

Continual Dynamics Of Prefrontal Oxyhemoglobin Patterns During Emotion And Feeling In Humans

Continual prefrontal activity during emotion and feeling

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Abstract— Human brain activity patterns during the dynamics of continual emotional or feeling stimuli remain obscure. In this study, 15 subjects were exposed to pleasant or unpleasant feelings, and near infrared spectroscopy (NIRS) showed changes in oxyhemoglobin in the prefrontal cortex (PFC). When these subjects were exposed to images invoking pleasant feelings followed by unpleasant feelings, oxyhemoglobins moved from negative to positive. Conversely, exposure to the opposite order of images rarely resulted in a negative oxyhemoglobins value. In addition, randomized images showed less oxyhemoglobins alteration. Two questionnaires were employed to determine whether the images used for the feeling tests inspired fear emotion and memory. Pleasant feelings were markedly increased with the relief emotion, while unpleasant feelings were enhanced with fear emotion and memory. These findings suggest that unpleasant feelings are predominantly associated with fear emotion and memory and that these processes result in dynamic changes of oxyhemoglobin in the PFC.

Keywords—prefrontal cortex; oxyhemoglobin; near infrared spectroscopy; feeling, emotion

I. INTRODUCTION

Emotion implicates various psychological states. These physiological phenomena have been associated with neuronal activities in the cerebral cortex [1]. Although these emotions are known to influence a complex state of feelings, the associative mechanisms for their activity patterns in neuronal cells are among the major topics of exploration in the field of psychology and neuroscience.

Recent physiological and physiological studies have suggested that emotion is associated with neuronal brain activity patterns in brain regions such as the amygdala, cingulate cortex, orbitofrontal cortex, and prefrontal cortex [2,3]. Local neural circuits among these brain regions may play roles in emotional processing [4]. In a previous anatomical study, neuronal excitation in the amygdala, projected to the hippocampus and cingulate cortex, was found to participate in the emotional process. In addition, this emotional process affects memory [5], while relevant memory critically controls emotion [6]. Hence, emotional arousal is tightly associated with acquired memory [7], and these emotional processes may influence both pleasant and unpleasant feelings [8].

“Feeling” as the subjective experience of an emotional state [8] is detected by a physical signal of the body reacting to external stimuli. Hoshi (2011) demonstrated that pleasant or unpleasant feelings evoked by emotional pictures influence the neurophysiological phenomena in the dorsolateral and ventrolateral prefrontal cortex [9].

Hemoglobin (Hb) is an iron-containing oxygen transport metalloprotein present in red blood cells. When oxygen binds to the heme component of Hb, oxygenated hemoglobin (oxy-Hb) is formed. Neuronal cells in the brain lack internal reserves of energy and require more energy from oxidative phosphorylation during their firing. Based on these facts, blood oxygenation level-dependent (BOLD) contrasts between oxy-Hb and deoxygenated hemoglobin (deoxy-Hb) have been conducted using near-infrared spectroscopy (NIRS) imaging to determine brain activity patterns. This NIRS imaging technique uses the near-infrared region of the electromagnetic

spectrum from 700 nm to 1000 nm. This region of the spectrum exhibits relatively good transparency in biological materials, permitting sufficient noninvasive photon transmission and/or reflection through organs such as the brain [10]. Functional NIRS (fNIRS) enables the measurement of the hemodynamic responses and alteration of oxy-Hb (Δ oxy-Hb) that are typically associated with neuronal behavior [11,12] and might therefore be useful for measuring neuronal activities during feeling [9].

Pleasant and unpleasant feelings seem to be tightly affected by memory [13], and the associative brain functions related to each feeling have been specified. However, the brain activity patterns that underlie the actual continual dynamics of emotion determination and/or the predomination of pleasant and unpleasant feelings remain to be clarified.

In the present study, we examined whether continuously altered emotional dynamics produce specific brain activity patterns in the prefrontal cortex for pleasant or unpleasant feelings using fNIRS and evaluated the associations of these brain activity patterns with relevant memories.

