Chemical Stimulus Determinants of Cat Neural Taste Responses to Meats[1]

J.C. BOUDREAU, Sensory Sciences Center, Graduate School of Biomedical Sciences, University of Texas Health Science Center, Houston, TX 77030

ABSTRACT AND SUMMARY

The cat taste system was studied by recording single unit pulse signals from neurons innervating chemoreceptors on the fungiform papillae on the tongue. On the basis of neurophysiological measures, these units have been divided into three separate functional groups. Group I units respond to acids in general, but at neutral pH the most effective stimuli are certain nitrogen compounds. Compounds with an imidazole ring such as L-histidine, 1-methyl imidazole, anserine and carnosine prove to be effective group I stimuli. Group II units are responsive to amino acids, especially L-proline and L-cysteine, to the di- and triphosphate nucleosides, and to some inorganic salts. Group III unit stimuli are less well defined but these units are among those maximally discharged by nucleotides. The most effective compounds for stimulating both Group I and Group II units are certain nitrogen heterocycles.

INTRODUCTION

Flavor results from the interaction of a chemical and an organism. In studying flavor the usual procedure is to smell or taste various chemical substances and report on the psychophysical sensations elicited by these substances. The psychophysical sensations evoked are a product of the chemical receptor properties and neural processing of the resultant sensory signals. An alternate method of determining an organism's response to food chemicals is to measure the elicited neural activity. This method gives us a much more exact and quantitative measure of the sensory effect of chemical substances.

To determine the nature of taste active compounds in the cat, single unit spike responses were recorded from neurons in the geniculate ganglion, a small cranial sensory ganglion located near the inner ear. These neurons innervate, via the chorda tympani nerve, chemoreceptors in the fungiform papillae of the tongue (1). The recorded spike potentials are neurally transmitted signals that represent certain chemical properties of the solutions applied to the tongue.

RESULTS

The chemoresponsive units of the geniculate ganglion have been divided into three functionally distinct neural groups on the basis of various neurophysiological measures (2). These neural groups respond to different types of chemical substances and innervate, with different diameter fibers, fungiform papillae on different but overlapping areas of the tongue (Fig. 1). These unit groups can be considered as three distinct sensory systems measuring different chemical aspects of ingested foods. The chemical stimulus determinants of spike discharge within each group have been investigated to elucidate the chemical nature of the taste active substances present in the cat's natural diet. Although these investigations are still continuing, much has been discovered concerning the types of taste active chemicals and various chemical properties of their solutions (3-5). In the pages to follow, the present knowledge of cat taste chemistry will be briefly reviewed.

Many chemoresponsive units will discharge to tongue application of aqueous solutions of various animal tissues such as muscle, liver, kidney, etc. (1). An extensive study of the different compounds found in aqueous extracts of animal tissues (6) was undertaken to determine what types of compounds are taste active in the cat. A wide variety of compounds was found to activate the various neural units. Many of these stimulating substances (e.g., amino acids, nucleotides, inorganic ions, etc.) are common constituents of meats and have been implicated in human flavors (6). In part, neural units from the different unit groups are selectively responsive to the different solutions, but some solutions will activate units from two or more groups. There is evidence that the different unit groups are responsive to different properties of the chemical solutions applied to the tongue and that when more than one group is activated more than one chemical solution property is present.

Group I units preferentially innervate fungiform papillae on the rear center and sides of the tongue with large diameter fibers (Fig. 1). They are responsive to a wide variety of chemical compounds dissolved in water. Among the most stimulating compounds in low pH solutions are compounds with carboxylic and phosphoric acid groups. The response to these compounds is pH sensitive since neutralized solutions of carboxylic acids are nonstimulatory and neutralized solutions of phosphoric acids are only marginally stimulatory. The neural response seems proportional to the concentration of the proton donating form of the molecule in the region of its pKa (4,5).

In the pH region from 5 to 7, effective group I stimuli are certain nitrogen and nitrogen-sulfur compounds. Among the nitrogen-sulfur compounds that stimulate are taurine, thiamine pyrophosphate, and glutathione (5). Compounds with a heterocyclic component are especially effective at neutral pH. The most stimulatory compounds we have yet discovered at pH's near neutrality are pyridine, thiazolidine, and a variety of compounds with an imidazole ring such as L-histidine, 1-methyl-L-histidine, 1-methyl-imidazole, and various histidine dipeptides including carnosine (beta-alanyl-L-histidine) and anserine (beta-alanyl-methyl-L-histidine). The response to these nitrogen compounds is also pH dependent, indicating that the nitrogen compounds are also only stimulatory in the protonated form (pKa values for the imino groups of these compounds fall between 5.0 and 7.0). An example of a group I unit discharging to a solution of anserine nitrate is presented in Figure 2.

