Effects of stimulus complexity on human olfactory evaluation and description

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Effects of stimulus complexity on human olfactory evaluation and description

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Preface

Olfaction is remained to be unrevealed greatly compared to vision and audition. Although past studies have elucidated the basic structure and function of olfactory system, it is unknown in detail how the sense of smell is created from various odorant molecules and how olfaction is related with emotion, memory, and learning.

To clarify human olfactory system, past studies investigated the relationship between olfactory perception and cognitive function. Owing to the studies, it was revealed that human olfaction can be modulated by olfactory experience and learning. For example, sommeliers who have experience in special olfactory training can discriminate and verbalize a lot of odors, but naïve people cannot. On the other hand, the manner that the first order reaction of olfactory neurons influences olfactory recognition is poorly understood. Though functional groups of chemical molecules (*e.g.,* alcohol and ester) can be an index of odorant categorization, a clear regulation between odorant molecular characteristics and the recognition is uncovered. To consider the effect of multiple processing from periphery (*i.e.,* olfactory receptor neurons and olfactory bulb) to center (*i.e.,* olfactory areas such as piriform cortex, amygdala, and orbitofrontal cortex) comprehensively, we investigated the effects of stimulus complexity on olfactory recognition using the complicated olfactory stimuli by conflict of dual emotional evaluations (first experiment) and mixing odorants (second experiment).

We first investigated the relationship between odor-evoked emotion and olfactory recognition. Emotion evoked by odors can be determined or modulated by several factors including odorant-receptor interactions and olfactory experiences. Because of these factors, some odors can induce an emotional discrepancy such as a

conflict between innately determined and experience-based emotions. We examined whether the difference between two subjective ratings, pleasantness and liking, for an odor can be related with the olfactory recognition to explore the effect of the complicated odors evoked by the discrepancy in emotional evaluations. We conducted an olfactory experiment, in which participants were asked to note the difference between pleasantness and liking, whereby the former referred to instinctive and innate feelings and the latter to experience-based and acquired feelings. Ten odorants exhibited no significant difference between pleasantness and liking ratings. Another 11 odorants exhibited a significant relationship between the choice of olfactory perceptual descriptors (*e.g.*, fruity and woody) and intensity; this was not true of the 10 discrepant odorants. We firstly showed that differences in pleasantness and liking ratings can be related with the selection of olfactory descriptors according to odor intensity, though the findings may be preliminary due to the number of participants and odorants.

We next examined whether the recognition of odor mixtures can be changed by structural complexity of odorant molecule. Odor mixtures can evoke smells that differ from those of their individual odor components. Two types of perceptual modes were proposed by past studies, in which a mixture can be perceived as either the original smells of its individual components (elemental) or as a novel smell (configural). We examined whether the structural complexity of an odorant molecule can affect the recognition of odor mixtures. We conducted olfactory experiments, in which different groups of participants were provided olfactory perceptual descriptions of low-, medium-, and high-complexity odor mixtures or components, respectively. Then, the participants' evaluations were compared between mixtures and components via two types of analyses. First, we compared each olfactory description following quantification via principal

component analysis. Second, we compared data based on seven major olfactory perceptual groups. The analyses suggest that odor mixtures composed of low-complexity odorants were perceived as relatively novel smells than medium- and high-complexity mixtures.

This thesis examined that complicated olfactory stimuli can affect human olfaction. The findings may help to understand how olfactory stimuli is processed from peripheral to central systems to determine the sense of a smell.

Table of contents

1. General introduction

Olfaction is known to be as a primitive sense and highly conserved from invertebrate to human[1,2]. The main role of olfaction would be to detect the beneficial or adverse resources from the volatile chemical substances, which is shown in diverse animals. For example, nematodes show attractive or aversive behavior according to odorants[3,4], fruit flies explore foods with the clue of chemicals in the air[5], and rodents exhibit fear behavior by substances derived from predators' body wastes[6,7]. We empirically know that human also can utilize olfactory cues, such as detection of hazardous materials by smells of rotten foods. Due to the commonality of olfactory system in organisms, basic structure of the system and physiological processes were revealed by past animal and human studies.

In this chapter, I review the knowledge about olfaction. First, I introduce the basic structure of olfactory system and manner of sensing smells. Then, past olfactory studies performing psychophysical experiments and neural activity measurement are mentioned. I finally summarize the aim of the present study.

1.1. Fundamental knowledge of olfactory system

In mammal, olfactory stimuli are broadly processed in the three stages, olfactory receptors in olfactory epithelium, olfactory bulb, and olfactory areas (Fig. 1). The basic structure of the system and manner of the processing are mentioned in this section.

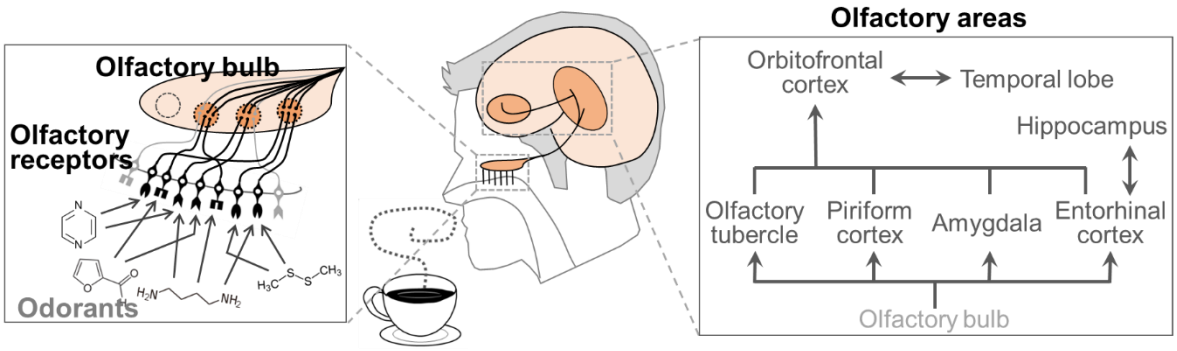

Fig. 1. Outline of olfactory system. Basic structure of olfactory system is described, where the olfactory signaling pathway from the receptor to brain is shown.

1.1.1. Olfactory receptor

The process for olfactory sensation is initiated by odorant-receptor interaction in olfactory epithelium. The olfactory receptor, expressed in olfactory receptor neuron, was found by L. Buck and R. Axel[8]. Mammal shares the olfactory receptor belonging to the class of G protein-coupled receptors with seven-transmembrane domain, and being specifically expressed in olfactory epithelium. It was known that the number of the expressed receptor types was dependent on the species (*e.g.,* mice: about 1000 types, human: 300–500 types)[9,10]. The correspondence between the receptors and odorants is complicated. One type of receptor can be activated by several types of odorants, and one type of odorant can activate several types of olfactory receptors. Such odorant-receptor interaction resulted in that the activities of olfactory receptor neurons, induced by an odorant, were encoded as population. However, the correspondences between the

receptors and odorants were scarcely elucidated. The numerous chemical features of an odorant, such as types of atom components, carbon structure, electrical charge, and so on, may cause difficulty in clarifying the regularity determining the correspondence between the receptors and odorants. Furthermore, it was reported that additional factors can influence the correspondence; according to the concentration of odorants, the activated receptor was switched to another type of receptor[4]; chemical transformation of odorants by enzymatic metabolism in olfactory mucosa can vary the population of activated receptors[11]; an odorant can act as agonist or antagonist to olfactory receptors[12]. Because of the various factors, the comprehensive correspondence between olfactory receptors and odorants still be unknown, although huge researches such as genome analysis and coupling analysis have been conducted[4,9,10,13–17].

1.1.2. Olfactory bulb

Next to the activation of olfactory receptors, olfactory bulb receives the odorant-evoked activities. In olfactory bulb, a number of glomeruli are formed, in which synaptic connections between axon of olfactory receptor neuron and dendrite of interneurons such as mitral or tufted cell are observed. The mitral and tufted cells are excitatory neurons, whereas other interneurons including periglomerular and granule cells are inhibitory neurons[18,19], enabling the inhibitory modulation termed as lateral inhibition. It should be noted that only one type of olfactory receptors is expressed in an olfactory receptor neuron, and the olfactory receptor neurons with the same type of receptors are projected to the same glomeruli in mammal[20]. This structure resulted in that an odorant triggers the activation of the definite glomerular group, meaning that olfactory bulb shows spatial activity pattern according to odorants. Indeed, previous studies using various types of

odorants demonstrated that rodent olfactory bulb showed odorant-specific spatial activity pattern[21–24]. Representation of the spatial activity pattern may be underlain by the lateral inhibition which can help to highlight the boundary between the activated and inactivated neurons. The spatial activity pattern in olfactory bulb was important for olfactory perception. When the spatial activity patterns were overlapped by receiving some odorants simultaneously, the mice cannot discriminate the individual odors[25]. From these studies, olfactory bulb would represent the odorant-specific spatial neural activity to be important for olfactory recognition.

It was also reported that olfactory bulb showed plasticity. MRI studies revealed that human olfactory bulb had plastic structure where the volume of olfactory bulb related to individuals' olfactory function. In past studies using Sniffin' Sticks test, which enables to assess olfactory performance[26,27], the score of the test was significantly correlated with the volume of olfactory bulb[28,29]. Although some neurodevelopmental hypotheses suggested that neurogenesis occurring at the level of olfactory epithelium, olfactory bulb, and lateral ventricle may have roles in the plasticity of olfactory bulb, the detailed mechanism remained to be unclear[29].

1.1.3. Olfactory area

Several olfactory areas, including olfactory tubercle, piriform cortex, amygdala, and entorhinal cortex, are projected from olfactory bulb. Olfactory tubercle receives monosynaptic input from olfactory bulb, and has a three-layered cortex-like structure[30–32]. Due to the presence of olfactory tubercle in ventral striatum, it was argued that olfactory tubercle has a role in olfactory goal-directed behavior[31,33]. Piriform cortex receives inputs from both olfactory bulb and other olfactory area[34]. In the piriform cortex,

olfactory information such as odor quality was categorized and represented[35,36]. Piriform cortex also exhibited associative and predictive activity by non-olfactory cue or just imaging a smell[37,38]. Amygdala has a role in emotional valence evoked by olfactory stimuli. A previous study reported the significant correlation between ensemble pattern activity in the amygdala and rating of subjective valence[39]. It was also reported that amygdala is involved in emotion-related learning, where amygdala neurons can encode odor cues related with positive or negative taste[40,41]. Entorhinal cortex receives inputs from olfactory bulb and piriform cortex, and is conceived as the nodal point between hippocampal formation and other cortical areas[42,43]. Although it can be hypothesized that entorhinal cortex could have a role in olfactory memory due to the connection with hippocampus, the detail functional role of entorhinal cortex still be unknown.

It was shown that these olfactory areas (olfactory tubercle, piriform cortex, amygdala, and entorhinal cortex) cooperate with higher-level regions for olfactory perception or recognition. Orbitofrontal cortex had a role in integration of sensory information and collaborated with amygdala to discriminate component smells from an odor mixture[44,45]. Anterior temporal lobe, which has connection with olfactory tubercle, piriform cortex, and orbitofrontal cortex, played a role in olfactory semantic-representation and verbalization[45,46]. Both activations of orbitofrontal cortex and piriform cortex were important for generating the predictive stimulus template with the clue of non-olfactory cue[37]. On the other hand, it was indicated that other sensory regions can influence the olfactory sensation. For example, olfaction can be affected by modulation from visual cortex, where stimulating the visual cortex by transcranial magnetic stimulation could improve the performance of olfactory discrimination from odor mixture[47], and simultaneous reception of gustatory, olfactory and somatosensory stimuli

can be an integrated sense, called as flavor[48,49]. Recognition such as semantic or contextual concordance can also influence olfaction[45,46,50]. Taken together, it has been suggested that the sense of smell is generated by cooperative processing within various brain region.

Although past animal studies greatly contributed to the understanding of olfactory system, there are clear differences between human and non-human in the system. Previous studies showed that human has reduced and shortened olfactory system compared to non-human, in terms of the number of olfactory receptors[10], the volume of olfactory bub[29,51,52], and connections in the central neural circuit[31,34,43,53]. Therefore, the human research is essential to reveal the human olfaction. In the next sections, I focus on and introduce the human research.

1.2. Olfactory psychophysical studies

Due to the technical difficulties of non-invasive recordings in human olfactory system, psychophysical approach mainly has been conducted to investigate and elucidate how human response to and evaluate smells. The analysis of the subjective ratings can provide olfactory cognitional profiles such as the primal axis of olfactory recognition and manner of semantical output of olfactory stimuli. In this section, I mention the knowledge revealed by past olfactory psychophysical studies.

1.2.1. Evaluation axis in olfactory psychophysics

To measure the sense of a smell as a score, some subjective indexes, such as pleasantness, intensity, familiarity, and edibility, have been used in olfactory psychophysical experiments. The pleasantness is a measurement for hedonic or offensive

feelings. The intensity is the subjective strength of a smell. The familiarity is used to measure the extent of the memory or experience concerned with the smell. The edibility is the subjective evaluation of being fit to eat or not. Many olfactory studies used these subjective indexes[41,54–58] and some studies suggested that the subjective indexes can be the primal axes for olfactory perception[59,60]. Examples of those olfactory evaluation axis are described in Fig. 2.

In addition to the subjective indexes, olfactory perceptual descriptors such as "citrus" and "earthy" also have been utilized to express the perceptual profiles of a smell. Several databases provide the various perceptual descriptors. For example, *Atlas of odor character profile* (Andrew Dravnieks) provides 146 olfactory descriptors and *Sigma Aldrich Ingredients Catalog: Flavors & Fragrances* (Sigma Aldrich) does 107 descriptors[61]. When participants evaluated a smell by the perceptual descriptors, they were often instructed to refer to a descriptor list, otherwise they could provide only few descriptors due to the poor ability of olfactory verbalization[45,54]. The limited ability of olfactory verbalization may be the reason why those subjective indexes mainly have been used in the olfactory experiments.

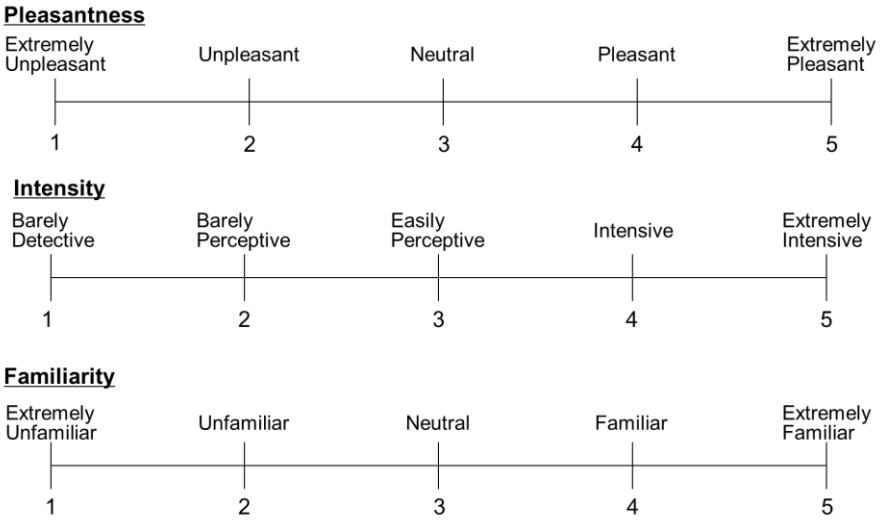

Fig. 2. Examples of subjective evaluation axis. Examples of pleasantness, intensity, and familiarity axis on 5-point-scale are described. Participants may be instructed to choose each score based on the smell they feel.

1.2.2. Odor profile determining olfactory recognition

Many researchers have aimed to elucidate the odor characteristics determining olfactory perception and recognition. It was reported that the chemical or structural feature of an odorant had a role in the olfactory recognition. Some studies indicated that amino acid sequence of the olfactory receptor binding site was important for the odorant-receptor interaction[17,62], and amino acid substitution in the receptor can vary the olfactory perception and recognition[63]. Other studies showed that the odorant-receptor interaction was affected by molecular volume or carbon structure[14,64] and the structural features such

as enantiomer and molecular structural complexity was involved in olfactory perception and recognition[54,60,65]. These studies suggested that peripheral odor coding or processing at the level of odorant-receptor interaction is important for olfactory perception and recognition.

On the other hand, it was also reported that higher-level processing, relating with experience, memory, learning, and so on, is essential for olfactory recognition. A previous report showed that odor mixture perception was modulated by pre-exposure of the components, and argued that olfactory experience can shape the olfactory recognition[66]. Another study exhibited that mere pre-exposure can vary the pleasant ratings in some odors[67]. Furthermore, several studies compared olfactory ratings between normal and expert participants, and found the effect of olfactory training or history on olfactory recognition and performance[12,68–70]. From these studies, olfactory perception and recognition would be determined by olfactory processing at the level of both peripheral and central systems.

1.2.3. Major olfactory perceptual group

In olfaction, the standard unit of stimuli, such as the three primary colors in vision and five basic tastes in gustation, has not been defined. The visual and gustatory sensory neurons have stimuli-type specific receptors. In vison, three types of cone cells in retina individually show light wave-specific responses. In gustation, each type of gustatory receptors in taste buds specifically respond to ligands such as glutamate, glucose, sodium, and so on. Due to the elucidated and simple correspondence between the receptor and stimuli, basic perceptual descriptors, such as “red” or “bitter”, were determined in vison and gustation. On the other hand, as described in the previous section,

multi-types of receptors intricately respond to various type of chemicals in olfaction. Such many-to-many correspondence may be the reason why numerous olfactory perceptual descriptors exists[61] and there is a difficulty in defining the major olfactory perceptual groups.

Although past physiological studies imply the difficulty in classifying the major olfactory perceptual group, researchers have aimed to define the major perceptual group with psychophysical approach. M. Zarzo and D. T. Stanton applied principle component analysis to calculate the distances between individual olfactory perceptual descriptors using a data of 881 odor samples and 82 perceptual descriptors, and made olfactory perceptual maps[71]. J. B. Castro, *et al*. reduced the dimension of olfactory perceptual descriptors by non-negative matrix factorization, and obtained 10 dimensional representation of olfactory perceptual space[72]. R. Kumar, *et al.* found 7 major olfactory perceptual group by the modularity maximization algorithm, using a data of several hundred perceptual descriptors and several thousand odor samples[61]. As these past studies, efforts for defining the major perceptual group have been performed. However, decisive conclusion about the perceptual group is not made. A previous review article indicated that the perception-based classification studies were subjective to 4 factors, individual differences within participants, stimuli characteristics, the manner of data collection, and analytical method[73]. Indeed, olfactory perception and recognition can be affected by various individual differences such as genetic variation in olfactory receptors, learning, experience, and so on[45,63,66]. Furthermore, there are a number of types of odorant and perceptual descriptors[61]. Because of the effects of the various factors on olfactory perception and recognition, comprehensive and careful analysis might be needed to establish the major olfactory perceptual group.

1.3. Studies of olfactory neural activity

To reveal the manner how olfactory stimuli is processed to generate the sense of a smell, the analysis of the neural activity is needed. Previous human olfactory studies have used some techniques to record and analyze the activity of olfactory neurons or brain region. In this section, I introduce the techniques and knowledge elucidated by the techniques.

1.3.1. Functional magnetic resonance imaging

Functional magnetic imaging (fMRI) enables to visualize and analyze the brain activity with high spatial resolving power, even if the target brain area is small and placed in deep region. Based on the hemodynamic response function, the brain activity is recorded in individual tiny areas of cubic millimeters (termed as voxel) respectively. A number of the voxels forms the three dimensional data of the brain activity, resulted in the high spatial resolution.

