Oxytocin encourages maternal learning

Oxytocin is often called the 'bonding hormone' because it is involved in many social, sexual and maternal behaviors in mammals. Scientists have long documented the presence and effects of oxytocin during specific physiological conditions and behavioral responses, but little is known about the specific mechanisms by which this neuropeptide functions. Recently, however, researchers at New York University (NY) teased apart some of the physiology by which oxytocin promotes maternal behaviors in mice (*Nature* **520**, 499–504; 2015).

As with humans, parenthood for mice involves a learning curve, and virgin mice often do not exhibit the maternal behaviors that experienced mothers demonstrate. For example, experienced mothers often notice the distressed call of an isolated pup and will promptly retrieve the pup, whereas virgin mice generally fail to notice or retrieve isolated pups.

Researchers Robert Froemke and colleagues were able to elicit this behavior in virgin mice by housing them with experienced mothers and litters. This

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behavior was more common and arose sooner among virgins with artificially increased oxytocin levels compared with controls. "It was remarkable to watch how adding oxytocin shifted animal behavior, as mice that didn't know how to perform a social task could suddenly do it perfectly," said Bianca Marlin, the first author of the paper, in a press release.

The researchers also identified a key location where this behavioral response takes place. By pharmacologically inactivating only the left auditory cortex, they impaired the retrieval behavior in experienced maternal mice and, using antibody labels, they confirmed that the left auditory cortex contains more oxytocin receptors than the right.

This is not to say that oxytocin simply causes maternal retrieval behavior, however. When the researchers used antagonists to block oxytocin receptors in the left auditory cortex, experienced mothers continued exhibiting the retrieval behavior. It seemed, therefore, that oxytocin chiefly encourages females to notice the stimulus and learn the behavioral response, but it is not needed to summon that response each time.

"Oxytocin turns up the volume of social information processed in the brain," said Froemke, and his team confirmed this by monitoring individual neurons in the auditory cortex during oxytocin administration. These findings reveal how oxytocin participates in 'bonding' behaviors and demonstrate a general mechanism by which neuromodulators can promote attention and learning. Froemke considers this a strong example for future studies and intends to continue exploring the role of oxytocin in the brain.

Gregory D. Larsen

GENETIC PREDISPOSITION TO LIVER CIRRHOSIS

Chronic alcohol abuse can damage the liver, leading to fat accumulation, inflammation, fibrosis (as healthy tissue is replaced with scar tissue) and, eventually, cirrhosis, a late-stage disease in which fibrosis is extensive and irreversible. Not all cases of liver disease progress to cirrhosis, however. Findings of a new study suggest that specific genetic mutations might predispose some people to developing cirrhosis. The presence of these mutations could potentially be used to identify those individuals at greater risk. Chandrashekhar R. Gandhi (University of Cincinnati and Cincinnati Children's Hospital Medical Center, OH) led the team that carried out the study. "It will be a major breakthrough if there are reliable diagnostic markers and a known genetic disposition that puts some alcoholics at increased risk to develop irreversible cirrhosis," he said in a press release.

A lack of suitable animal models has limited study of liver cirrhosis. Gandhi's team developed a mouse model in which a protein called augmenter of liver regeneration (ALR) was depleted. ALR is required for survival of liver cells, and depletion of ALR led to the development of liver disease, including fatty liver, inflammation and fibrosis, in mice. The researchers hypothesized that deficiency of ALR might accelerate liver damage in response to stress such as alcohol abuse. To test that hypothesis, they provided ALR-deficient and wild-type mice with alcohol for a period of 4 weeks and then examined their livers. ALR-deficient mice had extensive liver fibrosis that resembled cirrhosis in people, whereas wild-type mice had accumulation of fat in the liver but did not develop fibrosis.

The researchers next investigated whether ALR was compromised in people. They searched for mutations in the gene encoding ALR and identified several single-nucleotide polymorphisms (SNPs) that had not been previously identified. Gandhi explained, "We postulate that some of these SNPs could be responsible for the predisposition to develop cirrhosis." To test this idea, the team intends to compare the frequency of the ALR SNPs in people with and without alcoholic liver disease. Should the SNPs turn out to occur more frequently in people with liver disease, they could be used to identify those at greater risk of developing cirrhosis, allowing earlier intervention to stop or slow the progression of disease.

The results were presented by Sudhir Kumar, a member of Gandhi's team, at the American Society for Investigative Pathology Annual Meeting, part of Experimental Biology 2015 (28 March 2015; Boston, MA).

Monica Harrington