Medical Xpress

Scientists capture glimpse of how brain cells embody thought

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Cedars-Sinai neurologist Chrystal Reed, MD, Ph.D., with a patient in the epilepsy monitoring unit. Credit: Cedars-Sinai.

The coordinated activity of brain cells, like birds flying in formation, helps us behave intelligently in new situations, according to a study led by Cedars-Sinai investigators. The work, published in *Nature,* is the first to illuminate the neurological processes known as abstraction and inference in the human brain.

"Abstraction allows us to ignore irrelevant details and focus on the information we need in order to act, and inference is the use of knowledge to make educated guesses about the world around us," said Ueli Rutishauser, Ph.D., professor and Board of Governors Chair in Neurosciences at Cedars-Sinai and co-corresponding author of the study. "Both are important parts of cognition and learning."

Humans often use these two cognitive processes together to rapidly learn about and act appropriately in new environments. One example of this is an American driver who rents a car in London for the first time.

"The English drive on the right-hand side of the car and on the left-hand side of the road, the opposite of the way we do in the U.S.," Rutishauser said. "For someone from the U.S., driving in London means reversing many of the rules they have learned, and making that mental shift requires abstraction to focus on driving-sidedness, and making inferences to avoid pulling directly into oncoming traffic."

In the study, investigators worked with 17 hospitalized patients who had electrodes surgically implanted in their brains as part of a procedure to diagnose epilepsy. In total, the researchers recorded the firing of thousands of brain cells as participants performed an inference task on a computer.

Looking at the activity of so many brain cells required the use of artificial intelligence to extract the responses that were relevant, allowing investigators to see the coordination between the neurons during successful inference.

"These are high-dimensional geometrical shapes that we cannot imagine or visualize on a computer monitor," said Stefano Fusi, Ph.D., a principal investigator at Columbia University's Zuckerman Mind Brain Behavior Institute and co-corresponding author of the study. "But we can use mathematical techniques to visualize simplified renditions of them in 3D."

During the recordings, participants were repeatedly shown four pictures—a person, a monkey, a car and a watermelon. In response to each picture, they were asked to press a left-hand or right-hand button. Individuals then received a "correct" or "incorrect" message.

Through repetition, participants eventually learned the correct response for each of the four pictures. At that point, the rules of the game were reversed without the participants being informed, and the opposite response for each picture was counted as correct.

After the switch, some participants were able to quickly figure out the rule change and infer the correct responses without relearning them, meaning they performed inference.

Investigators saw striking geometric patterns in the brains of those participants. Groups of neurons were firing together, much like birds flying in formation or a crowd of people spontaneously taking up a chant at a sporting event.

The way the neurons coordinated their activity and encoded the relevant information indicated that the subjects had gained the conceptual knowledge needed to perform the task. Investigators saw no such patterns in the brains of participants who were not successful in using inference.

"Building conceptual knowledge is an important aspect of learning," said

Hristos Courellis, Ph.D., a researcher at Cedars-Sinai and first author of the study. "In our study, we identified a neural basis for this process, which in cognitive psychology is referred to as abstraction."

Some subjects were initially not able to perform inference from experience with the task alone. For these subjects, investigators provided verbal instructions that allowed the subjects to then infer the correct answers.

"A remarkable discovery was that the same neural geometries emerged in participants who received verbal instructions as in those whose ability to infer was based on experiential learning," said Adam Mamelak, MD, director of the Functional Neurosurgery Program and professor of Neurosurgery at Cedars-Sinai and co-author of the study.

"This crucial discovery shows that verbal input can result in neural representations that otherwise might take a long time to learn through experience."

The study, which relied on data from Cedars-Sinai and the University of Toronto, was led by Cedars-Sinai and conducted as part of a multi-institutional consortium.

"This study provides new insights into how our brains allow us to learn and carry out tasks flexibly and in response to changing conditions and experiences," said Merav Sabri, Ph.D., program director for The BRAIN Initiative. "These insights build on the body of knowledge that could one day lead us toward interventions for neurologic and psychiatric conditions that involve deficits in memory and decision-making."

A surprise to investigators was the discovery that these particular patterns of brain activity emerged only in the hippocampus, a region deep in the center of the brain that is known to be crucial for the formation of new long-term memories.

"Our finding expands our knowledge of the role of the hippocampus in learning," Rutishauser said.

"This is the first direct demonstration of the involvement of the human hippocampus in the learning of abstract knowledge and inference behavior. Many neurological conditions, including Alzheimer's disease, obsessive-compulsive disorder and schizophrenia, affect this brain region, and our finding could help explain the impaired decision-making we see in these patients."

More information: Ueli Rutishauser, Abstract representations emerge in human hippocampal neurons during inference, *Nature* (2024). DOI: 10.1038/s41586-024-07799-x.
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