Title

PART III. ASSESSING IRRITATION: Sensory Irritation: Relation to Indoor Air Pollution

Permalink

https://escholarship.org/uc/item/3w999934

Journal

Annals of the New York Academy of Sciences, 641(1 Sources of In)

ISSN

0077-8923 1749-6632

Authors

COMETTO-MUÑIZ, J. ENRIQUE
CAIN, WILLIAM S

Publication Date

1992-04-01

DOI

10.1111/j.1749-6632.1992.tb16539.x

Annals of the New York Academy of Sciences **641:**137-151, 1992

Sensory Irritation: Relation to Indoor Air Pollution

J. Enrique Cometto-Muñiz*[1] and William S. Cain*

John B. Pierce Laboratory and Yale University, New Haven, CT 06519
*Present Affiliation: University of California, San Diego, CA

Address for correspondence:

Dr. J. Enrique Cometto-Muñiz
John B. Pierce Laboratory
and Yale University
290 Congress Ave.
New Haven, CT 06519

Running Head: Sensory Irritation and Indoor Pollution

---

[1] Member of the Carrera del Investigador Científico, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), República Argentina.

Introduction

The existence of indoor air pollution in any particular place characteristically becomes known through complaints of occupants. It has become commonplace to hear that persons in an office experience eye, nose, and throat irritation, rhinitis, lassitude, loss of mental capacity, headache, and the like in connection with their occupancy of the space. The occupants normally suspect a chemical cause for their symptoms and in some instances a cause may prove specifiable. In many cases, however, no cause emerges. Indeed, even in the majority of cases where a cure such as increased ventilation may ameliorate symptoms, the actual offending agent eludes specification. Was it a vapor? A mixture of vapors? Vapors and particles?

Although scientists wish to link complaints to specific chemical causes, various sources of uncertainty plague the effort. First, the mere variety of the complaints engenders uncertainty. How should we count them? Should we aggregate complaints of fatigue with those of eye irritation or should we keep the complaints separate and seek a different cause for each? Does one complaint drive another? Does irritation cause lassitude? Second, people often experience the symptoms of concern outside problem buildings, as well as inside them. There is therefore little control over whether the symptoms, even if valid, arise strictly from exposure to agents in any particular building. Third, we can rarely validate the symptoms objectively. Without such means, we will always have the potential problem of over-reporting and embellishment. Although one person may seem more sensitive than another, the difference may lie in a greater proclivity to complain.

Although the varied complaints about indoor pollution may resist aggregation, sensory irritation figures prominently among them and even forms a common denominator. Irritation lends itself to measurement psychophysically in humans and animals, functionally in animals, and, when severe, clinically in humans. Because of its prominence and scientific accessibility, irritation can provide the focus for both basic and applied research on reactions to indoor contaminants. Only when the mechanism for irritation becomes known will we have the tools to avert irritative symptoms of indoor pollution completely. If irritation in buildings came about only from substances known as frank irritants, such as formaldehyde, we could avoid or eliminate the problem quickly. It appears instead that irritation from indoor pollution must arise from the aggregate effect of low concentrations of materials not normally considered irritants. Volatile organic compounds (VOCs), such as the ingredients in common solvents, ubiquitous in the indoor environment, are prime candidates.

Human studies of irritation can focus on the functional characteristics of the irritant sense (e.g., differences in stimulating potential from one chemical to another, change in sensory effect during exposure), on validation of symptoms, on mechanisms of irritation, and on screening of materials that might find their way into the indoor environment. Insofar as screening may rely upon psychophysical judgments of irritation, it may seem to have the same limitations as symptom reporting, viz., possible embellishment and over-reporting. If a person becomes irritated at his desk, he may call it a symptom. If he becomes irritated in an environmental chamber where he has given his consent to experience odors and irritation, he may call it a sensation. We can usefully distinguish between unintended sensations (symptoms) vs. intended ones. Until we develop objective measures of symptoms, we can try to create them in the lab and look at the functional rules of these sensations without the added burden of their occurring at the wrong time and in the wrong place. If we look at matters prospectively in such simulated environments, we can often learn things that are obscured in the field. The chamber approach has guided considerable research on ventilation requirements with a reasonably satisfactory outcome [12, 16]. Participants in such investigations seem to be surprisingly honest.

In this paper, we will review some salient functional aspects of the human irritant sense. Topics of interest will include a physical correlate for irritation, comparison of sensory irritation with olfaction, temporal properties of irritant perception, the psychophysical function for irritation, an objective measure of nasal irritation, and the role of age, smoking, and sex in irritant perception.

Nomenclature and Sensory Quality

Among persons interested in airborne chemoreception, the term irritant sense enjoys less popularity than the term common chemical sense. Parker [52] introduced the term common chemical sense (CCS) to describe the chemical sensitivity of the mucosae (ocular, nasal, oral, respiratory, genital, and anal). In the mucosae of the head and face - ocular, nasal, and oral - common chemical sensitivity is mediated by free nerve endings of the trigeminal nerve. The CCS lacks the specialized receptor cells of olfaction and taste.

Stimulation of the nasal CCS evokes sensations such as stinging, irritation, burning, piquancy, prickling, freshness, tingling and the like. As a group, these can be referred to as **pungent** sensations. There is also oral or buccal pungency.

Studies have separately addressed nasal pungency [6, 8, 18-20, 23, 27, 28, 50] and oral pungency [25, 32, 38, 43-45, 47, 55-57, 59, 60]. An almost odorless [13] and tasteless stimulus, the relatively harmless substance carbon dioxide, has served well for the study of nasal pungency [17, 24, 33, 37, 61, 62], oral pungency [22], and eye irritation [14].

Almost all airborne pungent substances can also stimulate the olfactory sense and will therefore often cause sensations from both sensory channels simultaneously [13]. In everyday life, we often fail to notice that a smell may have a little sharpness that implies co-activation of the CCS as well as olfaction. Personal products and cleaning products will sometimes signal their efficacy by a sharp "clean" or "refreshing" aroma that results from a CCS component. Commonly in psychophysical experiments, participants may be asked to assess the odorous and pungent attributes of a given stimulus separately [6, 18, 21, 23]. In a few studies, the use of subjects with unilateral destruction of the trigeminal nerve [4] or of subjects without olfactory function, i.e., anosmics [19, 20, 27, 28], have permitted a more direct look at the independent functioning of the nasal CCS.

Thresholds

For those substances with capacity to stimulate both olfaction and the CCS, the odor threshold typically falls below the pungency threshold . Until anosmic subjects were used, it was impossible to establish true nasal CCS thresholds. Anosmic persons lack the sense of smell either congenitally or secondary to another cause (e.g., head trauma, nasal sinus disease), so their only way to detect airborne chemicals is through the CCS.

We have charted how well normal, i.e., normosmic, and anosmic participants can detect homologous series of aliphatic alcohols and acetate esters [19, 20]. Figure 1 depicts thresholds for odor (normosmics), nasal pungency (anosmics), and eye irritation (obtained from a third, normosmic, group). Clearly, the thresholds decline with carbon chain-length. The eight-carbon molecule, for example, is a thousand or more times more effective than the one-carbon molecule, irrespective of the sense organ. Such a basic observation says much about the physicochemical basis for all three chemosensory reactions. The figure reveals as well a striking similarity in the absolute values of the thresholds for corresponding sensations in the acetate and alcohol series. The gap between odor and pungency, however, varies from about one order of magnitude to about four orders. Within the acetates series, eye irritation thresholds fell close to those for nasal pungency.

Insert Figure 1 about here

The thresholds in Figure 1 refer to vapor phase concentration. In order to reach the appropriate receptors, the stimuli must penetrate the mucus layer and then reach the lipid bilayer of the receptive membrane. The mucus comprises both viscous and watery layers [49, 53]. The effective concentration at the receptors will therefore reflect the net effect of partitioning between air and viscous mucus, between the viscous mucus and watery mucus, and between the watery mucus and the lipid membrane. The filtering effect will vary from very water soluble molecules - such as methanol or methyl acetate - to lipid soluble molecules - such as 1-octanol or dodecyl acetate.

Both the odor and pungency thresholds change logarithmically with carbon chain-length as do thresholds for narcosis [3, 34] and various toxic phenomena [48, 54]. The relative thresholds for such phenomena seem to result from an equilibrium between heterogeneous phases - reflecting water solubility, vapor pressure, surface activity, and partition coefficients - and are largely determined by a distribution equilibrium between an external phase and a susceptible biophase. In such cases, the thermodynamic activity of the stimulus is the same in all phases involved in such equilibrium - air, mucus, lipid membrane - while concentration can differ vastly from one phase to another.

The ratio of partial vapor pressure at a threshold effect - e.g., threshold of pungency or narcosis or toxicity - to saturated vapor pressure provides an index of thermodynamic activity, assuming ideal gas behavior. Figure 2 shows the odor, nasal pungency, and eye irritation thresholds expressed as percentage of saturated vapor at threshold. The thresholds for nasal pungency, unlike odor thresholds, are elicited at a fairly constant percentage of saturated vapor irrespective of molecular size or functional group. Eye irritation thresholds roughly coincide with those for nasal pungency, although there was slightly higher relative sensitivity for the middle acetates. In view of the strong role played by thermodynamic activity, it appears that the pungency evoked by these relatively nonreactive chemicals arises from a nonspecific, physical interaction between the stimuli and susceptible mucosal target sites.

