

## Cognitive aspects underlying pain and neuro-physiological responses

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### ABSTRACT

Health Psychology has intensely investigated the possible cognitive factors involved in, or responsible for, individuals' physical, emotional and behavioural well-being. The studies of pain have been addressed as a major point of concern in this area because they are reliant on individual differences and susceptible to subjects' interpretations of pain. Research identified that different cognitive mechanisms play a role in individuals' reports of pain signals. The impact of cognition on individuals' perceptions of pain might even trigger neurological-driven responses which, in some cases, could be avoided by the usage of certain cognitive strategies. This paper outlines the main cognitive aspects and processes of pain and neuro-physiological responses.

**Keywords:** Health Psychology; Pain; Cognitive Strategies; Neuro-Physiological.

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Aspectos cognitivos e respostas neurofisiológicas subjacentes à dor

### RESUMO

A Psicologia da Saúde tem investigado intensamente os possíveis fatores cognitivos envolvidos em – ou responsáveis por – bem-estar físico, emocional e comportamental dos indivíduos. Um importante fator de preocupação dessa área tem sido os estudos sobre a dor, pois sua análise é dependente de diferenças individuais e é suscetível a interpretações pessoais dos sujeitos. Pesquisas identificaram que diferentes mecanismos cognitivos desempenham um papel nos relatos de sinais de dor dos indivíduos. O impacto da cognição sobre a percepção de dor dos indivíduos pode desencadear respostas neurológicas que, em alguns casos, poderiam ser evitadas pelo uso de certas estratégias cognitivas. Este artigo descreve os principais aspectos e processos cognitivos da dor e suas respostas neurofisiológicas.

**Palavras-chave:** Psicologia da Saúde; Dor; Estratégias cognitivas; Neurofisiológico.

Respuestas cognitivas y neurofisiológicos subyacentes al dolor

## RESUMEN

La Psicología de la Salud ha investigado intensamente los posibles factores cognitivos implicados en, o responsables de, bienestar físico, emocional y comportamental de los individuos. Los estudios sobre el dolor se abordaron como un factor importante de preocupación en este ámbito, debido a que la construcción depende de diferencias individuales y susceptibles de poseer interpretaciones de los sujetos. Investigaciones han identificado que diferentes mecanismos cognitivos juegan un papel en los relatos de señales de dolor de los individuos a. El impacto de la cognición en la percepción del dolor de individuos puede incluso provocar respuestas neurológicas, que en algunos casos podrían evitarse mediante el uso de ciertas estrategias cognitivas. Este artículo describe los principales aspectos y procesos cognitivos del dolor y las respuestas neurofisiológicas.

**Palabras** claves: Psicología de la Salud; Dolor; Estrategias cognitivas; Neurofisiológico.

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A vast amount of research has investigated the reasons why pain might be reported so differently depending on the individual (Lumley et al., 2011; Sharpe, 2016; Sobol-Kwapinska, Babel, Plotek, & Stelcer, 2016). Pain is a vital mechanism for human survival which works as an alert sign that something is not functioning properly in the body. Note that pain might be defined as the organic or psychogenic response to a threat of tissue damage (Sarafino, & Smiths, 2014). The term organic refers to the actual physiological tissue damage, whereas psychogenic relates to the psychological processes involved in pain responses. It is now known that psychogenic pain is mainly caused by cognitive factors, even when there is no perceived physical harm in any of the individual's systems. Pain might as well be classified according to its intensity and duration. Acute pain is a short-duration discomfort, or alarm, characterized by a less-than-six-month existence, which would be caused by physical injuries or tissue damage. On the other hand, chronic pain may be described as a persistent, long-lasting period of soreness followed by neuropsychological and social implications, which might vary from feelings of helplessness to experience of anxieties (Lumley et al., 2011; Merskey, & Bogduk, 2012). Given the ample magnitude of possible causes of pain, chronic pain has been subdivided into different categories according to particular specificities, such as: sites of pain in the body; the body system in which pain manifests; temporal aspects of pain – patterns and length of (re)occurrence; intensity and onset of pain; and etiology of pain conditions (Merskey, & Bogduk, 2012). For instance, chronic recurring pain (regularly or irregularly) refers to repeated occurrences of pain due to benign causes, such as migraine, muscular tension or premenstrual pain. Continuous chronic pain may cause constant discomfort with oscillating levels of intensity, also possibly due to non-malignant conditions such as chronic back pain. Additionally, chronic progressive pain is experienced in cases of malignant conditions and tends to increase over time, with transition from acute to chronic pain. Classic examples of this sort of pain would be rheumatoid arthritis and cancer (Bérubé, Choinière, Laflamme, & Gélinas, 2016; Merskey, & Bogduk, 2012; Sarafino & Smiths, 2014).