II. METHODOLOGY AND EXPERIMENTAL DESIGN

A. Participants

The participants consisted of 15 healthy students enrolled at Kyoto University Medical School (7 males, 8 females, age: 21–25 years old). Questionnaires regarding past neurological medical history, including epilepsy and strokes, were conducted, and only healthy subjects (i.e., those with no history of medical treatment) participated in the study.

B. Ethics statement

Experimental procedures were conducted in accordance with the Declaration of Helsinki and were in agreement with the Ethical Guidelines of Kyoto University. All subjects in the study participated voluntarily and provided written informed consent prior to enrollment. Approval was obtained from the ethics committee of the Kyoto University Medical School (Approval document No. 1318).

C. Emotional stimuli

Nine pictures based on a story from a famous horror movie, *The Ring* (Fig. 1A), were used in the present study. This movie uses a well built of brick as a symbol from which a girl called "Sadako" (in Japanese) or "Samara" (in English) appears. We chose this movie because it has a simple story, symbolized by the brick well, and was likely to stimulate both unpleasant feelings and emotions of fear in the subjects.

The nine pictures used for the stimuli were classified into the following three groups: 1) neutral

(i.e., no emotion and feeling): picture 1; 2) pleasant: pictures 2–5; and 3) unpleasant: pictures 6–9. The three groups were arranged from pleasant to unpleasant in the first trial and from unpleasant to pleasant (i.e., the reverse order) in a second trial conducted six months later (Fig. 1B). Finally, a randomized test (third trial) in which the order of the pictures was determined using LabVIEW software (National Instruments, Austin, TX, USA) was conducted six months after the second trial (Fig. 1C).

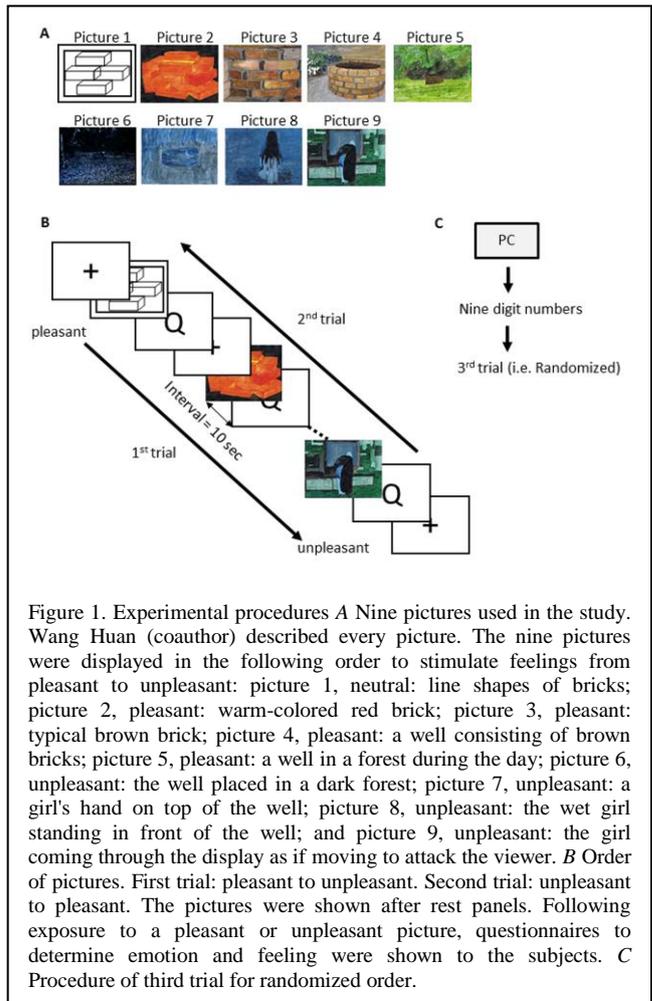


Figure 1. Experimental procedures A Nine pictures used in the study. Wang Huan (coauthor) described every picture. The nine pictures were displayed in the following order to stimulate feelings from pleasant to unpleasant: picture 1, neutral: line shapes of bricks; picture 2, pleasant: warm-colored red brick; picture 3, pleasant: typical brown brick; picture 4, pleasant: a well consisting of brown bricks; picture 5, pleasant: a well in a forest during the day; picture 6, unpleasant: the well placed in a dark forest; picture 7, unpleasant: a girl's hand on top of the well; picture 8, unpleasant: the wet girl standing in front of the well; and picture 9, unpleasant: the girl coming through the display as if moving to attack the viewer. B Order of pictures. First trial: pleasant to unpleasant. Second trial: unpleasant to pleasant. The pictures were shown after rest panels. Following exposure to a pleasant or unpleasant picture, questionnaires to determine emotion and feeling were shown to the subjects. C Procedure of third trial for randomized order.

