Taste preferences of the cat for neurophysiologically active compounds

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Six naturally occurring compounds which have been observed to be physiologically active in the anesthetized cat are also demonstrated to be behaviorally active in terms of preference and avoidance. Using a two-bottle long-term preference experiment, concentrations of .5, 5, 50 mM L-proline, L-lysine, L-histidine, L-tryptophan, L-isoleucine, and adenine (all in 50 mM NaCl) were compared against 50 mM saline. At 50 mM concentration, those chemicals which elicit an increase in spike output from geniculate ganglion chemoresponsive group II units (L-proline, L-lysine, and L-histidine) were found to be preferred, while L-tryptophan, L-isoleucine, and adenine, which decrease group II discharge, were avoided. The preference response to L-proline was then observed over a concentration range extending to 500 mM. Maximum response was observed at 50 mM, with preference decreasing as concentration was either increased or decreased.

The cat has been considered somewhat an oddity in behavioral taste research because, unlike most species of animals tested, the cat exhibits no preference for sucrose over water in a two-bottle choice situation. The insensitivity of the cat to sucrose has also been demonstrated in neurophysiological experiments in that sugars elicit little or no neural discharge from single neural units in the chorda tympani or geniculate ganglion (Bartoshuk, 1971; Boudreau, Bradley, Bierer, Kruger, & Tsuchitani, 1971; Cohen, Hagiwara, & Zotterman, 1955; Pfaffmann, 1941; Zotterman, 1935). Recent neurophysiological investigations (Boudreau & Alev, 1973) have revealed that although the cat may not be sensitive to sucrose, many of the chemical compounds (i.e., amino acids, nucleotides, etc.) it is likely to meet in its natural diet do have a marked effect on peripheral neural discharge.

In the present experiment, some of these neurophysiologically active compounds were offered to the cat in a two-bottle preference experiment. These compounds were chosen on the basis of their ability to affect the neural discharge of the geniculate ganglion group II units. Group II units innervate the fungiform papillae on the anterior two-thirds of the tongue and are the only units highly responsive to a variety of amino acids (Boudreau, 1974). Because of the relatively high spontaneous activity rates of group II units (Boudreau & Alev, 1973), chemicals placed on the tongue may increase, decrease, or elicit no change in neural discharge of these units. The chemicals tested in the preference experiment were chosen according to their ability to excite or inhibit group II activity.

The object of this behavioral experiment was to determine if these neurophysiologically active compounds could be detected by the cat (as indicated by preference behavior) and whether the direction of neural effect (excitation or inhibition) induced by the chemicals could be correlated with the cat's preference behavior.

METHODS

Six reagent grade chemicals, L-proline, L-lysine, L-tryptophan (Sigma Chemical Co.), L-isoleucine, L-histidine, and adenine (ICN Nutritional Biochemicals Co.), were presented as test stimuli in concentrations of 0.5, 5.0, and 50.0 mM. Three 12.5-mM adenine solutions were tested after 50 mM adenine proved to be an unsatisfactory test solution due to low solubility in water. Selection of these chemicals was made on the basis of neurophysiological response: L-proline, L-lysine, and L-histidine excite group II neurons of the geniculate ganglion, while L-tryptophan, L-isoleucine, and adenine inhibit these units (Boudreau, 1974). The solvent for each test solution, as well as the alternate solution in each choice situation, was a 50.0-mM solution of NaCl in deionized, glass-distilled water.

The two-bottle, long-term exposure technique was chosen as the method of presentation. Two identical glass bottles of 500 ml capacity, one containing the test solution, the other 50.0 mM NaCl, were fitted with Vollrath drinking tubes (5/8 in. diam) and attached to the cages, with the initial relative positions (left or right) being randomly assigned. The bottles remained on the cages for 48 h, with a position reversal at 24 h to avoid positional bias. Immediately upon removal of these solutions, two new bottles, one containing distilled water, the other saline, were placed on the cage for 48 h.

