equimolar sodium chloride, or both. These results suggest that gustatory stimulation by MSG and sucrose interact somewhere in taste transduction, perhaps within taste receptor cells or gustatory afferent pathways.

Introduction

Monosodium glutamate (MSG) is a naturally occurring amino acid that, in small quantities, has long been incorporated into Asian cuisine to enhance flavor (Maga, 1983). It is also a natural constituent of many protein-rich food items such as meats, cheese and some vegetables. Glutamate is said to possess a taste distinct from sweet, sour, salty and bitter. Researchers have recognized glutamate taste for its distinctiveness and termed its unique quality 'umami' (Yamaguchi, 1967). The ability of an organism to detect glutamate is important because its taste would signal the presence of dietary protein. Despite its importance as a food additive and as a substance present naturally in many foods, relatively little is known about the peripheral mechanisms responsible for the taste of MSG.

Ionotropic glutamate receptors have been identified in taste buds, but most evidence to date implicates metabotropic glutamate receptors in umami taste transduction (Brand *et al*., 1991; Faurion, 1991; Bigiani *et al*., 1997; Chaudhari and Roper, 1998; Lin and Kinnamon, 1999; Stapleton *et al*., 1999; Nakashima *et al*., 2001). Chaudhari *et al*. found a Type III metabotropic glutamate receptor (mGluR4) in taste receptor cells in rats and behavioral studies implicated this receptor in umami taste (Chaudhari *et al*., 1996). More recently (Chaudhari *et al*., 2000), they

characterized a novel variant of mGluR4 in rat taste receptor cells. This taste-specific variant has a truncated N-terminus and, when expressed in Chinese hamster ovary (CHO) cells, is stimulated by concentrations of MSG that matched behavioral taste assays. Further, in rats, a conditioned taste aversion (CTA) to MSG generalizes to L-2-amino-4-phosphonobutyrate (L-AP4), a potent agonist for mGluR4 receptors, but does not generalize to agonists for ionotropic glutamate receptors (Chaudhari *et al*., 1996; Nakashima *et al*., 2001). Finally, in taste, MSG is noted for its ability to interact synergistically with ribonucleotide monophosphates such as 5′-inosine monophosphate (IMP). Behavioral studies indicate that L-AP4 displays a similar synergistic relationship with IMP (Kurihara and Kashiwayanagi, 1998; Delay *et al*., 2000). Collectively, these data support the hypothesis that mGluR4 is involved in transducing MSG taste.

However, it is now well-established that if amiloride is mixed with MSG, a CTA to MSG generalizes strongly to sucrose, a prototypical sweet stimulus, and vice versa (Yamamoto *et al*., 1991; Chaudhari *et al*., 1996; Stapleton *et al*., 1999). Amiloride, undetectable to rats at concentrations <100 μM (Markison and Spector, 1995), blocks sodium channels and thereby reduces the intensity of the sodium

component of MSG taste (Heck *et al.*, 1984). The generalization of CTA between MSG and sucrose suggests that MSG may have taste characteristics that are shared with sucrose. This notion has also been advanced by recent reports that indicate the synergistic taste responses elicited by glutamate and IMP and recorded in the chorda tympani nerve are blocked by extracts of *Gymnema sylvestre*, a sucrose antagonist (Yamamoto *et al.*, 1991; Sako and Yamamoto, 1999; Sako *et al.*, 2000). Thus, electrophysiological and behavioral findings suggest that, in addition to activating glutamate receptors, MSG may interact in some manner with afferent mechanisms signaling sucrose taste.

CTA methods are excellent for determining whether two substances taste similar to each other in nonhuman species. That is, the more alike two substances taste, the more an aversion for one substance will generalize to the other taste stimulus. Similarities in taste sensations are generally thought to be the result of activation of the same taste receptors or other afferent signaling processes within the gustatory system. While CTA can reveal whether substances such as MSG and sucrose taste similar, it does not indicate the extent to which perceptual differences exist between two stimuli. Stimulus discrimination methods are better suited to determine perceptual differences, because the subject associates a different response and response consequence with each stimulus. The present experiments used discrimination procedures to ask how well rats can distinguish between the tastes of MSG and sucrose under different conditions in the presence or absence of amiloride. The results support the hypothesis that there is an interaction between sucrose and MSG at some level of taste transduction.