Due to the high resolution, past studies can examine the functional profiles of the small and deep-placed olfactory areas, including piriform cortex and amygdala. Among researchers using fMRI for human olfaction, Jay A. Gottfried's research group has contributed to the understanding of the olfactory perception and recognition. The research group combined psychophysical techniques and fMRI, and examined the olfactory neural mechanisms by showing the relationship between the olfactory performance and brain activity. Especially, his group seemed to focused on piriform and orbitofrontal cortices to investigate how brain codes the odor quality and integrates the sensory representations[45,46,74–76]. To achieve it, the groups often utilized the multivariate techniques in fMRI analysis[36]. The multivariate techniques enabled to provide pattern-

based activity where the data were averaged across space (voxels), time (scans) and participants, whereas the conventional (univariate) techniques potentially included obscuring information at the level of voxels, scans, and participants. Using the multivariate techniques, the group demonstrated the odorant-specific spatial maps in posterior piriform cortex[36], predictive stimulus templates triggered by non-olfactory cue in piriform cortex[37], and discrimination of odor components from the mixture performed by the connectivity between orbitofrontal cortex and amygdala[44]. These studies can help to understand how human brain processes the olfactory information and generate the sense of a smell.

However, some limitations should be noted in fMRI analysis. First, the temporal resolution of fMRI is on the level of seconds. This temporal resolution is derived from the fact that fMRI signals are calculated by hemodynamic response function based on the oxygenic consumption in the cerebral blood flow[77]. The delay of seconds would be critical obstacles in the analysis of olfaction because the sense of smells can be dynamically and momentary changed by the neural adaptation and recovery from the adaptation[78,79]. When the olfactory brain activity is examined, it must be considered whether the delayed activity data makes a biased conclusion. Second, a positive false error can be easily made in the statistical analysis of fMRI data. When the multiple comparison correction is performed to detect the significant activity among the numerous voxels, the threshold for statistical significance should be statistically and strictly determined. Previous studies alerted the occurring of the false positives by arbitrary threshold, and demonstrated that neural activity can be detected in a dead salmon by the arbitrary threshold[80,81]. Although fMRI enables to examine the functional activity even in small and deep-placed olfactory areas, those limitations should be considered to avoid

biased results.

1.3.2. Event-related potential

Event-related potential (ERP), which can be recorded via electroencephalogram, enables to investigate cognitional functions. It is known that physiological events, such as perception and recognition, trigger the synchronized activation of a million of neurons, resulting in an electrical response in the order of microvolts on the scalp. The ERP components were characterized by the peak amplitude and latency, and the physiological means of the components were established by past visual or auditory studies. For example, the P3 wave is a positive wave component appeared approximate 300 milliseconds after an event and indicated the process of attention[82]. The N4 wave is a negative component appeared approximate 400 milliseconds after an event and reflected semantical concordance[83].

Olfactory ERP studies have been performed mainly by Thomas Hummel's group. In an early study, his group showed the different ERP amplitude between normal participants and psychosis-prone subjects, in which pleasant odor (vanillin) induced significant large P1N1 amplitude in the subject group than health participant group[84]. After the study, the group reported a series of the olfactory ERP studies; using 95 healthy participants and two types of chemosensory stimuli (hydrogen sulfide as olfactory stimuli and carbon dioxide as trigeminal irritant), they showed that behavioral task and N1P2 amplitude exhibited age-related decrease in olfactory and trigeminal functions[85]; using an odorant which can be sensed as pleasant (sweet smell) or unpleasant (body odor) according to individuals, they demonstrated that the olfactory P3 component was significantly larger when the odorants sensed as unpleasant[86]; using different cultural

participant group (Algerian versus French) and smell of mint, they examined the effect of the experience in which longer P2 latency in response to smell of mint was observed in Algerian group[57]. From these studies, it can be suggested that subjective valences such as pleasantness and familiarity has important roles in the olfactory ERP responses. In recent studies, the group utilized the ERP as physiological index of olfaction; they investigated the interstimulus intervals whether participants can discriminate the former and later odor or they sensed the smells as one odor[87]; they found that the olfactory habituation induced by repeated long-term stimulation decreased the ERP amplitude[88]. Furthermore, the group examined olfactory memory maintenance focusing on N700 components[89].

Although several olfactory ERP studies were performed as previous description, the number of the studies are much less compared to the study of other sensory modalities such as vision and audition. The reason of few olfactory ERP study may be derived from some technical problems. First, it is difficult to regulate olfactory stimuli. Unlikely to the light or sound, the quantitative regulation of the amount of chemicals in the air is technically effortful. To avoid this problem, an expensive olfactometer will be necessary. Second, ERP might have some disadvantages to detect the electronic signals from small and deep-placed olfactory areas. Because most olfactory areas including olfactory tubercle, piriform cortex, and amygdala are relatively small and placed in deep region, ERP might be inconvenient to detect the olfactory first-order response from those areas. Dual recordings of both ERP and fMRI might be suitable to evade the disadvantage, like as a study performed by Gottfried *et al*[46].

1.3.3. Electro-olfactogram

Electro-olfactogram (EOG) is electric response derived from olfactory sensory

neurons, and can be recorded in olfactory epithelium. In the early works, animals such as frogs, rabbits, and dogs were used for the research[90,91] and Ottoson firstly used the words of “electro-olfactogram”. The animal studies revealed the biophysical origin of EOG, in which a group of neighboring olfactory receptor neurons was activated by odorants resulting in a small negative voltage transient[91].

In human, a few EOG studies performed[91] and only Thomas Hummel’s group recently performed the study[91–94]. In the most recent study, his group examined the profile of olfactory epithelium responses to various odorants[95]. In the study, the group set an electrode into nasal cavity, and recorded the electronic responses to odorants. They found that human olfactory epithelium showed odorant-specific response according to its zone, and the zone-specific responses were significantly correlated with pleasantness ratings. From these results, they concluded that human olfactory epithelium would reflect the axis of the olfactory pleasantness.

Although the recording of EOG by Thomas Hummel *et al*.[95] can be a powerful method to investigate the profiles of olfactory response in human, the technical difficulty is remained. Due to the vulnerability of the recordings in nasal cavity, more than 50% of the recorded data were discarded (successful 801 trials from all 1974 trails). Furthermore, the experimenter may be required to have clinical license to put the electrode into the nasal cavity. To avoid these problems, more easy and stable manner to record EOG should be established.

1.4. Aim of the present study

To investigate the profile of human olfaction, factors determining olfactory recognition should be explored. Past human olfactory studies mainly focused on cognitive

factors such as experience, memory, learning, culture, and language[57,68,69,96–98]. The cognitive factors affecting olfactory perception would be caused by neural processing in central nervous system such as piriform cortex, amygdala, and orbitofrontal cortex[45,46,50,99–101]. On the other hand, recent studies suggested that peripheral neural activity and odorant-receptor interaction also can determine or modulate olfactory perception[12,28,54,95,102–104], and animal studies demonstrated that neural activity in receptor neurons and topographic activity pattern of olfactory bulb are important for olfactory perception and odor discrimination[12,25,105–108]. The interaction or relationship between peripheral and central olfactory processing should be comprehensively investigated to elucidate the factors determining olfactory recognition, though there are technical difficulties in recording and analyzing the peripheral and central processing. To investigate the effect of the olfactory processing from periphery to center, we focused on the complexity of olfactory stimuli. Olfactory information is represented by collective neural activity in olfactory receptor neurons and olfactory bulb, and olfactory perception and recognition are made by several olfactory areas such as piriform cortex, amygdala, and orbitofrontal cortex. Due to such multiple processing of olfactory system, we hypothesized that the complexity of olfactory stimuli can influence olfactory recognition. To test it, we examined the effect of odor-evoked emotion and odorant molecular feature. The odor-evoked emotion can be primary axis of olfactory perception[59]. To investigate the emotion, various types of emotional evaluations (*e.g.,* pleasantness and liking) have been used in past studies. Using dual emotional evaluations, we aimed to investigate whether complicated emotional states can affect olfactory recognition. Molecular features of odorants can directly determine the activity pattern of olfactory receptor neurons[54]. We focused on the molecular structural complexity and tested whether the molecular

complexity can influence odor recognition. Independent experiments of olfactory evaluation investigating the effects of both emotion and odorant feature should be important to clearly show that olfactory recognition is determined or modulated by a complexity of olfactory stimuli. Such approach of both emotion and molecular feature would be a first step to understand how the interaction between peripheral and central processing affects olfactory recognition.

First, from the aspect of emotional feelings, we aimed to examine the effect of the discrepancy of similar but different two emotional evaluations. Previous studies suggested that olfactory emotion can be determined by innate factors such as genetic encoding of olfactory receptors and odorant-receptor interaction[54,63,109] and acquired factors such as experience and learning[57,68,100]. Because few studies assessed the odors showing the difference between the innate and acquired olfactory emotions, odors showing the difference of the emotions failed to be established scientifically. Examination of such odors exhibiting the emotional discrepancy can provide the mechanism how the innate and acquired factors interact each other to determine olfactory recognition. To investigate the relationship between the emotional states and olfactory recognition, we conducted an olfactory experiment where 12 healthy volunteers participated and 36 mono-odorants were used. In the experiment, we asked the participants to note the pleasantness as innate emotion and the liking as the acquired emotion. The participants were instructed to sniff each odor and provide 4 items for odor evaluation; the pleasantness and liking score on 5-point-scale, the olfactory perceptual descriptors (*e.g.,* "citrus" and "earthy") and the intensity score for the individual descriptors on 5-point-scale. We then performed the correlation analysis among the scores.

Second, we investigated whether the recognition of odor mixtures can be

affected by the molecular complexity. The smell of an odor mixture can be changed from the original smell of the odor components according to the combination of the components[12]. However, the regularity how the recognition of odor mixture is determined was unknown. We thus focused on the odorant molecular structural complexity. It was reported that mono-odorants with the more value of the complexity activated the more number of the olfactory receptors, and induced more variable olfactory perceptual descriptors[54]. From this previous study, it can be suggested that the molecular complexity has an effect on the odorant-receptor interaction, resulting in the influence on olfactory recognition. We thus hypothesized that the molecular complexity of odor components has a role in the determination of the mixture recognition. To assess it, we prepared 12 odor components and 18 binary odor mixtures, which were divided into three groups according to their molecular complexity scores (low, medium, and high). We then conducted two types of olfactory experiment, where participants were asked to sniff the component or mixture, and evaluate the smell by selecting some olfactory perceptual descriptors from a list and ranking the intensity for the selected descriptors. The selected descriptors and intensity ranks were compared between components and mixtures to examine the difference of the olfactory recognition.

The present thesis is mainly based on the paper of Hamakawa *et al.* published in Flavor and Fragrance journal. My contributions are designing and conducting the experiments, interpretation of the results, data analysis, and writing the manuscript.

2. Olfactory perceptual descriptions related with the difference between emotional evaluations

2.1. Introduction

In the brain, subjective valence is represented according to external sensory stimuli for decision-making or appropriate behavior. Various types of sensory stimuli, such as light, sound, smell, and taste are associated with reward or punishment, and pleasantness and liking are representative examples of this emotional valence in the brain[41,110,111].

Among several sensory modalities, olfactory stimuli can elicit emotions directly. Previous studies showed that olfactory sensory signals were sent to the limbic cortex without being relayed via the thalamus[41,45,105], and parts of the cortex associated with olfaction, such as the piriform cortex, were strongly connected to the limbic and paralimbic regions[34,45]. Indeed, pleasantness has been identified as a primal axis of olfactory perception in humans[59], and a number of olfactory studies have used it as an index to evaluate positive or negative emotion evoked by smells[39,44,57,59,95,101,112].

Emotions evoked by smell can be modulated or decided by various factors. Previous studies have indicated that some smells were innately perceived as attractive or aversive. The smells from body wastes of predators were genetically coded to induce fear in prey[7]. Humans and mice have shown similar hedonic ratings for some odors[109], indicating that olfactory hedonic ratings could be predetermined in mammals that share the same types of olfactory G protein-coupled receptors[8]. On the other hand, experience and learning also have been found to modify olfactory ratings or behavior. Preference for

an odor can be altered by reward or punishment conditioning in mice[108], and humans have been shown to vary their subjective ratings of odors according to pre-exposure to those odors[57,113]. These previous studies indicated that olfactory ratings and behavior were affected by innate or acquired factors. However, few studies have focused on differences between the emotions evoked by instinctively and innately determined factors or experience- and learning-based factors.

In the past olfactory studies, individual hedonic dimensions for the emotions may not be defined clearly. In the studies, the 'pleasantness' dimension was used most frequently to evaluate the emotional valence induced by smell[39,41,44,57,59,95,101,112]. Some studies have used pleasantness to examine innate odor-evoked emotion[54,59,60], whereas others have used pleasantness to test acquired emotion[57,67,113]. On the other hand, several studies used the 'liking' dimension to evaluate the emotional valence[114–116].

In this experiment, to investigate the relationship between the emotional discrepancy and olfactory recognition, we examined whether the significant difference between dual emotional evaluations (pleasantness and liking) is related with olfactory evaluations. We conducted an olfactory experiment with 12 participants and 36 mono-odorants. In the experiment, participants were asked to simultaneously evaluate the pleasantness, liking, olfactory descriptors (*e.g.,* woody), and intensity for an odor. We then analyzed the relationship between the concordance of the emotional evaluations and olfactory descriptors.

2.2. Materials and methods

2.2.1. Participants

Twelve healthy volunteers (six women and six men, mean age = 22.0, standard error of the mean = 0.71 years) participated in an olfactory experiment. All participants reported normal olfaction, and none reported a history of psychiatric disorders. All participants' data were included in the analysis. The ethics committee for the Faculty of Arts and Science at Kyushu University approved the experimental stimuli, protocols, and procedures (201510R2). Written informed consent was obtained from all participants. All methods of this research were performed in accordance with the approved guidelines.

2.2.2. Olfactory stimuli

A total of 36 odorants were used in the study (Table 1). The concentration of each odorant was determined based on a previous study examining human olfactory discrimination[117]. Each odorant was presented to participants using a simple olfactometer constructed by the researchers, as follows. A total of 10.0 μL of each odor solution was pipetted onto a cotton cloth (2 cm x 2 cm), and the cloth was placed into a sealed 50-ml vial at room temperature (set to 25°C using an air-conditioner). The vial containing the gaseous odorant was connected to the olfactometer, which consisted of a tank of pressurized air, a pressure-regulator (GF2-2506-RX-V, Yutaka Engineering Corporation), a digital flow meter (MF-FP10NH06-050-AI-ANV, Horiba STEC Co. Ltd.), odorless deodorant material (Muko-Kukan Nioi-Gui, Kobayashi Pharmaceutical Co. Ltd.), and an odorless tube (Fig. 3). Each odorant was presented to participants at a pressure of 2.0 L/min. The value of airflow pressure was decided by previous studies[36,39].

Table 1. List of 36 odorants used in this study.

Odorant	C.A.S.	% odorant	Solvent
(-)-α-Pinene	7785-26-4	15	Mineral oil
1,8-Cineol	470-82-6	2	Mineral oil
1-Octen-3-ol	3391-86-4	0.04	Mineral oil
2,4-Trans-trans-decadienal	25152-84-5	0.5	Mineral oil
2-Ethylpyrazine	13925-00-	0.4	Mineral oil
4-Nonanolide	104-61-0	0.5	Mineral oil
Acetophenone	98-86-2	0.15	Mineral oil
Benzaldehyde	100-52-7	0.25	Mineral oil
Decanal	112-31-2	1	Mineral oil
Diphenylether	101-84-8	1	Mineral oil
Ethyl propionate	105-37-3	0.25	Mineral oil
Heptanal	111-71-7	0.04	Mineral oil
Hydroxy citronellal	107-75-5	50	Mineral oil
Isoamyl acetate	123-92-2	0.1	Mineral oil
Isoamyl phenylacetate	102-19-2	0.5	Mineral oil
Isophorone	78-59-1	3	Mineral oil
Isovaleric acid	503-74-2	0.01	Mineral oil
Limonene	5989-27-5	5	Mineral oil
γ-Undecalactone	104-67-6	10	Mineral oil
2,3-Dimethylpyrazine	5910-89-4	0.2	1,2-Propanediol
4-Ethyl-2-methoxyphenol	2785-89-9	0.1	1,2-Propanediol
4-Methyl-3-penten-2-one	141-79-7	1	1,2-Propanediol
Butyl acetate	123-86-4	1	1,2-Propanediol
Caryophyllene	87-44-5	15	1,2-Propanediol
Dimethyl benzyl carbinyl butyrate	10094-34-5	20	1,2-Propanediol
Dimethyl trisulfide	3658-80-8	0.001	1,2-Propanediol
Ethyl acetate	141-78-6	0.5	1,2-Propanediol
Indole	120-72-9	0.5	1,2-Propanediol
Methyl heptanoate	106-73-0	10	1,2-Propanediol
Pentyl butyrate	540-18-1	1	1,2-Propanediol
Propane-1-thiol	107-03-9	0.0005	1,2-Propanediol
Strawberry aldehyde	77-83-8	1	1,2-Propanediol
Acetone	67-64-1	25	Water
Butanoic acid	107-92-6	1	Water
Propan-1-ol	71-23-8	15	Water
Trimethyl amine	75-50-3	0.025	Water

C.A.S. is Chemical Abstracts Service Number.

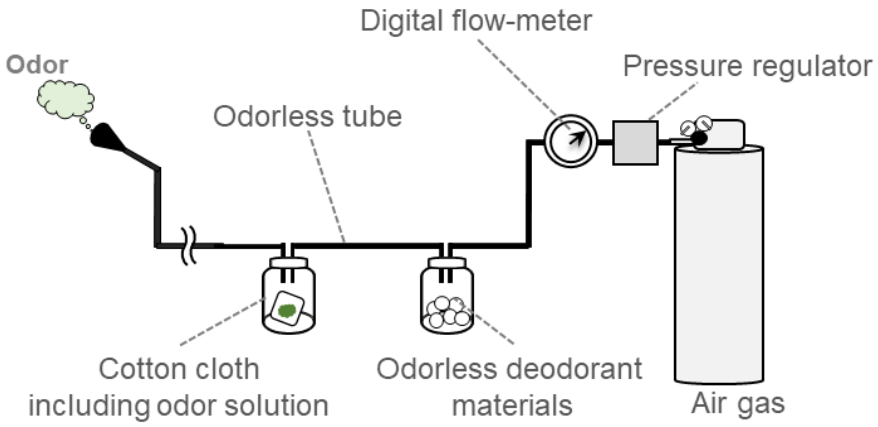

Fig. 3. The olfactometer constructed by the researchers. The olfactometer was used to present the odors (2.0 L/min).

2.2.3. Experimental procedure

The experiment was conducted in a well-ventilated room. The order in which the 36 odorants were presented was randomized (via computer-generated randomization) for each participant. During the evaluation of each odorant, participants were instructed to hold the tube 1 cm beneath one nostril, sniff the content, and evaluate the odor's smell and pleasantness and indicate their liking for the odor. Participants evaluated odor pleasantness and liking using five-point scales (1 = very unpleasant/disliked, 2 = unpleasant/disliked, 3 = neutral, 4 = pleasant/liked, 5 = very pleasant/liked). Participants were also asked to note differences between pleasantness and liking, with pleasantness defined as an instinctive and innate emotion, and liking defined as emotion resulting from individual experiences or circumstances (*e.g.,* the smell of a cigarette could be unpleasant

and liked, because it could be perceived as offensive and noxious but most smokers would like the smell). Participants then selected olfactory descriptor(s), such as “citrus” and “minty,” from a list and evaluate their intensity. The list was generated based on the *Atlas of Odor Character Profiles* (Andre Dravnieks) and included 146 olfactory descriptors. Participants evaluated the intensity of the descriptors using a five-point scale (1 = very weak, 2 = weak, 3 = easily detectable, 4 = strong, 5 = very strong) for each olfactory descriptor selected.

Participants were allowed 15 s to sniff each odorant, and 1 min to complete the sniffing/evaluation process. After each evaluation, participants rested outside the experimental room for 2 min to eliminate the effects of residual odors. In total, the experiment lasted approximately 2 h per participant.

