Lifelong Learning

CPD ARTICLE NUMBER TWO

Is Chronic Pain Simply Persisting Acute Pain?

The idea that 'pain is pain' and that chronic pain is simply acute pain continuing too long is archaic and wrong.

Traditionally the word pain was used as an all inclusive, blanket term. Pain was often described as being protective, serving as a warning that something else is wrong – a symptom of another underlying condition. This pain should, and usually does, resolve once the underlying condition has been dealt with and healed. In modern parlance we'd use the term 'acute pain' to describe this condition.

Sometimes this does not happen and the pain persists unusually long after healing or recovery. The pain is then called 'chronic' if, by definition, it persists more than three months. This time-based definition is totally arbitrary and unreasonable. Sometimes chronic pain is present before the three months have elapsed (eg, de-afferrentation pain – see below) and sometimes the mechanism for chronic pain is present from the outset without any time having elapsed.

This is because chronic pain is not simply a symptom of another underlying condition or pathology. Chronic pain is a medical entity; a clinical condition and a pathology in itself - not simply persisting acute pain. Chronic pain is **not** protective - it **does not** serve as a warning of an underlying condition because often there is **no underlying condition**. Chronic pain, like any other disease, should rather be considered as destructive, usually serving no purpose at all. It progressively damages first the body and then the psyche and lives of people afflicted with it.

Neuropathic pain is often used as a synonym for chronic pain, but neuropathic pain is only one type of chronic pain.

Pain processing

Chronic pain is a condition of *altered pain processing* due to physical changes mostly in the spinal cord, and more specifically the dorsal horn grey matter in the spinal cord. Altered processing can also take place in the brain, usually after brain injury or stroke.

Pain and other sensory stimuli enter the spinal cord via the dorsal nerve root and are processed in the dorsal or posterior spinal cord grey matter. This processing is quite complex. The pain stimuli are then transmitted up the cord to a number of pain centres in the brain.

In chronic pain, the changes that take place in the dorsal horn causing facilitated pain processing are termed 'central sensitisation' or, 'central wind-up'. This leads to increased perception of pain, facilitated transmission of pain signals to the brain or the origination of new pain impulses in the dorsal horn which are then transmitted to the brain.

If unresolved, central sensitisation becomes increasingly difficult to reverse and can eventually become permanent. Chronic pain and central sensitisation must, therefore, be diagnosed early and *appropriate* therapy initiated as soon as possible.

Central sensitisation origins

Central sensitisation is the reason chronic pain does not usually respond well, if at all, to normal analgesics and anti-inflammatory drugs (including epidural steroids) and sometime not even to opiates. Chronic pain requires treatment with a pharmacological arsenal different to that used for acute pain and often requires specific pain interventions to manage it or to reverse it. This will be the topic of a future article.

Central sensitisation can be either nociceptive or neuropathic in origin.

Nociceptive central sensitisation

Nociceptive pain is pain that arises due to stimulation of pain receptors (the nociceptors) in the tissues. Constant nociceptive input into the dorsal horn is termed 'afferent barrage'. It is a constant hammering on the dorsal horn system by incoming pain impulses from the periphery. Depending on its intensity and duration, this afferent barrage, causes central sensitisation of varying degrees.

Key points

- Chronic pain is not simply acute pain persisting for too long, but has a pathology of its own.
- Normal analgesics, NSAIDs, etc. have limited or no effect on chronic pain.
- A completely different group of pharmacological agents as well as interventions need to be applied to provide relief from chronic pain.

