Temporal processing of odor mixtures in humans

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Abstract

There is evidence that odorants in a mixture produce their sensations at different times. If true, then temporal processing may be an important component of olfactory decoding. Starting with binary odorant mixtures at which subjects had equal probability to detect one compound or the other, Equal Odd Ratio (EOR), we prepared solutions of each component separately and puffed these separated solutions at different times between 0 to 800 ms (latency times) and different concentration ratios. The results indicate a linear relationship between latency and concentration ratios confounding the meaning of the temporal delays reported in earlier psychophysical experiments.

Introduction

Human perceptions of odorant mixtures are created from olfactory receptor output combined with information from many brain functions, i.e. memory, emotion, other sensory input, etc. and each of these can operate at different speeds. Using four different odorant pairs Laing in 1994 observed a latency ranging from 92 ms (Carvone-Limonene) to 580ms (Carvone-Benzaldehyde). [1] Twelve years later, Rinberg studied the speed-accuracy tradeoff in mice and observed that the time required to reach the maximal accuracy can be up to 600 ms (harder tasks). [2] In 2015, Resulaj demonstrate that mice process odor information in 70-90ms after odor inhalation indicating that mice can make decisions surprisingly fast. [3] This evidence of temporal differences in human and murine response to different odorants led us to use a sniff olfactometer (SO) to study the effect of stimulus onset time for 3 odorant-pairs and compare these differences between mixtures of the same odorants at different concentration ratios. [1,3,4]

Experimental

Materials

The three odorants tested had thresholds that ranged over 10,000 fold: benzaldehyde (threshold 350 ppb), R(-)-carvone (threshold 2 ppb) and 2,4,6,-trichloroanisole (threshold 0.027ppb). They were tested starting at 5 times their threshold in binary mixtures and at concentration ratios above and below their equal odds ratio (EOR) in Experiment 1 and as pairs of single component solutions puffed simultaneously in Experiment 2. They were dissolved in ethanol and aliquots diluted to a target concentration with 7% ethanol and water to yield 7% ethanol for all samples tested.

Psychophysics

Four subjects participated in this study; 3 females and 1 male ranging from 25 to 32 years old. None of them were smokers and reported any olfactory dysfunction. They were students and employees of Cornell University's Department of Food Science and did not have any prior experience with this type of psychophysical testing. [5] Figure 1 shows a cartoon of the Sniff Olfactometry (SO) used. The SO delivers a 15ml puff of headspace gas from above 50 ml solutions of odorants with a duration of 70ms. The puffs were presented 500ms after a visual cue directing the subjects to inhale was shown on the monitor. After an additional 750 ms the subjects were asked to answer a question using

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the mouse. Shown on the right in Figure 1 is Binomial Generalized Linear Model (B-GLM) plot of the responses to the cue, "which is stronger: the 'mint' or the 'almond' smell?" replicated 9 times for each of 4 sessions covering a range of responses from 100% "mint" to 100% "almond". The dotted lines indicate the outer limits of the 95% prediction interval for the data. In Experiment 1 they were asked, "which odor was the strongest" but in Experiment 2 they were asked "which odor came first". They answered either "mint" or "almond".

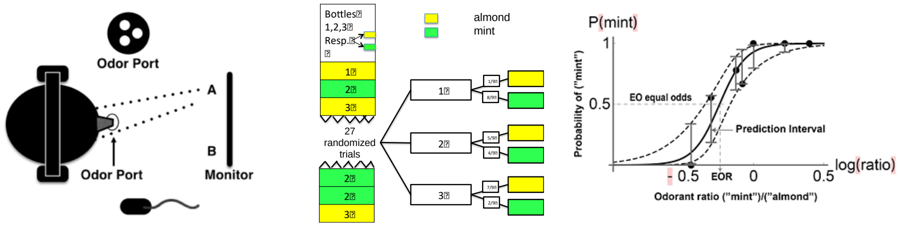

Figure 1: The Sniff Olfactometer, DATU, Inc., Geneva, NY, shown in the cartoon on the left shows a subject from above waring noise-canceling headphones, the mouse used for input, the shape and location of the odor port and the monitor used to provide cues to the subject. [4] In the center is shown the script for the 27 randomized trials each replicated 9 times. When testing mixtures, each bottle contains a different concentration ratio. [6] On the right is Binary-GLM fit of the carvone-benzaldyde data showing the probability of "mint", the EOR and the prediction interval (between the dotted lines).