2.2.4. Data analysis

We analyzed the correlation between olfactory pleasantness and liking for the 36 odorants using Spearman’s rank correlation coefficients (rho) and calculated p values for each odorant using JMP 12 (SAS Institute Inc., NC, USA). The rho and p values were calculated for 12 pairs (*i.e.,* the number of participants) of pleasantness and liking scores. We identified 10 odorants for which pleasantness was not significantly correlated with liking. We assigned the odors showing no significant difference between the emotional evaluations to the discrepant group (Table 2, D1−D10, $p > 0.05$). Subsequently, the hierarchical cluster analysis using Ward method was performed using JMP 12 (SAS Institute Inc., NC, USA).

We then examined the characteristics of olfactory recognition in the discrepant and correlation groups. We performed Spearman’s rank correlation analysis to examine the

relationships between the numbers and intensity of the olfactory descriptors selected using JMP 12 (SAS Institute Inc., NC, USA).

To examine the reproducibility of the selected olfactory descriptors among participants, we regarded descriptors chosen by only one participant as temporally and transiently selected (defined as transient descriptors, which are the non-colored descriptors in Appendix A). The proportion of transient descriptors ($TD_{Intensity,Odor}$) was calculated within each intensity score (*Intensity*: from 1 to 5), for each odorant (*Odor*: an odorant classified into discrepant or correlation group) as follows:

$TD_{Intensity,Odor}$ = (number of descriptors selected by only one participant for *Odor*) / (number of descriptors scored as *Intensity* for *Odor*).

The score of *TD* can range from 0 (all descriptors were selected by more than two participants) to 1 (all descriptors were selected by only one participant). For example, in Appendix A, the 6 perceptual descriptors scored as 1 in terms of intensity for acetophenone were “chemical,” “perfumery,” “peach (fruit),” “varnish,” “kerosene,” and “hay.” Of the 6 perceptual descriptors, the 3 descriptors “peach (fruit),” “kerosene,” and “hay” were provided by only one participant for the acetophenone, so $TD_{1,Acetophenone}$ was calculated as 3/6 = 0.5.

2.2.5. Statistics

Because the experimental data were not normally distributed, we used nonparametric tests in the statistical analyses. The Wilcoxon signed-rank test ($\alpha = .05$) was performed to compare the correlation and discrepant groups using JMP 12 (SAS Institute Inc., NC, USA).

2.3. Results

We examined whether the discrepancy between the pleasantness and liking influences the olfactory recognition. Here, the pleasantness was defined as instinctive and innate feelings and the liking was done as individual experience-based ones. Using 36 odorants for olfactory stimuli (Table 1), we performed an experiment in which 12 volunteers participated. Each odorant was presented by a simple self-made olfactometer (Fig. 3). Participants were asked to score the pleasantness (from 1: unpleasant to 5: pleasant) and liking (from 1: disliked to 5: liked) for each odorant, and selected olfactory descriptor(s) from a list generated based on the *Atlas of odor character profiles* (Andre Dravnieks). They were also asked to evaluate the intensity for each olfactory descriptor they selected (from 1: weak to 5: strong).

To examine the relationship between pleasantness and liking scores in each odor, we conducted Spearman's rank correlation analysis using the score of the pleasantness and liking. We obtained 10 odorants showing no significance in the correlation between the pleasantness and liking. The 10 odorants were classified into discrepant group (discrepant group; Table 2, D1−D10, $p > 0.05$). We then performed a cluster analysis among the other 26 odorants and classified 11 odorants for which the correlation was positive and highly significant into the correlation group (Fig. 4, Table 2, C1–C11).

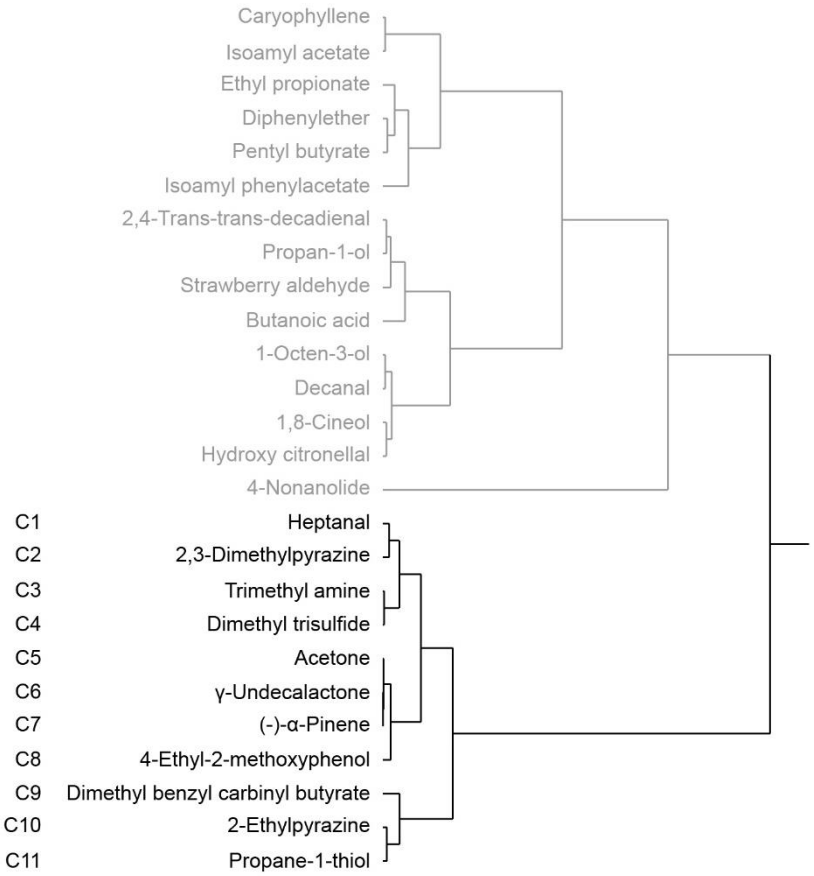

Fig. 4. The Cluster analysis for classification of the correlation group. Among the 26 odorants (except for discrepant group odorants) showing the significance between pleasantness and liking scores, the 11 odorants (C1–C11) was assigned to the correlation group.

Table 2. Correlations between pleasantness and liking for the 36 odorants

Odorant	Pleasantness mean ± SD	Liking mean ± SD	rho	*p*	ID
Acetophenone	2.75 ± 0.72	3.17 ± 0.80	**0.332**	**0.2917**	**D1**
Benzaldehyde	3.08 ± 0.76	3.08 ± 0.86	**0.389**	**0.2115**	**D2**
Limonene	4.17 ± 0.55	4.33 ±0.47	**0.431**	**0.1621**	**D3**
Ethyl acetate	2.83 ± 0.55	2.67 ± 0.75	**0.454**	**0.1384**	**D4**
Isophorone	3.17 ± 0.90	3.00 ± 0.82	**0.472**	**0.1212**	**D5**
Butyl acetate	2.25 ± 0.60	2.67 ± 0.85	**0.496**	**0.1009**	**D6**
Methyl heptanoate	3.50 ± 1.04	3.50 ± 0.96	**0.515**	**0.0866**	**D7**
4-Methyl-3-penten-2-one	2.33 ± 0.75	2.67 ±0.85	**0.530**	**0.0766**	**D8**
Iso-valeric acid	1.50 ± 0.65	1.67 ± 0.62	**0.532**	**0.0748**	**D9**
Indole	2.17 ± 0.69	2.42 ± 1.04	**0.541**	**0.0695**	**D10**
Caryophyllene			0.580	0.0480	
Isoamyl acetate			0.584	0.0462	
Ethyl propionate			0.623	0.0305	
4-Nonanolide			0.323	0.0304	
Diphenylether			0.637	0.0258	
Pentyl butyrate			0.645	0.0237	
Isoamyl phenylacetate			0.672	0.0235	
2,4-Trans-trans-decadienal			0.700	0.0113	
Propan-1-ol			0.706	0.0103	
Strawberry aldehyde			0.715	0.0089	
Butanoic acid			0.739	0.0061	
1-Octen-3-ol			0.767	0.0036	
Decanal			0.771	0.0033	
1,8-Cineol			0.777	0.0030	
Hydroxy citronellal			0.783	0.0026	
Heptanal	2.18 ± 0.72	2.00 ± 0.71	**0.812**	**0.0014**	**C1**
2,3-Dimethylpyrazine	3.17 ± 1.07	3.33 ± 1.03	**0.823**	**0.0010**	**C2**
Trimethyl amine	2.17 ± 0.99	2.33 ± 1.03	**0.837**	**0.0007**	**C3**
Dimethyl trisulfide	2.08 ± 0.76	2.08 ± 0.76	**0.839**	**0.0006**	**C4**
Acetone	3.08 ± 0.64	3.00 ± 0.91	**0.858**	**0.0004**	**C5**
γ-Undecalactone	3.08 ± 0.64	2.67 ± 0.94	**0.859**	**0.0003**	**C6**
(-)-α-Pinene	2.75 ± 0.72	2.83 ± 0.80	**0.859**	**0.0003**	**C7**
4-Ethyl-2-methoxyphenol	2.92 ± 0.86	3.33 ± 0.94	**0.870**	**0.0002**	**C8**
Dimethyl benzyl carbinyl butyrate	2.50 ± 1.12	2.25 ± 0.72	**0.887**	**0.0001**	**C9**
2-Ethylpyrazine	2.92 ± 0.95	3.00 ± 1.15	**0.909**	**<0.0001**	**C10**
Propane-1-thiol	1.92 ± 0.95	2.08 ± 1.26	**0.916**	**<0.0001**	**C11**

We performed Spearman's rank correlation analysis to determine the discrepant (upper bold odorants) and correlation (bottom bold odorants) groups.

We next investigated the characteristics of olfactory recognition in the discrepant and correlation groups respectively. Previous studies suggested that the sense of smells such as odor qualities (*e.g.,* “citrus”, “woody”, and so on) can be varied according to the intensity[12,118]. We therefore performed Spearman’s rank correlation analysis on the relationship between the intensity and olfactory descriptors. The results of the correlation analysis of the relationship between the number and intensity of olfactory descriptors showed that the number of olfactory descriptors selected was not significantly correlated with the mean intensity score in the discrepant group (Spearman’s rank correlation analysis, rho = −0.08, $p = 0.39$, Fig. 5A). In contrast, the number of descriptors selected was significantly correlated with the mean intensity score in the correlation group (Spearman’s rank correlation analysis, rho = −0.29, $p = 0.002$, Fig. 5B). The raw data for the selected descriptors and intensity scores are shown in Appendix A and pleasantness and liking scores in Appendix B.

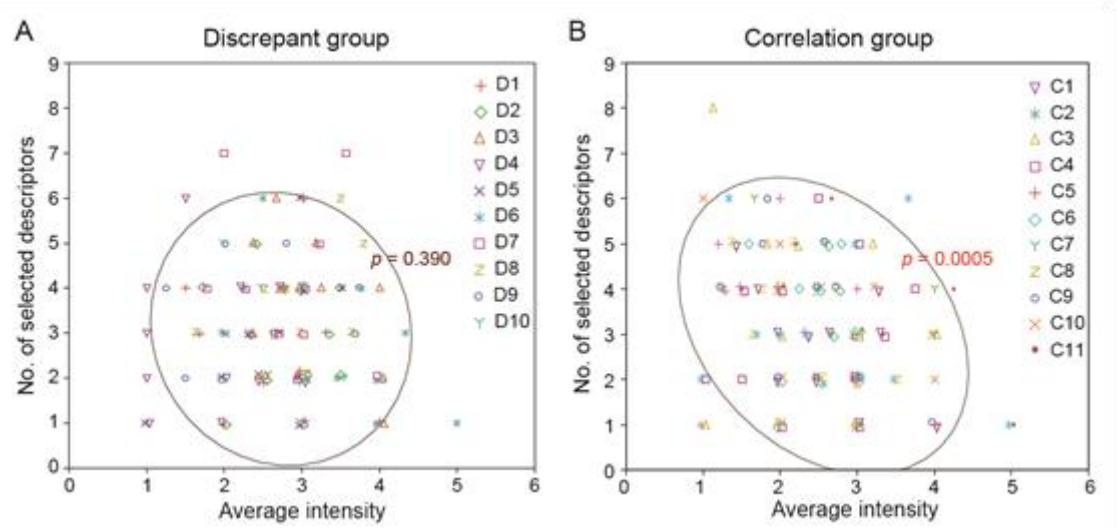

Fig. 5. The effect of the difference between pleasantness and liking on the choice of olfactory descriptors according to intensity. Spearman's rank correlation analysis revealed that the number of olfactory descriptors selected was not correlated with mean intensity scores in the discrepant group (A) but was significantly correlated with mean intensity scores in the correlation group (B). C1–C11 and D1–D10 represent the odorants in each group.

Based on the relationship between the number of descriptors and average intensity in the discrepant and correlation groups (Fig. 5), we then hypothesized that the choice of olfactory descriptors by participants was almost random, regardless to intensity, in discrepant groups, whereas the choice of descriptors was converged to a few descriptors when the participants sensed the smell strongly and clearly in the correlation group. To test the hypothesis, we focused on the reproducibility of the selected olfactory descriptors between participants. We regarded descriptors chosen by only one participant as temporally and transiently selected ones (defined as transient descriptors), and examined

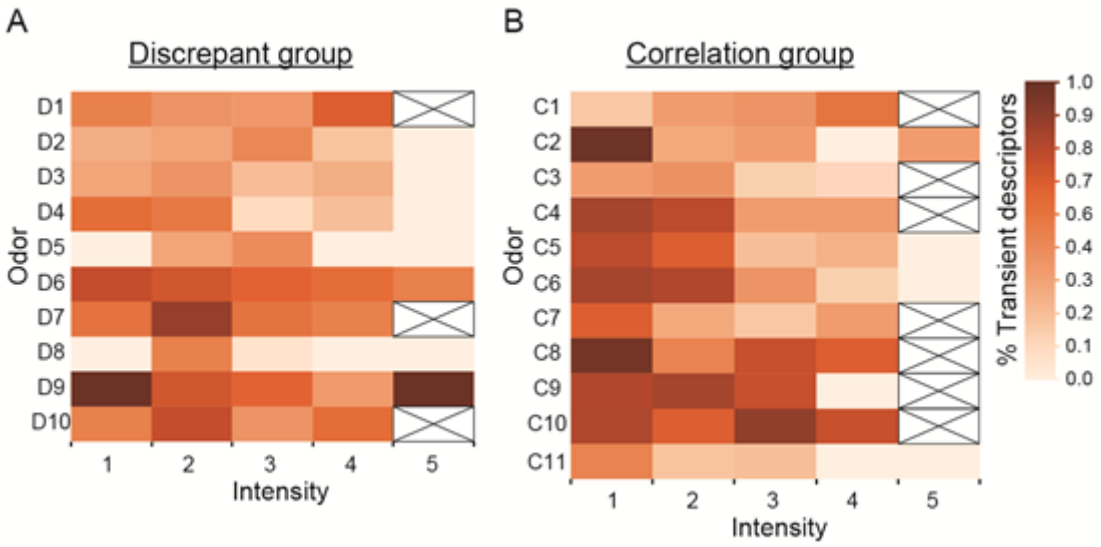

Fig. 6. Distribution of the ratio of transient descriptors within each intensity score for each odor. In the discrepant group (A), there was no trend in the distribution of intensity and the ratio of transient descriptors. In the correlation group (B), most odors showed high ratios for low-intensity scores and low ratios for high-intensity scores. C1–C11 and D1–D10 indicate the odorants in each group. The crosses in the white cells indicate that no participants rated the intensity of the odor; "% Transient descriptors" represents the ratio of transient descriptors within the intensity score for each odor.

the ratio of the transient descriptors in each intensity score of each odorant (see 2.2.4. Data analysis for detail). The results of the comparison of the reproducibility of the selected olfactory descriptors between groups showed that the discrepant group seemed to show no trend, and descriptor intensity was not associated with the ratio of transient descriptors (Fig. 6A). In addition, high and low ratios of transient descriptors were observed for odors with low and high intensity scores, respectively, in the correlation group (Fig. 6B).

2.4. Discussion

In this section, we discuss whether no significant difference between pleasantness and liking was related with olfactory recognition. We analyzed the correlation between odor pleasantness and liking to determine two groups, a discrepant group, which showed no significant correlations between these factors, and a correlation group, which showed significant correlations between these factors. The number of olfactory descriptors selected was not significantly correlated with mean intensity scores in the discrepant group, but it was significantly negatively correlated with mean intensity scores in the correlation group. In addition, reproducibility of the choice of olfactory descriptors according to intensity differed between the discrepant and correlation groups. Therefore, the findings suggested that the discrepancy between pleasantness and liking had relation with the choice of olfactory perceptual descriptors according to intensity.

We identified odorants that induced no significant difference between emotional evaluations, pleasantness and liking; however, the factors that caused this no significant difference remain unknown. We cannot exclude a possibility that ambiguity of smells may cause the no significant difference between pleasantness and liking because there seemed to be no clear differences between average scores of the evaluations (Table 2). Although we aimed to strictly control the intensity of the 36 odors by using the conditions based on a previous study and equivalent air-pressure from the self-made olfactometer, each intensity of the odors might not be uniform between participants. Preliminary test could be needed to survey the odor intensity and manner of odor presentation to regulate the ambiguity of smells. Otherwise, we can propose another possibility that chemical features of the odorants may induce the odors of the discrepant groups. For example, four types

of odorants, isovaleric acid, indole, trimethylamine, and propane-1-thiol, could reflect the effects of these factors on olfactory emotion. In general, the smells of these four odorants were malodorous, and the participants in the experiment evaluated as them as unpleasant (Appendix B). However, these odorants were grouped differently, as the former two odorants were in the discrepant group, and the latter two odorants were in the correlation group. The reason for the difference in grouping could have depended on the potential for conversion from malodorous to pleasant smells. The smell of isovaleric acid can become fruity via esterification, and the smell of indole can be perceived as floral in very low concentrations. In addition, this finding could have occurred because these two types of odorant can be bound to classes of olfactory receptors that signal pleasantness or unpleasantness. Furthermore, isovaleric acid could evoke fermentation odors, such as that of cheese, based on the *Sigma Aldrich Ingredients Catalog: Flavors & Fragrances* (http://www.sigmaaldrich.com)
and *The Good Scents* (http://www.thegoodscentscompany.com/), and emotional evaluation of isovaleric acid could depend on individual participants' diet histories. A large and comprehensive survey, including genetic variation in olfactory receptors, individual olfactory history, and the chemical properties of odorants, is required to elucidate the odorant-receptor interaction and experience factors involved in emotional discrepancy. Although our findings identified odors that could evoke emotional gaps, further research is required to examine the factors that cause these gaps.

The results for the correlation group could have occurred because of limited ability in olfactory verbalization. Previous studies reported that it was more difficult to verbalize olfactory stimuli, relative to other sensory modalities such as vision[45]. In the visual system, the occipital, parietal, temporal, and frontal cortices are strongly and

reciprocally interconnected, which allows feature-selective and detailed verbalization of visual stimuli [119,120]. In contrast, the connections between olfactory cortices and cortical areas involved in lexical-semantic representation are weak[45]. Moreover, previous studies have shown that the verbalization of olfactory stimuli was particularly difficult for naïve people[54]. This limited ability to verbalize olfaction could have led to the relationship between the selection and intensity of olfactory descriptors in the results (Figs. 5B and 6B). When the smells used in the experiment were weak and ambiguous, the participants chose a higher number of descriptors that did not overlap with those selected by other participants. This could mean that the participants made temporal and transient choices of higher numbers of olfactory descriptors because of the obscurity of the smells. When the odors were strong and clear, the participants tended to select only a few descriptors that overlapped with other participants' choices, even though they chose from a list of 146 descriptors. The finding that the choice of olfactory descriptors intensely perceived smells was limited to a few descriptors is consistent with the difficulty in olfactory verbalization observed in naïve people in previous studies[54]. Based on these results, olfactory verbalization or the choice of descriptors could have been influenced by subjective odor intensity in odorants for which pleasantness was correlated with liking.

