

Silent pain

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Is there really a point to pain? Yes, argue most. Pain warns you that something is not right. It teaches children not to put their hands on a hot plate because they know heat hurts. It urges you to consult your doctor when pain persists in any part of your body. Yes, but what about pain that accompanies something which has already been diagnosed? What about the persistent pain that frequently escorts chronic conditions, such as a sore back or cancer? Who can see the good in that kind of pain? Though there may be instances when it seems superfluous and even cruel, the sensation of pain is more necessary than it is not. It is a clear indicator that there is something wrong, and that it needs to be seen to. In the absence of pain, no alert signals are given off – which could ultimately put your life in danger. It is a complex sensation with many a meaning and many a pathway. One particular pathway was discovered when members of a family were incapable of feeling pain – a singular and rare condition due to the loss of function of a protein known as SCN9A or Nav1.7.



Hanky Panky, Brenda York

Courtesy of the artist

One of the very first medical descriptions of such an affliction was described in the literature in the 1930s. The article depicted a man who had an act as a human pincushion in a circus. Another similar case was discovered more recently in Pakistan where a young street performer entertained crowds by running knives through his arms or walking on red hot coal – and ended up in hospital on a regular basis for medical care. He died at the early age of fourteen when he threw himself off a roof. A study carried out on his family revealed other cases of seemingly total indifference to pain. In the past few years, yet other occurrences of this peculiar condition have been described. The disease is congenital, very rare – so far only 30 cases have been described worldwide – and though it sounds ideal never to be under the grasp

of pain, life is not necessarily easier for those who suffer from it.

It took many centuries before it was acknowledged that pain could be useful and – in some ways – even protective. For Aristotle, pain was merely part of a man's lot while on earth. Christianity transcended the belief by stating that pain was a divine gift. Although Hippocrates (460-379 BC) had already suggested that pain was the announcement of some form of physical disorder, it was only at the beginning of the second millennium that Galen of Pergamum (129-200 AD), a Roman physician, actually suggested that a network of nerves in our body lead to the brain. Such nerves were capable of distributing three types of perception: locomotion, sensibility and pain, where the purpose of pain was understood as a means of survival. The notion of the 'usefulness' of pain – such as the memory of what can harm or the telltale sign of a physical disorder – only emerged in the 18th century once Science had set itself free from the Church.

Individuals suffering from indifference to pain have already been depicted in the scientific literature but their condition was always accompanied with other serious drawbacks, such as mental retardation for instance. However, the difference between these cases and what the Pakistani street performer was suffering from is that he was otherwise perfectly normal. People with congenital indifference to pain (CIP) present no mental disadvantages. They can discern a dull touch from a pin prick, feel their limbs moving

and even discriminate hot from cold. Their cardiac rhythms are perfectly normal as is their capacity to sweat. The only other deficiency that may be linked to CIP is perhaps a slight loss of smell. But not every individual presents this slight anosmia.

So what is at the heart of this particular case of indifference to pain? A protein: SCN9A, otherwise known as 'sodium channel protein type 9 subunit alpha'. SCN9A is a transmembrane protein found in neurons. It forms a channel through which sodium ions flow, following the membrane's electric gradient. SCN9A seems to be concentrated in peripheral neurons and may well be at the very beginning of the electric impulse which triggers off the pain message and sends it off to the brain. In CIP, SCN9A is truncated and the channel is unable to function. Consequently, the sensation of pain isn't sent to the brain. Scientists were surprised to discover that only one protein seems to be responsible for a sensation which belongs to a pathway that is otherwise so complex. In this instance, SCN9A acts a little like an on/off switch. Certainly, SCN9A is at the very heart of pain perception since another mutation actually heightens the sensation – a condition known as erythralgia.

Pain has many facets. There are many neuronal pathways which trigger off pain. There are many other types of sodium channels involved in its transmission. What is more, polymorphisms may well endow different individuals with differences

in pain perception. Perhaps we all suffer differently. Be that as it may, pain is essential and the bearer of news which is better not to disregard. Babies and young children who suffer from CIP can bite off parts of their lips, chop off the tips of their tongues or burn their hands – which all go unnoticed unless a third party is present. And these are only surface wounds. What of broken bones or bowel blockage for instance?

The scarcity of CIP is precious for the design of drugs such as painkillers. Indeed, any rare disease whose phenotype can pinpoint only one protein – in this case, a sodium channel – is a godsend for scientists. If a drug can be designed to block SCN9A specifically, the side effects could be minimal. Currently, there are many analgesics that can silence pain by blocking other types of sodium channels, but the secondary effects can be big. However, the question arises: is it such a good thing not to feel pain? Imagine a chronic disease. Taking away all sensation of pain could turn out to be a catastrophe. A cardiac arrest could go unnoticed for instance. Perhaps, then, the population should be informed differently on the advent of a common harmful condition? Instead of describing the pain felt in your chest, for instance, why not put more of a stress on the other symptoms which accompany a heart attack? Undoubtedly, there is more to pain than meets the brain. And though, at times it may seem heartless, a life without pain would be like a ship without its hull.

Cross-references to Swiss-Prot

Sodium channel protein type 9 subunit alpha, *Homo sapiens* (Human) : Q15858

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