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Temporal integration of pungency

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Abstract

Four experiments explored possible temporal summation in olfaction and the common chemical sense. In one experiment, participants judged the perceived magnitude of various concentrations and durations (1.25 - 3.75 s) of the pungent odorant ammonia and the nonpungent odorant isoamyl butyrate. The perceived magnitude of ammonia increased during an inhalation whereas the magnitude of isoamyl butyrate did not. Time-intensity trading relations for ammonia indicated nearly perfect temporal summation. In another experiment, modulation of the concentration of ammonia during an inhalation led to assessments of perceived magnitude that confirmed the high degree of temporal summation seen in the first experiment. That is, approximately equal time-integrated mass of inhaled ammonia led to approximately equal perceived intensity. A third experiment indicated that temporal summation for ammonia arose from its pungency rather than from its odor, a fourth that trigeminally-mediated reflex apnea in response to ammonia also exhibits temporal summation. The degree of temporal summation measured with the reflex came very close to that assessed psychophysically. When stimulated with ammonia, the common chemical sense behaves more like a total mass detector than a concentration detector. The investigation raises the possibility that the short-term sensory reaction to most pungent stimuli may follow this simple rule.

Introduction

Inhaled chemicals often give rise both to odor and to some pungency, a sensory attribute of the common chemical modality. Certain evidence indicates that the two attributes, odor and pungency, behave differently as a function of concentration and time. For example, pungency generally grows more rapidly than odor with concentration (Katz and Talbert, 1930). The pungent attribute also has a longer latency and, unlike odor, perceived pungency may grow from one inhalation to another (Cain, 1976; Cain and Murphy, 1980).

deVries and Stuiver (1961) reported that olfaction exhibits some temporal summation at threshold over durations up to a few hundred milliseconds. These investigators studied four odorants. Within the interval 5 - 20 ms, concentration could be traded almost perfectly with time in order to maintain detectability constant. At such short intervals, therefore, temporal summation was approximately perfect. At longer intervals, temporal summation declined progressively towards zero and number of molecules per unit time became a better determinant of threshold than merely number of molecules *per se*. Schneider *et al.* (1966) noticed the same trend toward diminishing temporal summation as duration increased over the range 250— 1000 ms. The electro-olfactogram (EOG), a gross receptor potential measured in response to suprathreshold stimulation, was found to reach its peak in human subjects in the time interval between ~ 100 ms and a few seconds, depending on the stimulus (Osterhammel *et al.*, 1969; Kobal, 1981).

If receptor events alone determined the point in time beyond which no further summation occurred perceptually (i.e., a critical duration), then we might expect this point to coincide roughly with that necessary to achieve peak amplitude of the EOG. Only one investigation has addressed the issue. Kobal (1981) measured the EOG to hydrogen sulfide and simultaneously obtained estimates of its perceived magnitude (one subject participated). Perceived magnitude did indeed increase through the very early stages of stimulation, but reached a peak faster than the EOG. This finding and others in the same investigation led Kobal to conclude that a fast-acting process of adaptation, arising from a neural locus central to the receptors, accounted for temporal disparity between the EOG and sensation. Nevertheless, Kobal's experiment gave some encouragement to the possibility that suprathreshold olfactory stimulation might lead to temporal integration over a period as long as 2 —3 s. An assertion of Bekesy's (1964) also gave such encouragement. Choice of stimulus could prove crucial here, but no rules for the choice have yet emerged.

Although temporal summation in the common chemical sense has received no quantitative attention, Elsberg *et al.* (1935) reported that the pungency aroused by a dry, odorized airstream blown into the nose typically increased during the first 20 s or so. The stimulating procedure could have led to pungency *via*

progressive drying of mucosal tissue as well as *via* chemical stimulation. Taken at face value, however, the observations of Elsberg *et al.* (1935) can be seen as support for the conclusion that the perceptual 'time-constant' for integration in the common chemical sense must exceed that of olfaction considerably.

The present investigation asked whether pungent and nonpungent odorants would give evidence of temporal summation throughout inhalations of durations common in everyday situations. The quantitative characteristics of summation held particular interest. If, for instance, there existed a simple reciprocity between concentration and time for constant perceived magnitude, then we could consider one modality or the other a mass detector rather than a concentration detector.