Experiment (1):

As outlined on the left in Figure 2 the odorant pairs were tested as a mixed head space above a solution containing both. Iterative tests (n=9) of a range of odor ratios yielded response probabilities for 3 odorant pairs and 4 subjects.

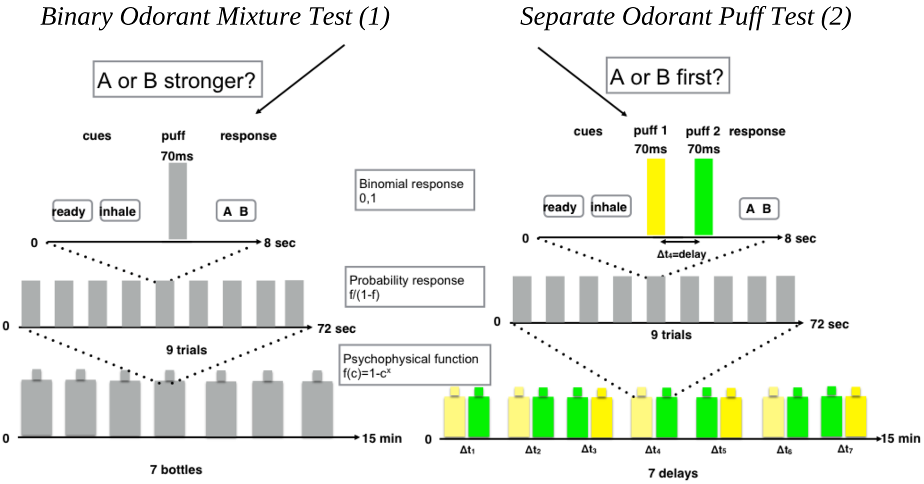
Binary Odorant Mixture Test (1) *Separate Odorant Puff Test (2)*

Figure 2: Shows the two experimental protocols: 1) used to determine the response probability at different concentration ratios of a binary mixture and 2) used to determine the response probability to the binary odorants puffed separately at various times.

Experiment (2):

To test the temporal effect on binary odorant detection, separate solutions were prepared at their EOR concentrations determined in Test (1). These solutions were placed in separate bottles and instead of puffing a mixture two bottles with separate odorants were puffed simultaneously. Then, they were puffed with different latencies between the puffs. The right side of Figure 2 is a cartoon of this experiment showing the randomly interlaced puffs of single odorants at different delay but all at same concentration ratio, in contrast to Experiment 1 where the samples were presented as single puffs of mixture at different ratios.

Results and discussion

Figure 3. summarizes the results of Experiment 1 (a. and b.) and Experiment 2 (c. and d.). The plots are generalized linear model fits to the binomial data produced from the SO. Dotted lines indicate the extent of the 95% prediction intervals and the 3 colors in a. and c. indicate different odorant pairs of the three odorants tested. The 4 colors shown in b. and d. indicate the four different subjects used in the study.

