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# Associations among central nervous, endocrine, and immune activities when positive emotions are elicited by looking at a favorite person

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#### **Abstract**

Recent studies on psychoneuroimmunology have indicated that positive psychological events are related to immune functions; however, limited information is available regarding associations among the central nervous, endocrine, and immune systems when positive emotions are elicited. In the present study, we demonstrated associations among these systems by simultaneously recording brain, endocrine, and immune activities when positive emotions were evoked in participants as they watched films featuring their favorite persons. Interestingly, the activity of peripheral circulating natural killer cells and the peripheral dopamine level were elevated while participants experienced positive emotions, and these values were positively correlated. The following brain regions were significantly activated in the positive condition relative to the control condition: medial prefrontal cortex, thalamus, hypothalamus, subcallosal gyrus, posterior cingulate cortex, superior temporal gyrus, and cerebellum. Further, covariate analyses indicated that these brain regions were temporally associated with endocrine and immune activities. These results suggest that while an individual experiences positive emotions, the central nervous, endocrine, and immune systems may be interrelated and attraction for favorite persons may be associated with the activation of the innate immune function via the dopaminergic system.

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#### 1. Introduction

Studies on psychoneuroimmunology have revealed that the central nervous, peripheral autonomic nervous, endo-

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crine, and immune systems are interrelated via complex biochemical pathways (Ader, 2000). Some have also revealed that acute psychosocial stressors such as public speaking, examinations, and even short-term mental arithmetic are sufficient to effect changes in immunological parameters (Goebel and Mills, 2000; Downing and Miyan, 2000; Isowa et al., 2004, 2006; Kimura et al., 2005). These stressors can activate the sympathetic nervous system and the hypothalamus–pituitary–adrenal (HPA) axis and

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increase the levels of circulating catecholamines (Maisel et al., 1990). Prolonged elevation of sympathetic nervous activity by such stressors induces extremely high levels of catecholamines. Additionally, via a  $\beta$ -adrenergic mechanism, it reduces the number of circulating lymphocytes and the activity of natural killer (NK) cells, a subgroup of lymphocytes essential to the cellular immune defense against virus-infected cells, bacteria, and tumor cells (Vivier et al., 2004), thereby decreasing immune defense (Maisel et al., 1990). Furthermore, chronic psychological distress might cause or facilitate diseases such as cancer (Jacobs and Bovasso, 2000). Therefore, it is suggested that negative emotions lead to the deterioration of human immune functions and health.

In contrast, recent findings suggest that positive psychological events are also related to immune functions and health in humans. It has been reported that individuals with a great tendency to experience positive emotions such as happiness and joy are less vulnerable to viral infections (Cohen et al., 2003; Doyle et al., 2006; Marsland et al., 2006). Furthermore, NK cell activity significantly increases after individuals laugh by watching comic films (Takahashi et al., 2001; Berk et al., 2001), and the proportion of circulating NK cells increases after positive emotions are experienced due to sexual arousal (Haake et al., 2004). However, whether the central nervous and immune systems are actually interrelated via neurochemical networks remains obscure because studies that focus on the association between central nervous and immune systems have not vet been conducted. Moreover, it is still obscure whether every positive emotion is related to the immune system.

Seeing one's favorite person such as a love interest or favorite actor/actress may evoke positive emotions and occasionally lead to a feeling of elation (Esch and Stefano, 2005a,b; Stefano and Esch, 2005; Planalp et al., 2006; Aron et al., 2006). Recent neuroimaging studies have demonstrated that such events activate reward-related regions in the brain (Bartels and Zeki, 2004; Aron et al., 2005; Fisher et al., 2005); based on this, attraction toward certain persons may be highly rewarding. In the present study, we attempted to examine positive emotions elicited on seeing a favorite person and the psychological and physiological responses, including central nervous, endocrine, and immune parameters, during these emotions. There have been no investigations on whether seeing a favorite person can indeed evoke positive emotions. In addition, to our knowledge, associations among central nervous, endocrine, and immune systems during experiencing those emotions have not been investigated to date. It is possible that a certain immune parameter is stimulated even when we see our favorite persons. In this study, the participants themselves selected persons whom they found attractive, and positive emotions were manipulated by the viewing of a film featuring these attractive persons. We have recently established a method that can simultaneously record brain activity by using <sup>15</sup>O-water positron emission tomography (PET) and peripheral physiological activity including immune activity (Ohira et al., 2006); thus in order to reveal associations among central nervous, endocrine, and immune systems, we simultaneously recorded various parameters such as mood states, brain activity, peripheral circulating NK cell activity, and the serum level of catecholamines when male participants watched films featuring people whom they perceived as attractive.

#### 2. Methods

#### 2.1. Participants

Twelve healthy male volunteers (right handed; age range: 20–29 years) participated in the study. The participants' self-reports in a questionnaire and an interview by a psychiatrist confirmed that they had no past history of psychiatric or neurological illnesses and were not receiving any medication. Two participants were excluded from the catecholamine analyses because of technical difficulties. All the participants provided written informed consent in accordance with the Declaration of Helsinki, and they were paid 15,000 Japanese Yen for participation. The participants received no medication during the experimental period. This study was approved by the Human Studies Committee of Aichi Medical University and the Ethics Committee of Kizawa Memorial Hospital.

#### 2.2. Task procedure

Participants were instructed not to eat 2 h before the scanning session, but they were allowed to consume non-alcoholic and caffeine-free fluids. In the present study, all participants underwent two PET scans. In the last minute of a 3-min rest period (pre-film-watching period), the first blood sample (for assays of endocrine and immune parameters) was obtained, and the participants were asked to evaluate their present mood state on a visual analogue scale (VAS). They then watched either an emotionally neutral film (control film), or a film featuring people they found attractive (positive film). The films were screened for 4 min on a 15-inch. display placed at a distance of approximately 60 cm (film-watching period). In the 2–3 min of the film-watching period, a PET scan (duration: 60 s) was performed. In the last minute of the film-watching period, a second blood sample was obtained. After watching the film, the subjects evaluated their mood state and the watched film on the VAS, and a rest period of 3 min (post-film-watching period) was set. The next pre-film-watching, film-watching, and post-film-watching periods began 5 min after the previous post-film-watching period. The order of the two types of films was counterbalanced across participants.

#### 2.3. Stimuli

We compiled 4-min audiovisual clips. The positive film featured a person whom each participant subjectively considered attractive. By free response, the participants themselves selected this person before the day of the experiment. All the selected persons were famous actresses. By the day of the experiment, we compiled an individual 4-min video film from TV programs and movies for each participant. In order to demonstrate the maximum effect, we did not standardize the actions performed by the actresses in the movies, but the films did not contain erotic and sexually suggestive scenes. For example, one film contained scenes of the favorite person smiling. In addition, we compiled audiovisual clips because we thought that the favorite person's voice was important for participants. The control film was a TV news program with a newscaster whom participants considered not so attractive. Since the newscaster being reported concerned weather in the past, rather than any new information, the participants remained uninterested in the film. In order to delete the activations in the non-emotional brain regions, such as the visual and auditory cortices, the PET images obtained during the control condition

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