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Self-Selection of Food and Water Flavored with Monosodium Glutamate

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The recognition and acceptance of food mainly depends on its chemostimulatory characteristics. Therefore, taste and flavor perception are important in food discrimination (2,5,24). The flavor can be said to motivate ingestion and may serve as a protector against the consumption of foods of questionable quality. Experimental evidence suggests that the flavor characteristic of a nutrient may be paired with its nutritive value (13,36,49), helping the animal to regulate his diet selection according to physiological needs (18,35,48,56).

Taste and oral stimulation can also reflexively initiate certain digestive and metabolic processes even before food reaches the stomach (39,42,44). This includes the stimulation of gastric acid secretion (16,47), release of gastrin (43,47), increase in pancreatic exocrine output (3,38,40,44,53), and mobilization of insulin from the endocrine pancreas (20,60).

Monosodium glutamate (MSG) is widely used as a flavor in cooking, presumably as a taste stimulant and a flavor enhancer. Possible mechanisms for the ability of MSG to stimulate taste receptors have recently been discussed by Cagan (6). L-Glutamic acid, the free acid of MSG, is a constituent of protein, and also occurs as a free amino acid (0.01 to 0.2%) in a variety of vegetables, meat, and seafood (17,31). Milk from lactating human females contains 0.007 to 0.02% free L-glutamate (59). It has been suggested by Fagerson (10) that only the form of glutamate with both carboxyl groups ionized is active as a taste stimulant in humans. Taste thresholds of MSG for humans are in millimolar concentrations (30). Electrophysiological measurements in rats showed that MSG is effective in stimulating the chorda tympani nerve (54). The taste of some other amino acids has been referred to as an MSG-like taste (25). A favorable effect of MSG as a flavor enhancer for meat, poultry, seafood, and vegetables has been reported (15,58). A synergistic effect between MSG and 5′-ribonucleotides in enhancing food flavor has been demonstrated (27).

Relatively little consideration has been given to MSG preference in animals,

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although animal models are commonly employed in the analysis of food intake mechanisms. Scott and Quint (55) showed that 1% MSG did not influence the diet preference of rats. Hiji and Sato (19) demonstrated that female rats select 5×10^{-2} to 1.5×10^{-1} M MSG-flavored water over water in two-choice, long-term preference tests. This preference for MSG solutions was observed only in a situation where solutions containing MSG were offered in an ascending concentration sequence. No such preference was shown in the descending concentration sequence. Weanling calves, beginning at 3 weeks of age, selected more of a 0.2% MSG-flavored diet than a nonflavored diet (61). The taste responses of pygmy goats to sucrose and quinine hydrochloride solutions were moderated by adding 5, 50, 500 ppm MSG (32).

In this chapter we will consider both the sensory and possible postingestional properties of MSG in an attempt to understand the consummatory responses to MSG by rats. Experimental data of a recent study by Ohara and Naim (41) will be discussed in some detail.

FACTORS AFFECTING THE SELECTION OF NUTRIENTS

The control of the ingestion of nutrients is known to be subject to the influences of taste, smell, and texture, as well as postingestional factors (18,23,33,48,56). Postingestional factors refer to those effects occurring after materials are ingested, including gastrointestinal tract processes or postabsorptive metabolic effects (9,22,33).

To ensure that any ingested food will not be poisonous, the animal uses at least two mechanisms. First, there are learning processes that make use of flavor as a cue, such that any postingestional consequences can be associated with food previously eaten. The rat accepts novel food slowly. This usually assures him of enough time to make a quality assessment. This type of learning has been termed "conditioned taste aversion" (13,14). Second, as a result of innate response, when an animal is given a choice of two foods, one of which is adulterated with an aversive taste stimulus, the animal will prefer the unadulterated (more "palatable") food. Many aversive taste stimuli are also poisons. This type of protective mechanism (i.e., simple rejection of adulterated food without apparent learning) might thus have had survival value in the phylogenetic history of vertebrates and, therefore, was genetically retained. Innate, learned, and postingestional responses can therefore influence the preference-aversion curves derived from preference tests.

