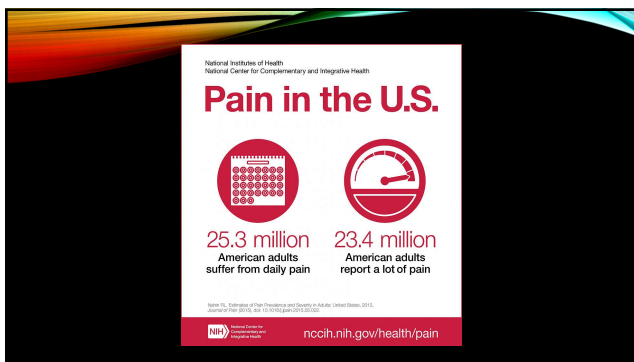
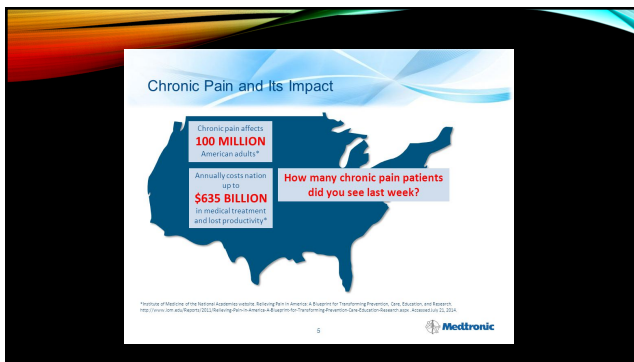


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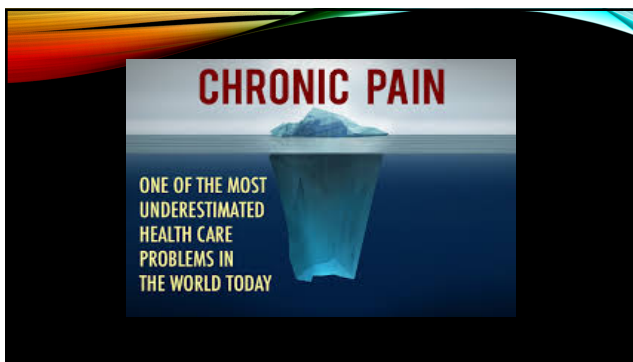
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4



5

CHRONIC PAIN

- It is now defined as pain that persists longer than the normal course of time associated with a particular type of injury.
- Chronic pain is essentially caused by the bombardment of the central nervous system (CNS) with nociceptive impulses, which causes changes in the neural response.
- The pain subsequently provokes changes in the behavior of the patient, and the development of fear-avoidance strategies.
- As a result, the patient may also become physically atrophied and deconditioned.

Source: https://www.sciencedaily.com/terms/chronic_pain.htm

6

WHAT CAUSES NEUROPATHIC PAIN?

- Anything that leads to loss of function within the sensory nervous system can cause neuropathic pain. As such, nerve problems from carpal tunnel syndrome or similar conditions can trigger neuropathic pain. Trauma, causing nerve injury, can lead to neuropathic pain. Other conditions which can predispose patients to developing neuropathic pain include diabetes, vitamin deficiencies, cancer, HIV, stroke, multiple sclerosis, shingles, and cancer treatments.
- In the spinal cord, the area which interprets painful signals is rearranged, with corresponding changes in neurotransmitters and loss of normally-functioning cell bodies; these alterations result in the perception of pain even in the absence of external stimulation. In the brain, the ability to block pain can be lost following an injury such as a stroke or trauma. Over time, further cellular damage occurs, and the sense of pain persists.

Source: https://www.medicinenet.com/neuropathic_pain_nerve_pain/article.htm#what_are_the_signs_and_symptoms_of_neuropathic_pain

7

SPINAL CORD MECHANISMS

The sensory input from primary sensory neurons is transferred, via their central axons, to second-order neurons in the dorsal horn of the spinal cord. The synaptic contacts made between afferent central terminals and dorsal horn neurons are highly organized, both topographically and functionally to maintain accurate transfer of information regarding the peripheral noxious stimuli. Following peripheral nerve lesions, synaptic processing in the spinal cord can be subject to diverse forms of functional, chemical, and structural plasticity that are highly involved in the production of hypersensitivity to sensory input, increased synaptic efficacy (the phenomenon of central sensitization), loss of inhibitory mechanisms, alterations in synaptic contacts, and the activation of nonneuronal cells all play major roles in producing increased pain sensitivity in neuropathic pain.

Source: Clinical Pain Management, Chronic Pain, 2nd edition, Eds. Wilson, Watson, Haythornthwaite, and Jensen, 2008 Hodder Arnold

8

WHAT CAUSES CENTRAL SENSITIZATION?

- Central sensitization involves specific changes to the nervous system. Changes in the dorsal horn of the spinal cord and in the brain occur, particularly at the cellular level, such as at receptor sites.
- How do injuries and conditions associated with the peripheral nervous system lead to changes in the central nervous system, which, in turn, lead to chronic pain in the isolated area of the original injury?
- How do migraine headaches become chronic daily headaches?
- How does an acute low back lifting injury become chronic low back pain?

Source: <https://www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain/central-sensitization>

9

CENTRAL SENSITIZATION: IMPLICATIONS FOR THE DIAGNOSIS AND TREATMENT OF PAIN

- Central sensitization manifests as pain hypersensitivity, particularly dynamic tactile allodynia, secondary punctate or pressure hyperalgesia, aftersensations, and enhanced temporal summation.
- It can be readily and rapidly elicited in human volunteers by diverse experimental noxious conditioning stimuli to skin, muscles or viscera, and in addition to producing pain hypersensitivity, results in secondary changes in brain activity that can be detected by electrophysiological or imaging techniques.
- Studies in clinical cohorts reveal changes in pain sensitivity that have been interpreted as revealing an important contribution of central sensitization to the pain phenotype in patients with fibromyalgia, osteoarthritis, musculoskeletal disorders with generalized pain hypersensitivity, headache, temporomandibular joint disorders, dental pain, neuropathic pain, visceral pain hypersensitivity disorders and postsurgical pain.