About the author

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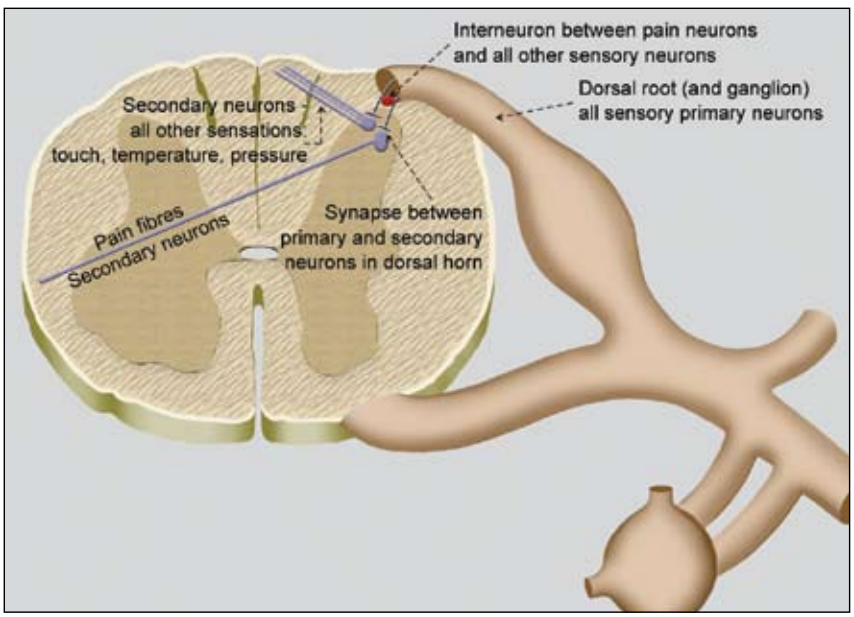


Figure. Schematic of anatomy of the dorsal root of the spinal cord.

Nociceptive pain causes central sensitisation in two main ways.

Chronic afferent barrage

A chronic condition eg, arthritis, can cause *chronic afferent barrage* resulting in central sensitisation. This means that chronic nociceptive conditions like arthritis have both a nociceptive element (destruction of the joint), and a central sensitisation component. This, for example, is why osteoarthritis pain in the knee responds so well to duloxetine, an antidepressant, due to its effect on the dorsal horn.

Acute afferent barrage

Acute pain that is not adequately treated also causes an afferent barrage, the intensity of which depends on the acute underlying problem. Intense untreated acute pain like post operative pain can cause central sensitisation in the dorsal horn very quickly – in a matter of hours to days.

Neuropathic central sensitisation

Neuropathic pain that may arise in sick or injured nerves may also cause central sensitisation.

Nerve injury

Nerve injury (from accidents as well as surgery) may cause central sensitisation. This type of chronic pain is called CRPS – Chronic Regional Pain Syndrome and has two subclassifications. In Type 1 CRPS a nerve injury is suspected but not immediately apparent whereas in Type 2 the nerve injury is apparent. Otherwise, clinically the types are identical.

Severed nerves (de-afferrentation pain - loss of all afferent input into the dorsal horn)

- **In phantom pain** the nerve to the area is cut through causing changes in the dorsal horn of the corresponding level. With loss of all afferent input, the small interneurons are never activated and so never inhibit pain impulses. This means that the 'pain gate' is constantly open (see below). Pain impulses then originate in the dorsal horn in the nerve that originally arose in the amputated area. These impulses are then transmitted to the brain which perceives the pain impulse as originating at the amputated body part.
- **Anaesthetica Dolorosa** occurs when nerves are severed for reasons other than amputation. This leads to an area of no feeling (anaesthetica) because all the afferents have been severed, but which is painful due to the central sensitisation as in phantom pain.

Nerve pathology (neuropathy)

There are many causes and types of neuropathy but most important is peripheral neuropathy. If the pain fibres are sick this may lead to afferent barrage and central sensitisation.

Central sensitisation in Chronic Pain

In chronic pain, treating a peripheral condition is not very effective without also addressing and treating the central sensitisation.

Mechanisms of sensatisation

Central sensitisation is mediated by two main mechanisms:

- Sensitisation and activation of NMDA receptors.
- Inhibition or death of the interneurons (Figure 1 - Opening the pain gate).

