

# Chapter 4

## The Emotional Perception of Phantom Limb Pain

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**Abstract** Chronic pain is a continuous learning state in which aversive emotional meanings are continuously associated with incidental events. In this chapter, I define “emotion” as an integrated neurobiological and functional adaptive process capable of generating physiological and experiential changes in constant interaction with neural systems and the external environment. The interaction of internal (neuronal) and external (environmental) dynamic networks may modulate the intensity and the experiential qualities of chronic pain, including its meaning and perception. Phantom-limb pain might be associated with an increased functional correlation of brain regions involved in the processing and integration of sensory, emotional, cognitive and socio-cultural components. The distinction between sensation and perception is essential for understanding the complexity of the neuro-mental processes of chronic pain, including phantom-limb pain. In the mental representation of phantom limb pain, body-perception may contribute to the development of an emotional and neuro-mental circuit in the brain leading to pain, which may elicit chronic phantom-limb pain.

### 1 Amputations and Phantom Limb Pain

Descriptions of phantom limb were first published in the sixteenth century. The surgeon Ambroise Pare is credited as having been the first to describe the clinical features of phantom pain (Paré 1551). However, it was surgeon Silas Weir Mitchell who first coined the term “phantom limb” (Mitchell 1872).

In Western countries, the main cause of amputations is peripheral vascular disease. It is expected that the augmentation of the number of amputations increase due to the growth of diabetes cases in the population (Jensen et al. 1985). At

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present, war and mine explosions around the world have also increased the incidence of traumatic amputations in individuals (Clasper and Ramasamy 2013).

Amputation is followed by phantom sensations, which can be painful, or not. These sensations are present in almost all patients. The phantom phenomenon may occur after the amputation of any part of the body, sometimes even after the amputation of internal organs. The complexity of the perception of a phantom limb indicates that the phantom image is produced by the brain, but we do not yet know all the underlying mental mechanisms. A series of peripheral and central mechanisms are involved in the generation of phantom pain. It is likely that the first events occur in the periphery, and then initiate a cascade of events in a central direction involving cortical brain structures. An important aspect of the phenomenon of phantom limb comes from the reorganization of the primary somatosensory cortex after amputation. This particular cortical reorganization takes place just days after the amputation and suggests a correlation between pain intensity and the degree of reorganization (Flor 2002, 2003; Flor et al. 2006).

Currently, phantom pain is a major global health problem because it is one of the most difficult chronic pains to manage. Despite ongoing physiological research in this area, there is very little evidence of long-term positive outcomes using available pharmacological treatments for phantom limb pain. In general, current treatments for phantom pain are based on analgesics and tricyclic antidepressants. Prescribed medication is effective in some patients, but many remain resistant, and many medications—especially opioids—produce harmful side effects (Sanzone 2016). Unfortunately, random treatments such as transcutaneous electrical nerve stimulation (TENS), hypnosis, feedback therapy (mirror box),<sup>1</sup> have little long-term efficacy in amputated patients with phantom pain. The effects on pain reduction are positive, but temporary. I believe the reason for these results is that the mental nature of chronic pain is neglected by phantom pain researchers. This problem includes the integration of psychological with physiological studies of phantom pain. I claim that the mental nature of chronic pain is the essence of phantom limb pain.

## 2 Characteristics of Phantom Limb Pain

The phenomenon of phantom limb is the persistence of sensory and motor perceptions in an amputated limb. After amputation, about 90% of the subjects perceive the existence of the missing limb (Melzack and Bromage 1973). Phantom sensations such as paresthesia, heaviness, heat, cold, or cramps, sometimes may be accompanied by the perception of very severe pain. Phantom pain may vary in

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<sup>1</sup>Experiments performed from a simple box with a mirror in the middle to cause a visual feedback in amputees (Ramachandran and Rogers-Ramachandran 1996; Ramachandran and Altschuler 2009).

intensity, frequency, duration of episodes and sensations. They fluctuate continuously from paroxysmal to more sustainable and from low to severe. The reported sensations are often described as sensations of tension, crushing, electric shock, twisting, or burning (Melzack and Bromage 1973).

The phantom often follows transformations usually within 6–12 months after the amputation. Its position and size can change. This is called *telescoping* (Harvie and Moseley 2014). A large number of phantom limbs become totally static and painful, sometimes in unimaginable positions. The positions of the phantom generally depend on the position that the limbs had before the amputation, for instance, during an accident, if an accident was the reason of the forthcoming amputation.

During my research at the Salpêtrière hospital in Paris and at the Institute of Neuroradiology and Diagnostic in Greifswald, Germany, I had the opportunity to interview more than 200 patients with chronic pain as well as 15 amputees with phantom limb pain. To my question about whether they dream of their body as intact (as it was before the amputation), or as it is after the amputation, most of the patients responded that they always dreamed of their body as it was before the amputation, in some cases even 12 or 15 years after the amputation. Other studies have shown similar results (Mulder et al. 2008). The responses of these patients reveal the existence of a neural representation of the body, which is at least partially genetically determined and relatively insensitive to changes in sensory input (Melzack and Bromage 1973). This also indicates the existence of complex interactions between the physical body appearance and the mental body representation.