Simple questionnaires were included after each picture (Fig. 5A) in which the participants assigned a numerical score to their feelings after being exposed to the image. The pictures and questionnaires were alternated every 10 s. The questionnaire results were analyzed to test whether each feeling corresponded to the dynamics of the oxyhemoglobin levels on the NIRS recordings. Six months after the first trial, an additional questionnaire was included asking about the fear or relief memory associated with each picture to examine the effect of implicit memory on the onset of emotion (i.e., fear or relief memory, Fig. 5B).

D. Experimental conditions

Each participant sat on a chair in a dark room to view each image following a 5-minute period of relaxation before the start of the experiment. The

display monitor (horizontal: 33.5 cm × vertical: 57.3 cm) was positioned 60.0 cm from the participant. Crosses (for a rest), test images, and questionnaires were each displayed on the monitor for 10 s. The experimenter recorded the answers.

E. fNIRS recording

fNIRS recordings were conducted in accordance with experimental procedures described elsewhere [9]. In brief, a multichannel fNIRS imaging system (FOIRE-3000, Shimadzu, Kyoto, Japan) was used in this study. Seven illuminator and detector pairs were tightly attached to the skin surface of the head according to the international 10-20 method [14], in which the positioning of the illuminators and detectors with respect to the forebrain is determined after measurement of the distance between the nasion and inion and between the two earlobes. According to the 10-20 method, channel numbers correspond to the typical brain regions as follows: ch. 6, left ventrolateral prefrontal cortex (VLPFC); ch. 19, left dorsolateral prefrontal cortex (DLPFC); ch. 1, right VLPFC; ch. 14, right DLPFC. After the experiments, the position of detector and illuminator were investigated again whether each position was placed on the right place. When the position of detector and illuminator was extremely moved, its data was discarded. All fNIRS data were transferred to a PC and analyzed with FOIRE-3000 software (Shimadzu, Kyoto, Japan). To reduce the effects of individual variation on the fNIRS data, normalization calculations were performed as described elsewhere [15]. In brief, the mean oxy-Hb value at the resting state was subtracted from the measurements during the task periods, and the results were then divided by one standard deviation of oxy-Hb. Thus, the mean value of the standardized measurements of oxy-Hb was 0, and the standard deviation was 1.

F. Statistical analysis

Values are shown as means ± standard errors. Differences were assessed by the Dunnett test, with a value of $P < 0.05$ taken to indicate statistical significance.

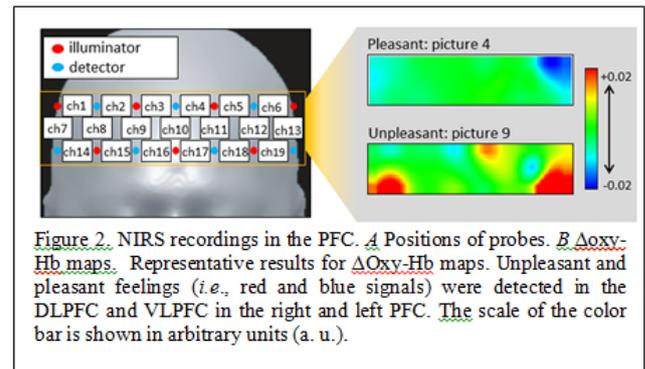


Figure 2. NIRS recordings in the PFC. *A* Positions of probes. *B* Δ oxy-Hb maps. Representative results for Δ oxy-Hb maps. Unpleasant and pleasant feelings (*i.e.*, red and blue signals) were detected in the DLPFC and VLPFC in the right and left PFC. The scale of the color bar is shown in arbitrary units (a. u.).

