SUMMARY

Pain has a representation in the central nervous system within some of the most ancient structures developed over the phylogenetical history. Also, it is the most important symptom for which patients seek medical attention. However, there are pathologies in which pain stops being the alarm and becomes a medical issue, perhaps the most dramatic example of this would be the presence of pain in a part of the body that is no longer present, this is known as ‘phantom limb pain’.

Over history, much attention has been given to pain understanding by well-known personalities and phantom limb itself was described first by Ambroise Paré in the 16th Century and later described by Silas Weir Mitchell in the 19th Century and thoroughly addressed by Livingston in the first half of the 20th Century.

The non-painful phantom limb phenomena are reported by almost all amputees and there is pain in 50 to 80%, no matter the nature of the amputation. We face a puzzling public health problem. The major cause of limb amputations comes from vascular and neuropathic complications provoked by diabetes, followed in frequency by trauma, all astonishingly prevalent in the general working population in productive ages. A worrying cause of trauma and the phantom limb in some developing countries is caused by anti-personnel mines leading people, a majority of civilians with a considerable amount of children, to a living hell accompanied by a painful phantom.

Phantom limb pain represents a challenge that involves a huge scope of study related to both public health and neuroscience. It is an entity that involves peripheral, central and psychological factors. Neuroscientific research has studied the system from the amputated peripheral nerve, where a neuroma develops, to the cerebral cortex in which there are changes in the somatosensory cortex after limb amputations, related to a decreased activation of the area that would represent the missing limb. Besides, this problem has caused the development of theories such as the ‘neuromatrix’ that is activated in the absence of peripheral sensory information. In this sense, the anterior cingulate cortex has been proposed as a key structure in the development of phantom nociception in animals.

After a huge amount of research, only 30% of patients benefits for a good number of interventions.

Phantom limb pain is a clear example that consciousness can indeed become ill and that the clinical frequency, importance and transcendence make research on the neuroscience of consciousness of vital importance.

The painful phantom represents a tool and challenge in the neuroscientific field, opens the door for the study on consciousness, supports the need for improved healthcare and allows us to think about war and its consequences in the development of society.

Key words: Phantom limb, pain, neuroscience, consciousness.

RESUMEN

El dolor es representado en el Sistema Nervioso Central en algunas de las estructuras más antiguas desarrolladas a lo largo de la historia filogenética. Además, es el síntoma más importante por el que los pacientes buscan atención médica. Sin embargo, existen patologías en las que el dolor deja de ser la alarma y se convierte en un problema médico; probablemente el ejemplo más dramático sea la presencia de dolor en una parte del cuerpo que no está presente, esto se conoce como “miembro fantasma doloroso”.

A lo largo de la historia, se ha prestado mucha atención en el entendimiento del dolor por renombradas personalidades. El miembro fantasma fue descrito por primera vez por Ambroise Paré en el siglo XVI; en el siglo XIX hizo lo mismo Silas Weir Mitchell, y posteriormente fue revisado con mayor profundidad por Livingston a inicios del siglo XX.

El fenómeno del miembro fantasma no doloroso es reportado prácticamente por todas las personas amputadas, y el doloroso en 50 a 80% de los casos, sin importar la naturaleza de la amputación. Nos encontramos frente un importante problema de salud...
Pain is an experience that represents an essential alarm to actual or potential tissue damage (9), however, the problem is when the alarm becomes the illness.

Pain has a representation in the Central Nervous System within some of the most ancient structures developed over the phylogenetical history of animals, such as the peripheral nerves and the spinal cord. Should pain not have developed over the history of life, perhaps life itself would have not succeeded until our days. Furthermore, pain is the most important symptom for which patients seek medical attention and, in many cases, they would not care about their disease were it not for the presence of pain. However, there are pathologies in which pain stops being the alarm and becomes a medical issue, perhaps the most dramatic example of this would be the presence of pain in a part of the body that is no longer present, this is known as "phantom limb pain" (3, 4, 8).

Over the centuries, much attention has been given to pain understanding. Aristotle thought that the heart was the seat for feelings and argued that pain was an emotion. In contrast, Galen recognized the brain as the organ of feeling and placed pain into the sphere of sensation. Avicenna noted that, in disease, pain can dissociate from touch or temperature recognition, and proposed pain to be an independent sensation. Further progress in its thinking awaited the development of scientific tools and several old concepts were substituted by proposals such as that of Newton and Hartley, that neuronal messages were vibrations of substance in nerves (11).

Regarding phantom pain, its first description was given by Ambroise Paré, in the 16th Century who postulated that peripheral factors, as well as a central pain memory, might be causing it (4). In more modern times, the acknowledgement of phantom limb pain was not formally described until 1866, when Silas Weir Mitchell chose to publish his findings in the newspaper The Atlantic Monthly, under a pseudonymous, due to fear of being considered as a charlatan. Public response did not wait, since many of the soldiers wounded during the American Civil War stood for the new ideas, allowing then a proper publication in a scientific journal in 1872 (4, 8). This phenomenon was more thoroughly revised in the beginning of the 20th century by Livingston (6), exemplified by the story of Nick, a personal friend and patient. He made clear how catastrophically this entity is suffered and how it can become a chronic and incapacitating disease.