It appears that, in a choice situation, animals are often able to select nutrients according to their physiological needs (18,48,56). This is specially true for rats. The immediate recognition of sodium by sodium-deficient rats has been argued to be an innate response via taste mechanisms (for review, see ref. 36). More common are the mechanisms wherein the animal associates the sensory quality of the food with postingestional consequences. For example, a 24-hr preference test indicated that glucose is preferred over sucrose (50), whereas during a brief exposure (i.e., 1 hr),

sucrose is preferred over glucose (57). Harris et al. (18), and later Scott and Verney (56), reported that, when given several choices, rats deficient in the B vitamins were able to select the food containing these vitamins. Figure 1 illustrates a recent study (37) in which rats were given a choice between two diets differing not only in flavor, but also in nutritional potential (46). One diet contained defatted raw soybeans as a protein source with the addition of 0.35% (w/w) sodium saccharin (appealing taste). The other diet contained defatted heated soybeans with the addition of aversive stimulus of either 2.0% (w/w) sucrose octaacetate or 0.02% quinine sulfate. Raw soybeans have a lower nutritive value than the cooked soybeans because the raw contain digestive enzyme inhibitors and other undesirable physiological factors (4,28,29,46). Given a choice between these two diets, the rats initially preferred the diet with the better taste (bad nutrition). However, after 6 to 7 days, the rats changed their preference to the diet with the "better nutrition," even though it contained sucrose octaacetate (Fig. 1A). This may be explained by assuming that postingestional factors eventually influenced the animals to choose the diet offering better nutrition. If so, the rats associated the appealing taste with "bad nutrition" and the aversive taste with "good nutrition." When quinine sulfate was substituted for sucrose octaacetate in the above regimen (Fig. 1B), this change in preference was not seen. This might be explained by suggesting that no sensory habituation

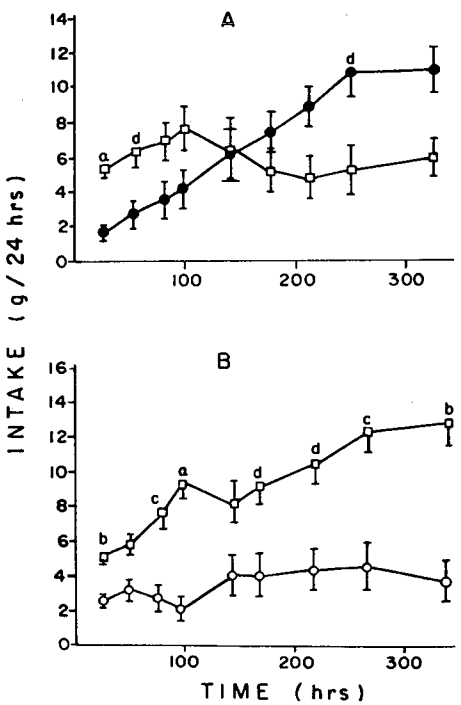

FIG. 1. Preference tests for diets containing unground raw soybean flakes (RS) mixed with an appealing taste stimulus vs. diets containing heated soybean meal (HS) mixed with an aversive taste stimulus. **A:** HS + 2.0% (w/w) sucrose octaacetate (●) vs. RS + 0.35% sodium saccharin (□). **B:** HS + 0.02% quinine sulfate (○) vs. RS + 0.35% sodium saccharin (□). Values are average food intake in grams ± SEM of 12 to 14 rats [$a = p < 0.001$, $b = p < 0.01$, $c = p < 0.02$, $d = p < 0.05$]. Diets were present at all times in the cages. Position of the diet cups was alternated daily. Water was available at all times. (From Naim, et al., ref. 37.)

occurred to the aversive taste of quinine. Alternatively, quinine might have produced postingestional information, e.g., pharmacological effects (52), alerting the rats that the combination of heated soybeans with quinine is less nutritious or, perhaps, even harmful.

Preference tests are often used for making qualitative sensory judgements on the properties of a specific flavor. The brief-exposure experiments, where the taste stimuli are available for only a few minutes, are considered to be more valid measurements of taste, with little confounding by postingestional factors (45).