III. RESULTS

G. Pleasant or unpleasant feelings in the prefrontal cortex

To examine how sequential viewing of the nine pictures (Fig. 1A and B) stimulated brain physiological functions, fNIRS recordings were conducted in the prefrontal cortex (PFC) of each subject using 19 detectors placed on the forehead (Fig. 2, left panel). This approach was based on previously described guidelines [9]. In fNIRS measurements, the oxy-Hb dynamics indicate the alteration of brain activity [12]. We detected the alteration of oxy-Hb levels (Δ oxy-Hb) during the viewing of pleasant and unpleasant images, and an example of fNIRS data was shown (Fig. 2, right panel). The Δ oxy-Hb level was markedly reduced when viewing the representative pleasant picture 4 at Ch 6 (*i.e.*, left VLPFC). Conversely, an unpleasant picture (*e.g.*, picture 9) increased Δ oxy-Hb bilaterally at Ch 14 and Ch 19 (*i.e.*, left and right DLPFC).

These findings suggest that pleasant feelings are associated with decreased oxy-Hb in the left VLPFC and that unpleasant feelings are clearly detectable as an oxy-Hb increase in both DLPFCs.

A. Stronger effect of unpleasant feelings on oxyhemoglobin

To investigate the effects of emotional dynamics on oxy-Hb levels, the subjects were continuously exposed to nine colored pictures, as shown in Fig. 1. The results for exposure to the nine images in the pleasant to unpleasant order are shown in supplemental Movie 1, and the analyses of oxy-Hb alteration (Fig. 3B) in representative areas (*i.e.*, Ch 1, 6, 14, and 19) are shown in Fig. 3C.

When the displayed pictures progressed from pleasant to unpleasant, Δ oxy-Hb showed a negative transient peak with the pleasant pictures (*e.g.*, picture 2, white arrow head), especially at Ch 1 and 14. The Δ oxy-Hb levels were almost unaltered for pictures 3 through 5, while Δ oxy-Hb at Ch 1, 6, 14, and 19 were significantly increased by exposure to unpleasant pictures (*e.g.*, picture 9, black arrow heads).

Conversely, displaying the pictures in the unpleasant to pleasant order resulted in increased Δ Oxy-Hb for pictures 2 and 9. Δ Oxy-Hb for picture 3 also tended to positive values, especially in Ch 6 and 14. Supplemental Movie 2 shows the dominant positive trend for Δ Oxy-Hb during this presentation order. These findings suggest that repetitive

