Study on the Relationship Between DNA Methylation and Pain

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**Abstract.** Chronic pain has become a great threat to people health. Research has proved that epigenetic regulation may explain the pathogenesis of pathological pain, which may lead to the development of its therapeutic means. DNA methylation is the popular type of epigenetic. Research has proved that DNA hypermethylation exists in pain state widely. In this article, reviewed the latest research progress of epigenetic regulation of chronic pathological pain from DNA methylation.

**Introduction**

In recent years, more and more studies on the mechanism of pain development and maintenance. With the rapid development of epigenetics, the epigenetic mechanism of pain has been further studied. The progress of epigenetic mechanism of pain in this paper Make a review.

**Chronic Pain Is a Great Threat to People Health**

Chronic pain is a serious threat to human health diseases, not only to patients with physical and mental pain, reduce the quality of life, while increasing the economic burden of family and society. Recent studies have shown that the prevalence of chronic pain is on the rise. Schopflocher D [1] found that the prevalence of chronic pain in Canada was 18.9\% by telephone questionnaire. The common pain areas in the three areas Is the waist, neck and knee. The current clinical treatment of pain drugs are antidepressants, NMDA antagonists, opioid analgesics, etc., mainly through their interaction with NMDA receptors or opioid receptors play an analgesic effect. However, most of these drugs have more adverse reactions, limiting their wide range of applications. Chronic pain also increases the financial burden on patients and society. According to the US Council on Medical Consumption, as of 2008, 100 million people in the United States suffer from chronic pain, pain patients and non-pain patients per person per year increased 261-300 dollars in medical expenses, because of pain caused by the loss of productivity Of the value of 299 billion -355 billion US dollars.

**Chronic Pain and Epigenetics Are Closely Related**

Recent studies have shown that [2], chronic pain and epigenetics are closely related. Epigenetics refers to the DNA sequence does not change, but gene expression has undergone a genetic change, mainly in the DNA methylation, histone modification, non-coding RNA regulation, gene imprinting, X chromosome inactivation and so on. DNA methylation is the most
thoroughly studied epigenetic mechanism in vertebrates. DNA methylation occurs in the CpG island cytosine fifth carbon (C5) on. DNA methylation is catalyzed and maintained by DNA methyltransferase (Dnmt). It is generally believed that mammalian Dnmt has 4 species, divided into two families: Dnmt1 and Dnmt3. The Dnmt1 family maintains its methylation during DNA replication and repair; the Dnmt3 family catalyzes Cpg de novo methyla- tion. Dnmt3 includes two de novo methyltransferases Dnmt3a, Dnmt3b and a regulatory protein Dnmt3. DNA methylation is generally believed to inhibit gene expression through two pathways. The first is a direct inhibition of transcription factors and methylated CpG island binding, direct inhibition of gene expression; the other is through the recruitment of DNA methyl-binding protein (Methyl-CpG-binding proteins, MBP) and some hinder complexes to prevent The transcription factor binds to a specific DNA sequence and indirectly inhibits gene expression.

**DNA Methylation and Pain Have a Close Relationship**

Studies have shown that DNA methylation and pain have a close relationship: 1. Pain patients, animal models, the degree of DNA methylation increased. Studies have shown that [3] sustained pain state of spinal dorsal horn cells CpG island methylation, CpG island methyl binding protein (MeCP2) increased. 2. Hypermethylation of pain-related gene promoter DNA, leading to decreased pain-related gene expression. Aging induced disc degeneration and back pain model [4], extracellular matrix protein SPARC promoter methylation increased, SPARC expression decreased. 3. DNA methylation inhibitors have a role in the treatment of pain. Studies have shown that [5], DNA methylation transferase (DNMT) inhibitor 5-azacytidine can inhibit the level of DNA methylation and DNMT expression, to reduce the pain effect. 4. DNA methylation is closely related to synaptic plasticity, and synaptic plasticity is one of the important mechanisms of chronic pain.

Bai[6] found that rat sciatic nerve chronic constriction injury, CCI)spinal cord extensive DNA methylation, daily intrathecal injection DNMTs inhibitor 5 - azacytidine (5 - azacytidine, 5 - AZA) can significantly reduce the degree of DNA methylation and weaken the CCI caused hyperalgesia. 5 - AZA can relieve pain caused by nerve injury in rats Pain suggests that DNMTs inhibitors are expected to be epigenetic drugs [7-8]. Zhong [9] found that the descendants of CCI female rats Compared with the control group showed an increase in anxiety or anxiety behavior in the hypothalamus in the nucleus of oxytocin levels decreased; In addition, CCI female offspring apricot Increased expression of DNMT1 in the nucleus of the nucleus causes DNA methylation levels upregulated, indicating that the parental neuropathic pain may pass through endocrine mechanisms and brain nuclei of epigenetic changes affect the emotions of future generations. Related behavior, initially revealed that chronic pathologic pain is parental inherited Epigenetic regulation mechanism. Moloney [10] induced IBS-like viscera in water stress the methylation of the GR promoter was found in the amygdala of the rat model increased expression of GR and decreased negative expression of HPA axis. The methylation level of the CRF promoter was decreased at its mRNA level increased, the two together to make a lot of glucocorticoid secretion, HPA axis of the decreased ability to show that GR and CRF DNA methylation changes in the expression of the state and its associated genes may cause visceral pain, but its specific mechanism remains to be further studied. While in the back of the model rats in the root ganglion neurons, DNMT1 mediates the analgesic gene in cannabinoids Receptor 1 (cannabinoid receptor 1, CNR 1) upstream promoter methylation, thereby downregulating the expression of CNR 1, making it to TRPV1 of the inhibitory effect weakened, causing IBS visceral pain symptoms.
In summary, pain is a complex physiological and psychological activity that involves multipart and more level, multi-level role, the mechanism is extremely complex. To explore the body was nuisance changes in epigenetic modification after stimulation and its regulation of gene expression will be clarify the mechanism of pain and provide a new direction and new ideas for its treatment.

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References


