Introduction

Chronic pain is a debilitating, complex condition that is an increasingly significant public health concern particularly in countries with an aging population. The burden on society in terms of loss of productivity and health-care costs due to chronic pain provides only a partial measure of its toll on the quality of life of its sufferers. A variety of diseases can lead to chronic pain states, including chronic inflammatory diseases (e.g. rheumatoid and osteoarthritis, pancreatitis), neuropathies resulting from injury to peripheral nerves (e.g. physical trauma, tumors), infections (herpes zoster) or disease (diabetes), as well as injuries within the central nervous system including multiple sclerosis and spinal cord injury. The cause of some chronic pain syndromes such as temporal mandibular joint pain, and other painful conditions such as fibromyalgia and migraine, remain to be established. Therapeutic interventions in other disease states, such as chemotherapy or surgical procedures may induce pain and, paradoxically, even the use of opioid analgesics can result in unexpected pain that is often different in quality and location from the pain associated with the original complaint.

Unlike acute pain, chronic pain serves no protective function and does not offer survival advantage to the organism. On the contrary, because many chronic pain syndromes are intractable or very difficult to manage within the tolerability of side effects associated with currently available therapeutics, chronic pain may actually contribute to morbidity and mortality and can itself be considered a disease. The mechanisms that promote chronic pain states associated with different pathologies are like-

ly to be diverse, and while current therapeutics such as COX inhibitors, opiates, sodium channel blockers, calcium channel blockers, and interventions which block the actions of TNF-alpha offer insight into some of these mechanisms, clearly much research is needed in order to establish better targets for effective therapeutic interventions and perhaps ultimately leading to approaches which can produce disease modification including, for example, gene therapy.

This issue of *NeuroSignals* has been compiled to provide expert opinion on selected topics within a very diverse field related to chronic pain. The first three reviews focus on chronic inflammatory pain and illustrate the importance of both peripheral and spinal mechanisms, and the contributions of glial function and the immune system to these pain states. The supra-spinal/spinal modulation of sensory processing, and possible alterations in this complex ascending/descending relay that may contribute to chronic pain states is discussed in the review by Suzuki and Dickenson. The supra-spinal/spinal plasticity in a central pain syndrome due to spinal cord injury is discussed by Yeziarski. The final review by King and colleagues focuses on the potential mechanisms that underlie chronic pain due to sustained opioid exposure, and the possible relationship between such paradoxical pain states and the development of opioid tolerance. We hope that these reviews can give a sense of the complex issues related to mechanisms underlying chronic pain states and some of the current thinking that can eventually lead to improved therapy.

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