Research identifies brain cells related to fear

July 11 2008

The National Institute of Mental Health estimates that in any given year, about
40 million adults (18 or older) will suffer from some form of anxiety disorder, including debilitating conditions such as phobias, panic disorders and post-traumatic stress disorder (PTSD). It is estimated that nearly 15 percent of U.S. soldiers returning from Iraq and Afghanistan develop PTSD, underscoring the urgency to develop better treatment strategies for anxiety disorders. These disorders can lead to myriad problems that hinder daily life – or ruin it altogether – such as drug abuse, alcoholism, marital problems, unemployment and suicide.

Functional imaging studies in combat veterans have revealed that the amygdala, a cerebral structure of the temporal lobe known to play a key role in fear and anxiety, is hyperactive in PTSD subjects.

Potentially paving the way for more effective treatments of anxiety disorders, a recent Nature report by Denis Paré, professor at the Center for Molecular and Behavioral Neuroscience at Rutgers University in Newark, has identified a critical component of the amygdala's neural network normally involved in the extinction, or elimination, of fear memories. Paré's laboratory studies the amygdala and how its activity impacts behavior. His research was published online by *Nature* on July 9, 2008 and is scheduled to appear in the print edition later in July.

Earlier research has revealed that in animals and humans, the amygdala is involved in the expression of innate fear responses, such as the fear of snakes, along with the formation of new fear memories as a result of

experience, such as learning to fear the sound of a siren that predicts an air raid.

In the laboratory, the circuits underlying learned fear are typically studied using an experimental paradigm called Pavlovian fear conditioning. In this research model on rats, a neutral stimulus such as the sound of a tone elicited a fear response in the rats after they heard it paired with an noxious or unpleasant stimulus, such as a shock to the feet. However, this conditioned fear response was diminished with repetition of the neutral stimulus in the absence of the noxious stimulus. This phenomenon is known as extinction. This approach is similar to that used to treat human phobias, where the subject is presented with the feared object in the absence of danger.

Behavioral studies have demonstrated, however, that extinction training does not completely abolish the initial fear memory, but rather leads to the formation of a new memory that inhibits conditioned fear responses at the level of the amygdala. As such, fear responses can be expressed again when the conditioned stimulus is presented in a context other than the one where extinction training took place.

For example, suppose a rat is trained for extinction in a grey box smelling of roses, and later hears the tone again in a different box, with a different smell and appearance. The rat will show no evidence of having been trained for extinction. The tone will evoke as much fear as if the rat had not been trained for extinction.

"Extinction memory will only be expressed if tested in the same environment where the extinction training occurred, implying that extinction does not erase the initial fear memory but only suppresses it in a context-specific manner," notes Paré.

Importantly, it has been found that people with anxiety disorders exhibit

an "extinction deficit," or a failure to "forget." However, until recently, the mechanisms of extinction have remained unknown.

As reported by *Nature*, Paré has found that clusters of amygdala cells, known as the intercalated (ITC) neurons, play a key role in extinction. His findings indicate that ITC cells inhibit amygdala outputs to the brain stem structures that generate fear responses. Indeed, Paré and his collaborators have shown that when ITC cells are destroyed with a targeted toxin in rats,
extinction memory is impeded, mimicking the behavior seen in PTSD.

Source: Rutgers University