The possibility of objective measurement of temporal summation in the common chemical sense also held interest. Stimulation of the trigeminal nerve, the afferent pathway for the common chemical sense in the nose, can trigger various cardiac, vasomotor, and respiratory reflexes (Angell-James and Daly, 1975). Irritants of sufficient intensity can cause reflex inhibition of respiration, even transitory apnea, both in animals and human beings (Allen, 1928, 1929). Reflex transitory apnea in human beings apparently occurs *via* closure of the glottis (Ranson, 1921). Sensitivity of this reflex has, in previous experiments, fallen closely in register with psychophysical data on pungency (Cometto-Muniz and Cain, 1982; Garcia Medina and Cain, 1982). In brief, the reflex has occurred at a constant level of pungency. The results have raised the tempting possibility that the reflex could serve as an objective index of common chemical sense functioning. If psychophysical data imply temporal summation in the common chemical sense, then so should the reflex.

Experiment I

Method

Participants. Sixteen young adults (nine males, seven females; average age, 21.8 yr) participated.

Apparatus. Participants sat under a ventilated hood during the experiments. A two-channel air-dilution olfactometer delivered various concentrations of isoamyl butyrate (9.6, 24.8, and 71.9 ppm determined by gas chromatography) and ammonia (47, 99, 225, and 434 ppm determined by the NIOSH [1974] wet chemistry procedure). The three concentrations of isoamyl butyrate evoked no apparent pungency in the investigators whereas the four concentrations of ammonia did. The stimuli flowed from 7 mm diameter o.d. teflon tubes at 4 l min⁻¹.

Procedure. Each participant served in two sessions, identical except for order of stimulus presentation. At the beginning of a session, the participant learned to coordinate his/her inhalations to the beats of a metronome and had to exhibit an

ability to inhale with uniform flowrate throughout the durations of interest. We made no attempt to fix flowrate at any particular value. The participant could inhale at whatever flowrate seemed comfortable as long as he/she sought to maintain it constant. The goal was to achieve proportionality between duration and volume of air inhaled. A separate experiment performed with six participants showed that almost exact proportionality would occur when inhalations were paced by the metronome. In that experiment, participants inhaled odorless air through a Fleisch tube at the durations used in the odor/pungency experiment. Each participant made six or seven inhalations. Figure 1 shows the outcome, derived from the integrated area under flow-duration curves. On average, volume varied with time according to the relation $V = 0.29 t^{0.96}$, $r = 0.997$. For perfect proportionality, the exponent would equal 1.0.

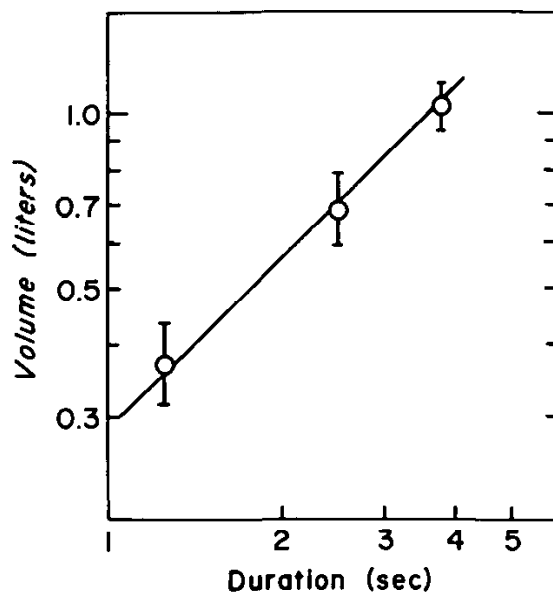


Figure 1. Relation between inhaled volume of air and duration. Variation, shown by standard errors, occurred almost exclusively in the levels rather than in the slopes of the relations for individual participants. Slope varied over the range $\pm 11\%$.

The durations of interest for the inhalation of ammonia equalled 1.25, 2.50, and 3.75 s. The durations of interest for the inhalation of isoamyl butyrate equalled 1.25 and 3.75 s. During testing, the participant picked up the appropriate tube upon signal, placed the tube into one nostril, and inhaled for 1, 2, or 3 beats of the metronome (1.25 s/beat). The first combination of concentration and duration was chosen irregularly. The participant assigned the intensity of this stimulus any number he/she deemed appropriate. Thereafter, the participant assigned numbers proportional to perceived magnitude, i.e., in accordance with the method of magnitude estimation (Stevens, 1975). The perceived magnitude of interest was that achieved at the end of an inhalation.