At a mental and unconscious level, it also reveals the non-acceptance of the loss, even if most of those patients responded to having accepted their amputation. Phantom limb pain may disappear within weeks or months. However, it can also remain the same, intolerable and persist for the entire life of the individual. Many factors can influence the experience of sensation and perception of phantom pain; for instance, pain in other parts of the body, the use of alcohol, in some cases the use of a prosthesis, and very often emotions play an important role in the intensity of phantom pain. In the process of subjective perception of chronic pain, it is imperative to emphasize the difference between chronic physical pain and chronic mental pain; that is to say, the difference between physical pain and suffering, both can also be related forming a noxious circuit, as I explain in the following pages.

### **3 Distinction Between Chronic Physical Pain and Suffering or Mental Pain: The Interaction Between Neuronal and Mental Processes**

We know that acute pain is necessary as a warning and signal for protection. Despite the acute sensation that hurts, we do not typically “suffer” from it. Suffering is a distressing personal, mental state that extends over time, in which the permanence of a pending state causes hope that this state ceases. In other words, suffering

is a subjective state and therefore, an individual (private) state. Its quality and intensity depend on our character, our past, our memories, our educational level and beliefs. All this will affect the vision of our future. Suffering is present in all human beings and most likely to extent in some animals. “Suffering is the substance of all life,” said Schopenhauer (2014).

In chronic pain processes, consciousness is involved and the suffering caused by chronic pain can change the perception of our bodies, of our lives, and the whole perception of the world. However, the reverse may also be possible, as the circuit operates in both directions. A mental state of chronic suffering can also be the cause of chronic physical pain that creates a neuro-mind circuit.

Scientific understanding of chronic pain is poor, partly because we seek to study it only in the brain, neglecting its interactions with the environment, which form dynamic mental states. Chronic pain forms not only in the brain; it also forms elsewhere. External factors that modify our mental states are also responsible for intensifying pain and altering its experiential qualities. We also neglect the possibility that the suffering caused by dramatic life experiences of an individual can be the cause of chronic pain. This is not surprising, given that the same structures of the limbic system are involved in the emotional process (suffering) and in the perception of pain (Fasick et al. 2015). Study of the interactions between depression and chronic pain show that both disorders activate neuro circuits (e.g. the hypothalamic-pituitary-adrenal axis, the structures of the limbic system, the ascending and descending pain tracks) as well as neurochemicals (e.g. monoamines, cytokines, and neurotrophic factors), and are associated with psychological alterations related with the control of emotions (Robinson et al. 2009).

There is another model that can help understand the intrinsic relationships and communication between the neurophysiological process and external factors. The concept of allostasis supports this model. Allostasis describes a cascade of cause and effect factors that commence with primary stress mediators, such as catecholamines and cortisol, to primary effects, secondary and tertiary outcomes (Seeman et al. 2001). Allostasis has been studied in a group of patients affected by chronic pain and depression who accumulated allostatic load through internal and external stressors (Robinson et al. 2009). This study highlighted the importance of treating all manifest symptoms of a patient using different kind of therapies.

Neurotransmitters that modulate pain, dopamine, norepinephrine, gamma-aminobutyric acid ( $\gamma$ -Aminobutyric acid) (GABA) and serotonin, are also involved in the modulation of emotions, thoughts and mood. Serotonin is a stabilizer that helps the mind to return to its homeostatic state. Studies have shown that migraine attacks, their frequency and chronicity relate to serotonin dysfunction and agonists of the 5-HT<sub>1F</sub> receptor (serotonin) are effective in the treatment of migraine, and receptor activation GABA has an anti-nociceptive role in the modulation of pain (Sivilotti and Woolf 1994; Hasanein and Parviz 2014; Tso and Goadsby 2014; Zhang et al. 2014).

