Life with No Pain: Congenital Insensitivity to Pain

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Abstract

Pain is mostly associated with unpleasant feelings and is largely despised and feared due to the emotional distress of sensations. However, without pain, humans wouldn't be able to separate harmful actions from non-harmful ones and wouldn't let their bodies heal. The sensation of pain is very crucial to the human body as it acts as a defense mechanism by alerting the body of on-going damage to the tissue or potential damage. The importance of pain is even more obvious when diagnosing patients with congenital insensitivity to pain, as their life is filled with terror of being hurt but being unable to detect it, which could ultimately lead to their death. This article dives into this disorder and how it can affect the normal daily lives of human beings, further revealing the vital importance of pain.

Background

According to the International Association for the Study of Pain, "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." It is very vital that scientists started considering it as 'the sixth sense' [1]. Pain serves a critical survival purpose: it protects our body from risky or damaging situations by prompting it to withdraw and escape these situations. For instance, if a person touches a hot object, a potentially endangering situation, they would displace their hand immediately as an attempt to reduce the damage caused by it. Furthermore, pain helps protect that part of the body after the incident. It informs the brain that this part of the body is damaged and requires time to recover. Therefore, the sensation of pain would alert that person to avoid utilizing it for a while, thus speeding up healing. The final function of pain is pretty straightforward: it helps humans learn to prevent similar damaging situations in the future [1].

When people understand that this sensation is just a neat way for the human body to indicate dangers, it can help to remove some of the worries that often accompany the pain. However, humans should never ignore pain. Unlike an alarm that can be turned off, pain should not be overlooked as it can lead to hazardous consequences such as permanent tissue damage and potentially permanent loss of function.

Before trying to comprehend the mechanism of pain, it is essential to understand the difference between pain and nociception. Pain is the state of agony usually followed by an injury; however, nociception is the subconscious detection of actual or likely tissue damage. Although they might seem very closely related at first, they can occur independently from each other. For example, some people with severe tissue damage might report having no pain or vice versa. Those are believed to be experiencing nociception, but no actual distresses of pain [2].

Mechanism

Pain occurs when special fibers called nociceptors respond to stimuli that can potentially cause tissue damage. Nociceptors are different from the usual neurons as they have a cell-like body with a peripheral axon and an ending that responds to diverse stimuli and is additionally the transmitter of the pain-related information to the central nervous system as shown in figure 1 [3]. Various discrete nociceptors respond to different stimuli like thermal, mechanical, and polymodal nociceptors. Thermal nociceptors mostly respond to heat or cold stimuli and notify the body about it, while the mechanical nociceptors are activated by sharp pinprick-type stimuli. Polymodal nociceptors are responsible for responding to any stimuli that are already causing tissue damage, leading to a slow-burning type of pain [5]. These

nociceptors are the same receptors that also respond to chemicals released in chilly or spicy food like hot pepper, which induces a burning sensation [6].

C-fibers, characterized by unmyelinated axons, are the most abundant subclass of nociceptors, conducting slowly and responding to noxious thermal, mechanical, or chemical stimulation arising from neural crest cells. After the C-fibers, the second most abundant subclass of nociceptors is the thinly myelinated nociceptors that are characterized by their fast conduction and are more likely to convey more sudden pain [3].

When tissue damage occurs, it triggers the release of different chemicals at the site of damage, causing inflammation. Some of these chemicals are Prostaglandins, which enhance the sensitivity of receptors to tissue damage, making humans feel pain more intensely. When those receptors are activated, they transmit an impulse to the brain. The signals travel up the spinal cord and reach the brain, which then processes the information and assesses how dangerous it is. Modern brain imaging has indicated that there is no specific area in the brain that processes pain. Instead, it is a complex array of reactions that take place in several parts of the brain which correspond with emotions, thought processes, etc. [6].

In this process, experience plays an essential role as it indicates if the stimulus was dangerous in the past or not. If the brain thinks that the event is dangerous or potentially damaging, it will evoke the sensation of pain and send impulses out to the peripheral cells that might compel that person to pull away or yell out in distress. Since pain is such a significant signal to the human being, it does not get subjected to the same kinds of filtering that occurs with the other senses. For instance, most senses will adapt to a stimulus that exists for a long time, and it starts to ignore it more and more over time, but in the case of pain, it is never neglected by the nervous system.

