Neuronal activity gives clues to working memory

June 7 2007

A newly discovered interplay of cells in one of the brain's memory centers sheds light on how you recall your grocery list, where you laid your keys, and a host of important but fleeting daily tasks.

Scientists at Weill Cornell Medical College say their experiments with common goldfish are uncovering the secrets of a form of short-term recall known as "working memory."

"We've now identified a mechanism that can organize the activity of groups of cells involved in this important form of recall," says lead researcher Dr. Emre Aksay, assistant professor of computational neuroscience in the HRH Prince Alwaleed Bin Talal Bin Abdulaziz Al-Saud Institute for Computational Biomedicine at Weill Cornell Medical College in New York City.

"Furthermore, because deficits in working memory are often a precursor of schizophrenia, drugs that target this mechanism might someday help fight that debilitating disease," he says.

The findings have been published in Nature Neuroscience.

Humans rely on their working memory every day to keep track of faces and names, tasks at school or in the workplace, and other important bits of information. "This process is distinct, neurologically speaking, from the storage and retrieval of longer-term memories," explains Dr. Aksay, who is also assistant professor of physiology and biophysics at Weill

Cornell.

Experts in labs around the world have developed theories as to how this process works. "Its basis lies in the ability of specific neurons to maintain a level of activity in the absence of input -- a persistent firing rate -- that's finely coordinated across related groups of cells," Dr. Aksay says.

But how do these brain cells communicate which each other to coordinate this activity"

To find out, Dr. Aksay, along with colleagues Dr. David Tank of Princeton University, and Dr. Mark Goldman of Wellesley College, turned to the common goldfish.

"It's really quite difficult to test the function of individual brain cells in primates and higher animals during behavior, but the goldfish's memory centers are much more accessible to research," Dr. Aksay explains. "We looked specifically at the fishes' oculomotor system -- the neural circuitry that directs the fish to shift its eyes left or right based on stimuli in the local environment." Because stimuli can be ever-changing and fleeting, the fish relies on its short-term memory to help guide these eye movements.

Two groups of cells are involved in this oculomotor memory, one in each half of the brain. Each group contains two types of neurons -- inhibitory cells and excitatory cells, and it is the inhibitory neurons that allow the two groups to interact. "In our experiments, we used pharmacologic means to interrupt either excitatory or inhibitory pathways, and then we watched what happened to persistent firing," Dr. Aksay says.

When the excitatory pathways were dampened, the persistence was impaired -- suggesting that excitation is essential to the sustained firing

that working memory requires.

"The real surprise came when we turned off many of the inhibitory pathways," Dr. Aksay says. In that case, persistent firing remained, but was often present at inappropriate times.

"It appears that the inhibitory cells are not key or even required to generate persistent firing," the researcher says. "Instead, they send a message from one group to the other that helps coordinate two sides: the role of inhibition in this system is to make sure that only one group is generating persistent activity at a given time. In this way, the goldfish doesn't get a mixed signal telling it to move its eyes in both directions at once."

This new finding has big implications for our understanding of the neural processes underlying working memory and the instantaneous decision-making that goes on based on that knowledge.

It might also have broader applications for psychiatric illness, Dr. Aksay notes.

"Many schizophrenic individuals, for example, show severe deficits in working memory, and children with working memory problems are at heightened risk of developing schizophrenia as adults," he says. Dysfunction in key inhibitory pathways that link brain cells has long been associated with these problems.

"These findings suggest that it is necessary to address not only deficits in excitatory pathways that lead to a lack of persistent firing but also dysfunction in inhibitory pathways that lead to a lack of coordination among groups of cells," Dr. Aksay explains. "This strategy could provide improved treatment options for people with schizophrenia."

Source: New York- Presbyterian Hospital/Weill Cornell Medical Center/Weill Cornell Medical College