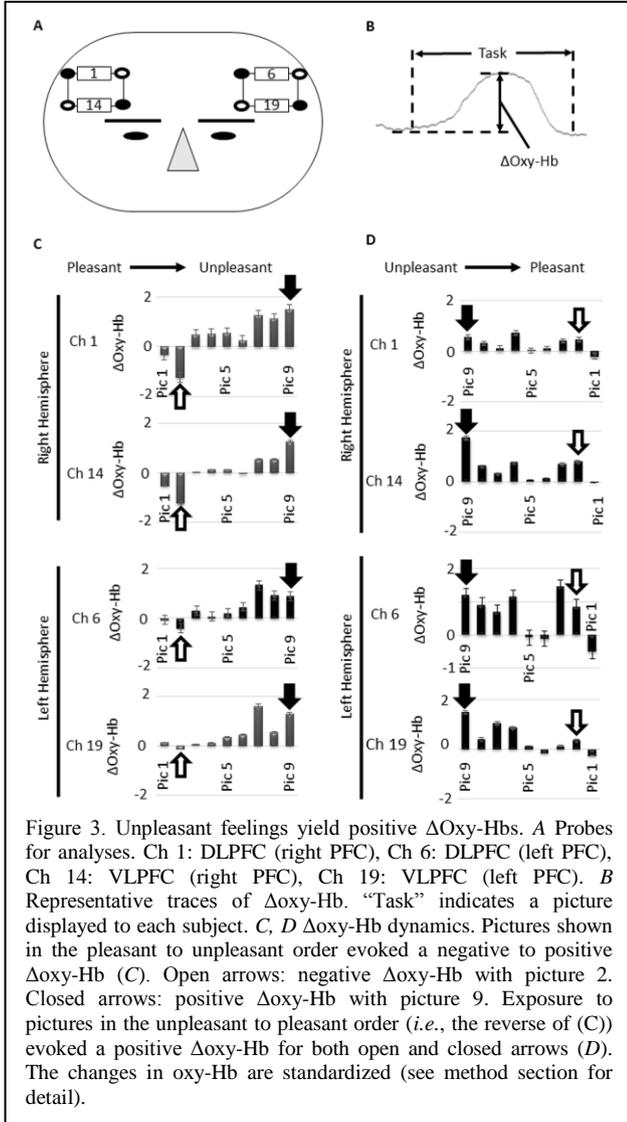


Figure 3. Unpleasant feelings yield positive Δ Oxy-Hbs. **A** Probes for analyses. Ch 1: DLPFC (right PFC), Ch 6: DLPFC (left PFC), Ch 14: VLPFC (right PFC), Ch 19: VLPFC (left PFC). **B** Representative traces of Δ Oxy-Hb. "Task" indicates a picture displayed to each subject. **C, D** Δ Oxy-Hb dynamics. Pictures shown in the pleasant to unpleasant order evoked a negative to positive Δ Oxy-Hb (C). Open arrows: negative Δ Oxy-Hb with picture 2. Closed arrows: positive Δ Oxy-Hb with picture 9. Exposure to pictures in the unpleasant to pleasant order (*i.e.*, the reverse of (C)) evoked a positive Δ Oxy-Hb for both open and closed arrows (D). The changes in oxy-Hb are standardized (see method section for detail).

unpleasant feelings predominantly lead to increasing Δ Oxy-Hb in the PFC.

H. Randomized picture order resulted in less prefrontal Δ Oxy-Hb

To determine whether the significant alteration of Δ Oxy-Hb occurred due to the stimulation pattern, summarized by the pleasant or unpleasant feelings shown in Fig. 1, an experiment was conducted using a randomized picture order (Fig. 4). In a representative result of this randomized test, the Δ Oxy-Hb values were relatively small, and the positive values for picture 2 and 9 were not significantly different from that that for picture 1. Other randomized tests also showed similar results (data not shown). These findings suggest that a randomized picture order caused less alteration of Δ Oxy-Hb in the PFC.