From trial to trial, the substance, ammonia or isoamyl butyrate, concentration, and duration varied in irregular order. The participant judged each combination four times per session. About 30 s elapsed between successive presentations.

Data analysis. For this experiment, and for experiments 2 and 3 below, the measure of interest was the geometric mean of the magnitude estimations given to a stimulus. Variability that arose from differences in the choice of the initial judgment in a session was eliminated by customary multiplicative means of normalization (Cain and Moskowitz, 1974).

Results

Figure 2 depicts how perceived magnitude varied with duration of inhalation. Ammonia showed clear growth with time. A threefold increase in duration caused, on average, a 61% increase in perceived magnitude. The increase varied systematically from 33% for the weakest concentration to 96% for the strongest. An analysis of variance revealed significant effects of concentration ($F[3,90] = 46.5, p < 0.0001$), time ($F[2,90] = 15.4, p < 0.0001$), and the interaction of concentration with time ($F[6,90] = 13.5, p < 0.0001$). In contrast, a threefold change in duration of isoamyl butyrate caused only a 7%, statistically insignificant, increase in perceived magnitude. An analysis of variance revealed

significance for concentration only ($F[2,30] = 34.9, p < 0.0001$).

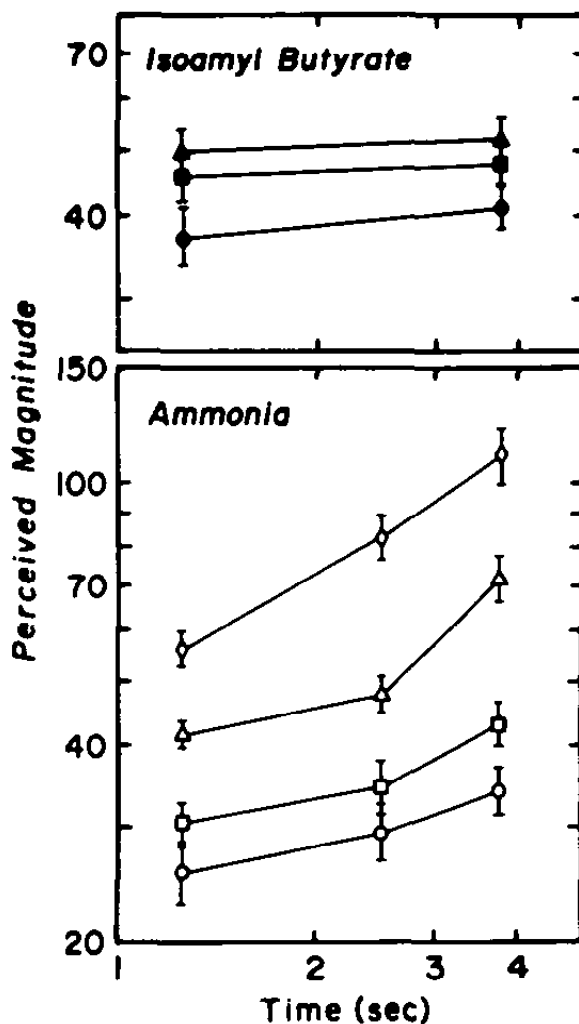


Figure 2. Perceived magnitude (geometric means \pm standard errors) as a function of duration of inhalation. The parameter in both graphs is concentration. From top to bottom, concentration equaled 71.9, 24.8, and 9.6 ppm, respectively, for isoamyl butyrate and 434, 225, 99, and 47 ppm, respectively, for ammonia.

Figure 3 displays perceived magnitude plotted against concentration for each duration. In the log-log coordinates of the figure, the functions for ammonia exhibit upward concavity, whereas those for isoamyl butyrate exhibit some downward concavity. Cain (1978) speculated that upward concavity may reflect increasing relative trigeminal (common chemical sense) involvement in the overall sensory impact of certain stimuli. As the third experiment in this report will show, the relative pungency of ammonia does indeed increase to a much greater degree than odor at higher concentrations.