Material and methods

Subjects

Male albino Sprague–Dawley rats were obtained from Harlan Sprague–Dawley (Indianapolis, IN). At the beginning of the experiment all subjects were ~90 days of age and weighed between 250 and 300 g. One week prior to testing, the rats were placed on a 20 h water deprivation schedule that was maintained for the duration of the experiment. Purina Lab chow was provided *ad libitum*. The subjects were housed individually in separate cages in the colony and the lighting was set on a 12 h light–dark cycle, with the lights turned on at 7 a.m. Each rat was tested at the same time each day between 9 a.m. and 1 p.m.

Apparatus

All testing occurred in three computer-controlled Knosys Ltd gustometers (Brosvic and Slotnick, 1986) housed in individual benchtop stations. The system consists of a Plexiglas operant chamber ($25.4 \times 15.9 \times 20.6$ cm) with a fan mounted in the ceiling to reduce olfactory cues. A small circular opening (2.2 cm diameter) in one wall, centered 11.4 cm from the floor of the chamber, permitted access to a drinking spout positioned 3 mm behind the portal. Each taste solution was stored in one of eight 10 ml, unpressurized pipettes. The bottom of the pipettes were at least 15 cm above the drinking spout. Solenoids, located at least 20 cm from the chamber, regulated the flow of solution from each tube through capillary tubing to individual 24 gauge stainless steel tubes within the drinking spout. The tips of these tubes were flush with the end of the spout. Each taste stimulus ('tastant') was presented as a 50 µl aliquot delivered over 0.45 s. Licks were counted when the animal's tongue made contact with the drinking spout and completed a 64 nA contact current through a stainless steel plate on the floor of the chamber. If the animal correctly identified the positively reinforced tastant ('S+'), a 70 µl water reinforcer was delivered to the spout. If the animal failed to identify the tastant associated with shock ('S–'), a 30–35 mV shock was delivered through the lick spout to the animal's tongue. The shock intensity was adjusted for each animal by increasing the intensity until the rat stopped licking when shock was applied. All testing was conducted under 30 ± 5 lx illumination from a white incandescent bulb inside the station in which the operant equipment was housed. A 75 ± 5 dB masking noise (Radio Shack Sleep Machine) was also present during all testing.

Procedures

Experiment 1: detection thresholds

The purpose of the first experiment was to establish detection thresholds for sucrose and MSG. This experiment also tested whether the addition of amiloride would affect stimulus detection.

Five animals were tested with sucrose as the S– and water as the S+ and four animals were tested with MSG as the S– and water as the S+. The concentrations of sucrose and MSG were 0.001, 0.01, 0.1, 1, 2.5, 5, 10, 25, 50 and 100 mM, in deionized water. Detection thresholds for each substance were first determined without amiloride, then with 50 µM amiloride in each solution.

Rats were initially trained to discriminate four S– concentrations (10, 25, 50 and 100 mM) from deionized water until they reached 80% detection rate for each concentration in two consecutive sessions. The water-deprived rats licked on a variable ratio 10 reinforcement schedule to initiate the delivery of the taste stimulus. Once the taste stimulus was delivered, the rat had 2 s to decide if the tastant was an S+ or an S–. When the S+ solution was presented, the rat was required to lick the spout during the last 0.4 s of the decision period to receive a water reinforcer (i.e. correct detection of the S+). When the S– substance was delivered, a correct detection was registered if the rat did not lick during the last 0.4 s of the decision period. Shock was always delivered to the spout for 2 s following the end of the decision period of each S– trial. The animal only experienced shock if it licked the spout during the shock

presentation. A 10 s intertrial interval occurred before the start of the next variable ratio 10. A test session ended after the animal completed 200 trials or an hour had elapsed, whichever occurred first.

During each test session, four of the eight stimulus tubes contained different concentrations of the taste stimulus (S–) and four contained deionized water (S+). Three of the four S– tubes were high concentrations (10–100 mM) and one was a low concentration (0.001–5 mM). The order of stimulus presentations within a session was randomized with a Latin Square design. Different concentrations and orders were tested each day and each concentration was stored in a different 10 ml pipette from day to day to minimize the possibility that a rat can discriminate a tastant on the basis of the location of stimulus delivery within the spout. After the subject had been tested, it was returned to its home cage where, after another hour, it received an additional 2 h of access to water. All rats received at least 14 days training on the discrimination task before data collection began. All data were collected within the next eight sessions.

At the end of the experiment, an additional test session was conducted to determine if any of the rats were able to discriminate between stimulus tubes on the basis of location or some equipment generated cue. All experimental parameters were maintained, except that water was presented from each stimulus tube and S+ and S– assignments were randomized.

