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Environmental Pollutants Alter Taste Responses in the Gerbil

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SCHIFFMAN, S. S., M. S. SUGGS, M. B. ABOU DONIA, R. P. ERICKSON AND H. T. NAGLE. *Environmental pollutants alter taste responses in the gerbil.* PHARAMACOL BIOCHEM BEHAV 52(1) 189–194, 1995.—Taste and smell are chemical senses that play a crucial role in food selection. Damage to taste and smell receptors can impair food intake, nutritional status, and survival. The purpose of this study was to determine the effects of 11 environmental pollutants (nine insecticides and two herbicides) on electrophysiological taste responses in the gerbil. Integrated chorda tympani (CT) recordings were obtained from gerbils to a range of tastants before and after a 4-min application of 1 of 11 environmental pollutants. The taste stimuli were: sodium chloride (100 mM), calcium chloride (300 mM), magnesium chloride (100 mM), HCl (10 mM), potassium chloride (500 mM), monosodium glutamate (MSG) (50 mM), sucrose (100 mM), fructose (300 mM), sodium saccharin (10 mM), quinine HCl (30 mM), and urea (2 M). The nine insecticides included organophosphorous, carbamate, and pyrethroid insecticides. The seven organophosphorous insecticides tested were: acephate, carbofuran, chlorpyrifos, chlorpyrifos oxon, demeton, malathion, and methamidophos. The carbamate insecticide carbaryl and the pyrethroid insecticide fenvalerate were also tested. Two herbicides, paraquat and glyphosate, were tested, and dose–response curves for each of these two herbicides were also determined. All of the 11 insecticides and herbicides had an effect on some of the taste stimuli tested. Application of 10 mM methamidophos exhibited the greatest amount of suppression on the 11 taste solutions. Each taste stimulus was significantly suppressed with the exception of 2 M urea. Herbicides paraquat and glyphosate also reduced responses to several tastants. These data indicate that environmental pollutants can modify taste responses in the gerbil.

Taste Insecticides Herbicides Pollutants Electrophysiology Gerbil

A BROAD RANGE of pollutants have been reported to impact the upper alimentary and respiratory tracts (13,24,38,40). Pollutants also have been implicated in a variety of symptoms including irritation of the eyes, nose, and throat; asthma-like conditions; and unpleasant odor and taste sensations (13, 24,38). Chronic exposure to metallurgic compounds, dusts, nonmetallic inorganic compounds, organic compounds, and by-products of manufacturing processes can damage the olfactory system, causing permanent anosmia (loss of smell) or hyposmia (reduction in ability to smell) (1-3,9,15,21,22,25, 34,35,39,41,42,46). Laboratory studies have documented a broad range of anatomic and physiological changes in the olfactory system resulting from environmental pollutants. These include damage to the olfactory epithelium (5,7,8,11, 17,26,27,32,37,45,49), accumulation of pollutants in the olfactory mucosa and bulbs (6,14,47), altered neurotransmitter levels (43,44,48), malignant neoplasms in the olfactory regions (12,28), and electrophysiologic changes in activity from olfactory receptors (4,8). The compounds that damage the olfactory system include a broad range of pesticides such as insecticides, soil fumigants, herbicides, and fungicides (5,6,32,45, 48,49).

Thus, most studies of the effect of pollution on the chemical senses have focused on the olfactory rather than the taste

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system. The purpose of the present study was to extend the previous olfactory studies to investigations of the impact of pesticides on the taste system. Pesticides are known to occur in a variety of food products including grain, watermelon, wine, fish, chili peppers, and apples (10). Patient complaints of taste aberrations after pesticide exposure are not uncommon (38), with altered taste perception or persistent bitter and metallic tastes as the presenting symptoms. Hexachlorocyclohexanes, which are used in insecticides, have been shown to bind to the squamous epithelia of the tongue (6). The present study was designed to assess the effect of pesticides on the electrophysiologic taste activity recorded from the chorda tympani nerve of the gerbil.

METHOD

Animals

Female Mongolian gerbils, *Meriones unguiculatus*, were obtained from Tumblebrook Farm (West Brookfield, MA). The gerbils were 10–12 weeks old and weighed 45–65 g.

