Discovery of neurons that allow mice to recognize others

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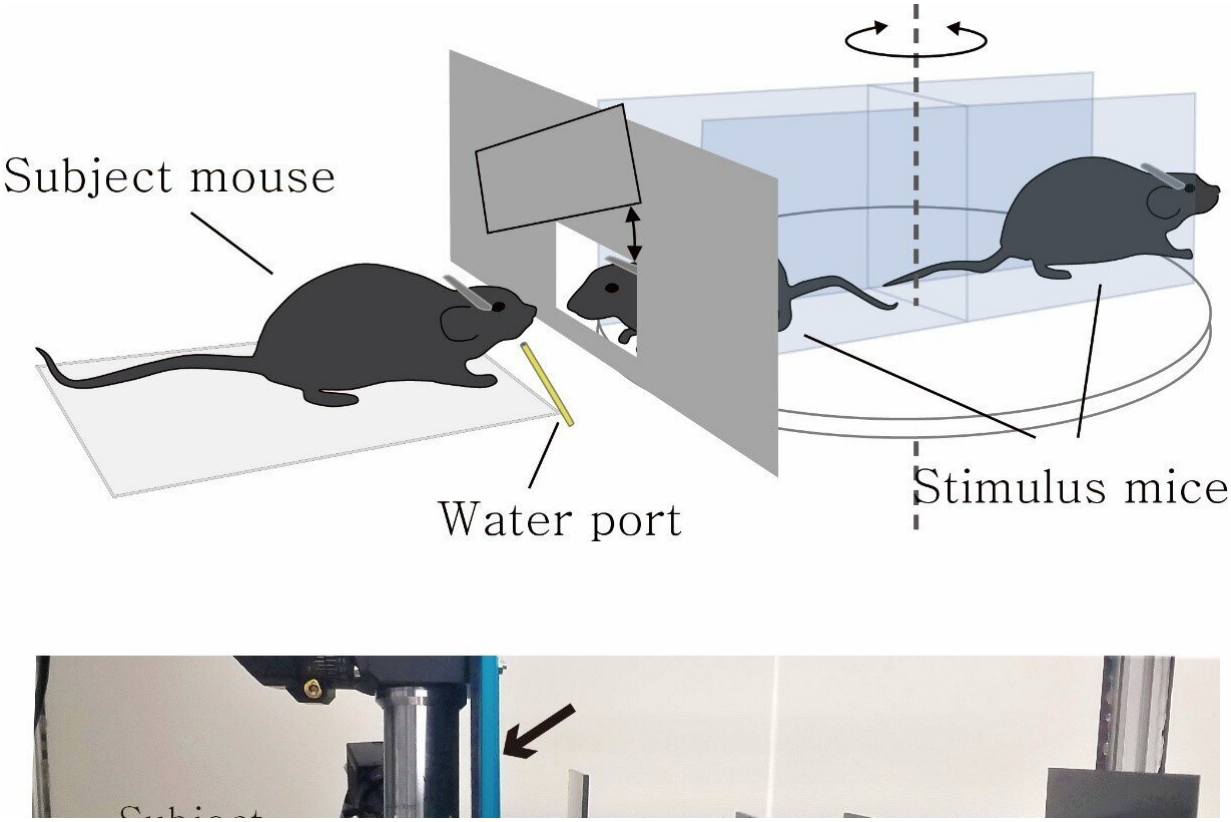


One of the two immobilized mice is presented to the subject mouse in random order. The subject mouse learns to recognize the presented mouse and associates it with the availability of water reward. Credit: Institute for Basic Science

Researchers from the Center for Cognition and Sociality (CCS) within the Institute for Basic Science (IBS) recently announced the discovery of