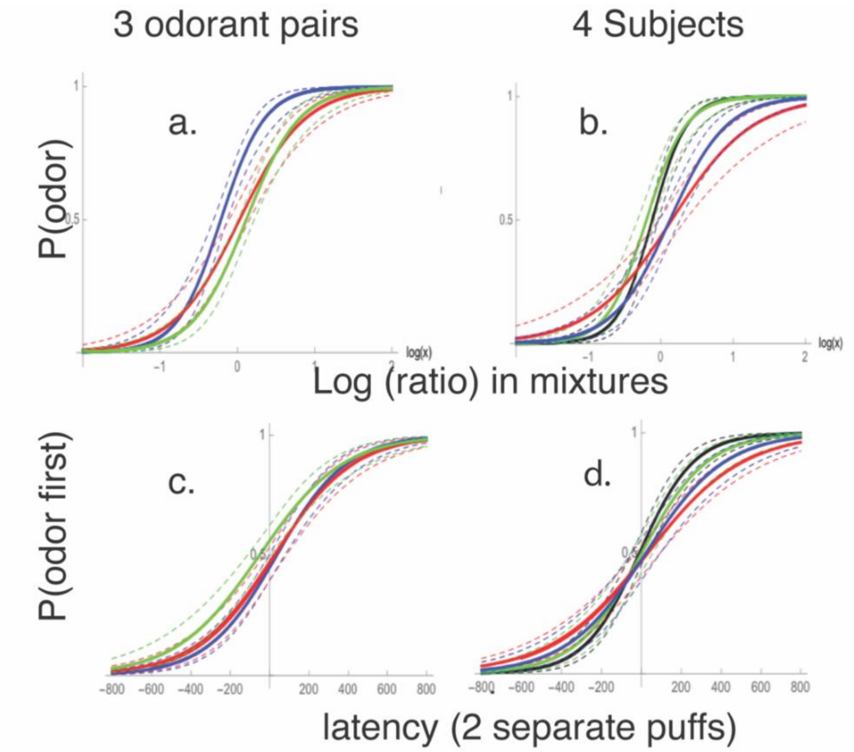

Figure 3: Summarizes the resutls of Experiment 1. and 2. Plots a. and b. show the combined Binomial-GLM plots for responses to mixtures of odorant. In a., blue, red and green, are the data from the 3 odorant pairs and b. shows the compined data GLM plots for the 4 different subjects. The EOR concentrations produced by subject "black" was used (arbitrarerly) to define the concentration ratio used in Experiment 2.

It is well documented that odorants differ greatly in their odor potency therefore we would expect the response probabilities for the 3 odorant pairs plotted in Fig.1(a.) to have different plots and indeed they do. Exactly how these differences affect odorant mixture perception remains to be determined but that behavior is compositionally determined is clear. Furthermore, Figure 1 (b.) shows an even greater difference in the perceptions for different subjects to the same odorant pair, a result also well documented in the literature. Far from being a confounding factor it implies that SO studies may be an excellent way to investigate individual differences. Speed is the main advantage SO tests have over more traditional sensory testing but SO studies require knowledge of the key odorants in a mixture.

In Experiment 2 the subjects were presented with single puffs separated in time by a range of latencies from -800ms to +800ms. All experiments began with odorants in separate bottles at their EOR determined in Experiment 1 for each odorant pair. For every pair and each subject, the response probability was 0.5 when separate puffs of single odorants were presented to the subject as it was when single puffs of mixtures were presented. At the EOR concentrations all the models were within the prediction interval at a 95% probability. In this study, no difference in temporal response different odorants or by different subjects. It is as though the brain does not distinguish between the sensations produced by a puff of air containing a uniform mixture of two different odorants and the sensations produced by two puffs of air each containing uniform sample of a single odorant. Whatever the mechanism that translates odorant composition from a sniff into a perception the intensity of each odorant is concentration dependent and independent of the delivery mechanism, i.e. individually or in a mixture. The receptor system evaluates each odorant separately and the two puffs in the SO do not dilute each other. Such a mechanism would allow organisms to perceive turbulent mixing of odorant sources as undiluted by the turbulence and indicative of the source composition. At least until diffusion completely dilutes the odorants and the gas is uniform.

As both figures c and d indicate the puffing of odorant pairs with different latencies has a marked effect on which odorant is perceived most frequently as first to be detected. All 3 pairs of odorants and all 4 subjects showed the same relationship between probability of detection and latency within a 95% prediction interval and reaching 100% detection of one odorant first with a 600-800ms separation. In light of these results from 4 subjects and 3 odorants it is not clear if the 580ms carvone-benzaldehyde latency measured by Laing was caused by differences in concentration ratios or differences in temporal processing. A better psychophysical experiment may be one that measures the effects of odorant composition on reaction time. [1]

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