Source: Woolf, c.j., Pain, 2011 mar; 142(3 suppl): s2-15

10

CENTRAL SENSITIZATION: IMPLICATIONS FOR THE DIAGNOSIS AND TREATMENT OF PAIN

- Prior to the discovery of central sensitization, the prevailing view on pain processing in the central nervous system was of a largely passive neural relay that conveyed by encoded action potentials, information on the onset, duration, intensity, location and quality of peripheral noxious stimuli, much like a telephone wire, from one site to another.
- The spinal gate control theory by Melzack and Wall in 1965 had highlighted that this sensory relay system could be modulated.
- Furthermore, first Perl then others showed that nociceptor peripheral terminals could become "sensitized" after injury, reducing their threshold, mainly to heat stimuli, and only within the site of the injury where the terminal was exposed to inflammatory modulators, the zone of primary hyperalgesia.

Source: Woolf, c.j., Pain, 2011 mar; 142(3 suppl): s2-15

11

CENTRAL SENSITIZATION: IMPLICATIONS FOR THE DIAGNOSIS AND TREATMENT OF PAIN

- The realization that synapses were subject to a form of use-dependent plasticity that could increase their strength or efficacy had steadily gained ground by the early 1980's.
- This was followed by the discovery of windup in dorsal horn neurons by Mendell and Wall in 1965, where repeated low frequency stimulation of a nerve at constant C-fiber strength were found to elicit a progressive increase in action potential firing over the course of the stimulus.

Source: Woolf, c.j., Pain, 2011 mar; 142(3 suppl): s2-15

12

Chronic pain is defined in the literature. As pointed out by both of the AMA Guides (5th and 6th editions), and a raft of literature on the impact of chronic pain.

It is a disease of the central nervous system (the spinal nerves and the brain). The central nervous system controls the entire body, including coordination of the upper extremities.

Chronic pain, through its negative effect on the central nervous system, impacts dexterities, or the ability to effectively use the hands and fingers.

Dexterities and coordination of the upper extremities are critical to much sedentary work. We must constantly remind the jury that severe chronic pain affects every aspect of a person's life: physical, mental, coordination, and performance. It destroys the ability to function at a competitive job level in all of these spheres. It becomes a disease in itself, independent of the injury site. This is part of central sensitization and its impact on employability of any kind.

13

"Processes have been identified by which unilateral inflammation, trauma, or illness can lead to pain and sensitivity in uninvolved, often contralateral structures. Physiologic processes underlying such symptoms, which were often dismissed as "not real", have been found at the level of the dorsal horn, thalamus, and sensory cortex...These findings are of major import. They demonstrate that pain need not be symptomatic of a disease or injury, but, in fact, can become a disease unto itself."

Guides to the Evaluation of Permanent Impairment, 5th Edition, American Medical Association, pages 567-568.

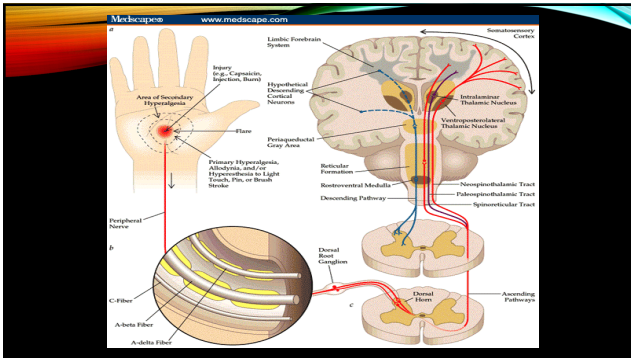
14

"The processes of peripheral and central sensitization are a normal consequence of tissue injury, and they offer significant protection to the organism; after tissue injury, sensitization serves as a reminder that the region is injured and should be closely guarded until the tissue has healed. However, the same neuronal mechanisms can lead to persistent pain even after all evidence of the initial inciting disease or injury have resolved."

"Chronic pain has been linked with significant disability. Although pain has been traditionally regarded as a symptom that serves as a warning signal of an underlying disease process, there is accumulating evidence that persistent pain should be considered a disease entity in its own right."

Guides to the Evaluation of Permanent Impairment, 6th Edition, American Medical Association, page 34.

15



16


PAIN IS INEVITABLE
SUFFERING IS OPTIONAL

17

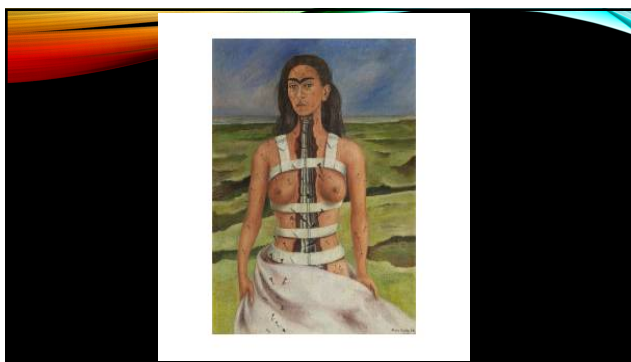
The Dalai Lama is 84 years old. He suffers pain daily. He needs walking assistance at times. But he does not suffer. At least that is what he says. (I don't think he would lie.) He says the purpose of life is happiness. Not hedonistic pleasure, which can lead to both pain and suffering. But in promoting kindness and in so doing, helping to reduce the suffering of others.

18

On September 17, 1925, Kahlo and Gómez Arias were traveling together on a bus when the vehicle collided with a streetcar. She suffered serious injuries as a result of the accident, including a broken spinal column, a broken collarbone, broken ribs, a broken pelvis, eleven fractures in her right leg, a crushed and dislocated right foot, and a dislocated shoulder. Also, an iron handrail pierced her abdomen and her uterus. After staying at the Red Cross Hospital in Mexico City for several weeks, Kahlo returned home to recuperate further. She began painting during her recovery and finished her first self-portrait the following year.