The biological approach to explaining pain mechanisms suggests that pain is no different from the interpretation of noxious stimuli perceived by the nociceptor receptors in the body. Receptors send pain signals, via afferent nerve (A-delta, A-beta and

C-fibres), through the spinal cord to the brain. Once the signals are processed in the brain, they produce neural impulses which are sent back to the body through efferent nerves and manifested in forms of painful symptoms (Melzack, Walls, & Ty, 1982). The theoretical implications of the given theory are primarily concerned with biological responses to physical stimuli. What it fails to explain however, is how pain might also be experienced in the absence of an actual physical stimulus. Holmes and Wolff (1952, in Flor & Turk, 1989), discussed that unspecific hyper activation of the autonomic nervous system (sympathetic activation), for instance emotional instability or high levels of stress, might induce painful conditions. In this case, there is absolutely no physical stimulation causing the pain responses, although the symptoms are still perceived by the individual. The Stress-Pain Hypothesis (Keefe, & Gil, 1986) states that whenever individuals are exposed to a stressful condition, muscle activity is triggered which consequently leads to nociceptive stimulation. This stimulation provokes somatization, in other words, pain responses which are stressors per se, therefore, increasing pain in a vicious cycle.

A similar plausible explanation to perceived pain was proposed by Ax (1964) and Fahrenberg (1967, cited in Flor, & Turk, 1989). They argued that certain 'psychological' pain could be initiated due to motivation-specific psychophysiological responses. What they meant was stimuli might be perceived differently according to each individual, and also that the same stimuli could be experienced in many ways by the same person, depending on the given time. To put it simply, according to this viewpoint, physiological responses are generated as a result of an individual's subjective interpretations of the stimuli. Investigations with soldiers during the World War II have provided significant evidence consistent with this assumption. Beecher (1947) concluded that soldiers who were wounded in the battlefield reported less pain and did not request as many painkillers as civilians who had undergone surgical procedures and experienced similar conditions. He carried on stating that this would be because of the ways individuals perceived the pain. For the soldiers, the wound would perhaps represent the end of their threat of death in the battlefield, whereas for the civilians, it would mean the beginning of their rehabilitation processes (Brannon, Feist, & Updegraff, 2014).

Indeed, individuals' perceptions and expectations seem to play a major role in physiological responses to noxious stimuli (Sinke, Schmidt, Forkmann, & Bingel, 2016). Research has shown that cultural factors might hugely influence the pre-disposition of certain individual differences, for instance, the ability to best manage pain according to cross-cultural perspectives (Taylor, 2015). A critical example would be Mexican women experiences of giving birth. They usually anticipate labour with a great amount of fear which automatically translates into more sensitivity to painful experiences and, consequently more complications in contrast with women from other cultures (Straub, 2012; Taylor, 2015). Similarly, those women who see the act of giving birth as something ordinary and, therefore, less frightening, generally describe less pain during pregnancy (Straub, 2012; Taylor, 2015). Neuropsychological-based studies involving functional magnetic resonance imaging (fMRI) techniques have demonstrated how such expectations could potentially induce neural processing prior to noxious stimuli. Researchers have found that whenever signals of high expectation of pain are activated in the brain, it results in increased firing of certain brain areas which generate anticipatory responses to upcoming events. That is, the re-adjustment of sensory, cognitive and motor systems in order to provide satisfactory neural and behavioural responses (Atlas, & Wager, 2012; Ploner, Tracey & Wiech, 2008). The findings corroborate that individuals who were expecting to feel a high-level pain stimuli presented more activation in many brain areas related to pain processing, when compared to individuals who were not expecting a high intensity pain (Ploner, Tracey, & Wiech, 2008).

Furthermore, socio-cultural factors may contribute to shape individuals' attitudes towards pain and, in some cases, it results in the formulation of pre-concepts of pain.

