How memories are formed in the brain: A new role for the internal compass

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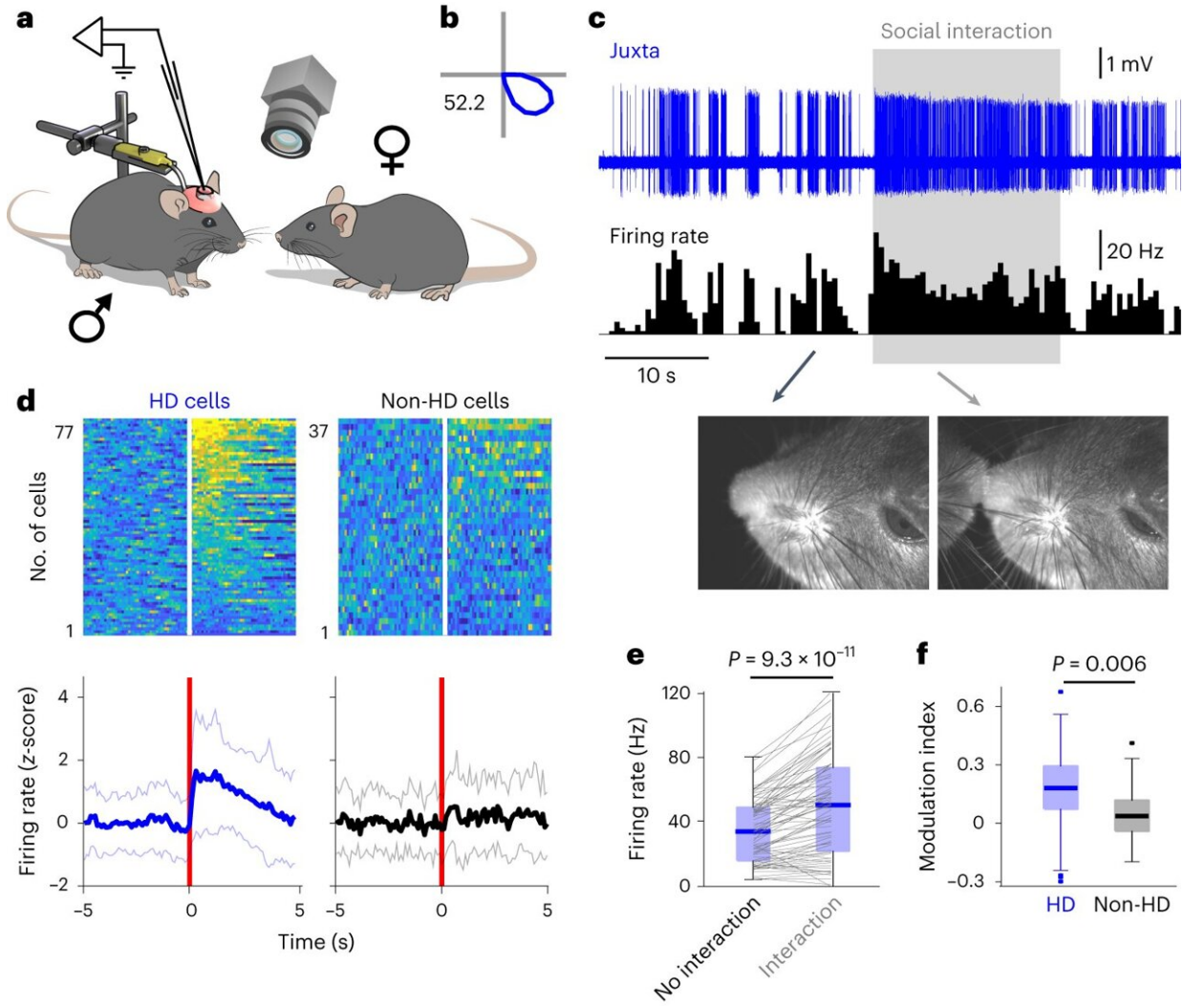

Social interactions dynamically modulated the gain of the HD representation. Credit: *Nature Neuroscience* (2024). DOI: 10.1038/s41593-023-01506-1

Since their discovery in the 1990s, the head-direction cells in the brain have been referred to as its "internal compass." These cells are activated when the head of an animal or human points in a certain direction, and are thought to be important for spatial orientation and navigation.

Now a team of neuroscientists at the University of Tübingen has discovered that head-direction cells in mice do more than this. They may be involved in relaying sensory and emotional information that is used to form memories of experiences, called "episodic memory."

The research team, led by Professor Andrea Burgalossi from the Institute of Neurobiology and the Werner Reichardt Center for Integrative Neuroscience (CIN), have published their study in the journal *Nature Neuroscience*.

In the external world of human experience, the senses together contribute to the formation of memories. The visual stimulus of a picturesque landscape, the echo of a laugh, the warmth of a hug—all these sensory impressions are brought together in one region of the brain, the hippocampus. This processing is crucial for transforming fleeting sensory perceptions into lasting memories.

"The hippocampus is a kind of neural curator that integrates the information," says Burgalossi. "During an experience, a memory trace is created in the hippocampus for that episode in our lives."

Previous assumptions called into question

In order to understand more precisely from where sensory information enters the hippocampus, the research team focused on one of its main input structures in the brain, the anterior thalamus.

"We have known for decades that this area is crucial for episodic

memory. Patients with damage to this region of the brain suffer from memory loss," says Dr. Patricia Preston-Ferrer, one of the lead authors of the study.

When scientists first recorded the activity of nerve cells in the anterior thalamus of rodents in the 1990s, they discovered the head-direction cells were located there. "Previously, it was assumed that these only encoded the animal's heading direction in its environment," says Preston-Ferrer. "But now our latest experiments show that this idea provides an incomplete picture."

When the Tübingen research team recorded the electrical activity in the mouse brain, they found that the head-direction cells in the thalamus became active when they exposed the mouse to sensory stimuli.

"In the case of a sound being played, as well as in the case of a tactile whisker on the mouse's snout being touched, only the head-direction cells were activated specifically and reliably and with a remarkably short delay," says CIN researcher and co-author of the study Giuseppe Balsamo. "We were surprised, as it had been assumed for decades that these neurons were unresponsive to sensory stimuli."

Possible connection between inner compass and episodic memory

The experiments revealed that in the anterior thalamus, only the head-direction cells responded to sensory stimuli. "This tells us that head-direction cells must have a special function," says CIN researcher and co-author of the study Dr. Eduardo Blanco-Hernandez.

"Their function must go beyond acting as an internal compass." The head-direction cells also responded with increased activity to aroused states

including social contacts such as encountering another mouse. "It is known that close attention and emotions have a great influence on the formation of memories and their quality. In such situations, we remember much more vividly than in an uninvolved, passive state," says Blanco-Hernandez.

All in all, the new results indicate that head-direction cells in the thalamus might constitute a key gateway for sensory, attention and arousal information entering the episodic memory system.

"To understand how a memory trace is formed, we need to know the pathways and nerve cells involved that transmit basic information to the hippocampus," says Burgalossi. "Based on our work, we believe the inner compass represents a key node in this process." Whether this node could be influenced, for example for therapeutic purposes, in order to better form and retrieve memories, will require further research.

More information: Eduardo Blanco-Hernández et al, Sensory and behavioral modulation of thalamic head-direction cells, *Nature Neuroscience* (2024). DOI: 10.1038/s41593-023-01506-1

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