Insert Figure 2 about here

Studies of anosmic persons offer a simple means to understand the functional characteristics of the nasal CCS.

Studies of additional chemical series in such subjects should eventually allow construction of quantitative structure-activity models for human pungency perception. The human data can be compared with relevant animal data when possible. Figure 3 shows the association between our nasal pungency thresholds and thresholds for the integrated trigeminal nerve response from rats (see [58]). The level of agreement encourages further comparisons.

Insert Figure 3 about here

Studies of the rules of additivity of pungency in mixtures should also stand high on the agenda. Regarding the possible role of VOCs in the creation of irritation, we need to ask whether subthreshold levels add up or even amplify each other to produce noticeable irritation. Do repetitive or continuous exposures to subthreshold concentrations increase sensitivity to those substances, so that they evoke pungency when they otherwise would not? Do the various mucosae - ocular, nasal, throat - differ in their sensitivity?

Suprathreshold Magnitude

Above the threshold, the perceived magnitude of nasal pungency increases with concentration much more sharply than does odor [4, 6, 8, 13, 17, 18, 21, 23, 24, 61, 62] (Figure 4). The function for pungency seems protective. A small increase in concentration may cause a rather large increase in sensation and hence in warning. By the same token, a fixed reduction in the concentration of an irritant will bring about a reasonable abatement in the magnitude of pungency (see [7]).

Insert Figure 4 about here

The bulk of the data imply that odor mixtures show hypoadditivity [42, 46]; the perceived odor intensity of a mixture falls below the sum of the perceived intensities of its components presented alone. Data on the perception of pungent odorants suggest that the nasal CCS shows mainly simple additivity and, at high concentrations, possibly hyperadditivity [21, 23] (see Figure 5). The perceived <u>pungency</u> of a mixture was as strong as the sum of the pungency of its components presented alone at the same concentration (simple additivity) or was even stronger (hyperadditivity). The perceived <u>odor</u> of the same mixtures always showed hypoadditivity.

Insert Figure 5 about here

Temporal Properties

For substances that can evoke both odor and irritation, the odor invariably precedes the irritation. This temporal disparity is apparently larger at lower levels of stimulation. At very low levels, the phenomena of adaptation to odor and temporal integration of pungency can cause odor to be present briefly, followed at some later point by irritation. Hence, after a very brief initial phase (seconds or less) of integration [26], odor may fade quickly [5, 41]. Nasal pungency, on the other hand, may begin after the odor fades and may grow sharply and over a long time [18]. Temporal integration in the CCS is apparent at the beginning of exposure (Figure 6) and can continue for hours, particularly for stimuli only very weak in initial pungency. Nevertheless, the CCS also does show adaptation. To illustrate, for a concentration of 1 ppm formaldehyde subjects found pungency to become progressively stronger for a while, then to remain about steady for a while, and finally to decline [14] (Figure 7).

Insert Figures 6 and 7 about here

Over long periods of exposure, subjects may develop tolerance to irritation, i.e., the same stimulus perceived as strongly irritating at first may become less so with exposure over a time-course that could range up to weeks and possibly even years. One such example is the relative insensitivity that smokers seem to develop to nasal pungency [17, 33].

Measurement of the Functional Status of the CCS

Standardized tests of smell functioning (e.g., [2, 9-11, 29-31]) ignore quantitative assessment of the nasal CCS largely because of the difficulty of measuring a CCS threshold without any contamination by olfaction. A reflex momentary apnea in response to CCS stimulation could offer an alternative. This reflex interruption of inhalation occurs when the stimulus reaches a critical and relatively high perceived strength [17, 18, 33, 37, 61] (see Figure 8). It holds promise as an objective indicator of the sensitivity of the CCS.

Insert Figure 8 about here

Results from the reflex transitory apnea have commonly agreed quantitatively with psychophysical data. For example, both types of measurements have indicated same degree of bilateral integration between the nostrils [37]. A higher threshold for the reflex found in smokers - compared to nonsmokers - agreed quantitatively with psychophysical judgments of perceived nasal pungency [17]. The threshold for the reflex displayed virtually the same degree of temporal integration as that seen psychophysically [18]; that is, time could be traded with concentration to achieve the threshold of the reflex or a criterion level of perceived pungency. Finally, higher CCS sensitivity in females than in males [33, 37] and in young subjects than in elderly subjects [61] with respect to the reflex apnea comported with psychophysical judgments of perceived nasal pungency [24, 61].

Age, Sex, and Smoking

Few studies have addressed whether smoking influences the perception of nasal pungency. Interestingly, one reason to focus attention on this matter (see [33]) was the existence of conflicting reports on the effect of smoking on olfaction [1, 35, 39, 40, 63]. A recent investigation suggests that smoking causes long term but reversible adverse effects on smell and that the negative results obtained in some of the previous studies might have derived from inclusion of persons with a history of smoking in the nonsmoking groups [36]. As indicated above, smokers have exhibited lower nasal CCS sensitivity than nonsmokers via the threshold for transitory apnea [17, 33]. Smokers also showed a decrease in the sensitivity from before to after smoking a single cigarette [17] (Table 1). Hence, in addition to a chronic reduction of pungency sensitivity measured after overnight abstinence from smoking, there is an acute desensitization. Modulation of CCS sensitivity by inhalation of various agents, including environmental tobacco smoke, would seem a suitable topic for further research.

Insert Table 1 about here

The psychophysical functions for nasal pungency in smokers and nonsmokers - whose thresholds for reflex apnea had also been measured - confirmed that smokers actually perceive irritants as weaker. Furthermore, the smokers found perceived pungency weaker by roughly a constant factor across concentrations [17] (Figure 9). The constancy of the difference suggested that the decreased sensitivity could have arisen from peripheral, possibly pre-neural factors - e.g., mucus thickness, lack of ciliary motility - which might play an obstructive role, impeding the transfer of molecules of inhaled irritants from the air to the free nerve endings.

Insert Figure 9 about here

The measurement of reflex apnea showed females to have a higher CCS sensitivity - i.e., to have lower thresholds - than males [33, 37]. Further studies revealed that females produced steeper psychophysical functions than males for nasal pungency, and that they experienced more nasal pungency from the same range of concentrations than their male counterparts [24] (Figure 10). No differences of either kind - steepness of the psychophysical function or relative magnitude of pungency - were observed between genders for buccally-evoked pungency.

Insert Figure 10 about here

Studies on the chemical senses and aging have generally focused on losses of olfaction and taste [15, 51, 64]. It is now clear, however, that aging takes a toll on the CCS also. One study that explored psychophysical functions for odor and nasal pungency in young (18-25 years) and elderly (65-83 years) subjects found chemical stimuli to seem only about half as intense to the elderly as to the young [62]. Using menthol, which elicits freshness via the CCS, Murphy [50] measured thresholds and psychophysical functions in young and elderly participants. The threshold was significantly elevated for the elderly and the median slope of the intensity function was steeper by a factor of two for younger adults.

When tested with the prickling and tingling stimulus carbon dioxide in the nose, a group of twenty elderly subjects (67 to 93 years) did not significantly differ from a group of twenty young persons (19 to 31 years) in their <u>detection</u> threshold [61]. However, the elderly did show a strong elevation of the <u>threshold</u> for the <u>reflex</u> transitory <u>apnea</u>, the average value for the elderly being 1.65 times that of the young (Figure 11). The elderly also showed a marked weakening of the perceived pungency of carbon dioxide (Figure 12).

Insert Figures 11 and 12 about here

Summary

All mucosae of the body possess chemical sensitivity provided by the common chemical sense (CCS). Airborne chemicals can stimulate the CCS through the ocular, nasal, and respiratory mucosae, evoking different pungent sensations, e.g., stinging, irritation, burning, piquancy, prickling, freshness, tingling. Pungent sensations elicited in the nose differ from odor sensations in various characteristics. They are achieved at considerably higher concentrations than those necessary to elicit odor, but they increase with the concentration of the stimulus in a steeper fashion than odor. Pungent sensations from mixtures of compounds show a higher degree of addition - relative to the pungency of the individual components - than that of odor sensations. Pungency is more resistant to adaptation than odor, and, unlike it, displays considerable temporal integration with continuous stimulation. Measurement of a reflex, transitory apnea produced upon inhalation of pungent chemicals holds promise as an objective indicator of the functional status of the CCS. Results from the measurement of this reflex have agreed quantitatively with sensory data in a number of studies, showing higher common chemical sensitivity in nonsmokers - compared to smokers -, in females - compared to males -, and in young adults - compared to elderly.

Research issues mentioned here include the following:

- We can rarely validate the symptoms putatively caused by indoor air pollution objectively. Without such means, we will always have the potential problem of over-reporting and embellishment. Although one person may seem more sensitive than another, the difference may lie in a greater proclivity to complain.

- Studies of anosmic persons offer a simple means to understand the functional characteristics of the nasal CCS. Studies of chemical series in such subjects should eventually allow construction of quantitative structure-activity models for human pungency perception. The human data can be compared with relevant animal data when possible.

- The rules of additivity of pungency in mixtures need explication. Regarding the possible role of VOCs in the creation of irritation, we need to ask whether subthreshold levels add up or even amplify each other to produce noticeable irritation. Do repetitive or continuous exposures to subthreshold concentrations increase sensitivity to those substances, so that they evoke pungency when they otherwise would not? Do the various mucosae - ocular, nasal, throat - differ in their sensitivity?

- Modulation of CCS sensitivity by long-term and short-term inhalation of various agents (e.g., environmental tobacco smoke) would seem a suitable topic for further research.