19

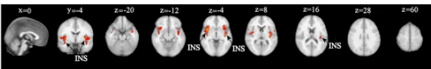


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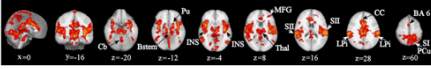
Increased Cerebral Activation as a Result of Central Sensitization in Healthy Subjects

Functional MRI

Normal nociceptive transmission (no hyperalgesia)



Central sensitization (secondary hyperalgesia)
60 g monofilament after 45' C-4 capsaicin



Zambreanu L, et al. Pain 2006;114:397-407. Medscape

21

Central Sensitization: Brain Illness

- Cortical Reorganization
- Pain matrix
 - No single pain generator
 - Multiple mutually reinforcing resonances

Grichewski et al. Abnormal brain chemistry in chronic back pain as in vivo proton magnetic resonance spectroscopy ... Pain (2005)
 Apkarian et al. Chronic Back Pain Is Associated with Decreased Prefrontal and Thalamus Gray Matter Density Journal of Neuroscience (2004)
 Balci et al. Beyond Feeling: Chronic Pain Hurts the Brain, Disrupting the Default-Mode Network Dynamics. Journal of Neuroscience (2008) vol. 28 (6) pp. 1398
 Linde et al. Theoretical dyslexia: A neurological and neuropsychological condition characterized by magnetoencephalography Proc Natl Acad Sci USA (1999) vol. 96 (24) pp. 13222-7
 Kuchner et al. Abnormal brain gray matter loss in fibromyalgia patients: preliminary study of the brain. J Neurosci (2007) vol. 27 (13) pp. 4004-7
 Schmidt-Wilcke et al. Altered connectivity and intensity of pain correlates with structural differences in gray matter in chronic back pain patients Pain (2004) vol. 113 (1-2) pp. 89-97

22

When we are talking about chronic pain syndrome and Central Pain Syndrome, we are talking about very similar phenomena.

23

- Pain is your body's normal reaction to an injury or illness, a warning that something is wrong. When your body heals, you usually stop hurting.
- But for many people, pain continues long after its cause is gone. When it lasts for 3 to 6 months or more, it's called chronic pain. When you hurt day after day, it can take a toll on your emotional and physical health.
- About 25% of people with chronic pain will go on to have a condition called chronic pain syndrome (CPS). That's when people have symptoms beyond pain alone, like depression and anxiety, which interfere with their daily lives.

(<https://www.webmd.com/pain-management/chronic-pain-syndrome-overview#1>)

24

CENTRAL PAIN SYNDROME INFORMATION PAGE
 NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

- Central pain syndrome is a neurological condition caused by damage to or dysfunction of the central nervous system (CNS), which includes the brain, brainstem, and spinal cord.
- Central pain syndrome is not a fatal disorder, but the syndrome causes disabling chronic pain and suffering among the majority of individuals who have it.

(<https://www.ninds.nih.gov/Disorders/All-Disorders/Central-Pain-Syndrome-Information-Page>)

25

INSTITUTE FOR CHRONIC PAIN

What is Chronic Pain Syndrome?

- In most cases, chronic pain starts with an acute injury or illness. If the pain of this injury or illness lasts longer than six months, it's then considered chronic pain. Sometimes, chronic pain subsequently causes complications. These complications, in turn, can make the pain worse. A chronic pain syndrome is the combination of chronic pain and the secondary complications that are making the original pain worse.
- Chronic pain syndromes develop in what we call a vicious cycle. A vicious cycle is the cycle of pain causing pain: chronic pain that causes secondary complications, which subsequently make the original chronic pain worse.

(www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain-syndrome)

26

WHAT ARE THESE SECONDARY COMPLICATIONS?

Chronic pain can lead to some common problems over time. For example, many people tend to have trouble sleeping because of pain. After a while, they become so tired, and their patience has worn so thin, that everything starts bugging them. They also find that coping with chronic pain gets harder and harder. Some people stop working. With job loss, they may experience financial problems. The stress of these problems keeps them up at night. Thinking too much in the middle of the night can make the original sleeping problem even worse. It can be hard to shut off the thinking even in the middle day.

(www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain-syndrome)

27

SECONDARY COMPLICATIONS CONTINUED

Chronic pain can also affect the roles people have in the family. They miss out on children's activities, family functions, and parties with friends. As a result, many people struggle with guilt. Guilt isn't the only emotion that is common to living with chronic pain. Patients tend to report some combination of fear, irritability, anxiety and depression. Patients also tend to express that they have lost their sense of direction in life. They are stuck. These problems are all common when living with chronic pain.

(www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain-syndrome)

28

SECONDARY COMPLICATIONS CONTINUED

These problems cause stress. They are called stressors, which means that they are problems that cause stress. These stressors can make pain worse because stress also affects the nervous system. It makes the nervous system more reactive and you become nervous. Now, pain is also a nerve related problem. Whatever its initial cause, pain travels along the nervous system to the brain, which is also part of the nervous system. Once reaching the brain, it registers as pain. When stress affects the nervous system, making it more reactive, the pain signals reach the brain in an amplified way. So, stress leads one to have more pain.

The vicious cycles of pain become clear. Chronic pain causes stressful problems, which, in turn, cause stress that makes the pain worse. This combination of chronic pain and the resultant problems that make pain worse is what we call chronic pain syndrome.