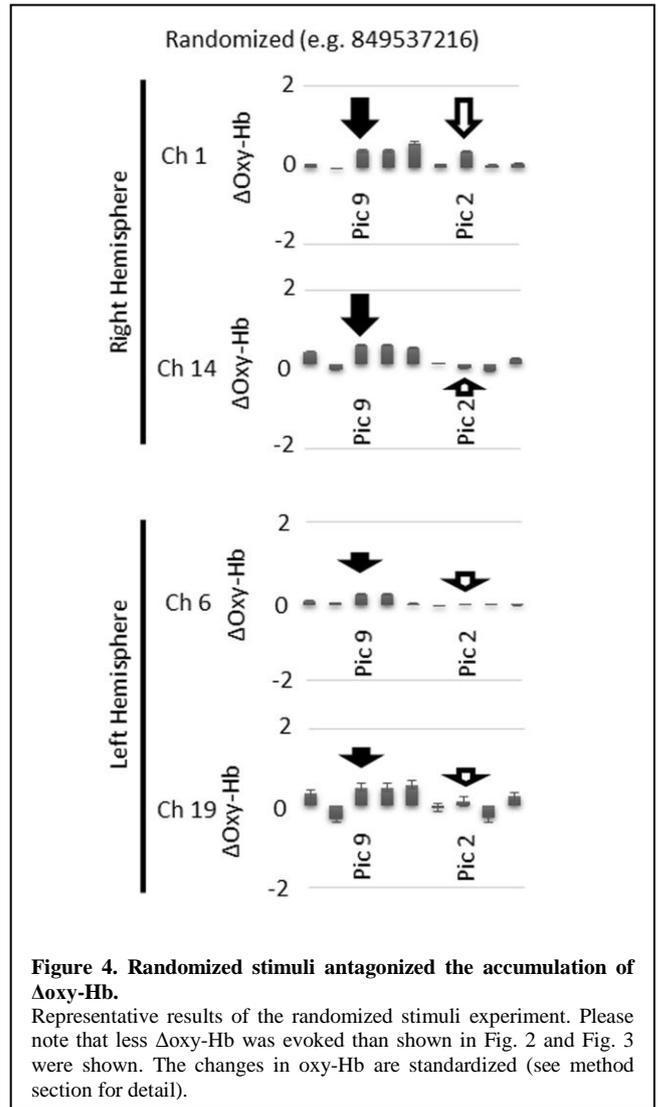


Figure 4. Randomized stimuli antagonized the accumulation of Δ Oxy-Hb. Representative results of the randomized stimuli experiment. Please note that less Δ Oxy-Hb was evoked than shown in Fig. 2 and Fig. 3 were shown. The changes in oxy-Hb are standardized (see method section for detail).

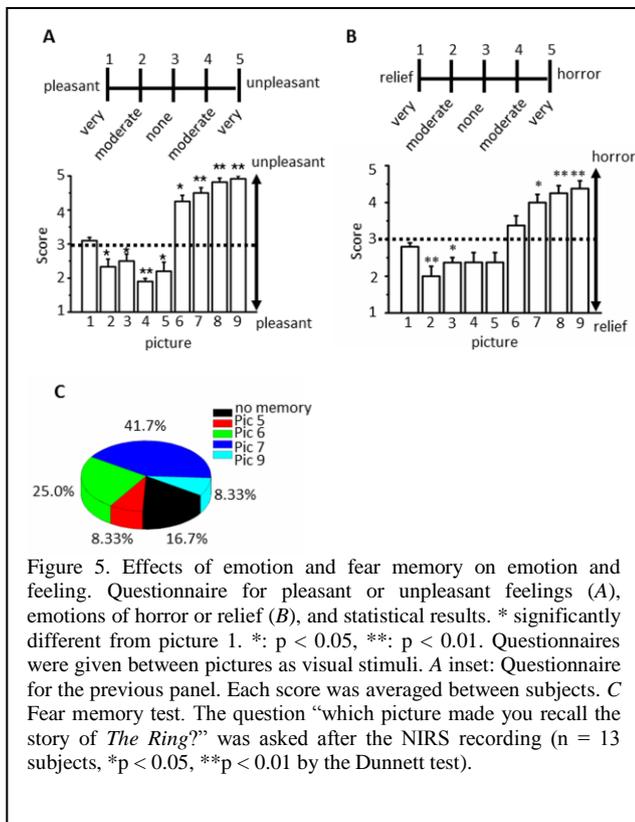
I. Similar effects for feeling and emotion

Following the fNIRS recordings, 15 subjects were exposed to each picture and answered questionnaires regarding their feelings (Fig. 5A). The averaged scores of the questionnaire were as follow : picture 1, 3.10 ± 0.09 ; picture 2, 2.33 ± 0.22 ; picture 3, 2.50 ± 0.20 ; picture 4, 1.90 ± 0.09 ; picture 5, 2.20 ± 0.25 ; picture 6, 4.25 ± 0.17 ; picture 7, 4.5 ± 0.15 ; picture 8, 4.81 ± 0.11 ; picture 9, 4.91 ± 0.08 . Because a value of 3 was set as neutral, < 3 was pleasant and > 3 was unpleasant. These findings suggest that picture 1 lead to neutral feelings, pictures 2–5 produced pleasant feelings, and pictures 6–9 inspired unpleasant feelings.

The questionnaire for emotion were also examined (Fig. 5B). Regarding emotion, the averaged scores of the questionnaire were similar to the values shown in Fig. 5A: picture 1, 2.87 ± 0.10 ; pictures 2–5, value < 3.0 ; pictures 6–9, value > 3.0 . Finally, we examined whether episodic fear memory affected these results. Half of the subjects held memories of fear for the fear-inducing picture (Fig. 5C). Altogether, horror feelings were similar to fear emotions, and these effects were partially determined by the fear memory.