Acknowledgements

Preparation supported by NIH Grant DC00284.

Figure Legends

Figure 1. Comparison between two homologous series: a) normal aliphatic alcohols from 1 = methanol to 8 = 1-octanol and b) acetates from 1 = methyl acetate to 8 = octyl acetate in terms of their ability to provoke threshold nasal pungency in an anosmic group, and threshold odor in a normosmic group. Eye irritation thresholds - measured in another group - are also shown for selected acetates. From Cometto-Muñiz and Cain [20].

Figure 2. Comparison between the homologous series in terms of thermodynamic activity at threshold odor from normosmics, at threshold nasal pungency from anosmics, and at threshold eye irritation. Thermodynamic activity was calculated as the ratio between vapor concentration at threshold odor, nasal pungency, or eye irritation, over saturated vapor concentration, multiplied by 100. From Cometto-Muñiz and Cain [20].

Figure 3. Comparison of human psychophysical thresholds obtained from anosmic subjects [19] and rat neural (trigeminal nerve) thresholds [58] for aliphatic alcohols from methanol (upper right) to 1-octanol (lower left).

Figure 4. Psychophysical functions for the odor and nasal pungency of ammonia (adapted from Cometto-Muñiz and Hernández [23]).

Figure 5. Relationship between the perceived intensity (psi) of formaldehyde-ammonia binary mixtures judged for (A) total nasal intensity, (B) odor, and (C) pungency, and, for corresponding attributes, the sum of the perceived intensities of the components. Odors were always hypoadditive - i.e., points fell below the identity line - whereas pungency was mainly additive - i.e., points lay around the identity line - and possibly hyperadditive at high enough levels - i.e., points lay above the identity line. From Cometto-Muñiz and Hernández [23].

Figure 6. Perceived magnitude as a function of duration of inhalation for the benign odorant isoamyl butyrate and the pungent odorant ammonia. The parameter is concentration: 10 to 72 ppm for isoamyl butyrate and 47 to 434 ppm for ammonia. The perceived magnitude of the pungent odorant increased markedly with inhalation time - thereby showing temporal integration over the duration explored. From Cometto-Muñiz and Cain [18].

Figure 7. Perceived pungency of 1 ppm formaldehyde over one and one-half hours (from Cain et al. [14]).

Figure 8. Breathing patterns (three breaths) detected by changes in temperature of a nasal thermocouple before, during, and after presentation of the tingling stimulus carbon dioxide at a concentration sufficient to elicit reflex, transitory apnea. The upper tracing shows a typical response whereas the lower tracing

shows a particularly pronounced disruption. From Cometto-Muñiz and Cain [17].

Figure 9. Upper portion shows psychophysical functions for the pungency of carbon dioxide, the loudness of a 1,000 Hz tone, and the odor of isoamyl butyrate in nonsmokers (empty symbols) and smokers (filled symbols). The subjects were instructed to judge all three types of stimuli on a single scale of intensity where they chose the size and range of numbers to use (free modulus). This use of the psychophysical method of magnitude estimation is called magnitude matching because it permits subjects to indicate matching levels of sensory magnitude across modalities. The difference in the levels of the functions for the two groups reflects in part differences in the choice of modulus, the unit of subjective intensity, and a simple normalization procedure eliminates it. In this case, olfaction was considered the normalizing modality, and the normalizing constant that brought judgments of odor intensity into coincidence between smokers and nonsmokers was applied to the judgments of the other modalities as well. Lower portion shows the same functions as above for the nonsmokers. The functions for the smokers were transposed upward by a factor that brought the judgments of odor intensity from the smokers into coincidence with those of the nonsmokers. The nasal pungency functions in smokers and nonsmokers still displayed a significant vertical difference. The outcome revealed that nonsmokers perceive the same array of carbon dioxide

concentrations as more pungent than do smokers by a roughly constant factor. From Cometto-Muñiz and Cain [17].

Figure 10. Left part. Psychophysical functions obtained by magnitude matching of the nasal pungency of carbon dioxide (circles) and sweetness of sucrose (triangles) in males (filled symbols) and females (empty symbols). In this case, taste was the normalizing modality. Right part. This side depicts the same functions as on the left for males. The functions for females were multiplied by a factor that brought the judgments of sweetness intensity from females into coincidence with those of males. This normalization was performed under the assumption of no intensity differences in sweetness perception between genders, and allows a meaningful comparison of pungency intensity along the ordinate. From Cometto-Muñiz and Noriega [24].

Figure 11. Individual thresholds for reflex apnea in a group of young (circles) and elderly (squares) subjects . Arrows indicate the averages for the groups. From Stevens and Cain [61].

Figure 12. Magnitude estimation of pungency by young and elderly as a function of carbon dioxide concentration delivered to the nose. Taste was the normalizing modality. From Stevens and Cain [61].

References

1. Ahlström, R., B. Berglund, U. Berglund, T. Engen and T. Lindvall. 1987. A comparison of odor perception in smokers, nonsmokers, and passive smokers. Am J Otolaryngol **8:** 1-6.

2. Amoore, J. E. and B. G. Ollman. 1983. Practical test kits for quantitatively evaluating the sense of smell. Rhinology **21:** 49-54.

3. Brink, F. and J. M. Posternak. 1948. Thermodynamic analysis of the relative effectiveness of narcotics. J Cell Comp Physiol **32:** 211-233.

4. Cain, W. S. 1974. Contribution of the trigeminal nerve to perceived odor magnitude. Ann N Y Acad Sci **237:** 28-34.

5. Cain, W. S. 1974. Perception of odor intensity and the time course of olfactory adaptation. ASHRAE Trans **80:** 53-75.

6. Cain, W. S. 1976. Olfaction and the common chemical sense: some psychophysical contrasts. Sens Process **1:** 57-67.

7. Cain, W. S. 1978. The odoriferous environment and the application of olfactory research. In Handbook of Perception. Vol.6A, Tasting and Smelling. E. C. Carterette and M. P. Friedman, Ed.: 277-304. Academic Press. New York.

8. Cain, W. S. 1981. Olfaction and the common chemical sense: similarities, differences, and interactions. In Odor Quality and Chemical Structure. H. R. Moskowitz and C. B. Warren, Ed.: 109-121. American Chemical Society. Washington, DC.

9. Cain, W. S. 1989. Testing olfaction in a clinical setting. ENT J **68:** 316-328.

10. Cain, W. S., J. Gent, F. A. Catalanotto and R. B. Goodspeed. 1983. Clinical evaluation of olfaction. Am. J. Otolaryngol. **4:** 252-256.

11. Cain, W. S., J. F. Gent, R. B. Goodspeed and G. Leonard. 1988. Evaluation of olfactory dysfunction in the Connecticut Chemosensory Clinical Research Center. Laryngoscope **98:** 83-88.

12. Cain, W. S., B. P. Leaderer, R. Isseroff, L. G. Berglund, R. J. Huey, E. D. Lipsitt and D. Perlman. 1983. Ventilation requirements in buildings: I. Control of occupancy odor and tobacco smoke odor. Atmos Environ **17:** 1183-1197.

13. Cain, W. S. and C. L. Murphy. 1980. Interaction between chemoreceptive modalities of odour and irritation. Nature **284:** 255-257.

14. Cain, W. S., L. C. See and T. Tosun. Year. Irritation and odor from formaldehyde: Chamber studies. In IAQ'86. Managing Indoor Air for Health and Energy Conservation. 126-137. American Society of Heating, Refrigerating and Air-Conditioning Engineers, Inc. Atlanta, Georgia, USA.

15. Cain, W. S. and J. C. Stevens. 1989. Uniformity of olfactory loss in aging. In Annals of the New York Academy of Sciences. Vol. 561. Nutrition and the Chemical Senses in Aging: Recent Advances and Current Research Needs. C. Murphy, W. S. Cain and D. M. Hegsted, Ed.: 29-38. The New York Academy of Sciences. New York.

16. Cain, W. S., T. Tosun, L. C. See and B. P. Leaderer. 1987. Environmental tobacco smoke: Sensory reactions of occupants. Atmos Environ **21:** 347-353.

17. Cometto-Muñiz, J. E. and W. S. Cain. 1982. Perception of nasal pungency in smokers and nonsmokers. Physiol Behav **29:** 727-731.

18. Cometto-Muñiz, J. E. and W. S. Cain. 1984. Temporal integration of pungency. Chem Senses **8:** 315-327.

19. Cometto-Muñiz, J. E. and W. S. Cain. 1990. Thresholds for odor and nasal pungency. Physiol Behav **48:** 719-725.

20. Cometto-Muñiz, J. E. and W. S. Cain. 1991. Nasal pungency, odor, and eye irritation thresholds in homologous acetates. Pharmacol Biochem & Behav **39:** (in press).

21. Cometto-Muñiz, J. E., M. R. García-Medina and A. M. Calviño. 1989. Perception of pungent odorants alone and in binary mixtures. Chem Senses **14:** 163-173.

22. Cometto-Muñiz, J. E., M. R. García-Medina, A. M. Calviño and G. Noriega. 1987. Interactions between CO_2 oral pungency and taste. Perception **16:** 629-640.

23. Cometto-Muñiz, J. E. and S. M. Hernández. 1990. Odorous and pungent attributes of mixed and unmixed odorants. Percept Psychophys **47:** 391-399.

24. Cometto-Muñiz, J. E. and G. Noriega. 1985. Gender differences in the perception of pungency. Physiol Behav **34:** 385-389.