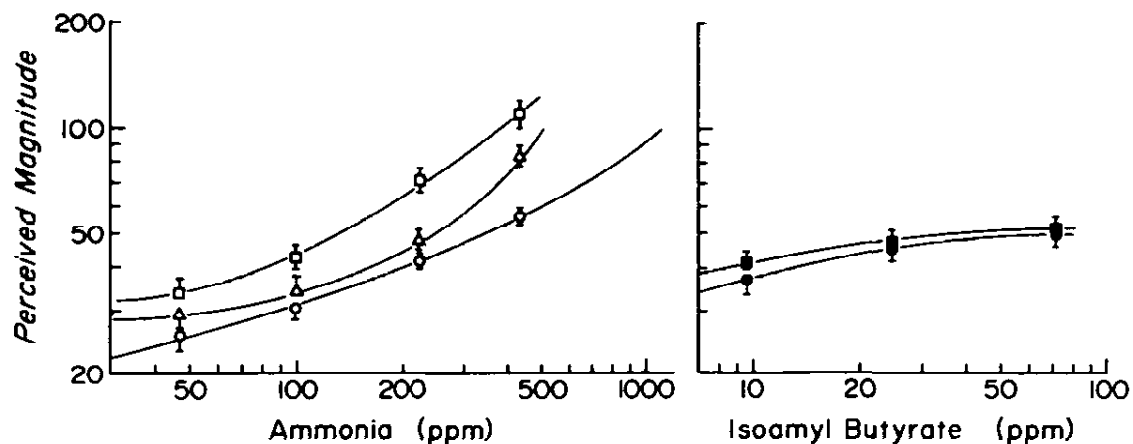


Fig. 3. Perceived intensity (geometric means \pm standard errors) as a function of concentration. The parameter is duration of inhalation. From top to bottom, duration of inhalation equalled 3.75, 2.50, and 1.25 s, respectively, for ammonia and 3.75 and 1.25 s, respectively, for isoamyl butyrate.

Isointensity (horizontal) cuts through the functions in Figure 3 permitted a view of how concentration of ammonia could be traded with duration in order to maintain perceived intensity constant. The trading relations for ammonia, shown in log-log coordinates in Figure 4, approximate straight lines for high intensities, but have downward concavity for low intensities. Whether or not such concavity represents the true form of the trading relations at low intensities can probably be settled only by the collection of more data. In any case, trading of concentration with time for the longest and shortest durations fell only slightly short of simple, or perfect, reciprocity. The average slope (exponent) of lines connecting the points at the shortest and longest durations equalled -0.96 , whereas -1.0 would represent perfect reciprocity.

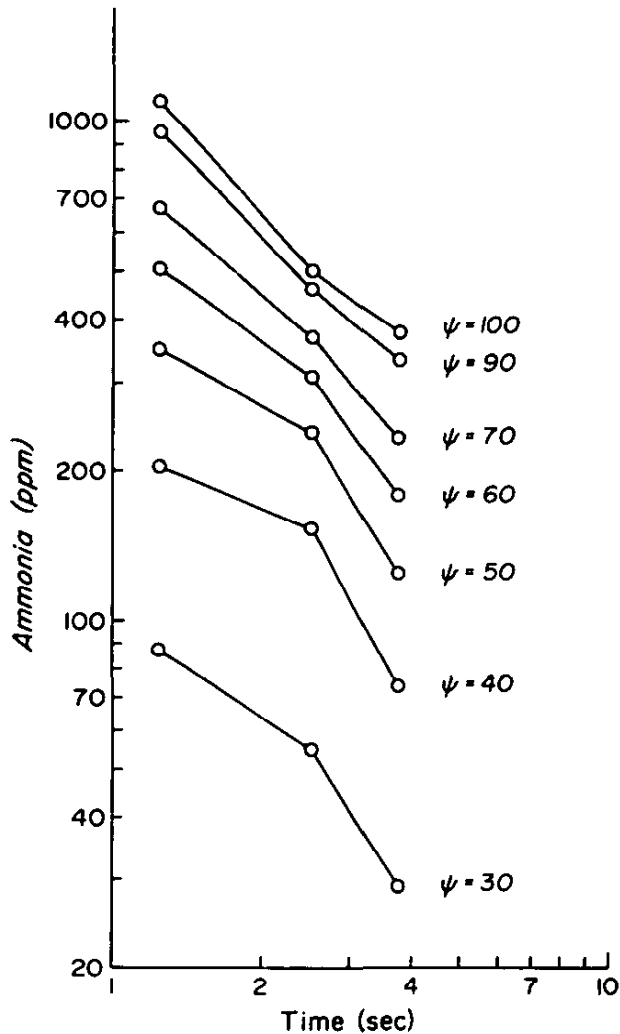


Figure 4. Trading relations showing how concentration could be traded with time in order to maintain perceived magnitude (ψ) constant at various levels.