For instance, it is known that in some particular cultures men adopt a certain role in society, in which, it becomes shameful for them not to be in control of themselves and their own lives. This personal control is described as an individual's locus of control, which might overlap with gender stereotyping (Brannon et al., 2014). In fact, a great deal of research has addressed the extent to which pain perception might be influenced by gender. It seems that in cold pressor tests, women tend to report higher levels of pain in contrast with men (Sarafino, & Smiths, 2014). More evidence for the gender-stereotype effect on pain perception comes from dental surgery patients, since it was found that, although gender did not influence the physiological responses to analgesics, women reported much more aggravated pain symptoms than male participants (Brannon et al., 2014). Nonetheless, this trend of results was not observed, when the gender of the experimenter was manipulated in controlled conditions. That is, both, women and men reported less pain when they were subjects of cold pressor pain tasks conducted by a male experimenter, when compared to a female experimenter (Vigil, Rowell, Alcock, & Maestes, 2014).

Interestingly, health-related studies have revealed that individuals who scored higher in perceived control tests, usually presented less activation in some brain regions associated with pain responses, such as, the right anterior part of the ventro lateral prefrontal cortex (VLPFC) (Ploner et al., 2008). In similar cases, individuals were assessed under controlled experimental conditions and the findings suggested that the idea of controllability – having control of – over the noxious stimuli reduced the activation in the insula, secondary somatosensory (SII) and anterior cingulate cortices (ACC), therefore, decreasing pain-related responses (Müller, 2011; Salomons, Johnstone, Backonja, & Davidson, 2004). In addition, it has been argued that gender might influence the specific cognitive strategies that men and women use to deal with pain. For instance, researchers have found that, in general, men tend to focus on the physical sensations of pain. In other words, men generally focus on the sensory characteristics of the stimuli, whereas women tend to rely on the emotional contents associated with pain, which may influence their perception of the stimuli (Keogh, Bond, Hanmer, & Tilston, 2005).

It is also worth noting that individual differences should be considered, while assessing pain as a general topic. Available data have shown that there seems to be a direct relationship between mood resulting from stressful life events, and physiological responses of pain. For this reason, mood changes were observed in an attempt to correlate behavioural with physiological outcomes. In that experiment, migraine patients rated their moods during specific times per day for a certain period of time. It was found that there was a significant correlation between migraine intensity and mood swings. Generally speaking, individuals who reported constant feelings of tiredness were more inclined to experience periodical headache (Harrigan, Rues, Ricks, & Smith, 1984). Similarly, Lavenson and Friesen (1983, in Keefe, & Gil, 1986) discussed that particular types of emotions, anger or fear for instance, would automatically result in physiological-specific responses. They argued that emotional content would trigger the repeated activation of systems, thereby promoting the dysfunction in homeostatic regulation, in other words, the breakdown in the equilibrium among systems in the body. According to this perspective, homeostatic deregulation was the fundamental reason why systems would present affected outcomes (pain responses), depending on how much individuals were exposed to stressors. Moreover, previous clinical evidences for the Deregulation of Systems Hypothesis showed that psychiatric patients did indeed present higher muscle activities, according to EMG results, whenever they were exposed to stressful stimuli (Malmo & Shagas, 1949, in Flor, & Turk, 1989).

Arguably, pain-specific responses may not only be elicited by hyper muscular activations, but also due to emotional suppression of affective responses, such as anger, research has revealed. In that, anger inhibition seems to be associated with over sensitivity to noxious stimuli (Braams, Blechert, Boden, & Gross 2012; Burns et al.,

2008). Gross (2002), carried out a series of investigations in which it was found that individuals who were supposed to suppress their behavioural responses to stressful stimuli during tasks, were more likely to present higher levels of arousal and translate those into reporting more pain. The underlying idea here is that increased anxiety levels, associated with affect suppression, would elicit sympathetic nervous system activation, as well as higher lower paraspinal muscle tension and systolic blood pressure (Burns et al., 2011). Not surprisingly, individuals who scored high marks in anxiety tests tend to report more pain and request more treatment than individuals who were classified as having a standard level of anxiety (Braams et al., 2012). Conversely, fear seems to inhibit pain responses, either in humans and animals, via the activation of endogenous opioids in the brain (Brannon et al., 2014; Rhudy, & Meagher, 2000). According to studies from the University of Bath – Bath Centre of Pain Research (Keogh, 2005), women are generally more fearful with regards to anxiety-related sensations and, as a result, tend to interpret those feelings with a greater extent of negativity thus, experiencing more intense pain compared to men. Equally surprising, a cognitive strategy, namely, acceptance, described as non-judgemental evaluations of one's thoughts, emotions and experiences, was found to decrease the expression of pain and distress in conditions of high stress (Braams et al., 2012).

