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# Section B: Extended Study

# SECTION 1: PAIN AND SENSATION

[**www.answers.com/topic/pain-1**](http://www.answers.com/topic/pain-1)

[**http://en.wikipedia.org/wiki/Gate\_control\_theory\_of\_pain#Physiology**](http://en.wikipedia.org/wiki/Gate_control_theory_of_pain#Physiology)

[**http://www.chiro.org/research/ABSTRACTS/Spinal\_Pain\_Syndromes.shtml**](http://www.chiro.org/research/ABSTRACTS/Spinal_Pain_Syndromes.shtml)

[**http://en.wikipedia.org/wiki/Referred\_pain**](http://en.wikipedia.org/wiki/Referred_pain)

[**http://www.iasp-pain.org//AM/Template.cfm?Section=Home**](http://www.iasp-pain.org//AM/Template.cfm?Section=Home)

[**http://www.ahs.uwaterloo.ca/~ranney/painanat.html**](http://www.ahs.uwaterloo.ca/~ranney/painanat.html)

## Pre-Study Questions

**Answer these question as best you can before beginning the section and then re-answer them when finished. This will give you an idea of the degree of improvement in you knowledge.**

1. Define pain
2. Describe the nociceptor
3. Were are nociceptors found
4. Describe the two parent nerves to the nociceptors
5. What is the result of the parent nerves different structures
6. Discuss fast pain and slow pain
7. Discuss the pain pathways from the nociceptor to the sensory gyrus
8. What stimuli excite nociceptors
9. Which chemicals excite nociceptors
10. What is hypersensitization and what is its mechanism of action
11. Discuss the articular receptors
12. Discuss the various methods of pain modulation
13. Discuss the role of endorphins in pain modulation
14. Discuss the gate control theory of pain modulation
15. Discuss how pain is processed in early, middle and late life

## Pain

According to the International Association for the Study of Pain, pain is:

*An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.* ***Note:*** *The inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment. Pain is always subjective. Each individual learns the application of the word through experiences related to injury in early life. Biologists recognize that those stimuli, which cause pain, are liable to damage tissue. Accordingly, pain is that experience we associate with actual or potential tissue damage. It is unquestionably a sensation in a part or parts of the body, but it is also always unpleasant and therefore also an emotional experience. Experiences, which resemble pain but are not unpleasant, e.g., pricking, should not be called pain. Unpleasant abnormal experiences (dysesthesias) may also be pain but are not necessarily so because, subjectively, they may not have the usual sensory qualities of pain.*

***“We all experience pain, but scientifically what is it? Most of us think of pain as an unpleasant sensation that originates in traumatized tissues and warns of injury, but it also has emotional qualities. Ancient philosophers mostly considered pain an emotion. Aristotle, for example, called it a passion of the soul. A contemporary writer described pain's qualities as including extreme aversiveness, an ability to annihilate complex thoughts and other feelings, an ability to destroy language, and a strong resistance to objectification (Scarry, 1985). Her perspective resonates with the lessons of everyday life: while pain has sensory features and lends itself to sensory description, it is above all else a powerful and demanding feeling state. Put more simply, pain is in part an emotion. The standard definition for pain, as developed by the International Association for the Study of Pain is as follows: "An unpleasant sensory and emotional experience normally associated with tissue damage or described in terms of such damage."***

***From the viewpoint of scientific inquiry, pain poses a significant challenge on several fronts. First, we need to view it multidimensionally. Our tools allow us to study it intensively and effectively at the level of sensory neurophysiology, but we are stymied as soon as we attempt to address it as an emotion (the central neurophysiology of emotion is formidably complex and still a frontier). Consequently, we risk developing an unbalanced knowledge base, filled with detailed information on the sensory neurophysiology of pain but void of content about pain's emotional nature. Second, pain is by definition a phenomenon of consciousness. It does not exist outside of the realm of awareness: it is not an observable phenomenon, it has no objective markers and it defies objective measurement. Our methods for measuring pain subjectively (recording reports of its quality, intensity, time course, and personal meaning) are primitive at best. Finally, we face a significant challenge in reconciling the progress in basic science areas with clinical application that improves pain control. For example, over the past two decades we have witnessed the publication of thousands of papers on endorphins along with elegant theory and speculation about the role of endorphins in pain and pain relief, but this has not led to a single drug or other product that improves the care of patients with pain. In this and many other areas, a gap exists between what we think we know and what we can achieve on the battlefield of clinical care. The answer, I suspect, lies with developing a truly multidisciplinary basic science and with integrating pain research with emerging research efforts in the fields of emotion and consciousness.***

***When one deals with pain as a clinical problem, subtle issues of definition take on enormous importance. Many physicians still hold the anachronistic and overly simplistic view that pain is merely an aversive sensation (a sensory problem). The usual therapeutic solution to an aversive sensation is to turn it off in one of the following ways: remove the origin of the noxious signaling, gate signal transmission from the peripheral tissues with opioid or other drugs, prevent such transmission with temporary nerve blocks, or introduce destructive lesions within the nervous system that prevent such transmission. This level of understanding, while not all wrong, is clearly incomplete. Pain proves notoriously unresponsive to conventional therapies that target its putative cause, can appear and persist without evidence of tissue trauma, and above all else it envelops the whole of the person who experiences it, interfering with normal living, functional capability and sleep. Recognizing this, Chapman and Stillman (1996) defined pathological pain as "severe persisting pain or moderate pain of long duration that disrupts sleep and normal living, ceases to serve a protective function, and instead degrades health and functional capability.." Because persisting pain causes true suffering, clinical intervention directed at pain needs to address the entire person -- protecting functional capability, psychological well being and overall health.”***

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Pain has been described in many ways by various authors but all tend to agree that pain is not a sensation but rather an emotional' experience. The most unique thing about pain is its degree of subjectivity. The degree to which pain is experienced depends on the person experiencing that pain, the situation that the person is in at the time, the cultural background from which that person comes and the intensity of the stimulus provoking the pain. One or more of these factors can outweigh all of the others so that it has been seen that in times of high stress such as in battle, a soldier can have the most horrific wounds and yet not experience pain at that time. It is not even necessary to have pain receptors stimulated to feel pain, sympathetic pregnancy pains in fathers and phantom limb pain' in amputees are two good examples of this. There has been work done to suggest that the intensity and period of pain following surgery is dependent on, all else being equal, whether the patient has a general or local anesthetic.

In the physical therapist's world, most pain results, at least initially, from the stimulation of nociceptors in the musculoskeletal system. In chronic pain states, there is some possibility that this stimulation has ceased but nevertheless the pain remains. In other individuals the stimulus may be very much present following quite severe trauma but the patient's experience is more pleasant than another who has a less significant injury but whose pain level is much higher. It is therefore apparent that it is impossible for the therapist to objectively judge the patient's pain level. It must be realised that however much of wimp we may feel that particular patient is, the intensity of their pain is very real to them and can be very disabling regardless of the severity of the causal injury.

CHEMICAL VS MECHANICAL PAIN

Most pain is generated by both chemical (inflammatory) and mechanical irritants. Exceptions to this are such causes as neurophysiological dysfunctions Such as phantom limb pain. Given the dichotomous and complex nature of pain, a clear line between chemical and mechanical pain is rarely encountered and only a distinction between pain primarily of one type or another can be made. With this reservation constantly in mind, the following is a summary of the characteristics of each type.

|  |  |  |
| --- | --- | --- |
|  | CHEMICAL | MECHANICAL |
| HISTORY | Constant or continuous Nocturnal  Unrelieved by rest.  Morning stiffness > 2 hours. Initially activity decreases pain then increases it. | Continuous or intermittent.  Morning stiffness < 2 hours.  Changed by activity, posture or rest. |
| VISUAL | Red (if infected or superficial) Swollen  Joint held in rest posture | No redness  No heat  May be thickened if any deformity |
| OBJECTIVE | Capsular or non-capsular pattern depending on joint involvement  Painful weakness on resisted testing if acute enough  Spasm end feel | Usually non-capsular or cold capsular pattern  Normal or painful strong resisted tests  Hard capsular or normal end feel |
| PALPATION | Hot  Swollen  May be pointing if infected | No heat  No effusion (there may be edema)  May be thickening |
| REACTION TO TREATMENT | Extremely irritable  Responds poorly to any manual treatment if hyperacute but may do OK if less acute | Good response to strong manual therapy |

### Mechanism

Pain is a protective mechanism that generally results from stimulation of nociceptors when this stimulation exceeds the systems reactive threshold. The purpose of pain is to make the animal aware of a situation's potential for causing tissue damage and tb provoke the animal into changing the situation so that this damage is avoided or minimized.

Pain has been categorized into acute (fast) and slow pain. Acute pain occurs within 0.1 seconds of stimulus application while slow pain takes a second or more and continues to increase over a relatively protracted period. Acute pain tends to be sharp such as when a pin is stuck into the skin and is usually not felt when deeper tissues are stimulated.

Slow pain is a deeper aching, burning or throbbing type of pain that is often associated with tissue damage and can be caused by stimulation of any innervated tissue and can last for prolonged periods.

**Nociceptors: (From Wikipedia, the free encyclopedia)**

A nociceptor is a [sensory receptor](http://en.wikipedia.org/wiki/Sensory_receptor) that sends signals that cause the perception of [pain](http://en.wikipedia.org/wiki/Pain) in response to a potentially damaging stimulus. Nociceptors are the [nerve](http://en.wikipedia.org/wiki/Nerve) endings responsible for [nociception](http://en.wikipedia.org/wiki/Nociception), one of the two types of persistent pain (the other, [neuropathic pain](http://en.wikipedia.org/wiki/Neuropathic_pain), occurs when nerves in the [central](http://en.wikipedia.org/wiki/Central_nervous_system) or [peripheral nervous system](http://en.wikipedia.org/wiki/Peripheral_nervous_system) are not functioning properly). Nociceptors are silent receptors and do not sense normal stimuli. Only when activated by a threatening stimulus do they invoke a [reflex](http://en.wikipedia.org/wiki/Reflex).