Experiment 2: sucrose versus MSG

This experiment tested how well rats could discriminate between sucrose and MSG. This experiment was conducted without amiloride to allow the Na$^+$ component of MSG to contribute fully to the taste of MSG.

Six of the nine rats tested in the threshold experiment (three were withheld from this experiment for health reasons) and an additional, naive seventh rat were the subjects for this experiment. All subjects from the threshold studies were tested with their respective S– tastants, but now the opposite tastant became the S+ stimulus instead of water. For example, if the subject had been trained with sucrose as the S–, then MSG became the S+. Sucrose was the S+ for animals originally trained with MSG as the S–. Three rats were tested with sucrose as the S– and four were tested with MSG as the S–.

The animals were tested in the same apparatus and under the same general protocol for the discrimination paradigm as stated in experiment 1 with the following exceptions. Concentrations of 5, 10, 25, 50, 100, 150, 200 and 300 mM sucrose and MSG were tested. Within a given session, three concentrations of S– solutions and three matched S+ solutions were presented to minimize intensity as a cue. These three included one low (5–25 mM), one intermediate (50–100 mM) and one high (150–300 mM) concentration randomly selected for each session. In addition, two of the delivery tubes contained water to use as the reinforcer. The order of presentation was determined with a Latin square and a different sequence was used each day. To help maintain licking even when the discrimination was difficult, one out of every four stimulus presentations was water treated as an S+. Every rat received at least 14 days training on the discrimination task before data collection began and all data were collected within the next 10 sessions. All other testing procedures were identical with those established during threshold experiments, including the water-only test the day after the last session.

Experiment 3: sucrose versus MSG with amiloride

This discrimination experiment repeated the procedures of experiment 2, but with 50 μM amiloride in each taste solution. The nine rats originally tested in the threshold experiments were subjects in this experiment. As in experiment 2, all subjects were tested with their original tastants as the S– and with the opposite tastant as the S+. Each solution, including water reinforcers, contained 50 μM amiloride. All other testing procedures were identical with those used in experiment 2. After 14 days of training, all data were collected over the next eight sessions.

Experiment 4: MSG versus sucrose with equimolar NaCl.

The results of the two previous experiments (see below) indicated that the sodium component of MSG may contribute to the ability of the rats to discriminate between sucrose and MSG. Moreover, others have reported that sweet substances can interact with sodium transduction in canine lingual epithelium (Mierson *et al*., 1988; Simon *et al*., 1989). Experiment 4 was conducted to determine if the addition of equimolar sodium chloride to sucrose might alter the discriminability of sucrose from MSG.

All 10 rats were tested in the same apparatus and under the same discrimination paradigm as stated previously. All concentrations and procedures conducted during experiment 2 were maintained for this experiment, except that NaCl was added to each sucrose solution to match the sodium component of the corresponding concentration of MSG. No amiloride was present in this experiment.

Experiment 5: MSG versus sucrose with equimolar NaCl and amiloride

The nine animals tested in the threshold experiments were also tested with procedures identical to those in experiment 4. As in experiment 4, an equimolar concentration of NaCl was added to each sucrose solution to correspond to the matched concentration of MSG and, in addition, 50 μM amiloride was added to all solutions.

Results

For each session, the percentage correct detection was calculated for each stimulus concentration. Data for a session were included only if the animal detected the S+ stimuli and the highest concentration of the S– in at least 80% of the respective trials. Each rat was trained until the detection rate

of each concentration had reached an asymptote. Data for every session in which the rat's performance met criteria, and no less than two sessions, were averaged to obtain a detection score for each stimulus concentration. Analysis of variance (ANOVA) procedures were performed on the data for each experiment. Simple effects tests and Newman–Keuls *post hoc* tests were used where appropriate.

Experiment 1: detection thresholds

Data for all eight sessions were included in the data analyses. Detection thresholds, defined as the concentration detected in 50% of the trials, for sucrose with or without amiloride were between 2.5 and 4 mM for all subjects (Figure 1). The ANOVA revealed a significant effect due to concentration [$F(9,36) = 184.5$, $P < 0.001$], but no effect for amiloride and no interaction between amiloride and concentration. Thus, the addition of amiloride does not appear to alter stimulus detection for sucrose.