Life with No Pain?

Children and even young adults have always wished to have superpowers like not feeling pain ever and similar abilities. This is a very common thought for people as they think that feeling no pain would relieve them from the emotional distress that follows it. Nonetheless, this

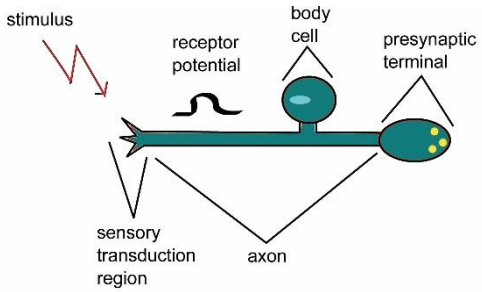

Figure 1: Schematic drawing of a nociceptor showing the four regions of the cell [4]

'super-ability' is not fictional. This rare 'super-ability' has occurred in almost 20 cases, all over the world [7]. However, this isn't something that people should wish for, as the inability to feel pain is extremely fatal and should never be considered as a 'superpower' but rather an exceedingly dangerous disorder.

Congenital Insensitivity to Pain (CIP), is a hereditary disorder where a person is not able to perceive any physical pain from birth. However, they can still feel touch and differentiate between sharp and dull objects, and hot and cold. On the other hand, they can't sense if a hot object is burning their body. As described before, one of the most essential functions of pain is teaching the human brain that doing this action again might injure the body. Hence, patients with CIP cannot comprehend if certain actions are dangerous or not, it leads to the accumulation of wounds and broken bones due to a lack of awareness of the danger and not expressing any discomfort. This ultimately decreases these patients' life expectancy. Most people born with this condition die during their childhood as they often do not realize their fatal injuries, such as broken bones until it is too late {1].

Recent research indicated that the prime cause behind this disorder is a gene mutation in different genes such as the PRDM12 gene, SCN9A, or the NTRK1 gene. Mutations more frequently occur in the NTRK1, the neurotrophic tyrosine receptor kinase 1 gene on chromosome 1, which is the receptor gene responsible for the nerve growth factor. In consequence, failure of differentiation and migration of neural crest cells occurs which induces the complete disappearance of small myelinated and unmyelinated nerve fibers causing the loss of pain sensation [8].

According to a study performed on a 1-year old with CIP, the most common symptoms accompanied by the

insensitivity to pain are frequent episodes of fever, mental retardation, and self-mutilating behavior. This specific child had the gene mutation in the PRDM12 gene, causing frequent tongue and perioral lesions, loss of teeth, and a habit of self-mutilation [8]. Moreover, self-mutilation such as frequent biting of the tongue, fingers, wrists, and feet is considered to be the most dangerous side-effect as it causes severe bleeding. This was evidently shown in a case documented of a 9-month-old boy, who suffered the aforementioned issue as he was reported with 3 months of prior self-mutilation. These further advances the idea that the dire effects of CIP only begin with the fruition of teeth in children as it permits them to hurt themselves through biting without awareness, resulting in scarring and deformation [9].

Unfortunately, there is no definite treatment for this disorder up until now due to the still largely unknown mechanism of pain perception and how such a disorder could cause the dysfunction of pain. However, alternative measures can be taken to help prevent self-mutilation and damage such as a new proposed mouthguard-like appliance that can prevent the biting. This appliance was applied extensively in a 16-month-old girl patient. Through several trials using different materials, the research found that the usage of methyl methacrylate for the mouthguard-like appliance proved to be successful as the 16-month-old girl accepted it and allowed her lesions to heal. It allowed her to enjoy a rather lesion-free life until she learned how to remove the appliance which gave rise to severe lesions and teeth loss. At that point, nothing could protect her from herself except her understanding of the situation and learning that removal of the appliance could injure her fatally [10]. One of the proposed solutions was full mouth extraction: the process of removing all the teeth in one's mouth. The procedure was not agreed upon by the parents due to the psychological and functional implications.

These cases are nothing more than proof to demonstrate that congenital insensitivity to pain isn't a blissful condition, but rather more of a curse to those who have it. A patient named Betz said, "People assume that feeling no pain is this incredible thing and it almost makes you superhuman. For people with CIP, it's the exact opposite. We would love to know what pain means and what it feels like to be in pain. Without it, your life is full of challenges" [11]

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