IV. DISCUSSION

This study aimed to investigate the prefrontal neural correlation of continuous affective stimuli. Therefore, we first carefully selected appropriate pictures that



effectively triggered pleasant and unpleasant feelings. Previous research has suggested that movies effectively activate the corticolimbic brain region related to emotion and feelings [16]. These external stimuli are important for the fine-tuning of appropriate sensations [17]. Therefore, our approach using various visual stimuli in this study was valid for examining human-specific sensations for the control of emotion and feeling. In addition, we performed randomized trials to determine whether patterns of colors or brightness affected brain functionality (Fig.1). This experiment carefully excluded the possibility of the mixture of sensations during presentation of the stimuli.

Brain functional measurements with fNIRS recordings from the PFC revealed oxy-Hb decreases during pleasant stimuli and oxy-Hb increases during unpleasant stimuli (Fig. 2). These findings are similar to those of a previous report [9], in which pleasant and unpleasant feelings specifically changed oxy-Hb in the PFC without affecting autonomic parameters.

Brain functioning during exposure to the various stimuli was examined. The pictures were arranged in three ways: 1) pleasant to unpleasant, 2) unpleasant to pleasant, and 3) randomized. For the pleasant to unpleasant order, we found that pleasant stimuli reduced oxy-Hb in the left lateral region of the PFC, while unpleasant stimuli increased oxy-Hb in both the left and right lateral PFC (Fig. 3). Recently, the lateral

frontal brain has been reported to serve as a neuronal activity region against various populations of sensory stimuli [18,19]. In light of these past reports, our present findings suggest that the lateral region of the prefrontal cortex plays an important role in detecting pleasant and unpleasant feelings.

However, the unpleasant to pleasant stimuli order persistently increased oxy-Hb, with less decrease (Fig. 4). This difference may be explained by the results of previous experiments. Past NIRS studies employing visual stimulation have revealed that the transient increase of oxy-Hb metabolism requires 13–19 seconds until the traces return to the baseline level [12,20]. In this study, we used 10-second intervals between stimuli. Taking into account the positive Δ oxy-Hb caused by unpleasant stimuli and the negative Δ oxy-Hb caused by pleasant stimuli in comparison to the baseline oxy-Hb, we believe that insufficient time was allowed for the recovery of oxy-Hb levels to the baseline. We also conducted a randomized trial study which may reduce the effects of functional hyperemia on oxy-Hb (Fig. 4). No potentiation of oxy-Hb amplitude in this condition supported this model. Therefore, repetitive unpleasant stimuli potentiated the baseline level of oxy-Hb. In addition, the effect size of the increase in oxy-Hb caused by unpleasant stimuli seemed to be larger than that of the decrease in oxy-Hb caused by pleasant stimuli. The former high, unpleasant oxy-Hb might neutralize the later low, pleasant oxy-Hb; however, the precise mechanism for the control of oxy-Hb during the presentation of various stimuli warrants further evaluation.

Finally, we examined two questionnaires for the association of emotions and feelings. Pictures which caused pleasant feelings tended to indicate an emotion of relief, whereas unpleasant feelings resulted in an emotion of fear (Fig. 5A and B). In addition, a memory test (Fig. 5C) showed that over half of the subjects answered that fear memory certainly affected these results. These findings are consistent with those of previous reports. For example, the neocortical brain area has been shown to participate in the encoding of memory for informational modulation of sensory functioning [21]. Hence, our findings may address novel associative mechanisms for feeling, emotion, and memory.

In conclusion, we characterized brain neurophysiological patterns for the different modalities of continual pleasant or unpleasant feelings, emotions of fear or relief, and memory. These brain activity patterns in response to specific stimuli will be useful as biomarkers for detecting changes in emotion or feeling.

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SUPPLEMENTAL MOVIE

Supplemental Movie 1. Δ oxy-Hb dynamics during switch from pleasant to unpleasant feelings. The images on which the subjects concentrated during this experiment were shown on a monitor (upper left). Lower left panel: NIRS imaging for Δ oxy-Hb.

Supplemental Movie 2. Δ oxy-Hb dynamics during switch from unpleasant to pleasant feelings. The images on which the subjects concentrated during this experiment were shown on a monitor (upper left). Lower left panel: NIRS imaging for Δ oxy-Hb.

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