In general the compounds that stimulate Group I units are similar to those eliciting a sour sensation in humans. Human psychophysical studies also indicate that sourness is a prominent component of the sensation elicited by L-histidine solutions and that sourness increases with a decrease in solution pH (7). The fact that basic nitrogen compounds, functioning as Brønsted acids (proton donors), elicit a sour sensation suggests a different role for the sour taste system than held traditionally, since low pH solutions are not necessary for activation of this system.

Group II units innervate chemoreceptors on the front part of the tongue with medium diameter nerve fibers. These units are characterized by high levels of spike discharge in the absence of experimenter applied stimulation. As a result of this high level of "spontaneous activity,"

[1]Presented at the AOCS Meeting, New Orleans, April 1976.

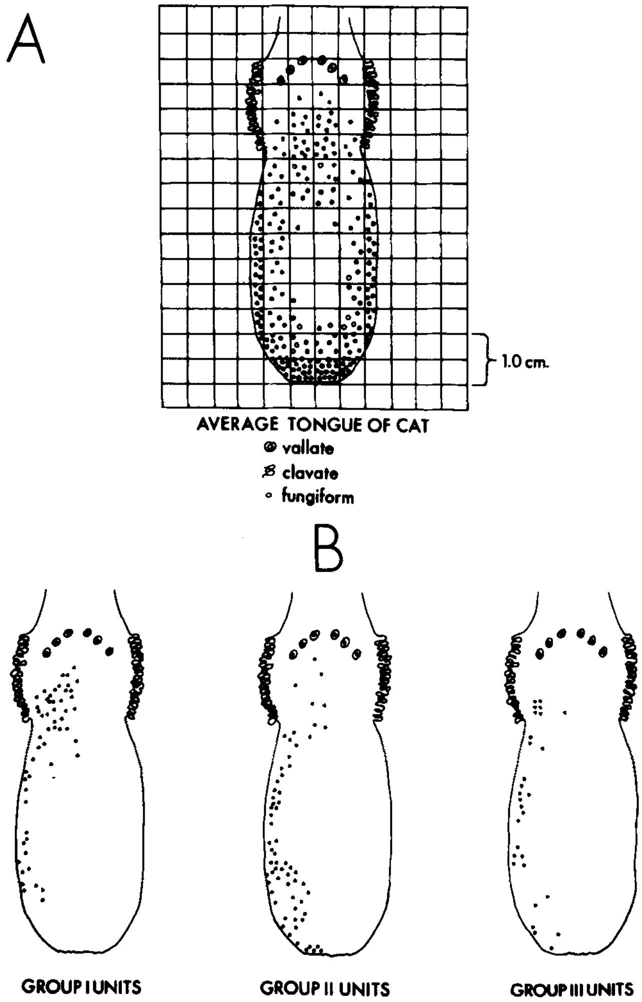

FIG. 1. (A) Schematic of the average cat tongue showing distribution of papillae. (B) Projection zones of the different neural unit groups in the geniculate ganglion. Each dot represents the approximate location of the papillae system of a single neural unit.

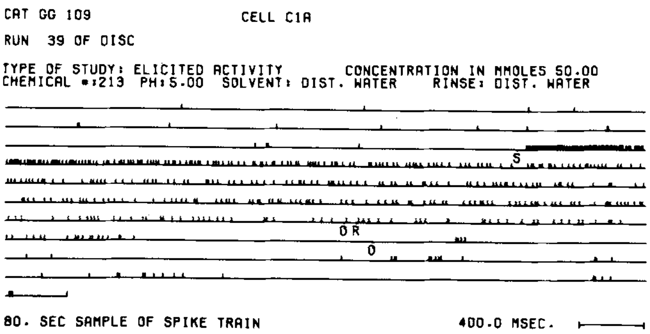

FIG. 2. Computer printout of the response of a Group I unit to a 50 mM solution of anserine nitrate (pH 5.0). Abbreviations: S = stimulus applied to tongue; R = rinse applied to tongue; O = stimulus or rinse flow off (times approximate only).

chemicals applied to the tongue can increase or decrease the number of spike discharged. The reduction in spike activity during the stimulation period is termed "inhibition" and the increase is termed "excitation."

Group II units are excited or inhibited by a variety of compounds although the most stimulatory natural substances we have yet encountered are the di- and triphosphate nucleosides and certain amino acids. Amino acids and various other nitrogen compounds are also the most effective inhibitory compounds. The chemical factor determining the nucleotide response is in part independent of the factor determining the response to the amino acids. Group II units are the units most responsive to inorganic salts such as $CaCl_2$ and NaCl. Phosphate salts will stimulate some members of all unit groups.

