

Pain can be highly variable and unpredictable. Genetics may be key to identifying pain mechanisms that control the intensity, duration, and physiologic response in individuals with chronic pain. Pharmacogenomics and precision medicine are permitting advances in pain control with analgesic drugs that have increased effectiveness and lead to decreased side effects. Knowledge of genetic variations related to how and why patients experience pain will aid in identifying those at risk, provide a better understanding of the phenomenon of pain, and possibly lead to innovative therapies to control pain.

AT A GLANCE

- Pain variability is influenced by heritability, environmental factors, and genetic polymorphisms in nociceptive and neurotransmitter genes.
- Genes controlling voltage-gated channels of neurons and genes regulating catecholamines, as well as cell membrane receptors, contribute to pain sensation and transmission.
- Healthcare providers should incorporate family pain history into the patient's overall assessment to identify potential genetic risk that could aid in providing personalized pain management strategies.

KEYWORDS

pain; genetics; pain assessment; pain management; precision medicine; pharmacogenomics

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Cancer-Related Pain

Understanding genetic influences and determining implications for practice

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In cancer care, nurses are familiar with pain management, yet many aspects about pain remain puzzling. For example, the ways in which individuals experience pain and the susceptibility of individuals to pain—and whether genetics play a role—are questions still under consideration. This article reviews findings related to the genetics of human pain that affect sensitivity and the nervous system's transmission of pain, as well as nursing implications concerning pain management therapies in clinical practice.

Pain Variability

Variability in the pain experience has long been attributed to a number of external factors. Pain variability may also be linked to behaviors attributed to certain personality types and is indirectly related to risk-taking behaviors (Devor, 2014). For example, men in many cultures are taught to be stoic and not express feelings of pain, even if pain is present (Devor, 2014).

Mogil (2012) reviewed the interactions between environmental causes and genetics that play a role in pain susceptibility, intensity, and variability. Heritability studies of pain have been conducted with human and animal models to examine the degree to which heritability is responsible for chronic pain. Heritability is the percentage of variation in a population's trait that can be attributed to inherited genetic factors; it is an estimate of what portion of a particular trait can be explained by a person's genetic variation (National

Cancer Institute, n.d.). These estimates are not indicators of disease risk, but they may indicate if a trait is highly heritable. In chronic pain disorders, pain sensitivity heritability estimates range from 9%–60% and increase with pain severity (Denk & McMahon, 2016).

Genetic Pain Studies

By studying chronic pain, researchers have been able to identify genes that could be responsible for pain conditions. Two groups of genes have emerged: ion channel subunits and nerve growth factor (NGF)-related genes (Denk & McMahon, 2016). The beta subunit of an NGF gene (*NGFB*) and a receptor gene (*NTRK1*) play a significant role in hereditary sensory automatic neuropathies (HSANs), specifically types 4 and 5, and cause insensitivity to pain (National Center for Advancing Translational Sciences, 2016).

Neurotransmitter-related genes also contribute to pain perception (James, 2013). Catecholamines (i.e., norepinephrine, epinephrine, and dopamine) affect pain sensitivity and perception through complex mechanisms in the central nervous system. Genes controlling the metabolism, function, and breakdown of catecholamines have been studied in several chronic pain conditions. For example, catechol-O-methyltransferase codes for enzymes that break down catecholamines, affecting pain sensitivity in fibromyalgia.

Altered ion channels and receptors can influence the excitability of pain-signaling neurons (Devor, 2014). More than 400