In contrast to the correlation group, pleasantness was not significantly correlated with liking (Fig. 5A) and there was no trend in the reproduced descriptors according to intensity (Fig. 6A) in the discrepancy group, which could reflect the relationship between olfactory verbalization and emotion. In addition, despite the poor connection between olfactory and lexical cortices, the connection between areas associated with olfaction and the limbic region, including the amygdala, was strong[34,45]. Consistent with the structure of the olfactory system, a previous study suggested that the primality of emotion was the

axis of olfactory perception[59], and numerous studies have used pleasantness as the axis in the evaluation of olfactory perception[39,44,57,59,95,101,112]. In our experimental design, pleasantness represented instinctive and innate emotion, and liking represented individual and experienced-based emotion. Participants were instructed to note the difference in their emotions and evaluate the pleasantness and liking simultaneously. Conflict between different emotional evaluations could be related with the choice of olfactory descriptors according to intensity, which could indicate that the emotional process has some relationship with lexical-semantic representation in the olfactory system.

To our knowledge, this approach was the first to use dual emotional evaluations to explore the effect of the difference between predetermined and experience-based emotions in human olfaction. Some studies have examined whether pleasantness evoked by smells was predetermined[63,109], while others explored the way in which olfactory experience or history influenced emotional ratings[57,113]. However, few studies have examined the profile of emotionally discrepant smells such as those that are preferred or considered unpleasant. The current study showed that the no correlation between emotional evaluations could be related with the choice of olfactory descriptors. This finding could help to understand the effect of emotional valence on olfactory recognition.

Previous studies showed that odor quality could vary according to intensity[12,118], which could indicate that our findings were derived from variability in olfactory perception according to intensity. To confirm this possibility, we listed and sorted the olfactory perceptual descriptors based on the intensity scores for the odorants (Appendix A). The results showed that most descriptors were reproduced across intensity scores from 1 to 5 for each odor, which indicated that no substantial change in olfactory descriptors occurred according to intensity. Therefore, our findings reflected the effect of the

discrepancy between pleasantness and liking rather than the change in olfactory recognition according to intensity.

2.5. Limitations

The study was subject to some limitations, which should be noted. Our findings might be derived from the ambiguity of odor intensity, meaning poor validity of our findings. To obtain more robust findings, a preliminary experiment should be performed to determine the experimental conditions for the equivalent odor intensity and inducing clear differences between pleasantness and liking scores. Next, we did not examine the neural mechanism underlying the finding that the difference between pleasantness and liking influenced the selection of olfactory descriptors according to average intensity. An analysis of brain activity should be performed to reveal this mechanism. In addition, examination of the interactions between instinctive and experienced-based emotions via neural imaging of the amygdala, hippocampus, and orbitofrontal cortex is required. Further, major olfactory perceptual space (*e.g.*, plant- and edibility-related odors) should be analyzed in future studies. In the current study, the olfactory perceptual descriptors were considered entirely different; however, some similar descriptors, such as “lemon” and “fruity (citrus),” were included. Similar to a previous study[61], the identification of a major olfactory perceptual group is required via the analysis of several olfactory descriptor databases including the *Atlas of Odor Character Profiles*. Moreover, a follow-up assessment using different odor concentrations for each odor sample is required. A previous study demonstrated that one type of olfactory receptor switched to another type of receptor according to odor concentration, which exerted a strong influence on olfactory behavior[4]. Therefore, confirmation that the choice of olfactory descriptors depends on

odor concentrations as well as subjective intensity evaluations is required. In addition, participants' backgrounds should be strictly controlled. Although all the participants in the study were Japanese students from Kyushu University, to ensure uniformity in the participants' backgrounds, detailed background information, such as genetic variation in olfactory receptors and olfactory history from infancy, were not considered. Future studies that classify participants according to their backgrounds are required.

2.6. Conclusion

We examined the relationship between discrepancy of emotional evaluations and olfactory descriptions according to intensity. The discrepant group showed no significant difference between the two types of emotional evaluations and no significant correlation between the number and intensity of the olfactory descriptors selected, while the correlation group, in which the two types of emotion were matched, showed a significant negative correlation between the number and intensity of the olfactory descriptors selected. In addition, the replication of selected descriptors differed according to intensity between the discrepant and correlation groups. These results can suggest that the discrepancy between the emotional evaluations was related with the choice of olfactory perceptual descriptors according to intensity. Previously, no olfactory studies used dual emotional evaluations, and our findings could be first step to elucidate the complicated emotional state evoked by smells. Further, these findings could help to elucidate the olfactory cognitive process that underlies the effect of emotional valence on olfactory recognition and verbalization.

3. The olfactory recognition of an odor mixture varies depending on the molecular complexity of its components

3.1. Introduction

Odor mixtures can evoke smells that differ from those of their individual odor components. Various research groups have proposed the existence of two different olfactory perceptual modes: elemental and configural[12,44,68,121–123]. In the elemental mode, a mixture is perceived as the original smells of its components, whereas in the configural mode, a mixture is perceived as a new smell. Previous studies have demonstrated that these perceptual modes occur not only alternatively, but also simultaneously[12,44,68,121,122]. Some studies have suggested that the capacity to identify the odor components of a mixture depends on the number of components[12,121,122], and others have suggested that the perceptual mode is determined based on an individual's olfactory background (*e.g.*, olfactory learning and pre-exposure)[12,68]. Although several studies have investigated the factors underlying perceptual mode selection, the essential factors associated with each perceptual mode remain to be elucidated.

An important first step towards understanding how the perceptual mode of an odor mixture is determined is to identify which properties of a single odorant molecule influence olfactory recognition. Research has indicated that process of olfactory perception is initiated by neural coding in the peripheral olfactory system via olfactory receptor neurons[8,20]. Information from the receptors is then sent to the olfactory bulb and eventually terminates in olfactory-related areas in the cerebral cortex[21,36,124]. Previous

studies have suggested that the pattern of neural activity in each stage of olfactory processing depends on the type of odorant (*i.e.*, an odorant's molecular structure and chemical properties)[106,124]. Additionally, various features of an odorant molecule—such as functional groups and carbon chain length[23,51,59]—can affect odor quality. Such findings imply that certain aspects of an odorant molecule determine how it is perceived. However, it remains unclear how odorant characteristics reflecting multiple molecular features play a role in determining the perceptual mode.

Molecular complexity is characterized by several structural features such as bond connectivity, symmetry, and atomic components[125]. Although some recent studies have reported that the complexity of monomolecular odorants indeed affects olfactory perception[54,60], to our knowledge, no studies have examined the relationship between the perceptual mode of odor mixtures and molecular complexity.

In this section, we therefore aimed to clarify whether the complexity of odorant molecules influences the perceptual mode of odor mixtures. To examine whether the odor description is changed by mixing, we compared the odor description between odor binary mixture and its components. We prepared 12 odor components and 18 binary odor mixtures, which were divided into three groups according to their molecular complexity scores (low, medium, and high). We then conducted an experiment wherein participants were instructed to describe the smells of the components or mixtures by selecting from among several linguistic expressions (referred to as olfactory descriptors: *e.g.*, "woody" and "citrusy"). Each participant was also asked to rank the selected olfactory descriptors based on the relative intensity of each perceived smell. We then examined differences in the relative intensity of olfactory descriptors between odor mixture and its component odors using two types of analyses: comparison of individual olfactory descriptors

quantified by principal component analysis; comparison based on major olfactory perceptual groups established in a previous study[61]. The analyses suggested that molecular complexity can play a role in determining the perceptual mode of odor mixtures.

3.2. Materials and methods

3.2.1. Participants

Fourteen healthy volunteers (eight women and six men, mean age ± standard error of the mean = 22.1 ± 0.57 years) participated in the odor mixture experiment, while an additional ten healthy volunteers (two women and eight men, mean age ± standard error of the mean = 21.9 ± 0.877 years) participated in the odor component experiment. Participants of the two experiments did not overlap. All participants reported having normal olfaction, and none reported a history of psychiatric disorders. No participants were excluded from the data analysis. The ethics committee of the Faculty of Arts and Science at Kyushu University approved all experimental stimuli, protocols, and procedures (201510R2). Written informed consent was obtained from each participant. All methods of this research were performed in accordance with the approved guidelines.

3.2.2. Olfactory Stimuli

A total of 12 odor components were used in the present study (see Table 3 for information regarding concentration, solvent, and associated olfactory descriptors). The 12 odor components were selected as follows: (1) Odorants with only two olfactory descriptors listed in a commercial-release database, *Sigma Aldrich Ingredients Catalog: Flavors & Fragrances* (http://www.sigmaaldrich.com), were extracted from the 128-odorant collection published in a previous report[117]; and (2) the extracted odorants were

sorted according to their molecular complexity. Note that methylsulfanylmethane (Chemical Abstracts Service Number = 75-23-8, complexity = 2.8) and decanoic acid (Chemical Abstracts Service Number = 334-48-5, complexity = 110) were removed because the former was deemed hazardous to the participants, and the latter could not be detected via gas chromatography/mass spectroscopy (GC/MS) analysis, which was performed by Dr. Ishikawa and Ms. Kikuchi. The concentration of each odor component was determined based on the 128-odorant collection, in which participants could smell each odor component when they were mixed. Olfactory descriptors used in the present study were obtained from the Sigma Aldrich database, although participants were also permitted to provide their own terms.

Table 3. Odor components and their associated properties and solvent conditions.

No.	Odorant	C.A.S	Complexity	Olfactory descriptors (% Odorant, Solvent)
1	Propan-1-ol	71-23-8	7.2	Alcohol, Sweet (15%, Water)
2	Propane-1-thiol	107-03-9	7.2	Cabbage, Onion (0.0005%, 1,2-Pro)
3	Dimethyl trisulfide	3658-80-8	12.4	Meaty, Sulfurous (0.001%, 1,2-Pro)
4	Propan-2-one	67-64-1	26.3	Apple, Ethereal (25%, Water)
5	4-Methyl-3-penten-2-one	141-79-7	96.7	Vegetable, Vanilla (1%, 1,2-Pro)
6	Acetophenone	98-86-2	101	Almond, Hawthorne (0.15%, MO)
7	4-Ethyl-2-methoxyphenol	2785-89-9	114	Meaty, Smoky (0.1%, 1,2-Pro)
8	Diphenylether	101-84-8	116	Geranium, Green (1%, MO)
9	Isoamyl phenylacetate	102-19-2	181	Honey, Rose (0.5%, MO)
10	Dimethyl benzyl carbinyl butyrate	10094-34-5	215	Herbaceous, Plum (20%, 1,2-Pro)
11	Strawberry aldehyde	77-83-8	245	Strawberry, Sweet (1%, 1,2-Pro)
12	Caryophyllene	87-44-5	293	Spicy, Woody (15%, 1,2-Pro)

C.A.S. is Chemical Abstracts Service Number. 1,2-Pro is 1,2-Propanediol. MO is mineral oil.

The molecular complexity values of the odorants were obtained from the PubChem database of chemical molecules (https://pubchem.ncbi.nlm.nih.gov). The molecular complexity of an odorant in the database was calculated based on its structure, including its bond connectivity, diversity of non-hydrogen atoms, and symmetry[125].

We categorized the selected odorants (ranges given in parentheses) into the following three groups based on molecular complexity values: The four lowest

complexity odorants were classified into the low group (7.2–26.3), the four highest complexity odorants were classified into the high group (181–293), and the four odorants with complexities of approximately 100 were categorized into the medium group (96.7–116). This manner of classification is consistent with methods reported in a previous study[54]. The four odorants in each complexity category were combined to create six binary odorant mixtures (18 mixtures in total). All odor mixtures used in the present study are listed in Table 4. The complexity score of an odor mixture was defined as the sum of its binary components.

Table 4. Odor mixtures used in the present study.

No.	Component 1	Component 2	Sum of complexity
1	Propan-1-ol	Propane-1-thiol	14.4
2	Propan-1-ol	Dimethyl trisulfide	19.6
3	Propane-1-thiol	Dimethyl trisulfide	19.6
4	Propan-1-ol	Propan-2-one	33.5
5	Propane-1-thiol	Propan-2-one	33.5
6	Dimethyl trisulfide	Propan-2-one	38.7
7	4-Methyl-3-penten-2-one	Acetophenone	197.7
8	4-Methyl-3-penten-2-one	4-Ethyl-2-methoxyphenol	210.7
9	4-Methyl-3-penten-2-one	Diphenylether	212.7
10	Acetophenone	4-Ethyl-2-methoxyphenol	215
11	Acetophenone	Diphenylether	217
12	4-Ethyl-2-methoxyphenol	Diphenylether	230
13	Isoamyl phenylacetate	Dimethyl benzyl carbinyl butyrate	396
14	Isoamyl phenylacetate	Strawberry aldehyde	426
15	Dimethyl benzyl carbinyl butyrate	Strawberry aldehyde	460
16	Isoamyl phenylacetate	Caryophyllene	474
17	Dimethyl benzyl carbinyl butyrate	Caryophyllene	508
18	Strawberry aldehyde	Caryophyllene	538

We prepared the mixtures as follows: A total of 5.0 μL of each of the two component solutions was pipetted onto a cotton cloth (1 cm x 1 cm), following which the two cloths were placed together in a sealed 20-mL vial at room temperature (set to 25°C using an air-conditioner) for 5 min. After 5 min, the cotton cloths were removed, and the vials containing the gaseous odor mixtures were presented to each participant. The preparation of individual odor components was same to the mixtures.

3.2.3. Experimental procedure

Two types of experiments were performed: an odor mixture experiment and an odor component experiment.

The odor mixture experiment was conducted in a well-ventilated room over the course of 2 days, with sessions separated by 24 h. The order in which the 18 odor mixtures were presented was randomized (computer-generated) from day to day for each participant. During the evaluation of each mixture, participants were instructed to open the vial containing the mixture, sniff the content, and select at least four olfactory descriptors from the list of 22 olfactory descriptors generated based on the Sigma Aldrich database, which was presented to the participants on a computer screen. According to the Sigma Aldrich database, some odor components shared the same olfactory descriptors. (For example, both propan-1-ol and strawberry aldehyde evoked “sweet” descriptors, while both 4-ethyl-2-methoxyphenol and caryophyllene evoked “meaty” descriptors.) Therefore, the total number of listed descriptors was 22 rather than 24. Participants were allowed to provide their own olfactory descriptors if the smells they perceived were not on the list. Participants were also asked to rank the descriptors they had provided based on their relative intensity. They were instructed to enter the rankings using a computer. Participants were allowed 30 s to sniff each mixture, and a total of 1 minute to complete the sniffing/evaluation process (Fig. 7). After each 1-min evaluation, participants were asked to rest outside the experimental room for 2–3 min to eliminate the effect of residual odors. During the rest period, we aimed to control the olfactory condition using each participant’s own body odor. During the first minute of the rest period, participants were instructed to bury their face in their own clothes and smell them. In total, the experiment lasted approximately 1.5 h per participant.

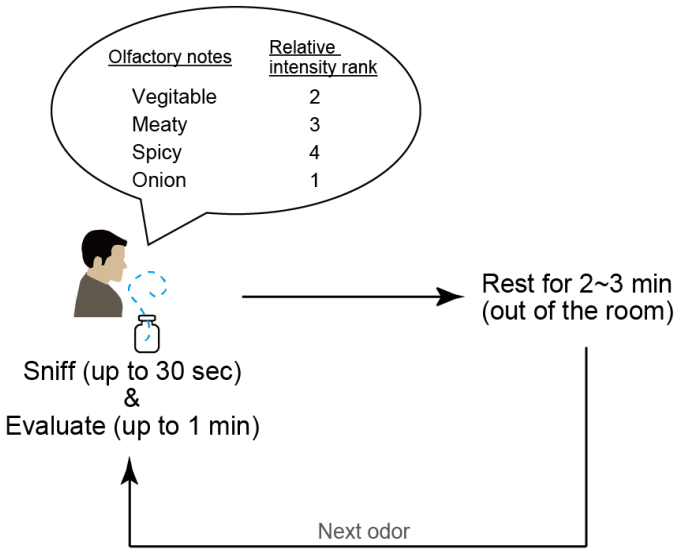

Fig. 7. The outline of the experiment. Participants sniffed each olfactory stimulus of 18 mixed odors or 12 single odors for up to 30 s, following which they evaluated the olfactory stimulus by selecting olfactory descriptors and providing a relative intensity ranking for the olfactory stimulus during the remainder of the 1-min period. After the evaluation, participants rested outside of the experimental room, and the process was repeated for a different olfactory stimulus 2-3 min later.

A similar design was utilized for the odor component experiment, except that the experiment was not repeated, and participants were asked to select/provide at least two olfactory descriptors.

3.2.4. Data analysis

The outline of data analysis is shown in Fig. 8. To compare the olfactory evaluations for odor mixture and its components, we first defined the pseudo mixture and real mixture (Fig. 8A). The pseudo mixture was derived from the data of the odor component experiment, and the real mixture was derived from the data of the odor

mixture experiment. We then compared the pseudo and real mixtures to confirm whether the odor description was different between pseudo mixture (odor components) and real mixture (odor mixture) at the level of individual olfactory descriptors and major perceptual group (fig. 8B).

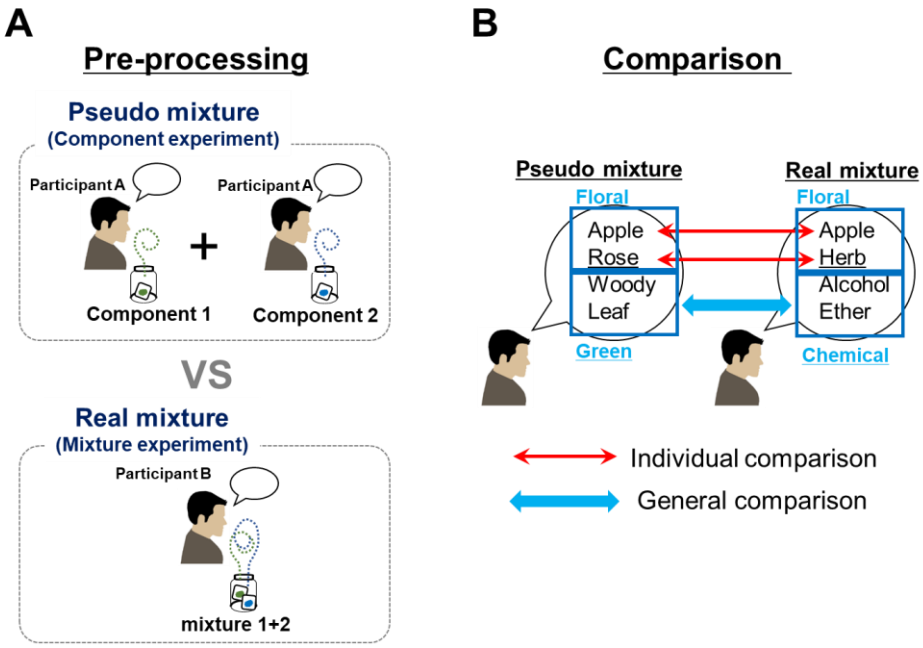

Fig. 8. The concept of data analysis. (A) We defined the pseudo and real mixtures. The pseudo mixture was derived from the data of the component experiment and the real mixture was derived from the mixture experiment. (B) We compared the pseudo and real mixtures at the level of individual descriptors and major perceptual group.

We defined the relative intensity score (RIS) of an olfactory descriptor as follows:

$$\mathrm{RIS}_{\mathrm{descriptor}} = \frac{X_{\max} - X_{\mathrm{descriptor}} + 1}{X_{\max}}, \quad (1)$$

where *descriptor* represents the focal olfactory descriptor, $X_{\max}$ represents the number of olfactory descriptors selected by the participant per odor component or mixture, and $X_{\mathrm{descriptor}}$ represents the rank of the olfactory descriptor provided by the participant based on relative intensity. If the olfactory descriptor was not selected by the participant,

the RIS was zero. We then compiled the $m \times n$ RIS data set (m = number of the provided descriptors, n = number of participants) for each mixture or component.