Experiment 2

Perfect temporal summation would imply that perceived magnitude depends on the integrated mass of stimulus inhaled, irrespective of how the mass is distributed in time. Hence, a stimulus modulated in concentration over the course of an inhalation would lead to the same perceived intensity as an unmodulated stimulus of equal time-integrated mass.

In Experiment 1, ammonia exhibited almost, though not quite, perfect temporal summation for the two extreme durations, 1.25 and 3.75 s. We might therefore expect this substance to produce approximately equal intensities for approximately equal inhaled mass, modulated or not.

If, however, a counterposing process such as adaptation occurred concurrently with temporal integration, then modulated stimuli might fall below expected

values derived from Experiment 1. This might occur particularly in a case where a modulated stimulus started at a high level and ended at a lower level (Cain, 1970). The experiment below explored whether modulation of the concentration of ammonia during an inhalation would lead to perceived intensity anticipated on the basis of temporal summation alone.

Method

Participants. Eighteen young adults (6 males, 12 females; average age, 24.9 yr) participated in one session each. None had participated in the first experiment.

Procedure. The apparatus and psychophysical procedures were the same as in Experiment 1. In this case, however, the participant sampled the stimulus from two tubes successively on each inhalation. The first tube of a pair, presented for 2.5 s, delivered either air alone or 223 ppm ammonia and the second, presented for 1.25 s, delivered 125, 290, or 670 ppm ammonia. The participant learned at the outset to switch from one tube to the other virtually instantaneously. The six stimuli (0 ppm/125 ppm, 0 ppm/290 ppm, 0 ppm/670 ppm, 223 ppm/125 ppm, 223 ppm/290 ppm, and 223 ppm/670 ppm) were presented four times each in irregular order. The participant judged the magnitude achieved at the end of an inhalation.

Results

Figure 5, left side, depicts perceived magnitude versus the inhaled mass of ammonia. The circles represent the stimuli (0 ppm/125 ppm (7.2 μg integrated mass), 0 ppm/290 ppm (16.8 μg), and 0 ppm/670 ppm (58.9 μg). In those cases, stimulation with ammonia lasted 1.25 s. The triangles in the figure represent the stimuli 223 ppm/125 ppm (33.1 μg), 223 ppm/290 ppm (42.7 μg), and 223 ppm/670 ppm (64.8 μg). In those cases, stimulation with ammonia lasted 3.75 s.

If perfect temporal summation had occurred, then one function could have described all six points. This did not occur. Nevertheless, the data still implied considerable summation, an amount compatible with the data of experiment 1 (Figure 4). The degree of summation in Figure 4 equalled 0.94 (i.e., 94%) for the $\psi = 50$ contour, 0.95 for the $\psi = 70$ contour, and 0.97 for the $\psi = 100$ contour. These three contours are approximately equal to the perceived magnitudes of the long-duration stimuli of low (33.1 μg), middle (42.7 μg), and high (64.8 μg) mass, respectively, in Figure 5. Use of these fractions to adjust actual mass to 'effective' mass brought the long-duration stimuli more closely into register with the data for the short-duration stimuli (right side of Figure 5). Hence, within a first approximation, it appears that the perceived intensity of ammonia depends on time-integrated mass. Slight departures from this rule would seem a worthy topic for a comparison between ammonia and other pungent stimuli.

