Chapter 1 : Neurobiological Basis for Chronic Pain

Chapter 1 provides the pain clinician with a brief overview of the basic information about pain neurophysiology (including the nervous system areas involved in the experience of pain, peripheral mechanisms, spinal mechanisms, supraspinal mechanisms, cortical processes, global activation, plasticity) and chronic pain classifications (neuropathic pain, nociceptive pain, psychogenic pain, and.

While this is unlikely to be an exclusive list of influential psychosocial factors, these are well researched and evidenced. This page will review each of these in turn. Fear avoidance Pain and Fear Fear is a typical emotional response to an experience that is perceived to be threatening, such as one that leads to a pain sensation [4] [5]. This pattern can lead to fear and avoidance of work-related activities, movement, and re-injury [6]. Kinesophobia is a term used interchangeably with fear avoidance in health and pain literature. The individual will rest and protect the painful area as an adaptive behaviour to allow tissue healing to occur [3]. For others, they may be unable to overcome the fearful emotion and the resulting avoidance behaviour persists [6]. A cycle of continued activity avoidance and fearful emotions may ensue, the longstanding effect of which in patients with chronic pain may have an adverse effect on the musculoskeletal and cardiovascular system disuse syndrome [8] , which fundamentally increases disability [3] [6]. Vlaeyen and Linton [6] have described the interconnections contributing to fear avoidance as follows: Due to hypervigilance, the avoidance behaviour begins to occur in anticipation rather than in response to pain. As there are fewer and fewer opportunities to correct the wrongful association of pain with the avoided activity, the behaviour perpetuates itself and fear avoidance persists. Studies have shown that high levels of fear avoidance can be a predictor for future episodes of pain [14] [15] [16] [17] [18] but on the contrary, studies [19] that showed more support for the link of depression with poor function and disability at this early stage [20] [21] In the learning pathway model, fear avoidance becomes a conditioned response through association of pain with movement [6] [4] [20]. The behaviour of avoiding expected pain-provoking movement or activities to prevent new episodes of pain is learned through experience [22] The individual may anticipate similar experiences and associate non-painful or non-harmful experiences with pain resulting in persistent fear avoidance behaviour. Any early fear avoidance behaviours, especially for those who have strong negative cognitions about their pain like anxiety and depression [23] [20] , could be identified. These patients could be monitored so they do not continue with this coping strategy once the acute stage has passed. Physiotherapists managing these patients may find it useful to categorise what kind of fear avoiders their patients are. Rainville et al [4] proposed the following categories: Furthermore, explaining how fear avoidance affects the physiological feelings they may be experiencing will help them to understand how their perception of pain may be altered. These mood changes could further affect perception of pain Disuse or disability from persistent avoidance behavior will experience pain with much less provocation than before lower the threshold for experiencing future pain. Several self-reported measures of fear avoidance could be used in the clinic to help assess fear avoidance. These include the following: Fear-Avoidance Beliefs Questionnaire FABQ identifies how beliefs about work and physical activity affect low back pain [25] Survey of Pain Attitudes SOPA assesses patients attitudes towards pain control, pain-related disability, medical cures of pain, solicitude of others, and medication for pain [26] Tampa Scale for Kinesiophobia TSK assesses fear of re-injury due to movement [7] Anxiety and Depression Anxiety Anxiety is described as a general term for several disorders that include; uneasiness, apprehension, nervousness, fear and worrying. Unfortunately much of this literature does not solely focus on anxiety alone. A study which aimed to evaluate the prediction of chronic pain looked at anxiety, depression and social stressors as risk factors and the severity of pain at 3, 6 and 12 months in patients. They found a strong correlation between baseline anxiety which predicted pain severity at 12 months. Interestingly no correlation was found for social stressors or depression. In a TMsI study, anxiety was found to predict pain intensity at different time-frames post injury whereas depression, social support, length of hospital stay and self-efficacy had no substantial effect. They summarised that pain predicted anxiety and depression in the first year, but anxiety only predicted pain intensity from months. Anxiety symptoms were therefore hypothesised