Stimuli

Eleven common pesticides were tested to determine if they alter taste responses to common tastants found in food. The pesticides included seven organophosphorous insecticides: acephate (1 mM and 10 mM), carbofuran (1 mM), chlorpyrifos (10 μM, 100 μM, and 1 mM), chlorpyrifos oxon (100 μM and 1 mM), demeton (2 mM), malathion (100 μM, 500 μM, and 1 mM), and methamidophos (10 mM). Also tested was the carbamate insecticide carbaryl (1 mM). Fenvalerate, a pyrethroid insecticide, was tested at 1 mM. Paraquat and glyphosate, which are both herbicides, were each tested at 1 and 10 mM. Dose-response curves for each of the two herbicides were determined at concentrations ranging from 0.156 to 10 mM.

Acephate, methamidophos, paraquat, and glyphosate were each dissolved in deionized water. All other pesticides were first dissolved in ethanol. Deionized water was then added gradually to obtain the final concentration desired. The ethanol concentrations used to dissolve each compound were: 1 mM carbofuran (8%), 10 μM, 100 μM, and 1 mM chlorpyrifos (0.01%, 0.1%, and 1%, respectively), 100 μM and 1 mM chlorpyrifos oxon (0.1% and 1%, respectively), 2 mM demeton (8%), 100 μM, 500 μM, and 1 mM malathion (1%, 8%, and 8%), 1 mM carbaryl (8%), and 1 mM fenvalerate (8%). Each of the solutions was prepared just prior to application to the gerbil tongue.

The effect of these environmental pollutants on a range of tastes was examined. The taste solutions tested were: sodium chloride (100 mM), calcium chloride (300 mM), magnesium chloride (100 mM), HCl (10 mM), potassium chloride (500 mM), monosodium glutamate (50 mM), sucrose (100 mM), fructose (300 mM), sodium saccharin (10 mM), quinine HCl (30 mM), and urea (2 M). A total of 11 stimuli were tested. All solutions were delivered to the tongue at 72°F. The taste solutions were dissolved in deionized water.

Experimental Procedure

Gerbils were anesthetized with an IP injection of ketamine HCl (Ketalar at 50 mg/ml) at a dose of 330 mg/kg body weight. Two doses were administered 15 min apart. Supplementary injections of sodium pentobarbital (Nembutal at 5 mg/ml) were delivered to maintain a surgical level of anesthesia. Integrated electrophysiological recordings from the chorda tympani nerve were made using the techniques described by Jakinovich and Oakley (19). Recordings from an average of four gerbils were obtained for the each of the pesticides to evaluate the effect on the taste stimuli.

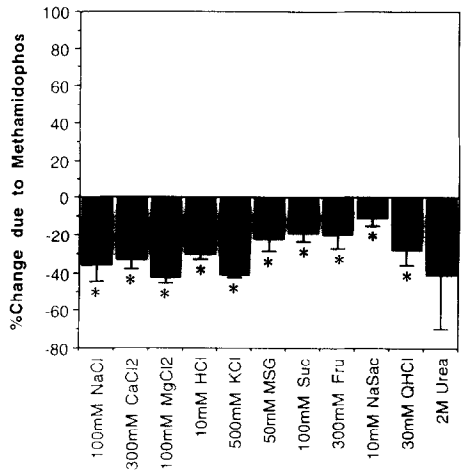

FIG. 1. Percent change in integrated chorda tympani responses after a 4-min application of 10 mM methamidophos. Abbreviations: NaCl, sodium chloride; $CaCl_2$, calcium chloride; $MgCl_2$, magnesium chloride; HCl, hydrochloric acid; KCl, potassium chloride; MSG, monosodium glutamate; Suc, sucrose; Fru, fructose; NaSac, sodium saccharin; QHCl, quinine hydrochloride; Urea, urea.

During a given trial, each of the 11 taste stimuli was applied to the gerbil tongue with a 1-min interstimulus rinse with deionized water or solvent. A pesticide was then applied for 4 min as a rinse to the gerbil tongue, followed by the 11 taste solutions with an interstimulus rinse of the pesticide. The stimuli were delivered in 2.0-ml samples by a gravity flow system at a rate of 0.20 ml per s.