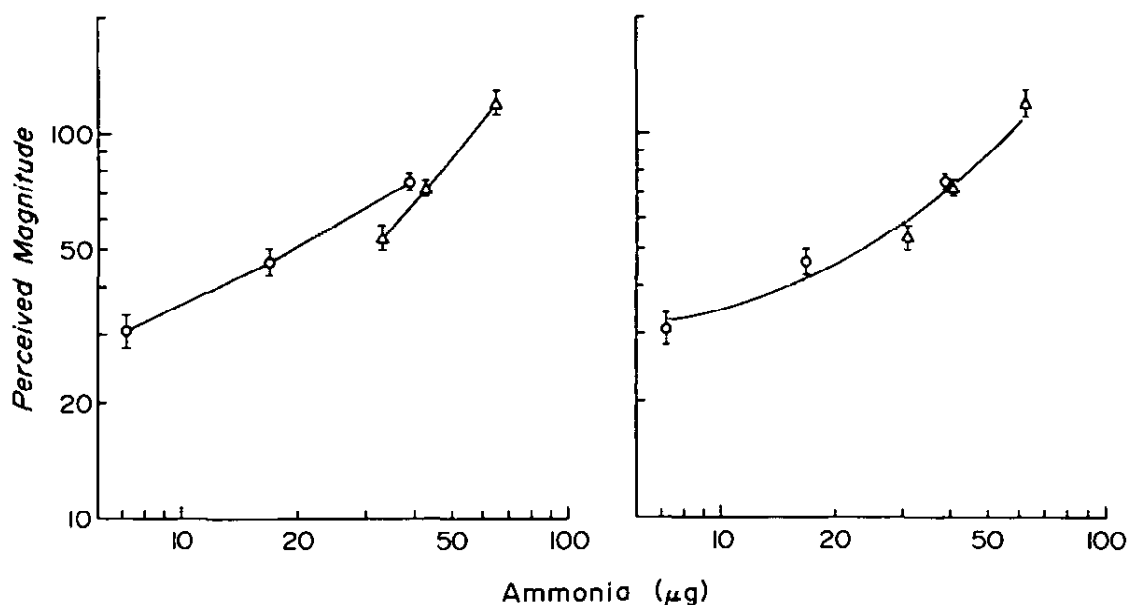


Figure 5. Left side shows perceived magnitude (geometric means \pm standard errors) of ammonia as a function of total mass inhaled in 3.75 s. Circles depict magnitude obtained from inhalation of air for 2.50 s followed immediately by 125, 290, or 670 ppm of ammonia for 1.25 s. Triangles depict magnitude obtained from inhalation of 233 ppm of ammonia for 2.50 s, followed immediately by 125, 290, or 670 ppm for 1.25 s. On the right side, the circles are plotted exactly as on the left side and triangles are plotted at values of integrated mass derived from the isointensity contours in Figure 3. The curve on the right side was fitted by eye.

Experiment 3

It seemed likely that the large degree of temporal integration found with ammonia in the first two experiments stemmed primarily from its influence on the common chemical sense rather than from its influence on olfaction. In order to assess this matter directly, the participants in experiment 3 judged pungency and odor separately (Cain, 1976).

Method

Participants. Ten young adults (6 males, 4 females; average age 27.1 yr) participated in one session each. Two had participated in the previous experiment.

Procedure. The stimuli comprised the following: 99 ppm of ammonia inhaled for 1.25 s, 99 ppm inhaled for 3.75 s, 434 ppm inhaled for 1.25 s, and 434 ppm

inhaled for 3.75 s. Each appeared five times per session in irregular order. Participants employed magnitude estimation to judge total intensity, intensity of odor, and intensity of pungency on each trial.

Results

The histogram in Figure 6 reveals the following: (1) total perceived intensity increased with duration of inhalation for both 99 and 434 ppm; (2) odor accounted for half or more of total intensity at the lower concentration, but far less than half at the higher concentration; and (3) unlike odor, pungency increased substantially with both duration and concentration. These results leave little doubt that the impact of ammonia on the common chemical sense accounts in large measure for the relatively rapid rate of growth of perceived intensity with concentration (see Figure 3) and for the rise in perceived magnitude with time (see Figure 2).