For MSG, the detection thresholds with and without amiloride were between 1 and 2.5 mM for all rats (Figure 2).
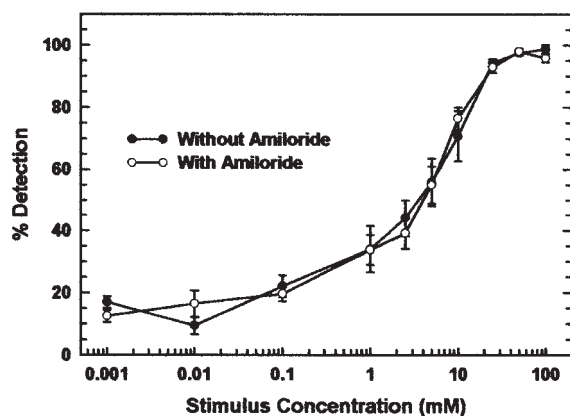

Figure 1 Mean (± SEM) correct detection of sucrose with and without the presence of 50 μM amiloride. Thresholds for all rats were between 2 and 4.5 mM sucrose under both conditions of amiloride.
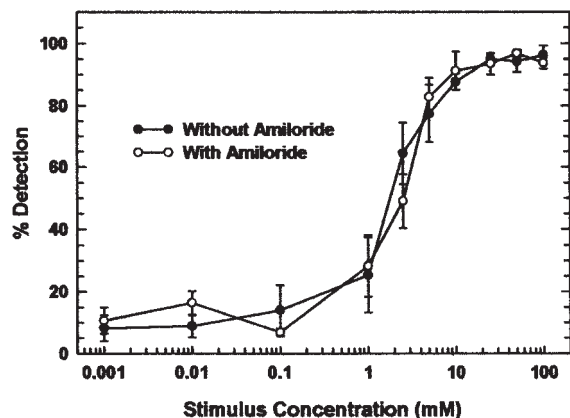
There was a significant effect for concentration [$F(9,27) = 132.7$, $P < 0.001$], but no effects of amiloride. Thus, amiloride had no effect on the detection thresholds of either MSG or sucrose. These data also show that the threshold for MSG is similar to that for sucrose.

Experiment 2: sucrose versus MSG

Data from eight of the ten sessions were included in the analysis. Equipment malfunction forced the elimination of data from one session and the session immediately following. Initial analyses did not reveal group differences related to the specific substance serving as the S+ or S– solutions. Therefore, the data for all rats were combined and organized to compare detection of the S– stimulus with that of the S+ (stimulus valence factor). A two-way, within-subject ANOVA examining stimulus valence (2) and concentration (8) revealed significant effects for concentration [$F(7,42) = 16.64$, $P < 0.001$] and an interaction between stimulus valence and concentration [$F(7,42) = 4.46$, $P < 0.001$]. Simple effects tests showed that the detection of the S+ was significantly greater than the detection of the S– at 10 mM [$F(1,6) = 10.27$, $P < 0.025$] and 5 mM [$F(1,6) = 3.90$, $P < 0.05$; Figure 3]. In brief, at 5 and 10 mM concentrations, rats had some difficulty distinguishing MSG from sucrose.

Another way to determine how difficult the discrimination task was at each concentration of tastant is to analyse error scores. Error scores are the average of the percentage error for detecting the S+ and S– at each concentration:

$$\text{error score} = ((100 - \text{percentage detection of S+}) + (100 - \text{percentage detection of S–}))/2.$$

A within-subject ANOVA detected a significant difference in errors related to concentration, [$F(7,42) = 16.64$, $P < 0.001$]. *Post hoc* testing showed that the error rate remained
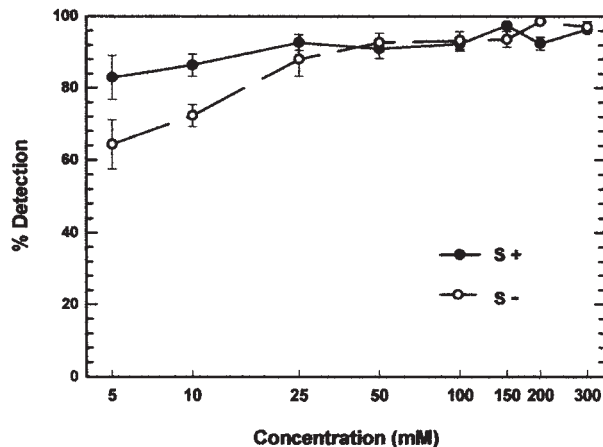

Figure 2 Mean (± SEM) correct detection of MSG with and without the presence of 50 μM amiloride. Thresholds for all rats were between 1 and 2.5 mM MSG under both conditions of amiloride.