A wide variety of amino acids stimulate group II neurons. Among the most excitatory stimuli are L-cysteine, L-proline, L-lysine, L-ornithine, L-histidine, and L-alanine. Among the most inhibitory substances are L-tryptophan, L-isoleucine, L-tyrosine, and L-phenylalanine. In testing compounds related to proline and histidine it was found that the heterocyclic ring components, pyrrolidine and imidazole, were as stimulatory as the parent amino acids. To further specify the properties of excitatory stimuli many other simple heterocyclic compounds were tested. Optimum heterocyclic excitatory stimuli, with the exception of imidazole, were four to six member non-aromatic nitrogen compounds. Neural discharge to nitrogen heterocycles was related to two factors: (a) a steric factor (in particular, ring size); and (b) the relative basicity of the compounds as indicated by pKa values. Maximum inhibition has also been obtained from solutions of nitrogen heterocycles. Heterocycles inhibiting group II units discharge were those with low pKa values (pyrrole) or those with a seven or eight member ring (azacycloheptane and azacyclooctane).

There are certain similarities between the chemical stimuli that taste sweet or bitter to humans and the compounds that excite or inhibit group II neurons. The amino acids that taste bitter for instance are those that inhibit group II neurons, whereas those that excite group II neurons taste sweet or bitter-sweet. This analogy between sweet and bitter and group II discharge is further strengthened by the fact that in behavioral testing the cat consumes solutions of group II exciters but avoids group II inhibitors (8). Many of the compounds that are sweet to the human, however, are inactive or repellent for the cat (9,10), no doubt reflecting his carnivoral heritage.

Group III neurons innervate chemoreceptors on the sides of the tongue with small diameter fibers. As presently described, Group III units constitute a heterogeneous group and may be subject to further functional subdivision. Some group III units are responsive to only a few of the compounds tested. In general, amino acids tend to be ineffective. Like the other unit groups, group III units respond to a variety of compounds. Among the compounds that are most stimulatory are nucleotides (including the monophosphate nucleotides), phosphate salts, butyryl choline chloride, and a variety of other compounds. Group III units are the units most responsive to nucleotides and discharges have been obtained to them at or below their concentrations in animal tissues. Preliminary indications are that the response to compounds like butyryl choline chloride is determined more by the butyryl group than the choline group. Three to six member hydrocarbon chains with carbonyl groups are common features of many nonphosphate group III stimuli. These facts make group III units those most responsive to lipid derived compounds. There is no obvious relationship between group III unit activation and any common human taste sensation, although the Japanese report that low levels of nucleotides are important in eliciting the "umami" or "delicious" sensation (11). Group III stimuli seem in part similar to human taste intensifier compounds.

DISCUSSION

While ingesting food, the organism measures various chemical aspects of the food with a complex set of chemoreceptors in the oral and nasal cavities. The taste receptors are primarily responsive to water soluble compounds and the olfactory receptors to volatiles. Many compounds are present in water extracts of animal tissues, but those most

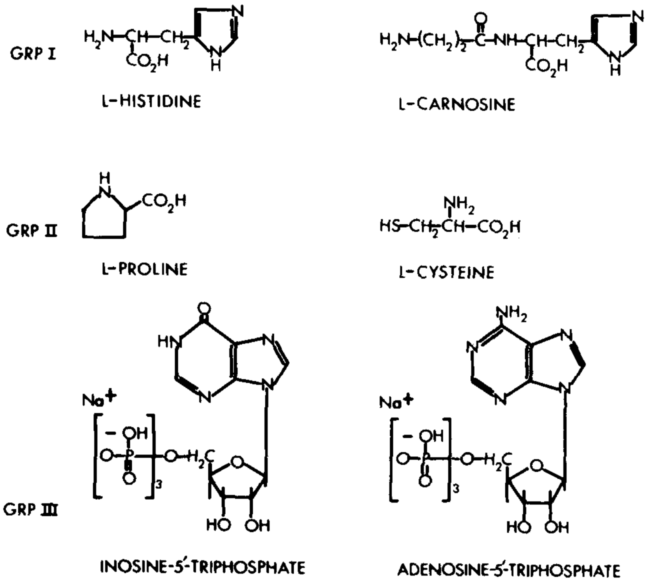

FIG. 3. Structural formulae of some of the compounds commonly found in animal tissues. These compounds are also among the compounds most stimulatory for the three different neural unit groups as indicated.

