

Reporting Summary

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Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (<i>n</i>) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒ Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection	No software was used for data collection in the behavioral assessments. E-prime 2.0 was used to control odor deliveries, present visual prompts and record responses in the fMRI experiment.
Data analysis	SPSS (Version 26), JASP (Version 0.13), Matlab 2014a, SPM 12, and AFNI 20.2.08.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [guidelines for submitting code & software](#) for further information.

Data

Policy information about [availability of data](#)

- All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:
- Accession codes, unique identifiers, or web links for publicly available datasets
 - A description of any restrictions on data availability
 - For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

All presented data and analysis scripts are available at <https://doi.org/10.57760/sciencedb.13818>.

Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

Reporting on sex and gender	The study examines the perception and neural representation of odor molecules. Sex and gender were not considered in the study design. Participants self-reported their sex. 51.6% of those who took part in the behavioral assessments and 50% of those in the fMRI experiment were female. No sex- and gender-based analyses have been performed as the study is not designed to probe sex- or gender-related differences.
Population characteristics	See above.
Recruitment	Participants were recruited via advertisement on social media.
Ethics oversight	The study was approved by the Institutional Review Board at the Institute of Psychology, Chinese Academy of Sciences (H18029).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☐ Life sciences ☒ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	The study presents quantitative data from nine behavioral experiments and an fMRI experiment where olfactory perception and neural representations of monomolecular odorants were compared before and after substructure adaptation, superstructure adaptation, and/or nonspecific olfactory adaptation.
Research sample	A total of 458 healthy non-smokers (236 female, mean age: 23.1 yrs, SD: 1.8 yrs) with no history of neurological disorders participated in the study. Of these, 386 participated in the main study and 36 in each of Supplementary Experiments 1 and 2. For the main study, 360 participants took part in the various behavioral assessments (36 participants per condition or task) and 26 participated in the fMRI experiment. They reported to have a normal sense of smell and no respiratory allergy or upper respiratory infection at the time of testing. Those who took part in unilateral adaptation and test also had no significant nasal septal deviation as measured by nasal spirometry, with nasal partitioning ratios ranging between -0.3 and 0.3.
Sampling strategy	Participants were selected based on the following criteria: 18-30 years old, nonsmoker, a normal sense of smell, no respiratory allergy or upper respiratory infection at the time of testing, no history of neurological disorders. In addition, for the unilateral adaptation and test experiment: no significant nasal septal deviation as determined by nasal spirometry; for the fMRI experiment: fulfillment of the MR safety criteria (e.g., no metal implant, no claustrophobia, etc). As to sample sizes, we were unaware of any previous study on substructure adaptation and odor quality change and thus could not perform a formal power analysis. The sample size in each experiment (or cell) was about twice the size used in previous studies on related topics (Cain & Polak, 1992; Gottfried et al., 2006; Howard et al., 2009; Li et al., 2008; Pierce et al., 1996; Pierce et al., 1995; Zelano et al., 2011).
Data collection	For the behavioral assessments, participants were individually assessed by an experimenter in a well-ventilated room (see Behavioral assessments for details). No one else was present during testing. The data were recorded by pen and paper. For the fMRI experiment, MR images were collected using Siemens Prisma 3T scanner; responses in the scanner were recorded using a keypad attached to the participants' right hand. No one was present in the scan room with the participants during scanning. Both the participants and the experimenters were blind to the chemical relationships among the olfactory stimuli and to the specific purposes of the experiments during data collection.
Timing	Data collection for the main study started in March 2019 and ended in August 2021. Supplementary experiments were performed from February to May 2023.
Data exclusions	No data were excluded from the analyses.
Non-participation	Five participants dropped out of the 2-session behavioral experiments due to time conflicts.
Randomization	Participants were randomly allocated into different experimental groups where applicable.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☐	☒ MRI-based neuroimaging

Magnetic resonance imaging

Experimental design

Design type

Slow event-related fMRI design.

Design specifications

The fMRI experiment comprised two scanning sessions held on two separate days, with Comp.CP as the adapting odor in one session and P in the other session. Each session consisted of 6 runs of about 6 min each: 2 baseline runs without adaptation, followed by 4 adaptation runs where the adapting odor of that session was delivered (in place of purified air) before the start of the first trial and during all inter-trial intervals. Each trial began with a 2 s attentional prompt, after which participants were cued to take a 2 s sniff. They then indicated with a button press whether there was an odor (for baseline runs) or whether there was an odor different from the background odor (for adaptation runs). There were 14 trials per baseline run: Comp.CP, P, C, and purified air were each presented during the sniff cue in 4, 4, 4, and 2 trials, respectively, in a pseudo-randomized order, and the interstimulus interval was jittered between 18 to 30 s. There were 13 trials per adaptation run: Comp.CP, P, and C were each presented in 3, 5, and 5 trials, respectively, when Comp.CP was the adapting odor, and in 5, 3, and 5 trials, respectively, when P was the adapting odor. The interstimulus interval was jittered between 18 to 26 s.

Behavioral performance measures

Participants' button presses (Y/N) were recorded. Task performance was assessed with hit rate. Hit rates in the baseline runs and adaptation runs were respectively calculated and compared.