(www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain-syndrome)

29

SYMPTOMS

CPS affects your physical health, your emotions, and even your social life over time. The pain can lead to other symptoms such as:

- Anxiety
- Depression
- Poor sleep
- Irritability
- Guilt
- Loss of interest in sex
- Drug or alcohol abuse
- Marriage or family problems
- Job loss
- Suicidal thoughts

(www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain-syndrome)

30

- Central sensitization can lead to heightened sensitivities across all senses, not just the sense of touch. Chronic pain patients can sometimes report sensitivities to light, sounds and odors. As such, normal levels of light can seem too bright or the perfume aisle in the department store can produce a headache. Central sensitization is also associated with cognitive deficits, such as poor concentration and poor short-term memory.
- Central sensitization also corresponds with increased levels of emotional distress, particularly anxiety.
- After all, the nervous system is responsible for not only sensations, like pain, but also emotions. When the nervous system is stuck in a persistent state of reactivity, patients are going to be literally nervous – in other words, anxious.
- Lastly, central sensitization is also associated with sick role behaviors, such as excessive resting, malaise, and dysfunctional pain behavior.

Source: <https://www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain/central-sensitization>

31

- Central sensitization has long been recognized as a possible consequence of stroke and spinal cord injury. However, it has become increasingly clear that it plays a role in many different chronic pain disorders. It can occur with chronic low back pain, chronic neck pain, whiplash injuries, chronic tension headaches, migraine headaches, rheumatoid arthritis, osteoarthritis of the knee, endometriosis, injuries sustained in a motor vehicle accident, and after surgeries.
- Fibromyalgia, irritable bowel syndrome, and chronic fatigue all seem to have the common denominator of central sensitization as well.

Source: <https://www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain/central-sensitization>

32

THERE ARE LIKELY MULTIPLE FACTORS THAT LEAD TO THE DEVELOPMENT OF CENTRAL SENSITIZATION IN THESE SO-CALLED 'PERIPHERAL' CHRONIC PAIN DISORDERS. THESE FACTORS MIGHT BE DIVIDED INTO TWO CATEGORIES:

- Factors that are associated with the state of the central nervous system prior to onset of the original injury or pain condition
- Factors that are associated with the central nervous system following onset of the original injury or pain condition.

Source: <https://www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain/central-sensitization>

33

PREDISPOSING FACTORS

- There are likely biological, psychological, and environmental predisposing factors.
- Low and high sensitivity to pain, or pain thresholds, are likely in part due to multiple genetic factors. While there is no research as of yet to support a causal link between pre-existing pain thresholds and subsequent development of central sensitization following an injury, it is largely assumed that one will be found.

Source: <https://www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain/central-sensitization>

34

PREDISPOSING FACTORS CONTINUED

- Psychological factors, such as the stress-response, are also apt to play a role in the development of central sensitization. Direct experimental evidence on animals and humans, as well as prospective studies on humans, have shown a relationship between stress and lowering of pain thresholds. Similarly, different types of pre-existing anxiety about pain is consistently related to higher pain sensitivities.
- All these psychophysiological factors suggest that the pre-existing state of the nervous system is an important determinant of developing central sensitization following the onset of pain. If the stress response has made the nervous system reactive prior to injury, then the nervous system might be more prone to become centrally sensitized once onset of pain occurs.
- The common denominator between chronic pain, anxiety, trauma, and depression is the nervous system. They are all dysfunctional conditions of the nervous system, particularly a persistently altered, or dysregulated, nervous system.

Source: <https://www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain/central-sensitization>

35

FACTORS LEADING TO CENTRAL SENSITIZATION FOLLOWING ONSET OF PAIN

- Conditions such as depression, fear-avoidance, anxiety, and other stressors can, in turn, further exacerbate the reactivity of the nervous system, leading to central sensitization.
- Poor sleep is also a common consequence of living with chronic pain. It is associated with increased sensitivity to pain as well.

Source: <https://www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain/central-sensitization>

36

Cognitive impairment in chronic pain patients has been associated with sleep disturbance / partial sleep deprivation, major depression, mood change / emotional distress, medication use, somatic preoccupation and pain catastrophization and perceived interference with daily activities that are potential sources of chronic stress."
(Hart et al, 2000, 2003; Nicholson & Martelli, 2004, 2006; Mooney et al, 2005; Kunderman et al, 2004)

37

Recent reviews have also indicated that the associated symptoms of chronic pain, singly and in combination, may be more important than pain severity in producing cognitive and other impairment, including hyperalgesic changes and disruption of serotonergic and opioidergic processes
(Pilcher & Huffcutt, 1996).

38

"Available evidence from acute, as well as chronic animal and human pain studies involving experimental, clinical and neurophysiological studies strongly supports the conclusion that pain and pain-related symptomatology, independent of TBI or neurological disorder, can and often do produce impairment of cognitive functioning as assessed on neuropsychological and functional tests, especially on measures of attentional capacity, processing speed, memory, and executive functions."
(Martelli, Nicholson, Zasler, 2007)

39

"Chronic pain is associated with significant morbidity. Patients with chronic pain often have lower quality of life and greater fatigue than their healthier cohorts...In addition, psychiatric comorbidities are common...(examples of chronic pain comorbidities include) depression, panic disorders, anxiety, and post-traumatic stress disorder."
(Argoff and McCarberg, 2010)

40

"Perhaps the most exciting and revealing data have come from studies of chronic pain patients, in which imaging has provided strong evidence that pain leads to brain changes that could have functional significance."
(Schweinhart and Bushnell, 2010)

41

"These technologies have indicated that chronic pain patients have altered pain modulatory circuits, both at forebrain and brain stem levels...Finally, imaging studies are beginning to identify biochemical alterations associated with chronic pain that could underlie neurotoxicity caused by long-term activation."
(Schweinhart and Bushnell, 2010)

42

“...chronic pain has a much larger impact on an individual than the direct effects of the pain itself. There is now accumulating evidence that chronic pain actually changes the structure and function of the central nervous system...Associated with these neurological changes are deficits in long- and short-term memory and emotional decision making.”
(Catherine Bushnell, 2009)

43

“Chronic pain patients who are depressed secondary to their condition are more likely to physically function more poorly and demonstrate more significant levels of physical disability.”
(Sitley Brown, 2008)

44

Chronic pain has also been associated with decreased brain function. In a study of brain volume in chronic pain conditions, Apkarian et al (2004) found a decrease in gray matter volume in patients with chronic back pain equivalent to brain atrophy over 10 to 20 years of normal aging.