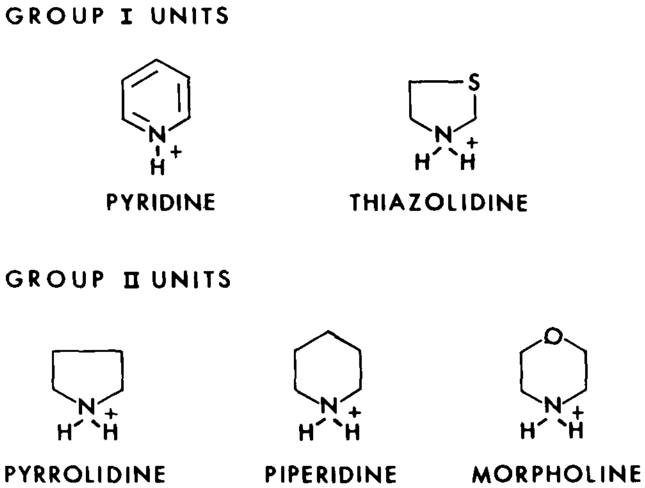

FIG. 4. Some of the most stimulatory compounds yet discovered for cat neural taste units.

common and present in the largest quantity are various inorganic ions, peptides, amino acids, nucleotides, pyridine compounds, organic acids, and various interactive and breakdown products of these compounds. As shown, many of these compounds will activate cat taste systems (Fig. 3). The information from the taste systems, together with information from olfactory and other sensory systems, is utilized by the organism in a sensory chemical analysis of food. A food flavor is a composite sensation resulting from activation of several separate sensory systems. Thus any meat flavor will have properties in common with other meat flavors as well as distinctive properties depending upon the chemical composition of the meat and the sensory systems activated.

Meat flavor to a flavor chemist usually means cooked meat flavor. Cooking meat produces a variety of chemical changes that are important in the flavor of meat (12-16). Although cooked meat flavor compounds are usually considered in terms of their olfactory qualities, many of these compounds would also have taste activity. Two factors that would promote stimulation of the cat taste systems would be decarboxylation and cyclization (3,4,5). Although few of the heat produced heterocyclic compounds reported to be important in human meat flavor perception have been tested on the cat, those with chemical properties similar to the cat taste active heterocycles in Figure 4 should stimulate.

ACKNOWLEDGMENTS

We thank J. Oravec, C. Madigan, J. Lucke, H.v. Nguyen, W. Anderson, and J. Watkins for assistance on various aspects of this work which was supported in part by NSF Research Grant BNS73-01296.

REFERENCES

1. Boudreau, J.C., B.E. Bradley, P.R. Bierer, S. Kruger, and C. Tsuchitani, Exp. Brain Res. 13:461 (1971).
2. Boudreau, J.C., and N. Alev, Brain Res. 54:157 (1973).
3. Boudreau, J.C., W. Anderson, and J. Oravec, Chem. Senses and Flavor 1:495 (1975).
4. Boudreau, J.C., V. Collings, J. Oravec, W. Anderson, and T.E. Nelson, "Sulfur, Nitrogen, and Phenolic Compounds in Food Flavor, ACS Symposium Series," Amer. Chem. Soc., Wash. D.C., 1976.
5. Boudreau, J.C., and T.E. Nelson, Chem. Senses and Flavor (In press).
6. Solms, J., "Gustation and Olfaction, an International Symposium," Academic Press, New York, NY, 1971, pp. 92-110.
7. Ninomiya, T., S. Ikeda, S. Yamaguchi, and T. Yoshikawa, Rep. 7th Sensory Evaluation Symposium, JUSE, 109-123 (1966).
8. White, T.D., and J.C. Boudreau, Physiol. Psychol. 3:405 (1975).
9. Carpenter, J.A., J. Comp. Physiol. Psychol. 48:139 (1956).
10. Bartoshuk, L.M., Ibid. 89:971 (1975).
11. Yamaguchi, S., T. Yoshikawa, S. Ikeda, and T. Ninomiya, J. Food Sci., 36:846 (1971).
12. Chang, S.S., Symposium on the Instrumental Analysis of Flavor and Flavor Stability of Fats and Fatty Foods, AOCS Spring Meeting, New Orleans, April 1976.
13. Hashida, W., Food Trade Rev. 44:21 (1974).
14. Herz, K.O., and S.S. Chang, Adv. in Food Res. 18:1 (1970).
15. Wilson, R.A., and I. Katz, Flavour Industry 5:1 (1974).
16. Wilson, R.A., J. Agr. Food Chem. 23:1032 (1975).

[Received October 19, 1976]