Where is hidden the ghost in phantom sensations?

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Abstract

The term phantom sensations (PS) refers to sensations in a missing body part. They are almost universal in amputees and can be both painful and not painful. Although PS have been frequently described in limb amputees, they can also occur in other clinical conditions and several pathophysiological interpretations have been proposed, with a predominance of theories based on a central origin. Actually, different mechanisms are able to create a phantom sensation. After an amputation, PS are frequently generated by the genesis of ectopic action potentials in the interrupted nerve fibers but the PS generator can also be more proximal. Sometimes PS are not created by the stimulation of somatosensory fibers with a missing territory, but they can be the result of central sensitization or neuroplastic changes that allow for the convergence of impulses coming from different body parts (referred sensations), one of which is missing. In conclusion, PS can be generated by both neuropathic and non-neuropathic mechanisms developed in the amputated body part or in other parts of the nervous system. Since these mechanisms are not pathognomonic of amputation there are no hidden ghosts to look for in phantom sensations. The only interpretative rule is just to follow the pathophysiological principles.

Key words: Phantom sensations; Phantom pain; Neuro-pathic pain; Referred pain; Pain pathophysiology

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Core tip: The term phantom sensations (PS) refers to sensations in a missing body part. They are almost universal in amputees and can be both painful and not painful. Several pathophysiological interpretations have been proposed, with a predominance of theories based on a central origin. Actually, PS can be generated by both neuropathic (ectopic) and non-neuropathic (referred) mechanisms developed in the amputated body part or in other parts of the nervous system. Since these mechanisms are not pathognomonic of amputation there are no hidden ghosts to look for in phantom sensations. The only interpretative rule is just to follow the pathophysiological principles.

The term phantom sensations (PS) refers to sensations in a missing body part, phenomena that obviously appear paradoxical (but also intriguing) for the most part of the people. A literary example is in the very famous book "Moby Dick, or the whale" (1851) by Herman Melville, who describes in a short sentence the PS of the Captain Ahab who had a leg amputated by the whale: "here is only one distinct leg to the eye, yet two to the soul".

PS are almost universal in amputees and can be both painful and not painful\textsuperscript{[1-3]}. More precisely, patients can describe their PS in several ways, according to the anatomical and pathophysiological characteristics of the amputation: burning\textsuperscript{[4]}, tingling\textsuperscript{[5]}, or painful\textsuperscript{[6]} sensations, illusory limb movement\textsuperscript{[7]}, visual hallucinations\textsuperscript{[8]}, and so forth.

Although PS have been frequently described in limb amputees, they can also occur in other clinical conditions such as after orchiectomy\textsuperscript{[9]}, mastectomy\textsuperscript{[10]}, tooth’s root canal treatment\textsuperscript{[11]}, penis amputation\textsuperscript{[12]}, ocular evisceration or enucleation\textsuperscript{[13]}. Several pathophysiological interpretations have been proposed for PS, with a predominance of theories based on a central origin, including psychiatric explanations\textsuperscript{[14]}. Actually, different mechanisms (neuropathic or non-neuropathic) are able to create a phantom sensation in a missing body part.

It is largely accepted that any neuropathic mechanism is characterized by the ectopic generation of action potentials in somatosensory afferent fibers\textsuperscript{[15]}. In amputees, neuropathic pain mechanisms of PS can be localized at the level of amputation or more proximally. Sometimes they are strictly linked to the amputation, sometimes not.

After an amputation, PS are frequently generated by the genesis of ectopic action potentials in the interrupted nerve fibers, as demonstrated by human micro-neurographic recordings\textsuperscript{[16]}. Nevertheless, several studies suggested that the PS generator can be proximal to the amputation site. On a pathophysiological point of view, this is not at all strange. In physiology, it is well known that the direct (ectopic) stimulation of a sensory nerve fiber induces a sensation localized in the territory of the stimulated fiber, i.e., in the body part where the receptors are located. When Penfield and Rasmussen described for the first time the sensory homunculus, they reported patients’ sensations evoked in different body parts during the electrical stimulation of the somatosensory cortex\textsuperscript{[17]}. All that considered, when the territory of the stimulated nerve fibers is missing, the adequate ectopic stimulation of somatosensory nerve fibers always creates a phantom sensation, wherever the stimulation is applied.