45

"...Grinding pain can take its toll on energy and concentration."
(Vash and Crewe, 2004)

46

"We all experience pain as arising from "out there," and, in consequence, imagine that it is actually triggered by noxious stimuli where we feel the pain. Central sensitization reveals, however, that this in many cases is a sensory illusion; specific alterations in the CNS can result in painful sensations occurring in the absence of either peripheral pathology or noxious stimuli, and the target for treatment in these situations must be the CNS not the periphery."
(Latremoliere and Woolf, 2009)

47

"Central sensitization can also occur after **surgery**, contributing to pain on movement or touch, in **migraine attacks** where brushing hair is often painful, and in some patients with **nerve damage** where even blowing on the skin produces excruciating burning pain."
(Woolf, 2006)

48

"Central sensitization describes changes that occur in the brain in response to repeated nerve stimulation...The resulting changes in brain wiring and response are referred to as *nerve plasticity*...or central sensitization...The changes of central sensitization occur after repeated experiences with pain."
(Gudin, 2004)

49

Indeed, permanent changes in the responsiveness of both the peripheral and central nervous systems can persist even after all tissue healing has ensued; thus, persistent pain can become a self-perpetuating condition.

50

"In neuropathic pain, by definition, the nervous system has been damaged and is dysfunctional."
(Galer and Dworken, 2006)

51

"Chronic pain involves errant reprogramming in the brain and spinal cord..."

(Kasdan, Morton, L; Occupational Hand & Upper Extremity Injuries & Disease (1998). Hanley & Belfus, INC. Philadelphia, p. 37 – 38.)

52

"...what is clear is that the brains of chronic pain patients whose analgesic needs are largely unmet with current treatment options are very sick, both in terms of neurotransmitter systems and potential extensive neurodegeneration, as now shown in several studies across varying pain conditions." (Tracey, 2008)

53

"Research shows that cortical abnormalities associated with chronic pain are responsible for specific cognitive and behavioral changes including depressive symptoms, anxiety, and hypervigilance." (Przekop & Przekop (2013). In "Chronic Pain: A Neurocognitive Perspective")

54

“...chronic pain patients are more anxious, have more depression, and suffer from poorer sleep, compared with healthy control subjects...Depression may evoke chronic pain by increasing pain sensitivity and lowering pain-tolerance thresholds. Secondary depression may occur as a reaction to chronic pain. Thus, pain may be specified both as a cause and as an effect of depression.”
(Sayar, Arikian & Yontem, 2002)

55

“Persistent pain is common. Whereas acute pain may only impact by interrupting current activity, episodic and persistent pain is likely to interfere with one or more aspects of a person's life and to affect his or her sense of identity.”
(British Pain Society, 2009)

56

“The comorbidity of chronic pain and MDD (major depressive disorder), PTSD, or GAD (generalized anxiety disorder) is common. These conditions cause neurodysregulation and neurodegeneration in the CNS. The underlying pathophysiology of these conditions is central sensitization. Central sensitization syndrome is a complex, neuroimmunologically mediated condition.”
(Kaplan & Heimur, 2013)

57

"...when CNP is a disease (CNP-D), there is no identifiable peripheral pain generator, or, if there is an identifiable peripheral event, it is insufficient to produce pain in a person with an intact, normally functioning nervous system. The nervous system is either injured or sensitized to such a degree that normally non-painful stimuli produce pain. The key element is that the nervous system is not functioning in a normal manner (i.e., it is diseased) and the pain is no longer adaptive, but maladaptive."
(Twillman, 2017),

58

"Stress develops from continual pain because of hyperarousal of the SNS, a process known as "HPA overdrive" because of the involvement of the hypothalamic-pituitary-adrenal axis."
(Ginsberg, 2017)

59

HPA overdrive causes excess glucocorticoid signaling, receptor downregulation, an end to normal negative feedback regulation of the stress response, inhibition of descending cortical pain modulation ("nociceptive braking"), and proliferation of peripheral pro-inflammatory cytokines by catecholamines.
(Ginsberg, 2017)

60

"The list of chronic pain conditions that can become sensitized is quite large, including abdominal pain, fibromyalgia, phantom pain, headache, irritable bowel syndrome, and back pain to name just a few." (Ginsberg, 2017)