Next, we defined the pseudo-mixtures as an idealized mixture in which the olfactory descriptors of its components had been completely preserved (Appendix C-A). The pseudo-mixture was compared to the true mixture evaluated by participants in order to determine whether the olfactory descriptors of odor components had changed in the mixture. Pseudo-mixture values were calculated as follows: we obtained the matrix $C_{m,n}^{x}$ which consisted of the $m \times n$ RIS data set for each odor component, where x represents the number of odor samples (1–12), m represents the number of the provided descriptors (row data), and n represents the number of participants (column data). The RIS data sets in $C_{m,n}^{x}$ were derived from the results of the component experiment. Using $C_{m,n}^{x}$, we calculated the RIS-matrix for pseudo-mixture $P_{m,n}^{x}$ as

$$P_{m,n}^{x} = C_{m,n}^{k} + C_{m,n}^{l} , \quad (2)$$

where k and l represent the number of odor components from 1 to 12 ($k \neq l$). The combination of x, k, and l was based on the data presented in Table 4. For example, pseudo-mixture 1 was regarded as the sum of the RIS-matrices of odor components 1 and 2 ($P_{m,n}^{1} = C_{m,n}^{1} + C_{m,n}^{2}$). In contrast to that of the pseudo-mixture, we defined the RIS-matrix of the real mixture based on the actual results of the mixture experiment. Therefore, the RIS data sets for the real and pseudo-mixtures ranged from No. 1 to No. 18, respectively.

To evaluate the differences between the real and pseudo-mixtures, we performed comparison based on both individual olfactory descriptors and major olfactory perceptual groups (Fig. 8B). To compare the individual olfactory descriptors, each olfactory descriptor was quantified via principal component analysis (PCA) (Appendix C-B). We

applied PCA to reduce the dimensions of participants (*n*) and integrated participant responses for each olfactory descriptor. PCA was performed based on the correlation coefficient matrix using JMP 12 (SAS Institute Inc., NC, USA). We then obtained multi-dimensional eigenvalue vectors for each olfactory descriptor. The number of vector dimensions was determined based on the individual cumulative contribution ratio (≥ 80%), respectively. We compared the Euclidean distance of each eigenvalue vector for each pair of real and pseudo-mixtures (*e.g.,* real mixture 1 versus pseudo mixture 1). Descriptors of "unknown" provided by participants were excluded from statistical analysis.

For comparisons based on major olfactory perceptual groups, we classified the olfactory descriptors into previously established "perceptual communities" [61] (Appendix C-C). In this previous study, the seven major olfactory perceptual communities (termed communities *a* to *g*) were identified based on odor qualities (*e.g.,* community *a* included plant-related odors such as "herb", "wood", etc.). In our study, 90 olfactory descriptors (22 descriptors were derived from the Sigma Aldrich database, and 68 descriptors were provided by participants) were categorized into the seven communities based on the methods of Kumar *et al*. (2015). The degrees of correspondence between the olfactory descriptors and the communities are listed in Table 3. Non-typeable descriptors such as "the smell of a hospital" were less than 10% each for real and pseudo-mixture RIS data sets and excluded from the comparison between real and pseudo mixtures. In each pair of real and pseudo-mixtures, the RIS data sets were compared according to perceptual community.

Table 4. List of olfactory descriptors and perceptual communities.

Olfactory descriptors	Community	Derived	Olfactory descriptors	Community	Derived
Alcohol	g	S. A.	Gelatin	X	F. A.
Almond	f	S. A.	Ginger	d	F. A.
Apple	c	S. A.	Hay	a	F. A.
Cabbage	f	S. A.	Ink	X	F. A.
Ethereal	g	S. A.	Insect repellent	e	F. A.
Geranium	c	S. A.	Iron	b	F. A.
Green	b	S. A.	Energy drink	X	F. A.
Hawthorne	c	S. A.	Leaf of marigold	b	F. A.
Herbaceous	a	S. A.	Lemon	d	F. A.
Honey	c	S. A.	Minty lip balm	X	F. A.
Meaty	f	S. A.	Magnolia	c	F. A.
Onion	f	S. A.	Manicure	X	F. A.
Plum	g	S. A.	Marker pen	X	F. A.
Rose	c	S. A.	Felt tip pen	X	F. A.
Smoky	a	S. A.	Nail polish remover	X	F. A.
Spicy	a	S. A.	Oil	d	F. A.
Strawberry	g	S. A.	Ointment	X	F. A.
Sulfurous	e	S. A.	Paint	e	F. A.
Sweet	g	S. A.	Peach	g	F. A.
Vanilla	g	S. A.	Pickle	X	F. A.
Vegetable	b	S. A.	Pomegranate	X	F. A.
Woody	a	S. A.	Pop	X	F. A.
Almond jelly	X	F. A.	Powder medicine with syrup	X	F. A.
Ammonia	f	F. A.	Red wine	g	F. A.
Antisepsis before injection	f	F. A.	Roast	f	F. A.
Baloon	X	F. A.	Rotten	f	F. A.
Banana	g	F. A.	Rubber	f	F. A.
Bandage	X	F. A.	Seirogan	X	F. A.
Burnning garbage	X	F. A.	Similar to Mmixture 17	X	F. A.
Candy	g	F. A.	Smell of grandmather's house	X	F. A.
Carrot	b	F. A.	Smell of hospital	X	F. A.
Cherry	g	F. A.	Smell of new bag	X	F. A.
Cinnamon	a	F. A.	Smell of new shoes	X	F. A.
Coarse tea	c	F. A.	Smell of new shop	X	F. A.
Coconut	e	F. A.	Smell of roast	f	F. A.
Coin	X	F. A.	Smell of rubber boot	f	F. A.
Coke	X	F. A.	Sour fruit	X	F. A.
Compress	X	F. A.	Sweat	e	F. A.
Detergent	X	F. A.	Taping	X	F. A.
Earth	f	F. A.	Unknown	X	F. A.
Farm	X	F. A.	Varnish	X	F. A.
Fish	f	F. A.	Vegetable juice	X	F. A.
Food waste	f	F. A.	Vinegar	e	F. A.
Gummed tape	X	F. A.	Welsh onion	f	F. A.
Garlic	f	F. A.	Yoghurt	e	F. A.

The correspondence between olfactory descriptors used in this study and the "perceptual communities" defined in the previous study of Ritesh Kumar *et al*. is listed. In the "Community" column, "X" represents the non-typeable descriptors in the previous study. In the "Derived" column, "S.A." represents the *Sigma Aldrich Ingredients Catalog: Flavors & Fragrances* and "F.A." represents the freely answered by participants.

3.2.5. Re-analysis of data of mammal olfactory bulb

To consider the neural mechanism that molecular complexity influences the olfactory recognition, we examined the relationship between odorant complexity and the number of activated glomeruli based on the findings of a previous study[106]. In the previous study, 72 odorants were used and two types of glomerular clusters were observed, where the one responded to one type of odorant selectively, and the other responded to several types of odorants or had uncharacterised responses. In the individual two types of the glomerular clusters, the regression line was fit using the least squares method using JMP 12 (SAS Institute Inc., NC, USA), and the goodness of fit of the models was evaluated.

3.2.6. Statistics

Because our experimental data did not exhibit a normal distribution, we used non-parametric tests for statistical analyses. The Wilcoxon signed-rank test ($\alpha = 0.05$) was performed to compare the Euclidean distance of each eigenvalue vector from the PCA. Wilcoxon text with Bonferroni α correction were performed to compare data based on perceptual communities. The corrected α levels were as follows: 0.05/7 = 0.0071 in pair of 6 and16 of 1st-day real mixture vs pseudo-mixture; 0.05/6 = 0.0083 in pair of 1, 2, 4, 5, 8, 10, 13, 14, 15, and 18 of 1st-day real mixture vs pseudo-mixture and pair of 1, 2, 4, 5, 6, 12, 14, 17, and 18 of 2nd-day real mixture vs pseudo-mixture; 0.05/5 = 0.01 in pair of 3, 7, 9, 11, 12, and 17 of 1st-day real mixture vs pseudo-mixture and pair of 3, 7, 8, 9, 10, 11, 13, 15, and 16 of 2nd-day real mixture vs pseudo-mixture. Wilcoxon signed-rank tests and Wilcoxon tests were performed using JMP 12 (SAS Institute Inc., NC, USA).

3.3. Results

We compared the real and pseudo-mixtures by each olfactory descriptor quantified by PCA (Fig. 8B). The analysis of PCA revealed that low-complexity mixtures had significance or marginal significance (pseudo vs 1st-day real; pair 1: $p = 0.031$, pair 3: $p = 0.0092$, pair 5: $p = 0.081$, pair 6: $p = 0.086$, pseudo vs 2nd-day real; pair 1: $p = 0.089$, pair 3: $p = 0.0472$, pair 4: $p = 0.0071$, pair 5: $p = 0.025$, Wilcoxon signed-rank test, Table 5).

Table 5. The result of statistical comparison between real and pseudo mixtures with PCA.

Complexity group	Mixture pair (real vs pseudo)	Real (1st day) vs Pseudo		Real (2ns day) vs Pseudo	
		df	*p* value	*df*	*p* value
Low complexity	1	23	0.0312*	22	0.0885 †
	2	23	0.166	21	0.963
	3	16	0.0092*	17	0.0472*
	4	25	0.163	24	0.0071*
	5	23	0.0809 †	23	0.0249*
	6	24	0.0864 †	24	0.274
Medium complexity	7	30	0.238	26	0.542
	8	25	0.256	24	0.556
	9	24	0.179	26	0.0014*
	10	29	0.594	28	0.452
	11	25	0.912	25	0.630
	12	23	0.300	26	0.0338*
High complexity	13	24	0.0002*	22	0.077 †
	14	19	0.151	23	0.307
	15	19	0.748	27	0.517
	16	22	0.649	22	0.626
	17	23	0.0497*	28	0.353
	18	20	0.0703 †	21	0.095 †

The left column shows the number of mixture pair (*e.g.* real-mixture 1 vs pseudo-mixture 1). The *df*s were based on the number of quantified olfactory descriptors. * indicates the significance and † do the marginal significance.

We then compared the real and pseudo-mixtures by major olfactory perceptual groups, "perceptual community" [61] (Fig. 8). Analysis of each "perceptual community" revealed significant and marginally significant differences in community *b* (including green-related odors such as "fresh" and "vegetable") and community *g* (including sweet-related odors such as "sweet" and "fruit") of the low-complexity group (pseudo vs 1st-day real in Table 6; community *g* in pair #1: $p = 0.0001$, community *b*: $p = 0.012$ and community *g*: $p = 0.0016$ in pair #2, community *f*: $p = 0.012$ and community *g*: $p = 0.004$ in pair #4, pseudo vs 2nd-day real in Table 7; community *g* in pair #1: $p = 0.0035$,

community *b*: $p = 0.012$ and community *g*: $p < 0.0001$ in pair #2, community *g* in pair #4: $p = 0.0038$, community *g* in pair #6: $p = 0.0051$, Wilcoxon rank sum test with Bonferroni α correction Table 6 and 7).

Table 6. The result of statistical comparison by the perceptual community between real (1st day) and pseudo mixtures.

Real (1st day) vs Pseudo											
Low				Medium				High			
Pair	Com.	*p* value	Rel.	Pair	Com.	*p* value	Rel.	Pair	Com.	*p* value	Rel.
1	*a*	0.123		7	*a*	0.204		13	*a*	0.455	
	b	0.0309			*b*	0.620			*b*	0.177	
	c	0.465			*c*	0.371			*c*	0.427	
	d	-			*d*	-			*d*	0.447	
	e	0.855			*e*	-			*e*	-	
	f	1.00			*f*	0.719			*f*	0.913	
	g	1E-04*	R < P		*g*	0.0488			*g*	0.461	
2	*a*	0.648		8	*a*	0.247		14	*a*	0.188	
	b	0.0116 †	P < R		*b*	0.525			*b*	0.176	
	c	0.855			*c*	0.203			*c*	0.131	
	d	-			*d*	-			*d*	0.272	
	e	0.272			*e*	0.447			*e*	-	
	f	0.635			*f*	0.0413			*f*	0.148	
	g	0.0016*	R < P		*g*	0.459			*g*	1.00	
3	*a*	0.212		9	*a*	0.315		15	*a*	0.0284	
	b	0.443			*b*	0.150			*b*	0.590	
	c	0.903			*c*	0.778			*c*	0.791	
	d	-			*d*	-			*d*	0.272	
	e	-			*e*	-			*e*	-	
	f	0.0214			*f*	0.198			*f*	0.139	
	g	1.00			*g*	0.575			*g*	0.150	
4	*a*	0.967		10	*a*	0.100		16	*a*	0.516	
	b	0.144			*b*	0.383			*b*	0.768	
	c	0.754			*c*	0.900			*c*	0.0402	
	d	-			*d*	0.447			*d*	0.447	
	e	0.333			*e*	-			*e*	0.447	
	f	0.0119 †	P < R		*f*	0.0547			*f*	0.0978	
	g	0.002*	R < P		*g*	0.576			*g*	0.859	
5	*a*	0.487		11	*a*	0.906		17	*a*	0.263	
	b	0.488			*b*	0.536			*b*	0.438	
	c	0.154			*c*	0.636			*c*	0.143	
	d	-			*d*	-			*d*	-	
	e	0.272			*e*	-			*e*	-	
	f	0.745			*f*	0.228			*f*	0.386	
	g	0.199			*g*	0.008*	R < P		*g*	0.929	
6	*a*	0.175		12	*a*	0.574		18	*a*	0.337	
	b	0.303			*b*	0.383			*b*	0.917	
	c	0.441			*c*	0.0447			*c*	0.456	
	d	0.447			*d*	-			*d*	0.807	
	e	0.272			*e*	-			*e*	-	
	f	0.702			*f*	0.833			*f*	0.879	
	g	0.0314			*g*	0.228			*g*	0.0032*	R < P

The column of “Pair” indicates the number of mixture pair (*e.g.*, real-mixture 1 vs pseudo-mixture 1). The column of “Com.” indicates the perceptual community. Wilcoxon rank-sum tests were performed to compare relative intensity scores between real mixtures (N = 14) and pseudo-mixtures (N = 10). The α level was Bonferroni corrected. Dashes indicate “0” responses, which were excluded when Bonferroni correction was performed. In the “Rel.” column, “Rel.” represents the relation of the relative intensity scores between each pair of real and pseudo mixture, “R” refers to the real mixture, while “P” refers to the pseudo-mixture. The relation was shown only in the perceptual community exhibiting significant difference.

Table 7. The result of statistical comparison by the perceptual community between real (2nd day) and pseudo mixtures.

Real (2nd day) vs Pseudo											
Low				Medium				High			
Pair	Com.	*p* value	Rel.	Pair	Com.	*p* value	Rel.	Pair	Com.	*p* value	Rel.
1	*a*	0.166		7	*a*	0.016 †	P < R	13	*a*	0.882	
	b	0.284			*b*	0.0993			*b*	0.203	
	c	0.727			*c*	0.443			*c*	0.976	
	d	-			*d*	-			*d*	-	
	e	0.807			*e*	-			*e*	-	
	f	0.203			*f*	0.522			*f*	0.386	
	g	0.0035*	R < P		*g*	0.0592			*g*	0.859	
2	*a*	0.478		8	*a*	0.311		14	*a*	0.004*	R < P
	b	0.0119	P < R		*b*	0.0409			*b*	0.0368	
	c	1			*c*	0.589			*c*	0.0468	
	d	-			*d*	-			*d*	0.272	
	e	0.272			*e*	-			*e*	-	
	f	0.173			*f*	0.0384			*f*	0.0367	
	g	< 1E-04*	R < P		*g*	0.404			*g*	0.859	
3	*a*	0.594		9	*a*	0.0686		15	*a*	0.692	
	b	0.557			*b*	0.105			*b*	0.387	
	c	0.272			*c*	1.00			*c*	0.813	
	d	-			*d*	-			*d*	0.272	
	e	-			*e*	-			*e*	-	
	f	0.0216			*f*	0.103			*f*	-	
	g	0.636			*g*	0.517			*g*	0.157	
4	*a*	0.113		10	*a*	0.658		16	*a*	0.059	
	b	0.471			*b*	0.306			*b*	0.215	
	c	0.948			*c*	0.647			*c*	0.0305	
	d	-			*d*	-			*d*	-	
	e	0.099			*e*	-			*e*	-	
	f	0.0787			*f*	0.347			*f*	0.0523	
	g	0.0038*	R < P		*g*	0.0217			*g*	0.516	
5	*a*	0.859		11	*a*	0.258		17	*a*	0.394	
	b	0.0796			*b*	0.688			*b*	0.202	
	c	0.613			*c*	0.576			*c*	0.157	
	d	-			*d*	-			*d*	0.447	
	e	0.272			*e*	-			*e*	-	
	f	0.536			*f*	0.0523			*f*	0.272	
	g	0.138			*g*	0.105			*g*	0.594	
6	*a*	0.0588		12	*a*	0.638		18	*a*	0.455	
	b	0.722			*b*	1.00			*b*	0.322	
	c	0.266			*c*	0.0170			*c*	0.125	
	d	-			*d*	0.447			*d*	0.272	
	e	0.272			*e*	-			*e*	-	
	f	0.239			*f*	0.611			*f*	0.807	
	g	0.0051*	R < P		*g*	0.0133			*g*	0.0043*	R < P

The column of “Pair” indicates the number of mixture pair (*e.g.,* real-mixture 1 vs pseudo-mixture 1). The column of “Com.” indicates the perceptual community. Wilcoxon rank-sum tests were performed to compare relative intensity scores between real mixtures (N = 14) and pseudo-mixtures (N = 10). The α level was Bonferroni corrected. Dashes indicate “0” responses, which were excluded when Bonferroni correction was performed. In the “Rel.” column, “Rel.” represents the relation of the relative intensity scores between each pair of real and pseudo mixture, “R” refers to the real mixture, while “P” refers to the pseudo-mixture. The relation was shown only in the perceptual community exhibiting significant difference.

The findings of these two analyses can suggest that low-complexity odor mixtures would be perceived as new smells more easily than medium- or high-complexity mixtures (Table 8).

Table 8. The ratio of significant change between real and pseudo mixtures.

Complexity	Comparison with PCA	Comparison based on community
Low	41.7% (5/12)	58.3 % (7/12)
Medium	16.7 % (2/12)	8.3 % (1/12)
High	16.7 % (2/12)	25.0 % (3/12)

We next investigated the relationship between odorant complexity and the number of activated glomeruli by re-analyzing the data of a previous study[106]. Mammals shares the similar olfactory system such as the same type of olfactory receptors and the structure of periphery from receptor neurons to olfactory bulb, indicating that the study of the mammal system can contribute to understand human olfactory system. The re-analysis revealed that the fit of the line was significant for glomerular clusters that responded selectively to certain types of odorants (Fig. 9A, $p = 0.032$), where lower complexity odorants induced the more number of activated glomeruli. The fit of the line was not significant for clusters that responded to multiple types of odorants or clusters that exhibited uncharacterized responses (Fig. 9B, $p = 0.996$). From the results, molecular complexity can influence the spatial activity pattern in olfactory bulb.

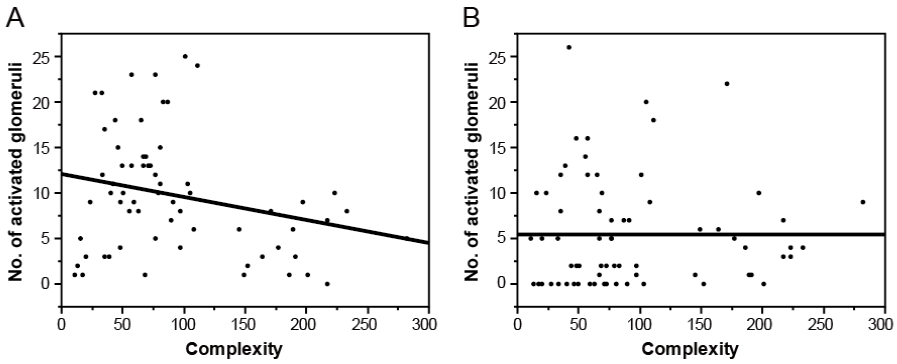

Fig. 9. Re-analyses of the data of Yuji K. *et al*. The regression line was fit using the least squares method, and the goodness of fit of the models was evaluated. The fit of the line was significant for glomerular clusters that responded selectively to certain types of odorants (A, $p = 0.032$), while the fit was not significant for clusters that responded to multiple types of odorants or clusters that exhibited uncharacterized responses (B, $p = 0.996$).