In fact, the idea of self-regulation towards painful symptoms has been extensively explored for decades. Back in the 1980's, Droste, Greenlee and Roskamm (1986, in Sheridan, & Radmacher, 1992) had already proposed that pain responses could be highly influenced by personal factors. It was argued that in the majority of cases of silent heart attacks (that is, when patients have heart attacks without noticing prior signals), individuals tended to be less responsive to any pain-related-stimuli such as electric shocks or muscular pain. Meaning that, individual sensitivity to stimuli might play a role in general experiences of pain. Furthermore, similar findings identified a number of personal traits which appeared to pre-dispose individuals to certain health conditions, such as high blood pressure and coronary heart disease (CHD) (Martin, Carlson, & Buskist, 2013). It was argued that individuals who were classified as the so-called Type A-Personality Pattern would present a higher need for control leading to anxieties and respective consequences as discussed previously. These sets of characteristics embody fundamental aspects for health-related conditions. Further research, however, must be carried out in order to attribute such health implications as to specifically derived from personality variables (Martin et al., 2013).

In addition, an important personality factor related to cognitive aspects directly related to pain experiences, is neuroticism. This personality factor relates to the tendency to expect, anticipate and experience anxiety (anxiety sensitivity), depression-like symptoms and distress (Muris, Meesters, Hout, Wessels, & Rassin, 2007; Payne, Seidman, Lung, Zeltzer, & Tsao, 2013). It seems that catastrophic perceptual responses to pain might result from personality traits, rather than, solely external nociceptive input (Pallegama, Ariyasinghe, Perera, & Treede, 2016). Even more remarkable is the fact that not only adults tend to exacerbate their reactions to pain, but also adolescents and children who undergo worries and frustrations, usually report more chronic pain symptoms (Payne et al., 2013). Studies (Muris et al., 2007) demonstrated the impact of extreme vigilance to pain and consequent behavioural outcomes. It was found that neuroticism was a major factor in reports of chronic pain according to results from the Pain Behavioural Inhibition and Behavioural Activation Scale (BIS-BAS, Muris et al., 2007). The findings revealed that perceptual sensitivity was significantly associated with cognitive factors, regardless of individuals' ages and physical conditions. Of similar importance, there are a number of fundamental points that need to be taken into account in terms of personality theory (Gray, 1991, in Muris et al., 2007). According to biological approaches, neuroticism-like traits rely on brain systems that help to regulate behaviour. The behaviour inhibition system (BIS) enhances individuals' alertness to possible danger, and works in a very similar

state to the neuroticism pattern. Consequently, it is thought that extreme activation of this system (BIS) may intensify neuroticism, thus sensitivity to pain leading to catastrophizing responses.

At present, however, empirical investigations suggest that there is a direct cognitive – physiological mechanism operating in nociception (sensory perception of pain). It has been revealed that not only the nervous system (NS) processes noxious stimuli sending the pain signals to the brain, but it also relies on inhibitory messages which reduce the electrical stimulation in the nervous system (Sheridan, & Radmacher, 1992). Scientists have found that endogenous opiate like substances, or endorphins, are fundamental neurochemicals generated in the brain and body glands, which promote the regulation of pain. For survival reasons, the pain suppression system is not always actively sending inhibitory messages to the brain. Nonetheless, particular factors, such as stressors, might trigger inhibitory activations in the brain. Researchers have found that stressful conditions might produce a state called “stress-induced analgesia” (SIA), when there is an increase in the brain’s endogenous opioids (Taylor, 2015; Yilmaz et al., 2010). Further possible functions associated with endogenous opioids are still unknown, nevertheless, evidences suggest that they might be released as the body’s physical response to stress, acting on the control of pain (Taylor, 2015). Similarly, cognitive strategies might be used in order to activate endogenous responses, hence reducing pain. It has been found that, in some cases, switching attention – distraction condition – from the noxious stimuli can lead to perceived stimulation of the Periaqueductal Grey (PAG) This is another fundamental brain region associated with analgesia-like symptoms and the release of serotonin, reducing pain-related symptoms (Taylor, 2015; Tracey et al., 2002; Yu, Gollub, Spaeth, Napadow, Wasan, & Kong, 2014). Additionally, scientists have addressed individuals’ attentional modulation of pain making use of modern neuroimaging techniques. They found that pain experiences might depend upon how much attention is given to the stimulus, in spite of the stimulus itself (Ploner et al., 2008).

