MedicalXpress

A better understanding of links between pain and anxiety reveals treatment opportunities

May 27 2015

Pain has both physical and emotional components. Anxiety is common in people suffering from chronic pain, and people with anxiety are more likely to suffer from chronic pain. Dr. Min Zhuo and his team at the University of Toronto have found the biological basis for this link in the connections between neurons in a brain region known as the anterior cingulate cortex (ACC). Better yet, they have identified a molecule that can reduce chronic pain-related anxiety. Dr. Zhuo's latest results were presented at the 9th Annual Canadian Neuroscience Meeting, on May 27th 2015 in Vancouver British Columbia.

"This study provides the first synaptic mechanisms to explain the multiple functions of ACC neurons in pathological conditions such as chronic pain" says Dr. Zhuo.

Chronic pain can be viewed as a learned memory: In the way that repetition of a piano piece enables you to learn it by facilitating transmission of the appropriate signals through your neurons, pain that persists can become chronic because your neurons become more efficient at transmitting pain signals. This strengthening of connections between neurons through repeated use is called Long Term Potentiation, or LTP. Previous work in the Zhuo lab has shown that in animal models of chronic pain, LTP occurs in a part of the brain called the Anterior Cingulate Cortex, or ACC, and that inhibiting LTP reduces chronic pain.

Interestingly, increased activity in the ACC is also seen in humans suffering from anxiety disorders and in animal models of anxiety.

However how LTP in the ACC differs in chronic pain and anxiety was not known, nor why the two would interact to result in more pain in anxiety sufferers, and more anxiety in pain sufferers.

The most common form of LTP is an increase in the number of receptors in neurons that are downstream of the synapse, which is the structure through which neurons communicate with each other. This is called post-LTP, because it is present after the synapse. Another less studied form of LTP occurs before the synapse, and involves the release of a larger amount of the signal from the neuron upstream. This is called pre-LTP. By using molecules that specifically block pre-LTP or post-LTP, Dr. Zhuo found a new form of pre-LTP that occurs in the ACC. Pre-LTP had previously only been seen in other brain regions.

"It is novel to demonstrate that both pre- and post-LTP can take place at the same cortical synapse!" says Dr. Zhuo. "As compared with post-LTP, pre-LTP employs a different set of molecules to induce and express the injury-related potentiation; it provides new opportunities for us to discover new drugs that may selectively control anxiety vs pain in future."

Dr. Zhuo's team also showed that pre and post-LTP were present in conditions of chronic pain, but that pre-LTP was only present when the pain became chronic, and not in cases of acute pain. They found that blocking pre-LTP reduced anxiety, and also that conditions that produced anxiety in animals (without pain) resulted in pre-LTP. These experiments led them to conclude that pre-LTP in neurons of the ACC mediates anxiety.

The discovery that two forms of LTP exist in the ACC, with pre-LTP associated with anxiety and post-LTP associated with pain, explains why these two conditions are linked, as both conditions result in an increase in transmission of the glutamate signal between neurons in the ACC.

Dr. Zhuo's team also found a novel molecule, called NB001, which can specifically block neuronal pre-LTP, and has powerful analgesic, or pain-reducing, effects in animal models of chronic pain. Further investigation of the signaling pathways of pre- and post-LTP should reveal new drug targets for treating pain and anxiety.

"This work is a result of a global collaboration with three different countries, each contributing valuable and novel research. This model of global collaboration is, is the future of excellence in scientific research" concludes Dr. Zhuo.

Provided by Canadian Association for Neuroscience