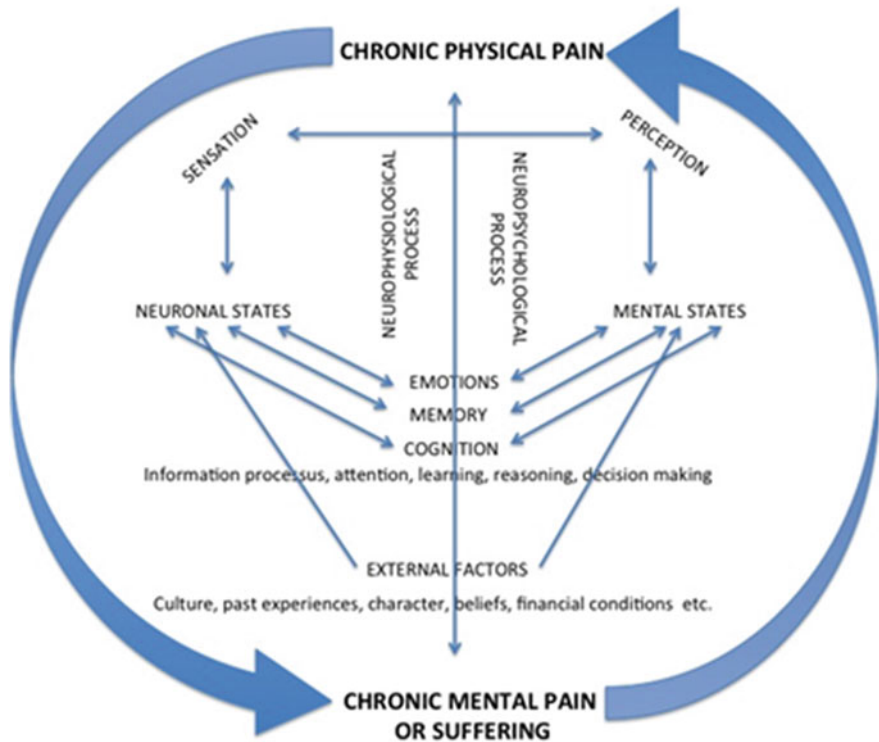
However, what is the importance of these studies, and what is their relationship to pain and suffering? The answer is that if the neurotransmitters associated with

depression and mood changes are also associated with the presence of certain chronic pains (as shown by these studies), it means that there is a pain-depression comorbidity, and that mental pain (suffering) may also be the cause of chronic pain. Neural states; namely, internal physiological mechanisms of pain, interact with mental mechanisms that are processed in the brain and which are in constant contact with socio-cultural networks (Bartra 2014). If we think of mental states as emergent properties of brain activity, sensitive to influence by external environmental factors, we can think that pain is a neuro-mental state. However, such emergence needs robust correlation with a well-defined neurophysiological process in which consciousness must be involved. For now, we have not achieved the theoretical understanding to underpin this assumption, in part because we do not have the means to build an experimental model of consciousness that can lead us directly to the mind-body problem. Since consciousness remains a scientific mystery, a good way to continue study of the mental nature of chronic pain would be to analyze the relationship between the brain and the universe around us. It is through this neuro-mental synergy (internal-external networks) which, in my opinion, consciousness and mind emerges. Therefore, it is advised to study interaction between mental states and neural states in chronic pain using the proposed neuro-mental theoretical model below (Fernández-Salazar 2015; Fig. 1).

This pattern of interaction between pain and suffering opens study of pain consciousness, to the analysis of the relationship between the qualitative nature of subjective mental states of painful experiences and their neurophysiological mechanisms. Perception is a process that affects and is affected by the state of mind of the person. Thus, the active selective perception of pain can alter the mental state of a person and change their perception of pain. In that process is included all the external events that a person can perceive just before the cognitive process, in which will exist an explanation and understanding of those perceptions.

It has been suggested that interactions of pain with other somatosensory sub-modalities and visual information about the body offer the possibility of modulating chronic pain (Haggard et al. 2013). A good example is the mirror box created by Ramachandran and Rogers-Ramachandran (1996) that manipulates the brain of amputees and, in many cases, reduces phantom limb pain as well as motor imagery which has been defined as the act of mentally play an action without executing it (Jeannerod 1994; Sirigu and Duhamel 2001) also in other kind of chronic pain (Moseley et al. 2008).

These studies support the hypothesis proposed in the above model that mental states could control and modify physical states, demonstrating the intimate relationship between body and mind. The suffering caused by the mental image of having an incomplete or distorted body, in the case of the strange phantom positions, could provoke an aversive mental state able to increase phantom pain intensity. Therefore, mental noxious states could be a cause of phantom limb pain. I believe that if we continue to investigate this model we may become capable through physical-mental therapy to modify the harmful mental conditions that cause chronic pain, and we may be able to prevent phantom limb pain.



**Fig. 1** Neuro-mental model of chronic physical pain and chronic mental pain or suffering. The process of pain involves unconscious nociception, and conscious pain. Emotions, cognition, memory, and external factors such as culture and social conditions influence our perception of consciousness of pain and its perception. Neural states interact with mental states in both directions, causing a noxious circuit that can start with mental pain (suffering) provoking chronic physical pain, or vice versa (Fernández-Salazar 2015)

#### 4 Pain as Homeostatic Emotion

Physiological changes generated during the unpleasant emotional experience caused by pain are part of a defence system that alerts the body to be prepared to confront aversive situations through behaviour of attack or retreat. The theory of emergence expressed by Cannon (1914) says that the body is programmed to maintain an optimal level of activation and adjustment at the time to experience intense emotions caused by pain. Through homeostasis, there is a series of internal adjustments in order to find optimal levels. Emotions function to prevent a particular emergency.