as the primary causative factor of persistent pain in this cohort study. It is therefore important to address patients anxiety early to prevent it persisting and causing a negative barrier to their recovery. One study examined the validity of a single question to screen for depression and anxiety [41]. Single question screening tools were compared with validated questionnaires such as mini-international neuropsychiatric interview, HAD scale and Hopkins symptom checklist. Therefore single question screening tools are fairly effective in identifying anxiety and could be utilised into early assessments with chronic pain patients. Depression Depression is described as a general term for mental disorders which include; sadness, loss of interest or pleasure, feelings of low self-worth and low mood. In a study examining the impact of anxiety and depression in phantom limb pain PLP patients mean depression scores were higher, although non-significant, in patients with non-PLP chronic pain syndromes. A study of low back pain observed higher prevalence of depression symptoms Pain, Anxiety and Depression Anxiety and depression appear to be overlapping conditions. In patients with chronic musculoskeletal pain, those with both anxiety and depression experienced the greatest pain severity, a highly significant finding. Furthermore combined psychiatric co-morbidity was strongly associated with disability days with; This study also found a significant correlation with reduced QoL when all three conditions presented together. Thus it comes into question as to why these psychiatric disorders; a present together, b develop with the onset of traumatic pain, c appear to cause acute pain to persist and d cause more severe functional deficit together than when presenting independently. Many studies have looked into the pathophysiology of pain, anxiety and depression to find answers and to facilitate more successful treatment of these complex conditions. Impact of Depression and Anxiety on the Pain Experience Anxiety A physiological model of anxiety may explain its role in pain perception; It is known that a state of acute anxiety stimulates the sympathetic nervous system SNS causing increased muscle tension, increased nociceptive input and increased sensitivity to pain stimuli , thus explaining why anxiety may correspond to increased pain perception. Corticosteroid hormones, for example, released after stress may play a part in pain modulation [46] as cortisol a steroid hormone known to stimulate the SNS has been found in higher levels in those with chronic pain [47]. Furthermore neurotransmitters, neuropeptides and pro-inflammatory cytokines have been found to either mediate or modulate pain. Therefore these physiological processes overlap in both anxiety and pain. There is evidence accumulating to show atypical sensory processing in the brain and dysfunction of skeletal muscle nociception, however the latter may not explain pain persistence in non-MSK pathologies where chronic pain has clearly been observed. A more permanent state of anxiety results in chronic muscle tension and anticipatory anxiety which leads to even more disability. Decreases in activities, especially those which provide meaning and reinforcement, may result in greater social isolation, decreased self-efficacy, increased feelings of uselessness and subsequent increases in anxiety and depression symptoms. Functional magnetic resonance imaging fMRI studies along with blood-oxygenated level dependent contrast BOLD techniques have been utilised in various studies to map common areas of brain activation by detecting changes in blood flow. These studies have been able to map similar areas of brain activation for anxiety and pain. It has been shown that there is exaggerated brain response in patients with social anxiety disorder [48] [. The areas identified were the midline cortical regions such as; the ventromedial pre-frontal cortex PFC , dorsomedial PFC, posterior cingulate cortex implicated in self-referential process , emotional centre amygdala and memory area hippocampal gyrus. This indicates that there are integrated neural pathways associated with anxiety, pain processing, memory and concept of the self â€” the latter potentially implicating personality traits into anxiety and pain. Depression There is less known evidence about the physiology of depression compared to anxiety however it has been postulated that people with depression or a depressive personality have a greater sensitivity to acute and chronic pain. Similarly to anxiety, excessive sympathetic activity and elevated pro-inflammatory cytokine production is also postulated in the aetiology of depression thus providing a potential physiological link between all three conditions and a possible reason for the overlapping prevalence within patient presentations. Despite these CNS observations It is known that in healthy, non-depressed human volunteers pain-intensity related haemodynamic changes have been observed in all of the above brain sites [49] Further studies compared the response of brain areas with BOLD techniques; 13 patients suffering from an acute episode of major depressive disorder MDD were investigated during painful stimulus application and

compared to 13 control subjects [50]. The results demonstrated increased activation of the pain matrix and increased thermal pain thresholds compared to healthy subjects. They speculated that the brain area activation may be linked to an underlying prefrontal psychopathology in depression. In another BOLD study [51] patients with diagnosed MDD showed greater activation of pain-related brain sites right insular, dorsal anterior cingulate, right amygdala during anticipation of painful, heat stimuli compared with healthy subjects. Furthermore in MDD subjects, greater activation of the amygdala was associated with greater levels of perceived helplessness. This implies anticipation of pain may further pain experience and activation of the pain matrix potentially contributing to persistence of pain. In other studies the cingulate and PFC has also been implicated in pain modulation and may contribute to chronic pain associated with fibromyalgia syndrome. The brain is perceived as a mediator for nociceptive pain, but also for pain behaviours which are known to influence pain itself, likely causing its persistence. It is clear from research studies that physiology of depression, anxiety and pain is overlapping. However it is difficult to establish which the primary cause is and which is secondary. Catastrophising "Pain catastrophizing refers to a negative cognitive-affective response to anticipated or actual pain [52]. It was formally introduced by Albert Ellis and was used to describe a mal-adaptive cognitive style in those with anxiety and depressive disorders [53]. The research focussed on the fact that catastrophizing was an exaggerated and negative cognitive and emotional response during an actual or anticipated painful stimulation. Catastrophizing is often characterised by people magnifying their feelings about painful situations and ruminating about them which can combine with feelings of helplessness [54]. However, it is also apparent that fear avoidance and depression are important predictors of pain intensity and disability [56]. High correlations between fear avoidance and pain catastrophizing have been found [57] , however only pain catastrophizing predicted pain intensity [58]. This highlights the importance of a multifactorial approach to pain management and the significance catastrophizing has in moulding the pain experience. How can we assess the levels of catastrophizing? Research has developed self-report instruments that can be used in various populations [63]. This incorporates magnification, rumination and helplessness. Highlighting the need for a multifactorial approach, participants are asked to rate the extent to which they experience each item by recalling previous experiences with pain [64]. The more negative experiences with pain can correlate with higher levels or pain intensity and disability [65] Why does this happen? There are various theoretical mechanisms of action including the appraisal theory [66] where the levels of helplessness the person is feeling will affect their ability to cope. Evidence has also suggested that there is an increased nociceptive transmission via spinal gating mechanisms and a central sensitisation of pain. This may represent a central nervous mechanism which is contributing to the development, maintenance and aggravation of persistent pain [70] [71] [72]. It is therefore apparent that both psychological and physiological factors play a huge part in the perception, maintenance, experience and management of pain and both directly influence each other. It is important to recognise these factors in both the acute and chronic pain patient in order to understand what aspects of their pain are a barrier to their recovery. Chronic Stress and Pain A physiologic stress response may be evoked by fear or perceived threat to safety, status, or well-being and elicits the secretion of sympathetic catecholamines epinephrine and norepinephrine and neuroendocrine hormones cortisol to promote survival and motivate success. Cortisol is a potent anti-inflammatory that functions to mobilize glucose reserves for energy and modulate inflammation. Cortisol also may facilitate the consolidation of fear-based memories for future survival and avoidance of danger. Although short-term stress may be adaptive, maladaptive responses eg, magnification, rumination, helplessness to pain or nonâ€”pain-related stressors may intensify cortisol secretion and condition a sensitized physiologic stress response that is readily recruited. Ultimately, a prolonged or exaggerated stress response may perpetuate cortisol dysfunction, widespread inflammation, and pain. The sympathetic nervous system promotes catabolic tissue breakdown and fat metabolism to mobilize glucose for energy and promote arousal, alertness, motivation, and goal-directed behavior. Cortisol is a vital catabolic hormone produced by the adrenal cortex of the kidney. In the presence of a physical or psychological threat, cortisol levels surge to provide the energy and substrate necessary to cope with stress-provoking stimuli or escape from danger. Exaggerated or recurrent negative cognitions, rumination or worry, magnification, and helplessness are all maladaptive catastrophizing

responses to pain or nonâ€”pain-related stress that may prolong cortisol secretion. Prior to addressing nonâ€”pain-related stress in pain management, it is important to identify patients most likely to benefit from stress management. Objective measures of cortisol may be obtained from blood, saliva, urine, or hair; however, laboratory tests may not be appropriate for the physical therapy setting, and each test has specific limitations. Alternatively, there are a multitude of subjective measures of self-reported stress that may be easily integrated into the screening process. Following the identification of stress or maladaptive coping skills during initial screening, educating patients about the role of stress in the pain experience may allow for cortical inhibition of emotional fear-based responses to nonthreatening stimuli. Journal of Hand Therapy ; A pain neuromatrix approach to patients with chronic pain. Manual Therapy doi:

Chapter 2 : The Anatomy and Physiology of Pain - Pain and Disability - NCBI Bookshelf

TY - JOUR. T1 - The biological basis of pain. AU - Covington,Edward C. PY - Y1 - N2 - Pain is characterized not only by location and quality, but also in emotional terms (terrifying, unbearable, agonizing).

Biological Evolution Human beings are animals. This is not a reference to our behavior although, of course, some people do act like animals. It is a reference to the fact that humans are biological creatures, as much as crocodiles, cougars, and capybara. We are the product of millions of years of evolution, our physical make-up changing to make us fitter to survive and reproduce. However, although humans are animals, we also have something that no other animal has: We gather in families, tribes, clans, nations. We have an incredibly sophisticated method of interacting -- speech. We can communicate over time and distance through printing and broadcasting. Our memories are the longest, our interactions the most intricate, our perception of the world simultaneously the broadest and most detailed. The combination of biology and society is what makes us what we are and do what we do. Biology guides our responses to stimuli, based on thousands of generations of ancestors surviving because of their responses. Our social structures dictate restrictions on and alterations in how we carry out our biological responses. Neither biology nor society stands without the other. For some people, this is a contradiction -- either nature biology controls people, or nurture society does. But in fact we filter everything through both to determine how we react to stimuli. The following is a discussion of the two sides of human nature: I will discuss each in turn. The latter includes mentally or economically healthy. Since human beings are very social creatures, we may also apply self-preservation to other people, such as our families. However, I will discuss that in the next chapter. A doe, unaware of the danger lurking in the grass, separates slightly from the herd. With a rush, the lioness bursts into a run to take down the doe. The startled doe bounds away, running and swerving, trying to escape. The lioness, unable to keep up the pace, gives up, and the doe escapes back into the herd. A zebra is not so lucky, and the pride feasts. The Donner Party was a group of settlers trekking to California in Trapped by snow in the Sierra Nevada Mountains , they survived as best they could. This included resorting to cannibalism when they ran out of food, eating the bodies of those who had died. To be successful as a species, the members of that species must have a desire to survive long enough to pass on their genes to offspring. A species with a death-wish dies out rather quickly. It is from those individuals and therefore species that all living things are descended. The desire to stay alive is an instinctive one, built into the psyche of the organism. The organism will seek those elements of its environment that will enhance its chances for survival. These include food, water, oxygen, and periods of rest to allow the body to repair any wear and tear on the tissues. Alternately, it will avoid or evade those elements that might reduce its chances for survival. Such dangers include predators, starvation, dehydration, asphyxiation, and situations that can cause damage to the body. These seek or avoid drives influence the behavior of organisms: The desire to stay alive is also a selfish instinct, since it is personal survival that the organism is seeking. Survival Through Evolution A phrase that has often been misquoted, "Survival of the Fittest," actually means survival of the fit. By fit, I mean an organism has those attributes that allow it to get the most out of its environment: The better it is at doing this, the more fit it is. At this point I should discuss the niche. A niche is a position within an environment that calls for certain attributes to exploit that environment. An environment can contain any of a variety of elements: It can also contain animal life, from the tiniest insects to blue whales and everything in between. It is the combination and degree of each of these elements that create niches. Say there are many small animals, like mice, in an area. A small carnivore like a wildcat could find a lot of food. Thus, it would fit into this niche and thrive. However, when the number of mice decreases, the wildcat can find less food, and has a lesser chance of survival. If the wildcat has competition from other small carnivores, like foxes, the one that is particularly good as a predator, through cunning or speed or some other attribute, will catch more food. This lessens the amount of food available for the competition, and thus drives the competition out. If the fox is better at catching mice that is, more fit than the wildcat, the wildcat will either die or have to move to another niche in which it will be the better predator. On the other hand, if there are no small animals but many big animals, like antelope, neither a fox nor a wildcat would have much success preying on them. However, large