It has been revealed that attention works as a cognitive tool which allocates processing resources to percept and cognition. By doing so, it then maximises responses to desired stimuli (the ones that are being attended) and, consequently, minimises the awareness of irrelevant stimuli. Functional imaging investigations suggest that distraction from the noxious stimuli results in decreased neuro activities in the primary and secondary somatosensory cortices (SI and SII), thalamus, insula and anterior cingulate cortex (ACC). These brain regions are related to sensory and cognitive aspects of pain, hence, their lower activation indicate less noxious responses (Ploner et al., 2008). Additionally, further analyses revealed that, apart from the reduction of functions in certain brain areas, other cerebral regions seemed to be hyper activated during distraction tasks. Those areas are particularly the ones involved in the descending pain modularity system. This complex network comprises the prefrontal cortex (PFC), ACC and PAG, all of which work to stimulate opioid – induced analgesia which is the body’s natural painkiller through the spinal cord (Ploner et al., 2008). Having said that, attention might modulate noxious perception due to the stimulation of opioid-descending pathway, which controls nociceptive processing in the central nervous system.

In this perspective, there is plentiful evidence to suggest that individuals’ attentional focus may result in altered physiological responses to pain. In that, alternative approaches in medicine (integrative medicine) have attempted to explore the beneficial effects of cognition on the control of pain. It has been emphasized that some placebo drugs may produce analgesia depending on individuals’ cultural and personal attributes (Ploner et al., 2008). Note that placebo drugs are flawed samples of chemicals, which may still produce behavioural outcomes although they do not present any pharmacological active principal (Martin et al., 2013). It therefore remains under investigation as to why some placebo drugs present great effects on

the management of pain. It could be that placebo outcomes result from individuals' beliefs and inferred meaning of the drug, rather than the pharmacological components of the drugs (Martin et al., 2013). For this reason, the placebo effect represents an example of cognitive pain modulation through a non-invasive method, in which there is an alteration of brain activities without any chemical intervention (Ploner et al., 2008). Interestingly, it has been found that red placebo pills are more likely to stimulate responses than blue pills, due to the implicit perceptual meaning attached to it. Usually red colour suggests 'hot' or 'danger', and that might be interpreted as more efficient on the control of pain. That again, the perceived drug effects are no different to individuals applying meaning and expectations to the efficacy of a given drug.

Equally important, there are pain conditions that do not correspond to explanations proposed by bio-physiological perspectives. In certain cases, pain that originates from internal organs could end up being perceived in a body part other than the responsible organ itself. This is described as "Referred Pain" (Sarafino, & Smiths, 2014). This phenomenon usually happens in cases of heart attack, when the pain is referred to the shoulders, chest and arms. Pain in the lower back can also result from stomach problems, for instance. The etiology of referred pain has been alleged as a product of misleading sensory impulses in the spinal cord. A possible explanation to this condition is that, once internal organs and the skin use the same spinal pathway to reach the brain, simultaneous messages are perceived much more easily in the skin in contrast with internal organs. Hence, the stimuli are decoded as if coming from the skin instead of the damaged organ (AMA, 2003; Tortora & Grabowski, 2003, in Sarafino, & Smiths, 2014). This viewpoint accounts for the conductivity of sensory stimuli, however, it does not provide sufficient amount of detail to explain cases of neuralgia or causalgia for instance. Neuralgia is a condition in which the patient experiences extreme shooting pain along a particular nerve, after infection of this peripheral nerve, or as a result of degenerative conditions. The episodes are sudden and without any apparent cause. Causalgia, on the other hand, is a syndrome characterized by unexpected feelings of strong burning pain. Both conditions may be triggered by the simplest stimuli such as a puff of air (AMA, 2003; Melzack & Wall, 1982, in Sarafino, & Smiths, 2014).