RESULTS

Of the seven organophosphorous insecticides tested, 10 mM methamidophos exhibited the greatest amount of sup-

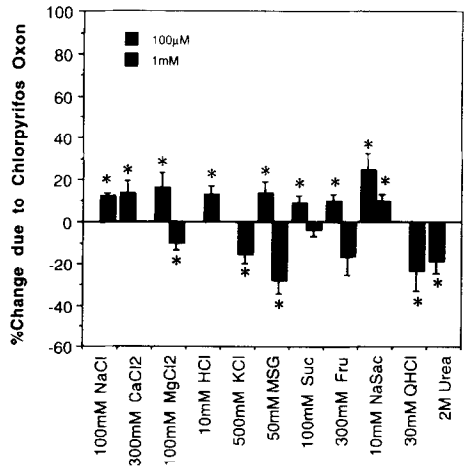

FIG. 2. Percent change in integrated chorda tympani responses after a 4-min application of 100 μM and 1 mM chlorpyrifos oxon.

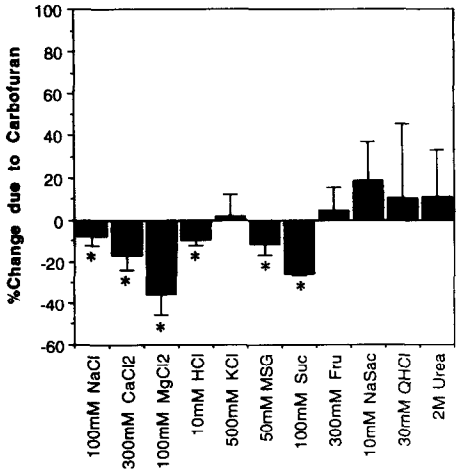

FIG. 3. Percent change in integrated chorda tympani responses after a 4-min application of 1 mM carbofuran.

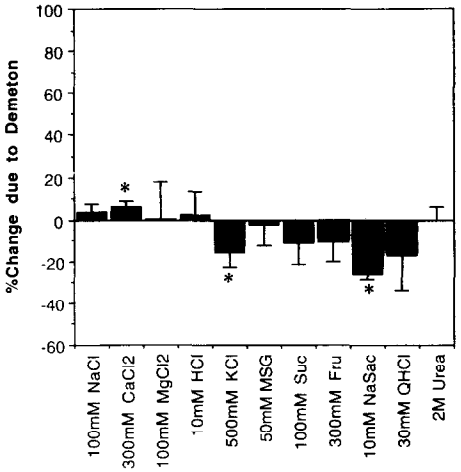

FIG. 5. Percent change in integrated chorda tympani responses after a 4-min application of 2 mM demeton.

pression on the 11 taste solutions. Each compound was significantly suppressed, with the exception of 2 M urea (Fig. 1).

Chlorpyrifos oxon was applied to the tongue at 100 μM with significant enhancements in response to: 300 mM calcium chloride (14%), 100 mM magnesium chloride (17%), 50 mM MSG (14%), 100 mM sucrose (9%), 300 mM fructose (10%), and 10 mM sodium saccharin (25%). A significant suppression in response was seen with 2 M urea (18%). Chlorpyrifos oxon was also applied to the tongue at 1 mM with significant enhancements in responses to: 100 mM sodium chloride (13%), 10 mM HCl (13%), and 10 mM sodium saccharin (10%). The 1 mM concentration of chlorpyrifos oxon also significantly suppressed responses to: 100 mM magnesium chloride (10%), 500 mM potassium chloride (15%), 50 mM MSG (28%), and 30 mM QHCl (24%) (Fig. 2).

Application of 1 mM carbofuran for 4 min to the tongue significantly blocked the responses to: 100 mM sodium chloride (8%), 300 mM calcium chloride (17%), 100 mM magnesium chloride (35%), 10 mM HCl (9%), 50 mM MSG (12%), and 100 mM sucrose (26%) (Fig. 3).

