Editorial

An Update on Precision Pain Medicine: Na^+ Channel Disorders

I will not ease your pain
I will not give up on my friend until I die

I have a "pain" in memory of the "friend".
That I will not cure that pain for a hundred thousand treatments

Rumi, 1207-1273

There has been an explosion in our understanding of the genomic, molecular, and cellular biology data to diagnose health and disease conditions in the last few decades.

The article by N. Mohamad et al., on MDMA neurotoxicity, is a true example of this new area of medicine (1). Pain Medicine concepts are also shifted to better understanding pain syndrome and treatment based on understanding the cellular dysfunction at the level of channels.

First, it started with an interesting report on a rare phenomenon of complete congenital inability to sense pain in three consanguineous families from northern Pakistan. Cox paper in nature (2). showed the mutation gene SCN9A would affect the alpha-subunit of the voltage-gated sodium channel (Na V1.7) and loss its function, which is essential in controlling the upstroke of action potential and transmitting current waves alongside all neuron subunits. The study by McDermott also supports of channelopathy induced by a mutation in the sodium channels can produce complete insensitivity to pain by looking at the fMRI (3).

Another rare functional mutation in the Na V1.7 channel is “Familial Erythromelalgia,” which can cause severe proximal pain, redness, and swelling on the extremities. These patients get more robust action potential with minimal stimulation (<65pA). (4).

So, there is tremendous excitement regarding targeting NaV1.7 to treat pain. Lee et al. used the monoclonal antibody that targets the voltage-sensor paddle of NaV1.7 and effectively suppressed the inflammatory and neuropathic pain in mice (5). Although the results in humans have been mixed, possibly results from the block of Na V1.7 showed to be very profound to see the effect clinically.

Pain Channelopathy is a new and evolving concept of pain, and a wide variety of new diseases are regularly reported, such as paroxysmal extreme pain disorder (NaV1.7 channelopathy), Familial Episodic Pain Syndrome (TrpA1 channelopathy), and familial hemiplegic Migraines (P/Q Ca Channels, NaV1.1 channelopathy) (6).

Mild mutation of sodium channels (NaV1.7 and NaV1.8) are also seen in more common diseases, such as small fiber neuropathy (7).

Understanding the changes in the function and spatiotemporal patterns of these ion channels' expression could be the key to controlling the nociception excitability and, eventually, how to alter the pain status.

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A. Sassan Sabouri, M.D.
Assistant Professor
Department of Anesthesia, Critical Care and Pain Medicine,
Massachusetts General Hospital and Harvard Medical School,
Boston,
MA 02114
The United States
Email: asabouri@mgh.harvard.edu

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