The concept of homeostasis means a steady state of processes, which stabilize by the synchronization and the organization of self-regulating physiological mechanisms. Homeostasis allows the body to maintain its functional integrity in the

internal environment (*milieu intérieur*), and the external fluctuating environment. Claude Bernard and Walter Cannon noticed that the constancy of the cell environment must be preserved and that the internal environment is key to this (Bernard 1859; Cannon 1926). Regulatory organs whose actions appear complementary and coordinated provide homeostasis in phantom limb pain. These organs (e.g. kidneys, lungs, gastrointestinal tract) interface between the external environment—where changes are permanent—and the interior environment, which must remain fixed. As Claude Bernard noted, the internal environment is the necessary condition to the “free and independent life.” “The constancy of the internal environment is the prerequisite for independent living” (Bernard 1859).

The importance of homeostatic mechanisms involved in the control of chronic pain should be noted. In order to maintain the constancy of the internal balance of the body, it is important to consider the internal and external mechanical, thermal and chemical changes, as well as stimuli that cause pain. In the case of a nociceptive stimulus, the body is in an alert state, and the endogenous mechanisms that modulate the unpleasant sensation are activated. This occurs with some hormones, which have an analgesic effect, for example, oxytocin, which the paraventricular nucleus of the hypothalamus (PVN) releases. When the PVN is stimulated, it inhibits pain information that reaches the spinal cord producing an analgesic effect (Condés-Lara 2008, 2009). PVN neurons activated by noxious stimuli can suppress the activation of A-delta and C fibres, inhibiting nociceptive signals that may transform into pain, thus completing an endogenous analgesia system. This mechanism shows that the PVN, as other brain structures, participates in the mechanism involved in pain and analgesia. The same situation applies for other substances such as norepinephrine or serotonin (Fields et al. 2006).

These examples show the importance of homeostasis in controlling pain at an endogenous level. We talk about homeostatic “feelings” in reference to the perception of temperature, to itching, to distension, hunger, thirst, to touch and pain (Craig 2003). In the case of phantom limb pain, a process of internal regulation (homeostasis) occurs wherein an emotional component is essential. The emotion represents the amount of information received (pain) by which the body tries to adapt better to the level of the received stimulation. As Damasio (2000) puts it:

The pervasiveness of emotions would be remarkable if only the “natural” and “acquired” inducers caused them. I submit, however, that what we call emotions and moods are not only caused by these easily recognizable kinds of stimuli but are also caused by the process of regulating life itself. Certain conditions of internal state, engendered by the ongoing processes of maintaining homeostasis and by the organism’s interactions with the environment that are pertinent to homeostatic regulation, induce collections of responses that are formally comparable to the conventional emotions we have been considering (Damasio 2000, p. 18).

Emotions are inseparable from the states of pleasure and pain and represent the mechanisms of life regulation. They constitute a complex survival and adaptation system that is always linked to homeostasis, but also depends on social and cultural influences. As for acute pain, I prefer to consider it not as a whole emotion, but as a homeostatic emotional process with a negative connotation, but necessary and

protective for the body. In contrast, chronic pain is an emotional process but is useless, aversive, and destructive to the body and manifests maladaptive homeostasis. If we compare pain and emotion, both consist of chemical and neural responses that aim to sustain life in an organism and have characteristic adaptive behaviours. Therefore, endogenous balance or homeostasis may decrease chronic pain and contribute to changing the contents of the emotions caused by pain and improving the quality of the life of individuals.

## 5 The Mental Representation of Phantom Limb Pain in the Brain

The neural representation of pain in the brain seems to be formed by a neuromatrix, which describes functional relationships of various sensory areas of the brain, cognitive, emotional and volitional (Melzack 1990). Phantom limb pain indicates that the neuromatrix activates, not only through peripheral receptors, but also intrinsically, so that the brain generates experiences without the need of a lesion to produce pain or a body-part to feel a body. There are no individualized centres or single tracks of “accurate representation” of pain in the brain. In fact, numerous experimental data in the fields of nociception indicate that a single burning stimulus activates several populations of neurons in different regions. In the brainstem, there are probably at least several tens of areas, which activate by that stimulus. These areas include the brainstem, and in the brain, hundreds of neuronal groups (including many thalamic nuclei, the hypothalamus, the amygdala, the hippocampus, the striatum and the cortex) which activate in parallel. There is no *pain centre* in the brain. It is probably the simultaneous activation of all these structures, which constitute the neural correlate of that pain (Bouhassira and Calvino 2009).