History

Nociceptors were discovered by [Charles Scott Sherrington](http://en.wikipedia.org/wiki/Charles_Scott_Sherrington) in 1906. At the time scientists believed that animals were mechanical devices that transformed sensory stimuli into motor responses. That transitioned into more specific research where it was determined that different types of stimulation to a receptive field led to different responses. One of these stimuli had an intensity and quality sufficient to trigger autonomic reflex withdrawal, and pain. Sherrington used many different styles of experiments to discover that this pain was a nociceptive reaction and was sensed through specific receptors called nociceptors.[[1]](http://en.wikipedia.org/wiki/Nociceptor#cite_note-0)

Location

In mammals, nociceptors are sensory [neurons](http://en.wikipedia.org/wiki/Neuron) that are found in any area of the body that can sense pain either externally or internally. External examples are in [tissues](http://en.wikipedia.org/wiki/Biological_tissue) such as [skin](http://en.wikipedia.org/wiki/Skin) ([cutaneous nociceptors](http://en.wikipedia.org/wiki/Cutaneous_nociceptor)), [cornea](http://en.wikipedia.org/wiki/Cornea) and [mucosa](http://en.wikipedia.org/wiki/Mucosa). Internal nociceptors are in a variety of organs, such as the [muscle](http://en.wikipedia.org/wiki/Muscle), [joint](http://en.wikipedia.org/wiki/Joint), [bladder](http://en.wikipedia.org/wiki/Urinary_bladder), [gut](http://en.wikipedia.org/wiki/Gut) and continuing along the digestive tract. The cell bodies of these neurons are located in either the [dorsal root ganglia](http://en.wikipedia.org/wiki/Dorsal_root_ganglia) or the [trigeminal](http://en.wikipedia.org/wiki/Trigeminal_nerve) ganglia.[[2]](http://en.wikipedia.org/wiki/Nociceptor#cite_note-Jessell-1) The trigeminal ganglia are specialized nerves for the face, whereas the dorsal root ganglia associate with the rest of the body. The axons extend into the peripheral nervous system and terminate with the dendrites wherever a receptive field is found.

Types and functions

The peripheral terminal of the mature nociceptor is where the noxious stimuli are detected and transduced into electrical energy. When the electrical energy reaches a threshold value, an [action potential](http://en.wikipedia.org/wiki/Action_potential) is induced and driven towards the CNS. This leads to the train of events that allows for the conscious awareness of pain. The sensory specificity of nociceptors is established by the high threshold only to particular features of stimuli. Only when the high threshold has been reach by either chemical, thermal, or mechanical environments are the nociceptors triggered. Majority of nociceptors are classified by which of the environmental modalities they respond to. Some nociceptors respond to more than one of these modalities and are consequently designated polymodal. Other nociceptors respond to none of these modalities (although they may respond to stimulation under conditions of inflammation) and have thereby earned the more poetic title of sleeping or silent nociceptors.

Nociceptors have two different types of axons. The first are the [Aδ fiber](http://en.wikipedia.org/wiki/A_delta_fiber) axons. They are myelinated and can allow an action potential to travel at a rate of about 20 meters/second towards the CNS. The other type is the more slowly conducting [C fiber](http://en.wikipedia.org/wiki/C_fiber) axons. These only conduct at speeds of around 2 meters/second.[[4]](http://en.wikipedia.org/wiki/Nociceptor#cite_note-3) This is due to the light or non-myelination of the axon. As a result, pain comes in two phases. The first phase is mediated by the fast-conducting Aδ fibers and the second part due to (Polymodal) C fibers. The pain associated with the Aδ fibers can be associated to an initial extremely sharp pain. The second phase is a more prolonged and slightly less intense feeling of pain as a result from the damage. If there is massive or prolonged input to a C fiber there is progressive build up in the spinal cord dorsal horn. This phenomenon is similar to tetanus in muscles but is called wind-up. If wind up occurs there is a probability of increased sensitivity to pain.[[5]](http://en.wikipedia.org/wiki/Nociceptor#cite_note-Fields-4)

Thermal

Thermal nociceptors are activated by noxious heat or cold at various temperatures. There are specific nociceptor transducers that are responsible for how and if the specific nerve ending responds to the thermal stimulus. The first to be discovered was TRPV1, and it has a threshold that coincides with the heat pain temperature of 42°C. Other temperature in the warm-hot range is mediated by more than one TRP channel. Each of these channels express a particular C-terminal domain that corresponds to the warm-hot sensitivity. The interactions between all these channels and how the temperature level is determined to be above the pain threshold are unknown at this time. The cool stimuli are sensed by TRMP8 channels. Its C-terminal domain differs from the heat sensitive TRPs. Although this channel corresponds to cool stimuli, it is still unknown whether it also contributes in the detection of intense cold. An interesting finding related to cold stimuli is that tactile sensibility and motor function deteriorate while pain perception persists.

Mechanical

Mechanical nociceptors respond to excess pressure or mechanical deformation. They also respond to incisions that break the skin surface. The reaction to the stimulus is processed as pain by the cortex, just like chemical and thermal responses. Many times these mechanical nociceptors have polymodal characteristics. So it is possible that some of the transducers for thermal stimuli are the same for mechanical stimuli. The same is true for chemical stimuli, since TRPA1 appears to detect both mechanical and chemical changes.

Chemical

Chemical nociceptors have TRP channels that respond to a wide variety of spices commonly used in cooking. The one that sees the most response and is very widely tested is [Capsaicin](http://en.wikipedia.org/wiki/Capsaicin). Other chemical stimulants are environmental irritants like [acrolein](http://en.wikipedia.org/wiki/Acrolein), a [World War I](http://en.wikipedia.org/wiki/World_War_I) [chemical weapon](http://en.wikipedia.org/wiki/Chemical_weapon) and a component of cigarette smoke. Besides from these external stimulants, chemical nociceptors have the capacity to detect endogenous ligands, and certain fatty acid amines that arise from changes in internal tissues. Like in thermal nociceptors, TRPV1 can detect chemicals like capsaicin and spider toxins.[[3]](http://en.wikipedia.org/wiki/Nociceptor#cite_note-Woolf-2)

Sleeping/silent

Although each nociceptor can have a variety of possible threshold levels, some do not respond at all to chemical, thermal or mechanical stimuli unless injury actually has occurred. These are typically referred to as silent or sleeping nociceptors since their response comes only on the onset of inflammation to the surrounding tissue.[[2]](http://en.wikipedia.org/wiki/Nociceptor#cite_note-Jessell-1)

Pathway

[Afferent](http://en.wikipedia.org/wiki/Afferent_nerve) nociceptive fibers (those that send information *to*, rather than *from* the brain) travel back to the [spinal cord](http://en.wikipedia.org/wiki/Spinal_cord) where they form synapses in its [dorsal horn](http://en.wikipedia.org/wiki/Dorsal_horn). This nociceptive fiber (located in the periphery) is a first order neuron. The [cells](http://en.wikipedia.org/wiki/Cell_%28biology%29) in the dorsal horn are divided into physiologically distinct layers called laminae. Different fiber types form [synapses](http://en.wikipedia.org/wiki/Chemical_synapse) in different layers. Aδ fibers form synapses in laminae I and V, C fibers connect with neurons in lamina II, Aβ fibers connect with lamina I, III, & V.[[2]](http://en.wikipedia.org/wiki/Nociceptor#cite_note-Jessell-1) After reaching the specific lamina within the spinal cord, the first order nociceptive project to second order neurons and cross the midline. The second order neurons then send their information via two pathways to the [thalamus](http://en.wikipedia.org/wiki/Thalamus): the dorsal column medial-lemniscal system and the anterolateral system. The first is reserved more for regular non-painful sensation, while the lateral is reserved for pain sensation. Upon reaching the thalamus, the information is processed in the ventral posterior nucleus and sent to the [cerebral cortex](http://en.wikipedia.org/wiki/Cerebral_cortex) in the brain. As there is an ascending pathway to the brain that initiates the conscious realization of pain, there also is a descending pathway that modulates pain sensory. The brain can request the release of specific [hormones](http://en.wikipedia.org/wiki/Hormones) or chemicals that can have analgesic effects, which can reduce or inhibit pain sensation. The area of the brain that can release some of these hormones is the [hypothalamus](http://en.wikipedia.org/wiki/Hypothalamus).[[6]](http://en.wikipedia.org/wiki/Nociceptor#cite_note-5)

This effect of descending inhibition can be shown by electrically stimulating the [periaqueductal grey](http://en.wikipedia.org/wiki/Periaqueductal_grey) area of the midbrain. The periaqueductal grey in turn projects to other areas involved in pain regulation, such as the [nucleus raphe magnus](http://en.wikipedia.org/wiki/Nucleus_raphe_magnus) (which also receives similar afferents from the [nucleus reticularis paragigantocellularis](http://en.wikipedia.org/w/index.php?title=Nucleus_reticularis_paragigantocellularis&action=edit&redlink=1) (NPG). In turn the nucleus raphe magnus projects to the [substantia gelatinosa](http://en.wikipedia.org/wiki/Substantia_gelatinosa) region of the dorsal horn and mediates the sensation of spinothalamic inputs. The periaqueductal grey also contains [opiod receptors](http://en.wikipedia.org/wiki/Opioid_receptors) which explains one of the mechanisms by which opiods such as [morphine](http://en.wikipedia.org/wiki/Morphine) and [diacetylmorphine](http://en.wikipedia.org/wiki/Diacetylmorphine) exhibit an analgesic effect.