Figure 3 Mean (± SEM) correct detection of the S+ and S– taste stimuli when rats had to discriminate between sucrose and MSG (experiment 2).

<20% at concentrations above 10 mM (Figure 4, filled circles). Error rates increased significantly at 10 and 5 mM ($P < 0.01$). These data indicate that rats had some difficulty discriminating MSG from sucrose at low but suprathreshold concentrations (5–10 mM) for detection of both tastants. At concentrations of 25 mM and above, rats readily distinguish sucrose from MSG.

Experiment 3: sucrose versus MSG with amiloride

All data for the eight sessions were included in these analyses. The ANOVA of the discrimination data collected with 50 µM amiloride present in each solution also found significant effects due to stimulus valence [$F_{(1,8)} = 90.08$, $P < 0.001$], concentration [$F_{(7,56)} = 18.22$, $P < 0.001$] and valence by concentration [$F_{(7,56)} = 20.39$, $P < 0.001$; Figure 5]. In contrast to the data without amiloride, simple effects tests found the S+ was detected (mean ± SEM = 91.7 ±

2.1%) significantly more ($P < 0.005$) than the S– (73.4 ± 5.3%) at 100 mM ($P < 0.005$). This difference increased significantly ($P < 0.001$) as the concentration decreased. These data indicate that, in the presence of amiloride, rats had difficulty in discriminating MSG from sucrose up to 100 mM, well above detection threshold.

As with experiment 2, the analysis of the error scores in experiment 3 showed a significant increase in task difficulty related to concentration [$F_{(7,56)} = 18.22$, $P < 0.001$]. In this experiment, however, error rates increased significantly at 50 mM ($P < 0.01$) and continued to increase significantly at each lower concentration (Figure 4, open circles). Importantly, these analyses show that it was much more difficult for rats to discriminate sucrose from MSG when amiloride was present.

Experiment 4: MSG verses sucrose with equimolar NaCl

Experiments 2 and 3 suggested that the taste of Na^+ may be an important cue that rats use to distinguish sucrose from MSG, especially at lower concentrations of these tastants. In experiment 4, NaCl was added to each concentration of sucrose to match the concentration of sodium in MSG solutions to reduce differences in Na^+ taste between the taste solutions. This tested whether the presence of sodium influenced the ability of rats to discriminate MSG from sucrose (Figure 6). A two-way, within-subject ANOVA indicated that there were significant effects for stimulus valence [$F_{(1,9)} = 101.32$, $P < 0.001$], concentration [$F_{(7,63)} = 44.69$, $P < 0.001$] and the interaction between the two [$F_{(7,63)} = 31.86$, $P < 0.001$]. Simple effects tests indicated that identification of the S+ and S– was comparable for concentrations of 100 mM and higher. At 50 mM, however, detection rates (Mean ± SEM = 71.6 ± 4.8%) for the S– were significantly less than those (92.7 ± 2.0%) for the S+ [$F_{(1,9)} = 17.8$, $P < 0.005$] and this disparity in the discrimination of S+ and S– taste stimuli increased as the concentration
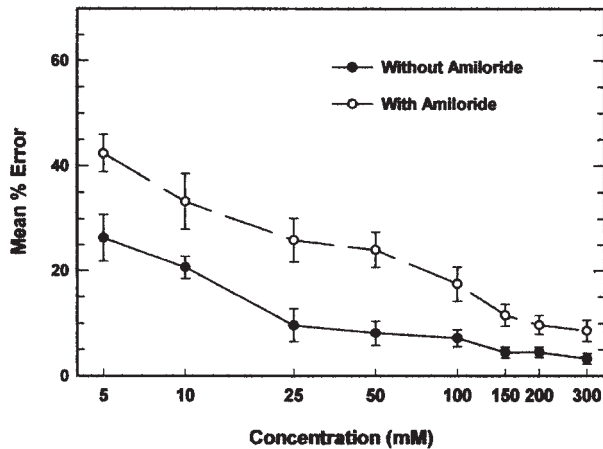

