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Anatomical and Physiological Basis of Chronic Pain Mechanisms

Nurul Aisyah Rahman*

Department of Medical Physiology, Penang Health Sciences University, George Town, Penang, Malaysia

DESCRIPTION

Chronic pain is a major global health concern that affects hundreds of millions of individuals and represents one of the leading causes of disability and reduced quality of life. Unlike acute pain, which serves as a protective physiological response to tissue injury, chronic pain persists beyond the normal healing period and often becomes a disease in its own right. Advances in anatomy, neurophysiology, molecular biology and pain neuroscience have substantially improved our understanding of the complex mechanisms underlying chronic pain. Rather than resulting solely from damaged tissues, chronic pain is now recognized as a multidimensional condition involving intricate interactions among peripheral nerves, the spinal cord, the brain, immune cells and the musculoskeletal system. These emerging insights are reshaping both pain research and clinical management. The anatomical foundation of pain begins with specialized sensory receptors known as nociceptors. These free nerve endings are widely distributed throughout the skin, muscles, joints, fascia, periosteum and visceral organs. Nociceptors detect potentially harmful mechanical, thermal, or chemical stimuli and transmit signals through A δ and C nerve fibers to the dorsal horn of the spinal cord. Under normal physiological conditions, this pathway enables rapid detection of injury and initiates protective reflexes. However, persistent activation of nociceptors following tissue damage or inflammation can alter neural function, contributing to the transition from acute to chronic pain.

One of the most significant discoveries in pain physiology is the concept of peripheral sensitization. Following injury, inflammatory mediators such as prostaglandins, bradykinin, cytokines and nerve growth factor reduce the activation threshold of nociceptors, making them increasingly responsive to normally non painful stimuli. This heightened sensitivity contributes to hyperalgesia and allodynia, common features of chronic pain disorders. Anatomically, changes also occur within peripheral nerves, including altered ion channel expression and abnormal nerve sprouting, further amplifying pain transmission. Central sensitization represents another fundamental mechanism in chronic pain. Repeated nociceptive input induces functional and structural changes within neurons of the spinal dorsal horn and higher pain processing centers. Increased excitatory neurotransmission, reduced inhibitory signalling and enhanced synaptic plasticity result in exaggerated responses to sensory stimuli. Consequently, pain may persist even after the original tissue injury has healed. From my perspective, central sensitization has fundamentally transformed pain research by demonstrating that chronic pain often reflects maladaptive changes within the nervous system rather than ongoing peripheral damage alone. Modern neuroimaging studies have further expanded understanding of the anatomical basis of chronic pain. Functional Magnetic Resonance Imaging (fMRI), Positron Emission Tomography (PET) and Diffusion Tensor Imaging (DTI) reveal altered activity and connectivity within multiple brain regions, including the somatosensory cortex, anterior cingulate cortex, insula, prefrontal cortex, amygdala, thalamus and hippocampus. These interconnected regions collectively form the "pain matrix," integrating sensory, emotional, cognitive and behavioral aspects of pain perception. Chronic pain is therefore increasingly viewed as a disorder of neural network dysfunction rather than isolated sensory processing.

The musculoskeletal system also plays a significant role in chronic pain physiology. Altered biomechanics, muscle weakness, fascial dysfunction, joint degeneration and connective tissue remodeling contribute to persistent nociceptive input. Conversely, chronic pain itself may induce muscle inhibition, reduced mobility and compensatory movement patterns that perpetuate tissue stress and functional impairment. This reciprocal relationship between anatomy and physiology highlights the importance of addressing both structural abnormalities and neural mechanisms during rehabilitation. Another emerging area involves neuroimmune interactions. Immune cells, including macrophages, mast cells, microglia and astrocytes, actively participate in pain modulation by releasing cytokines, chemokines and growth factors that influence neuronal excitability.

Correspondence to: Nurul Aisyah Rahman, Department of Medical Physiology, Penang Health Sciences University, George Town, Penang, Malaysia, E-mail: nurul.rahman@phsu.my

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