Sensitivity

Nociceptor neuron sensitivity is modulated by a large variety of mediators in the extra cellular space.[[7]](http://en.wikipedia.org/wiki/Nociceptor#cite_note-6) Peripheral sensitization represents a form of functional plasticity of the nociceptor. The nociceptor can change from being simply a noxious stimulus detector to a detector of non-noxious stimuli. The result is that low intensity stimuli from regular activity, initiates a painful sensation. This is commonly known as [Hyperalgesia](http://en.wikipedia.org/wiki/Hyperalgesia). Inflammation is one common cause that results in the sensitization of nociceptors. Normally Hyperalgesia ceases when inflammation goes down, however, sometimes genetic defects and/or repeated injury can result in [Allodynia](http://en.wikipedia.org/wiki/Allodynia): a completely non-noxious stimulus like light touch causes extreme pain. Allodynia can also be caused when a nociceptor is damaged in the peripheral nerves. This can result in deafferentation, which means the development of different central processes from the surviving afferent nerve. With this situation, surviving dorsal root axons of the nociceptors can make contact with the spinal cord, thus changing the normal input.[[5]](http://en.wikipedia.org/wiki/Nociceptor#cite_note-Fields-4)

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### Referred Pain

Pain perceived distant to the source of the pain, it may or may not (usually is) be felt to be contiguous with the local pain. It is felt in a dermatomal or quasidermatomal distribution and is potentiated by the following three factors:

* Centrality (structures close to the spinal cord are better able to refer pain)
* Depth (the deeper the structure the greater the potential)
* Intensity of pain

The pain is not a function of the nerve transmitting pain downwards (or at least this is very unlikely) but a very consistent characteristic apart from its distribution is that stressing the pain source causes referral and/or increases the intensity of the referred pain. However, pain that spreads in a non-dermatomal distribution is generally not considered referred but still stressing causes an increase in the pain level. It may be that radiating pain is caused by lateral recruitment in the sensory gyrus.

From Wikipedia, the free encyclopedia

Referred pain is a term used to describe the phenomenon of pain perceived at a site adjacent to or at a distance from the site of an injury's origin. One of the best examples of this is during [ischemia](http://en.wikipedia.org/wiki/Ischemia) brought on by an [angina pectoris](http://en.wikipedia.org/wiki/Angina_pectoris), or heart attack. Even though the [heart](http://en.wikipedia.org/wiki/Heart) is directly affected the pain is often felt in the neck, shoulders and back rather than the chest. The [International Association for the Study of Pain](http://en.wikipedia.org/wiki/International_Association_for_the_Study_of_Pain), as of 2001, has not officially defined the term; hence several authors have defined the term differently. Despite an increasing amount of literature on the subject there is no definitive answer regarding the mechanism behind this phenomenon. This phenomenon is also known as "reflective pain"[[1]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Arendt-Neilsen-0)

[Physicians](http://en.wikipedia.org/wiki/Physician) and scientists have known about referred pain since the late 1880s yet the true origins and causes of referred pain is unknown.

Characteristics

* The size of referred pain is related to the intensity and duration of ongoing/evoked pain.[[1]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Arendt-Neilsen-0)
* Temporal summation is a potent mechanism for generation of referred muscle pain.[[1]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Arendt-Neilsen-0)
* Central hyperexcitability is important for the extent of referred pain.[[1]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Arendt-Neilsen-0)
* Patients with chronic musculoskeletal pains have enlarged referred pain areas to experimental stimuli. The proximal spread of referred muscle pain is seen in patients with chronic musculoskeletal pain and very seldom is it seen in healthy individuals.[[1]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Arendt-Neilsen-0)

Modality specific somatosensory changes occur in referred areas, which emphasize the importance of using a multimodal sensory test regime for assessment.[[1]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Arendt-Neilsen-0)

Mechanism

There are several proposed mechanisms for referred pain. Currently there is no definitive consensus regarding which theory may be correct.

Convergent-projection

This represents one of the earliest theories on the subject of referred pain. It is based on the work of W.A. Sturge and J. Ross from 1888 and later TC Ruch in 1961. This theory proposes that afferent nerve fibers from tissues converge onto the same spinal neuron. This theory explains why referred pain is believed to be segmented in much the same way as the spinal cord. Additionally, experimental evidence shows that when local pain (pain at the site of stimulation) is intensified the referred pain is intensified as well.

Criticism of this model arises from its inability to explain why there is a delay between the onset of referred pain after local pain stimulation. Experimental evidence also shows that referred pain is often unidirectional. For example stimulated local pain in the anterior tibial muscle causes referred pain in the ventral portion of the ankle; however referred pain moving in the opposite direction has not been shown experimentally. Lastly, the threshold for the local pain stimulation and the referred pain stimulation are different, but according to this model they should both be the same.[[1]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Arendt-Neilsen-0)

Convergent-facilitation

In 1893 J MacKenzie created an alternate theory based on the ideas of Sturge and Ross. He believed that the internal organs were insensitive to stimuli. Furthermore, he believed that nonnociceptive afferent inputs to the [spinal cord](http://en.wikipedia.org/wiki/Spinal_cord) created what he termed "an irritable focus". This focus caused some stimuli to be perceived as referred pain. However, the theory did not gain widespread acceptance from critics due to its dismissal of visceral pain.

Recently this simple idea has regained some credibility under as a new term, central sensitization. This theory, therefore, explains why changes in somatosensory sensibility could be undergoing processes similar to the dorsal horn and the [brainstem](http://en.wikipedia.org/wiki/Brainstem). Additionally, the delay in appearance of referred pain shown in laboratory experiments can be explained due to the time required to create the central sensitization.[[1]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Arendt-Neilsen-0)

Axon-reflex

This theory suggests that the afferent fiber is bifurcated before connecting to the [dorsal horn](http://en.wikipedia.org/wiki/Dorsal_horn). Bifurcated fibers do exist in muscle, skin, and intervertebral discs. Yet these particular neurons are rare and are not representative of the whole body. Axon-Reflex also does not explain the time delay before the appearance of referred pain, threshold differences for stimulating local and referred pain, and somatosensory sensibility changes in the area of referred pain.[[1]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Arendt-Neilsen-0)

Hyperexcitability

This theory hypothesizes that referred pain has no central mechanism. However, it does say that there is one central characteristic that predominates. This theory is derived from experiments involving noxious stimuli and recordings from the dorsal horn of animals. Experiments revealed that referred pain sensations began minutes after muscle stimulation. Pain was felt in a receptive field that was some distance away from the original receptive field. According to the theory new receptive fields are created as a result of the opening of latent convergent afferent fibers in the dorsal horn. This signal could then be perceived as referred pain.

Several characteristics are in line with this theory of referred pain such as dependency on stimulus and the time delay in the appearance of referred pain as compared to local pain. However, the appearance of new receptive fields, which is interpreted to be referred pain, conflicts with the majority of experimental evidence from studies including studies of healthy individuals. Furthermore, referred pain generally appears within seconds in humans as opposed to minutes in animal models. Some scientists attribute this to a mechanism or influence downstream in the supraspinal pathways. Neuroimaging techniques such as [PET scans](http://en.wikipedia.org/w/index.php?title=PET_scans&action=edit&redlink=1) or [fMRI](http://en.wikipedia.org/wiki/FMRI) may visualize the underlying neural processing pathways responsible in future testing.[[1]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Arendt-Neilsen-0)

Thalamic-covergence

This theory suggests that referred pain is perceived as such due to the summation of neural inputs in the brain, as opposed to the spinal cord, from the injured area and the referred area. Experimental evidence on this theory is lacking. However, pain studies performed on monkeys revealed several pathways converging on both subcortical and cortical neurons.[[1]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Arendt-Neilsen-0)

Examples

* [Myocardial ischaemia](http://en.wikipedia.org/wiki/Myocardial_ischaemia) (the loss of blood flow to a part of the heart muscle tissue) is possibly the best known example of referred pain; the sensation can occur in the upper chest as a restricted feeling, or as an ache in the left shoulder, arm or even hand.[[2]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Wiki_Pain-1)
* “Ice cream headache” or “[brain freeze](http://en.wikipedia.org/wiki/Brain_freeze)” is another example of referred pain, in which the [vagus nerve](http://en.wikipedia.org/wiki/Vagus_nerve) is cooled by cold inside the throat. [[2]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Wiki_Pain-1)
* [Phantom limb pain](http://en.wikipedia.org/wiki/Phantom_limb_pain), a type of referred pain, is the sensation of pain from a limb that has been lost or from which a person no longer receives physical signals. It is an experience almost universally reported by amputees and quadriplegics. [[2]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-Wiki_Pain-1)
* Dr. Janet Travell and Dr. David Simons have mapped out very detailed pain referral patterns associated with the many muscles involved in myofascial pain. Their textbooks have many illustrations that assist in the diagnosis and treatment of these common afflictions.

Use in Clinical Diagnosis and Treatments

Referred pain can be indicative of nerve damage. A case study done on a 63 year old man with a sustained injury during his childhood developed referred pain symptoms after his face or back was touched. After even a light touch, there was shooting pain in his arm. The study concluded that the reason for this man's pain was possibly due to a neural reorganization which sensitized regions of his face and back after the nerve damage occurred. It is mentioned that this case is very similar to what phantom limb syndrome patients suffer. This conclusion was based on experimental evidence gathered by V. Ramachandran in 1993. With the difference being that the arm that is in pain is still attached to the body.