Several examples can be given. For instance, in a recent paper, selective peripheral nerve blockades suggested a major role played by dorsal root ganglia in the generation of PS in a group of amputees\textsuperscript{[18]}. Very interesting is also the recently described case of a patient with an old hip disarticulation amputation due to a malignant sarcoma\textsuperscript{[19]}. After 1.5 years from amputation, this patient started to complain a severe phantom limb pain, mainly localized at the right phantom thigh. Computed tomography and magnetic resonance imaging showed the presence of a metastatic spinal mass involving the L3 vertebra with stenosis of the right lateral recess. Importantly, the resection of the vertebral mass completely resolved the phantom limb pain, demonstrating that the pain generator was in the sensory nerve fibers compressed at the lateral recess of the lumbar spine and not at the site of amputation.

Moving proximally in the central nervous system, the electrical stimulation of the thalamus during functional stereotactic mapping constantly evoked various PS, including pain, in a group of amputees\textsuperscript{[20]}.

Sometimes PS are not created by the stimulation of somatosensory fibers with a missing territory, but they can be the result of central sensitization or neuropathic changes that allow for the convergence of impulses coming from different body parts (referred sensations), one of which is missing. All that happens because the conscious representation of the body lies in the activation of one or more parts of the sensory cortex, independently from what really occurs in the periphery. This seems to be clearly confirmed in patients with arm amputation where the stimulation of face and trunk can evoke a phantom sensation. Since face and trunk are close to the hand in the cortical representation of the human body, the interpretation for this referred sensation was again the change of cortical representation after the amputation\textsuperscript{[21]}.

On a neurobiological point of view, great importance has been attributed to the rearrangement of the central nervous system in response to the loss of inputs coming from the periphery\textsuperscript{[22]}, but it is important to underline that any injury can induce a change in the cortical body representation, independently from PS occurrence\textsuperscript{[23]}. It is also worth highlighting that referred sensations are not neuropathic per se and can also be observed in healthy subjects, although only in special situations\textsuperscript{[24]}. Since the beginnings of the 20\textsuperscript{th} century it was clear that a painful sensation can be complained in a part of the body as a consequence of a disease in another\textsuperscript{[25]}. This is confirmed by several studies on experimental pain demonstrating how the intense stimulation of some tissues is able to evoke a painful sensation not only in the stimulation site, but also at a distance from it\textsuperscript{[26,27]}. Nowadays referred pain is truly considered a rather common complaint in several clinical conditions.

Moreover, the (traumatic) amputation of a body part is not necessary for the development of PS as demonstrated by the evidence that patients with congenital limb absence can experience PS after minor trauma or minor surgery\textsuperscript{[28,29]}. Interestingly, cortical representation changes can also explain other quasi-phantom phenomena. For instance, in patients with complete spinal cord injury the stimulation of body parts above the lesion can evoke a
sensation below the injury level\textsuperscript{[27]}. All that considered, referred sensations can thus represent an additional pathophysiological basis of PS in amputees.

In conclusion, PS can be generated by both neuropathic and non-neuropathic mechanisms developed in the amputated body part or in other parts of the nervous system. Since these mechanisms are not pathognomonic of amputation there are no hidden ghosts to look for the amputated body part or in other parts of the nervous system.

All that considered, referred sensations can thus represent an additional pathophysiological basis of PS in amputees. In this respect, since PS are generally very stressful for patients, according to Sherman\textsuperscript{[4]}, physicians have an important role in easing the patients’ suffering by educating them about the PS pathophysiology in order to explain that their sensations are not so strange as they appear.

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