carnivores such as lions would. Of course, nothing stays the same forever. Niches alter through geologic, climatic and, in the present day, man-made changes in land, water and air. A volcano can create a new island. An ice age can lock up huge quantities of water in ice caps and glaciers, creating areas of land where oceans once rolled. Continental drift can push seabeds to the tops of mountains. Humans can chop down forests and build cities. All these changes alter the niches, the environmental conditions under which the life in those niches live. Of course, this means the life has to change as well, to match the new conditions. An example is a moth in England. It was originally a mottled white, which allowed it to blend into the light bark of the trees in its area. However, in the 19th century factories in this area began to belch out soot from their chimneys that settled on the trees, changing the tree bark from mottled white to mottled black. The moth could no longer blend in and thus was easy prey to birds. However, some of the moths were darker and thus less noticeable. After a few generations of these darker moths surviving and passing on their genes, the standard color changed to mottled black, and the moth, now blending into the dark bark, survives. Note that such changes are not conscious decisions made by the organism: Some of those variations are detrimental: However, as the conditions in a niche change, those same variations can become advantageous, enhancing rather than weakening chances for survival. If no variations exist in a species that contribute to survival when conditions change, or if conditions change too quickly for advantageous variations to be passed on to enough descendants, 1 the species can die out. Survival Through Strategy Other changes in an organism can develop over time. For example, some animals have perfected the technique of hibernating during periods when the food supply is low. Marmots have developed a social structure that provides lookouts who watch for predators and sound a warning when one appears. Prairie dogs dig their burrows with multiple entrances and exits so if a predator comes in one door, the dogs can leave through another. These survival strategies are adaptations to niche conditions, but unlike physical changes are not necessarily genetic changes. However, some survival strategies are learned behaviors. That is, the young learn them from older animals that learned them from their ancestors. For example, most predators teach their young the techniques of successful hunting. In general, it appears the higher the complexity of the nervous system of the animal, the more likely strategies are learned rather than instinctive. Sharks, with a relatively simple nervous system, hunt by instinct and need no instruction on how to go about it. Lions, with a complex system, must learn the techniques of stealth, stalk, and attack. Again, in most animals, the strategies are not conscious decisions, but responses to stimuli such as hunger, thirst, asphyxiation, fear, or exhaustion. If conditions change so the instinctive strategy is dangerous rather than beneficial, the animal can die. The musk ox strategy is to form a stationary circle with the young in the center and the older members facing outward, rather than running away. This is excellent against wolves, but deadly when faced with spears and guns perfect, however, for the human survival strategy of group hunting with weapons. For example, the genetically dictated instinctive reaction to a threat to self-preservation is the "fight or flight" syndrome. The changes include an increased rate of respiration to provide more oxygen to the muscles, an accelerated heart beat to speed up the blood flow, a lessening in sensitivity to pain, and changes in the blood stream, including an injection of adrenalin and diversion away from the organs to the muscles. These physiological changes prepare the animal to either fight for survival or run away from danger. For example, an amoeba will avoid an electric field automatically -- an instinctive reaction unmitigated by a survival strategy. A starving rat, however, will run across an electrified grid that gives it painful shocks if there is food on the other side. Humans are subject to the same stimuli and reactions as any other animal. Hunger, thirst, asphyxiation, fear, and exhaustion are physical sensations that cause instinctive physical reactions. Thus you eat when hungry, drink when thirsty, fight for air, run from dangerous situations, sleep. These responses are instinctive, and we have no more control over them than we do over our eye color. Actually, we do have control over our eye color. The reason we do is why our approach to self-preservation is different from all other creatures.

Chapter 3 : Are We Close To A Complete Understanding Of The Biological Basis Of Pain? - ABC News

Introduction. The International Association for the Study of Pain (IASP) definition of pain highlights the multidimensional components of pain. The interaction of these dimensions (sensory/discriminative: intensity, location, quality and behaviour of pain, cognitive-evaluative: thoughts of the pain as influenced by previous experiences and knowledge, and motivational-affective: emotional.

Exploring Phantom Limb Pain Psychology Nearly all amputees report having a phantom limb experience, and for the majority, it is excruciatingly painful. In fact, according to neurologist Vilayanur S. Ramachandran at the Center for the Brain and Cognition at the University of California, San Diego, nearly 70 percent of amputees continue to suffer from intermittent pain in a limb decades after it has been removed. Unfortunately, most current treatments are ineffective because the biological basis for the pain is not completely understood. According to Nicolelis, most scientists believe that phantom limb perceptions stem from residual activity in the regions of the neuromatrix formerly assigned to the missing limb. In addition, he suggests that future phantom limb treatments may include brain remapping techniques. Nicolelis cites the results of several experiments performed on the peripheral nervous system to support the theory that a complex neuromatrix develops and controls our body image, including: Amputees with a severed peripheral nervous system continued to suffer from phantom limb pain, which suggests the source is more likely the brain; When different, but specific, areas of the brain are damaged, a drastic change in body image and perception occurs, which indicates that they are result of a complex, interactive network in the brain, rather than just the function of one localized region; When a person experiences a drastic change in body structure, corresponding changes can be observed in the brain, which supports the theories of neural plasticity and brain remapping. Additional research by Ramachandran indicates the likelihood of phantom limb pain is significantly reduced in young children, suggesting that the body image neuromatrix is formed during the first our first eight years of development. In the past, scientists believed that once the neuromatrix was fully developed, it could not be reconfigured. As a result, treatments ranging from prescription drugs and acupuncture to electric spinal cord stimulation SCS were used to treat phantom limb pain â€" all with marginal success. Based upon experiments that show sensory input activates nearby areas of the Penfield map of the motor cortex after a limb is amputated, scientists now believe that the brain is more flexible, and therefore, the neuromatrix can be reorganized. Treatment for Phantom Limb Pain This research and insight into the organizational structure of the brain creates a huge opportunity for a new and exciting treatment for phantom limb pain â€" illusions. For example, Ramachandran and his colleagues are using mirrors to create the illusion that the phantom limb is real. Because severity of pain before amputation is a major risk factor, the best treatment for phantom limb pain begins before the phenomenon starts. Before surgery, patients should be as pain-free as possible. In addition, special care should be taken to ensure the patient heals quickly and without complications. Finally, if phantom limb pain develops, it may be most effectively treated by reorganizing the brain. While this may currently require the use of rudimentary illusion methods like the mirror box, there is no doubt that a better understanding of the neuromatrix and advancements in technology may enable future treatments like stimulation of specified brain regions and enhanced methods of creating illusions, perhaps by integrating the use of holograms, lasers and things perhaps we can only dream of at this point in time. Implications for Future Treatment of Phantom Limb Pain These advancements in treatment of phantom limb pain also have larger implications for science and medicine. The more we understand about the organizational function of the brain, the more effective we will be at treating any disorder, including pain.

Chapter 4 : Psychological pain - Wikipedia

Pain is characterized not only by location and quality, but also in emotional terms (terrifying, unbearable, agonizing). Pain has an essential duality. It is both sensation and emotion.

