Imaging Pain

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KEYWORDS

• Chronic pain • Neuroimaging • MRI • Resting-state networks • MVPA
• Brain-based therapies

KEY POINTS

- No single region within the central nervous system is responsible for chronic pain; altered brain structure and function occurs across many regions of the brain, brainstem, and spinal cord.
- Resting-state functional MRI (fMRI) has revealed multiregional alterations in brain function within various resting-state networks, including the salience, executive control, and default-mode networks.
- Multivariate pattern analysis (MVPA) is a new and powerful technology that allows for a whole-brain approach to identify altered brain structure and function in chronic pain. MVPA may ultimately help to develop brain-based objective biomarkers of pain and achieve the goal of precision pain management.
- Researchers are now using neuroimaging to identify brain targets for novel and effective treatments for chronic pain, such as transcranial magnetic stimulation, real-time fMRI, and other neuroimaging-based therapies.

INTRODUCTION

Chronic pain affects more than 100 million adults and accounts for approximately $600 billion annually in medical costs and lost productivity.[1]

The complex neural mechanisms that occur to amplify and maintain chronic pain are poorly understood. Neuroimaging pain research holds great promise for the development of new and effective treatments through advancing our understanding of these complex mechanisms.

Neuroimaging research findings show that chronic pain is different from acute pain. Chronic pain can become a disease in its own right that occurs following initial injury, which then progresses to a chronic state within the central nervous system (CNS). Although other body systems are also involved in the initiation and maintenance of

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chronic pain,[2] neuroimaging has allowed for increased understanding of how the CNS is involved in chronic pain.

Types of neuroimaging used to study chronic pain
- PET
- Electroencephalography (EEG)
- Magnetoencephalography (MEG)
- Single-photon emission computed tomography (SPECT/CT)
- MRI

Examples of chronic pain conditions studied using neuroimaging
- Chronic low back pain (cLBP)[3]
- Fibromyalgia (FM)[4]
- Osteoarthritis (OA)[5]
- Complex regional pain syndrome (CRPS)[6]
- Phantom limb pain, chronic migraine[7]
- Chronic pelvic pain (CPP)[8,9]
- Peripheral neuropathy (PN)[10]

In addition to advancing the study of chronic pain, the evolution of neuroimaging technology has opened a window to the brain that allows us a more complete understanding of the basic physiologic and pathophysiologic mechanisms of pain signal processing and the related subjective experience of pain itself.

Examples of neuroimaging research of pain processing
- Acute pain in healthy volunteers[11]
- Acute pain in animals[12]
- Animal models of chronic pain[13]

Several experiential factors influence the experience of pain. Neuroimaging has allowed for the study of how these factors interact with and impact pain perception by studying related changes in brain activity.

Examples of pain modulatory factors studied using neuroimaging
- Attention[14]
- Anticipation[15]
- Empathy[16]
- Placebo[17]
- Effects of meditation[18]
- Fear/anxiety[19]
- Reward[20]

The present review focuses specifically on the use of neuroimaging, specifically the most widely used neuroimaging technology of MRI, and observed CNS changes in various chronic pain conditions (**Box 1**) As used here in this review, we refer to "neuroimaging" as meaning imaging of the spinal cord, brainstem, and brain. Neuroimaging of peripheral nerves is beyond the scope of this review.

ANATOMIC AND FUNCTIONAL SUBSTRATES

Basic Sequence of Mechanisms and Structures Involved in Pain Processing

1. Noxious stimuli trigger signals in the peripheral nerves. Peripheral nerves that relay nociceptive information include the following:
   - A-delta nerve fibers: These fibers transmit "first-pain" signals, the pricking, sharp sensations felt immediately after a stimulus.