Orthopedic Diagnosis

From the above examples one can see why understanding of referred pain can lead to better diagnoses of various conditions and diseases. In 1981 physiotherapist [Robin McKenzie](http://en.wikipedia.org/w/index.php?title=Robin_McKenzie&action=edit&redlink=1) described what he termed centralization. He concluded that centralization occurs when referred pain moves from a distal to a more proximal location. Observations in support of this idea were seen when patients would bend backward and forward during an examination. Studies have reported that the majority of patients that centralized were able to avoid spinal surgery due to isolation of the area of local pain. However, the patients that did not centralize had to undergo surgery in order diagnose and correct problems. As a result of this study there has been a lot of research into the elimination of referred pain through certain body movements. One example of this is referred pain in the calf. McKenzie showed that the referred pain would move closer to the spine when the patient bent backwards in full extension a few times. More importantly, the referred pain would dissipate even after the movements were stopped. [[5]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-4)

General Diagnosis

As with [myocardial ischaemia](http://en.wikipedia.org/wiki/Myocardial_ischaemia) referred pain in a certain portion of the body can lead to a diagnosis of the correct local center. Somatic mapping of referred pain and the corresponding local centers has led to various topographic maps being produced in order to aid in pinpointing the location of pain based on the referred areas. For example local pain stimulated in the esophagus is capable of producing referred pain in the upper abdomen, the oblique muscles, and the throat. Local pain in the prostate can radiate referred pain to the abdomen, lower back, and calf muscles. Kidney stones can cause visceral pain in the urethra as the stone is slowly passed into the excretory system. This can cause immense referred pain in the lower abdominal wall. [[6]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-5) In addition to this, recent research has found that [ketamine](http://en.wikipedia.org/wiki/Ketamine), a sedative, is capable of blocking referred pain. The study was conducted on patients suffering from [fibromyalgia](http://en.wikipedia.org/wiki/Fibromyalgia), a disease characterized by joint and muscle pain and fatigue. These patients were looked at specifically due to their increased sensitivity to nociceptive stimuli. Furthermore, referred pain appears in a different pattern in fibromyalgic patients than it does in normal people. Often this difference manifests as a difference in terms of the area that the referred pain is found (distal vs. proximal) as compared to the local pain. The area is also much more exaggerated owing to the increased sensitivity.[[7]](http://en.wikipedia.org/wiki/Referred_pain#cite_note-6)

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7. [^](http://en.wikipedia.org/wiki/Referred_pain#cite_ref-6) Graven-Nielsen, T et al. (1999).Ketamine reduces muscle pain, temporal summation, and referred pain in fibromyalgia patients. Pain. 85, 483-491.

The following are potential area for referral from varying viscera.

|  |  |
| --- | --- |
| HEART | Under the sternum, base of the neck, over the shoulders, over the pectorals and down one or both arms L>R. |
| ESOPHAGUS | Pharynx, lower neck, arms midline chest from the upper to the lower sternum |
| GASTRIC | Lower thoracic to upper abdominal |
| *GALL* BLADDER | Upper abdominal, lower scapular and thoracolumbar |
| PANCREAS | Upper lumbar or upper abdominal. |
| KIDNEYS | Upper lumbar, occasionally anterior abdominal about 2 inches lateral to the umbilicus |
| URINARY BLADDER | Lower abdomen and occasionally to the groin and testicles |
| UTERUS | Lower abdominal or low lumbar. |

### Transmission Pathways

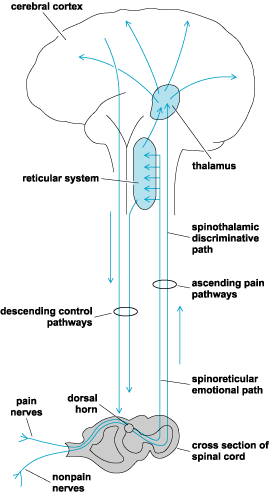
From Answes.com [**www.answers.com/topic/pain-1**](http://www.answers.com/topic/pain-1)

Acute pain is a useful warning system. There are specific nerve paths for conducting this sensation (see illustration). Pain receptors in the skin and other tissues are nerve terminals which lack any special characteristics, and they are probably triggered by a chemical stimulus when potential tissue damage occurs. There appear to be two types of terminals: one responds to many types of painful stimuli, whereas the other specifically responds to either mechanical or thermal energy. When the terminals are [stimulated](http://www.answers.com/topic/stimulate), the pain (that is, nociception message) is carried along specific small sensory fibers called A-delta and C fibers. The A-delta fibers are larger and transmit the “first pain” or “fast pain” The smaller C fibers transmit a secondary [dull](http://www.answers.com/topic/dull) continuous pain. These nerve fibers were traditionally believed to enter the spinal cord through the dorsal root, but it now seems that many also enter through the [ventral root](http://www.answers.com/topic/ventral-root) into the spinal cord.

*Neurophysiology of incoming pain. Sensation from peripheral receptors travels along specific pain nerves, and is modulated throughout the spinal cord and brain.*

Having entered the spinal cord, these fibers relay in the dorsal horn of the spinal gray matter, an area of considerable regulation and modulation of the incoming pain stimulus which is influenced by other incoming sensory stimuli; that is, touch or pressure sensations can suppress the transmission of signals in the small pain fibers. This helps to explain why when a person is hurting, the pain can be reduced by [rubbing](http://www.answers.com/topic/rubbing) the affected part, and this phenomenon forms the basis of some of the treatment strategies of stimulation-produced [analgesia](http://www.answers.com/topic/analgesia). In addition, the incoming pain signal in the spinal cord is also modulated by descending signals from the brain. At times of [anxiety](http://www.answers.com/topic/anxiety), these pain signals may be augmented. From these relay stations in the dorsal horn, the pain signal is carried by two nerve paths up to the brain. The classical [pathway](http://www.answers.com/topic/pathway) is the [spinothalamic tract](http://www.answers.com/topic/spinothalamic-tract), on the side of the spinal cord opposite to the incoming stimulus, and this leads to the posterior part of the [thalamus](http://www.answers.com/topic/thalamus) in the brainstem, and from there nerve paths radiate the pain sensation to many parts of the [cerebral cortex](http://www.answers.com/topic/cerebral-cortex), where the pain is appreciated. In addition to this direct path, there is also a [diffuse](http://www.answers.com/topic/diffuse) ascending path known as the spinoreticular tract which relays to many of the [basal ganglia](http://www.answers.com/topic/basal-ganglia) in the brain, and from there to areas of the brain connected with motivational and affective behavior such as the [hippocampus](http://www.answers.com/topic/hippocampus) and the [cingulate gyrus](http://www.answers.com/topic/cingulate-gyrus). It is possible that narcotic [analgesics](http://www.answers.com/topic/analgesic) exert some of their action on this ascending spinoreticular tract because these drugs tend to reduce the suffering aspects of pain, but still preserve many of the discriminative qualities so that individuals can still feel the pain, but it does not [bother](http://www.answers.com/topic/bother) them so much. *See also* [Analgesic](http://www.answers.com/topic/analgesic); [Narcotic](http://www.answers.com/topic/narcotic).

Certain parts of the brainstem around the central canal appear to [exert](http://www.answers.com/topic/exert) a strong [inhibitory](http://www.answers.com/topic/inhibit) effect on incoming pain signals. Stimulation of these areas probably releases [endorphins](http://www.answers.com/topic/endorphin-1), which are morphinelike substances produced by the body and liberated at various sites on the incoming pain path to suppress these signals. *See also* [Endorphins](http://www.answers.com/topic/endorphin-1).



### 

SPINAL CORD TRANSMISSION

The impulse enters the spinal cord via the posterior root ganglion and ascend or descend one to three segments in the tract of Lissauer posterior to the dorsal horn. The fibers terminate in neurons in the dorsal horn and are transmitted cranially in one of two pathways.

Posterior Laminae

These are found in the dorsal horn of the spinal cord and number 1 through 5.

Lamina 1

These receive impulses mainly from the A-delta fibers that carry nociceptive information especially concerning skin damage. Most of the fibers arising from this lamina cross the spinal cord but a few go direct to higher centers on ipsilaterally.

Laminae 2 and 3

These laminae are collectively known as the substantia gelatinosa. For the most part, this area receives fibers' from the slow pain system, the C fibers almost all of which terminate here. It is here that the gate control theory suggests that a modification of pain impulse occurs.

Lamina 4

The cells of this lamina respond to stimulation of large A-beta fiber impulses. There is no change in the frequency of response of these cells when A-delta or C fiber impulses are stimulated.

Lamina 5

This lamina has the most complex responsiveness of all of these posterior laminae. Almost all nociceptive and mechanoreceptive impulses eventually reach this lamina, a few of the fast pain impulse by-pass this lamina to go directly to higher centers. The response of the cells in lamina 5 depends in a large part to the intensity of the stimulus. High intensity stimulation leads to facilitation of the cell and relative ease of signal transmission across the spinal cord to the opposite side of the cord while more gentle stimulation inhibits this transmission. This inhibition is, according to this theory, the result of pre and post-synaptic effects produced by the cells of lamina 2 and 3. In addition, where the pulses originate will also determine whether facilitation or inhibition occurs. If from the nociceptive system ie. the small diameter A-delta or C fibers successive impulses have a “windup" effect in that successive impulses occur for a longer duration and so the transmission is facilitated. If the signal arises from the A-beta fibers, a silent period follows each discharge and so tends to inhibit transmission.

The fast pain fibers terminate in laminae 1 and 5 of the dorsal horn. Here they excite neurons that send long fibers to the opposite side of the cord and then upwards to the brain in the lateral division of the anterolateral sensory pathway (the lateral spinothalamic tract).

The slow signal's C fibers terminate in laminae 2 and 3 of the dorsal horn (the substantia gelatinosa). Most of the signals then pass through another short fiber neuron to terminate in lamina 5. Here the neuron gives of f a long axon most of which join with the fast signal axons to cross the spinal cord and continue on upwards in the brain in the same spinal tract. However, the fast and slow fibers remain differentiated from each other in the spinothalamic tract with the fast fibers having large diameter and so faster transmission rates.

TERMINATION IN THE BRAIN STEM AND THALAMUS

About 75 to 90% of all pain fibers terminate in the reticular formation of the medulla, pons and me encephalon. From here other neurons transmit the signal to the thalamus, hypothalamus and cerebrum. A small number of fast signals are passed directly to the thalamus and from here to the sensory cortex. It is thought that these signals are important for localizing but not interpreting the pain. Of the slow signals, none or at least very few are passed directly to the thalamus but must go through the reticular system before this.