By Ana Sandoiu Chronic fatigue syndrome is a debilitating disorder characterized by severe fatigue that lasts for more than 6 months. The condition is also accompanied by a range of symptoms, from muscle pain and headaches to cognitive dysfunction. The illness can sometimes be difficult to diagnose, and its cause is not yet known. However, new research finds the biological basis for two subgroups of chronic fatigue syndrome, which may in the future help clinicians to diagnose the disease and treat it more effectively. New research shows that there may be two subgroups among patients with chronic fatigue syndrome and investigates the biological evidence for the condition. Chronic fatigue syndrome CFS , also sometimes referred to as myalgic encephalomyelitis ME , affects more than 1 million people in the United States. The disease is usually most prevalent in women in their 40s and 50s, with CFS being four times more frequent in women than in men. Symptoms include joint pain, painful lymph nodes, having trouble sleeping, and headaches , as well as difficulty concentrating and remembering things. Medical professionals do not yet know what causes the disease. CFS is difficult to identify as there is no test for it, and because it shares some of its symptoms with other illnesses. However, new research investigates the biological basis for the illness and identifies two subgroups of CFS that go on to develop differently: Mady Hornig, director of translational research at CII and associate professor of epidemiology at the university. The results were published in the journal Translational Psychiatry. Those with atypical CFS found to have lower levels of immune molecules Hornig and team performed immunoassays to measure 51 immune biomarkers in the cerebrospinal fluid of 32 people with classical CFS, and another 27 with atypical CFS. The tests showed lower levels of immune molecules in those with atypical CFS than in those with the classical variant. The analyses revealed drastically lower levels of interleukin 7 a protein that plays a key role in the adaptive immune response to infections , interleukin 17A, and chemokine ligand 9 molecules with a key role in the adaptive immunity to neurological illnesses. Additionally, these biological features were accompanied by different trajectories of disease history and comorbidities. Those with atypical CFS tended to have a history of viral encephalitis and tended to fall ill after traveling abroad or receiving a blood transfusion. Furthermore, people with atypical CFS went on to develop simultaneous conditions such as seizure disorders, several types of cancers , or demyelinating disorders - that is, multiple sclerosis-like diseases that damage myelin , the protective sheath around the nerve cells in our brains and spinal cords. Ian Lipkin, also explains the contribution of the findings: However, only people with classical CFS displayed the previously discovered 3-year mark of CFS - namely, after 3 years of having an "overzealous" immune system, CFS patients show signs of immune "exhaustion," with dramatic drops in their levels of immune molecules. In this new study, only those with classical CFS had this drop in immune molecules after 3 years, whereas those with atypical CFS displayed steady or increased levels of cytokines and chemokines - proteins that control the development and activation of immune cells. She also suggests that genetic predispositions may cause the immune system to respond differently in atypical individuals. Researchers at CII continue to investigate other subgroups of CFS patients, such as patients with allergies, cognitive impairment, and gastrointestinal problems. Learn how altered gut bacteria could cause CFS.

Chapter 5 : The biological basis of mood disorders By OpenStax (Page 5/27) | blog.quintoapp.com

Abstract. The understanding of human pain perception, nociceptive systems, and analgesia is complicated by the variety of psychological, social and contextual variables that may interact with noxious sensory input to produce inexplicable changes in the strength, unpleasantness or quality of pain that is experienced.

George Boeree Pain is a perception, and like any perception, it is rooted in sensation, and on the biological level, in the stimulation of receptor neurons. Also like other forms of perception, pain is sometimes experienced when there is no corresponding biological basis! Nociceptors In the skin and other tissues of the body, there are special sensory neurons called nociceptors. These neurons translate certain stimuli into action potentials that are then transmitted to more central parts of the nervous system, such as the brain. There are four kinds of nociceptors: Thermal nociceptors are sensitive to high or low temperatures. Mechanical nociceptors respond to strong pressure to the skin that comes with cuts and blows. These receptors respond quickly, and often trigger protective reflexes! Chemical nociceptors respond to a variety of chemicals released with tissue damage, as well as to external chemicals such as capsaicin the chemical that makes hot peppers "hot" and spider venom. Polymodal nociceptors can be excited by strong pressure, by heat or cold, and by chemical stimulation as well. Silent or sleeping nociceptors stay quiet - hence the name - but become more sensitive to stimulation when they are surrounded by inflammation. When there is significant damage to tissue, several chemicals are released into the area around the nociceptors. This develops into what is called the "inflammatory soup," an acidic mixture that stimulates and sensitizes the nociceptors into a state called hyperalgesia, which is Greek for "super pain. Prostaglandins are released by damaged cells Potassium is released by damaged cells. Serotonin is released by the blood platelets. Bradykinin is released by blood plasma. Histamine is released by mast cells. In addition to all this, the nociceptors themselves release "substance P," which causes mast cells to release histamine, which in turn stimulates the nociceptors! Histamine is interesting in that, when it stimulates nociceptors, it is experienced as an itch rather than pain. We use antihistamines, of course, "to relieve the itch. In the lungs, for example, there are "pain receptors" which cause you to cough, but do not cause you to feel pain. Transmission upwards The nerves that carry messages from the nociceptors up the spinal cord follow several different tracts. Most go to the thalamus, where they are distributed to various higher centers. Some also go to the reticular formation which, among other things, governs alertness and to the amygdala a part of the limbic system involved in emotion. Referred pain, such as the pain that people sometimes feel in their left arms and shoulders when they are having a heart attach, is due to the way in which nerves come together in the spinal cord. The brain sometimes loses track of where the pain is coming from. Gate theory is based on this idea of confusion of neural signals. It seems that some non-pain stimulation can sometimes interfere with the experience of pain. This is the explanation behind such phenomena as the benefits of rubbing a painful area, the use of hot or cold compresses, acupuncture, and acupressure. There are people who have had damage to some part of these tracts, often after a stroke, who feel tingling or a burning pain that is aggravated by touch. Other people have damage higher in the brain that lets them feel pain like everyone else, but eliminates the connections to the emotional centers. Phantom pain - the pain amputees sometimes feel in the very limb they are missing - is due to the fact that, when nociceptors are damaged or missing, the neurons in the spinal cord that transmit pain messages sometimes become hyperactive. In the brain and spinal cord, there are certain chemicals called opioids, or more specifically enkephalin, endorphin, and dynorphin. When they are released into synapses, they diminish the levels of pain transmitted, exactly like heroin. There are actually a variety of things which diminish the experience of pain: A reduced experience of pain is called, logically, hypoalgesia. And there are people who are born with a genetic inability to feel pain at all. It is very rare, and at first sounds like a blessing. But the rate of early death is quite high in these people, usually because injuries that normal people would attend to small ones, like sprains go unattended and develop into more serious problems. That, of course, is the reason why pain has evolved as it has: It warns us to sit down, rest, attend to an injury, avoid things that cause pain, and so on. On the other hand, pain is not always useful. The cancer patient, for example, knows about his or her disease and

is taking care of it. The often excruciating pain is totally unnecessary, and we should do what we can to get rid of it!

