

Pain regulation and research: Decoding the brain's response to pain

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Professor Patrick Stroman from the Centre for Neuroscience Studies at Queen's University shares insights into his research on the neural basis of human pain and pain regulation, which is supported by functional magnetic resonance imaging

The research being carried out by Dr Patrick Stroman at Queen's University is focused on understanding the neural basis of human pain and how it is altered in chronic pain conditions. Carrying out this research in humans requires the use of a non-invasive neuroimaging method such as functional magnetic resonance imaging (fMRI). Over two decades, he has developed the necessary methods and has applied them to obtain new insights into neural signaling involved with pain.

Why we feel pain

Pain is a complex process that motivates us to avoid or reduce injury and to protect wounds while they heal; it is both a sensory and emotional response. The pain that we experience can depend on diverse factors such as our mood, past experiences, state of health, and attention focus.

Neural processes involved in nociception (neural signaling resulting from potentially noxious stimuli) and pain (the related unpleasant sensory and emotional experience) are now known to involve all levels of the central nervous system: the brain, brainstem, and spinal cord. Research in the 1960s showed that receptors in our skin that respond to noxious stimuli send neural signals to our spinal cord, where they are processed and relayed up to our brainstem and then our brain.⁽¹⁾

These signals are also regulated (turned up or down) by descending signals from the brain and brainstem to the spinal cord. This feedback changes our pain depending on our situation (such as being afraid, in danger, relaxed, or safe).

Functional magnetic resonance imaging



Figure 1: Example of functional MRI data spanning the brainstem and spinal cord using methods developed by P. Stroman.

The first application of functional MRI for studying activity involved in pain responses in the brain was reported only a few years after fMRI was first developed.⁽²⁾ However, the MRI methods that were developed to provide images in a rapid sequence to observe signal changes in time are susceptible to errors in the vicinity of bone or air, such as low in the skull and near the spine. In order to carry out fMRI in the brainstem and spinal cord, Dr Stroman modified the methods to improve the image quality at the cost of speed.⁽³⁾

It was also necessary to adapt data analysis methods, and as such, Dr Stroman developed the 'Pantheon' analysis software package.^(4,5) There is now a large body of evidence demonstrating the ability to detect MRI signal variations related to neural activity in the brainstem and spinal cord.⁽⁶⁾

Pain regulation in healthy people

Evidence of fMRI's sensitivity in detecting influences on nociception and pain has come from several studies with surprising results. The MRI signal responses were observed to depend on the timing and temperature of heat stimuli, as expected.

However, the signals also varied in time when stimuli were not applied. It was determined that these signal variations could not be attributed to errors but demonstrated changes in neural activity in response to a person being told to expect to feel a noxious hot stimulus a short time later.^(7,8) The results showed that neural signaling contributing to how a person feels pain is a continuous process in the brainstem and spinal cord.

A person's state of pain sensitivity is constantly being adjusted in relation to their perceived environment, mood, attention focus, expectations, etc., even while they are not feeling pain. The same neural signaling pathways involved with continuous regulation of spinal cord neurons and feedback to brainstem regions are expected to play an important role in chronic pain conditions.

Cognitive and emotional influences on pain

The influence of cognitive and emotional processes on nociception and pain has been investigated in several studies, including a recent study of the effects of listening to music.⁽⁹⁾ This study involved fMRI of the lower brain and brainstem regions while participants listened to their choice of music while feeling a noxious heat stimulus on their hand. Participants rated their pain slightly (~14%) lower while listening to music, compared to not listening to music, and fMRI results showed differences in neural activity.

The regions identified as being influenced by listening to music included brain regions and brainstem regions known to contribute to pain regulation. The results showed that the influence of listening to music on pain perception likely involves cognition, emotion, memory, and salience. This provided new insights into human pain regulation.

Chronic pain conditions

The developments described above have enabled studies of people with fibromyalgia syndrome (FM) in collaboration with Dr Roland Staud at the University of Florida (Gainesville) and with provoked vestibulodynia (PVD) in collaboration with Dr Caroline Pukall at Queen's University. These studies consistently demonstrated heightened heat pain sensitivity in people with FM and altered nociceptive processing in the brainstem and spinal cord regions.⁽¹⁰⁻¹²⁾

Overall, the results provide evidence of altered descending pain regulation in FM, and that altered arousal/stress responses and autonomic regulation may influence the descending regulation. The studies of PVD⁽¹³⁾ and comparisons with FM⁽¹⁴⁾ showed differences in neural signaling compared to HC participants and between FM and PVD. Whereas PVD appeared to involve altered signaling related to arousal and salience, FM seemed to have distinct differences in the autonomic influence on pain.

The methods that have been developed can therefore reveal specific aspects of the neural basis of altered pain in FM, as well as differences between the pain conditions of FM and PVD.

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