SELF-SELECTION OF MSG-FLAVORED WATER

As mentioned above, comparisons between the brief-exposure preference tests and long-term exposure tests can often separate sensory effects from postingestional ones. In our study (41) the brief-exposure, two-choice preference test was carried out according to the method described by Cagan and Maller (7). Forty-two rats (200 to 250 g) were individually housed. Animals were divided into three equal groups. After 8 hr of water deprivation, rats were subjected to a preference test between a single concentration of MSG in water versus water for a period of 10 min. Rats were tested three times during the week on alternate days. Each group of rats was subjected sequentially from lower to higher concentrations of MSG in the following percentages:

Group 1: 0.005, 0.05, 0.5, 5.0, 50.0 (2.7×10^{-5} to 2.7 M).
Group 2: 0.001, 0.02, 0.1, 1.0, 8.0, 16.0 (5.3×10^{-5} to 8.6×10^{-1} M).
Group 3: 0.005, 0.25, 3.0, 12.0 (2.7×10^{-4} to 6.4×10^{-1} M).

In long-term preference tests, 126 weanling rats (40 to 50 g) were used. Rats were divided into nine groups. Each group was subjected to a two-choice preference test between a single concentration of MSG in water versus water for a period of 14 days. During this period, the rats were maintained *ad lib.* on rat chow. The following percentage concentrations of MSG in water were used: 0.005, 0.02, 0.05, 0.1, 0.25, 0.5, 1.0, 3.0, and 5.0 (2.7×10^{-4} to 2.7×10^{-1} M).

Figures 2 and 3 indicate that rats show a strong preference-aversion response to the taste of aqueous solutions containing MSG, in both short- and long-term testing. These results are qualitatively compatible with electrophysiological measurements of the chorda tympani nerve in rats (54). The results of long-term tests using male rats are similar quantitatively to those obtained by Hiji and Sato (19) with female rats.

Positive responses to MSG solutions were observed when MSG served as a single taste stimulus in deionized water, suggesting that under these circumstances MSG was a taste stimulant rather than a taste enhancer (15). The Na^+ alone cannot simply account for the sensory response for MSG (1). In a different experiment (41), rats