Because most of the fast and all of the slow signals pass through the reticular system, they have a wide ranging and potent effect on almost the entire nervous system as the reticular system transmits activating signals into all parts of the brain. Signals that pass through this system can only be localized to gross body areas and are therefore of little use in pain localization but are more important in interpreting pain and producing an awareness of ongoing destructive processes.

REFERRED PAIN

This is basically a mislocalization of pain and generally follows the main innervating segment's dermatome although in more severe pain, several dermatomes may be affected. Visceral referral is thought to be produced by the following mechanism. The nociceptive fibers from the viscera synapse in the spinal cord with some of the same neurons that receive pain fibers from the skin. When the' visceral nociceptors are stimulated, some are transmitted by the same neurons that conduct skin nociception and so take on the characteristics of those impulses and appear to originate from the skin.

VISCERAL PAIN

The viscera tend to have only pain and no other sensory nerve endings. Visceral pain differs from superficial pain in that highly localized damage to an organ may produce no pain at all or at worse non-acute pain. However, a stimulus that causes diffuse nociceptor response may cause extremely severe pain. Stimuli that can produce this are chemical damage, ischemia, spasm of smooth muscle and distension. All visceral pain from the abdominal or thoracic cavities is transmitted through small C fibers in the Sympathetic nerves and cause slow pain.

Pain originating from problems in the peritoneum, pleura or pericardium is different from that of other viscera. These parietal walls are supplied extensively with fast and slow pain nerve endings, which have their fibers in spinal rather than sympathetic nerves. These structures can therefore produce the sharp pain of the superficial tissues.

### Sensitization and Hypersensization

For easy reading see <http://www.wellcome.ac.uk/en/pain/microsite/science4.html>

Nociception should cease once the stimulus (heat, mechanical or chemical) is removed but hypersensitization may occur and pain occur with what should be non-painful stimuli and even in the absence of external stimuli.

1. Central Sensitization

This is increased excitation of neurons within the CNS causing strengthened synaptic relationships.

1. Peripheral Sensitization

Increased excitation of neurons in the peripheral system.

Changes that cause hypersensitization include:

* Nociceptor damage
* Nerve damage
* The presence of inflammatory chemicals such as ATP, dynorphin, and prostaglandin E causing increased sensitivity of the nociceptors and opening up sodium ion channels to a greater extent and for longer periods
* Release of neurotransmitter substances and substance P in the spinal cord increasing excitation of the central neurons.

Changes to the proteins being produced by the nociceptor and dorsal root ganglion (AXT involved).

Pain levels need to be sufficient to cause concern in the individual but must be appropriate to the stimulus and the stage of healing. In acute injury increased pain states force the individual to take care of the wound and in non-acute injuries to avoid damaging habits. But sustained long-term severe pain levels once healing has occurred are pointless and often disabling.

Hypersensitization occurs in two ways:

1. lowering of thresholds where non-painful stimuli become painful (allodynia)
2. raising of responsiveness so that painful stimuli cause an exaggerated perception (hyperalgesia)

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## Sensory Receptors and Pathways

**Somatosensory system**: sensory system that provides information about touch and body position

-projects to the *primary somatosensory cortex*

**Touch:**

-the sensation of touch varies over two "dimensions"   
-*quality*:

-pressure, vibration  "simple sensations"   
-also, more complex: smoothness, wetness

-*spatial*:

-ability to locate sensations on the surface (or inside) the body   
-*two-point discrimination* shows that this dimension varies across the body

-Skin:

-three layers:

-**epidermis**: outer layer of the skin, thinnest   
-**dermis**: middle layer, contains nerve fibers, blood vessels, and connective tissue   
-**subcutaneous tissue**: fat cells   
-receptors:

-**Pacinian corpuscles**: in the dermis, around joints and muscles, and around the gut

-fast response, delivered to fast-conducting nerve fibers   
-vibration and deep pressure

-**Meissner's corpuscles** and **Merkel's discs**:

-fine spatial discrimination   
-Merkel's discs are *slow adapting*, innervate slower nerve fibers

-**nerve endings**: detection of pain, heat, and cold   
-**Ruffini's endings**: detect stretching of the skin   
-*receptors vary across receptive field size* (large or small) *and adaptation speed* (fast or slow)

Sensory Pathways: two systems

**1) dorsal column system**: inputs enter the dorsal part of the spinal cord, and synapse in the medulla

**-**fibers then cross over the midline, and terminate in the thalamus

**2) anterolateral / spinothalamic system**: inputs synapse on cells in the spinal cord, cross over, ascend anterolateral columns of spinal cord

Mapping:

-inputs from the periphery are mapped onto spinal nerves in **dermatomes**   
-cortical cells are mapped with spatial relations preserved   
-columnar organization

-columns respond to particular *qualities* and *spatial locations*   
-all cells in the column respond similarly   
-Area 3b receives input from fast- and slow-adapting skin receptors   
-Area 3a receives input from stretch receptors (muscles)   
-*maps of the somatosensory system are repeated throughout the nervous system*: dermatomes, thalamus, several cortical areas

Complexity:

-like all sensory system, there is increasing complexity in neuron response to stimulus

-initially, cells may respond to particular quality at a particular location

-then, cells become more selective: may only respond to a combination of qualities, or across spatial locations

Modulation of Pain: the reduction of pain sensations can be accomplished in a number of ways

-**opioids**: exogenous and endogenous opiates act as **analgesics**

-analgesic effect of exogenous opioids suggest that endogenous opioids are a way the brain modulates pain   
-injection of opioids into the **periaqueductal gray** produces analgesia:

-hypothesized mechanism: projection from the p.g. to the medulla, activates neurons which project down the spinal cord (*descending fibers*), modulating pain sensations at the spinal cord synapses

-analgesic opioids can also be injected directly into the spinal cord, eliminating side effects (*epidurally* and *intrathecally*)

-**electrical stimulation**: may block signals electrically, or stimulate pain modulation mechanisms   
-**placebos**:

-inactive agent that can alleviate pain in some circumstances   
-use of an opiate receptor antagonist suggests that placebos work on opioid systems   
-other evidence suggests a second, non-opioid system

-**stress**:

-stress can modulate pain sensations   
-animal models use noxious stimuli to inflict stress, then test pain modulation   
-opioid modulation: stresses effect on pain declines over time, as with opioid use

-also, cross-tolerance exists between opioids and stress (in pain reduction)

-non-opioid pain modulation is also likely, since opioid antagonists do not block the effect

-*opioid and non-opioid modulations is likely*; the above evidence, along with lesion evidence, suggests two distinct pathways

### Articular Receptors

|  |  |  |  |  |
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| TYPE | MORPHOLOGY | LOCATION | PARENT NERVE | FUNCTION |
| 1 | Thinly encapsulated globular corpuscles in 3-6 clusters | Superficial layers of the joint capsule | 6-9u small and myelinated | Static and dynamic mechanoreceptors of low threshold and slowly adapting. Proprioceptive |
| 2 | Thickly encapsulated conical corpuscles in 2-4 clusters | Deep layers of joint capsule and fat pads | 9-12u medium and myelinated | Dynamic mechanoreceptors of low threshold and rapidly adapting. Kinesthetic. |
| 3 | Thinly encapsulated fusiform corpuscles | Intrinsic and extrinsic joint ligaments | 13-17u large and myelinated | Dynamic mechanoreceptors of high threshold and very slowly adapting. Acts as the joint counterpart to the Golgi tendon organ. Inhibits antagonistic muscles to the stretched ligament |
| 4 | Simple nerve endings found in plexi and individually. | Fibrous capsule, ligaments, fat pads, blood vessel walls, bone, periosteum | 2-5u very small and myelinated and <2u extremely small and unmyelinated | Nociceptors of high threshold and non-adapting. Pain sensors. |

PERIPHERAL TRANSMISSION

The common free nerve endings have two distinct pathways into the central nervous system that correspond to the two different types of pain.

The acute pain signals are .transmitte4 in the peripheral nerves by small A fibers at velocities between 6 and 30 meters per second while the slow pain impulses travel in C fibers at much slower velocities of between 0.5 and 2 meters per second. The fast pain impulse is an emergency signal telling the subject that there is a threat present and provoking an almost instantaneous and often reflexive reaction to remove themselves from the pain source. This is often followed a second or more later by a duller pain that tells or either tissue damage or continuing stimulation if it lasts more than a few seconds.

## Pain Modulation

Peripheral

Accommodation is a characteristic common to all nerve fibers and is thought to be due to the current flow itself closing the sodium channels in the nerve and thereby preventing sodium exchange and hence polarization of the nerve. Thus while the nociceptors themselves may be non-adapting, the nerves which transmit their signal is.

Spinal

The effect of pain signals at lamina five tends to facilitate transmission upwards, this is truer, the greater the intensity. However, milder intensities and mild to moderate input from the mechanoreceptors tend to inhibit lamina five as far as pain transmission is concerned. Thus, the net effect at lamina five will determine whether or not the signal is relayed upwards. If mild mechanoreceptor input dominates, the pain signal is stopped at this point, if pain input dominates or if the mechanoreceptor input is to strong, transmission occurs.

Central

Chemical

There are three main components in this system. The periaqueductal gray area of the upper pons send signals to the raphe magnus nucleus in the lower pons and upper medulla which relays the signal down the cord to a pain inhibitory complex located in the dorsal horn of the cord. Stimulation of the periaqueductal gray area either directly or indirectly from higher centers initiates the process of signal transmission. The nerve fibers derived from the gray area secrete encephalin and serotonin while the raphe magnus release encephalin only. The fibers terminating in the cord's dorsal horn secrete serotonin, which has been shown to act on another set of cord neurons that in turn release encephalin. This encephalin is believed to produce presynaptic inhibition of the incoming pain fibers to laminae 1 through 5 thereby blocking pain signals at their entry point into the cord. It is further believed that the chemical releases in the upper end of the pathway can inhibit pain signal transmission in the reticular formation and the thalamus. The inhibition from this system is effective on both slow and fast pain signals.

