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Effects of olfactory stimulation with isovaleric acid on brain activation in informed and naïve conditions: A functional MRI study

Yoriko Murata [a,*], Fumino Okutani [b], Mitsuhiko Nakahira [c], Takahiro Ushida [d], Tatsunori Ikemoto [d], Isamu Yokoe [a], Taizo Takeda [c], Hideto Kaba [b], Toshikazu Tani [d], Yasuhiro Ogawa [a]

[a] *Department of Radiology, Kochi Medical School, Japan*
[b] *Department of Integrative Physiology, Kochi Medical School, Japan*
[c] *Department of Otolaryngology and Head & Neck Surgery, Kochi Medical School, Japan*
[d] *Department of Orthopaedics, Kochi Medical School, Japan*

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Abstract

Objective: To investigate the differences in regions of brain activation in response to olfactory stimulation by functional magnetic resonance imaging in conditions of prior warning of an odor and without.
Methods: Participants were 17 normal right-handed volunteers; 8 participants received prior warning of the odor (informed condition) and 9 participants were not pre-warned (naïve condition). The odorant used was isovaleric acid.
Results: In the informed condition with prior warning, activation was observed in the putamen extending to the insula, amygdala, and inferior frontal gyrus, and there was instant reification of the odor, while in the naïve condition without prior warning, activation was observed in the anterior cingulate cortex, entorhinal cortex, putamen and inferior frontal gyrus, and recognition of the odor was difficult.
Conclusions: These results suggest that the condition prior to olfactory stimulation, i.e., with or without prior warning, can affect recognition and regions of brain activation in response to olfactory stimulation using isovaleric acid. Differences in recognition and regions of brain activation between both conditions could be associated with response latencies, or degree of attention, expectation and/or concentration.

Keywords: Olfactory stimulation; Isovaleric acid; Functional magnetic resonance imaging; Prior information

1. Introduction

Our response to various odors may change our emotions and behaviors in daily life, and our response may differ depending on whether we expect to smell an odor or not. Previous research has indicated that odor perception is in fact associated with memory of odors [1,2] and that it could be affected by emotion [3]. Odors are known to be important in emotional processing [3], with subjects responding more rapidly to olfactory stimulation when the target was presented in the expected rather than in the unexpected modality [4]. Thus, information processing in response to olfactory stimulation might be distinctly different under informed and naïve conditions.

Various recent studies using functional magnetic resonance imaging (fMRI) have begun to clarify the human brain mechanism in response to odor [5–10]. Recently research of attentional modulation in olfactory fMRI is intriguing. Zelano et al. reported a dissociation in primary olfactory cortex that revealed attention-dependent and attention-independent subregions [11]. Sabri et al. reported that the posterior and central orbitofrontal cortex and the subgenual cingulate were significantly activated, and the right orbitofrontal cortex in ignore conditions [12]. However, these previous studies have not focused on the important issue of whether information about an odor prior to odor stimulation affects the brain mechanism involved.

* Corresponding author. Tel.: +81 88 880 2367; fax: +81 88 880 2368.
E-mail address: muratay@kochi-u.ac.jp (Y. Murata).

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The present study therefore sought to investigate whether activation of brain areas associated with odor response differs according to whether the subject anticipates smelling an odor (by giving prior warning of odor stimulation) or not. The odor used was selected on the basis of past research findings. Most odors are usually labeled as pleasant or unpleasant [3] and unpleasant odors are assessed more rapidly than neutral or pleasant odors [13]. In addition, response times for unpleasant odors are significantly shorter than for pleasant odors during affective judgement [14] and we are more highly sensitive to unpleasant odors than to neutral or pleasant ones [13]. Thus we selected isovaleric acid, which smells like sweaty socks, for use in the present study since we considered it to be a typical smell causing widespread discomfort. Using fMRI, we investigated whether any distinctions exist in recognition between naïve and informed conditions in response to olfactory stimulation.

2. Materials and methods

2.1. Subjects

Participants were 17 healthy right-handed volunteers (4 men and 13 women) who were assessed to have normal olfactory function by T&T olfactometry. All subjects and a parent whose daughter was under 20 years old gave informed consent to procedures that were approved by the local ethics committee of Kochi Medical School.