25. Cowart, B. 1987. Oral chemical irritation: Does it suppress taste intensity? Chem Senses **12:** 467-479.

26. de Vries, H. and M. Stuiver. 1961. The absolute sensitivity of the human sense of smell. In Sensory Communication. W. A. Rosenblith, Ed.: 159-167. Wiley. New York.

27. Doty, R. L. 1975. Intranasal trigeminal detection of chemical vapors by humans. Physiol Behav **14:** 855-859.

28. Doty, R. L., W. E. Brugger, P. C. Jurs, M. A. Orndorff, P. F. Snyder and L. D. Lowry. 1978. Intranasal trigeminal stimulation from odorous volatiles: psychometric responses from anosmic and normal humans. Physiol Behav **20:** 175-185.

29. Doty, R. L., R. E. Frye and U. Agrawal. 1989. Internal consistency reliability of the fractionated and whole University of Pennsylvania Smell Identification Test. Percept Psychophys **45:** 381-384.

30. Doty, R. L., M. G. Newhouse and J. D. Azzalina. 1985. Internal consistency and short-term test-retest reliability of the University of Pennsylvania Smell Identification Test. Chem Senses **10:** 297-300.

31. Doty, R. L., P. Shaman and M. Dann. 1984. Development of the University of Pennsylvania smell identification test: A standardized microencapsulated test of olfactory function. Physiol Behav **32:** 489-502.

32. Dunér-Engström, M., B. B. Fredholm, O. Larsson, J. M. Lundberg and A. Saria. 1986. Autonomic mechanisms underlying capsaicin induced oral sensations and salivation in man. J Physiol **373:** 87-96.

33. Dunn, J. D., J. E. Cometto-Muñiz and W. S. Cain. 1982. Nasal reflexes: Reduced sensitivity to CO_2 irritation in cigarette smokers. J appl Toxicol **2:** 176-178.

34. Ferguson, J. Year. Relations between thermodynamic indices of narcotic potency and the molecular structure of narcotics. In Proc Symp sur le Mechanisme de la Narcose. 25-39. CNRS. Paris.

35. Fordyce, I. D. 1961. Olfaction tests. Brit J Industr Med **18:** 213-215.

36. Frye, R. E., B. S. Schwartz and R. L. Doty. 1990. Dose-related effects of cigarette smoking on olfactory function. JAMA **263:** 1233-1236.

37. García-Medina, M. R. and W. S. Cain. 1982. Bilateral integration in the common chemical sense. Physiol Behav **29:** 349-353.

38. Green, B. G. 1986. Sensory interactions between capsaicin and temperature in the oral cavity. Chem Senses **11:** 371-382.

39. Joyner, R. E. 1963. Olfactory acuity in industrial population. J Occup Med **5:** 37-42.

40. Joyner, R. E. 1964. Effect of cigarette smoking on olfactory acuity. Arch Otolaryngol **80:** 576-579.

41. Köster, E. P. 1971. Adaptation and Cross-Adaptation in Olfaction. Ph.D. thesis. University of Utrecht.

42. Laing, D. G., H. Panhuber, M. E. Willcox and E. A. Pittman. 1984. Quality and intensity of binary odor mixtures. Physiol Behav **33:** 309-319.

43. Lawless, H. 1984. Oral chemical irritation: Psychophysical properties. Chem Senses **9:** 143-155.

44. Lawless, H., P. Rozin and J. Shenker. 1985. Effects of oral capsaicin on gustatory, olfactory and irritant sensations and flavor identification in humans who regularly or rarely consume chili pepper. Chem Senses **10:** 579-589.

45. Lawless, H. and D. A. Stevens. 1984. Effects of oral chemical irritation on taste. Physiol & Behav **32:** 995-998.

46. Lawless, H. T. 1987. An olfactory analogy to release from mixture suppression in taste. Bull Psychonom Soc **25:** 266-268.

47. Lawless, H. T. and D. A. Stevens. 1988. Responses by humans to oral chemical irritants as a function of locus of stimulation. Percept & Psychophys **43:** 72-78.

48. McCreery, M. J. and W. A. Hunt. 1978. Physico-chemical correlates of alcohol intoxication. Neuropharmacology **17:** 451-461.

49. Morgan, K. T., D. L. Patterson and E. A. Gross. 1986. Responses of the nasal mucociliary apparatus to airborne irritants. In Toxicology of the Nasal Passages. C. S. Barrow, Ed.: 123-133. Hemisphere Publishing Corporation. Washington, DC.

50. Murphy, C. 1983. Age-related effects on the threshold, psychophysical function, and pleasantness of menthol. J Gerontol **38:** 217-222.

51. Murphy, C., W. S. Cain and D. M. Hegsted (Eds.). 1989. Annals of the New York Academy of Sciences. Vol. 561: Nutrition and the Chemical Senses in Aging: Recent Advances and Current Research Needs. The New York Academy of Sciences. New York.

52. Parker, G. H. 1912. The reactions of smell, taste, and the common chemical sense in vertebrates. J Acad Nat Sci Phila **15:** 221-234.

53. Proctor, D. F. 1982. The mucociliary system. In The nose. Upper Airway Physiology and the Atmospheric Environment. D. F. Proctor and I. Andersen, Ed.: 245-278. Elsevier Biomedical Press. Amsterdam.

54. Rang, H. P. 1960. Unspecific drug action. The effects of a homologous series of primary alcohols. Br J Pharmacol **15:** 185-200.

55. Rozin, P., L. Ebert and J. Schull. 1982. Some like it hot: A temporal analysis of hedonic responses to chili pepper. Apetite **3:** 13-22.

56. Rozin, P., M. Mark and D. Schiller. 1981. The role of desensitization to capsaicin in chili pepper ingestion and preference. Chem Senses **6:** 23-31.

57. Rozin, P. and D. Schiller. 1980. The nature and acquisition of a preference for chili pepper by humans. Motivat & Emot **4:** 77-101.

58. Silver, W. L., J. R. Mason, M. A. Adams and C. A. Smeraski. 1986. Nasal trigeminal chemoreception: Responses to n-aliphatic alcohols. Brain Res **376:** 221-229.

59. Sizer, F. and N. Harris. 1985. The influence of common food additives and temperature on threshold perception of capsaicin. Chem Senses **10:** 279-286.

60. Stevens, D. A. and H. T. Lawless. 1986. Putting out the fire: Effects of tastants on oral chemical irritation. Percept & Psychophys **39**: 346-350.

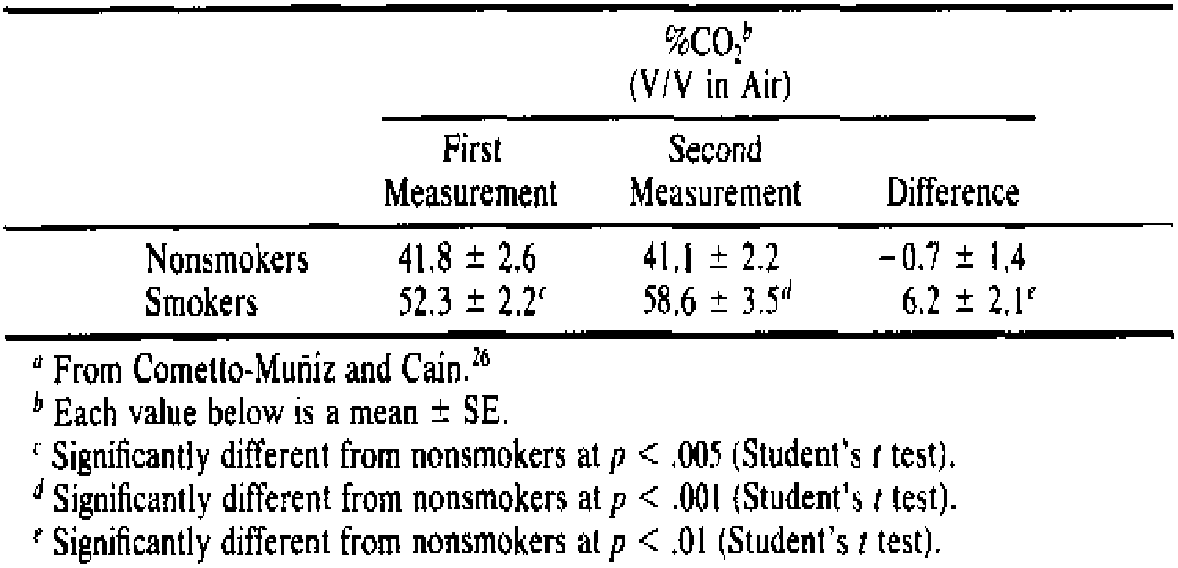
61. Stevens, J. C. and W. S. Cain. 1986. Aging and the perception of nasal irritation. Physiol Behav **37**: 323-328.

62. Stevens, J. C., A. Plantinga and W. S. Cain. 1982. Reduction of odor and nasal pungency associated with aging. Neurobiol Aging **3**: 125-132.

63. Venstrom, D. and J. E. Amoore. 1968. Olfactory threshold in relation to age, sex or smoking. J Food Sci **33**: 264-265.

64. Wysocki, C. J. and A. N. Gilbert. 1989. National Geographic Smell Survey. Effects of age are heterogenous. In Annals of the New York Academy of Sciences. Vol. 561: Nutrition and the Chemical Senses in Aging: Recent Advances and Current Research Needs. C. Murphy, W. S. Cain and D. M. Hegsted, Ed.: 12-28. The New York Academy of Sciences. New York.