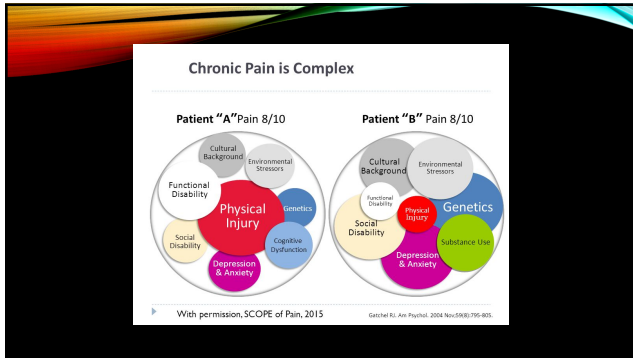
61

"MEASURE WHAT YOU CAN, AND MAKE MEASURABLE THAT WHICH YOU CANNOT."—GALILEO

62

	0	1	2	3	4	5	6	7	8	9	10
	No pain. Feeling perfectly normal.	Very light barely noticeable pain, like a mosquito bite or a poison ivy itch. Most of the time you never think about the pain.	Minor pain, like tightly pinching the fold of skin between the thumb and first finger with the other hand, using the fingernails.	Very noticeable pain, like an acupuncture needle to the nose causing a bloody nose, or a doctor giving you an injection. The pain is not so strong that you change your behavior.	Strong, deep pain, like an average toothache, the initial pain from a bee sting, or minor trauma to part of the body, such as rubbing your toe red. So strong you notice the pain all the time and cannot completely ignore it.	Strong, deep, piercing pain, such as a torn muscle when you stand on a wrong, or mild back pain. Not only do you notice the pain all the time, you are now preoccupied with managing that pain. Normal activities is curtailed. Temporary personality disorders are frequent.	Strong, deep, grinding pain as intense as seems to partially dominate your senses, causing you to think somewhat unclear. At the point you begin to have trouble holding a job or maintaining normal social relationships.	Same as 6 except the pain completely dominates your senses, causing you to think unclear about the time.	Pain so intense you can no longer think clearly at all, and you often undergo personality change. If the pain has been present for a long time, suicide is frequently contemplated and sometimes tried. Compulsive or suicidal.	Pain so intense you cannot tolerate it and demand pain killers or surgery, no matter what the side effects or risk.	Pain so intense you will go unconscious shortly. Most people have never experienced this level of pain. Those who have suffered a major accident and lost consciousness as a result of the pain and not blood loss, have experienced level 10.
Minor											
Does not interfere with most activities; able to adapt to pain psychologically.											
Moderate											
Interferes with many activities. Requires lifestyle changes but patient remains independent. Unable to adapt to pain.											
Severe											
Unable to engage in normal activities. Patient is disabled and unable to function independently.											

63



67

The effects of chronic or intractable pain may include poor sleep, restricted mobility, decreased activity, poor mood, greater use of medications and more health practitioner visits.

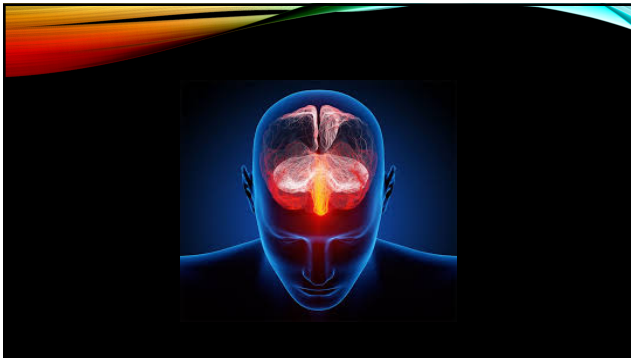
(<https://www.practicalpainmanagement.com/resources/diagnostic-tests/measuring-clinical-outcomes-chronic-pain-patients>)

68

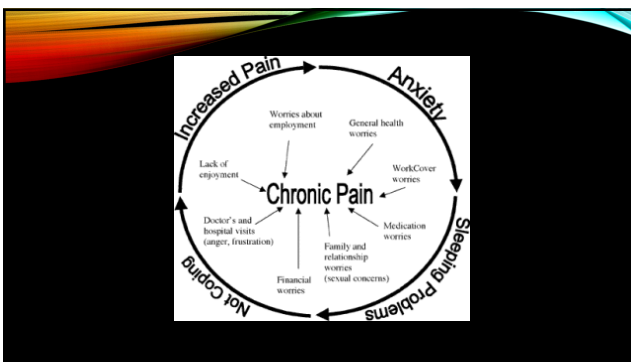
The psychophysical part of our study supported the hypothesis that the NAc signal difference between the two groups reflects differences in the predicted valuation of the offset of the acute painful stimulus; in chronic pain patients, it reflects the prediction of worsening the ongoing back pain, as if the patients were disappointed that the painful stimulus was discontinued, while in the control subjects it reflects the prediction of relief," explains Dr. Apkarian. "These findings point to a potential dysfunctional associative learning process in chronic pain patients."

("Hurts so good: Chronic pain changes brain response to acute pain." ScienceDaily, 15 April 2010)

69



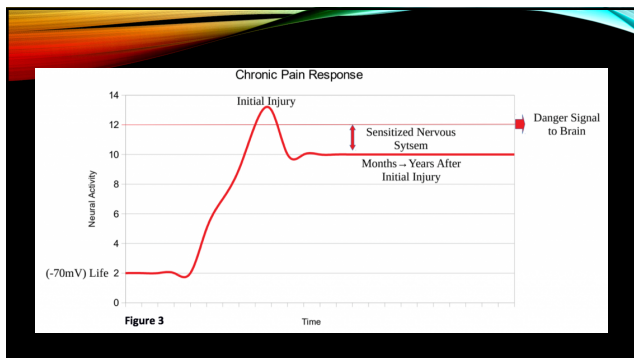
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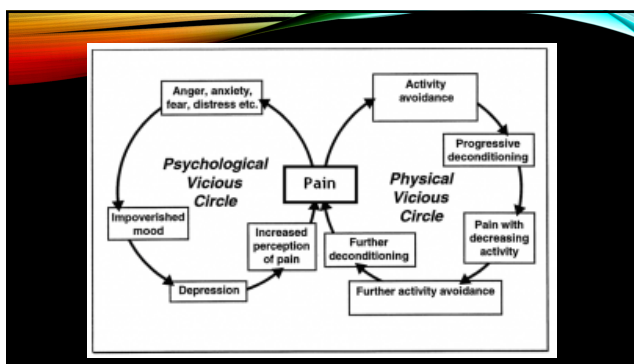
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Effects of Chronic Pain on the Patient	
Physical Functioning <ul style="list-style-type: none"> • Ability to perform activities of daily living • Sleep disturbances 	Psychological Morbidity <ul style="list-style-type: none"> • Depression • Anxiety • Anger • Loss of self-esteem
Social Consequences <ul style="list-style-type: none"> • Relationships with family and friends • Intimacy/sexual activity • Social isolation 	Societal Consequences <ul style="list-style-type: none"> • Healthcare costs • Disability • Lost workdays