Odor stimulation was performed under the following two conditions: with immediate prior warning for eight ''informed'' subjects (two men and six women; mean age 24 years; range 16–28 years) and without prior warning for the remaining nine ''naïve'' subjects (two men and seven women; mean age 23 years; range 21–27 years). The following instructions were given to all the subjects before the experiment: 'We would like you to participate fMRI study on olfaction'. Additional instruction to informed subjects only was 'During the scan you will receive the smell of sweaty socks'.

2.2. Odor administration and task design

Odor was delivered via a mask using an olfactometer that enabled alternation between odorant stimulus and clean air. The task consisted of seven 8-s activation periods with 32-s interstimulus intervals, resulting in a total acquisition time of 5 min (20-s baseline period before the first stimulus) (Fig. 1). The flow-rate of the odorant and air supply was kept constant at 4 l/min such that the same degree of somatosensory stimulation was delivered throughout. Subjects reported the valence of a series of olfactory stimulations with isovaleric acid, rating each stimulation as either pleasant, unpleasant or neither unpleasant nor pleasant.

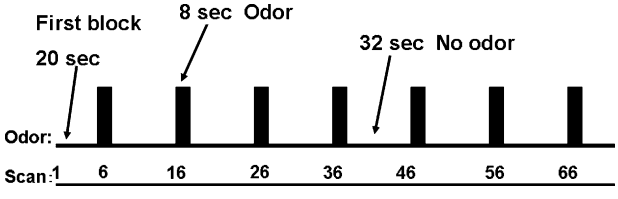

Fig. 1. Experimental design. Isovaleric acid was delivered for 8 s in the activated condition, alternated with 32 s of clean air in the off condition, for seven cycles. Images acquired during baseline periods were not used in analysis.

2.3. Odorant selection

Odorant used was 13.5% isovaleric acid diluted in propylene glycol. This concentration is adopted for the strongest intensity used in T&T olfactometry.

2.4. fMRI data acquisition and analysis

MRI data were obtained using a 1.5T GE Signa scanner using a T2* sequence (TR/TE = 4000/40, flip angle = 90°, width 7 mm, gap 1 mm, 17 slices). The first 4 scans were discarded due to T1 saturation effects, leaving a total of 80 scans that were analyzed for brain activation. Each set of imaging data was analyzed using FEAT, a part of FMRIB'S Software Library ($p < 0.01$, cluster, z value > 2.3).

3. Results

3.1. Stimulation with prior warning

In the informed condition, group analysis across all eight subjects revealed significant activation in the bilateral

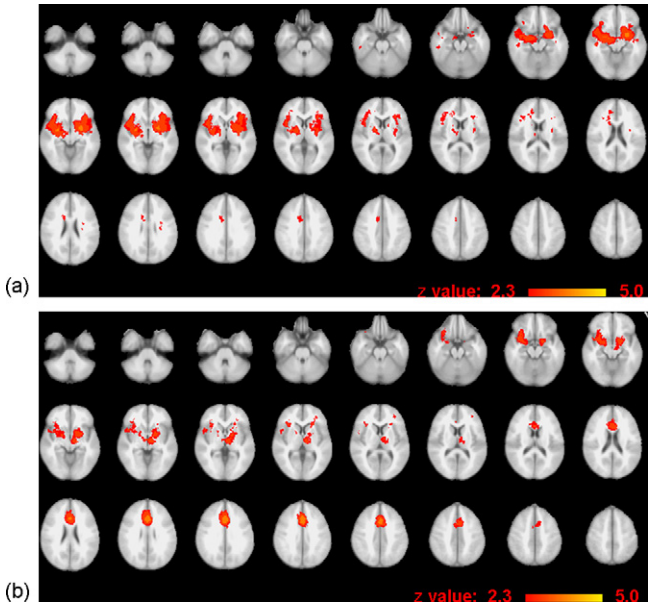

Fig. 2. (a) Activation in the informed condition. Figure shows the group activations across the eight informed subjects. Activations were thresholded at $p < 0.01$ to reveal the extent of the activations. (b) Activation in the naïve condition. Figure shows the group activations across the nine naïve subjects. Activations were thresholded at $p < 0.01$ to show the extent of the activations.