Application of 500 μM malathion for 4 min to the tongue significantly blocked responses to: 500 mM potassium chloride (14%) and 100 mM sucrose (5%), while enhancing the response to 100 mM magnesium chloride (13%). Malathion was also tested at 1 mM with significant blockages seen in the response to: 300 mM calcium chloride (9%) and 100 mM magnesium chloride (23%). Increases in response was seen with 10 mM sodium saccharin (21%) and 2 M urea (22%) (Fig. 4).

There were significant suppressions to several compounds after the application of 2 mM demeton. These suppressions were: 500 mM potassium chloride (15%) and 10 mM sodium saccharin (26%) (Fig. 5). Acephate and chlorpyrifos did not show any consistent results (Figs. 6 and 7).

The carbamate insecticide carbaryl (1 mM) significantly suppressed responses to 300 mM calcium chloride (11%), 100 mM magnesium chloride (19%), and 10 mM HCl (20%) (Fig. 8). Fenvalerate (1 mM) significantly enhanced the responses to 10 mM HCl (13%) and 500 mM potassium chloride (18%) (Fig. 9).

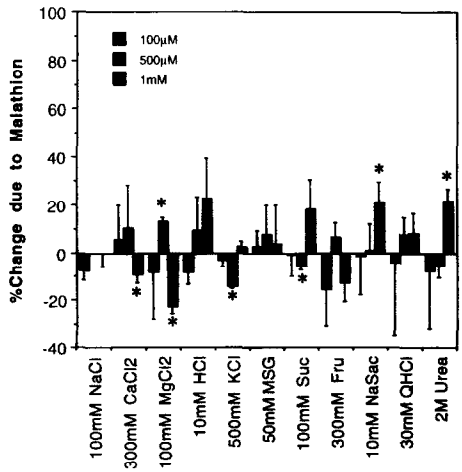

FIG. 4. Percent change in integrated chorda tympani responses after a 4-min application of 100 μM, 500 μM, and 1 mM malathion.

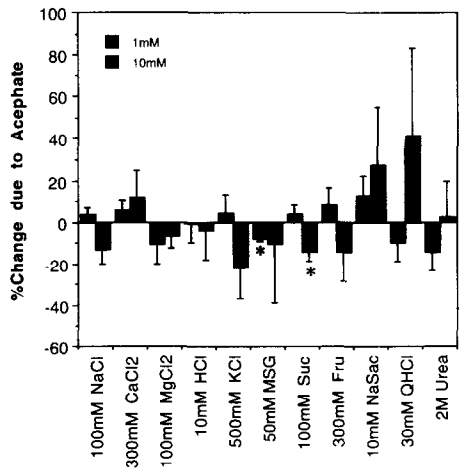

FIG. 6. Percent change in integrated chorda tympani responses after a 4-min application of 1 and 10 mM acephate.

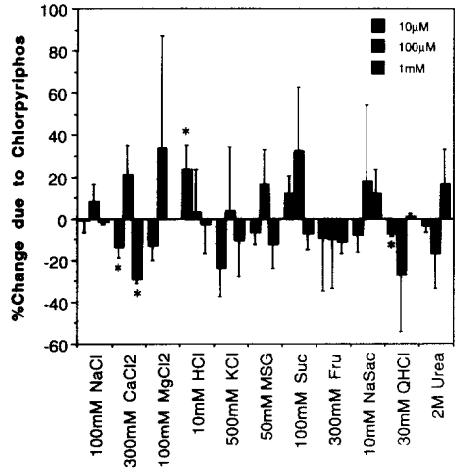

FIG. 7. Percent change in integrated chorda tympani responses after a 4-min application of 10 μM, 100 μM, and 1 mM chlorpyrifos.

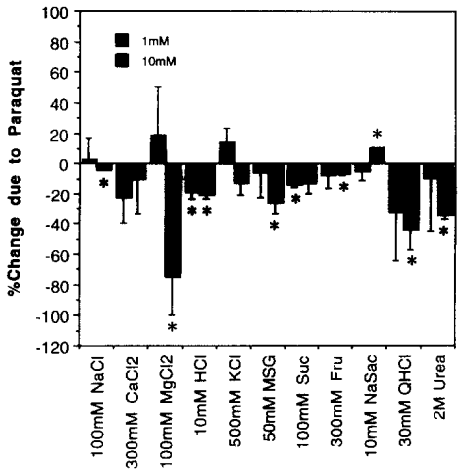

FIG. 10. Percent change in integrated chorda tympani responses after a 4-min application of 1 and 10 mM paraquat.