NMDA receptors

NMDA receptors are a group of ionotopic glutamate receptors that occur in both peripheral tissue and the central nervous system. They occur both pre- and post synaptically and are responsible for excitatory synaptic transmission. They play an important role in pain transmission and sensitisation. They also play a role in neuroplasticity and neuro-degeneration (apoptosis).

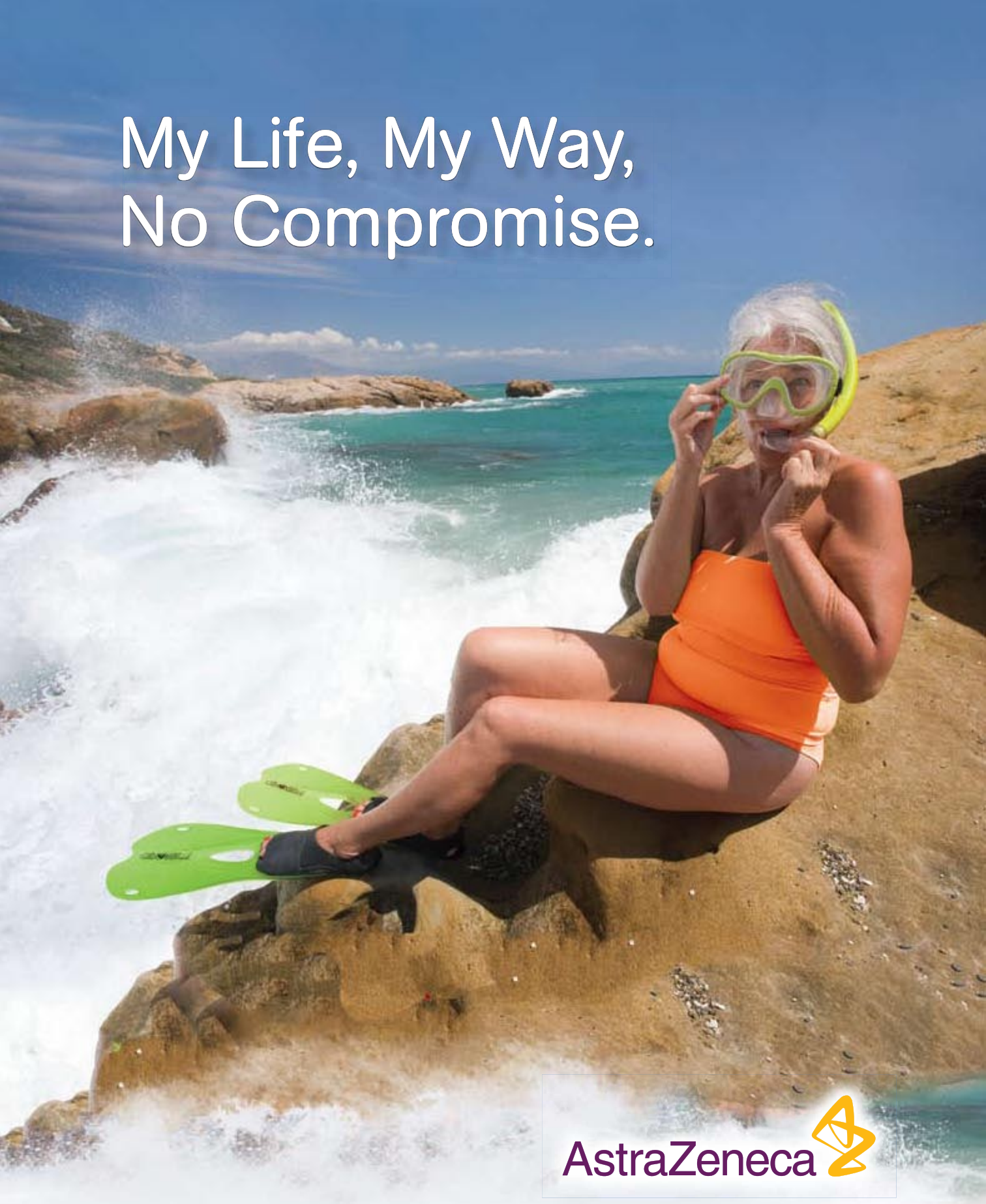
Activation of NMDA receptors after tissue injury and inflammation enables facilitated processing in the spinal cord or central sensitisation.

