Neuroscience

Gabrielle Strobel reports from Washington, D.C., at the annual meeting of the Society for Neuroscience

Pugnacious mice lack serotonin receptor

Disturbances in serotonin's complex web of action have been blamed for many disorders, including migraines, depression, and schizophrenia. As researchers discover more types of receptor molecules for this neurotransmitter—14 are currently known—scientists are gaining greater insights into how a single transmitter can be involved in myriad functions.

Now, researchers say they have new evidence that serotonin's action on one of these receptors, called 5HT1b, helps dampen aggression. The absence of that receptor leads to increased aggressiveness in mice, reports René Hen of the Institut de Chimie Biologique in Strasbourg, France.

Hen and his colleagues created "knockout" mice, genetically engineered animals that lack the gene for the 5HT1b receptor. These animals don't produce the receptor, enabling researchers to study serotonin in new ways. Previous pharmacological studies often were confounded by the variety of similar serotonin receptors, explains Hen. This made it difficult to interpret exactly which receptors responded to any given drug.

"These knockout mice develop, feed, and mate normally, but when challenged in aggression tests, [they] show a clear-cut difference in their behavior," Hen says. When confronted with an intruder, the mutant mice attacked faster, more often, and more intensely than their normal cousins. Moreover, the mutant mice showed less anxiety under stress, Hen reports.

These results confirm earlier studies suggesting that this receptor is a molecular target through which serotonin controls aggression, he states.

"We know there is a link between aggression and decreased [concentrations of] serotonin in humans as well. Knocking out the serotonin receptor has the same effect as reducing serotonin [concentrations]," he says. There is no evidence suggesting that mutations in serotonin receptors are a major cause of abnormal aggression in humans, he adds.

Young brain sports marijuana receptors

The smoke from a marijuana cigarette may impart only a transient high to adults, but it could have more lasting effects on infants, warn neuroscientists at the University of British Columbia in Vancouver.

Max S. Cynader and Zheng Chen report that newborn kittens and monkeys have many more receptors for cannabinoid molecules—which give marijuana its mind-altering punch—in their immature brains than do adult animals. Using a radioactive label to localize such receptors, they found that numbers peak just when the brain is most malleable. Their study focused on the cortex, the area involved in learning and cognition.

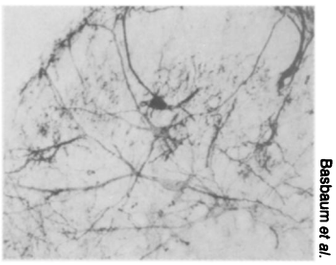
"There is a striking temporary concentration of these receptors in the visual cortex during a critical period, when the brain fine-tunes its structure and function," says Cynader. "Stimuli at that time determine how well [the brain] will work forever."

The receptors lie in the subplate, a transient scaffolding that underlies the developing cortex. "The subplate is particularly important, because the final architecture of the cortex is being assembled from this zone," Cynader says.

As the cortex takes shape, the subplate gradually degenerates and receptor numbers dwindle. In kittens, receptor numbers peak around 40 days after birth. The presence of the receptors in human infants has not been proved, but Cynader notes that the subplate is well developed at birth and performs functions similar to those in kittens and monkeys.

The pattern of receptor expression in animals suggests that endogenous cannabinoids may play a role in setting up the cortex. But the researchers are still puzzling over just what that role may be. To unravel the mystery, they will test how drugs that stimulate or block the receptors affect cortical development, Cynader explains.

Pain message travels via diffuse signal



Basbaum et al.

Antibody against substance P receptor reveals the whole morphology of nerve cells in rat spinal cord.

Have you ever experienced pain from an injured finger that slowly spread until your whole hand hurts? You may have "sensed" the diffusion of substance P, a neurotransmitter that helps relay pain messages to the brain, says Allan I. Basbaum.

Basbaum, a neuroscientist at the University of California, San Francisco, studied the distribution of substance P and its receptor molecules in the spinal cord. There, peripheral nerve fibers carrying pain messages release substance P onto receptors on so-called projection neurons, which then forward the unpleasant news along the spinal cord to the brain.

In many neural transmissions, nerve endings lie close to a tiny receptor-containing region of the target cell. Thus, the released transmitter only needs to cross a narrow gap to reach the receptor molecule. Substance P, however, works differently, Basbaum holds.

Labeling substance P receptors on spinal cord neurons with an antibody, Basbaum and his co-workers noticed that the receptors cover most of the surface of the nerve cells — in contrast to the tiny receptor patches in traditional neural communication. "The antibody reveals the entire morphology of the substance P neurons," Basbaum explains.

Moreover, the group saw receptor molecules inserted into a neuron membrane without any synapse nearby. Conversely, when labeling substance P itself, they found it in synapses next to membranes devoid of the substance P receptor.

"There is considerable mismatch between the distribution of substance P and this receptor," Basbaum says. "That mismatch is a strong anatomical indication that substance P generally acts by diffusing away from its site of release."

Though the effects of this diffusion remain largely unknown, Basbaum says some evidence suggests that it contributes to an oversensitivity to pain. As for the throbbing hand, he says, the initial pain sensation relates only to the original injury. But as the problem persists, more substance P gets released, diffuses farther away, and excites distant neurons that normally answer to stimuli from areas beyond the injury.

Different memories go different places

Someone shows you a phone number that you must remember. You will probably "say" the number in your head until you can write it down. This "inner-voice" mechanism of remembering a string of numbers takes place in a brain area separate from the one that stores the original visual image.

Using positron emission tomography (PET), Eraldo Paulesu and co-workers at Hammersmith Hospital in London, England, have confirmed earlier findings suggesting that different cortical regions harbor verbal and purely visual short-term memory.

When researchers asked volunteers to look at and remember a series of English letters, PET scans revealed activity in two small regions in the brain's verbal domain, the left hemisphere. In contrast, when presented with a string of Korean letters — verbally meaningless to people who don't speak Korean — a small area in the right hemisphere lit up, Paulesu says.