Of the more important morphine like substances that act in synaptic receptors is beta-endorphin, met-encephalin, leu-encephalin and dimorphic. The two encephalin are found in the system described above, beta-endorphin is found in the hypothalamus and the pituitary gland and dynorphin is found only in minute quantities in nervous tissue but is an extremely powerful analgesic. . Endorphins interact with opiate receptor neurons to reduce the intensity of pain: among individuals afflicted with chronic pain disorders, endorphins are often found in high numbers.

Neurophysiological

A feedback system exists in the cortex called the corticofugal system. This originates at the termination point of the various sensory pathways. Excessive stimulation of this feedback loop results in a signal being transmitted down to the posterior horn of the stimulated cord cells and produces lateral or recurrent inhibition of the cells adjacent to the stimulated cell thereby preventing the spread of the signal. This is the automatic gain control system to prevent overloading of the sensory cortex.

The Gate Control Theory

This theory is dependent on the interaction of signals from the mechanoreceptor and the nociceptor systems at the substantia gelatinosa and the net inhibitory or facilitatory effect at this level. A net inhibitory impulse will result in the failure for pain impulses to be transmitted to the level where action results while a net facilitatory effect will allow transmission of these signal to higher levels. It is complimentary to the chemical analgesic system in that it is capable of blocking the impulse before it reaches the conscious or reactive level while the chemical system is triggered by impulses reaching these higher centers and then modifying the pain. In effect, the gate control mechanism is responsible for ensuring that insignificant pain impulses do not cause the organism to respond.

As we have seenpain impulses reach the substantia gelatinosa via the small C fibers. In addition, signals from non-nociceptive nerve endings, the mechanoreceptors have to reach the spinal cord and do so by even larger and myelinated A-beta fibers. It the relative amounts of activity in the A-beta fibers compared with that in the C fibers that in part determines whether the pain signal reaches the target cells in lamina five and from there the activation system (the spinal arc and or the reticular formation). In some circumstances, the system is dominated by descending influence from the higher centers such as the chemical analgesia produced by the periaqueductal system or by the effect of situation, personality, culture etc..

The aggregate of the mechanoreceptor and nociceptor impulses reaching the substantia gelatinosa (laminae 2 and 3) determine whether further transmission will be facilitated or inhibited. Impulses from the A-beta fibers facilitate the cells of the substantia gelatinosa while those from the C fibers inhibit these cells. Transmission from the substantia gelatinosa into lamina 5 tends, all else being equal to have an inhibitory effect on further transmission across the spinal cord and hence to higher centers. If this inhibitory effect is enhanced (facilitated) a very strong inhibition is placed on lamina 5 and transmission to the action centers is prevented. Therefore if the A-beta effect is greater than the C the gate is effectively closed to transmission. However, if the inhibitory effect of the substantia gelatinosa is inhibited by a relatively larger effect of the C fibers, the cells of lamina 5 are facilitated and the gate is opened for transmission upwards.

Therefore, the greater the mechanoreceptor input, the less chance there is of pain reaching the conscious level. This explains how a mother can rub away a child’s pain when he or she falls over or how massage, TNS, oscillatory mobilizations, exercises or frictions can reduce or eliminate pain. It also explains why fast pain is least affected by these mechanical strategies as a proportion of these fibers by-pass lamina 5.

The only problem with this theory is that the impulses from the mechanoreceptors carried in the A-beta fibers do not pass through the substantia gelatinosa but pass directly to lamina five from lamina 1.



Suprathreshold simulation of large and small (that is mechanoreceptor and nociceptor) receptors and their nerve fibers results in transmission along both pathways. If the stimulation is light to moderate the mechanoreceptor input dominates and then stimulates the inhibitory interneurons I the substantia gelatinosa (laminae 2 and 3) which in turn results in inhibition of the transmission cells in lamina 5. If the stimulus is larger, the nociceptor input dominates and inhibits the inhibitory interneuron and so no inhibition of lamina 5 cells occurs and pain is passed on to the activation system. The theory is somewhat outdated and inadequate but is still a useful working model.

PAIN BASED TREATMENTS

Manual and Exercise Therapy

Both manual techniques and exercises can be considered as sub-barrier and barrier techniques while manual techniques may also be used as an extra-barrier technique. Sub-barrier techniques do not reach the point where they impart any mechanical stress on the restrictive structures. Barrier techniques do reach the restrictive barrier and then stress it to varying degrees. Extra-barrier techniques, manipulation, push through the abnormal restrictive barrier.

Sub-barrier (Grade 1 and 2 and if done correctly Grade 3 and 4) techniques have a neurophysiological but no direct mechanical effect on the restrictive tissue. Barrier and Extra-barrier techniques (Grade 3+ and 4+ and 3 and 4, if done the way they are normally incorrectly done with some stretch on the restrictor, and manipulation Grade 5) have, in addition to the neurophysiological effect, a mechanical effect.

The usually model to explain the pain relieving effects of sub-barrier and barrier techniques is the gate control theory. Here the exercise or manual technique stimulates the Type 1 and 2 receptors. If the technique is properly graded it will not stimulate nociceptors or increase inflammation. The stimulation of the large nerves results in a net inhibitory effect at lamina 5 and a closing of the gate. The technique is always oscillated so as to overcome the rapid adaptation of the type 2 receptors. The barrier and extra-barrier techniques will have the same neurophysiological effect but at the same time produce a mechanical stress and deformation of the restrictive tissue. However, the mechanical effect may well increase nociception if the tissue is too acutely affected for the technique. So while the technique is likely to be more effective at generating mechanoreception it is also more risky. Manipulation has both strong mechanical effects and strong neurophysiological ones. In addition it is postulated that manipulation will have an effect on the corticofugal system as well as a direct stimulatory effect on the endorphin system. However, it has a large mechanical effect that may well exacerbate the condition if too acute.

The direction of the manual technique or exercise may also be a matter of determining the effect required. If a neurophysiological effect is required then the direction of the treatment can be arbitrary providing that the appropriate spinal segments are being stimulated. However, in an acute condition, it is safer if the direct of the treatment chosen is the least painful and irritable. If a mechanical effect is required then the direction of the treatment must be against the restricting tissue.

Basing treatments on pain levels means to a large extent determining the degree of inflammation and hence irritability. From here the appropriate decision regarding grading and direction of motion can be determined.

## ABSTRACTS

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| Riley JL 3rd :  **The stages of pain processing across the adult lifespan.**  J Pain, 1(2):162-70, 2000. 47 References  Division of Public Health Service, College of Dentistry, JHM Health Science Center, 1600 SW Archer Road, Gainesville, FL 32610 jriley@dental.ufl.edu (JL Riley III, PhD)  The authors claim no financial interest or other relationship with any manufacturer(s) of any commercial product(s) related to this article.  Studies and have found that the prevalence of and intensity of musculoskeletal pain increases with age. However, other studies have found that older adults are less likely than younger to report headache, backaches, and stomach pain and that pain complaints might be most prevalent in middle age and decrease thereafter. Other researchers have suggested that differences across age span are a function of sensory dulling with age. Research testing for age-related differences in ratings has found inconsistent results. Studies using a visual analog scale (VAS) have not found age differences, nor have studies using the McGill Pain Questionnaire (MPQ) or Multidimensional Pain Questionnaire (MPI).  Studies examining age-related differences on the affective response to pain have generally not found age differences for depression or anxiety. However, a recent a study has suggested that the relationship between pain and depression might vary depending on age cohort. A conceptual model that lends itself to the study of differences and the processing of chronic pain across the adult life span is the 4-stage model of pain of processing. This model consists of an initial sensory-discriminatory dimension, the major component of which is the perceived intensity of the pain sensation. The second stage of pain processing, termed immediate unpleasantness, reflects an individual's immediate affective response and involves limited cognitive processing. The third stage involves longer-term reflective or cognitive processes that relate to the meanings or implications that pain holds for one's life as a manifest by a negative emotions related to pain (e.g., depression, frustration, anxiety, fear, and anger). A final stage of this model is that of the overt behavioral expression of pain (e.g., frequency of moaning, lying down during the day, and the degree to which the individual is able to participate in daily responsibilities).  The purpose of this paper was to expand on previous work by testing for age-related differences in the magnitude and association of the 4 stages of pain processing. The authors were particularly interested in whether changes associated with age have a selective impact on the later stages of pain processing, as has been shown for personality traits. Concurrently, they were also interested in providing further validation of the 4-stage model.  The subjects in this study consisted of 1585 pain patients evaluated at a pain management clinic. The sample consisted of 689 men and 971 women, 52% of whom were currently married and/or living together. The average age was 53.58 years. Sixty-seven percent were Caucasian, 31% were African-American and 2% were Asian. Subjects were divided into 3 age cohorts: younger adults 18-44 years (n = 895), middle-aged adults 45-64 years (n = 538), and older adults 65-85 (n = 159). Demographics for each cohort are given in the article.  Pain intensity and pain unpleasantness, the first and second stages, were assessed with a VAS. The emotional factor, the third stage, was assessed using separate VASs for depression, anxiety, frustration, anger, and fear. Pain behavior was measured on 4 subscales from the Psychosocial Pain Inventory. This instrument was an interview format with individual items summed to subscale composite scores. These subscales measured the extent of pain behavior manifest by the patient at home, degree of social reinforcement for illness behavior, reduction in family related responsibilities, and impact of rest and avoidance activity on pain. Statistical analyses included ANCOVA, HSD, LISREL-8, GFI, and NFI tests.  No differences in magnitude or association were found for the 2 initial stages of pain processing. The results indicated statistically significant age-related effects on the third (emotional distress) and fourth (pain behavior) stages. The older age group reported less emotional distress and pain behavior than the younger or middle-age cohorts. The middle-aged group showed the highest association between their emotional response to pain and pain behavior and the elderly group showed the least association.  Because individuals interpret pain in the context of their lives, attitudes toward aging are likely to contribute to the emotional response to pain. The attribution of medical symptoms to the aging process has been shown to be greater for older than for younger medical patients and associated with reduced emotional response to these symptoms. The elderly might accept pain-related losses as an aging-related natural reduction in overall health and experience less negative emotion related to these symptoms. It is also possible that middle age is the time for the beginning of aches and pains of aging, making the symptoms of chronic pain more difficult to accept. Middle age is the time individuals are most susceptible to depression related to health problems.  Overall, these data support the 4 stages of pain processing. No age-related differences were found in the linear association between pain and emotional response to pain. An individual's emotional response to pain might be linked to the perceived effectiveness of one's ability to control pain, and therefore, the link between pain and pain-related emotions should be mediated by the ability to cope with pain. Although some studies have suggested the elderly use more externally mediated coping (i.e., hoping and praying), most studies have not found age-related differences in perceived ability to control pain or ratings of the effectiveness of coping strategies.  An important contribution to the pain and aging literature is the finding of the age-related differences in the linear association between emotional response to pain (third stage) and pain behavior (fourth stage). The authors were unable to find any other study reporting this finding. Older adults were found to be less likely to manifest signs of illness behavior to family and friends as a function of the emotional response to pain. It is possible that the elderly have different environmentally related contingencies reinforcing pain behavior than those in younger age groups. For example, older individuals might be less likely to have access to immediate social support and research suggests that the environmental influences are likely to play a complex role in moderating the expression of pain for all individuals. The finding that middle-aged adults have a stronger link between their negative affect and pain behavior, and that their overall level of emotional distress is greater than older adults have clinical implications for both age ranges. These data suggest that different treatment foci might be indicated based on the age of the patient. This might suggest that middle-aged patients might benefit more from pharmacological interventions aimed at managing affective distress. In contrast, the older group might need a relatively greater emphasis on behavioral interventions aimed at increasing function with a lesser focus on an affective distress. In older patients, for whom pain relief is the primary goal, they might be expected to have lesser affective contribution or complications to analgesia effectiveness. Middle-aged patients, with higher levels of pain-related negative emotions, might not respond to typical analgesic medications with the same efficacy because of the contribution from affective factors.  This study showed that age has statistically significant effects on the third and fourth stages of the 4-stage model of pain processing. Chronic pain patients in the older-age cohort reported less emotional distress and pain behavior than the younger or middle-age cohorts. In addition, the association between the emotional response to pain and subsequent pain behaviors work the highest for individuals in the middle-age group and lowest for those in the older age cohort. These differences are likely to be a function of differences in life circumstances, attitudes and beliefs about pain and/or aging, and age cohort-related differences in the methods used for coping with chronic pain.  [**Back to Module 3**](http://www.pain.com/cme/module.cfm?mod_year=2001&mod_month=1&mod_num=3) **or** [**Next Article**](http://www.pain.com/cme/article.cfm?article_next=24&mod_year=2001&mod_month=1&mod_num=3) |