Chapter 6 : Biological Basis of Pain - Oxford Clinical Psychology

Pain is a perception, and like any perception, it is rooted in sensation, and on the biological level, in the stimulation of receptor neurons. Also like other forms of perception, pain is sometimes experienced when there is no corresponding biological basis!

Beck, MD In reviewing all types of literature about pain, I sadly note the paucity of research from my field of Orthopedics. This is a shame since orthopedic surgeons have training in a number of sciences not commonly used in other medical specialties: In subsequent articles, I will describe how these sciences can be of use to all physicians in pursuit of better pain treatment for our patients. What problems do I see with solving pain issues using a conventional, symp-tom-based, pathoanatomical approach? It works well for acute injury but, it does not work for Chronic Pain. Pain does not show up on a MRI. What is the specific pathoanatomy in Fibromyalgia? Our classic approach ignores the enormous compensatory ability of the human nervous system and how some functions are protected at the sacrifice of others. In other words, the symptoms may not reflect the most important pathology. Chronic Pain is mostly the result of central compensatory strategies for survival, but pain itself is not a survival priority. These biological priorities dominate in how we adjust to any present threats but not pain avoidance. It stands to reason then that our focus on pain symptoms is misguided. Motor Control and Motor Learning in Rehabilitation. Their Functions Revealed by Electromyography, 4th Ed. Williams and Wilkin Baltimore. Functional Neurology for Practioners of Manual Therapy. Biagggioni, Burnstock, Low, and Robertson. Primer on the Autonomic Nervous System, 2nd Ed. Practical Biomechanics for the Orthopedic Surgeon, 2nd Ed. The Management of Chronic Pain, 2nd Ed. Bronner S and Brownsten B eds. The Application of Engineering to the Musculoskeletal System. Mobilisation of the Nervous System. Churchill Livingston, Longman Group. The Sensitive Nervous System. Neuroscience for Rehabilitation, 2nd Ed. Lippincott Williams and Wilkins, New York. Somatosensory Testing and Rehabilitation. Gamble JG and Rose J. Human Walking, 2nd Ed. Gilman S and Winans-Newman S. Development of the Nervous System, 2nd Ed. Atlas of Functional Neuroana-tomy, 2nd Ed. Proprioceptive Neuromuscular Facilitation, 3rd Ed. Jacobson M and Mahendra SR. Developmental Biology, 4th Ed. Principals of Neural Science, 2nd Ed. Knott M and Voss DE. Patterns and Techniques, 2nd Ed. Latash ML and Lestienne F. Motor Control and Learning. Diagnosis and Indications, 2nd Ed.

Chapter 7 : Biological basis of 'atypical' chronic fatigue syndrome revealed

Neurobiological Basis for Chronic Pain A new paradigm offers a unique perspective and postulates that the fundamental causation of most chronic pain is neurobiological. By John L. Beck, MD.

Pain has much in common with other sensory modalities National Academy of Sciences, First, there are specific pain receptors. These are nerve endings, present in most body tissues, that only respond to damaging or potentially damaging stimuli. Second, the messages initiated by these noxious stimuli are transmitted by specific, identified nerves to the spinal cord. The sensitive nerve ending in the tissue and the nerve attached to it together form a unit called the primary afferent nociceptor. The primary afferent nociceptor contacts second-order pain-transmission neurons in the spinal cord. The second-order cells relay the message through well-defined pathways to higher centers, including the brain stem reticular formation, thalamus, somatosensory cortex, and limbic system. It is thought that the processes underlying pain perception involve primarily the thalamus and cortex. In this chapter we review the anatomy and physiology of pain pathways. We also discuss some of the physiological processes that modify the pain experience and that may contribute to the development of chronicity. For obvious reasons, most of this information comes from animal experiments. However, in recent years, experimental studies of human subjects using physiological, pharmacological, and psychophysical methods indicate that much of what has been learned in animals is applicable to humans National Academy of Sciences, Research into basic mechanisms underlying pain is an increasingly exciting and promising area. However, most of what is known about the anatomy and physiology of pain is from studies of experimentally induced cutaneous skin pain, while most clinical pain arises from deep tissues. Thus, while experimental studies provide fairly good models for acute pain, they are poor models for clinical syndromes of chronic pain. Not only do they provide little information about the muscles, joints, and tendons that are most often affected by chronically painful conditions, but they do not address the vast array of psychosocial factors that influence the pain experience profoundly. To improve our understanding and treatment of pain we will need better animal models of human pain and better tools for studying clinical pain. Pain Processes Figure illustrates the major components of the brain systems involved in processing pain-related information. There are four major processes: Transduction refers to the processes by which tissue-damaging stimuli activate nerve endings. Transmission refers to the relay functions by which the message is carried from the site of tissue injury to the brain regions underlying perception. Modulation is a recently discovered neural process that acts specifically to reduce activity in the transmission system. Perception is the subjective awareness produced by sensory signals; it involves the integration of many sensory messages into a coherent and meaningful whole. Perception is a complex function of several processes, including attention, expectation, and interpretation. Figure Diagrammatic outline of the major neural structures relevant to pain. The sequence of events leading to pain perception begins in the transmission system with transduction lower left , in which a noxious stimulus produces nerve impulses in the primary more Transduction, transmission, and modulation are neural processes that can be studied objectively using methods that involve direct observation. In contrast, although there is unquestionably a neural basis for it, the awareness of pain is a perception and, therefore, subjective, so it cannot be directly and objectively measured. Even if we could measure the activity of pain-transmission neurons in another person, concluding that that person feels pain would require an inference based on indirect evidence. Transduction Three types of stimuli can activate pain receptors in peripheral tissues: Mechanical and heat stimuli are usually brief, whereas chemical stimuli are usually long lasting. Nothing is known about how these stimuli activate nociceptors. The nociceptive nerve endings are so small and scattered that they are difficult to find, let alone study. Nonetheless, there have been some studies of the effects of chemicals on the firing frequency of identified primary afferent nociceptors. A variety of pain-producing chemicals activate or sensitize primary afferent nociceptors Bisgaard and Kristensen, ; Juan and Lembeck, ; Keele, Some of them, such as potassium, histamine, and serotonin, may be released by damaged tissue cells or by the circulating blood cells that migrate out of blood vessels into the area of tissue damage. Other chemicals, such as bradykinin,