With these bases, pain is the subjective representation of a bodily injury which includes the sensory component, the *quale* (one can define *qualia* [plural of *quale*] as the phenomenal or qualitative aspects of our mental life that define what it is like to have a mental experience) as the core content of perceptions that we are sometimes unable to describe. For instance, what it is like to be in pain. However, what is the representation of the pain when it is not due to a physical lesion, as is the case of many types of chronic pain, such as fibromyalgia? The brain regions mentioned above also activate in spite of damage. There must be a kind of a mental representation of suffering or mental pain caused by the negative images, by memories, by the past and the present of the individual before mental pain becomes physical and transforms the neuronal networks. The representation of chronic pain without injury would be what each individual thinks about his/her pain; how they perceive it and the way he analyses or understands his suffering. Therefore, the meaning of this representation would be how it is like to be in pain. In the previous set of elements that includes pain, we face the mind-body connection.



To help identify the nature of phantom limb pain, the quality of chronic pain and its meaning needs study together with its neurobiological mechanisms, and the results integrated to produce a more complete understanding. I propose to study the possibility of a mechanism emerging from a neurophysiological and a mental phenomenon that have subjective and qualitative aspects. In this way, phenomenological and neurophysiological data can correlate non-reductively to form neuro-mental networks. Eventually, we can integrate the two perspectives: the objective perspective of chronic pain and the subjective perspective in a neuro-mental approach, i.e. both physical and mental at the same time. In this way, chronic pain is not only sensation, but also personal perception. This may “provide a richer and more precise description of the texture and structure of pain experiences, especially chronic pain experiences, and to relate pain to the brain” (van Rysewyk 2014).

I believe the distinction between sensation and perception is essential for understanding the complexity of the neuro-mental processes of chronic pain. Perception is more than the conscious and intuitive record of sensations. Perception is not only explained by the nature of the stimulus. In my view, the concept of perception must integrate mental and physiological approaches. It seems important to include consciousness in any definition of perception, even if we cannot accurately describe the phenomenon of consciousness of chronic pain.

Perception is physio-mental and cultural through which the use of the senses, the past of the individual, and his culture, link physical events with cognitive mechanisms. The cognitive process of perception includes attention (the selection of sensory information), interpretation (sensory information retained and transformed into impressions), comprehension (the meaning given to retained sensory information), storage (archiving in the brain sensory information understood and interpreted). The nature of perception is mental, and in the perceptive process, sensation turns into meaning and knowledge. In other words, the notion of perception implies that there is content and representation. In contrast, “pure” sensation may be organic, such as the sensations of hunger, thirst, satiety, nausea, muscle fatigue, orgasm, and tickling. However, it is not the same to have an empty sensation in the stomach as to have the mental representation of a meal, which informs us that we are hungry.

What is the meaning of chronic pain? The meaning of the physical painful representation could be the perceptual understanding of bodily injury. However, it could also consist in the aversive images that cause mental pain, and what we think these images mean. Pain has a fundamental component that characterizes it: the aversive emotion. Emotions are about something and thus, they have meaning. The meaning of pain could be bodily injury, or the illusion of a painful sensation, which one might call a false perception of pain, as in the case of phantom limb pain. It is not that phantom limb pain is false in its experiential qualities and meaning, but in the sense that I feel pain in my foot when the foot no longer exists. Thus, I would consider chronic pain as would I consider consciousness: both are neuro-mental phenomena. The emotional aspect of chronic pain is not just an organic emotional

response, but also an intrinsic quality of the physical sensation and its interpretation.

As we know, with certain surgical procedures such as the prefrontal lobotomy or cingulotomy one can dissociate the cognitive component of the emotional aspect of pain. After surgery, when we ask the patient if he continues to be in pain, he responds that the pain is still there, with the same intensity as before the surgery and he is able to describe it. The difference is that after the surgery the patient is no longer suffering, he does not care about his nociceptive sensation; that is to say, although the intensity of the pain is the same, it does not matter to the patient because what is missing is the affective meaning of pain (Foltz and White 1962). This proves that the most alarming component of pain is the emotional aspect, i.e., the perception and its content, but not necessarily the sensation nor the nociceptive process. In these cases, patients have a nociceptive sensation, but not a perception of pain, and the sensation of *pain* does not cause them to suffer.

Chronic pain is a process in which the different components link in various ways to integrate as a whole, a complex and distinctive representation, which may be the consciousness of pain (Chapman 2005). In this sense, the distinction of the components required to do an analysis is not clear, because the painful experience integrates through the merger of these components. A priori, “each of its components reveals itself as physical and mental, as neurophysiological and conscious at the same time, and pain as a result would be a versatile event perceived by a sensitive individual” (Díaz 2007). As in the case of consciousness, the location of pain can be quite disconcerting. Irrespective of the type of pain, whether acute, chronic or inflammatory, the individual who perceives it normally refers to the location of the lesion. However, neuroscience tells us that the brain produces pain (Butler and Moseley 2003), although the latter is an organ with a deficiency of sensitivity to lesions, which in itself is a rather strange and almost ironic situation. One could say that this is half-true, since pain is indeed produced by this painless brain, but its perception comes from the outside; it is caused, in part privately, individually, especially through mediators such as psychosocial-cultural factors.

