

## [Grant-in-Aid for Specially Promoted Research]

### Molecular and neural basis for olfactory communication in humans



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#### Purpose and Background of the Research

##### ● Outline of the Research

This research aims to understand the role of olfaction (sense of smell) in human communication, using a multidisciplinary approach including natural product chemistry, biochemistry/molecular biology, neuroscience/physiology, and behavioral psychology. We will investigate the role of body odors in human communication at the multilevel of molecules, receptors, brain, and behavior. The final goal of this project is to address the big question, "Are there pheromones in humans?" by specifically focusing on mother-child and gender relationships. We will target infants and women as sources of body odor and aim to identify body odor components with positive physiological and psychological effects such as attachment, bonding, comfort, and social buffering. In addition, we will identify their olfactory receptors, elucidate their neural connection patterns to the olfactory bulb, the primary center of olfaction, and investigate their mechanisms of action on the brain by using brain imaging techniques. In addition to the academic significance of elucidating the molecular and neural basis of olfactory communication between humans, the project is expected to lead to applications that support appropriate human communication.

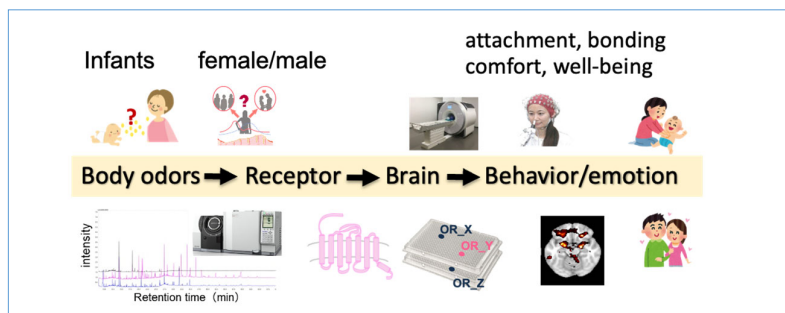


Figure 1. Project image

##### ● Background leading to the conception of this study

The question of whether humans have pheromones is often asked, but unfortunately, the sex pheromones that cause the often-discussed behavior of attracting the opposite sex do not seem to exist in humans. On the other hand, there has long been circumstantial evidence suggesting the existence of primer pheromones with physiological effects, such as the dormitory effect. In the first place, looking at primates as a whole, including humans, there have been no reports until recently proving the existence of a pheromonal substance at the molecular level. Our group succeeded in identifying odorants secreted by males and of interest to females during the mating season in the ring-tailed lemur, a New World monkey, which became the talk of the world as the first pheromone candidate in primates (Shirasu et al. Current Biol. 2019). This was achieved by narrowing down the active odorants by using the latest odor collection technology and analytical chemistry, and it was thought that this method could be applied to human body odor, which has been difficult to control until now.

Meanwhile, the JST ERATO Touhara Chemosensory Signal Project has launched human brain function imaging technology and established an experimental system that can measure olfactory responses with high spatiotemporal resolution using EEG and fMRI (Singh et al. Sci. Rep. 2016, Okumura et al. Chem. Senses 2017, Kato et al. PNAS 2022). Assay systems using stress indicators have also been established for physiological effects of odor (Hirasawa et al. Psychoneuroendo. 2019). Thus, technologies connecting pheromone molecules to physiology, such as natural product chemistry, receptor biochemistry, and neuroendocrinology, and a noninvasive measurement system for human brain function imaging have been established, and the foundation for challenging the identification of odorants used for olfactory communication in humans and the elucidation of their mechanisms of action has been established, leading to the conception of this study.

#### Expected Research Achievements

##### ● Research objectives and Targeted goals of project

The academic question is: What are body odor components that have positive effects among humans? What physiological, behavioral, and psychological effects do those body odor components have? What is the mechanism by which those substances are recognized? How are signals transmitted to the brain and how is the information processed? The target communication is the ones between infant and mother (related to mother's attachment, bonding, nurturing behavior) and between the opposite sex (related to comfort, peace of mind, well-being). The purpose of this study is to identify the odorants involved in each of these events from body odor, and to clarify the mechanisms by which these odorants are sensed by the receptors, transmitted to the brain, and processed to ultimately produce behavioral changes, psychological effects, and physiological changes. Furthermore, humans integrate and process multiple sensory information inputs in the real world, and we will try to elucidate how the olfactory signals we identify interact with other sensory inputs and the mechanism of sensory information integration.

##### ● Originality and Significance of the Study

The academic significance of this study is that it will answer the question of whether there are social signals of odor and pheromone in humans, who do not have the vomeronasal nervous system found in mice and other animals. From a neuroscientific point of view, it is not only significant that the mechanism of olfactory signal transmission from receptors to the brain, i.e., the olfactory bulb-cortical projection mode, which is completely unknown in humans, but it is also expected to elucidate a part of the sensory information integration mechanism in human communication. The biological and evolutionary significance of adding a new concept of olfaction to the infantile facial attractiveness ("baby schema") proposed by Dr. Lorenz, a well-known animal behaviorist, is considered.

##### ● Effects on human society

The evidence at the molecular, neural, and behavioral levels obtained in this study is expected to have a big effect on human society. Specifically, the clarification of infants' neurological representations, from smell to multisensory neural representations, will lead to improved well-being for caregivers and support for infant development. The identification of odors that induce positive psycho-behavioral changes among heterosexuals could lead to social implementation that would improve interpersonal relationships. This research is a multilevel, multidisciplinary, interdisciplinary study at the molecular and individual levels that asks the ultimate question of human pheromones and clarifies the role of the sense of smell in human interaction in terms of peace of mind, security, bonding, and well-being. The research is expected to have a large effect on social life from a new aspect and axis.

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