We confirmed whether differences in the number of selected olfactory descriptors affected the results. We found no difference of the selected descriptors among components (Fig. 10A) and mixtures (Fig. 10B).

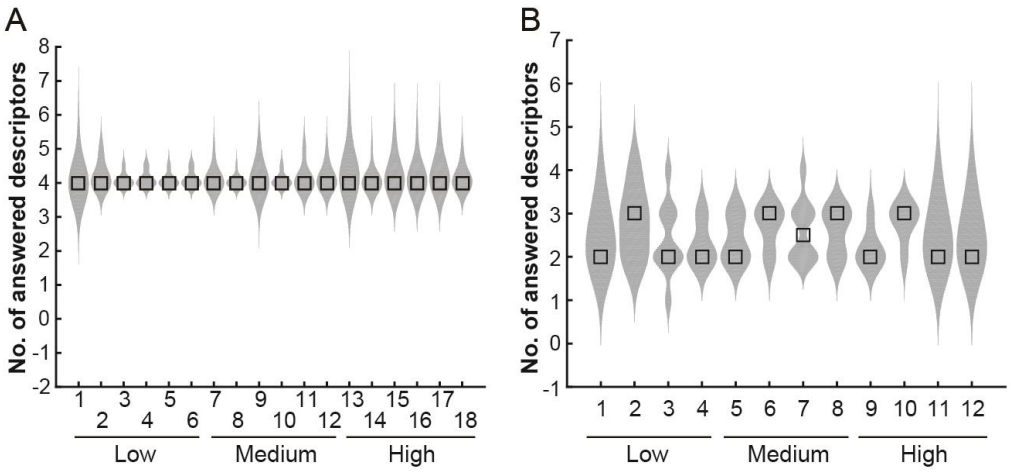

Fig. 10. The number of provided olfactory descriptors. The y-axis shows the total number of olfactory descriptors provided per mixture (A) or component (B). Wilcoxon tests revealed no significant differences among the mixtures or components (A: $p = 0.71$, B: $p = 0.58$).

3.4. Discussion

In this section, we demonstrated that odor mixtures composed of low-complexity odorants were perceived as relatively different smells from those of the original components. To determine whether the smells of odor components had changed when mixed with other components, we compared participant responses to a series of pseudo-mixtures, which were presumed to retain the olfactory descriptors of the individual components. PCA of individual olfactory descriptors revealed that real low-complexity

mixtures induced different olfactory descriptors than those indicated for pseudo-mixtures. Analysis of olfactory descriptors based on seven major perceptual communities[61] revealed that real and pseudo-mixtures of the low-complexity group differed significantly with regard to perceptual community. Thus, our findings suggest that humans have the olfactory capacity to detect a specific smell from among a mixture, depending on the complexity of its odor components.

Our results indicated that mixtures composed of low-complexity odorants were perceived as novel odors, and this result may be explained by odorant-specific spatial patterns of glomerular activity. In the olfactory system, odor information is generated in olfactory receptors, which directly project to the olfactory bulb, wherein odor information is represented as odorant-specific spatial patterns of glomerular activity[21,124]. Previous research has indicated that overlap of spatial activation patterns in the olfactory bulb can impede the detection of odor components when some odorants are sniffed simultaneously[25]. According to these studies, olfactory recognition may depend on the pattern of spatial activity in the olfactory bulb. Therefore, we hypothesized that overlap of glomerular activity results in differential odor recognition between the mixture and component, and that the extent of the activity overlap may depend on the molecular complexity of odor components. To test the hypothesis, we examined the association between odorant complexity and the number of activated rodent glomeruli based on the findings of a previous study. The authors of the study observed that some glomerular clusters selectively responded to one type of odorant, while other clusters responded to several types of odorants or exhibited uncharacterized responses[106]. Our additional analyses of their data confirmed that large numbers of glomeruli were activated by the lower-complexity odorants, whereas fewer glomeruli were activated by higher-

complexity odorants in the clusters that exhibited selective responses (Fig. 9A). These results suggest that low-complexity odor components increase the potential for spatial overlap in glomerular activity, relative to that observed for medium- or high-complexity components. Such differences may in turn underlie differences in odor recognition between low-complexity mixtures and medium- or high-complexity mixtures. However, these hypotheses are based on neural activity within the rodent olfactory bulb, as no study has directly investigated the neural response within the human olfactory bulb. Nonetheless, the fundamental principles of the olfactory system, including odorant-receptor interactions, population coding, and inhibitory processing, are usually shared among mammals[20,23,126]. Thus, the molecular complexity of an odorant may affect how it is processed in the olfactory bulb, and this may be an essential factor in determining the perceptual mode of a mixture.

Although previous studies have suggested that odorants of higher complexity bind to a larger number of olfactory receptors[54], this study cannot contradict with our result. Olfactory receptor neurons project to glomeruli in the olfactory bulb, where glomerular activation induced by the olfactory receptor neurons undergoes inhibitory regulation (*i.e.,* lateral inhibition). Thus, binding to a large number of olfactory receptors may result in relatively greater lateral inhibition.

As for our experiments, the two analyses conducted in the present study exhibited consistent results, in which low-complexity odorants were perceived as novel smells when individual components were mixed with one another. We examined differences between real and pseudo-mixtures by comparing data among individual olfactory descriptors or perceptual communities. Low-complexity mixtures 1, 4, and 6 exhibited significant or marginally significant differences in both comparisons of

individual olfactory descriptors and those based on perceptual community (Tables 5, 6 and 7). Our results suggest that participants perceived the smells of these mixtures as distinct from their components with regard to both specific and general odor qualities. For other low-complexity mixtures, significant differences in either olfactory descriptors or perceptual community were observed. In mixtures 3 and 5, we observed significant differences only in the comparison of olfactory descriptors. Such results indicate that the real and pseudo-mixtures were perceived as similar in quality, although participants were capable of differentiating the smells verbally. In the present study, participants carefully evaluated each smell by referring to a pre-determined list of olfactory descriptors. Furthermore, the number of olfactory descriptors selected from the list was much higher than the number of terms provided by participants (ratio of listed to provided descriptors = 13:3 in 1st-day real mixture 3; 12:5 in 2nd-day real mixture 3; 10:0 in pseudo mixture 3; 18:2 in 1st-day mixture 5; 18:2 in 2nd-day mixture 5; 14:3 in pseudo mixture 5). These results indicate that minor alterations in olfactory descriptors may have occurred within the perceptual community of mixtures 3 and 5. For mixture 2, significant differences were observed only in the analysis of perceptual communities. This result may be attributed to the property of the olfactory verbalization. Previous studies have demonstrated that the verbalization of aspects related to olfactory stimuli is more difficult than that for other senses such as vision[45]. Thus, limitations in olfactory verbalization may result in the recognition of real and pseudo-mixtures as qualitatively different, even if the difference cannot be verbalized when presented with a list of options. In contrast to findings observed for low-complexity mixtures, few medium- or high-complexity mixtures exhibited significant differences with regard to olfactory descriptors or perceptual community. Thus, these findings indicate that the smells of low-complexity mixtures are

perceived as different from those of their components with regard to specific (olfactory verbal expression) and/or general qualities (perceptual community).

We next discuss the validity of the methods used to analyze differences among individual olfactory descriptors and perceptual communities. PCA was applied to quantitatively evaluate data for each olfactory descriptor. In previous studies, PCA was utilized to identify the major olfactory perceptual groups or characterize odor profiles by reducing the dimensions of olfactory perceptual descriptors[56,59,71]. In the present study, we utilized PCA to quantify each olfactory descriptor by reducing the dimensions of participant responses, which enabled us to perform the statistical comparison between the real and pseudo-mixtures. By comparing individual olfactory descriptors, we aimed to increase the sensitivity of detecting alterations in olfactory recognition, even if the alteration was minor (*e.g.,* transformation from "Rose" to "Geranium"). In our subsequent analyses, we compared differences in perceptual communities between the real and pseudo-mixtures. The seven perceptual communities were established in a previous study by performing a network analysis of numerus olfactory descriptors obtained from several databases, including *Sigma Aldrich Ingredients Catalog: Flavors & Fragrances*[61]. By comparing the communities, we intended to examine whether general odor quality differed substantially between the real and pseudo-mixtures. Thus, the use of both analyses enabled us to detect both minor/specific and substantial/general alterations in olfactory recognition between the real and pseudo-mixtures.

The selection of olfactory descriptors can be affected by a participant's lexical knowledge[57]. In the present study, we limited the number of olfactory descriptors and instructed participants to select descriptors from among those on an existing list, enabling us to control for differences in the lexical background of participants. A previous study

reported that single, high-complexity odorants induced more descriptors[54]. This previous study focused on the number of olfactory descriptors, and participants were instructed to freely provide their own olfactory descriptors. In contrast, our study focused on the olfactory descriptors themselves rather than on the number of descriptors, and participants were instructed to select at least four (odor mixture experiment) or two (odor component experiment) olfactory descriptors from among those on the given list in the component or mixture experiment, respectively (although they were allowed to provide their own descriptors if they were not on the list). The selection of olfactory descriptors from the list would drive the participants towards elemental perception at the expense of configural perception[127]. However, we observed that low-complexity odor mixtures exhibited differences in both olfactory descriptors and perceptual quality between real and pseudo-mixtures. Furthermore, our analyses confirmed that the total number of olfactory descriptors provided by the participants did not significantly differ among the odor component and mixtures used in the present study (Fig. 10). Thus, our findings indicate that molecular complexity plays a role in determining the perceptual mode, and that the findings were not affected differences in the number of olfactory descriptors provided.

3.5. Conclusion and improvement points

The study of this section has several limitations. First, the number of odorants and mixtures investigated in our experiments may have been insufficient for deriving a definitive conclusion. To examine the association between molecular complexity and perceptual mode, we utilized odor components and mixtures with a discrete rather than continuous range of complexity scores. Although differences between real and pseudo-

mixtures were observed in the low-complexity group, we cannot exclude the possibility that other ranges of complexity scores (*e.g.,* 50–100) would yield different results. Furthermore, in our analysis of perceptual communities, the insufficient variety of odorants may explain why significant differences were observed only for community *g* in the low-complexity group. Comprehensive investigations using a greater number of odorants and mixtures may enable researchers to analyze the perceptual profiles of individual mixtures in detail. Such analyses are essential for demonstrating the robustness of the odorant-complexity-based regularity or identifying exceptions to this regularity, as represented in Fig 9B. The results of such comprehensive examinations can be used to establish a database that would enable investigators to predict the perceptual mode of a mixture based on its odor components. Second, we simplified the design of our study by including only binary odor mixtures, although odor mixtures in the real world are often composed of numerous odorants. Therefore, our finding that low-complexity mixtures induce configural perception may be restricted to binary odor mixtures. Although our findings partially elucidate the association between molecular features of odorant molecules and olfactory recognition, future studies should examine this association for mixtures of three or more odorants to improve the generalizability of our findings.

In conclusion, the findings in the section suggest that molecular complexity influences the olfactory perceptual mode of odor mixtures. Specifically, we observed that odor mixtures composed of low-complexity odorants were perceived as relatively novel odors, indicating that molecular complexity may influence how the odorant and receptor interact to produce the associated neural representation in the central olfactory system. Such information may further our understanding of the olfactory perceptual modes of odor mixtures at the receptor level.

4. General discussion

4.1. Summary of results and discussions

In this thesis, we explored the factors determining olfactory recognition and found that emotional states and odorant molecular feature had effects on olfactory recognition such as the selection of olfactory perceptual descriptors and recognition of odor mixtures.

For the investigation of emotional effect on olfactory recognition, we tested whether no significant difference between dual emotional evaluations, pleasantness and liking influenced olfactory recognition. After analyzing the correlation between odor pleasantness and liking obtained from subjective assessment, odorants belonging to the following two groups were identified: a discrepant group showed no significant correlations between the pleasantness and liking; and a correlation group showed significant correlations between the factors. In subsequent analysis, the number of olfactory descriptors selected was not significantly correlated with mean intensity scores in the discrepant group, whereas it was significantly negatively correlated with mean intensity scores in the correlation group. From these results, we can suggest that the discrepancy between pleasantness and liking would be related with the choice of olfactory perceptual descriptors according to intensity.

In our experiments of recognition of odor mixture, odor mixtures composed of low-complexity odorants were perceived as relatively different smells from those of the original components when they were mixed. We defined pseudo mixtures and real mixtures to compare participants' evaluations for the components and mixtures. The

former was presumed to retain the olfactory descriptors of the individual components, and the later was participant response to the odor mixtures. The pseudo and real mixtures were compared by each olfactory descriptors and major perceptual group, resulted in that real and pseudo mixtures of the low-complexity group showed significant difference. Furthermore, an analysis of mammal olfactory bulb activity suggested that low-complexity odorant induced spatially large neural activity which can contribute to configural perception. From these results, we can suggest that recognition of odor mixture that the smells of the components are changed or retained depends on the molecular complexity of the odor components.

4.2. General discussion

In this study, we examined whether the complexity of olfactory stimuli can be related with olfactory recognition from the aspects of emotion and odorant molecular feature. In the first experiment, we focused on the concordance between two types of emotional evaluations (*i.e.*, pleasantness and liking). The experiment may indicate that the emotional complexity evoked by olfactory stimuli. Emotional valence encoded in amygdala can be analyzed by multivariate fMRI analysis as ensemble pattern, whereas univariate fMRI analysis cannot detect the activity representing the difference of pleasantness in a previous study[39]. Such multivariate encoding in amygdala might reflect that the degree of olfactory stimulus complexity could be an index indicating the emotional state or processing. The degree of the correlation between pleasantness (defined as instinctive feeling) and liking (defined as experience-based feeling) in our experiment might be related with such ensemble activity pattern in amygdala. No significant difference in the correlation of emotional evaluations could indicate the

complexity of emotional state, which might confuse the selection of olfactory descriptors according to intensity in our findings (Figs. 5 and 6). In the second experiment, we focused on the structural complexity of odorant molecule. We suggested that low-complexity odorant induced a greater number of activated glomeruli in olfactory bulb and cause configural perception in mixed odors. Previous study reported that the molecular complexity can be an index to determine odorant-receptor interaction, and our findings suggested that the molecular complexity was also related with the activity of olfactory bulb (Fig. 9). Both experiments showed that the complexity of olfactory stimuli can be related with olfactory description. Our first experiment suggested that emotional complexity (no significance between pleasantness and liking) might confuse the selection of olfactory description (Figs 5 and 6), and our second experiment indicated that low-complexity odorant induce the change of olfactory description in mixed odors, suggesting that the complexity of olfactory stimuli might be an index reflecting how human describe olfactory stimuli. Our approach may be the first investigation of the olfactory recognition from the complexity of olfactory stimuli that would have importance to examine human olfaction as a novel axis of olfactory recognition. However, it should be noted that we cannot exclude the possibility that our findings might come from just fluctuation of participants' evaluations. To obtain more validity in our results, preliminary test may be needed to avoid the ambiguity of odor intensity and confirm the reproducibility of participant' evaluations.

The interaction between peripheral and central processing may be related with our results. It was known that central neural processing has dominance on olfactory recognition. For example, previous study indicated that primary axis of olfactory perception is hedonic evaluation[59], and the evaluation was modulated by memory and

experience[45,57,66]. Contrast to the past studies, the present thesis suggests that factors which can be derived from the olfactory peripheral processing can modulate or determine olfactory recognition. Such top-down and bottom-up modulation have been reported in olfactory recognition[45,50,54]. In our research of the discrepancy of emotional evaluations, participants were asked to note the difference of original definition of pleasantness and liking. Though the emotional evaluations could greatly depend on individual participants' subjective evaluation, such instruction for the emotional evaluations might make some top-down effects, resulted in the discrepancy of emotional evaluations. If such effect occurred, activity pattern of olfactory areas would be different between discrepant and correlation group. The piriform cortex which has role in encoding odor quality[36,45] has dense connection with amygdala and entorhinal cortex, whereas the piriform cortex is poorly connected with areas showing lexical-semantic representation[45]. Due to such structure of olfactory system, the alteration of emotional state could make some effects on the selection of olfactory descriptors (Fig. 1). Although previous studies showed that verbalization of olfactory stimuli was easily affected by olfactory memory and experience[45,54,69], few study revealed the relationship between the emotion and olfactory verbalization. Our findings might suggest that change of emotional state could influence the verbalization of olfactory stimuli. In the experiment of the molecular complexity and odor mixture recognition, bottom-up effect may occur, in which the peripheral neural activity seemed to have a dominance in determining the recognition of odor mixtures. We found that low-complexity mixtures were relatively perceived as changed smells from those of the components than medium- and high-complexity mixtures (Figs. 5 and 6). Due to the numerous combination of odorants, it was difficult to elucidate the regularity between odorant molecular feature and recognition of odor mixtures. Actually, most of

past studies focused on monomolecular odorant[54,59,103], and only a few studies revealed the mixture perception from the aspect of odorant molecule[12], although most of odors which is smelled by us in a real life would be mixtures. Our findings newly provide the molecular complexity as a factor which can determine the recognition of odor mixtures. Furthermore, our re-analysis of mammal olfactory bulb suggested that the molecular complexity determined the activity pattern of olfactory bulb (Fig. 9). These findings can help to understand how the molecular complexity affect olfactory central processing for the perceptual modes of odor mixture.

In the present thesis, olfactory perceptual descriptors (*e.g.,* sweet and woody) were mainly used to evaluate olfactory recognition. In most of past studies, other axes such as pleasantness and familiarity were used[36,67,101]. However, the axes might be insufficient to change the olfactory recognition induced by discrepant emotional states or configural/elemental perceptual modes. For example, “floral” and “woody” smells are qualitatively different, but some participant may evaluate both smells as pleasant and familiar odor. To avoid the failed analysis, we used the olfactory descriptors, which enabled to analyze the effect of emotion on olfactory verbalization and mixture perceptual modes caused by odorant molecular complexity.

Participants were instructed to select the listed olfactory descriptors, not to answer freely without the descriptor list. The selection of the descriptors from a list was important for the participants to fully evaluate the quality of a smell. Past studies showed that olfactory verbalization is too difficult for naïve participnat[45,54]. Actually, in a preliminary test, when participants were presented strawberry aldehyde, which is artificially made to give out the smell of strawberry, one out of ten participants can answer as “smell of strawberry”. Furthermore, previous studies reported that olfactory

verbalization can be affected by several factors such as language, culture, and individual background[57,68,97,98]. In all experiment of the present thesis, all participants were Japanese students at Kyushu university, which means that the backgrounds of culture and language were controlled, except for the individual background. To control the influence of the individual background on olfactory evaluations, participants were asked to choose the descriptors from a list. If the experiments for emotional effect and recognition of odor mixtures were performed without the olfactory descriptor list, it would be difficult to analyze the effect of discrepant emotional state and molecular complexity on olfactory recognition.

The present thesis may include some limitations. First, the reproducibility of participants' evaluations was not confirmed. To obtain more robust conclusion, the reproducibility should be tested. Second, we recorded no neural activity of olfactory receptor neurons, olfactory bulb, and olfactory areas. To elucidate the manner that emotional discrepancy affect the olfactory verbalization and low-complexity odorants induce configural perception, the activity of the olfactory areas including piriform cortex, amygdala, hippocampus, and orbitofrontal cortex should be recorded using fMRI. Third, the number of participants and odors might be insufficient to make robust and clear conclusion. In the investigation of emotional effect, only 12 participants were recruited. In the examination of recognition of odor mixtures, only 12 odorants and 18 mixtures were evaluated. The more number of participants and odorants would be needed to verify the effect of the emotional effect and molecular complexity robustly.

4.3. Future studies

The neural mechanism should be examined to fully understand the manner that

olfactory recognition is determined or modulated by some factors such as emotion and odorant molecular features.