Table 1. Threshold values for the Nasal Reflex before (First Measurement) and after (Second Measurement) a period of resting for the Nonsmokers and a period of smoking for the Smokers[a].



	%CO_2[b] (V/V in Air)		
	First Measurement	Second Measurement	Difference
Nonsmokers	41.8 ± 2.6	41.1 ± 2.2	−0.7 ± 1.4
Smokers	52.3 ± 2.2[c]	58.6 ± 3.5[d]	6.2 ± 2.1[e]

[a] From Cometto-Muñiz and Cain.[26]

[b] Each value below is a mean ± SE.

[c] Significantly different from nonsmokers at $p < .005$ (Student's *t* test).

[d] Significantly different from nonsmokers at $p < .001$ (Student's *t* test).

[e] Significantly different from nonsmokers at $p < .01$ (Student's *t* test).

FIGURE 1

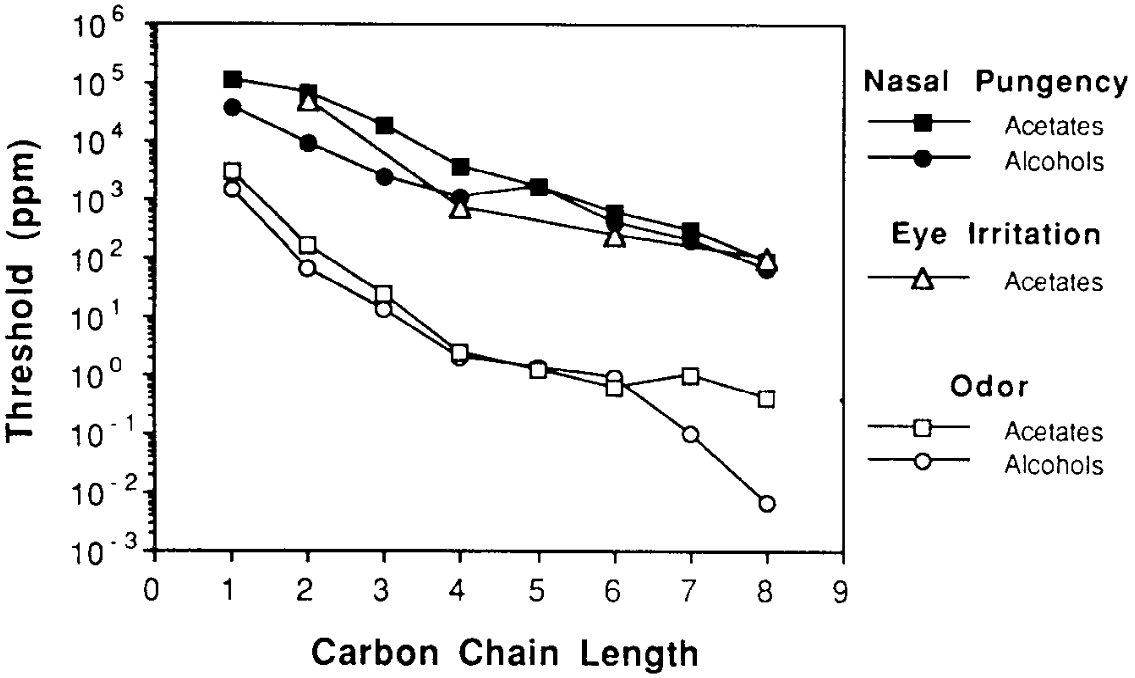

Threshold (ppm)
10^6
10^5
10^4
10^3
10^2
10^1
10^0
10^-1
10^-2
10^-3
0
1
2
3
4
5
6
7
8
9
Carbon Chain Length
Nasal Pungency
Acetates
Alcohols
Eye Irritation
Acetates
Odor
Acetates
Alcohols

FIGURE 2

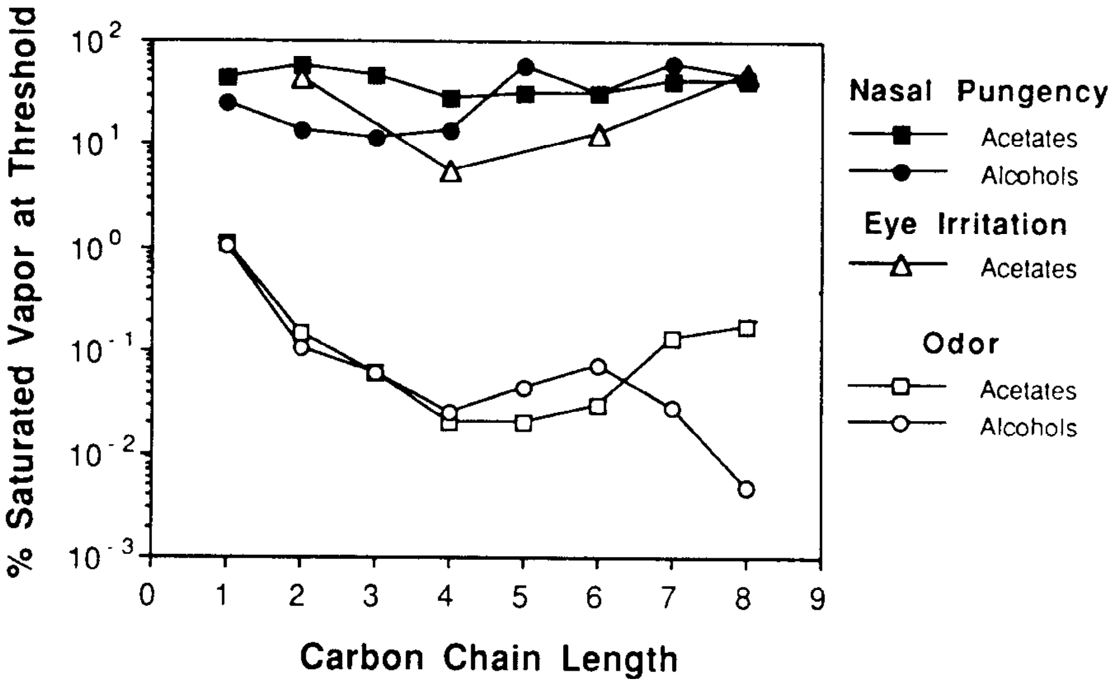

% Saturated Vapor at Threshold
10 2
10 1
10 0
10 -1
10 -2
10 -3
0
1
2
3
4
5
6
7
8
9
Carbon Chain Length
Nasal Pungency
Acetates
Alcohols
Eye Irritation
Acetates
Odor
Acetates
Alcohols

FIGURE 3

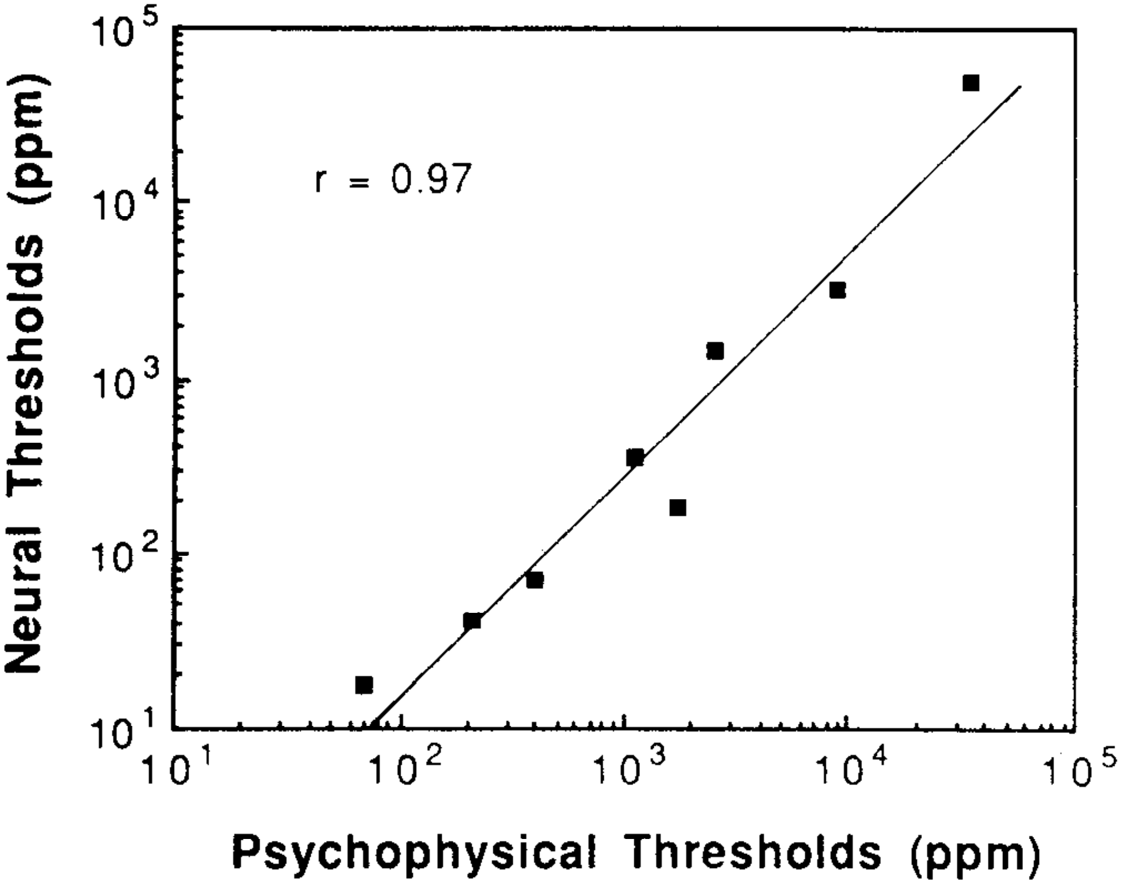

r = 0.97
Neural Thresholds (ppm)
Psychophysical Thresholds (ppm)
10^1
10^2
10^3
10^4
10^5
10^1
10^2
10^3
10^4
10^5

