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(Psychology and Neuroscience / Arts and Sciences)

Post-traumatic stress disorder (PTSD) is a major public health concern. The lifetime prevalence rate of PTSD is 8% in the general adult population, but the risk of PTSD is greatly increased to over 30% in military veterans who experience combat. The symptoms of PTSD include (a) exposure to a major trauma (b) re-experience of that trauma (c) avoidance of situations reminiscent of the original trauma, and (d) increased arousal and heightened startle behavior. Because these symptoms are chronic, patients with PTSD are also at risk for other disturbances such as anger and aggression, substance abuse, depression, and suicide.

Neuroimaging studies in humans implicate the over-activity in the amygdala in PTSD sufferers. The amygdala is an important limbic structure that has critical roles in fear and anxiety. The most widely-used animal model of PTSD is the fear conditioning model. Results of fear conditioning studies also implicate the critical role of the amygdala in PTSD. Medicinal compounds that are useful for treating PTSD in humans, such as the selective serotonin reuptake inhibitors (SSRIs), inhibit activity in the amygdala and disrupt normal fear conditioning. We have recently shown that decreasing serotonin in individually-housed rats increases fear-potentiated startle and increases neuronal activity in rat amygdala neurons, similar to that observed in human PTSD. The anticonvulsant phenytoin normalizes fear responses in PTSD rats. Further, we have shown that serotonin and glutamate receptors, and the hyperpolarization-activated current (IH) play an important role in excitatory mechanisms of the amygdala.

The overall purpose of this project is to test the hypothesis that neuronal hyperexcitability in the amygdala is associated with PTSD-like increased startle in rats. This hypothesis is tested by the following specific aims:

- Specific aim 1 is to investigate changes in amygdala neuronal membrane properties and excitatory neural input to the amygdala in control and PTSD rats using whole-cell voltage clamp.
- Specific aim 2 is to use voltage clamp recordings to compare the biophysical characteristics of IH in control and PTSD rats.
- Specific aim 3 is to correlate physiological changes in receptor and ion channel function with changes in protein expression in the amygdala using immunoblotting.

The results of these experiments will yield important new information about the functional role of excitability in the amygdala, and may lead to novel therapeutic targets for the treatment of PTSD.

Post-traumatic stress disorder (PTSD) is a major public health and military concern. The lifetime prevalence rate is 8% in adults and increases to over 30% in military veterans who experience combat. Both neuroimaging studies of PTSD in humans and fear-conditioning studies in rodents implicate the functional role of neuronal excitability in the amygdala in PTSD. We have recently shown that decreasing serotonin in individually-housed rats results in heightened fear conditioning and increased neuronal activity in rat amygdala neurons, similar to that observed in human PTSD, and that the anticonvulsant phenytoin can normalize fear responses in PTSD rats. Further, we have shown that serotonin and glutamate receptors, and the hyperpolarization-activated current (IH) play an important role in excitatory mechanisms of the amygdala.

The overall purpose of this project is to test the hypothesis that excessive neural activity in the amygdala is associated with PTSD-like increased startle in rats. This hypothesis is tested by the following specific aims: (1) investigate changes in amygdala neuronal membrane properties and excitatory neural input to the amygdala in control PTSD rats (2) compare the biophysical characteristics of IH in control and PTSD rats; and (3) correlate physiological changes in receptor and ion channel function with changes in protein expression in the amygdala. The results of these experiments will yield import