prostaglandins, and leukotrienes, are synthesized by enzymes activated by tissue damage Armstrong, ; Ferreira, ; Moncada et al. All of these pain-producing chemicals are found in increased concentrations in regions of inflammation as well as pain. Obviously, the process of transduction involves a host of chemical processes that probably act together to activate the primary afferent nociceptor. In theory, any of these substances could be measured to give an estimate of the peripheral stimulus for pain. In practice, such assays are not available to clinicians. It should be pointed out that most of our knowledge of primary afferent nociceptors is derived from studies of cutaneous nerves. Although this work is of general importance, the bulk of clinically significant pain is generated by processes in deep musculoskeletal or visceral tissues. Scientists are beginning to study the stimuli that activate nociceptors in these deep tissues Cervero, , ; Coggeshall et al. In muscle, there are primary afferent nociceptors that respond to pressure, muscle contraction, and irritating chemicals Kumazawa and Mizumura, ; Mense and Meyer, ; Mense and Stahnke, Muscle contraction under conditions of ischemia is an especially potent stimulus for some of these nociceptors. Despite progress in our understanding of the physiology of musculoskeletal nociceptors, we still know very little about the mechanisms underlying common clinical problems such as low back pain. Even when there is degeneration of the spine and compression of a nerve rootâ€”a condition generally acknowledged to be extremely painfulâ€”we do not know which nociceptors are activated or how they are activated. Neither do we know what it is about the process that leads to pain. Transmission Peripheral Nervous System The nociceptive message is transmitted from the periphery to the central nervous system by the axon of the primary afferent nociceptor. This neuron has its cell body in the dorsal root ganglion and a long process, the axon, that divides and sends one branch out to the periphery and one into the spinal cord Figure The axons of primary afferent nociceptors are relatively thin and conduct impulses slowly. Figure The primary afferent nociceptor. This is the route by which the central nervous system is informed of impending or actual tissue damage. Its peripheral process runs in peripheral nerves, and its peripheral terminals are present in most body structures more It is possible to place an electrode into a human peripheral nerve and record the activity of primary afferent nociceptors Fitzgerald and Lynn, ; Torebjork and Hallin, The nociceptor is characterized by its response to noxious heat, pressure, or chemical stimuli. There is a direct relation between the intensity of the stimulus and the frequency of nociceptor discharge Figure Furthermore, combined neurophysiological and psychophysical studies in humans have shown a direct relation between discharge frequency in a primary afferent nociceptor and the reported intensity of pain Fitzgerald and Lynn, ; LaMotte et al. Blocking transmission in the small-diameter axons of the nociceptors blocks pain, whereas blocking activity of the larger-diameter axons in a peripheral nerve does not. These identified primary afferent nociceptors are thus necessary for detecting noxious stimuli. Figure The relation of discharge frequency in primary afferent nociceptors to subjective pain intensity in human subjects. The skin of human subjects was subjected to brief, calibrated temperature increases. Subjects began to identify the temperature more Monitoring activity in identified primary afferent nociceptors is a potential tool for the evaluation of certain types of clinical pain. In fact, this method has been used clinically to demonstrate pain-producing neural activity arising from a damaged nerve Nystrom and Hagbarth, At present, this method should be considered just a research tool; however, it is technically feasible and is of great potential value for evaluating pain patients. It raises the possibility of actually demonstrating nociceptor activity coming from a painful area. This method could be an advance over other correlative techniques for assessing pain because it measures the presumed noxious input, that is, the neural activity that ordinarily causes pain. Most of the other measures assess responses that could be, but are not necessarily, caused by noxious stimuli. It is important to point out that 1 there can be pain without activity in primary afferent nociceptors, and 2 there can be activity in primary afferent nociceptors without pain. These phenomena occur when there has been damage to the central or peripheral nervous systems. In addition, the modulating system can suppress central transmission of activity elicited by nociceptor input. Thus, there is a variable relation between nociceptor input and perceived pain intensity. For this reason the method of recording primary afferent nociceptors could be used to confirm the presence of an input, but it could not be used to prove that pain was not present. Besides these theoretical limitations of trying to assess subjective pain intensity by recording primary afferent nociceptors, there are important practical problems in measuring either