After these events, although knowledge has grown in a considerable fashion to the massive extent that we have today, patients still suffer from treatment resistant pain syndromes and the knowledge about the neural mechanisms of phantom limb pain has not lead neither to a complete cure nor an effective way of preventing it. In addition, the non-painful phantom phenomena are reported by almost all amputees and there is pain in 50 to 80% of them, no matter the nature of the amputation. We face a puzzling public health problem. The genetic background in Latin America puts its population at a higher risk of diabetes, and the lack of efficient health resources leads many people to poor disease control, ending in vascular complications and neuropathies, which ultimately represent the major cause of limb amputations. Trauma follows diabetic foot as leading cause of limb amputations, being very important, since the highest incidence happens in working population at productive ages (5).

Another issue related to traumatic amputations cannot be left unmentioned, the constant presence of war in many developing countries has left, among other ethically highly questionable things, anti-personnel mines. These devices accounted for 7328 casualties worldwide only in the year 2005, taking those affected with traumatic amputations to being handicapped and
with phantom limb pain. The mentioned number has to be added to thousands more that were not recorded. The International Campaign to Ban Landmines estimates 15 to 20 thousand new landmine casualties every year. This problem is spread through 58 countries in four continents, with Afghanistan, Cambodia, and Colombia being the most affected nations. Furthermore, the expanding number of conflicts around the world has lead to an increasing number of cases related to anti-personnel mines; there are countries that still produce and use these weapons, which condemn civilians to a living hell. Therefore, the problem has to be dealt with in those places where the conflicts are over and in those with arising ones. Amongst all the affected ones in 2005, just to give an example, the vast majority (81%) were civilians, with a considerable amount of children (15).

Phantom limb pain represents a challenge that involves a huge scope of study related to both public health and scientific knowledge, giving neuroscience a very important role. Considering the high prevalence and the transcendence of the problem, a considerable amount of research has been endeavoured in order to understand and effectively treat these patients. The issue is more than complex, it is an entity that involves peripheral, central and psychological factors (4).

From the times of Ramón y Cajal, the changes in the peripheral nerves after denervation were observed and described as a neuroma. More recently, several authors such as Devor (1), Wall (13) and Woolf (14), have suggested the mechanisms within the neuroma that play an important role in the genesis of the phantom. Besides, the role of other structures in the Nervous System has taken the researchers to look up to the roof and try to understand the phantom from the systems above the spinal cord. In this context, at the beginning of the nineties, Ronald Melzack proposed a theory in which a neural network distributed throughout several structures of the Central Nervous System processes parallel information to the sensory input. This signature was consigned as a ‘neuromatrix’ that codifies what has been described as the ‘genetic body of the brain’ which is, in other words, a reference of the body itself, determined genetically. The phantom would then appear when the neuromatrix is activated in the absence of peripheral sensory information (7). In addition, there is a cortical sensory map which was described by Penfield and colleagues as an homunculus. More recent evidence, provided by Herta Flor and her group, using functional magnetic resonance imaging, has demonstrated changes in this region after limb amputations, related to a decreased activation of the area that would represent the missing limb (2). The idea that there are new connections in the somatosensory cortex between the portion that represents the phantom and the adjacent area has been proposed by Ramachandran, as a possible etiology (12). Curiously, in an opposite manner to common research strategies, the above mentioned findings were first obtained from clinical studies that later lead to animal research in order to find the specific mechanisms involved. In this sense, Pellicer and colleagues have proposed that the anterior cingulate cortex is a key structure in the development of phantom nociception in animals. All this basic knowledge provides the fundamental physiological background in order to obtain a rational therapy focused in this difficult clinical entity (10).

Even after a huge amount of modern research and effort, treatment only benefits 30% of the patients after interventions such as local anaesthesia, sympatheticotomy, dorsal-root entry-zone lesions, cordotomy, rhizotomy and pharmacological treatments with anticonvulsants, barbiturates, antidepressants, neuroleptics and muscle relaxants (4).

The problem of phantom limb pain certainly represents a pathological state of human consciousness itself. An individual makes conscious a part of the body that is not there and just to make it worse, it has a good chance of making inexist powerful pain evident. This is a clear example that consciousness can indeed become ill and that the clinical frequency, importance and transcendence make research on the neuroscience of consciousness of vital importance. Consciousness represents a huge question mark which has been tackled by several disciplines. The holistic understanding of consciousness would lead to an unprecedented amount of knowledge from the philosophical, humanistic and scientific points of view regarding the understanding of life itself.

Considering the outstanding success for human nature that this would represent and giving its clinical relevance for millions that suffer from pathologies related to its malfunction, like those with painful phantoms, research in this field becomes an epistemic priority.

Phantom pain represents a powerful tool and a true challenge in several fields. The most obvious of them is the neuroscientific one, which with further time and effort should eventually elucidate the mechanisms involved. Also, the phantom opens a window for the understanding of consciousness. Above all, it provides us with two mainstreams in the social field; on the one hand, it supports the need for improved healthcare in developing societies in order to diminish the catastrophic consequences of not preventing properly chronic controllable diseases. On the other hand, it allows us to think about war and the weapons used in it, which cause severe consequences in the development of individuals and society.
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