Figure 4 Mean (± SEM) errors made by rats when trying to discriminate between MSG and sucrose without (closed circles, experiment 2) and with (open circles, experiment 3) 50 µM amiloride in all solutions.
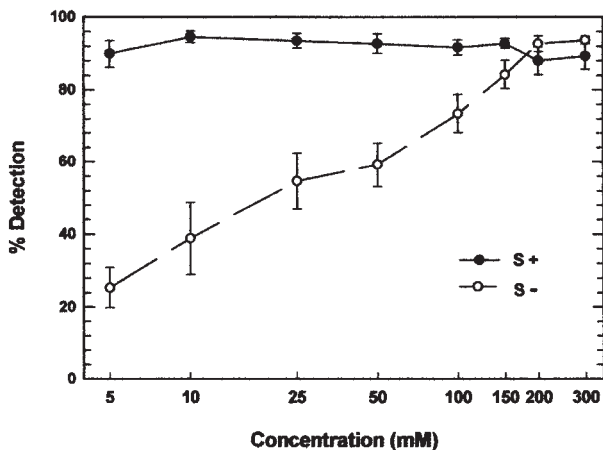

Figure 5 Mean (± SEM) correct detection of the S+ and S– taste stimuli when rats had to discriminate between sucrose and MSG with 50 µM amiloride added to all solutions (experiment 3).
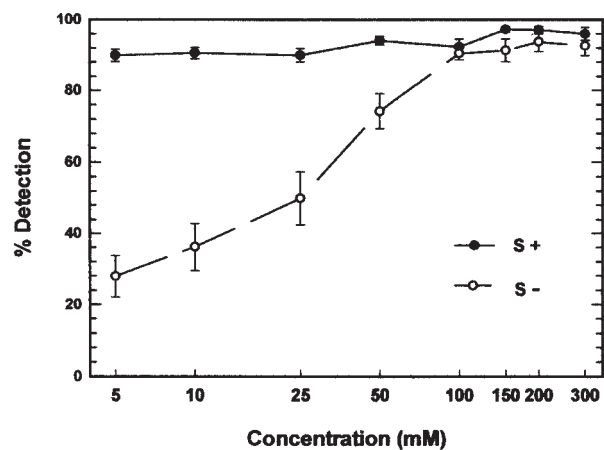

Figure 6 Mean (± SEM) correct detection of the S+ and S– taste stimuli when rats had to discriminate between MSG and sucrose with equimolar NaCl added to each concentration of sucrose (experiment 4).

decreased ($P < 0.001$ in all cases). These results indicate that the addition of sodium chloride to sucrose impaired the ability of rats to distinguish this mixture from MSG. This also can be seen in the analysis of error scores, which revealed a significant increase in errors [$F_{(7,63)} = 44.70$, $P < 0.001$] at each concentration below 100 mM (Figure 7, closed circles).

Experiment 5: MSG versus sucrose with equimolar NaCl and amiloride

As a final test of the effect of sodium ions on the ability of rats to discriminate MSG from sucrose, amiloride was added to all solutions of experiment 4 (Figure 8). The analysis of these data identified significant effects of stimulus valence [$F_{(1,8)} = 43.78$, $P < 0.001$], concentration [$F_{(7,56)} = 16.83$, $P < 0.001$] and the interaction between the two variables [$F_{(7,56)} = 18.64$, $P < 0.001$]. Simple effects tests revealed that the detection rates of the S+ were significantly better than those for the S– at all concentrations of 50 mM and below ($P < 0.005$). Thus, as might be expected, blocking amiloride-sensitive Na channels reduced the ability of rats to discriminate sucrose from MSG, whether NaCl was added to sucrose (Figure 8) or not (Figure 5).

This finding is also seen when analyzing the error rates. The ANOVA of the error scores uncovered a significant effect for concentration [$F_{(7,56)} = 16.83$, $P < 0.001$]. *Post hoc* tests ($P < 0.05$) indicate that, in agreement with the detection data, the error rate for discriminating between the taste solutions increased as the tastant concentrations decreased (Figure 7, open circles).
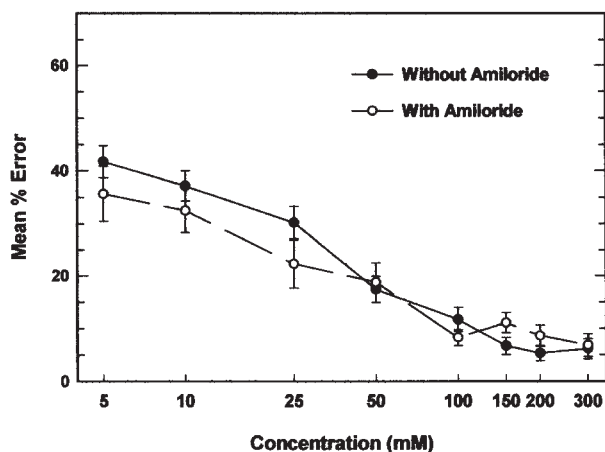
Comparisons across experiments