To elucidate the effect of peripheral neural activity on the central processing in olfaction, recording of electro-olfactogram (EOG) will be needed. EOG is a technique enabling to record the activity of olfactory receptor neurons directly induced by odorants. T. Hummel research group recorded EOG response from human olfactory epithelium, and suggested that the distribution of olfactory receptors in the epithelium surface reflected a primary perceptual axis as visual and auditory systems[95]. Use of this technique will enable to define and quantify the innately determined emotion and the effect of molecular complexity at the level of receptor neuron activity. Furthermore, the combination of EOG and central neural recording will help to understand human olfactory system comprehensively. For example, simultaneous recording of EOG and ERP revealed that indistinguishable odor enantiomers at the level of recognition can be discriminated at the level of receptor neuron activity[128]. To elucidate the mechanism that factors such as emotional state and molecular complexity determines or modulate olfactory recognition, olfactory neural recordings should be performed by both EOG and ERP.

To use EOG for investigation of peripheral neural activity, some improvements will be needed for conventional EOG method. Though the method of EOG, which was established by T. Hummel research group, is a powerful technique to examine the profile of peripheral neural activity, there are some technical difficulties. First, the medical license is needed. In the method of T. Hummel group, electrodes were put in nasal cavities. This treatment demands highly medical technique and knowledge, which will restrict non-licensed researchers to perform the EOG recording. Second, the recording of EOG from nasal cavities had low signal-to-noise ratio. In the study of T. Hummel group, 801

recordings were succeeded from 1974 odor events[95]. The recording of EOG from nasal cavities was vulnerable to several types of noise such as trigeminal neural activity, body movements, and respiratory airflow[91]. To resolve these technical difficulties, new methods for EOG recording will be needed. For example, put of the electrode on the face may lead to the new EOG method. Some researchers demonstrated that responses correlated with EOG from the epithelium can be recorded by placing external electrodes around the nose[91]. Such new EOG method will greatly help to investigate the manner that olfactory recognition is determined by emotional states and odorant molecular complexity.

5. Conclusions

The present thesis focused on the complexity of olfactory stimuli from the aspects of odor-evoked emotion and odorant molecular feature. We showed that conflict in emotional evaluations and odorant molecular complexity can be related with determining or modulating human olfactory recognition. The discrepancy in the dual axes of emotional evaluations (*i.e.,* pleasantness and liking) may contribute to induce complicated odor-evoked emotions, which could affect the selection of olfactory descriptors. Using the dual axes of emotional evaluations may help to investigate olfactory emotional states in future study. Odor mixtures composed of low-complexity odorants were relatively sensed as changed smell from the components, and neural activity of mammal olfactory bulb was subject to the molecular complexity, suggesting that the molecular complexity could determine the perceptual modes of odor mixtures. Using the original analyses to compare the olfactory descriptors between the components and mixtures, we demonstrated that odor qualities can be compared at the level of minor (each olfactory descriptor) and major (perceptual community) quality. This method can

help to the research investigating slightly different smells, such as smells of wine evaluated by sommeliers. Although no recording of neural activity was performed in this thesis, our findings, experimental design and analytical methods potentially enable to investigate human olfactory system from peripheral to central processing.

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Appendix A: The raw data of descriptors and intensity scores for the correlation and discrepant groups.

The table shows the selected olfactory descriptors, intensity scores, and participants for the discrepant (D1−D10) and correlation (C1−C11) groups. Colored descriptors were selected for one odor by more than two participants, and the colors differ according to descriptor type. The gray background indicates the omission of intensity scores that were excluded from the analyses.

Discrepant group (D1–D10)

Odor	Descriptors	Intensity	Participant ID
Acetophenone (D1)	Chemical	1	1
	Perfumery	1	1
	Peach (fruit)	1	4
	Varnish	1	5
	Kerosene	1	5
	Hay	1	12
	Alcohol-like	2	1
	Fruity (citrus)	2	1
	Perfumery	2	2
	Cologne	2	4
	Perfumery	2	4
	Etherish, Anaesthetic	2	7
	Heavy	2	8
	Cinnamon	2	10
	Spicy	2	10
	Fruity (other)	2	11
	Herbal, Green, Cut grass	2	12
	Woody, Resinous	2	12
	Cologne	3	2
	Fragrant	3	2
	Aromatic	3	2
	Rubbery (new rubber)	3	3
	Aromatic	3	5
	Cool, Cooling	3	7
	Chemical	3	9
	Rubbery (new rubber)	3	9
	Caramel	3	10
	Vanilla-like	3	10
	Rubbery (new rubber)	4	6
	Varnish	4	8
	Paint-like	4	8
	Coconut-like	4	10
	Sweet	4	10

Odor	Descriptors	Intensity	Participant ID
Benzaldehyde (D2)	Violets	1	1
	Rose-like	1	1
	Floral	2	1
	Medicinal	2	5
	Fragrant	2	7
	Nail polish remover	2	8
	Like mothballs	2	8
	Kerosene	2	9
	Chocolate	2	10
	Alcohol-like	2	12
	Chemical	2	12
	Disinfectant, Carbolic	2	12
	Cherry (berry)	3	1
	Cologne	3	2
	Floral	3	2
	Alcohol-like	3	3
	Chemical	3	3
	Rope-like	3	4
	Leather-like	3	4
	Cinnamon	3	6
	Nutty (walnut, etc)	3	6
	Coconut-like	3	7
	Vanilla-like	3	10
	Cinnamon	3	11
	Etherish, Anaesthetic	3	12
	Like Gasoline, Solvent	3	12
	Perfumery	4	2
	Aromatic	4	2
	Paint-like	4	4
	Varnish	4	8
	Paint-like	4	8
	Chemical	4	9
	Aromatic	4	10
	Cantaloupe, Honey Dew Me	4	11
	Sweet	5	10

Odor	Descriptors	Intensity	Participant ID
Limonene (D3)	Herbal, Green, Cut grass	1	1
	Lemon (fruit)	1	1
	Peach (fruit)	1	8
	Cool, Cooling	1	10
	Aromatic	2	1
	Fragrant	2	4
	Peach (fruit)	2	7
	Sweet	2	7
	Orange (fruit)	2	9
	Minty, Peppermint	2	10
	Eucalyptus	2	10
	Cool, Cooling	2	12
	Orange (fruit)	3	1
	Orange (fruit)	3	3
	Fruity (citrus)	3	3
	Grapefruit	3	4
	Lemon (fruit)	3	4
	Fruity (citrus)	3	4
	Orange (fruit)	3	6
	Fruity (citrus)	3	6
	Floral	3	7
	Cool, Cooling	3	8
	Fruity (citrus)	3	9
	Herbal, Green, Cut grass	3	10
	Herbal, Green, Cut grass	3	11
	Floral	3	11
	Perfumery	3	11
	Aromatic	3	11
	Orange (fruit)	3	12
	Grapefruit	4	1
	Orange (fruit)	4	2
	Grapefruit	4	2
	Lemon (fruit)	4	2
	Fruity (citrus)	4	2
	Orange (fruit)	4	5
	Grapefruit	4	8
	Lemon (fruit)	4	8
	Fruity (citrus)	4	8
	Grapefruit	4	10
	Grapefruit	4	12
	Fruity (citrus)	4	12
	Fruity (citrus)	5	1

Odor	Descriptors	Intensity	Participant ID
Ethyl acetate (D4)	Alcohol-like	1	1
	Paint-like	1	1
	Chemical	1	1
	Floral	1	1
	Celery	1	2
	Woody, Resinous	1	2
	Paint-like	1	5
	Chemical	1	7
	Minty, Peppermint	1	8
	Banana-like	1	11
	Grape-juice-like	1	11
	Floral	1	11
	Almond-like	1	12
	Like burnt paper	1	12
	Kerosene	1	12
	Animal	1	12
	Etherish, Anaesthetic	2	1
	Rubbery (new rubber)	2	4
	Sweaty	2	6
	Aromatic	2	6
	Light	2	8
	Alcohol-like	2	9
	Fishy	2	10
	Stale	2	10
	Medicinal	3	1
	Like Gasoline, Solvent	3	3
	Paint-like	3	3
	Alcohol-like	3	7
	Nail polish remover	3	7
	Nail polish remover	3	8
	Like cleaning fluid (carbona)	3	8
	Sweet	3	9
	Sour milk	3	10
	Varnish	4	7
	Alcohol-like	4	10

Odor	Descriptors	Intensity	Participant ID
Isophorone (D5)	Pineapple (fruit)	1	1
	Lavender	1	5
	Sweet	1	11
	Minty, Peppermint	1	12
	Fruity (other)	2	2
	Woody, Resinous	2	2
	Sooty	2	4
	Sharp, Pungent, Acid	2	7
	Burnt, Smoky	2	7
	Cool, Cooling	2	8
	Chemical	2	9
	Alcohol-like	2	10
	Nail polish remover	2	10
	Herbal, Green, Cut grass	2	12
	Caramel	3	1
	Musty, Earthy, Moldy	3	3
	Like burnt paper	3	4
	Burnt candle	3	4
	Cinnamon	3	6
	Aromatic	3	6
	Alcohol-like	3	8
	Eucalyptus	3	8
	Rubbery (new rubber)	3	9
	Like mothballs	3	10
	Cool, Cooling	3	10
	Cinnamon	3	11
	Raisins	3	11
	Cool, Cooling	3	12
	Cool, Cooling	4	2
	Incense	4	4
	Nail polish remover	4	8
	Disinfectant, Carbolic	4	10
	Medicinal	4	10
	Honney-Like	5	1
	Sweet	5	1
	Burnt rubber-like		4

Odor	Descriptors	Intensity	Participant ID
Butyl acetate (D6)	Chemical	1	1
	Nail polish remover	1	1
	Medicinal	1	2
	Varnish	1	8
	Alcohol-like	1	9
	Etherish, Anaesthetic	2	1
	Disinfectant, Carbolic	2	1
	Etherish, Anaesthetic	2	4
	Like Gasoline, Solvent	2	5
	Fragrant	2	8
	Varnish	2	9
	Alcohol-like	3	2
	Varnish	3	2
	Sharp, Pungent, Acid	3	4
	Chemical	3	4
	Like mothballs	3	8
	Banana-like	3	9
	Paint-like	3	9
	Etherish, Anaesthetic	3	10
	Varnish	3	11
	Medicinal	4	1
	Nail polish remover	4	3
	Nail polish remover	4	4
	Nail polish remover	4	5
	Varnish	4	6
	Nail polish remover	4	6
	Like Gasoline, Solvent	4	7
	Varnish	4	7
	Nail polish remover	4	10
	Alcohol-like	4	11
	Like Gasoline, Solvent	4	11
	Nail polish remover	4	11
	Alcohol-like	5	1
	Nail polish remover	5	2
	Nail polish remover	5	7
	Nail polish remover	5	12

Odor	Descriptors	Intensity	Participant ID
Methyl heptanoate (D7)	Lavender	1	8
	Lemon (fruit)	1	8
	Herbal, Green, Cut grass	1	11
	Lemon (fruit)	1	12
	Disinfectant, Carbolic	1	12
	Peach (fruit)	2	1
	Lemon (fruit)	2	1
	Sweet	2	1
	Perfumery	2	1
	Fruity (other)	2	2
	Alcohol-like	2	4
	Fruity (citrus)	2	5
	Sweet	2	7
	Cool, Cooling	2	8
	Chemical	2	9
	Floral	2	10
	Grape-juice-like	2	11
	Creosote	2	12
	Like Gasoline, Solvent	3	5
	Pear (fruit)	3	7
	PineApple (fruit)	3	3
	PineApple (fruit)	3	4
	PineApple (fruit)	3	9
	PineApple (fruit)	3	10
	Apple (fruit)	3	3
	Apple (fruit)	3	10
	Lemon (fruit)	3	2
	Fruity (citrus)	3	1
	Fruity (citrus)	3	2
	Fruity (citrus)	3	12
	Sweet	3	4
	Sweet	3	9
	Sweet	3	11
	Molasses	3	11
	Fragrant	3	1
	Fragrant	3	7
	Pear (fruit)	4	2
	PineApple (fruit)	4	2
	Grapefruit	4	4
	Lemon (fruit)	4	4
	Fruity (other)	4	4
	Kerosene	4	5
	PineApple (fruit)	4	6
	Fruity (other)	4	6
	Fruity (citrus)	4	10
	Fruity (citrus)	5	4
	PineApple (fruit)	5	8
	Chemical		1

Odor	Descriptors	Intensity	Participant ID
4-Methyl-3-penten-2-one (D8)	Alcohol-like	1	2
	Nail polish remover	1	2
	Fruity (citrus)	1	12
	Chemical	2	1
	Nail polish remover	2	8
	Paint-like	2	9
	Chemical	2	9
	Almond-like	2	10
	Etherish, Anaesthetic	2	10
	Tar-like	2	11
	Heavy	2	11
	Rubbery (new rubber)	2	11
	Hay	2	12
	Disinfectant, Carbolic	3	1
	Nail polish remover	3	1
	Woody, Resinous	3	2
	Varnish	3	3
	Nail polish remover	3	3
	Chemical	3	4
	Etherish, Anaesthetic	3	5
	Varnish	3	5
	Nail polish remover	3	5
	Paint-like	3	7
	Banana-like	3	8
	Nail polish remover	3	10
	Alcohol-like	3	12
	Etherish, Anaesthetic	4	1
	Medicinal	4	1
	Etherish, Anaesthetic	4	4
	Paint-like	4	4
	Sharp, Pungent, Acid	4	4
	Nail polish remover	4	4
	Chemical	4	6
	Nail polish remover	4	6
	Alcohol-like	4	7
	Like Gasoline, Solvent	4	7
	Rubbery (new rubber)	4	9
	Sweet	4	10
	Paint-like	4	11
	Creosote	4	12
	Alcohol-like	5	1

Odor	Descriptors	Intensity	Participant ID
Isovaleric acid (D9)	Musty, Earthy, Moldy	1	1
	Fermented (rotten) fruit	1	1
	Putrid, Foul, Decayed	1	1
	Sweaty	1	2
	Like blood, Raw meat	1	7
	Kerosene	1	9
	Sickening	1	12
	Lemon (fruit)	2	1
	Putrid, Foul, Decayed	2	5
	Putrid, Foul, Decayed	2	7
	Fermented (rotten) fruit	2	8
	Rancid	2	8
	Sour milk	2	10
	Yeasty	2	12
	Rancid	2	12
	Putrid, Foul, Decayed	2	12
	Stale	3	3
	Urine-like	3	4
	Stale	3	5
	Cadaverous, Like dead anin	3	5
	Rancid	3	5
	Fecal (like manure)	3	5
	Mouse-like	3	6
	Sickening	3	7
	Stale	3	8
	Cheesy	3	9
	Banana-like	3	10
	Fermented (rotten) fruit	3	10
	Stale	3	12
	Like ammonia	4	4
	Musty, Earthy, Moldy	4	4
	Sweaty	4	4
	Fermented (rotten) fruit	4	11
	Putrid, Foul, Decayed	4	11
	Rancid	5	2
	Putrid, Foul, Decayed	5	2
	Sweaty	5	6

Odor	Descriptors	Intensity	Participant ID
Indole (D10)	Varnish	1	1
	Chemical	1	8
	Chemical	2	1
	Household gas	2	1
	Kerosene	2	1
	Sooty	2	2
	Burnt rubber-like	2	2
	Grainy (as grain)	2	4
	Woody, Resinous	2	4
	Warm	2	5
	Sewer odor	2	7
	Chemical	2	9
	Household gas	2	10
	Grainy (as grain)	2	11
	Crushed grass	2	11
	Etherish, Anaesthetic	2	12
	Burnt, Smoky	2	12
	Medicinal	3	1
	Burnt, Smoky	3	2
	Stale	3	3
	Paint-like	3	6
	Grainy (as grain)	3	7
	Burnt candle	3	8
	Yeasty	3	10
	Sooty	3	10
	Burnt candle	3	10
	Bark-like, Birch bark	3	11
	Woody, Resinous	3	11
	Sooty	3	12
	Like burnt paper	3	12
	Like mothballs	4	5
	Chemical	4	6
	Rubbery (new rubber)	4	9

Correlation group (C1–C11)

Odor	Descriptors	Intensity	Participant ID
Heptanal (C1)	Grape-juice-like	1	1
	Chemical	1	1
	Sweet	1	1
	Almond-like	1	4
	Dry, Powdery	1	12
	Sweet	1	12
	Herbal, Green, Cut grass	2	1
	Raw cucumber-like	2	1
	Almond-like	2	2
	Soupy	2	2
	Rope-like	2	4
	Like mothballs	2	5
	Woody, Resinous	2	5
	Fruity (citrus)	2	6
	Bean-like	2	8
	Rope-like	2	11
	Heavy	2	11
	Alcohol-like	2	12
	Sour, Acid, Vinegar	3	2
	Dry, Powdery	3	4
	Chemical	3	6
	Mouse-like	3	7
	Cat-urine-like	3	7
	Rancid	3	7
	Heavy	3	8
	Chemical	3	9
	Varnish	3	10
	Like burnt paper	3	10
	Oily, Fatty	3	12
	Musty, Earthy, Moldy	4	3
	Cadaverous, Like dead anin	4	7
	Musty, Earthy, Moldy	4	10
	Rubbery (new rubber)	4	11

Odor	Descriptors	Intensity	Participant ID
2,3-Dimethylpyrazine (C2)	Peanut butter	1	1
	Burnt, Smoky	1	1
	Nutty (walnut, etc)	1	8
	Bakery (freash bread)	1	9
	Burnt, Smoky	1	9
	Hay	1	12
	Like burnt paper	1	12
	Heavy	1	12
	Oily, Fatty	1	12
	Almond-like	2	2
	Heavy	2	2
	Coconut-like	2	6
	Coconut-like	2	7
	Nutty (walnut, etc)	2	7
	Fragrant	2	7
	Peanut butter	2	8
	Coconut-like	2	10
	Peanut butter	2	10
	Herbal, Green, Cut grass	2	12
	Burnt, Smoky	2	12
	Peanut butter	3	2
	Almond-like	3	3
	Peanut butter	3	3
	Nutty (walnut, etc)	3	4
	Maple (as in syrup)	3	4
	Stale	3	6
	Almond-like	3	8
	Almond-like	3	9
	Nutty (walnut, etc)	3	10
	Coconut-like	3	11
	Almond-like	4	4
	Caramel	4	4
	Peanut butter	4	4
	Sweet	4	4
	Caramel	4	8
	Almond-like	4	10
	Sweet	4	10
	Nutty (walnut, etc)	4	11
	Nutty (walnut, etc)	5	5

Odor	Descriptors	Intensity	Participant ID
Trimethyl amine (C3)	Oak wood, Cognac-like	1	1
	Herbal, Green, Cut grass	1	1
	Hay	1	1
	Bark-like, Birch bark	1	1
	Woody, Resinous	1	1
	Mouse-like	1	5
	Bitter	1	8
	Stale	1	8
	Fecal (like manure)	1	8
	Sour, Acid, Vinegar	1	10
	Herbal, Green, Cut grass	1	12
	Garlic, Onion	2	1
	Sweet	2	1
	Seasoning (for meat)	2	4
	Burnt, Smoky	2	6
	Like burnt paper	2	7
	Burnt, Smoky	2	7
	Fecal (like manure)	2	7
	Fishy	2	9
	Cheesy	2	10
	Urine-like	2	10
	Cork-like	3	2
	Rope-like	3	2
	Leather-like	3	2
	Seminal, Sperm-like	3	3
	Black pepper-like	3	4
	Meaty (cooked, good)	3	4
	Heavy	3	8
	Putrid, Foul, Decayed	3	8
	Fishy	3	10
	Animal	3	10
	Soupy	4	4
	Fried chicken	4	4
	Fishy	4	5
	Sickening	4	11
	Rancid	4	11
	Putrid, Foul, Decayed	4	11
	Eucalyptus		1

