



- **FACT SHEET No. 17**

Visualization of Joint Pain and the Contribution From Widespread Pain and Hypersensitivity

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The high prevalence of joint pain directly affects the quality of daily lives of people worldwide. Degenerative joint disease (osteoarthritis) is a common cause of chronic pain, especially among the elderly. Cartilage destruction and changed biomechanical loading, and its associated synovial inflammation/periarticular muscular defense, are considered to account mainly for the underlying mechanisms of joint pain. However, recent research shows that certain neurophysiological mechanisms play an important role in the development of chronic joint pain.

To proceed with diagnosis and treatment of joint pain, diagnostic imaging is performed in clinical settings, such as those specializing in orthopedics and rheumatology, along with physical findings and hematologic examinations. The intensity of a patient's pain, however, is rarely evaluated through traditional radiological assessments. One large epidemiologic study revealed that approximately only one-third of cases that tested radiologically positive to knee osteoarthritis and lumbar spondylosis displayed pain symptoms[1, 2].

In preclinical studies of joint pathologies, abnormal neuronal firings from primary afferents have been recorded after noxious flexion and extension joint stress procedures[3]. Similar patterns of neuronal firings have been detected from inflamed joints and immobilized joints[4]. Moreover, spinal dorsal horn neuronal recordings reveal an enlargement of the neuronal receptive field and a lowered threshold to



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cutaneous mechanical stimuli after acute and chronic joint inflammation[5, 6], and these changes in neuronal properties were reported after joint contracture as well[7].

Under these conditions, spinal glia cell activation, several types of cytokine, and neurotransmitter releases are observed. Concomitantly, the pain behaviors show a lower pain threshold also on the side contralateral to the injury. Similar observations have been made in humans[8].

As joint pain is an “unpleasant sensation and emotion experienced in the brain,” various functional brain imaging studies have been conducted and show functional changes in patients with joint pain.

In an fMRI study, pressure stimulation applied to the painful site of OA knees showed activity in bilateral thalamus, secondary somatosensory cortex (SII), insula, supplementary motor area (SMA), anterior cingulate (ACC), and medial frontal gyrus as well as unilaterally in the right putamen and left amygdala[9]. This activity pattern is markedly different from pain-related activity observed in chronic back-pain patients but similar to acute pain activity in normal subjects. This suggests that manifestations of sensitization in joint pain take place through the entire nervous system.

Recently, central widespread pain and hypersensitivity have become recognized as important concepts for understanding chronic joint pain. Brain connection network analysis in patients by using the resting state fMRI method has revealed that the Default Mode Network (a set brain region involved in monitoring the internal environment for the detection of salient events) shows greater connectivity to the insular cortex, a brain region known to process evoked pain in individuals suffering from chronic pain conditions such as fibromyalgia[10]. In addition, a functional alteration of the nucleus accumbens and dysfunction of the pain inhibitory system (periaqueductal gray, etc.) results in failure to regulate pain and is a contributor to pain chronicity[11]. Since fibromyalgia is often accompanies poly-arthritis, it is important to be aware of the underlying central widespread pain and hypersensitivity during therapeutic management.

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