The separate results of experiments 2–5 imply that the ability of rats to discriminate MSG from sucrose in solutions above 10 mM is facilitated by the presence of sodium ions in MSG. To test this hypothesis more directly, the detection data for the six subjects tested in all four discrimination experiments were compared. Data for each concentration were analyzed with separate within-subject ANOVAs to detect any effects resulting from stimulus valence (2) and experiments (4). The interaction between these two variables was significant in each of the analyses for 5, 10, 25 and 50 mM [$F_{(3,15)} \geq 3.98$ in all cases; $P < 0.05$ or smaller]. In each case, *post hoc* tests showed that detection of the S– was significantly better in experiment 2 than in the rest of the experiments. Thus, reducing the intensity of the sodium component of MSG with amiloride (experiment 3), adding NaCl to sucrose to make the sodium component equivalent to that of MSG (experiment 4), or the combination of both manipulations (experiment 5) appeared to interfere with accurate discrimination between sucrose and MSG seen in experiment 2 at concentrations <100 mM.

Figure 7   Mean (± SEM) errors made by rats at each concentration of MSG and sucrose/NaCl in the absence (filled circles, experiment 4) and presence (open circles, experiment 5) of 50 µM amiloride. Equimolar NaCl was added to each concentration of sucrose in these experiments.
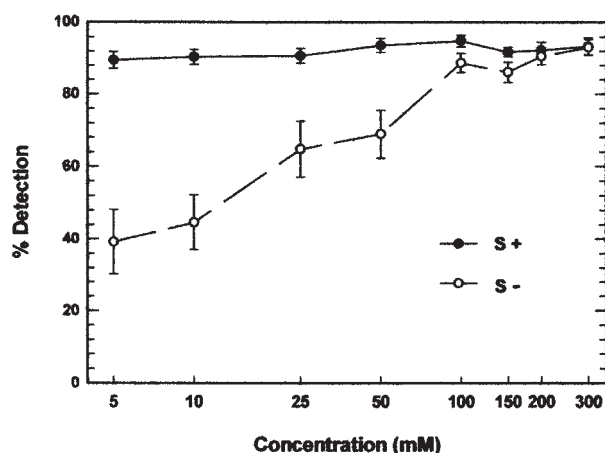

Figure 8   Mean (± SEM) correct detection of the S+ and S– taste stimuli when rats had to discriminate between MSG and sucrose with equimolar NaCl added to each concentration of sucrose and with 50 µM amiloride added to all solutions (experiment 5).

Discussion

This study measured the detection thresholds for sucrose and MSG in rats and tested the ability of rats to discriminate between these taste stimuli under a variety of conditions. The findings verify and extend previous results from conditioned taste aversion studies, indicating that there are marked taste similarities between sucrose and MSG. Importantly, when the sodium component of MSG is reduced as a potential cue, rats have difficulty discriminating MSG from sucrose at low to moderate concentrations of the two taste stimuli.

Rats displayed a detection threshold for sucrose, defined as the concentration detectable on 50% of the trials, at ~2.5–4 mM. The threshold for MSG was ~1–2.5 mM. This agrees well with other studies that report detection

thresholds of sucrose in rats (Campbell, 1958; Noma *et al.*, 1971; Brosvic and Slotnick, 1986; Thaw and Smith, 1992; Thaw, 1996) and estimated thresholds from studies of MSG (Hiji, 1967; Chaudhari *et al.*, 1996; Stapleton *et al.*, 1999). Moreover, thresholds of rats to detect sucrose or MSG solutions were not affected by the presence of 50 µM amiloride, a sodium channel blocker. Since amiloride raises the detection threshold for NaCl from ~5 to ~40 mM in rats (Geran and Spector, 2000) and altered MSG discrimination performance in experiments 3 and 5, it clearly affected Na^+ taste in the concentration range used in the present experiments. That amiloride did not affect the taste thresholds for MSG and sucrose in this study is of importance, especially for MSG, because it indicates that sodium taste is not necessary for the detection of these compounds. The implication for MSG is that rats may be detecting the anion, glutamate, at threshold concentrations of the tastant. On the other hand, sodium ions appear to contribute to the perception or taste quality of MSG. This is indicated by the influence of amiloride on the ability of rats to discriminate the tastant at all concentrations of MSG (e.g. Figure 4).

