Biomedicine

Carol Ezzell reports from New Orleans at the annual meeting of the Society for Neuroscience

Watching the remembering brain at work

Neuroscientists taking pictures of the human brain in action have confirmed for the first time that people use different brain areas to perform different types of memory tasks. They have also uncovered the first evidence in living brains that the hippocampus – a banana-shaped region deep within the brain – plays a key role in memory.

Last week, Larry R. Squire of the University of California, San Diego, and Marcus Raichle of Washington University Medical Center in St. Louis reported their observations of 18 volunteers performing word-completion tasks. Using an imaging technique called positron emission tomography (PET), Squire and Raichle found that the study participants used different areas of their brains to provide the endings of word fragments briefly flashed before them by the researchers. The brain areas used varied according to whether the volunteers were asked to provide the first word that came to mind, or to remember a word from a list they had scanned previously.

During the experiment, the researchers used PET scans to monitor changes in blood flow in the volunteers' brains. Areas of increased flow revealed the brain regions used during the various tasks.

When subjects drew upon their memories of previous lists to complete the fragment "mot-" as "motor," for example, the right sides of their hippocampi flooded with blood. This indicated that each subject used nerve cells there to remember the word, even though researchers usually attribute such verbal processing to the left brain. If the subjects were not searching their brains for a word they had already seen and instead gave the first word that came to them, blood flow did not increase significantly to either side of their hippocampi.

Interestingly, participants sometimes spontaneously recalled words from the lists even if they did not remember having seen the words before. During this phenomenon, which psychologists term "priming," PET scans revealed that the volunteers primarily used a brain area called the visual cortex.

"We are finding [in the living brain] that there is more than one kind of memory, and that separate neural regions are involved in each," Squire concludes.

Writer's cramp: Literally in your head

A new study suggests that the hand and arm spasms of chronic writer's cramp are not just psychosomatic symptoms, as some psychologists thought. Instead, this often debilitating disorder may result from abnormal functioning in part of the brain, report two neurologists from Washington University School of Medicine in St. Louis.

Lee W. Tempel and Joel S. Perlmutter used PET scans, which highlight areas of increased blood flow, to gauge brain activity in six people, aged 24 to 72, suffering from writer's cramp in the right hand. They compared these brain scans with those of an age-matched control group of eight people without writer's cramp. The researchers made the PET scans after stimulating the hands of both groups with a vibrator.

On average, the people with writer's cramp showed only two-thirds as much blood flow in the sensorimotor cortex – the brain region responsible for hand sensation and movement – compared with controls, Tempel and Perlmutter found.

Although the volunteers with writer's cramp experienced symptoms only in the right hand and arm, their PET scans revealed reduced blood flow in the sensorimotor cortex on both sides of the brain. "This was a surprise," Tempel says, adding that it might explain why writer's cramp sufferers who learn to write with their other hand eventually develop symptoms in that hand as well. Tempel says the results also suggest that writer's cramp is a form of focal dystonia, a brain disorder characterized by involuntary muscle spasms.

Receptor involved in brain injury found

Two independent research groups – one in Japan, the other in Kansas – have reported isolating two different forms of a specific nerve-cell receptor that may play a role in brain damage caused by stroke, epilepsy or head injury.

Both teams claim they have found in rats the receptor for glutamate, a neurotransmitter involved in nervous system development and memory storage. Brain cells appear to release glutamate in increased amounts after injury, and neurologists believe the so-called NMDA receptor (named for its ability to bind to the lab-made chemical N-methyl-D-aspartate) can kill nerve cells when overstimulated by glutamate.

Elias Michaelis of the University of Kansas in Lawrence says the NMDA receptor purified by his group can bind to both glutamate and NMDA. He and his colleagues found that they could block the binding of both chemicals by first adding antibodies that stick to the receptor. Further, they found that adding fibroblast growth factor – which also promotes nerve-cell growth – reduced the number of NMDA receptors on lab-cultured nerve cells, protecting them from death by overexcitation.

Michaelis and his colleagues published some of their results in the Nov. 7 NATURE. In the same issue, Shigetada Nakanishi and co-workers at Kyoto University reported purifying a candidate NMDA receptor with a very different structure.

Michaelis contends that both groups have uncovered NMDA receptors, but of different types. Neuroscientist Charles F. Stevens remains skeptical. Stevens, of the Salk Institute for Biological Studies in La Jolla, Calif., says he believes Nakanishi's team has found all or part of the real NMDA receptor, but he questions the Kansas researchers' finding because their candidate receptor bears no structural similarity to previously described receptors for other molecules.

Membrane molecule guides nerve growth

Nerve cells in the visual system of a developing embryo wire themselves properly by avoiding a specific molecule on the outer membranes of other nerve cells, new studies of chicks and fetal mice indicate.

The long, tail-like axons of nerve cells in the eye's retina plug into the correct sockets in a developing animal's optic tectum – the brain region that coordinates visual stimuli – by seeking out the lowest concentration of a chemical named "repulsive guiding molecule" (RGM), asserts Friedrich Bonhoeffer of the Max Planck Institute for Developmental Biology in Tubingen, Germany. Bonhoeffer reports that the axons of retinal nerve cells grown in the laboratory avoided high concentrations of membrane-bound RGM, preferring regions of a culture dish with low RGM levels.

He speculates that cells bearing RGM form one of two chemical gradients that sprouting retinal axons use to orient themselves. Bonhoeffer and his colleagues have used labeled antibodies to show that RGM levels increase steadily from the front to the back of an animal's optic tectum. He hypothesizes that a second, unidentified chemical may increase from the back to the front of the optic tectum, forming an opposite gradient.

By finding their optimal positions between these two gradients, retinal axons replicate in the optic tectum the same visual pattern that their cell bodies create in the retina itself, Bonhoeffer suggests. In this way, retinal cells convey a visual stimulus from a specific part of the retina to its corresponding part of the tectum, which allows an animal to tell where in its field of vision a given stimulus originated.

Bonhoeffer says it's too early to tell whether RGM might help reprogram the retinal axons of people with some vision disorders. But, he adds, "it would be interesting to see."