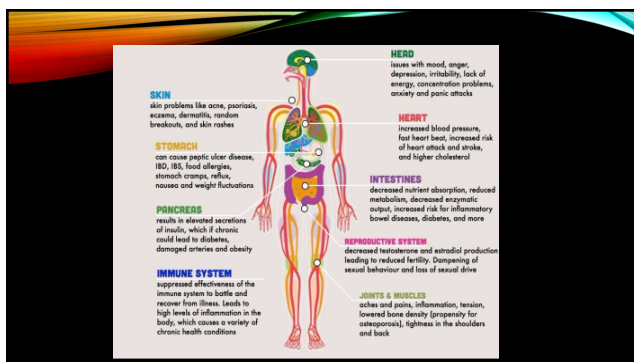
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Chronic Pain, Depression

- Potentiation of depression neurochemistry
 - Norepinephrine
 - Serotonin
 - Dopamine
- Likely 50-75%
- Clinical recognition problems
- Treatment problems
 - Opioid resistance
 - Reduced motivation

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PAIN / EMOTION CHART

STRESS

EMOTIONAL BURDEN

FINANCIAL WORRIES

FEAR OF CHANGE

BIG EGO

LACK OF PLEASURE

LACK OF FORGIVENESS

LACK OF EMOTIONAL SUPPORT

LACK OF FLEXIBILITY

ISOLATION

TENSION & JEALOUSY

DEPRESSION

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CLINICAL PAIN MANAGEMENT CHRONIC PAIN

Neuropathic pain is a form of chronic pain defined as, "Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system."

While the biological advantage to the organism of nociceptive pain is readily identifiable, it is less easy to do so for neuropathic pain and it is probable that, in broad terms, neuropathic pain is a result of a pathological process representing a disordered, regenerative response to neuronal damage.

Source: Clinical Pain Management: Chronic Pain, 2nd edition, Eds. Wilson, Watson, Haythornthwaite, and Jensen, 2008 Hodder Arnold

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EXCITATORY MECHANISMS

The afferent barrage associated with peripheral nerve injury is associated with the development of a sustained state of hyperexcitability of dorsal horn neurons, a process dubbed central sensitization.

In addition to events such as lowering of activation thresholds of spinal neurons, central sensitization is characterized by the appearance of "wind-up".

Source: Clinical Pain Management, Chronic Pain, 2nd edition, Eds. Wilson, Watson, Haythornthwaite, and Jensen, 2008 Hodder Arnold

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ANATOMICAL REORGANIZATION

This synaptic rearrangement means that second-order dorsal horn neurons that normally receive predominantly high threshold sensory input, now receive inputs from low threshold mechano-receptors. Such misinterpretation of information within the spinal cord may result in low threshold sensory information being interpreted as nociceptive, leading to the emergence of hypersensitivity after peripheral nerve injury.

Source: Clinical Pain Management, Chronic Pain, 2nd edition, Eds. Wilson, Watson, Haythornthwaite, and Jensen, 2008 Hodder Arnold

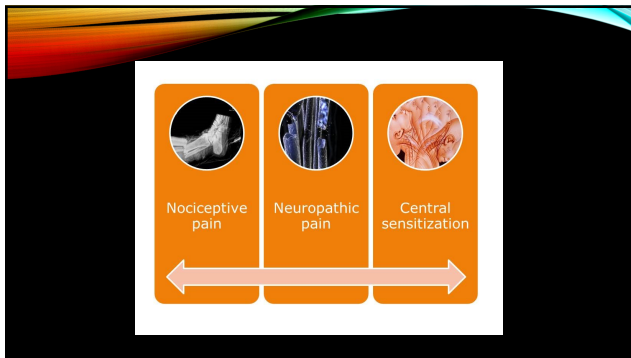
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THE ROLE OF NONNEURONAL CELLS

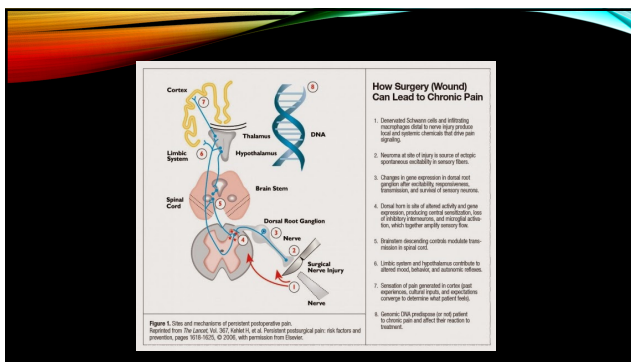
The status of microglia in the spinal cord has been examined in a variety of nerve injury models and substantial evidence, both direct and indirect, indicates that microgliosis fundamentally contributes to the pathophysiology of neuropathic pain.

Source: Clinical Pain Management, Chronic Pain, 2nd edition, Eds. Wilson, Watson, Haythornthwaite, and Jensen, 2008 Hodder Arnold

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What is central sensitization/dysfunctional pain?

Definition	Examples	Pain Quality
<ul style="list-style-type: none"> • Amplification of neural signaling within the CNS that elicits pain hypersensitivity 	<ul style="list-style-type: none"> • Fibromyalgia • Tension-type headache • Irritable bowel syndrome • Interstitial cystitis • Temporomandibular joint pain • May be present in many patients with chronic low back pain, osteoarthritis and rheumatoid arthritis 	<ul style="list-style-type: none"> • Often diffuse • Frequently with allodynia and/or hyperalgesia • Rarely burning, lancinating or electric shock-like

CNS = central nervous system
Source: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4591121/>