Accurate discrimination between two tastants is based upon the identification of salient features that are not shared by the two stimuli; the fewer differences in taste qualities, the more difficult the discrimination between the substances becomes. In this study, the experimental procedures were designed to keep the rat responding on task, even when the task became very difficult. That is, when discrimination between two stimuli became difficult, rats generally continued to respond well to the presentation of the S+, while showing a decrease in avoidance responding after the presentation of the S–, even though the animal will readily avoid the shock if it can identify the S–. It is possible that the intensities of the sucrose stimuli could have been perceived as different from the intensities of MSG within a session and served as a cue that would make the discrimination easier. This seems unlikely, though, since thresholds for these substances were similar and the concentrations of sucrose and MSG were matched within each session. But if intensity was a cue in these experiments, then the rats would find it easier to discriminate between the S+ and S– and thus qualitative differences between the tastes of MSG and sucrose would be even less than was observed at low to moderate concentrations in experiments 3–5.

The poorer performance at 5 and 10 mM in experiment 2 probably represents performance within the concentration range between detection and recognition thresholds of the two tastants. Between 10 and 100 mM, the presence of amiloride made it difficult for rats to distinguish between tastants. The experiments reported here extend and verify results from earlier CTA studies in which rats with a CTA to either MSG with amiloride or to sucrose showed a comparable degree of suppression to the same concentration of the opposite stimulus (Yamamoto *et al.*, 1991; Stapleton *et al.*, 1999). Generalization of CTA from one taste stimulus

to a second stimulus is directly related to the degree to which the two stimuli share common perceptual characteristics (Spector and Grill, 1988). Together, the results of previous CTA experiments and the present study indicate that rats perceive the taste of sucrose and MSG mixed with amiloride as quite similar. Moreover, these results indicate that to rats, the sugar, sucrose and the anion, glutamate, are difficult to distinguish under many conditions.

These experiments are not designed to study the mechanisms underlying the taste similarities of sucrose and MSG. We can only speculate as to why rats have difficulties making this taste discrimination. One might surmise that sucrose and the glutamate anion may share transduction mechanisms or information transmission at some point in the signaling pathway. For instance, whole nerve recordings of mixtures of MSG and IMP are suppressed in the presence of extracts of *Gymnema sylvestre*, a sucrose antagonist (Yamamoto *et al.*, 1991; Sako and Yamamoto, 1999). Thus, it is possible that glutamate and sucrose interact at the level of the apical membrane receptors of taste cells. Indeed, Sako and Yamamoto suggested that glutamate activates more than one type of taste receptor (Sako and Yamamoto, 1999). If this is the case, one explanation might be that, at lower concentrations, glutamate may activate receptors that also respond to sucrose, thus generating afferent signals for glutamate that are difficult to differentiate from sucrose. At the higher concentrations in experiment 3, it is possible that the improved discrimination performance resulted from an increase in the impact of the sodium component of MSG, especially at concentrations above the shift in threshold for NaCl induced by amiloride. However, the addition of NaCl to sucrose (experiment 4) to neutralize the uniqueness of the sodium component of MSG did not alter the discriminability of the two substances any more than the addition of amiloride to the solution to reduce the effects of sodium taste (experiment 3). Another possible explanation for the better discrimination at the higher concentrations is that a second receptor type, such as the taste-mGluR4 receptor (Chaudhari *et al.*, 2000), may begin to mask or contribute to the input of the first system. It is also possible that sucrose and MSG interact downstream of membrane receptor activation. For example, afferent signaling for these tastants may depend upon the net change of cAMP within the taste receptor cell. It also may be that the afferent signals from the taste receptor cells may interact on neurons some point within the afferent gustatory pathways in the brain stem or the cortex. However, this study cannot elucidate how this interaction might occur.

In summary, detection thresholds for sucrose and MSG are similar to each other and are unaffected by the presence of amiloride. Rats accurately discriminated between sucrose and MSG at 10 mM and greater when the substances were mixed only with deionized water, but can only accurately identify solutions >50 mM in the presence of amiloride, equimolar sodium ion concentrations, or both. These results

suggest that afferent processes activated by sucrose and MSG may interact within taste receptor cells or gustatory afferent pathways.

Acknowledgements

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