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Nav1.8, an analgesic target for nonpsychotomimetic phytocannabinoids

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Abstract

Pain impacts billions of people worldwide, but treatment options are limited and have a spectrum of adverse effects. The search for safe and nonaddictive pain treatments has led to a focus on key mediators of nociceptor excitability. Voltage-gated sodium (Nav) channels in the peripheral nervous system-Nav1.7, Nav1.8, and Nav1.9-play crucial roles in pain signaling. Among these, Nav1.8 has shown promise due to its rapid recovery from inactivation and role in repetitive firing, with recent clinical studies providing proof-of-principal that block of Nav1.8 can reduce pain in humans. We report here that three nonpsychotomimetic cannabinoids-cannabidiol (CBD), cannabigerol (CBG), and cannabinol (CBN)-effectively inhibit Nav1.8, suggesting their potential as analgesic compounds. In particular, CBG shows significant promise due to its ability to effectively inhibit excitability of peripheral sensory neurons. These findings highlight the therapeutic potential of cannabinoids, particularly CBG, as agents that may attenuate pain via block of Nav1.8, warranting further in vivo studies.

Keywords: cannabidiol; cannabigerol; cannabinol; sensory neurons; voltage-gated sodium channel.

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