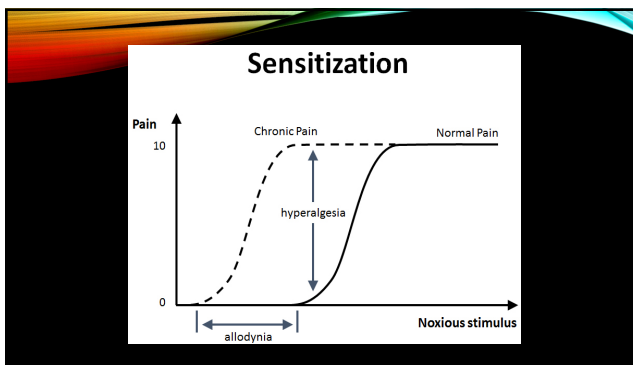
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Clinical Features of Central Sensitization/Dysfunctional Pain

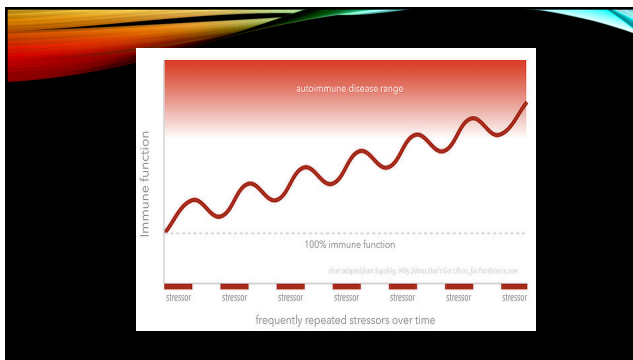
Pain <ul style="list-style-type: none"> • Pain all over body • Muscles stiff/ticky • Headaches • Pain in jaw • Pelvic pain • Back/urination pain 	Anxiety/depression <ul style="list-style-type: none"> • Sad or depressed • Anxiety • Stress makes symptoms worse • Tenses in neck and shoulder • Grind/clench teeth
Fatigue <ul style="list-style-type: none"> • Do not sleep well • Unrefreshed in morning • Easily tired with physical activity 	Other symptoms <ul style="list-style-type: none"> • Difficulty concentrating • Need help with daily activities • Sensitive to bright lights • Skin problems • Diarrhea/constipation

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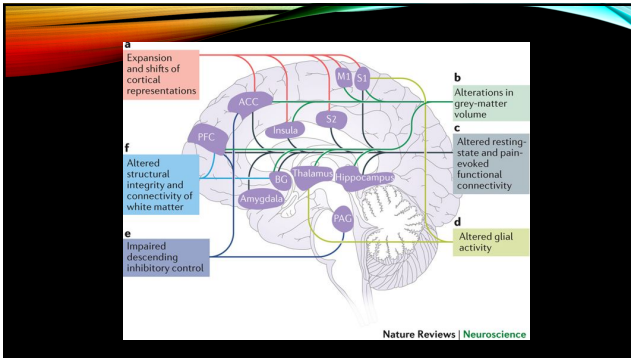
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Paul was on 90mg of oxycodone four times a day for his chronic pain. He gradually weaned himself off oxycodone using marijuana and now uses only marijuana to treat his pain. He has less pain and better quality of life than when he was on opioids. He lives in New York State where the medical marijuana law was updated to include chronic pain as a qualifying condition on 3/22/17.

Most people believe that the most powerful weapons we have against severe pain are opioids like Vicodin, Percocet, Hydrocodone and Oxycodone. But is this really true? It's an important question because opioids are highly addictive and taking too much can be fatal. Millions of Americans have become addicted to prescription opioids and most have been medical patients taking them as directed. Even worse, more than 200,000 Americans have died of accidental overdoses of these drugs.

(<https://www.paintreatmentdirectory.com/posts/marijuana-vs-opioids-for-pain-420>)

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A 2011 review of randomized controlled studies of cannabinoids for treatment of chronic noncancer pain found significant effects on pain relief as well as significant improvements in sleep. Most of the studies were of neuropathic pain, but one study each of fibromyalgia and rheumatoid arthritis also reported positive results. No serious adverse effects were reported.

A 2014 survey by the National Pain Foundation of fibromyalgia patients found that 62% of those who tried marijuana said it was very effective at treating their symptoms, 33% said it helped a little and only 5% said it didn't help at all.

(<https://www.paintreatmentdirectory.com/posts/marijuana-vs-opioids-for-pain-420>)

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A survey of 100 consecutive medical marijuana patients who were returning for their annual recertification in Hawaii found that 97% used marijuana primarily for relief of chronic pain. They reported an average 64% decrease in pain – a decrease on a 10-point pain scale from 7.8 to 2.8. Half also reported relief from stress and anxiety; 45% reported insomnia relief; and 71% reported no negative side effects. No serious adverse effects were reported. Some of the patients reported they were able to reduce or eliminate their use of opioids.

(<https://www.paintreatmentdirectory.com/posts/marijuana-vs-opioids-for-pain-420>)

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In a 2015 review of controlled studies of cannabinoids in the treatment of chronic neuropathic pain the authors concluded that cannabinoids provide significant pain relief in chronic neuropathic pain in conditions where other treatments do not work. They found that reported side effects in the reviewed studies were minor.

(<https://www.paintreatmentdirectory.com/posts/marijuana-vs-opioids-for-pain-420>)

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CHRONIC PAIN: TAKE HOME MESSAGE

- Involves complex changes in the brain and nervous system that lead to dysfunction
- May be difficult to detect underlying mechanisms
- Assessment and treatment address all dimensions of the biopsychosocial experience
- Complete relief and cure often unrealistic
- Treatment is aimed on empowering the patient to manage the pain using positive coping skills, lifestyle changes and judicious use of medications

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The very existence of the reality we experience is dependent on our past decisions, modified by the decisions we are making right now. Objective reality is fluid, and dependent on both the past and the present. One is unchangeable (even though we can revise the understanding of it in our minds); the other is dependent on that which we think and do this very instant, in limited and partial understanding of the reality defined by our past. This dependency creates an existential dilemma, wherein we are like Hamlet, not able to end the slings and arrows of outrageous fortune, and by opposing, end them. His dilemma, and ours, arises not in that sleep of death, but that of life, wherein what dreams may come.

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