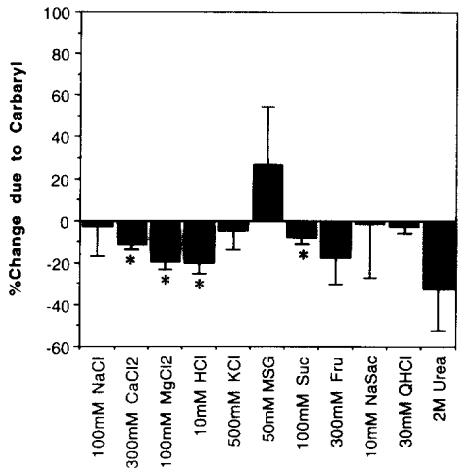

FIG. 8. Percent change in integrated chorda tympani responses after a 4-min application of 1 mM carbaryl.

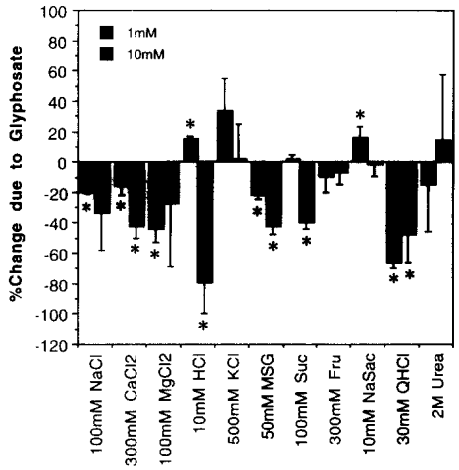

FIG. 11. Percent change in integrated chorda tympani responses after a 4-min application of 1 and 10 mM glyphosate.

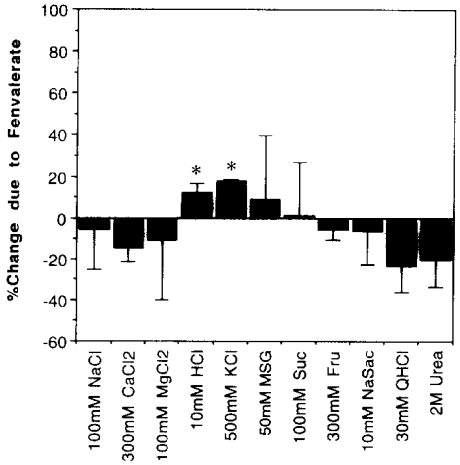

FIG. 9. Percent change in integrated chorda tympani responses after a 4-min application of 1 mM fenvalerate.

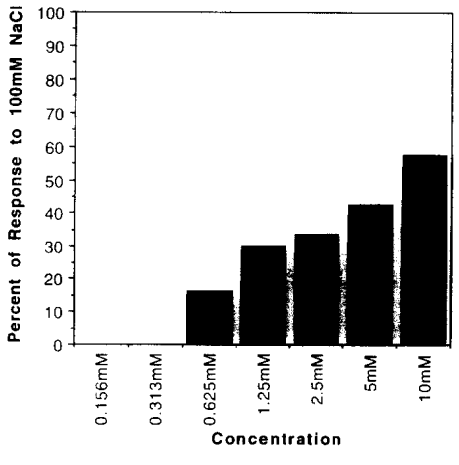

FIG. 12. Dose-response curve for paraquat, as a percent of 100 mM sodium chloride.