The 11 experimental animals, naive adult cats of mixed breed and weight from Houston, were fed ad lib on dry cat food (Purina Cat Chow). A total of 11 animals were used due to the unavailability of the same five cats for testing throughout the entire experiment. A 1-week period preceded preference testing to familiarize the animals with the drinking bottles. Only distilled water and saline were used during the familiarization period. Proficiency was observed after 3 days, with consumption averaging 150-300 ml per day. After the adjustment period, test solutions were presented on a random basis with no animal being tested twice at the same

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concentration. If a chemical was presented twice, the lower of the two concentrations always preceded the higher by at least 1 month.

RESULTS

The results of the preference tests at each of three concentrations of the test chemicals are shown in Figure 1. The ordinate for each graph depicts the amount of test solution ingested relative to the total fluid consumption over the 48-h test period. The preference region is defined as the area above the 50% line, while the avoidance region is the area below that line. The test chemicals are arranged along the abscissa in order of increasing neurophysiological response (see Figure 3). The five points above each chemical represent single trials on five different cats.

At 0.5 mM, no definite trend can be seen concerning responses towards the two groups of excitors and inhibitors, although values for individual trials indicate the possibility of discrimination by some of the cats. At 5.0 mM, the three excitors are slightly preferred, but the variability in response toward the inhibitors remains high. At 50.0 mM, a clear distinction is seen between the two groups of chemicals with the excitors preferred and the inhibitors avoided. The responses of individual cats were also examined for patterns, such as preference or avoidance for all chemicals at a given concentration, and no trends were observable other than those pointed out for the total group of cats in Figure 1.

At a concentration of 0.5 mM, great variability was shown by the animals for the chemicals, although some of the preference values (>90% or <10%) indicate that discrimination may be occurring. In a control study with water-water choice, preference values rarely exceeded 60% and never 80%. The two-bottle choice situation is inadequate for measuring discrimination thresholds (discrimination may be masked by equal preference), but these extreme preference values indicate that some animals were discriminating the presence of the chemical.

At 5.0 mM, the range of variability for the excitors decreases, with four of the five tests for each chemical demonstrating preference. The two other points for L-lysine and L-histidine are above the 40% level, while the other point for L-proline (at 16%) represented a trial in which the animal became ill with diarrhea (not associated with experimental procedure). All symptoms disappeared within 48 h and subsequent retesting of this animal resulted in a point in the preference region. The response toward the inhibitors does not show the same trend as seen for the excitors, since variability remained high with preference or avoidance dependent upon the animal tested.

At 50.0 mM, preference was demonstrated in 14 of the 15 trials, indicating that the excitors are clearly preferred at this concentration. Only one trial with

L-histidine showed avoidance. In addition, the variability in response equaled or was less than that shown at other concentrations. Similarly, the inhibitors are almost totally avoided with the exception of one test point for adenine (at 12.5 mM).

Figure 1. Results of two-bottle long-term exposure preference testing of the six test stimuli at three concentrations. The ordinate of each graph represents the percent of that concentration of test solution consumed relative to total fluid consumption (48-h period). Preference region is the area above the 50% line. All amino acids are of the L-stereoisomeric form. Open circles above adenine represent 12.5 mM (see text).

Figure 2. Results of preference testing for L-proline over a concentration range from 0.5 to 500.0 mM. Ordinate represents percent of test solution consumed relative to total fluid consumption (48-h period). Circles with line represent means of results at a given concentration.

A Fischer's exact probability test (Siegel, 1956) on a 2 by 2 contingency table plotting frequency of response greater than 50% and less than 50% against the groups "excitators" and "inhibitors" indicates that this result is highly significant ($p < .001$).

The preference shown to L-proline at each of the three concentrations led to a subsequent study, which investigated the response over a concentration range extending to 500.0 mM (Figure 2). The resulting curve of mean preferences (open circles) shows a maximum at 50.0 mM, with preference decreasing as concentration is either increased or decreased from this value. The variability in response at each concentration appears to be inversely correlated with the extent of preference.