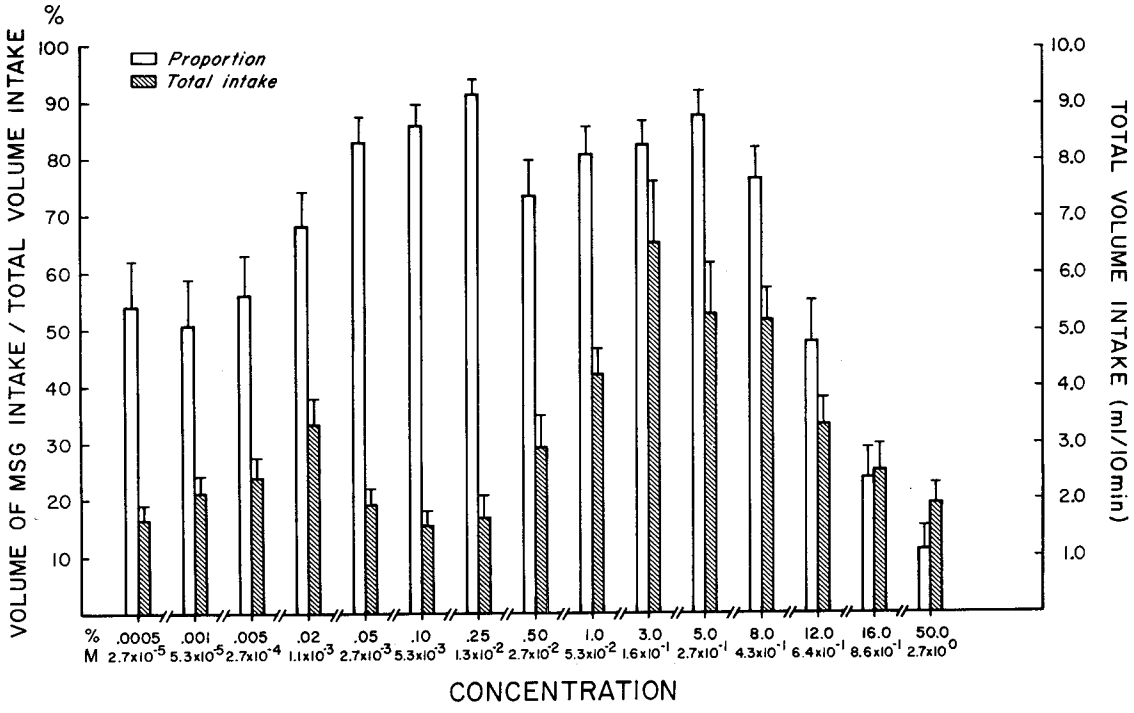

FIG. 2. Proportional intake of MSG-flavored water when paired with plain water, and total volume intake as a function of MSG concentration in brief-exposure tests. Values are the mean ± SEM of 13 rats per group. (From Ohara and Naim, ref. 41.)

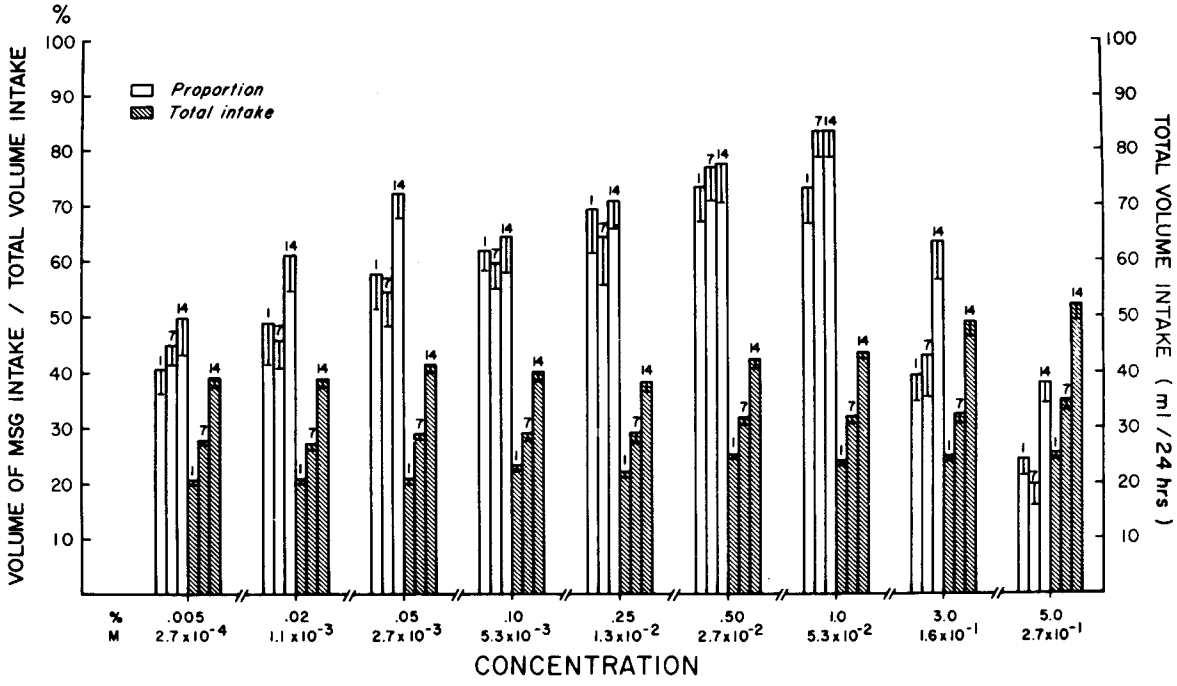

FIG. 3. Proportional intake of MSG-flavored water when paired with plain water, and total volume intake as a function of MSG concentration on days 1, 7, and 14 of long-term test. (From Ohara and Naim, ref. 41.)

could detect the difference between MSG, monosodium aspertate, sodium acetate, and sodium glutamate in situations where the Na^+ content and pH were kept equal.