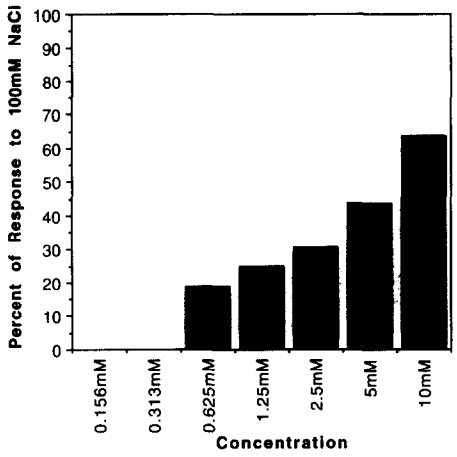

FIG. 13. Dose-response curve for glyphosate, as a percent of 100 mM sodium chloride.

Application of the herbicide paraquat (1 mM) significantly suppressed responses to: 10 mM HCl (19%) and 100 mM sucrose (14%). Paraquat was also tested at 10 mM with significant suppressions to: 100 mM magnesium chloride (75%), 10 mM HCl (21%), 50 mM monosodium glutamate (27%), 300 mM fructose (7%), 30 mM quinine HCl (44%), and 2 M urea (34%). A significant enhancement in response was seen with 10 mM sodium saccharin (10%) (Fig. 10). Glyphosate, another herbicide, was also tested at 1 and 10 mM. After the application of glyphosate at 1 mM, there were suppressions in responses to: 100 mM sodium chloride (20%), 300 mM calcium chloride (16%), 100 mM magnesium chloride (45%), 50 mM monosodium glutamate (22%), and 30 mM quinine HCl (66%). There were also significant increases in the responses to: 10 mM HCl (15%) and 10 mM sodium saccharin (16%). Glyphosate was also tested at 10 mM with significant decreases in the response to: 300 mM calcium chloride (43%), 10 mM HCl (79%), 50 mM monosodium glutamate (43%), 100 mM sucrose (40%), and 30 mM quinine HCl (48%) (Fig. 11).

A dose-response curve was determined for both paraquat and glyphosate at the concentrations 0.156, 0.313, 0.625, 1.25, 2.5, 5, and 10 mM. Sodium chloride was also tested at 100 mM as a control. Both herbicides gave an initial response at the concentration of 0.625 mM. The responses progressively increased from this concentration to the final concentration of 10 mM, which achieved approximately 60% of the level of 100 mM sodium chloride response in both cases (Figs. 12 and 13).

DISCUSSION

At the concentrations applied to the gerbil tongue in this study, the organophosphate methamidophos produced the greatest effect on taste by reducing electrophysiological activity to a broad range of compounds after 4-min applications. Significant reductions to a range of tastes were also found after treatment with carbaryl, carbofuran, fenvalerate, and the higher concentrations of the herbicides paraquat and glyphosate. For the 11 taste stimuli and 19 pollutant concentrations tested (209 experimental tests), a total of 74 significant changes (both suppressions and enhancements) were found after application of a pollutant to the gerbil tongue for 4 min. On the basis of chance, only 10 or 11 significant changes would be expected.

Although the majority of the statistically significant changes in electrophysiological activity to tastants indicated suppression of taste responses, there was considerable variability among pesticides and tastants. The lack of a clear trend in the direction of change in activity for a given taste stimulus after exposure to pesticides suggests that taste changes may be due to altered metabolic activity in taste cells or levels of neurotransmitters in a manner not related to mechanisms specific for taste transduction. Organophosphates are known to inhibit acetylcholinesterase (16,20,23,29,33,50) and neuropathy target esterase (NTE) activity (16,20,33,50). Certain organophosphates can also alter glutaminase activity levels (29) and lactate dehydrogenase levels (16). The carbamate insecticide carbaryl not only inhibits lactate dehydrogenase activity but also alters other metabolic profiles (30,31). The pyrethroid insecticide fenvalerate decreases adenylate energy charge (18), and the herbicide paraquat causes pulmonary lipid peroxidation and produces free radicals (36).

In conclusion, pesticides can significantly alter the pattern of electrophysiological activity to tastants (both reductions and enhancements) in a gerbil model. The alterations in taste are probably due to changes in metabolic activity in taste cells or levels of neurotransmitters, rather than modifications in the transduction systems. The variability of the pattern of effects from pesticide treatment may be responsible for dysgeusia that can occur after pesticide exposure (38,39).

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