Odor	Descriptors	Intensity	Participant ID
Dimethyl trisulfide (C4)	Mushroom-like	1	1
	Black pepper-like	1	1
	Sour, Acid, Vinegar	1	8
	Cooked vegetables	1	8
	Beery (beer-like)	1	9
	Aromatic	1	12
	Oily, Fatty	1	12
	Seasoning (for meat)	2	2
	Sickening	2	4
	Stale	2	4
	Fermented (rotten) fruit	2	4
	Rubbery (new rubber)	2	9
	Animal	2	10
	Eggy (freash eggs)	2	12
	Woody, Resinous	2	12
	Incense	3	1
	Burnt, Smoky	3	1
	Fishy	3	3
	Sweaty	3	4
	Seminal, Sperm-like	3	4
	Animal	3	4
	Chemical	3	5
	Musty, Earthy, Moldy	3	6
	Dirty linen-like	3	6
	Fecal (like manure)	3	7
	Garlic, Onion	3	10
	Sickening	3	10
	Putrid, Foul, Decayed	3	10
	Sour, Acid, Vinegar	3	11
	Cooked vegetables	3	11
	Sickening	4	6
	Sickening	4	7
	Rancid	4	7
	Putrid, Foul, Decayed	4	7
	Rancid	4	10

Odor	Descriptors	Intensity	Participant ID
Acetone (C5)	Raw cucumber-like	1	1
	Rope-like	1	2
	Fruity (other)	1	2
	Leather-like	1	2
	Stale	1	3
	Like ammonia	1	4
	Oily, Fatty	1	5
	Lemon (fruit)	1	8
	Sweet	1	8
	Light	1	8
	Fragrant	1	8
	Vanilla-like	1	10
	Incense	1	10
	Alcohol-like	1	12
	Tea-leaves-like	1	12
	Cool, Cooling	1	12
	Chemical	2	1
	Sweet	2	1
	Rubbery (new rubber)	2	2
	Woody, Resinous	2	7
	Coconut-like	2	8
	Alcohol-like	2	9
	Varnish	2	9
	Sweet	2	10
	Like mothballs	2	10
	Aromatic	3	1
	Alcohol-like	3	4
	Paint-like	3	9
	Chemical	3	10
	Nail polish remover	3	10
	Minty, Peppermint	3	12
	Chemical	4	4
	Rubbery (new rubber)	4	4
	Almond-like	4	6
	Cork-like	4	7
	Strawberry-like	4	11

Odor	Descriptors	Intensity	Participant ID
γ-Undecalactone (C6)	**Strawberry-like**	1	1
	Grape-juice-like	1	1
	Lavender	1	1
	Raisins	1	1
	Perfumery	1	5
	Varnish	1	8
	Banana-like	1	8
	Paint-like	1	8
	Chemical	2	4
	Rose-like	2	5
	Crushed weeds	2	5
	Herbal, Green, Cut grass	2	8
	Woody, Resinous	2	8
	Rubbery (new rubber)	2	9
	Sweet	2	12
	Fruity (other)	3	2
	Burnt candle	3	3
	Minty, Peppermint	3	4
	Sweaty	3	4
	Aromatic	3	5
	Floral	3	7
	Chemical	3	9
	Sweet	3	9
	Sweet	3	10
	Floral	3	11
	Aromatic	3	11
	Sweet	4	1
	Peach (fruit)	4	2
	Perfumery	4	6
	Fragrant	4	6
	Aromatic	4	6
	Aromatic	4	7
	Peach (fruit)	4	10
	Strawberry-like	5	2
	Sweet	5	7

Odor	Descriptors	Intensity	Participant ID
(-)-α-Pinene (C7)	Peach (fruit)	1	1
	Fresh green vegetables	1	1
	Medicinal	1	9
	Minty, Peppermint	1	12
	Fishy	1	12
	Herbal, Green, Cut grass	2	2
	Burnt rubber-like	2	4
	Varnish	2	5
	Woody, Resinous	2	6
	Rope-like	2	7
	Leather-like	2	7
	Cool, Cooling	2	7
	Minty, Peppermint	2	8
	Perfumery	2	8
	Aromatic	2	8
	Celery	2	10
	Hay	2	10
	Varnish	2	11
	Herbal, Green, Cut grass	2	12
	Aromatic	3	1
	Medicinal	3	1
	Celery	3	2
	Minty, Peppermint	3	2
	Medicinal	3	3
	Cool, Cooling	3	3
	Varnish	3	4
	Rope-like	3	4
	Rubbery (new rubber)	3	4
	Herbal, Green, Cut grass	3	9
	Minty, Peppermint	3	10
	Kerosene	3	11
	Woody, Resinous	4	5
	Lavender	4	8
	Herbal, Green, Cut grass	4	10
	Fruity (citrus)		1

Odor	Descriptors	Intensity	Participant ID
4-Ethyl-2-methoxyphenol (C8)	Fried chicken	1	1
	Kippery (smoked fish)	1	1
	Medicinal	1	2
	Metallic	1	7
	Yeasty	1	9
	Bakery (freash bread)	1	9
	Meaty (cooked, good)	1	10
	Rose-like	1	12
	Minty, Peppermint	1	12
	Woody, Resinous	1	12
	Incense	2	1
	Meaty (cooked, good)	2	1
	Sharp, Pungent, Acid	2	2
	Disinfectant, Carbolic	2	2
	Stale	2	3
	Meaty (cooked, good)	2	5
	Cheesy	2	6
	Incense	2	6
	Dry, Powdery	2	7
	Like mothballs	2	7
	Cheesy	2	8
	Rubbery (new rubber)	2	9
	Seasoning (for meat)	2	10
	Alcohol-like	2	12
	Herbal, Green, Cut grass	2	12
	Fruity (other)	3	2
	Medicinal	3	3
	Woody, Resinous	3	4
	Burnt, Smoky	3	5
	Burnt, Smoky	3	6
	Burnt, Smoky	3	8
	Chemical	3	9
	Burnt, Smoky	3	10
	Cheesy	3	11
	Meaty (cooked, good)	3	11
	Burnt, Smoky	4	4
	Meaty (cooked, good)	4	6
	Fragrant	4	8
	Cheesy	4	10
	Burnt, Smoky	5	1

Odor	Descriptors	Intensity	Participant ID
Dimethyl benzyl carbinyl butyrate (C9)	Green pepper	1	1
	Medicinal	1	1
	Yeasty	1	8
	Sweaty	1	8
	Heavy	1	8
	Minty, Peppermint	1	12
	Household gas	1	12
	Rubbery (new rubber)	1	12
	Lemon (fruit)	2	1
	Sweet	2	1
	Oily, Fatty	2	2
	Cork-like	2	4
	Banana-like	2	4
	Fruity (other)	2	5
	Woody, Resinous	2	5
	Stale	2	6
	Wet wool, Wet dog	2	8
	Herbal, Green, Cut grass	2	9
	Chemical	2	10
	Hay	2	10
	Like Gasoline, Solvent	2	12
	Fruity (other)	3	1
	Spicy	3	2
	Fruity (other)	3	4
	Leather-like	3	4
	Sweaty	3	6
	Chemical	3	9
	Aromatic	3	9
	Cool, Cooling	3	9
	Herbal, Green, Cut grass	3	10
	Like mothballs	3	10
	Woody, Resinous	3	10
	Sour, Acid, Vinegar	3	11
	Spicy	3	11
	Like burnt paper	3	12
	Medicinal	3	12
	Sour, Acid, Vinegar	4	2
	Burnt rubber-like	4	3
	Spicy	4	7

Odor	Descriptors	Intensity	Participant ID
2-Ethylpyrazine (C10)	Woody, Resinous	1	1
	Cinnamon	1	2
	Heavy	1	2
	Coconut-like	1	8
	Sweet	1	8
	Musty, Earthy, Moldy	1	10
	Grainy (as grain)	1	10
	Sooty	1	12
	Like burnt paper	1	12
	Black pepper-like	2	2
	Popcorn	2	6
	Nutty (walnut, etc)	2	8
	Burnt, Smoky	2	9
	Nutty (walnut, etc)	2	10
	Dry, Powdery	2	12
	Burnt, Smoky	2	12
	Peanut butter	3	1
	Popcorn	3	3
	Chemical	3	3
	Nutty (walnut, etc)	3	6
	Almond-like	3	7
	Peanut butter	3	7
	Almond-like	3	8
	Raw potato-like	3	11
	Bean-like	3	11
	Almond-like	4	2
	Almond-like	4	4
	Caramel	4	4
	Peanut butter	4	4
	Almond-like	4	6
	Nutty (walnut, etc)	4	7
	Peanut butter	4	8
	Almond-like	4	9
	Almond-like	4	10
	Caramel	4	10
	Sweet	4	10
	Nutty (walnut, etc)	4	11
	Almond-like	5	1
	Sweet	5	4
	Mouse-like	5	5

Odor	Descriptors	Intensity	Participant ID
Propane-1-thiol (C11)	Stale	1	4
	Sweet	1	12
	Stale	1	12
	Heavy	1	12
	Fermented (rotten) fruit	1	12
	Oily, Fatty	1	12
	Seasoning (for meat)	2	1
	Bitter	2	4
	Cooked vegetables	2	5
	Fecal (like manure)	2	6
	Stale	2	7
	Rancid	2	7
	Heavy	2	8
	Burnt, Smoky	2	8
	Burnt, Smoky	3	1
	Cooked vegetables	3	4
	Burnt, Smoky	3	6
	Garlic, Onion	3	9
	Sickening	3	10
	Rancid	3	10
	Putrid, Foul, Decayed	3	10
	Meaty (cooked, good)	4	1
	Fermented (rotten) fruit	4	2
	Rancid	4	2
	Stale	4	3
	Putrid, Foul, Decayed	4	3
	Fermented (rotten) fruit	4	10
	Sickening	4	11
	Fermented (rotten) fruit	4	11
	Rancid	4	11

Appendix B: The raw data of the pleasant and preference score for the correlation and discrepant groups.

The column of "Mean" is each average of the scores in the odor. The column of "SEM" is the standard error of the mean in the odor.

Discrepant group: pleasantness scores

ID	Odors	Participants (N = 12)												Mean	SEM
D1	Acetophenone	4	3	3	3	2	3	2	2	3	2	4	2	2.75	0.22
D2	Benzaldehyde	4	2	3	3	4	4	3	2	2	3	4	3	3.08	0.23
D3	Limonene	4	4	3	4	4	5	4	5	4	4	4	5	4.17	0.17
D4	Ethyl acetate	3	3	3	3	3	2	2	2	3	3	4	3	2.83	0.17
D5	Isophorone	5	3	2	3	3	4	3	2	2	4	3	4	3.17	0.27
D6	Butyl acetate	2	2	3	2	2	3	1	2	2	3	3	2	2.25	0.18
D7	Methyl heptanoate	5	4	4	1	2	4	4	4	3	4	4	3	3.50	0.31
D8	4-Methyl-3-penten-2-one	3	2	3	1	2	1	2	3	3	3	2	3	2.33	0.22
D9	Isovaleric acid	2	1	3	1	1	1	2	1	2	2	1	1	1.50	0.19
D10	Indole	1	2	2	3	2	2	2	2	2	2	4	2	2.17	0.21

Discrepant group: liking scores

ID	Odors	Participants (N = 12)												Mean	SEM
D1	Acetophenone	3	3	4	3	4	4	2	4	3	2	4	2	3.17	0.24
D2	Benzaldehyde	4	3	3	2	3	4	2	4	2	2	4	4	3.08	0.26
D3	Limonene	5	4	4	5	4	5	4	5	4	4	4	4	4.33	0.14
D4	Ethyl acetate	2	3	3	3	2	2	1	3	4	3	3	3	2.67	0.22
D5	Isophorone	5	3	2	3	3	3	2	4	2	3	3	3	3.00	0.25
D6	Butyl acetate	1	2	4	3	3	2	2	3	3	4	3	2	2.67	0.26
D7	Methyl heptanoate	5	4	4	1	3	3	3	4	4	4	3	4	3.50	0.29
D8	4-Methyl-3-penten-2-one	4	2	3	2	3	1	4	3	2	3	2	3	2.67	0.26
D9	Isovaleric acid	2	1	2	1	1	1	2	3	2	2	1	2	1.67	0.19
D10	Indole	1	2	2	2	5	3	2	2	2	2	4	2	2.42	0.31

Correlation group: pleasantness scores

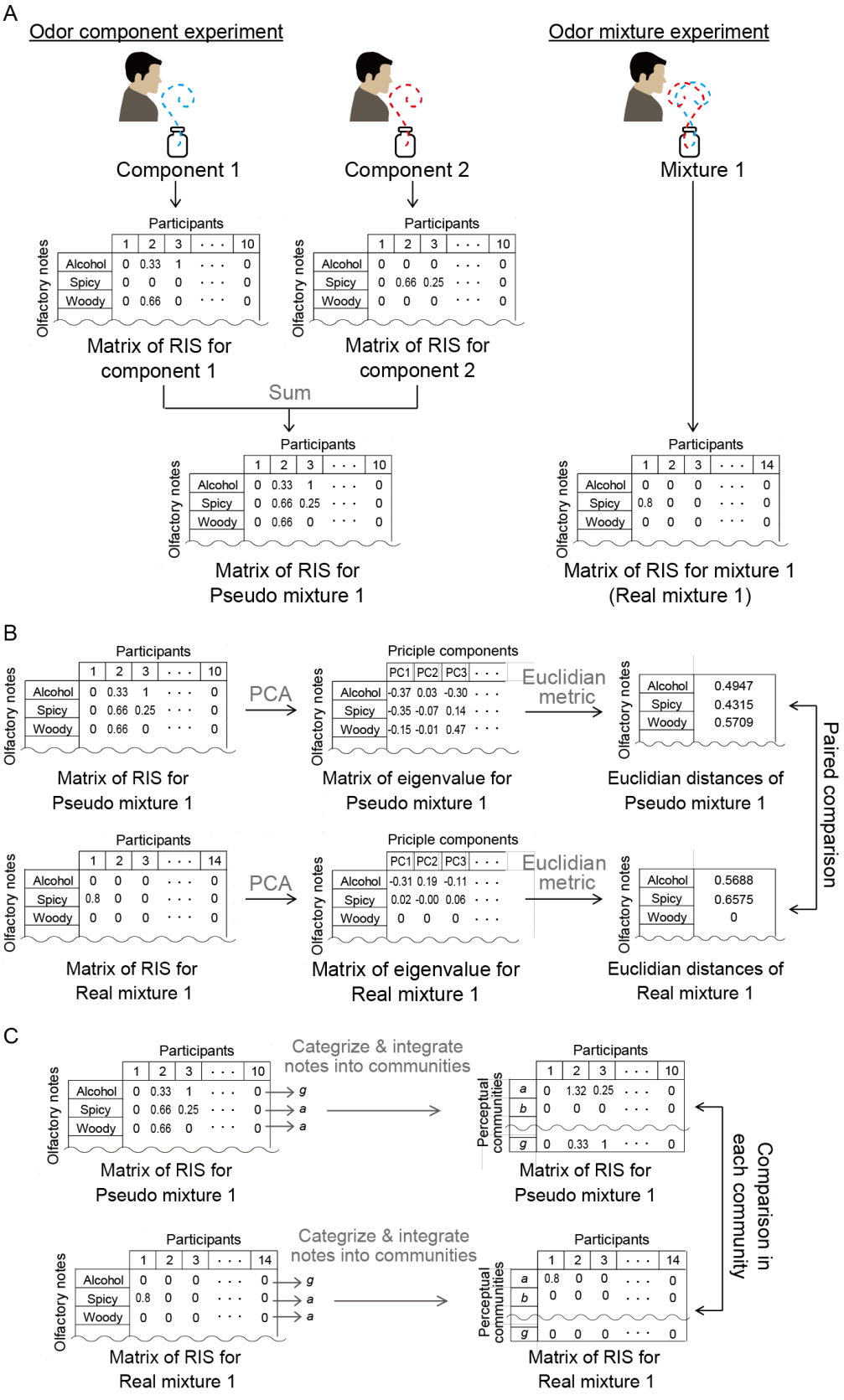
ID	Odors	Participants (N = 12)												Mean	SEM
C1	Heptanal	2	1	2	3	2	3	1	3	3	2	2	3	2.18	0.22
C2	2,3-Dimethylpyrazine	4	1	3	4	5	2	4	4	3	3	3	2	3.17	0.32
C3	Trimethyl amine	2	1	2	4	4	2	2	1	2	2	1	3	2.17	0.30
C4	Dimethyl trisulfide	2	3	2	2	3	1	1	3	2	1	2	3	2.08	0.23
C5	Acetone	3	3	3	2	3	3	3	4	2	3	4	4	3.08	0.19
C6	γ-Undecalactone	4	4	3	2	3	3	4	2	3	3	3	3	3.08	0.19
C7	(-)-α-Pinene	4	2	2	2	4	3	3	3	2	3	3	2	2.75	0.22
C8	4-Ethyl-2-methoxyphenol	3	2	2	4	3	5	2	3	3	3	3	2	2.92	0.26
C9	Dimethyl benzyl carbinyl butyrate	4	2	1	4	3	2	3	1	4	3	2	1	2.50	0.34
C10	2-Ethylpyrazine	4	1	3	4	2	4	3	3	4	2	3	2	2.92	0.29
C11	Propane-1-thiol	2	1	1	2	4	3	3	2	2	1	1	1	1.92	0.29

Correlation group: liking scores

ID	Odors	Participants (N = 12)												Mean	SEM
C1	Heptanal	2	1	1	3	2	3	1	3	2	2	2	2	2.00	0.21
C2	2,3-Dimethylpyrazine	5	2	3	5	4	2	3	4	4	3	3	2	3.33	0.31
C3	Trimethyl amine	2	1	3	4	4	3	3	1	2	2	1	2	2.33	0.31
C4	Dimethyl trisulfide	2	3	2	2	2	1	1	3	2	1	3	3	2.08	0.23
C5	Acetone	2	3	3	1	3	4	3	4	2	3	4	4	3.00	0.28
C6	γ-Undecalactone	4	4	2	1	2	2	4	2	2	3	3	3	2.67	0.28
C7	(-)-α-Pinene	3	2	2	2	4	3	4	3	2	4	3	2	2.83	0.24
C8	4-Ethyl-2-methoxyphenol	4	2	3	4	4	5	2	4	3	4	3	2	3.33	0.28
C9	Dimethyl benzyl carbinyl butyrate	3	2	2	3	3	2	3	1	3	2	2	1	2.25	0.22
C10	2-Ethylpyrazine	5	1	2	4	2	4	4	3	4	2	3	2	3.00	0.35
C11	Propane-1-thiol	4	1	1	2	5	3	2	2	2	1	1	1	2.08	0.38

Appendix C: The outline of data analysis.

(A) The manner to obtain the data sets of real and pseudo-mixtures is shown. Data sets of the real mixture were derived from the odor mixture experiment and those of pseudo-mixtures were done from the odor component experiment. (B) How to analyze using PCA is shown. Using PCA, we quantified each olfactory descriptor by decreasing the dimensions of participants, and then performed statistical paired comparison between real and pseudo-mixtures using the Euclidian distances. (C) The method of the comparison based on the "perceptual communities" is shown. According to the correspondence described in Table 4, we categorized the olfactory descriptors into perceptual communities (from a to g) and performed statistical comparison in each perceptual community.


A
Odor component experiment
Odor mixture experiment
Component 1
Component 2
Mixture 1
Participants
Olfactory notes
Matrix of RIS for component 1
Matrix of RIS for component 2
Sum
Matrix of RIS for Pseudo mixture 1
Matrix of RIS for mixture 1 (Real mixture 1)
B
PCA
Priciple components
Euclidian metric
Matrix of eigenvalue for Pseudo mixture 1
Euclidian distances of Pseudo mixture 1
Paired comparison
Matrix of RIS for Real mixture 1
Matrix of eigenvalue for Real mixture 1
Euclidian distances of Real mixture 1
C
Categrize & integrate notes into communities
Perceptual communities
Matrix of RIS for Pseudo mixture 1
Comparison in each community
Matrix of RIS for Real mixture 1