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| Endogenous mechanisms of sensory **modulation**. |

**Pain 1999 Aug;Suppl 6:S45-53**   (ISSN: 0304-3959)

Dubner R; Ren K [[Find other articles with these Authors](http://www.medscape.com/server-java/MedLineApp?/member-search/search.cgi?getcount=200&advanced=1&relevance=50&ray=off&earliestseg=UM667300%2C1960&latestseg=UMA0709W%2C2001&concept_mapping=on&searchlogic=boolean&wordvars=on&getchunk=20&relevance%20)]  
Department of Oral and Craniofacial Biological Sciences, University of Maryland Dental School, Baltimore 21201, USA. [rnd001@dental.umaryland.edu](mailto:rnd001@dental.umaryland.edu).

We provide evidence supporting the idea that the relationship between tissue damage, or the threat of tissue damage, and the response to such stimuli is variant and dependent on neuronal networks by which attentional, emotional and cognitive components of **pain** experience activate endogenous descending **modulatory** systems. Most previous studies have focused on responses to transient noxious stimuli with little information on the influence of descending **modulation** on behavioral responses to persistent **pain** and hyperalgesia after tissue or nerve injury. Utilizing correlative behavioral and neuronal studies we have demonstrated that (1) behavioral context modulates neuronal activity in nociceptive and non-nociceptive somatosensory pathways, supporting the hypothesis that responses in these pathways are not immutable; (2) descending **modulation** influences behavior and neuronal activity at spinal cord levels after inflammation and persistent **pain**; and (3) there are descending facilitatory as well as inhibitory influences on behavior and spinal cord neuronal activity that may impact on persistent **pain** particularly of deep muscle and visceral origin. Cortical as well as subcortical pathways are available by which dorsal horn activity can be modulated by attentional, motivational and cognitive factors. It appears that the same neuronal mechanisms in the forebrain and brain stem are available for behavioral **modulation** in a learned task involving the threat of tissue damage (transient noxious stimuli) as are available in the development and amplification of persistent **pain** produced by inflammation. These parallel brain mechanisms emphasize the saliency of **pain** experience as an important learned behavior for the survival of the organism, similar to sequential goal-directed behaviors in an operant task.

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| Towards a **pain** treatment based on the identification of the **pain**-generating **mechanisms**? |

**Eur Neurol 2001;45(2):126-32**   (ISSN: 0014-3022)

Dallel R; Voisin D [[Find other articles with these Authors](http://www.medscape.com/server-java/MedLineApp?/member-search/search.cgi?getcount=200&advanced=1&relevance=50&ray=on&earliestseg=UM989900%2C1999&latestseg=UMA0709W%2C2001&concept_mapping=on&searchlogic=boolean&wordvars=on&getchunk=20&relevance_%20)]  
Laboratoire de Physiologie Oro-Faciale, Faculte de Chirurgie Dentaire, Clermont-Ferrand, France. [radhouane.dallel@u-clermont.fr](mailto:radhouane.dallel@u-clermont.fr).

Despite continuous improvements in available **pain** treatments, many patients with chronic **pain** still remain insufficiently relieved. Although such therapeutic failures are often ascribed to pharmacological or psychological factors, difficulties in elucidating **pain**-generating **mechanisms** may be the main cause of insufficient **pain** management. These difficulties arise from several origins, including the unsuitability of the usual classification of **pain**, the exclusive use of etiology or symptom criteria as the main dimension of **pain** to guide the choice of therapeutic agents, the inadequate interpretation of sensory deficit, the lack of identification of the injured tissues, the absence of objective **pain** assessment by psychophysical methods. In this paper, we review briefly some fundamental knowledge to determine **pain** treatment based on the identification of the physiopathological **mechanisms** of **pain**. We advocate that once **pain**-generating **mechanisms** are known, it becomes possible to establish the appropriate treatment of **pain**.

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| **Pain** **mechanisms** and management: a central perspective. |

**Clin J Pain 2000 Sep;16(3 Suppl):S144-56**   (ISSN: 0749-8047)

Mannion RJ; Woolf CJ [[Find other articles with these Authors](http://www.medscape.com/server-java/MedLineApp?/member-search/search.cgi?getcount=200&advanced=1&relevance=50&ray=on&earliestseg=UM989900%2C1999&latestseg=UMA0709W%2C2001&concept_mapping=on&searchlogic=boolean&wordvars=on&getchunk=20&relevance_%20)]  
Neural Plasticity Research Group, Department of Anesthesia and Critical Care, Massachusetts General Hospital and Harvard Medical School, Charlestown 02129, USA.

Although **pain** is always intense and unpleasant, the capacity to experience this sensation is, under normal circumstances, fundamental to the preservation of bodily integrity. Clinically, however, after injury to peripheral tissue or directly to the nervous system, spontaneous and evoked **pain** manifest that serve no physiologic function, are crippling to patients, and are difficult to treat. Here, we review the specific role of the dorsal horn of the spinal cord in the **mechanisms** of nociceptive protective **pain** and the spinal plasticity that occurs after nerve and tissue injury. This spinal neuronal plasticity is shown to be a key contributor to pathologic **pain** hypersensitivity. The potential for the molecular **mechanisms** responsible for the spinal plasticity in revealing new targets for future treatment is also discussed.

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| Pathophysiologic **mechanisms** of neuropathic **pain**. |

**Curr Pain Headache Rep 2001 Apr;5(2):151-61**   (ISSN: 1531-3433)

Taylor BK [[Find other articles with this Author](http://www.medscape.com/server-java/MedLineApp?/member-search/search.cgi?getcount=200&advanced=1&relevance=50&ray=on&earliestseg=UM989900%2C1999&latestseg=UMA0709W%2C2001&concept_mapping=on&searchlogic=boolean&wordvars=on&getchunk=20&relevance_%20)]  
Division of Pharmacology, School of Pharmacy, University of Missouri-Kansas City, 64108, USA. [taylorb@umkc.ed](mailto:taylorb@umkc.ed).

New animal models of peripheral nerve injury have facilitated our understanding of neuropathic **pain** **mechanisms**. Nerve injury increases expression and redistribution of newly discovered sodium channels from sensory neuron stomata to the injury site; accumulation at both loci contributes to spontaneous entopic discharge. Large myelinated neurons begin to express nociceptive substances, and their central terminals sprout into nociceptive regions of the dorsal horn. Descending facilitation from the brain stem to the dorsal horn also increases in the setting of nerve injury. These and other **mechanisms** drive various pathologic states of central sensitization associated with distinct clinical symptoms, such as touch-evoked **pain**.