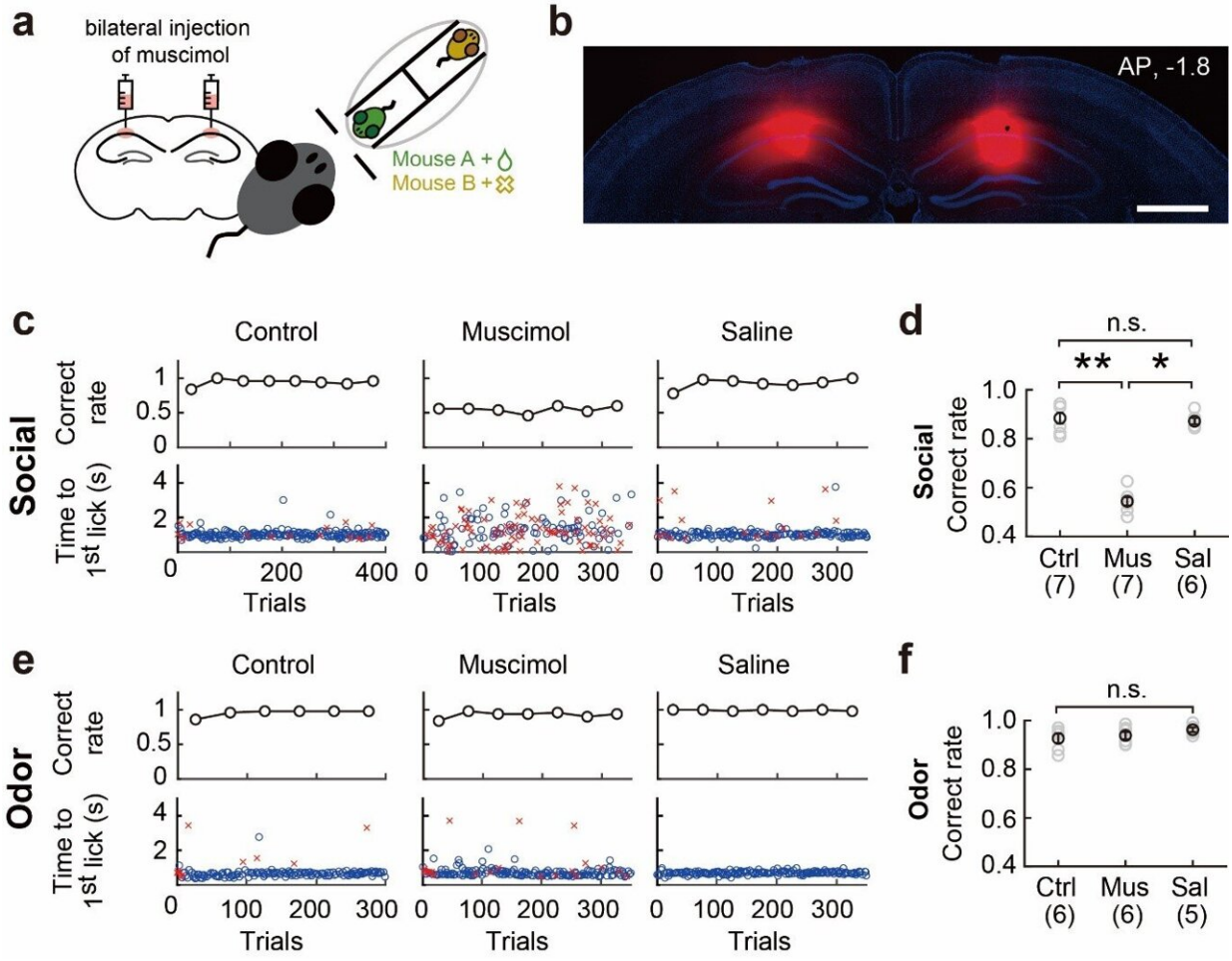
neurons that allow us to recognize others. The research team discovered that the neurons that deal with the information associated with different individuals are located in the CA1 region of the hippocampus.

Social animals, including humans, constantly engage in interactions with others. In this process, the ability to recognize the identity of the social counterpart, retrieve relevant information about them from memory, and update it from the current interaction is critical for establishing social relationships. However, there has been limited research on how these processes occur in the brain.

In order to answer this question, past efforts mostly focused on mouse brain studies, particularly in the hippocampus. The hippocampus was thought to be the answer, since it is a brain structure that is well-known to be responsible for memory formation. Within the hippocampus, the Cornu Ammonis (CA) fields, which are numbered CA1, to CA3, are involved in various functions related to memory and spatial processing and were hence key research interests.

So far, the mouse studies on the neural mechanisms of individual recognition mainly focused on the CA2 region of the hippocampus. However, previous studies have used behavioral experiments that only involve distinguishing unfamiliar mice from familiar mice, making it difficult to interpret whether the results reflect the animal's ability to perceive or truly recognize individual characteristics.

In this study, published in *Nature Communications*, the IBS-CCS research team developed a new behavioral paradigm using mice to better investigate their ability to recognize other individuals. Their new method involved having the subject mouse associate specific individual mice with rewards and studying their behavior after encountering reward-associated individuals and not associated individuals.



When neuroinhibitor muscimol is injected into the dorsal CA1 region of the hippocampus, the subject mouse becomes unable to distinguish the presented mice. However, when the same experiment was performed while presenting odor stimuli unrelated to social activity, this phenomenon was not observed. Credit: Institute for Basic Science

Specifically, two mice were immobilized on a spinning disk and were randomly presented to a subject mouse, which would recognize the neighbor through scent. Water is then supplied from the device to the subject mouse as a reward when licking in response to the reward-