Similarly, it has been argued that cognition may influence certain pain conditions which are not directly explained in terms of bio-physiological activation. Apart from its obvious changes in the body (increased anxiety levels, stress and so on), cognition may also enhance episodes of aggravated symptoms of pain. Here, a fundamental psychologically-associated condition is identified as Phantom Limb Pain (PLP) (Straub, 2012; Subedi, & Grossberg, 2011). This phenomenon occurs after the amputation of a limb or damage in the peripheral nervous system (PNS), resulting in cortical reorganization in the primary somatosensory and the motor cortex (Subedi, & Grossberg, 2011). Individuals usually report extreme feelings of pain in a limb that has been removed, or has no functioning nerves (Sarafino, & Smiths, 2014). The incidents may vary from being recurrent to persistent and, in this case, presenting enduring effects for months or even years. It remains unclear the exact reasons why the mentioned phenomena might happen. Nevertheless, there is evidence to suggest that neurophysiological changes may happen not only due to external stimuli, but also the ways in which they are interpreted at the cognitive level. Another plausible explanation to the PLP was suggested more recently by Melzack (2005) in his "neuromatrix and neurosignature" hypothesis, which states that a network of neurons work to integrate different inputs from various areas in the body, all of which include somatosensory, limbic, visual, and thalamocortical regions, resulting in pain responses and experiences. According to the theory, pain responses are constantly updated depending on the individual's awareness, perception of the body, and his/her experiences. Once incoming inputs were deprived from a particular amputated limb, abnormal neurosignature would be sent to the neuromatrix, ultimately resulting in the PLP (Melzack, 2005). Additionally, it is thought

that distress, anxiety, exhaustion, and depression tend to exacerbate PLP (Subedi, & Grossberg, 2011).

Additionally, recent findings revealed that particular factors contribute to the assimilation of cognitive variables resulting in the development of pain. Those variables might be developed as a result of operant conditioning, in which, whenever individuals receive reinforcement for a certain behaviour, it increases the chances that this behaviour will be repeated in the future. The relevance of this approach to pain is that, in some cases of chronic pain, patients may report more aggravated symptoms in order to avoid doing certain tasks, or to receive emotional reinforcement from peers, or family members. This also seems to be true for self-reports of pain intensity and facial expressions of pain (Kunz, Rainville, & Lautenbacher, 2011; Martin et al., 2013). Cautious considerations should be taken into account, bearing in mind context and individual-specific characteristics, so that further inferences in terms of conditioned responses to pain may be placed more thoroughly. Likewise, similar patterns of pain behaviour have been investigated since the 1980's, and findings suggest that there is a direct correlation between the sick-role (feelings of helpless and hopeless) and more aggravated descriptions of pain. The risks of adapting the sick-role is that of, the more individuals perceive that attention and compassion is given to them, the more likely it is that pain behaviour will become a habit in their lifestyles. If that becomes the case, whenever serious episodes of pain happen, physicians may interpret those as ordinary patterns of the individual's behaviours, disregarding the importance of the fact, also resulting in undesirable physical and emotional outcomes to the patient (Sarafino, & Smiths, 2014).

Moreover, in cases where Cognitive Behavioural Therapy (CBT) is applied instead of only pharmacological intervention to pain, it usually presents positive effects on readjusting individuals' maladaptive attitudes and behaviours towards pain-like symptoms. The impact of CBT in the perception of pain may reflect on subsequent decrease of chronic pain conditions, and medical assistance, or the use of drugs (Curran, Williams, & Potts, 2009; Halaszynski, 2013). Findings have suggested that patients who did not continue adhering to their re-adapted concepts/cognition after the CBT sessions, were more likely to experience distress and look for treatment in the near future (Curran, Williams, & Potts, 2009). This clinical evidence illustrates the possible effects of poor personal concepts/cognition towards pain, leading to increased physical perception of pain and consequent reduced well-being.

In summary, literature evidence indicates that various patterns of cognition and psychological aspects play a major role in individuals' general perception of pain. Cognitive processes of interpretation of pain are of particular interest and may drastically alter individuals' responses to noxious stimuli, in face of, or in the absence of, physical causes/stimuli of pain. Similarly, perception is culture and individual specific, and has a direct effect on interpretation and descriptions of pain. In addition, neurological findings have accounted for the possible consequences of attentional modulation, resulting in enhanced activities in pain-related areas in the brain. Certain personality traits and individual differences have also been found to result in increased or decreased sensitivity to noxious stimuli. Neuroticism, anxiety and distress are only a few examples of personal-specific, psychological variables that may influence the extent to which pain is differently experienced by individuals. It remains still unclear, though, the reasons why certain "psychological" pain phenomena might occur such as, Referred Pain, Neuralgia, Causalgia and Phantom Limb Pain. Alternative approaches in pain treatment suggest that pain might be best explained in terms of an interaction between the biological functions of the body-brain mechanisms, and the cognitive elements influencing physical changes. The need for future investigations in the fields of pain studies is of fundamental importance, as well as the application of sophisticated imaging techniques, to broaden the scope of understanding of neuro-physiological interactions with cognitive-emotional processes influencing pain outcomes.