pain-producing substances or primary afferent nociceptor activity. One is that the largest group of patients disabled by pain localize it to musculoskeletal structures in the lower back. Because the nerves innervating these structures are not near the skin, they are difficult to find. Another problem is that pain arising from deep structures is often felt at sites distant from where the tissue damage occurs. In contrast to the pain produced by skin damage, which is sharp or burning and well localized to the site of injury, the pain that arises from deep tissue injury is generally aching, dull, and poorly localized Lewis, When the damage to deep tissues is severe or long lasting, the sensation it produces may be misperceived as arising from a site that is distant from the actual site of damage Head, ; Kellgren, ; Lewis, ; Sinclair et al. This phenomenon, known as referred pain, helps to explain the frequent discrepancy between physical findings and patient complaints. The mechanism of referred pain is unknown for any particular case. Referred pain can be a major source of confusion in the examination of patients complaining primarily of pain. The fact that pain is referred from visceral internal organs to somatic body structures is well known and commonly used by physicians. For example, the pain of a heart attack is not always localized to the heart but commonly is felt diffusely in the chest, the left arm, and sometimes in the upper abdomen. Less widely recognized is the fact that irritable spots, such as myofascial trigger points, in skeletal muscles also cause feelings of pain in locations distant from the irritable spot. This was demonstrated experimentally in muscle and fascia by Kellgren in the late s Kellgren, Specific patterns of pain referred from particular muscles have been described clinically Travell and Rinzler, ; Travell and Simons, See Chapter 10 and Appendix. At least four physiological mechanisms have been proposed to explain referred pain: The latter two involve primarily central nervous system mechanisms. Sympathetic nerves may cause referred pain by releasing substances that sensitize primary afferent nerve endings in the region of referred pain Procacci and Zoppi, , or possibly by restricting the flow of blood in the vessels that nourish the sensory nerve fiber itself. Peripheral branching of a nerve to separate parts of the body causes the brain to misinterpret messages originating from nerve endings in one part of the body as coming from the nerve branch supplying the other part of the body. According to the convergence-projection hypothesis, a single nerve cell in the spinal cord receives nociceptive input both from the internal organs and from nociceptors coming from the skin and muscles. The brain has no way of distinguishing whether the excitation arose from the somatic structures or from the visceral organs. It is proposed that the brain interprets any such messages as coming from skin and muscle nerves rather than from an internal organ. The convergence of visceral and somatic sensory inputs onto pain projection neurons in the spinal cord has been demonstrated Milne et al. According to the convergence-facilitation hypothesis, the background resting activity of pain projection neurons in the spinal cord that receive input from one somatic region is amplified facilitated in the spinal cord by activity arising in nociceptors originating in another region of the body.

Chapter 8 : Psychology Exploring Phantom Limb Pain â€" .: 3iCreative :.

Pain is a subjective experience with two complementary aspects: one is a localized sensation in a particular body part; the other is an unpleasant quality of varying severity commonly associated with behaviors directed at relieving or terminating the experience.

A literal ton of research has been done on the causes of depression. Below is a brief discussion of the multiple biological, psychological and social factors that have been identified as being related to the development of depression. In context of the Diathesis-Stress hypothesis, the biological factors typically function as diatheses, the psychological factors may serve as diatheses or stressors, and sociological factors tend to function as stressors or triggers. Biology of Depression You may have heard that depression is the result of a simple imbalance of brain chemicals. Although brain chemicals are certainly part of the cause, this explanation is too simplistic. Even just considering the biological dimension of depression, the brain has multiple layers of complexity. Neurochemistry Neurotransmitters The brain uses a number of chemicals as messengers to communicate with other parts of itself and with the nervous system. Neurons are constantly communicating with each other by way of exchanging neurotransmitters. A tiny space called a synapse connects neurons to one another. In a simple scenario, one neuron the sender sends a neurotransmitter message across the synapse and the next neuron the receiver receives that message by way of a receptor embedded on its surface. Receptors are tiny molecules that function like a lock on a door. Receptors have chemical channels with particular shapes, which perfectly match the shape of neurotransmitter molecules that are sent across the synapse. As a result, the receptor becomes activated or opened, just like when a key enters a lock and turns to open it. When there are no neurotransmitter molecules around to unlock the receptors, the receptors remain in a closed or inactive state. There needs to be some quiet time between neurotransmitter messages for those messages to have any meaning. It is important that receptors be allowed to reset and deactivate between messages so that they can become ready to receive the next burst of neurotransmitters. The neurotransmitters are then repackaged and reused the next time a message needs to be sent across the synapse. Even though this seems like a complicated set of steps, this entire information transmission cycle occurs in the brain within in a matter of seconds. Any problem that interrupts the smooth functioning of this chain of chemical events can negatively impact both the brain and nervous system. Depression has been linked to problems or imbalances in the brain with regard to the neurotransmitters serotonin, norepinephrine, and dopamine. What we do know is that antidepressant medications used to treat the symptoms of depression are known to act upon these particular neurotransmitters and their receptors. The neurotransmitter serotonin is involved in regulating many important physiological body-oriented functions, including sleep, aggression, eating, sexual behavior, and mood. Serotonin is produced by serotonergic neurons. Current research suggests that a decrease in the production of serotonin by these neurons can cause depression in some people, and more specifically, a mood state that can cause some people to feel suicidal. In the s, the "catecholamine hypothesis" was a popular explanation for why people developed depression. This hypothesis suggested that a deficiency of the neurotransmitter norepinephrine also known as noradrenaline in certain areas of the brain was responsible for creating depressed mood. More recent research suggests that there is indeed a subset of depressed people who have low levels of norepinephrine. For example, autopsy studies show that people who have experienced multiple depressive episodes have fewer norepinephrinergic neurons than people who have no depressive history. However, research results also tell us that not all people experience mood changes in response to decreased norepinephrine levels. Some people who are depressed actually show hyperactivity within the neurons that produce norepinephrine. More current studies suggest that in some people, low levels of serotonin trigger a drop in norepinephrine levels, which then leads to depression. Another line of research has investigated linkages between stress, depression, and norepinephrine. Norepinephrine helps our bodies to recognize and respond to stressful situations. The neurotransmitter dopamine is also linked to depression. Dopamine plays an important role in regulating our drive to seek out rewards, as well as our ability to obtain a sense of pleasure. Recently, another neurotransmitter, glutamate, has been implicated in depression as well,

but more research is necessary at this time to determine the nature of this relationship.

Chapter 9 : The biological basis of pain â€" Case Western Reserve University

However, new research finds the biological basis for two subgroups of chronic fatigue syndrome, which may in the future help clinicians to diagnose the disease and treat it more effectively.