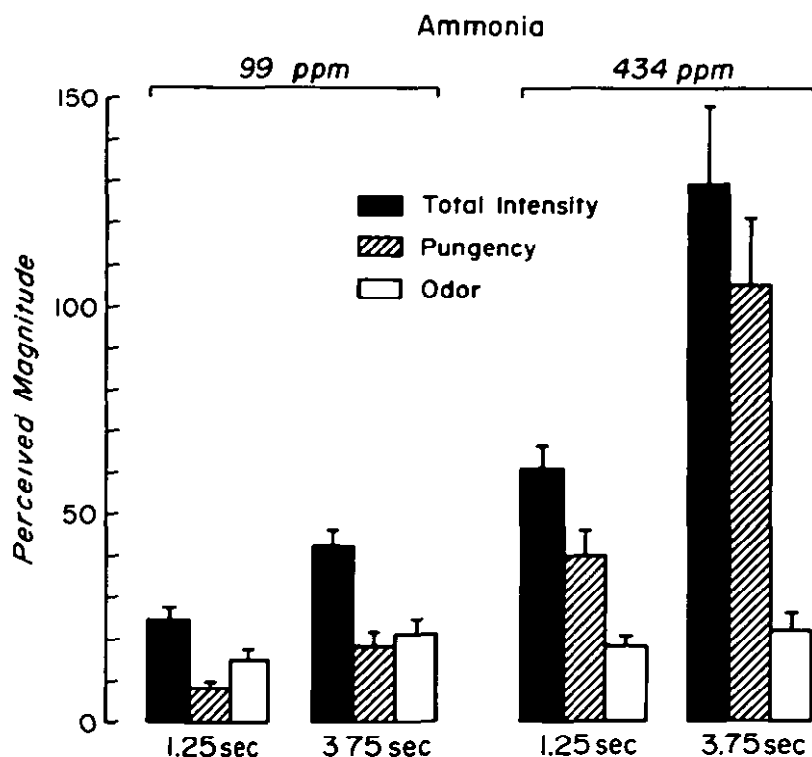


Figure 6. Perceived odor, pungency, and total intensity (geometric means \pm standard errors) for two concentrations of ammonia inhaled for two durations.

The failure of odor to show significant growth with concentration may have manifested an inhibitory influence of pungency on odor. In an experiment that manipulated pungency and odor independently, Cain and Murphy (1980) found a mutual inhibitory influence, with a stronger influence of pungency on odor than vice versa. If this were true in the present case, then use of a topical anesthetic in the nose should disinhibit odor. (Such anesthetics seem to leave olfaction

largely unimpaired.) We had no opportunity to pursue this problem, but consider it also worthy of study.

Experiment 4

Inhalation of an irritant at a high enough concentration will trigger a reflex momentary apnea (Dunn *et al.*, 1982). Virtually everyone has experienced this reflex though it has received little recent attention (Alarie, 1973). The reflex occurs readily, for example, upon the inhalation of smelling (ammonium) salts, where a prolonged inhalation is virtually impossible. The reflex appears to be trigeminally mediated and, as mentioned in the introduction, even shows close quantitative correspondence with aroused pungency (Cometto-Muniz and Cain, 1982; Garcia Medina and Cain, 1982). In view of this correspondence between psychophysical and reflex results, it appeared likely that the reflex would show temporal summation. That is, the concentration necessary to elicit the reflex during a long inhalation seemed likely to fall somewhat below the concentration necessary to elicit the reflex during a short inhalation.

Methods

Participants. Ten young adults (6 males, 4 females; average age 27 yr) participated in three sessions each. Five had participated in Experiments 2 or 3.

Apparatus. In addition to the apparatus used in the previous experiments, this experiment employed a thermocouple (Cu-Constantan) to monitor breathing. The thermocouple tip protruded through the inner wall of a small plastic sleeve that fitted snugly into one nostril, the unstimulated nostril. The arrangement allowed the thermocouple to sense the temperature of the air entering and exiting the nostril during inhalations and exhalations. The reference tip of the thermocouple sat in ice water. Voltage changes produced during breathing were recorded on a Grass polygraph. The pattern produced during normal or paced breathing had a sinusoidal character. Interruptions in inhalation produced by the reflex reaction to the pungent stimulus registered generally as notches in the otherwise smooth waves produced during inhalations.

Procedure. A trial consisted of either three successive inhalations of 1.5 s duration or three of 4.5 s. On the first inhalation of three, the participant inhaled from a tube that delivered just air. On the second inhalation, the participant inhaled from a tube that delivered one or another concentration of the ammonia, including 0 ppm (air). On the third inhalation, the participant inhaled again from the tube that delivered just air. This sequence offered the best means to detect the reflex when it occurred.

To determine the threshold for the reflex, the experimenter began with a test

concentration of 177 ppm and increased it by approximately 120 ppm increments until the reflex appeared. Test concentrations of 0 ppm occurred at random during the otherwise ascending series. A session entailed one determination of the threshold at the shorter duration of inhalation and one at the longer duration.

Results

For the shorter inhalations, threshold for the reflex equalled 795 ppm \pm 72 [SE] and occurred with an average latency of 1.33 s \pm 0.13 [SE]. For the longer inhalations, the threshold equalled 392 ppm \pm 34 [SE] and occurred with a latency of 2.86 s \pm 0.19 [SE]. This implies 94% temporal summation, an outcome that closely resembles the previous psychophysical data.

