An Alternative to Medical Marijuana for Pain?

Findings from a new study in Biological Psychiatry

Philadelphia, PA, March 4, 2015 – Medical marijuana is proliferating across the country due to the ability of cannabis ingestion to treat important clinical problems such as chronic pain. However, negative side effects and the development of tolerance limit the widespread therapeutic use of Δ⁹-tetrahydrocannabinol (Δ⁹-THC), the major psychoactive ingredient in cannabis.

THC’s side effects are produced via its actions at cannabinoid CB₁ receptors in the brain. Thus, scientists theorized that an agent with similar mechanistic actions, but that activate CB₂ receptors instead, may eliminate the unwanted side effects while maintaining an equivalent level of efficacy.

Dr. Andrea Hohmann and her colleagues at Indiana University tested this strategy and found that, unlike Δ⁹-THC, repeated dosing with the cannabinoid CB₂ agonist AM1710 suppresses chemotherapy-induced pain in mice without producing tolerance, physical withdrawal, motor dysfunction, or hypothermia. Moreover, the therapeutic effects of AM1710 were preserved in mice lacking CB₁ receptors but absent in mice lacking CB₂ receptors.

Their findings are reported in the current issue of Biological Psychiatry.

“Our study is important because it demonstrates beyond doubt that activation of cannabinoid CB₂ receptors suppresses neuropathic pain without producing signs of physical dependence (i.e., a withdrawal syndrome) or other unwanted side effects associated with activation of CB₁ receptors in the brain,” said Hohmann.

Their studies used animals that were treated with a chemotherapeutic agent (paclitaxel) to produce pain. When animals were given AM1710, a CB₂ agonist, its pain-suppressive effects were fully preserved and its therapeutic effects were maintained even after repeated dosing.

Alternatively, and as expected, when animals were given Δ⁹-THC, they developed complete tolerance to the pain-suppressing effects of THC and with repeated dosing, THC was no longer effective in suppressing neuropathic pain.

When the THC-treated animals were challenged with a drug that blocks CB₁ receptors in the brain, the animals showed a prominent withdrawal syndrome, indicating signs of physical dependence following removal of THC. Strikingly, this was not the case with the CB₂ agonist; blocking either CB₁ or CB₂ receptors produced no signs of withdrawal in animals treated chronically with the CB₂ agonist.

Hohmann added, “We think our data suggests that CB₂ receptors are an important target for suppressing chronic pain without unwanted side effects (e.g. psychoactivity, addiction).”

“It is important to know whether the benefits of cannabis ingestion for pain could be attributed in large part to the stimulation of CB₂ receptors,” commented Dr. John Krystal, Editor of Biological Psychiatry. “CB₂ agonists, in theory, would present less risk regarding addiction and intoxication than the ingestion of cannabis or THC.”

More work will be necessary before CB₂ receptor agonists could be prescribed for use in humans, but for now, these data support the therapeutic potential of CB₂ agonists for managing pain without the adverse effects associated with cannabis.

The article is “Chronic Cannabinoid Receptor 2 Activation Reverses Paclitaxel Neuropathy Without Tolerance or Cannabinoid Receptor 1–Dependent Withdrawal” by Liting Deng, Josée Guindon, Benjamin L. Cornett, Alexandros Makriyannis, Ken Mackie, Andrea G. Hohmann (doi:...