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| Central mechanisms of **pain** **modulation**. |

**Curr Opin Neurobiol 1999 Aug;9(4):436-41**   (ISSN: 0959-4388)

Mason P [[Find other articles with this Author](http://www.medscape.com/server-java/MedLineApp?/member-search/search.cgi?getcount=200&advanced=1&relevance=50&ray=off&earliestseg=UM667300%2C1960&latestseg=UMA0709W%2C2001&concept_mapping=on&searchlogic=boolean&wordvars=on&getchunk=20&relevance%20)]  
Department of Neurobiology, Pharmacology and Physiology, Committee on Neurobiology, The University of Chicago, 947 East 58th Street, Chicago, Illinois 60637, USA. [pmason@midway.uchicago.edu](mailto:pmason@midway.uchicago.edu).

Bulb spinal serotonergic neurons and two physiological classes of bulbospinal nonserotonergic cells interact to modulate **pain** transmission. Recent studies have begun to elaborate targets of descending **pain** **modulation** other than the well-studied flexion withdrawal pathways. Site-specific, naloxone-sensitive placebo analgesia, which is hard to reconcile with current models of descending **pain** **modulation**, presents an exciting challenge to the field.

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| Stimulation of human thalamus for **pain** relief: possible **modulatory** circuits revealed by positron emission tomography. |

**J Neurophysiol 1998 Dec;80(6):3326-30**   (ISSN: 0022-3077)

Duncan GH; Kupers RC; Marchand S; Villemure JG; Gybels JM; Bushnell MC [[Find other articles with these Authors](http://www.medscape.com/server-java/MedLineApp?/member-search/search.cgi?getcount=200&advanced=1&relevance=50&ray=off&earliestseg=UM667300%2C1960&latestseg=UMA0709W%2C2001&concept_mapping=on&searchlogic=boolean&wordvars=on&getchunk=20&relevance%20)]  
Departement de stomatologie, Faculte de medecine dentaire, Universite de Montreal, Quebec, Canada, H3C 3J7.

Stimulation of human thalamus for **pain** relief: possible **modulatory** circuits revealed by positron emission tomography. J. Neurophysiol. 80: 3326-3330, 1998. Stimulation of the somatosensory thalamus was used for more than 2 decades to treat chronic **pain** in the human. However, despite clinical reports of successful results, little is known about the actual mechanisms mediating this form of stimulation-produced analgesia. To reveal possible neuronal pathways evoked by thalamic stimulation, we measured regional changes in cerebral blood flow (rCBF) in five patients who received successful long-term relief of chronic **pain** with somatosensory thalamic stimulation. Positron emission tomography during thalamic stimulation revealed significant activation of the thalamus in the region of the stimulating electrodes as well as activation of the insular cortex ipsilateral to the thalamic electrodes (contralateral to the patients' clinical **pain**). For these patients, thalamic stimulation also evoked paresthesiae that included thermal sensations in addition to tingling sensations. Results of this study indicate that in some cases somatosensory thalamic stimulation may activate a thalamocortical **pain** **modulation** circuit that involves thermal pathways. These results are consistent with other recent reports suggesting that activation of thermal pathways may contribute to **modulation** of nociceptive information.

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| Possible deficiencies of **pain** **modulation** in fibromyalgia. |

**Clin J Pain 1997 Sep;13(3):189-96**   (ISSN: 0749-8047)

Lautenbacher S; Rollman GB [[Find other articles with these Authors](http://www.medscape.com/server-java/MedLineApp?/member-search/search.cgi?getcount=200&advanced=1&relevance=50&ray=off&earliestseg=UM667300%2C1960&latestseg=UMA0709W%2C2001&concept_mapping=on&searchlogic=boolean&wordvars=on&getchunk=20&relevance%20)]  
Department of Psychology, University of Western Ontario, London, Canada.

OBJECTIVE: To examine possible deficiencies in endogenous **pain** modulating mechanisms in fibromyalgia patients compared with matched **pain**-free control subjects. DESIGN/SUBJECTS/METHODOLOGY: **Pain** reduction was investigated in 25 female patients with fibromyalgia and 26 age-matched healthy women using the diffuse noxious inhibitory controls (DNIC) paradigm. Tonic thermal stimuli at painful and non-painful intensities, tailored to individual heat **pain** thresholds, were employed to induce **pain** inhibition. The anticipated effect was assessed by measuring the electrical **pain** threshold and detection threshold, using a double staircase method. Only non-tender control points were stimulated (thermode on the foot, electrodes on the inner forearm). RESULTS: The patients with fibromyalgia had significantly lower heat **pain** thresholds than the healthy subjects, but similar electrical detection and **pain** thresholds. The repeatedly applied electrical stimuli resulted in a degree of perceptual adaptation that was similar between the two groups. However, concurrent tonic thermal stimuli, at both painful and non-painful levels, significantly increased the electrical **pain** threshold in the healthy subjects but not in the fibromyalgia patients. The electrical detection threshold was not affected in either group. CONCLUSIONS: **Pain** **modulation**, produced by a concurrent tonic stimulus in healthy persons, was not seen in the fibromyalgia group. The patients either had deficient **pain** **modulation** or were unable to tolerate a tonic stimulus intense enough to engage a **modulatory** process. It remains to be established whether the **pain** reduction found in the healthy subjects was the conventional DNIC effect, another effect (e.g., distraction), or a combination of both.

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| [Current aspects of nociceptive transmission: peripheral mechanisms and spinal **modulation**] |

[Aspectos actuales de la transmision nociceptiva: mecanismos perifericos y modulacion espinal.]

**Rev Neurol 1996 Jul;24(131):769-78**   (ISSN: 0210-0010)

Banos-Diez JE; Navarro-Acebes X [[Find other articles with these Authors](http://www.medscape.com/server-java/MedLineApp?/member-search/search.cgi?getcount=200&advanced=1&relevance=50&ray=off&earliestseg=UM667300%2C1960&latestseg=UMA0709W%2C2001&concept_mapping=on&searchlogic=boolean&wordvars=on&getchunk=20&relevance%20)]  
Departament de Farmacologia i Terapeutica. Universitat Autonoma de Barcelona.

Nociceptive transmission shows unusual features of sensorial physiology, due to the complex **modulation**, which occurs from the start of the impulse until its final perception. In recent years the dynamic role played in nociception by peripheral structures, such as the 7 and spinal nociceptors and the second order neurons, has been recognized. It is fairly clear how a number of modulators activate and make nociceptors sensitive, accounting for the appearance of clinical features such as primary hyperalgesia, and their persistence. Thus eico sanoides, histamine, bradykinin and others allow considerable control of nociceptor activity. Also, the dorsal horn neurons play an important part in other clinical signs associated with **pain**, such as mechanical (secondary) hyperalgesia. At this level, some neurotransmitters such as glutamate or the neurokinins seem to be important in central sensibilization phenomena, which occur when a painful stimulus is maintained. In fact, continued release of these neurotransmitters implies the expression of certain genes and the production of certain proteins. Knowledge of the relationship between the different neurochemical systems and subsequent changes in their expression in different pathological situations may help to explain the pathophysiology of some clinical signs of neuropathic **pain** which are at present inexplicable.

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| Short term influence of **mechanical** factors on regional musculoskeletal **pain**: a study of new workers from 12 occupational groups. |

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OBJECTIVES: To determine the influence of short-term exposure to **mechanical** factors on regional musculoskeletal **pain**. METHODS: Full time newly employed workers were recruited from 12 occupational groups and information collected by questionnaire. Subjects indicated on a blank body manikin any low back, shoulder, wrist or forearm or both, or knee **pain**, which had occurred during the past month and had lasted more than 1 day. Data were also collected with a previously validated questionnaire on working postures, manual handling activities, and repetitive movements of the upper limb. The relations between **mechanical** factors and each area of **pain** were calculated as odds ratios (ORs) with 95% confidence intervals (95% CIs). Adjustment was made for age and sex. RESULTS: 1081 subjects (median age 23; interquartile range 20--27) were recruited to the study (a participation rate of 91%). 261 (24%) reported low back **pain**, 221 (20%) shoulder **pain**, 93 (9%) wrist or forearm **pain**, and 222 (21%) knee **pain**. Several specific manual handling activities were found to be associated with low back, shoulder, and knee **pain**. Carrying weights of more than 50 lbs (23 kg) on one shoulder was the factor which was most strongly associated with low back **pain** (OR 2.4 (95% CI 1.5 to 3.8)), shoulder **pain** (OR 3.1 (95% CI 1.9 to 4.8)), and knee **pain** (OR 3.5 (95% CI 2.2 to 5.5)), whereas forearm **pain** was most strongly associated with repetitive movements of the wrists (OR 1.8 (95% CI 1.04 to 3.1)). By contrast very few postures were associated with regional **pain**, although bending forwards in an uncomfortable position for at least 15 minutes was associated with shoulder **pain** (OR 1.6 (95% CI 1.2 to 2.2)) and kneeling for at least 15 minutes was associated with knee **pain** (OR 1.8 (95% CI 1.2 to 2.6)). Exposure to **mechanical** factors was most strongly associated with **pain** at multiple sites rather than with **pains** in individual regions. CONCLUSIONS: Even among workers with only short-term exposure to **mechanical** factors, musculoskeletal **pain** is increased.

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## Post-Study Questions

After re-taking the pre-study questions, answer the following. The purpose of these questions is for you to demonstrate your understanding of this Section of the module and your ability to apply the knowledge.

1. A patient presents in an acute pain state where the tissue resistance is felt to come on simultaneously with the pain onset.
   1. Describe the level of acuteness
   2. Describe an appropriate non-manual treatment
   3. Describe an appropriate manual treatment
2. Describe how you would progress both types of treatment as the patient progresses from this acute pain state to one of stiffness with minimal pain.
3. Post-Study Questions

**The purpose of these questions is for you to demonstrate your understanding of this Section of the module and your ability to apply the knowledge.**

1. **Describe how you would modify your mobilizations on a patient who, on presentation, complains of pain coming on simultaneously with tissue resistance on passive mobility testing and progresses to the point where pain is felt only on strong overpressure during the examination.**
2. **Discuss how your mobilizations decrease pain, increase range of motion and lead to permanent resolution of the problem.**