Discussion

The four experiments gave a rather uniform picture of temporal summation of pungency. The longer the pungent stimulus was inhaled, the greater was its perceived magnitude. This held true for durations up to 4.5 s and, judging from the functions in Figure 2, would probably hold true for considerably longer durations. It seems likely that a critical duration (a duration beyond which no further summation occurs), if one exists, will occur beyond time limits feasible with any single inhalation. It would therefore seem necessary to search for a critical duration only with a stimulus delivery system that would flow the stimulus into the nose for long periods of time and independently of the breathing cycle (see Mozell *et al.*, 1969). The humidity of any flow system must receive careful attention in order to preclude drying of the mucosa during stimulation. In such experiments, it would be of interest to learn whether the critical duration varies with concentration, whether it occurs at some criterion time-integrated mass, and whether it varies with the nature of the stimulus.

Although we found no evidence for temporal summation of odor, previous evidence indicates that it can occur (de Vries and Stuiver, 1961; Schneider *et al.*, 1966; Kobal, 1981). Its presence or absence during any interval presumably depends on the nature and level of the stimulus. The nature of the stimulus may have played a critical role in our finding of an absence of temporal summation of odor. Isoamyl butyrate yielded such flat psychophysical functions that even if time-integrated mass of odorant had determined perceived magnitude, the effect could have failed to become evident.

On the basis of personal observations, we can state that temporal summation occurs for the pungency of most odorous substances. A ready way to obtain pungency from odorants is to place the plain end of a male 14/35 standard taper joint into the neck of a bottle containing undiluted odorant and to inhale through the ground glass end, placing it in the nostril. This will cause pungency that

grows over time for virtually all odorous substances, including those that evoke no pungency when inhaled at the neck of the bottle without the glass joint.

For ammonia, it appeared generally true that temporal summation was nearly perfect. This finding would imply that the common chemical sense is virtually a mass detector rather than a concentration detector. Nevertheless, just as it is of interest to learn whether the critical duration varies with the nature of the stimulus, it would also be of interest to learn whether the approximation to perfect summation varies with the nature of the stimulus. If so, then it might become possible to implicate certain chemical properties (e.g., ability to break S-S linkages in proteins) or physicochemical properties (e.g., rate of diffusion through mucus and epithelial tissue) in the mechanism of stimulation of the common chemical sense (Alarie, 1973). At present, it is unclear whether inhaled molecules stimulate the free endings of the trigeminal nerve directly or via an intermediate step whereby the molecules first affect epithelial cells which in turn produce some stimulating (chemical) agent. Since the free nerve endings lie below the distal portion of epithelial cells (Beidler, 1965; Cauna *et al.*, 1969), either direct stimulation after diffusion into the epithelial layer or indirect stimulation could account for the relatively long latency of pungent sensations. Temporal properties, including latency, temporal summation, and any refractory period after stimulation, presumably hold clues to whether direct or indirect stimulation governs the sensory reaction to irritants. Such an issue has long been posed with respect to cutaneous pain (LaMotte, 1979).

Although low level pungency may not deserve the designation 'painful', moderate to high levels generally do. Should we therefore classify the common chemical sense as a pain modality? Jones (1954) seemed to favor that conclusion. If that is correct, then the production of pungency may signal tissue damage, just as painful stimulation of the skin generally does (Hardy *et al.*, 1952). Pain induced by immersion of the limb in hot water grows with time (Hardy *et al.*, 1968). This may be called temporal summation of pain, but such a benign term seems to neglect the likely possibility that the underlying phenomenon is progressive tissue damage. Such stimulation-induced hyperalgesia may also operate throughout the range of pungency. If so, then the term temporal summation would also seem inappropriate here. This matter awaits exploration.

This investigation marks the third time where the assessment of reflex transitory apnea yielded excellent agreement with psychophysical data. In the first case, the threshold for the reflex exhibited the same degree of bilateral integration as seen psychophysically (García Medina and Cain, 1982). In the second, cigarette smokers exhibited a higher threshold for the reflex than did nonsmokers, an outcome that also agreed quantitatively with psychophysical judgments of pungency in the two groups (Cometto-Muñiz and Cain, 1982). In the present case, the threshold displayed virtually the same degree of temporal summation as that seen psychophysically. These various findings lend strong encouragement to the conclusion that the reflex may offer an objective

physiological index of human chemosensory functioning.

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