As shown by the short-term tests (Fig. 2), the preference for solutions containing MSG occurred for a wide range of the offered concentrations. For brief-exposure experiments, there was a significant stimulation of the total liquid intake (MSG solution and water) over the range between 1 and 8% MSG as compared to lower concentration (0.05 to 1%). This suggests that solutions containing 1 to 8% MSG were most preferred in brief-exposure experiments. A solution containing 16% MSG was the minimum concentration required to cause a significant reduction of intake compared to water.

In long-term tests (Fig. 3), the total intake of liquid from both choices was slightly increased at high concentrations of MSG. This might be due to the necessity of diluting the concentrated solutions, since the proportional intake (intake of MSG solution as percentage of total intake) of solutions containing MSG was significantly reduced in that range. The proportion data suggested that in long-term tests solutions of 0.1 to 1% MSG are consistently preferred over water. A solution that contained 5% MSG was consistently less preferred than water.

Comparisons of the proportion data between brief-exposure and long-term testing suggest that solutions of 3 to 5% MSG might have produced, in long-term tests, postingestional feedback that reduced the amount of MSG intake. In short-term testing, these concentrations were still highly preferred. However, any analysis of the postingestional effects that might be caused by the ingestion of MSG requires a determination of the absolute amounts consumed. A relationship that expresses the ingestion of milliliters of taste stimulus solution versus milliliters of deionized water does not always give meaningful information. Therefore, the number of moles of MSG ingested as a function of the molar concentration of MSG in the solutions offered was calculated. Figure 4 shows that for brief exposure experiments the total number of moles of MSG consumed increased as the concentration of MSG solution rose, peaking at a concentration of about 3 to 5×10^{-1} M MSG. The total number of moles consumed was reduced when higher concentrations of MSG were presented. In the long-term experiments, the total number of moles of MSG consumed (Fig. 5) increased as a function of increasing MSG concentration. This includes the solution of 5% (2.7×10^{-1} M) MSG, which was less preferred than water in terms of milliliters ingested (Fig. 3).

Measurements of MSG intake were taken at concentrations that ranged 10^5-fold for brief-exposure tests and 10^3-fold for long-term tests. The data indicate that the total moles of MSG ingested peaked for both brief and long exposure at a similar concentration of MSG (Figs. 4 and 5). This suggests that the maximum intake of moles of MSG occurs at similar concentrations of MSG, whether or not the experiments were conducted over a 10-min period or over a 2-week period. It is therefore concluded that rats did not change their preference for ingestion of moles of MSG when exposed to long-term preference tests as compared to the short-term.