FIGURE 4

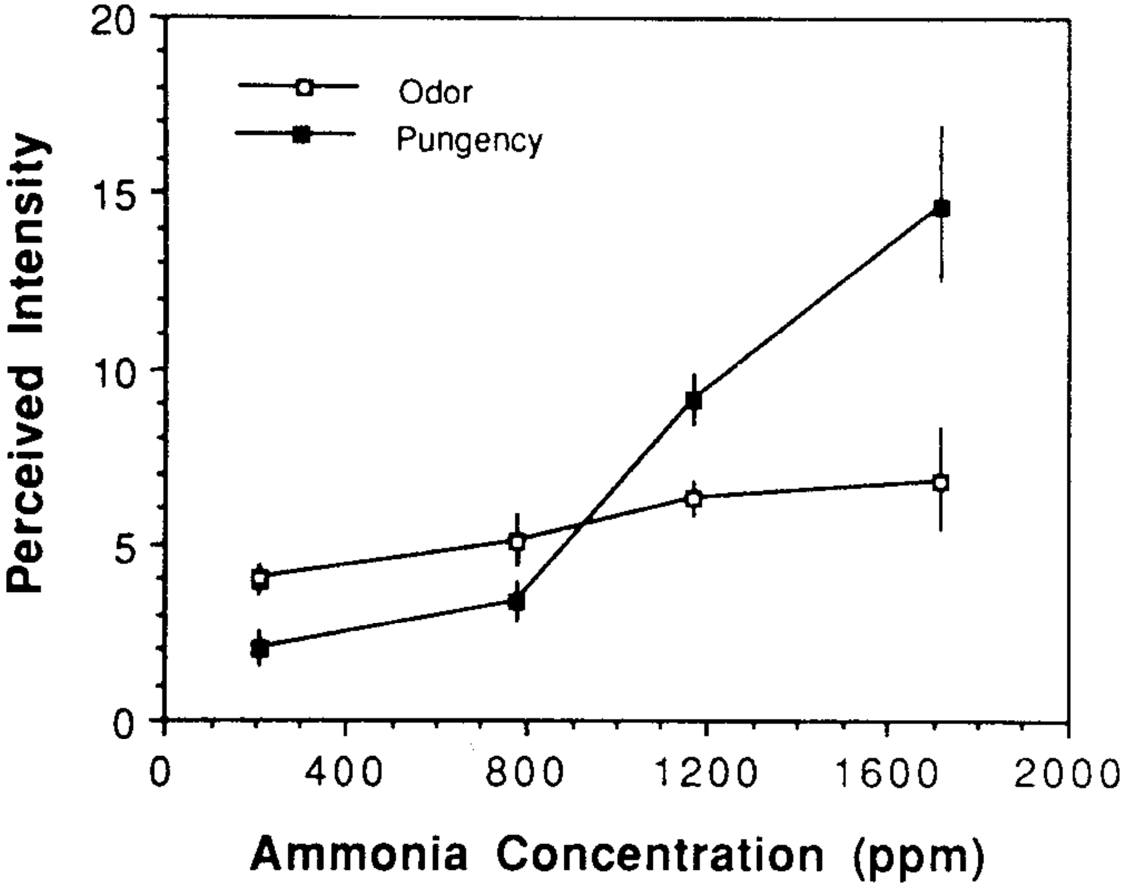

20
15
10
5
0
Perceived Intensity
0
400
800
1200
1600
2000
Ammonia Concentration (ppm)
Odor
Pungency

FIGURE 5

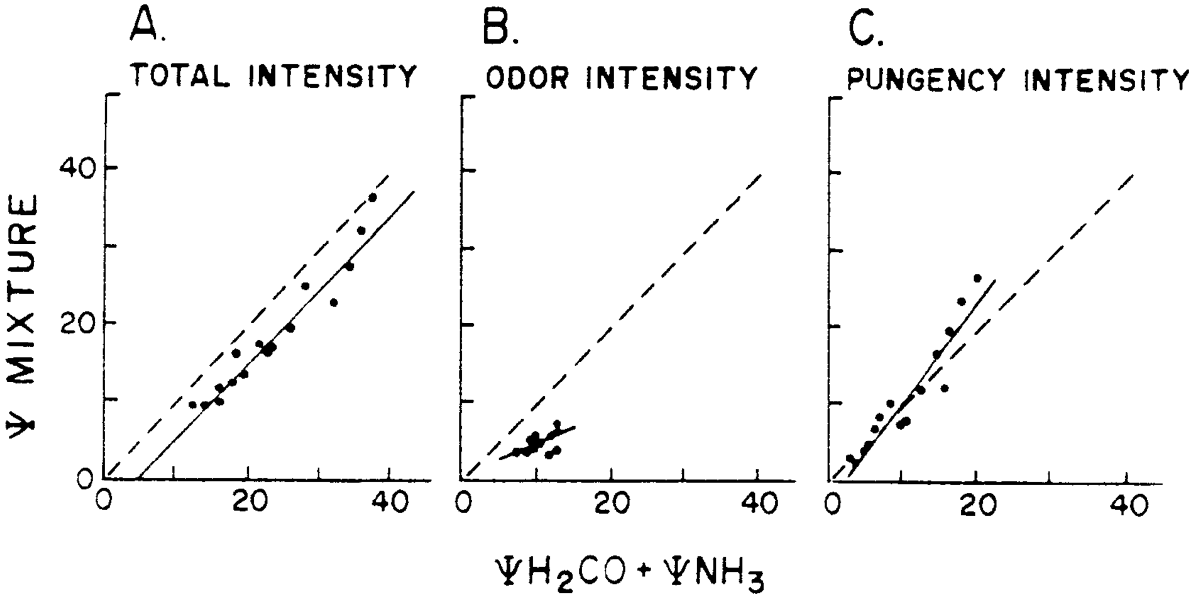

A.
TOTAL INTENSITY
B.
ODOR INTENSITY
C.
PUNGENCY INTENSITY
Ψ MIXTURE
0
20
40
0
20
40
$\Psi H_2CO + \Psi NH_3$

FIGURE 6

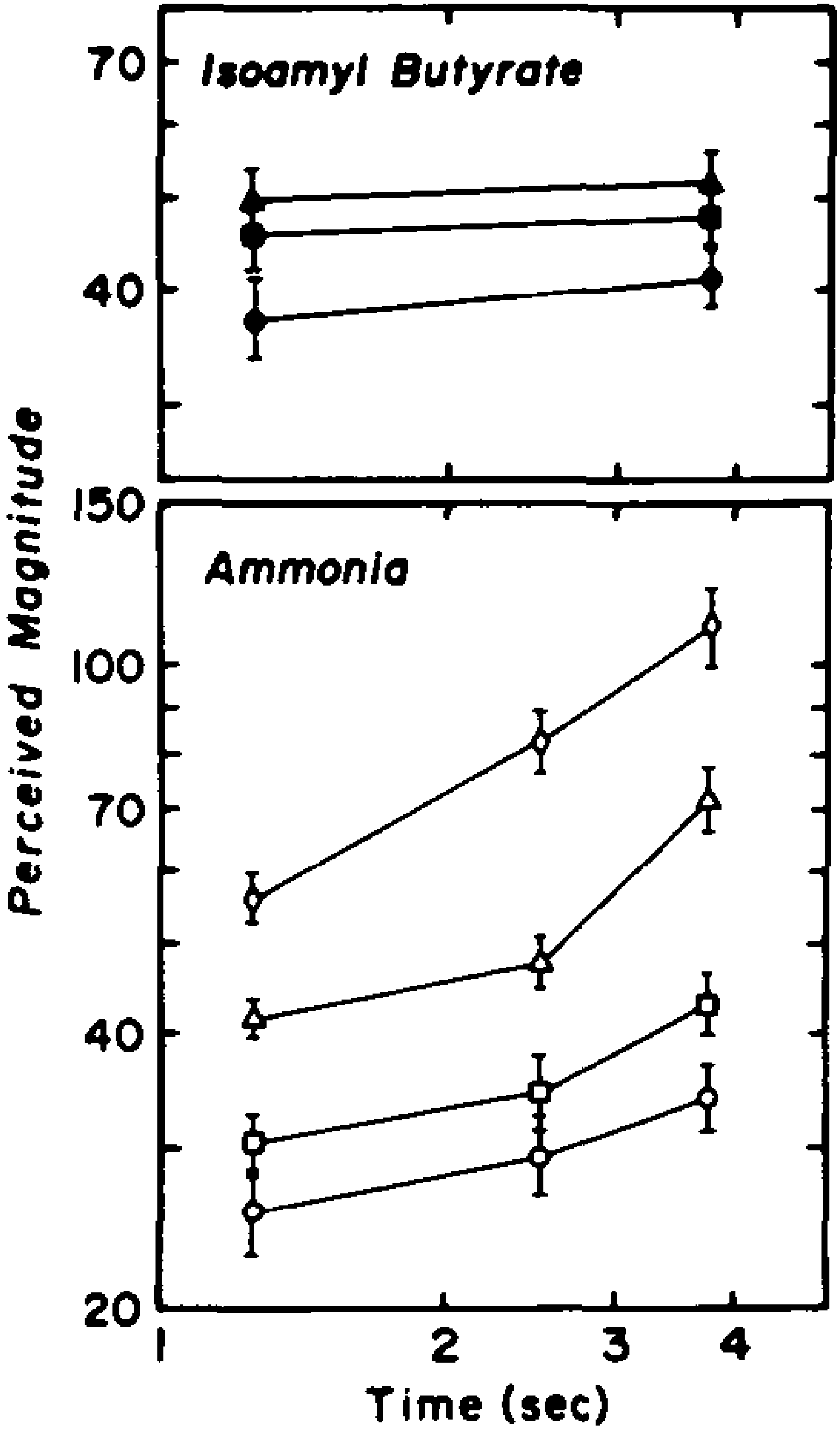

Isoamyl Butyrate
Ammonia
Perceived Magnitude
70
40
150
100
70
40
20
1
2
3
4
Time (sec)