DISCUSSION

Techniques

This experiment was designed and test solutions chosen on the basis of neurophysiological studies on the geniculate ganglion gustatory system of the cat (Boudreau, 1974; Boudreau & Alev, 1973). Three of the test stimuli, L-proline, L-histidine, and L-lysine, were chosen because they consistently increased neural discharge from group II neurons of the geniculate ganglion while the other three primarily inhibited neural response. Although these six represent only a limited number of chemicals to which group II units are responsive, they are among the most active, either excitatory or inhibitory. Certain other active chemicals were not chosen because of offensive odors (cysteine and methyl-cysteine), high variability in neural response (arginine), or uncontrollable activation of other neural groups within the ganglion (ATP and ITP). Responses from

other neural groups to the test stimuli are minimal or were controlled by the adjustment of pH and the use of saline as the solvent. L-histidine, for example, is an active group I excitator, but when the pH is adjusted to 8.5, response from these units is absent. 50-mM saline itself elicits no definite neural response from any group of neurons with the exception of an occasional inhibitory response from group I units. No significant preference is shown when cats are given a choice between water and 50 mM saline (Carpenter, 1956). Therefore, by control of pH and solvent, selective stimulation of group II neural units was maintained during the consumption of these solutions, provided that neural data from anesthetized cats accurately represents the situation in unanesthetized animals.

A comparison of the preference data with the neural data available at the beginning of the experiment can be seen in Figure 3. As can be seen

Figure 3. Comparison of neurophysiological data on response of group II neurons of geniculate ganglion (Boudreau, 1974) with behavioral preferences of cats to the six test stimuli. The solvent is indicated in the upper right corner of each graph. Means are indicated by theta symbols. Open circles above adenine represent 12.5 mM concentration. All amino acids are of the L-stereoisomeric form.

from these data, group II units of Pittsburgh cats show increased neural discharge to distilled water solutions of L-proline, L-lysine, and L-histidine, while presentation of solutions of L-tryptophan, L-isoleucine, and adenine are accompanied by decreases in discharge. Subsequent research on the group II neurons of Houston cats to the test stimuli in 50 mM saline indicates that the saline solvent potentiates response of these units to the excitors while reducing inhibition of response to the inhibitors (Boudreau, Anderson, & Oravec, Note 1). No data are yet available on the response of group II neurons to L-histidine at pH 8.5, but all other stimuli were presented at the same pH in both neurophysiological and behavioral experiments.

The Richter long-term exposure technique (Richter, 1939) was chosen for convenience and to directly compare our work on the cat with that of others. Dissimilar results may be obtained in preference experiments when using short- vs. long-term exposure of test stimuli. For example, sucrose is rated more effective for the rat than glucose with short exposure times (Cagan & Maller, 1974; Guttman, 1954; Hagstrom & Pfaffman, 1959), but glucose is more effective in long-term exposures (Richter & Cambell, 1940; Soulariac, 1947). The difference is usually attributed to postingestion factors (Collier & Bolles, 1968; Jacobs, 1962; McCleary, 1953; Shuford, 1959), which may or may not be operative in the present experiments.

Comparison of Results

Preference studies in the cat have been primarily directed towards the cat's ability or inability to taste sugars. Carpenter (1956) reported that cats were unable to discriminate between sucrose solutions and water. Kare (1961) also came to the conclusion that cats were indifferent to sucrose, and, citing Maller, reported that no sustained preferences were seen for solutions of glucose, xylose, fructose, lactose, or saccharin (Maller, cited in Kare, 1971). Bartoshuk (1971) also investigated this phenomenon and found that significant preferences could be obtained only by using high concentrations of sucrose (about 1M in .03 M NaCl solutions).

Compounds other than sucrose have not been extensively investigated. Carpenter (1956) also examined preferences for NaCl, KCl, saccharin, and quinine HCl. Only slight preferences were seen for NaCl and KCl below .1 M and for saccharin below .001 M. Quinine HCl, which elicits an inhibitory response from group II neurons (Boudreau et al., 1971), was avoided at all tested concentrations. Quinine is also avoided when directly added to foods, with rejection occurring at lower concentrations than when an aqueous solution is tested (Rofe & Anderson, 1970).