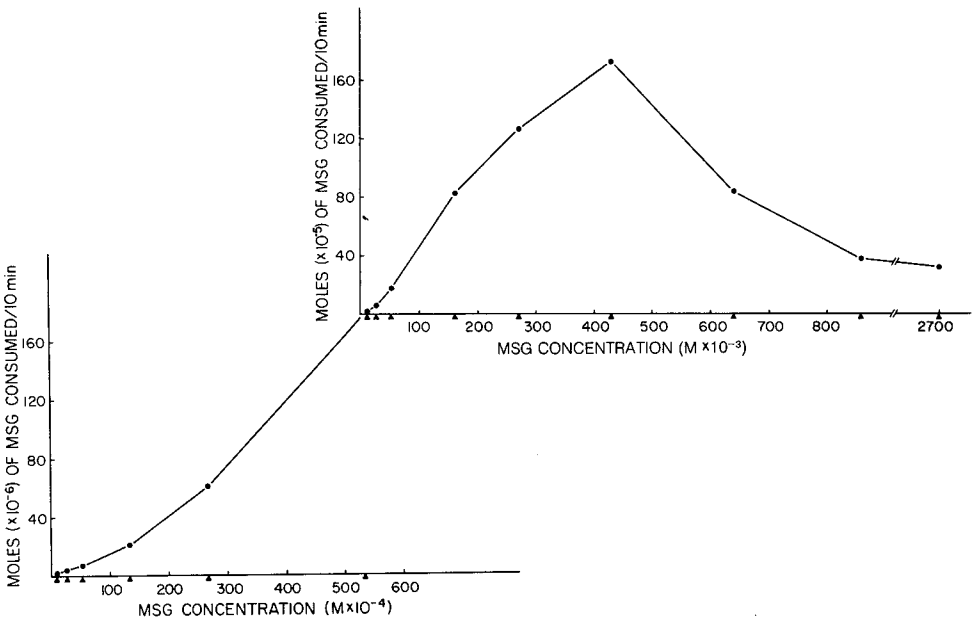

FIG. 4. The intake of moles of MSG as a function of MSG concentration in the solution offered during brief-exposure tests. Values are the mean of 13 rats per group. (From Ohara and Naim, ref. 41.)

This result thus rules out postingestional effects in long-term tests with solutions containing up to 5% MSG. The curve shape suggests sensory response (26).

At low concentrations of offered MSG, the curve is ascending linearly, whereas higher concentrations bring about the saturation of taste receptors (Figs. 4 and 5). In the very high MSG concentrations (tested only for brief exposure), the total moles of MSG consumed is significantly reduced. This cannot be explained by viscosity (texture) changes when the solutions became very concentrated, since the measured viscosity value of solutions containing 50% MSG (2.7 M) was 5.5 centistokes lower than those values necessary for preference by rats (C. M. Christensen, unpublished observation).

SELF-SELECTION OF MSG-FLAVORED DIET

Weanling rats were divided into two groups of 70 each. Each group was subdivided into five subgroups. Rats were given a two-choice preference test for a period of 7 days between a casein-based diet and a single concentration of MSG in the same diet. For one group the casein diet contained 9% protein, while for the second group it contained 18%. Each subgroup received a single concentration of MSG in their casein diet as a choice along with the diet without MSG. The following diet concentrations of MSG were used: 0.1, 0.5, 1.0, 3.0, and 7.0%.

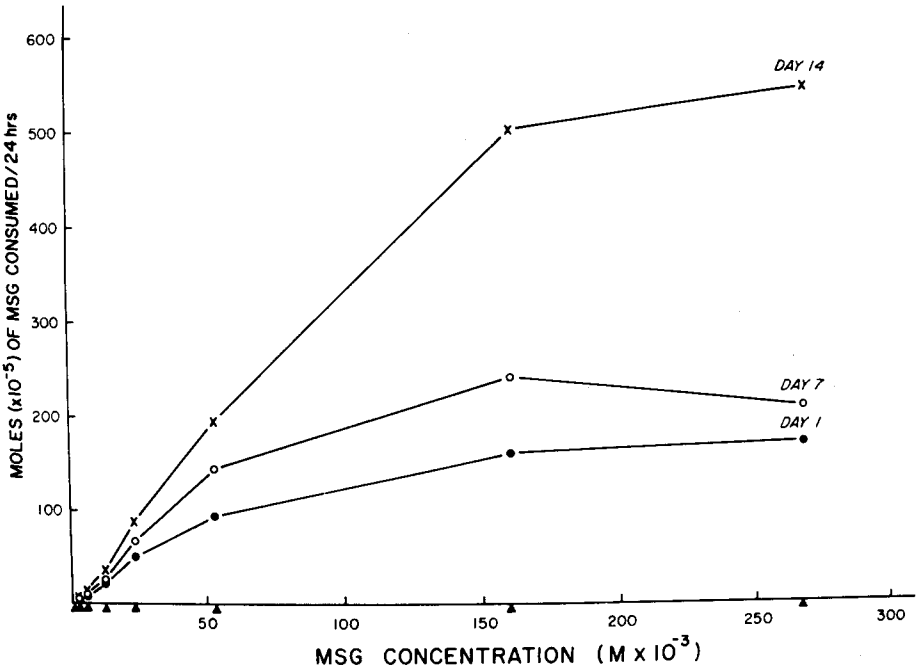

FIG. 5. The intake of moles of MSG as a function of MSG concentration in the solution offered during long-term tests. Values are the mean of 14 rats per group. (From Ohara and Naim, ref. 41.)