However, if we assume that pain is in the brain, it is because the nociceptive receptors arrive there. It is also in the brain that sensations and perceptions are received from outside the brain are subsequently integrated, although we do not yet have a good idea how this is produced, and even less how the distinctive quality of pain occurs; that is to say, its distinctive and unique *quale*.

In the mental representation of pain, when we speak of consciousness, either the consciousness of chronic pain or the awareness to perceive objects and all kinds of elements around us, it is not easy to distinguish between objects, mental representations, aversive images, the stimuli that cause these perceptions, the quality of these experiences and our social and cultural beliefs. It seems that it is precisely in the convergence of all these factors that chronic pain consciousness emerges (Chapman 2005).

The body schema, a part of consciousness, presents as “a system of motor function” as a set of mental representations that operate at the level of consciousness, a perceptual belief system of the body (Gallager and Meltzoff 1996). The body

schema allows us to have knowledge of the position of our body in space. In contrast, the body image consists of a system of perceptions, attitudes and beliefs about our own body, what we think about the mental representations of our body (Gallager and Meltzoff 1996). The concept of self-image can be perceived constructively or destructively. These mental representations are not always part of conscious processing; they form part of the unconscious perception processes of the individual to the extent that they are sets of beliefs or attitudes. It seems then that amputation would cause a discrepancy between the representation of the body image and the body schema. The body image in the amputated patient would remain as it was before the amputation (probably because of the unconscious non-acceptance of the loss of one of its limbs), thus causing the change of body image. Mental images of an integral body will then be processed by the brain that tries to “fill” the amputated portion corresponding to the part of the body in the body schema represented in the somatosensory cortex. This would be one cause of the *existence* of phantom limb pain. The possibility that the chronic mental pain or suffering caused by the visual and constant reality of a missing limb, so the incompleteness of the self body image becomes unbearable, provoking a chronic physical phantom pain. The mirror box and virtual reality are used to modify the body schema through visual feedback, mostly resulting in decreased phantom limb pain (Ramachandran and Rogers-Ramachandran 1996; Ramachandran and Hirstein 1998; Ramachandran and Altschuler 2009). This works only temporarily since once the patient is no longer in front of the mirror box its visual reality always refers him to the actual physical image; that is to say, to the incomplete self-image. So, the phantom pain returns.

## 6 Conclusion

Chronic pain, especially phantom limb pain, is usually treated with expensive medications, which are associated with undesirable side effects. To the extent that chronic pain affects the whole person (body-brain-mind), clinical treatment should be varied and particularly focused on the aversive meaning of pain in a multidisciplinary and holistic perspective. All pains are different because each person has his or her own story; much of chronic pain depends on the personal history of the individual.

Scientific investigation of pain has important limitations. I am as sceptical as Damasio regarding objectivity in the neurosciences (Damasio 1994). On one hand, the results obtained are only approximations; on the other, results are sometimes ambiguous, and there are many ways to interpret them. In the case of phantom limb pain, the limits of science are especially marked because every patient is different and personal subjectivity influences interpretation of the experimental results. Therefore, it is very difficult to make objective analyses. In the study of large populations of patients, some particular cases are sometimes overlooked. However, these cases may hold the key to the sought after results.

Emotions and mental representations that amputees have in relation to their distorted body image after amputation must be studied in order to have a better understanding of the emotional dimension of phantom limb pain. There are several studies showing evidence of distorted body image in people with chronic pain, as well as evidence of distortion of the neural representations of the body image (Lotze and Moseley 2007). It could be possible that phantom pain is produced by the mental pain engendered by the non-acceptance of the loss of a body part and lack of acceptance of the amended body image. If that is the case, the brain does not cause mental pain; but conversely, the mind would provoke physical chronic pain able to transform neural networks generating phantom chronic pain.

Neuroscience has made significant progress in understanding the neurophysiology of pain. We know quite well the physiological mechanisms involved in the process of pain, but we continue to ignore some aspects of the emotional nature of chronic pain, especially regarding phantom limb pain. A non-reductive, multidisciplinary approach is needed. However, it could be that the mind is so complex that we will never understand its mechanisms. However, in chronic pain, evidence indicates that mind dominates brain, not vice versa. The key may lie in brain plasticity. The brain constantly rebuilds. Some studies have shown that it is mental activity that controls brain activity (MacIver et al. 2008), which may lead to inadequate plasticity in patients with chronic pain. However, if mental activity is controlled, it may balance neuronal activity, and reshape the brain by restructuring certain neural networks. Since the mind is an enigma, which for the time being seems mostly inaccessible, a good way to continue the study of the mental nature of chronic pain would be to analyse the relationship between the brain and the universe around us. It is such neuro-mental synergy (internal-external networks) through which consciousness and mind emerges.