Acquisition

Imaging type(s)

Functional and structural MRI.

Field strength

3 Tesla.

Sequence & imaging parameters

Gradient-echo T2*-weighted echoplanar images (EPI) were acquired with two sets of parameters due to a major software update. For 17 participants: repetition time (TR), 2 s; echo time, 27 ms; flip angle, 90°; matrix, 96 × 96; field of view, 192 × 192 mm²; in-plane resolution, 2.0 × 2.0 mm²; slice thickness, 2 mm; gap, 0; number of slices, 34; and acquisition angle, 30° rostral to the intercommissural line. For 9 participants: a blipped-controlled-aliasing multiband EPI sequence was employed; TR, 2 s; echo time, 29 ms; flip angle, 80°; matrix, 128 × 128; field of view, 192 × 192 mm²; in-plane resolution, 1.5 × 1.5 mm²; slice thickness, 1.5 mm; gap, 0; number of slices, 88; and acquisition angle, 0° to the intercommissural line. A 1 mm³ isotropic T1-weighted anatomical volume, along with a field map, was also acquired for each participant.

Area of acquisition

For 17 participants, 34 slices were acquired at an oblique plane 30° rostral to the intercommissural line, which covered all regions of interest including the anterior piriform cortex, posterior piriform cortex, amygdala, and orbitofrontal cortex. For 9 participants, a whole-brain scan was acquired.

Diffusion MRI

☐ Used

☒ Not used

Preprocessing

Preprocessing software

SPM 12 (<http://www.fil.ion.ucl.ac.uk/spm>). Preprocessing involved slice timing correction, artifact removal, motion correction, and for univariate analysis, spatial smoothing (6-mm FWHM Gaussian kernel) and temporal filtering (128 s high-pass filter). For representational similarity analysis, no additional preprocessing was performed to preserve the spatial fidelity of the signals.

Normalization

Spatial normalization was not performed except for the purpose of displaying group-level odor-induced activations at

Normalization	baseline, in which case the images from the baseline runs were spatially normalized to a standard EPI template (MNI space).
Normalization template	ICBM152.
Noise and artifact removal	EPI images were corrected for geometric distortion due to susceptibility artifacts using participants' field maps and were spatially realigned to the first volume of the first session (first baseline run on Day 1) and unwarped to reduce movement related variance. In the GLM-based univariate analysis, movement parameters were entered as nuisance regressors.
Volume censoring	Not applied.

Statistical modeling & inference

Model type and settings	We performed both univariate analysis and multivariate representational similarity analysis. For univariate analysis, the 3 × 3 combinations of test odors (Comp.CP, P, C) and adaptation conditions (baseline, adaptation to Comp.CP, adaptation to P) were modeled with a set of impulse response functions from 0-16 s post stimulus that made no assumption about the shape of the response. Head motion parameters were included as nuisance regressors, and serial autocorrelations were modeled as an autoregressive process. For multivariate representational similarity analysis, we computed and compared the representational similarities between two test odors in an ROI under different adaptation conditions.
Effect(s) tested	We tested the effect of adaptation condition on odor-evoked percent signal changes in the ROIs with repeated measures ANOVAs and paired -sample t tests. In addition, the representational similarities (z-transformed Pearson correlations) between two test odors in each ROI were compared between adaptation conditions using the paired-samples t test.
Specify type of analysis:	☐ Whole brain ☒ ROI-based ☐ Both
Anatomical location(s)	The anterior piriform cortex and the posterior piriform cortex were manually drawn on each participant's anatomical scan, coregistered to his/her mean realigned EPI image, according to an anatomical atlas (Mai et al., 2008). The amygdala was defined using cytoarchitectonic probabilistic maps integrated in SPM Anatomy toolbox (Eickhoff et al., 2005). The olfactory orbitofrontal cortex was defined based on a meta-analysis of human neuroimaging studies on olfactory processing (Gottfried and Zald, 2005), drawn as 6-mm radius spheres centered on MNI coordinates (-22, 32, -18) and (24, 33, -12), respectively.
Statistic type for inference (See Eklund et al. 2016)	The structural masks of the ROIs were projected into each participant's native EPI space and functionally restricted to voxels that responded to odors at baseline (voxel-wise $p < 0.01$) (Zelano et al, 2011). The functionally restricted ROIs were employed in all subsequent analysis. Statistical inferences were based on odor-evoked percent signal changes and the representational similarities between two test odors extracted from the ROIs under different adaptation conditions.
Correction	Multiple comparisons across ROIs and conditions were Bonferroni corrected where applicable.

Models & analysis

n/a	Involved in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☐	☒ Multivariate modeling or predictive analysis
Multivariate modeling and predictive analysis	For multivariate representational similarity analysis, effects of no interest (motion regressors and low-frequency drift) were first subtracted out from the preprocessed functional data with AFNI programs 3dDeconvolve and 3dSynthesize. Values from post-stimulus TR 3, the time point that best captured signal variations across conditions, were then extracted from the voxels within each ROI for each of the combinations of test odors and adaptation conditions, which formed the input to representational similarity analysis. For each adaptation condition, we computed the representational similarity between two test odors in an ROI as the Pearson correlation across voxels within that region.