In inflammation, the number of NMDA receptors on peripheral nerve fibres increases as do those in the dorsal horn.

The nature of the NMDA receptors, their role in central sensitisation and drugs that can be used to block the NMDA receptors will be the subject of a future article.

Interneurons – the 'gates' (Figures 1 & 2)

The interneurons are in effect the 'gate' in the 'gate' theory of pain. They are small neurons connecting the neurons of all other sensations and the neurons of pain. Activity in the neurons of all the other sensations causes activity in the interneurons which in turn inhibit transmission in the pain neurons. This is why rubbing or stroking a hurt area reduces pain in the area.



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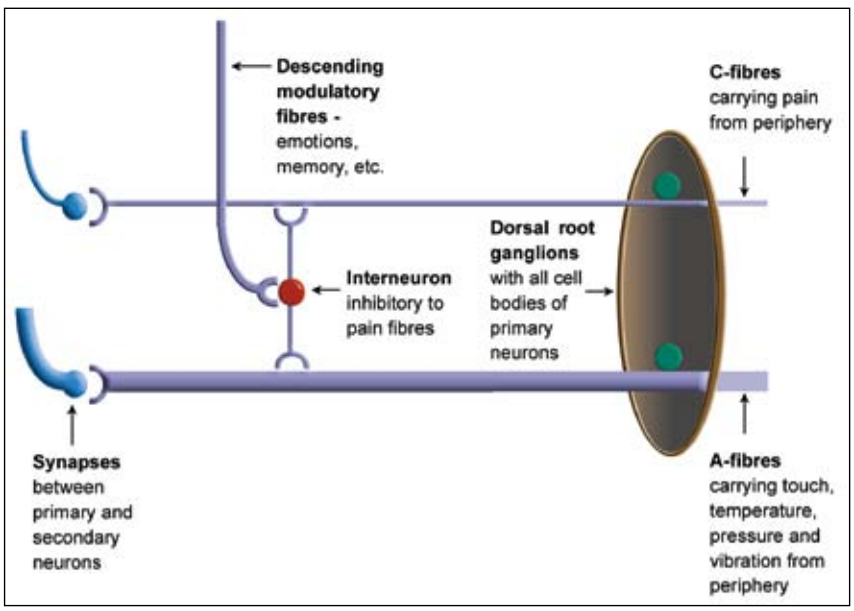

Figure 2. Schematic of the neural connections in the dorsal horn of the spinal cord.

Modulating fibres descending from the higher centres also have an effect on the interneurons. They can cause activity in the interneurons and so inhibit the pain neurons, or they can inhibit the interneurons and facilitate pain. This is why emotions, experience and memory have a inhibitory or facilitatory effect on pain by closing or opening the gate. This effect of emotions and the psyche on the pain gate is what makes successful treating of chronic pain often very difficult and why psychotherapy is an important part of chronic pain therapy.

If the interneurons are the gate, then if they are absent or non-functional, the gate to transmission of pain is open and pain flows freely from the periphery, through the open gate to the brain with increased perception of pain.

This is part of central sensitisation. Intense and prolonged afferent barrage causes the death of the interneurons leaving the gate to pain wide open. Should the barrage continue for a length of time, the inhibitory interneurons can even be replaced by facilitatory neurons, opening the gate even further.

This aspect of chronic pain condition is very difficult to treat as it is almost impossible to re-grow the interneurons.

Strategies for prevention of interneuron death and thus preventing chronic pain will be the subject of a future article.

Summary

From the above we see that chronic pain is **not** simply acute pain persisting for too long, but has a pathology of its own. It is then easily understood why normal analgesics, NSAIDs, etc. have limited or no effect on chronic pain. A whole different group of pharmacological agents as well as interventions need to be applied to provide relief for chronic pain.

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