The present study demonstrates that certain compounds which are neurally active in the cat at low

concentrations are also behaviorally active in terms of preference and avoidance. Neurophysiological responses to amino acids at comparable concentrations have also been demonstrated in the chorda tympani of the rat. Investigators have utilized chorda tympani fiber recordings in studying the response to MSG and its potentiation by 5' nucleotides (Yamashita, Ogawa, & Sato, 1973; Sato, Yamashita, & Ogawa, 1970). Both behavioral and neurophysiological responses to five amino acids—glycine, valine, alanine, methionine, and tryptophan—were reported by Halpern, Bernard, and Kare (1962). Electrophysiological response was found to increase with concentration up to 1.0 M for glycine and alanine but not for methionine. Differences in preference, dependent upon whether ascending or descending concentration series were used, were seen for methionine, glycine (between .01 M and 1.0 M only), and both D- and L-tryptophan. The rat significantly rejects L-tryptophan only if concentrations are presented in a descending order (.01 M - .005 M - .001 M), whereas the cat rejects this compound consistently only at the .05 M concentration regardless of prior exposure to a lower concentration. Comparison of our results with those of others is obviated by differences in species, choice of stimuli, and the neurophysiological measures utilized. On the basis of our data, the cat appears to be different from the rat in his gustatory response to amino acids.

Amino acids also possess taste qualities for humans as shown by psychophysical studies. In solution, L-proline is described as sweet, L-lysine as flat, and L-histidine as flat (Solms, Vuataz, & Egli, 1964), or slightly bitter (Berg, 1953; Ferguson & Lawrence, 1958). L-isoleucine tastes flat (Solms et al., 1964), bitter (Ferguson & Lawrence, 1958), or bitter and weakly astringent (Berg, 1953). L-tryptophan is bitter (Solms et al., 1964), flat (Berg, 1953), or simply not sweet (Lawrence & Ferguson, 1959). No data are available on adenine, though purine bases alone are reported to have no flavor activity (Kuninaka, 1967). These six stimuli were also tasted by personnel in this lab at 100-mM concentration in distilled water. L-proline was predominantly sweet; L-histidine was moderately sweet, flat, or moderately bitter; L-lysine was moderately sweet to flat; adenine was flat to weakly unpleasant; L-isoleucine was mildly bitter; and L-tryptophan was strongly bitter and unpleasant.

Interpretation of Results

The cat is a strict carnivore, whether in captivity or its natural ecological niche, living almost entirely on animal tissue (Boudreau & Tsuchitani, 1973; Ewer, 1973; Schaller, 1972; Scott, 1968). Nitrogenous compounds, such as those used in this experiment, are common constituents of animal tissue (Batzer, Santoro, & Landman, 1962; Jones, 1967; Solms, 1971). Therefore, a relationship seems to exist in the

cat between the chemical consistency of food consumed, the neural gustatory responses, and preferential behavior.

A great number of behavioral studies on diet selection have demonstrated that an animal is often capable of choosing between diets of different nutrient compositions (Harper, Benevenga, & Wohlhueter, 1970; Richter, 1943; Simpson & Booth, 1971, 1973). The rejection of diets with imbalanced amino acid patterns and the selection of corrected (balanced) diets have been thoroughly demonstrated. Although several factors enter into the selection of a diet, it is apparent from neurophysiological and behavioral work on the rat, hamster, and cat that much information concerning the chemical composition of a diet is available through chemosensory pathways of the nasal and oral cavities.

Young (1966) has pointed out that there appear to be at least four general determinants of diet selection: (1) organic conditions of the subject, (2) previous dietary experience, (3) bodily constitution, and (4) peripheral stimulation of the head receptors. The correlation between responsiveness of group II neurons and behavior encompasses only one subset of the total number of head receptors possibly involved in food acceptance. The olfactory and other airborne chemoresponsive systems (Tucker, 1971) were possibly stimulated in this experiment. The solutions had no characteristic odors for the experimenters, but informational input for the cat by these channels cannot be ruled out. In addition, the glossopharyngeal, trigeminal, and vagal nerves also innervate chemoreceptors in the oral cavity. No data are available on the response of neural units in any of these systems to the test stimuli. To this extent, the correlation can only be described as between a subset of the total neural network involved in food selection and resultant behavior.

Since group II excitors are preferred by the cat and group II inhibitors are avoided, it is possible to predict preference behavior from neurophysiological measures (other things being equal). That the direction of preference behavior can be predicted from neural response suggests that distinct sensations arise with the differential activation of group II neurons and that these sensations have hedonic attributes. A possible analogy lies in the human sensations of sweet and bitter frequently associated with organic nitrogen compounds.

REFERENCE NOTE

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