Table 1 indicates that rats do not show a preference for MSG-flavored diets over unadulterated diets. This was true for both low- or high-protein diets. This part of the study confirms the data of Scott and Quint (55). Since no preference for MSG-flavored diet was observed, the taste-enhancing phenomenon cannot be concluded from this study. Diets containing a high (7%) level of MSG were, in general, less preferred than unadulterated diets.

The lack of preference for MSG in solid food as compared to a strong preference in solution may be explained in two ways. Perhaps there is a competition between MSG and dietary components for the gustatory receptors that masks the sensory properties of MSG. Another possible reason for the lack of preference for an MSG-flavored diet might be an incomplete ionization of the MSG carboxyl groups in the diet compared to its aqueous state. This ionization has been reported by Fagerson (10) as necessary for taste sensation. A competition hypothesis is supported by the data showing a lower proportional intake (intake of MSG-flavored diet as a percentage of the total intake) of 9% protein—7% MSG diets than 18% protein—7% MSG. It is possible that, in the competition between protein components and MSG for gustatory receptors, MSG molecules were favored when the diet containing a low protein level. As a result, the rats could more easily detect the

TABLE 1. *Proportional intake of MSG-flavored diet when paired with plain diet, both containing either 9 or 18% protein**

		MSG concentrations in diet (%)				
	%	0.1	0.5	1.0	3.0	7.0
Day 1	9	$48 \pm 4^{a,\dagger}$	54 ± 4^{a}	58 ± 6^{a}	60 ± 6^{a}	46 ± 5^{a}
	18	54 ± 5^{a}	53 ± 5^{a}	51 ± 4^{a}	51 ± 4^{a}	41 ± 5^{a}
Days 2–3	9	43 ± 4^{a}	43 ± 5^{a}	50 ± 5^{a}	39 ± 6^{a}	22 ± 3^{b}
	18	47 ± 3^{a}	51 ± 3^{a}	53 ± 4^{a}	51 ± 3^{a}	38 ± 3^{a}
Days 4–7	9	56 ± 6^{a}	55 ± 7^{a}	60 ± 5^{a}	$40 \pm 8^{a,b}$	12 ± 2^{c}
	18	47 ± 3^{a}	51 ± 3^{a}	57 ± 4^{a}	$46 \pm 3^{a,b}$	30 ± 3^{b}

*Intake of MSG-flavored diet expressed as a percentage of total intake. Values are mean ± SEM of 13 to 14 rats per group.

†Comparisons following analysis of variance were made for each block of days across concentrations. All values not designated by the same superscript letter are different at least at the 5% level.

From Ohara and Naim, ref. 41.

aversive taste of 7% MSG. No differences were found for the total intake of diets, nor for body weight gains, as a function of MSG concentration in the diet. This might indicate that no amino acid imbalances occurred. Depression in food intake is known to occur within 3 hr in response to feeding a diet with amino acid imbalances (51). Thus, the thesis that the selection of MSG was by sensory means rather than postingestional feedback regulation is further supported in the diet experiments.

CONCLUSIONS

Different analyses resulted in two different expressions of MSG preference in rats. The expression of MSG acceptance by volume intake of MSG solutions, compared to deionized water, was different from that which expressed the intake of moles of MSG as a function of its concentration in solution offered. To separate the sensory properties of MSG from possible postingestional effects, it was suggested that acceptance is best expressed as the number of moles of MSG ingested for each solution.

It can be concluded from the data that in a two-choice situation, rats, by using sensory input, will not select high levels of glutamate. This may be an example of the sensory quality limiting consumption without the necessity of invoking post-ingestional feedback mechanisms. The suggestions that sensory, rather than post-ingestional factors, regulate the intake of MSG is compatible with other studies showing that an increase of glutamate in the diet does not usually lead to an increase of glutamate in the circulatory system (8,12,34). Since the rate of free amino acids crossing the intestinal wall diminishes with increasing electrical charge (11), glutamic and aspartic acids are slowly absorbed. These acids were also found to be the most rapidly excreted (21). Further confirmation is afforded by Windmueller

and Spaeth (62), who demonstrated that the intestine metabolizes nearly all absorbed dietary glutamate.

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