**Table.** Psychological aspects underlying biological-physiological responses of pain

<b>Author(s) (year)</b>	<b>Psychological aspects</b>	<b>Biological-physiological-behavioural responses</b>
Ax (1964) and Fahrenberg (1967, in Flor, & Turk, 1989); Beecher (1947)	'Psychological' pain due to subjective interpretations of pain	Physiological responses
Atlas, & Wager (2012); Ploner et al. (2008); Sinke et al., (2016)	High expectations of pain	Anticipatory responses to upcoming events; re-adjustment of sensory, cognitive and motor systems; neural and behavioural responses Higher levels of arousal and over sensitivity to noxious stimuli; increase anxiety, pain and distress; increase sympathetic nervous system activation, higher lower paraspinal muscle tension and systolic blood pressure
Braams et al. (2012); Burns et al., (2008; 2012)	Anger inhibition; high anxiety levels; suppression of affective responses	Men concentrate on the physical sensations of pain, (sensory characteristics of the stimuli); women concentrate on the emotional contents associated with pain (perception of the stimuli ); expression of pain and distress
Braams et al., (2012); Keogh et al. (2005)	Cognitive strategies; acceptance	Women reporting higher levels of pain in contrast with men in cold-pressor tests
Brannon, et al. (2014); Sarafino, & Smiths (2014)	Socio-cultural factors: pre-concepts of pain; locus of control; gender-stereotype effect on pain perception	Increased physical perception of pain
Curran et al. (2009)	Poor concepts/cognition towards pain	Increased ratings of acute pain
Gray (1991, in Muris et al., 2007); Pallegama et al. (2016); Payne et al. (2013)	Type A-Personality Pattern; Neuroticism; catastrophizing; anxiety sensitivity; depression-like symptoms; worries and frustrations; behaviour inhibition system (BIS)	Unspecific hyper activation of the autonomic nervous system (sympathetic activation)
Holmes and Wolff (1952, in Flor, & Turk, 1989)	Emotional instability or high levels of stress	Muscle activity and nociceptive stimulation
Keefe, & Gil (1986)	The Stress-Pain Hypothesis; exposure to stressful conditions	Increase facial pain displays and pain ratings
Kunz et al.(2011); Sarafino,& Smiths (2014)	Operant conditioning, reinforcement; sick-role	Repeated activation of systems, promoting the dysfunction in homeostatic regulation and breakdown in the equilibrium among systems in the body
Lavenson and Friesen (1983, in Keefe, & Gil, 1986); Lumley et al. (2011)	Mood instability, anger/fear	Stimulation of endogenous opioids in the brain
Lumley et al. (2011); Rhudy, & Meagher (2000)	Anxiety (activates) and fear (inhibits) pain responses	Phantom Limb Pain (PLP) - Cortical reorganization in the primary somatosensory and the motor cortex; abnormal neurosignature sent to the neuromatrix (integrate inputs from various areas, including somatosensory, limbic, visual, and thalamocortical) resulting in the PLP
Melzack (2005) ; Subedi, & Grossberg (2011)	Distress, anxiety, exhaustion, and depression, interpretations of external stimuli at the cognitive level; awareness and perception of the body and experiences	

Continue

Continuation

Müller (2011); Salomons, Johnstone, Backonja, & Davidson (2004)	Perceived control over the noxious stimuli	Reduced the activation in the insula, secondary somatosensory (SII) and anterior cingulated cortices (ACC), decreasing pain-related responses Stimulation of the Periaqueductal Grey (PAG); Release of Opiate like substances – endorphins – and serotonin; decreased neuro activities in the primary and secondary somatosensory cortices (SI and SII), thalamus, insula and anterior cingulated cortex (ACC); hyper activation of prefrontal cortex (PFC), anterior cingulated cortex (ACC) and PAG
Ploner et al. (2008); Tracey et al. (2002)	Attentional modulation	Inhibitory activations in the brain and Stress-induced analgesia (SIA)
Taylor (2015); Yilmaz et al., (2010)	Stressful conditions	Different pain sensitivity when exposed to male versus female laboratory personnel/experimenter
Vigil et al. (2014)	Gender differences in laboratory personnel/ experimenter	

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