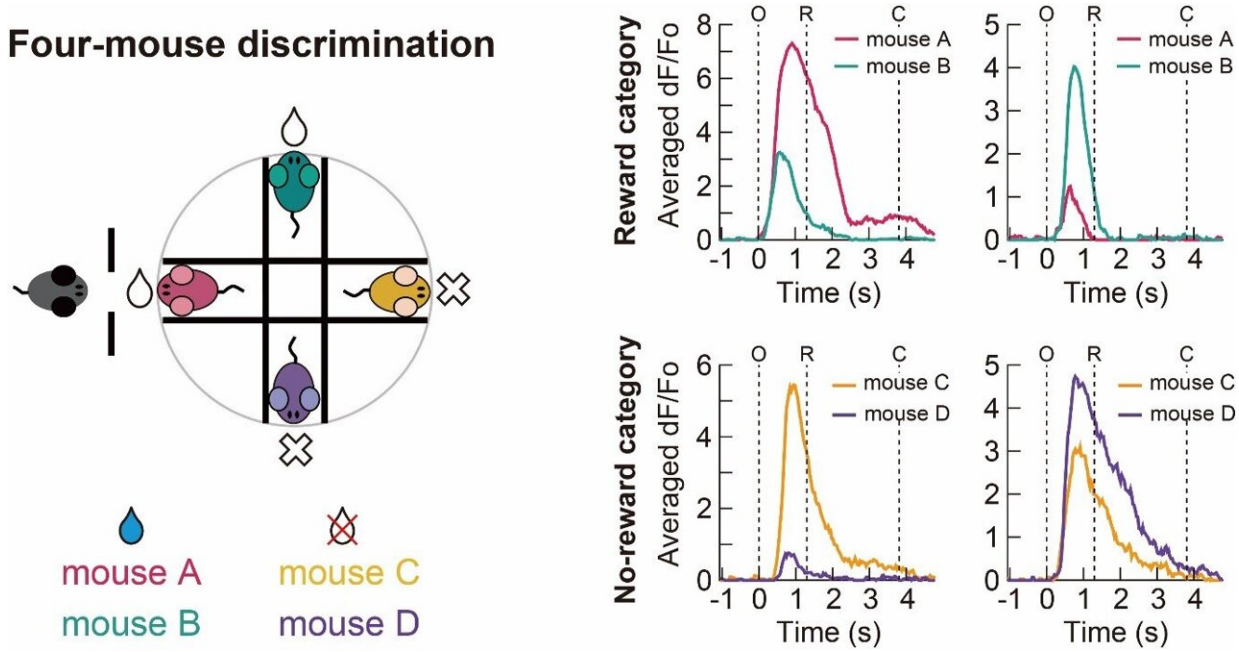
associated mouse, but not another. The researchers tried to determine whether the subject mouse could discriminate against different individuals and analyzed the brain cell activity during the experiment.

The stimulus mice on the spinning disk were male littermates and the subject mice were already familiar with the stimulus mice. This means that the subject mice distinguished between stimulus mice solely according to the unique characteristics of the stimulus mice, suggesting the high reliability of the experimental results.

Using this behavioral paradigm, the researchers clearly demonstrated that the dorsal CA1 region of the hippocampus plays an essential role in individual recognition. For example, when the hippocampal CA1 region is suppressed using a neuroinhibitor, the subject mouse was unable to distinguish its neighbor. Also by using a two-photon imaging technique that allows real-time observation of neural cell activity in the deep regions of the brain, the IBS-CCS team even identified the specific neuronal cells in the hippocampal CA1 region that is responsible for the recognition of individual mice.

This was an interesting addition to previous findings, which have proposed the dorsal CA2 region of the hippocampus to be the important brain area for social memory while reporting that the dorsal CA1 region does not play a significant role.

Furthermore, researchers in the past believed that social memories in rodents only last for a short period of time and that they do not form long-term memories about individual subjects. However, the latest study by the IBS-CCS has demonstrated that long-term memories about individuals can indeed be formed in mice.



Neurons in the dorsal CA1 region of the hippocampus were found to be responsible for distinguishing between two mice within the reward category or between two mice in the non-reward category. Credit: Institute for Basic Science

Dr. Lee Doyun, who led this research, stated, "We have revealed for the first time how value information about others obtained through positive or negative interactions with them is represented and stored in our brains. Furthermore, this provides significant insights into understanding the role of our brains in building and developing human relationships through various social interactions."

Beyond that, the researchers have also revealed the presence of specific neurons in the subject mouse's hippocampal CA1 region that process positive information associated with different individual mice. An important part of forming a social relationship is assigning a positive or negative value to a social encounter with another individual and updating that value. For example, just as it is essential to develop a friendship

with a particular individual, it is essential to evaluate how enjoyable and rewarding it was to interact with them.

These specific CA1 neurons were found to be responsive when encountering reward-associated individuals. However, such reward expectation responses were not observed when the subject was exposed to odors that are unrelated to social activity, such as citral or butanol. These findings indicate that the hippocampal CA1 region plays a selectively important role in the formation of associative social memories.

It is hoped that this new discovery can lead to a potential solution for the treatment of various brain disorders that cause difficulty in forming social relationships.

"Our results could be utilized to understand and propose treatment methods for mental disorders such as autism, which exhibit abnormalities in brain functions involved in processing memories and related information about others," explains Dr. Lee.

More information: Eunji Kong et al, Dynamic and stable hippocampal representations of social identity and reward expectation support associative social memory in male mice, *Nature Communications* (2023). DOI: 10.1038/s41467-023-38338-3

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