The mind is an endogenous and exogenous oscillatory system emerging from the brain, from the constant interaction of the brain with the natural systems of our environment, and with socio-cultural networks. We need a body to receive external stimuli decoded in a perceptual process that takes place in the brain. But a body alone in the wild would be just a mass of fat, bone, water and muscle, unable to perceive external information, and a brain without mind (without the interaction of external networks) would be only a machine. Therefore, it seems essential to conduct holistic study of the mind, of the interaction between the brain and the environment. We cannot content ourselves with a reductionist approach; we need to stop looking for answers only in the brain; we must also look beyond, in our relationships with others, in the biotic and physical structure of our environment, in our emotional dimension.

The challenge in phantom limb pain is to determine the type of emotion felt, and understand how the meaning of the emotion is related to the quality of pain. From a practical perspective, the hope is to modulate the emotion caused by the loss in order to better control phantom limb pain. The type of emotion depends on the environment and circumstances when suffering arises. The quality of the emotion, however, depends on the personal perception that we have about pain as well as on the history of the individual, since we know emotions link to the mechanisms of

memory. The emotion caused by suffering or mental pain will have a relationship with the type of the memories of the individual, which need to be revealed during clinical consultations. The control of those emotions will relate to the motivation of the individual in managing or eliminating physical pain, and of the capacity to identify and understand mental pain, by analysing the relationship between the perceptions that the patient has of his pain with the perception that he has of his environment. Such an objective requires advancement in our knowledge of the phenomenal mind using qualitative research methods. It is imperative that clinicians listen to patients, not only focusing on the list of his symptoms or experimenting with new medications. Understanding pain cannot be limited to knowledge obtained about neural structures and mechanisms using standard, quantitative methods. A deeper study of emotions, of consciousness, and mind and its correlation with the environment, in my opinion, will help resolve the problem of chronic pain and in particular phantom limb pain. We need to seek for answers not only in the brain, but also from studying relationships between the brain and the environment.

## References

- Bartra R (2014) *Anthropology of the brain, consciousness, culture and free will*. Cambridge Press, Cambridge
- Bernard C (1859) *Leçons sur les propriétés physiologiques et les altérations pathologiques des liquides de l'organisme*. Baillière, Paris
- Bouhassira D, Calvino D (2009) *Douleurs: physiologie, physiopathologie et pharmacologie*. p. 94 Arnette, Paris
- Butler DS, Moseley LS (2003) *Explain pain*. Noigroup Publications, Adelaide
- Cannon WB (1914) The emergency function of the adrenal medulla in pain and the major emotions. *Am J Physiol* 33:356–372
- Cannon WB (1926) Physiological regulation of normal states: some tentative postulates concerning biological homeostatics. In: *Jubilé Charles Richet* (ed) Editions Médicales, Paris, p 91
- Chapman CR (2005) “Psychological aspects of pain: a conscious studies perspectives” on the neurological basis of pain. McGraw-Hill, London, pp 157–171
- Clasper J, Ramasamy A (2013) Traumatic amputations. *Br J Pain* 7(2):67–73
- Condés-Lara M (2008) Nociceptive spinothalamic tract and post-synaptic dorsal column neurons are modulated by paraventricular hypothalamic activation. *Eur J Neurosci* 28(3):546–558
- Condés-Lara M, Rojas Piloni G, Martínez Lorenzana G, López Hidalgo M, Rodríguez Jiménez J (2009) Hypothalamospinal oxytocinergic antinociception is mediated by GABAergic and opiate neurons that reduce A-delta and C fiber primary afferent excitation of spinal cord cells. *Brain Res* 1247:38–49
- Craig AD (2003) Pain mechanisms: labeled lines versus convergence in central processing. *Rev Neurosci* 26:1–30
- Damasio A (1994) *L'erreur de Descartes. La raison des émotions*. Odile Jacob, Paris, p 16
- Damasio AR (2000) A second chance for emotion. In: Lane RD, Nadel L (eds) *Cognitive neuroscience of emotion*. Oxford University Press, Nueva York, p 18
- Díaz JL (2007) *La conciencia viviente*. FCE, Mexico