FIGURE 7

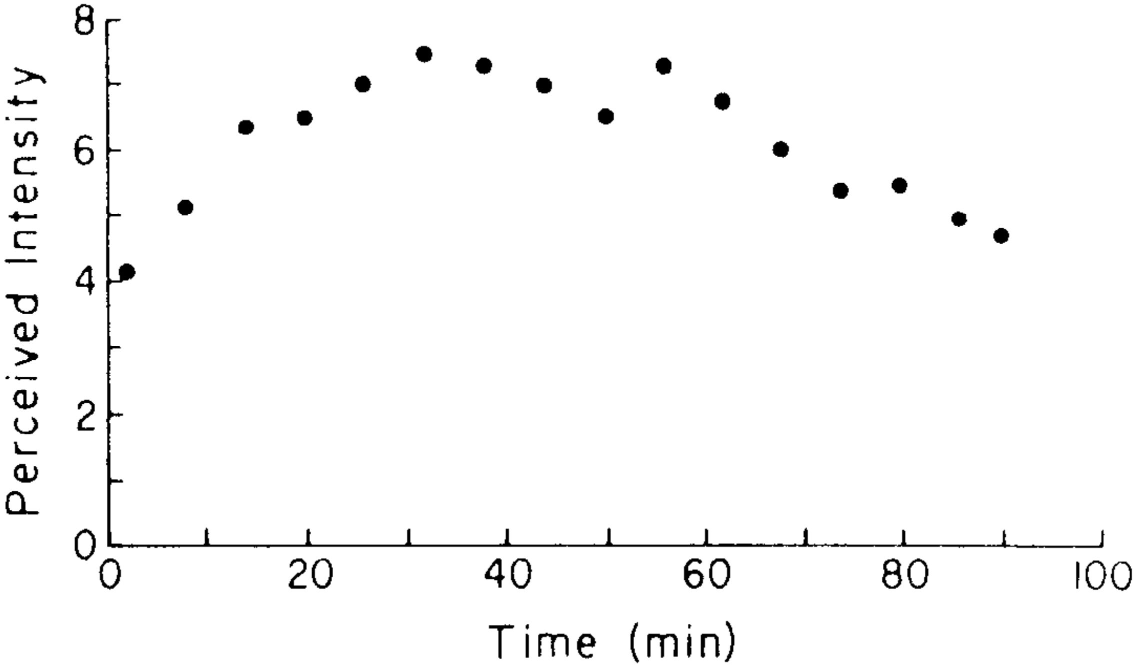


FIGURE 8

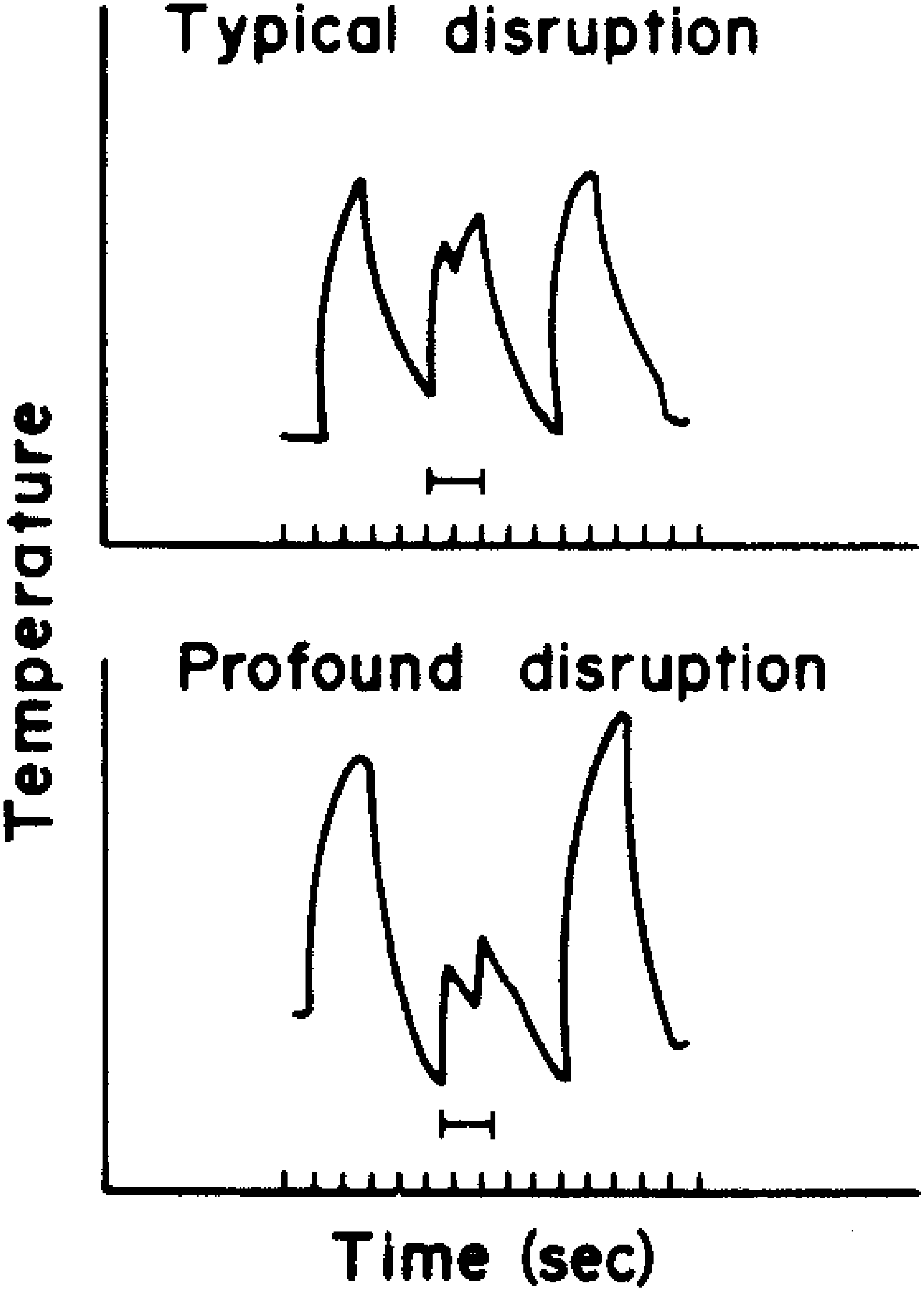

Typical disruption
Profound disruption
Temperature
Time (sec)

FIGURE 9

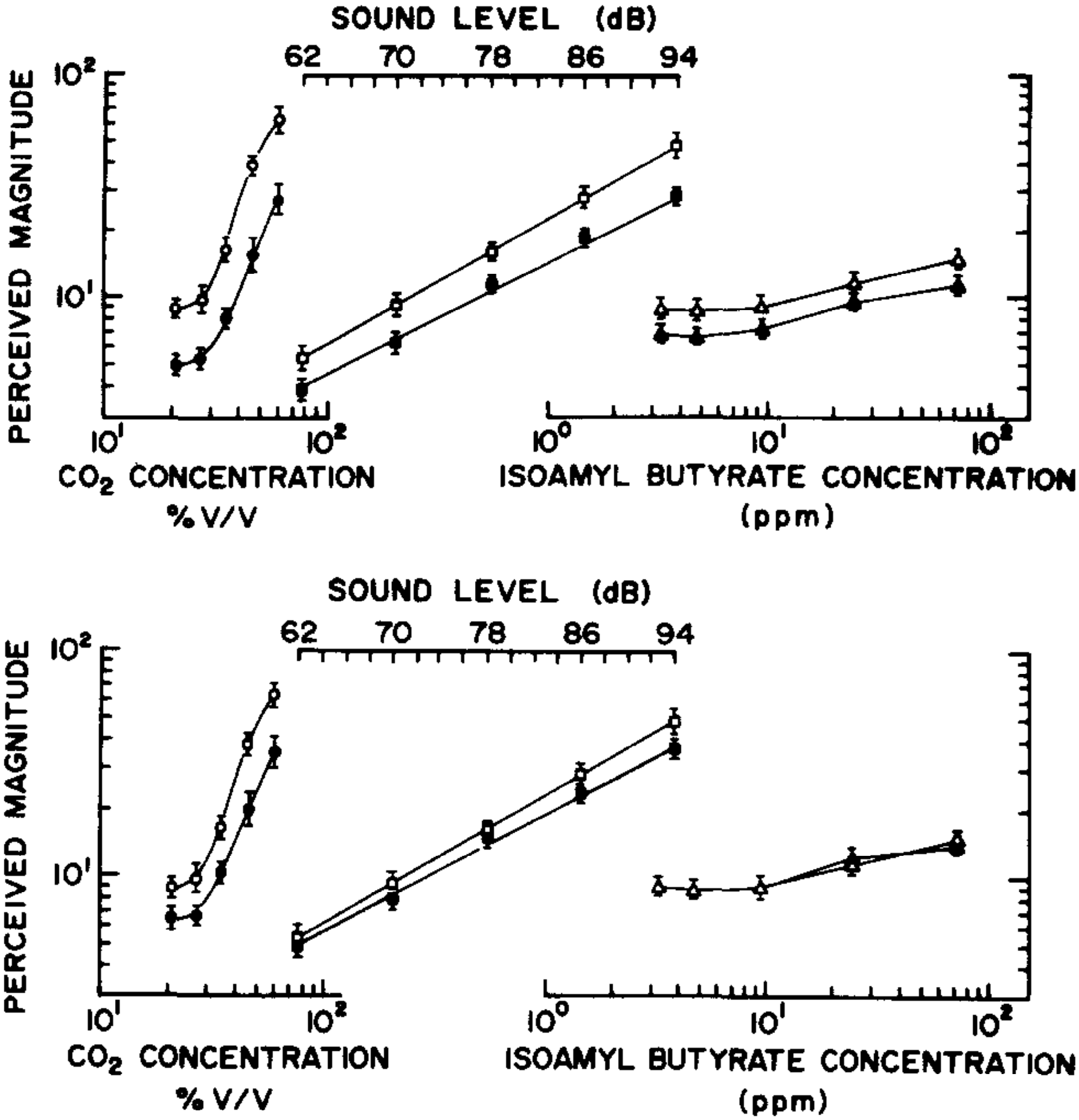

SOUND LEVEL (dB)
62
70
78
86
94
PERCEIVED MAGNITUDE
10^2
10^1
10^1
10^2
CO₂ CONCENTRATION
% V/V
10^0
10^1
10^2
ISOAMYL BUTYRATE CONCENTRATION
(ppm)
SOUND LEVEL (dB)
62
70
78
86
94
PERCEIVED MAGNITUDE
10^2
10^1
10^1
10^2
CO₂ CONCENTRATION
% V/V
10^0
10^1
10^2
ISOAMYL BUTYRATE CONCENTRATION
(ppm)

FIGURE 10

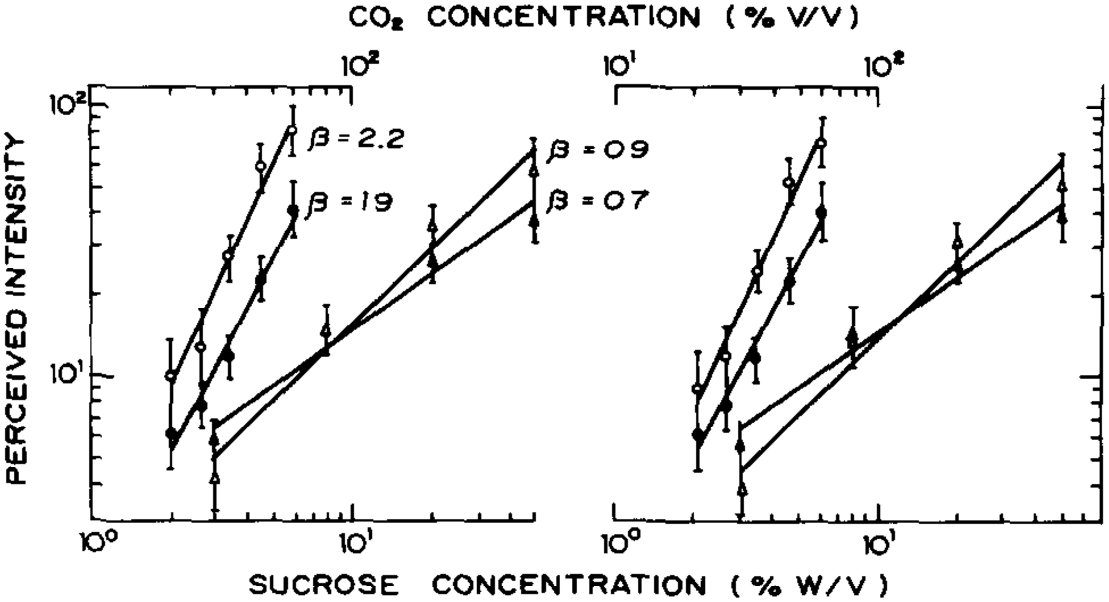
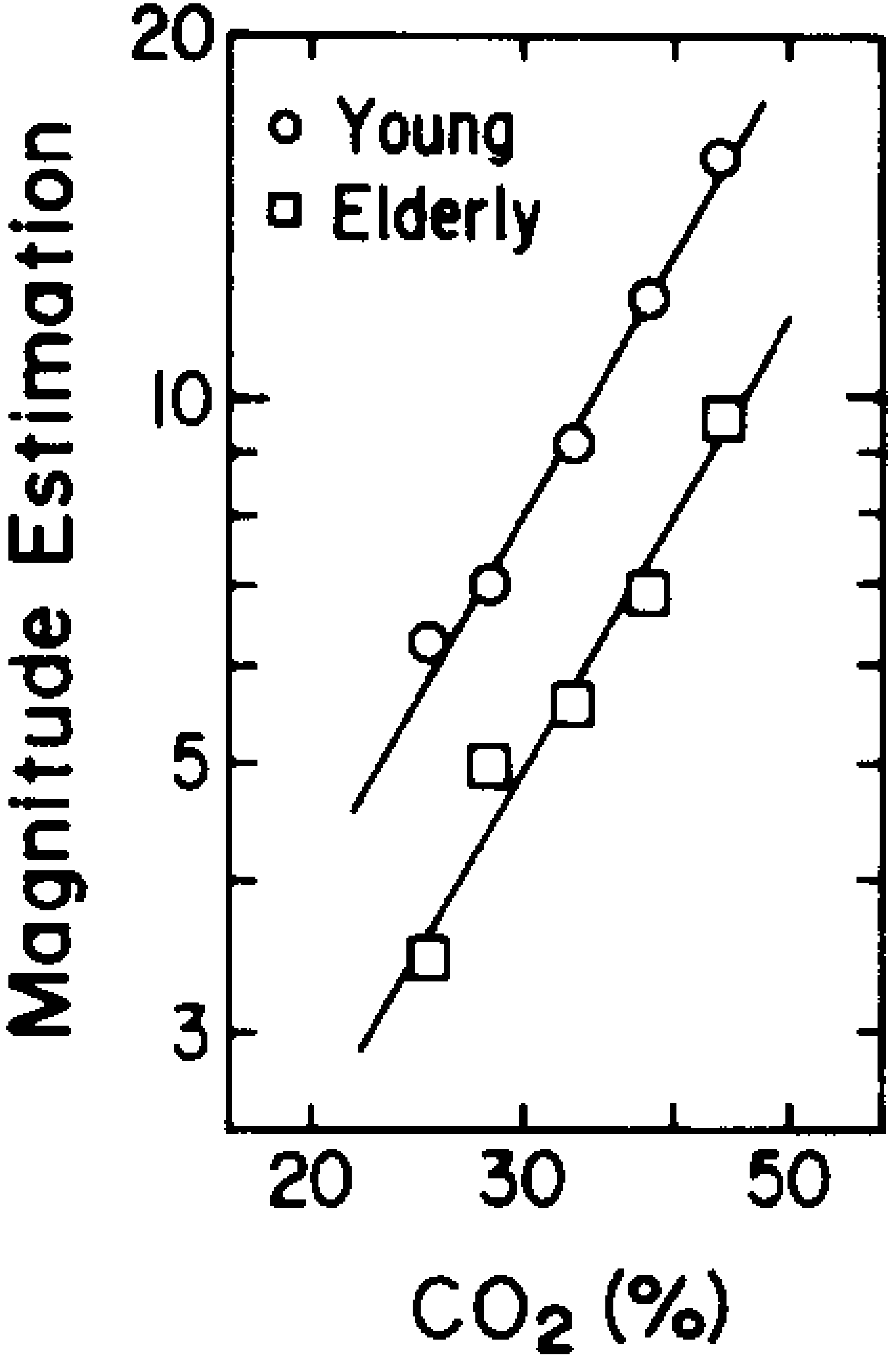

CO₂ CONCENTRATION (% V/V)
10²
10¹
10²
10²
10¹
PERCEIVED INTENSITY
β = 2.2
β = 1.9
β = 0.9
β = 0.7
10⁰
10¹
10⁰
10¹
SUCROSE CONCENTRATION (% W/V)

FIGURE 11

FIGURE 12



This is a pre-copyedited, author-produced version of an article accepted for publication in Annals of the New York Academy of Sciences following peer review. The version of record Annals of the New York Academy of Sciences **641**:137-151, 1992 is available online at: http://onlinelibrary.wiley.com/doi/10.1111/j.1749-6632.1992.tb16539.x/abstract - DOI: 10.1111/j.1749-6632.1992.tb16539.x