- Fasick V, Spengler RN, Samankan S, Nader ND, Ignatowsky TA (2015) The hippocampus and TNF: common links between chronic pain and depression. *Neurosci Biobehav Rev* 53:139–159
- Fernández-Salazar M (2015) Cortical plasticity related with chronic pain in a continuous interaction of neuronal and mental processes, vol. 8, Center for Cognitive Sciences, University of Minnesota
- Fields HL, Basbaum AI, Heinricher MM (2006) Central nervous mechanisms of pain modulation. In: McMahon SB, Koltzenburg M (eds) *Wall and Melzack's textbook of pain*, 5th edn. Elsevier, China, pp 125–142
- Flor H (2002) Phantom-limb pain: characteristics, causes, and treatment. *Lancet Neurol* 1:182–189
- Flor H (2003) Cortical reorganization and chronic pain: implications for rehabilitation. *J Rehabil Med Suppl* 41:66–72
- Flor H, Nikolajsen L, Jensen TS (2006) Phantom limb pain: a case of maladaptive CNS plasticity? *Nat Rev Neurosci* 7:873–881
- Foltz EL, White LE Jr (1962) Pain “relief” by frontal cingulotomy. *Neurosurgery* 19:89–100
- Gallagher S, Meltzoff AN (1996) The earliest sense of self and others: Merleau-Ponty and recent development studies. *Philos Psychol* 9(2):211–233
- Haggard P, Iannetti GD, Longo MR (2013) Spatial sensory organization and body representation in pain perception. *Curr Biol* 23(4):R164–R176
- Harvie D, Moseley GL (2014) Exploring changes in the brain associated with recovery from phantom limb pain—the potential importance of telescoping. *Eur J Pain* 18(5):601–602
- Hasanein P, Parviz M (2014) Role of GABAA receptor in modulation of acute thermal pain using a rat model of cholestasis. *Pharmacol Biochem Behav* 124:226–230
- Jeannerod M (1994) *The representing brain: Neural correlates of motor intention and imagery*. Cambridge Univ Press 17:187–245
- Jensen TS, Krebs B, Rasmussen J, Nielsen P (1985) Immediate and long-term phantom limb pain in amputees: incidence, clinical characteristics and relationship to pre-amputation limb pain. *Pain* 21(3):267–278
- Lotze M, Moseley GL (2007) Role of distorted body image in pain. *Curr Rheumatol Rep* 9(6):488–496
- MacIver K, Lloyd DM, Kelly S, Roberts N, Nurmikko T (2008) Phantom limb pain, cortical reorganization and the therapeutic effect of mental imagery. *Brain* 131(8):2181–2191
- Melzack R (1990) Phantom limbs and the concept of a neuromatrix. *Trends Neurosci* 13(3):88–92
- Melzack R, Bromage PR (1973) Experimental phantom limbs. *Exp Neurol* 39:261–269
- Mitchell SW (1872) *Injuries of nerves and their consequences*. J.B. Lippincott and Co., Philadelphia
- Moseley GL, Gallace A, Spence C (2008) Is mirror therapy all it is cracked up to be? Current evidence and future directions. *Pain* 138(1):7–10
- Mulder T, Hoschtenbach J, Dijkstra PU, Geertzen JH (2008) Born to adapt, but not in your dreams. *Conscious Cogn* 17(4):1266–1271 (Epub 2007 May 11)
- Paré A (1551) *La manière de traicter les playes faictes tant par hacquebutes que par fleches: et les accidentz d'icelles, comme fractures et caries des os, grangrene et mortification: avec les pourtraictz des intrumentz necessaires pour leur curation. Et la methode de curer les combustions principalement faictes par la pouldre à canon. La vefve Jean de Brie*. Bibliothèque interuniversitaire de médecine, Paris, p 131. <http://www.bium.univ-paris5.fr/histmed/medica/cote?extbmpoit6741>
- Ramachandran V, Altschuler EL (2009) The use of visual feedback, in particular mirror visual feedback, in restoring brain function. *Brain* 132:1693–1710
- Ramachandran VS, Hirstein W (1998) The perception of phantoms limbs. *The D.O. Hebb lectures*. *Brain* 12:1603–1630
- Ramachandran VS, Rogers-Ramachandran D (1996) Synaesthesia in phantom limbs induced with mirrors. *Proc Biol Sci* 263(1369):377–386
- Robinson MJ, Edwards SE, Ivengar S, Bymaster F, Clark M, Katon M (2009) Depression and pain. *Front Biosci (Landmark Ed.)*

- Sanzone AG (2016) Use of nonopioid analgesics and the impact on patient outcomes. *J Orthop Trauma* 1:S12–S15
- Schopenhauer A (2014) *Le monde comme volonté et comme représentation*, I, IV, 57. PUF, Paris, p 396
- Seeman TE, McEwen BS, Rowe JW, Singer BH (2001) Allostatic load as a marker of cumulative biological risk: MacArthur studies of successful aging. *Proc Natl Acad Sci USA* 98:4700–4775
- Sirigu A, Duhamel JR (2001) Motor and visual imagery as two complementary but neurally dissociable mental processes. *J Cogn Neurosci*, 13:910–919
- Sivilotti L, Woolf CJ (1994) The contribution of GABAA and glycine receptors to central sensitization and touch evoked allodynia in the spinal cord. *J Neurophysiol* 72(1):169–179
- Tso AR, Goadsby PJ (2014) New targets for migraine therapy. *Curr Treat Opt Neurol* 16(11):318
- van Rysewyk S (2014) Objective knowledge of subjective pain? Towards a subjective-neuroscience of pain. *Ngau Mamae*, Spring:10–20
- Zhang Z, Tao W, Hou YY, Wang W, Lu YG, Pan ZZ (2014) Persistent pain facilitates response to morphine reward by downregulation of central amygdala GABAergic function. *Neuropsychopharmacology* 39(9):2263–2271