Improved Endogenous Opioid Anti-Nociception with Reduced Neurodegeneration, Hyperalgesia, Allodynia and Tolerance

Published date: Feb. 1, 2012

Technology description

Endogenous opioid peptides and receptors evolved to modulate nociceptive input in response to injury. One of those peptides, dynorphin, acts on the kappa opioid receptor subtype to produce analgesia without sedation, respiratory depression or constipation. Prior to this invention, dynorphin was not an acceptable analgesic because of certain severe toxic side effects, when given in doses higher than physiological concentrations, mainly NMDA mediated neurotoxicity. Dynorphin produces its deleterious side effects by producing an NMDA mediated motor paralysis. In disease states such as stroke, spinal cord injury or neuropathic pain, activation of NMDA receptors by endogenous dynorphin may lead to neurodegeneration, hyperalgesia and allodynia. Tolerance to opiate drugs may also be mediated by the NMDA actions of dynorphin. This invention provides materials and methods to block NMDA receptor activation by dynorphin thus allowing the use of exogenous dynorphin as a beneficial nociceptive agent without side effects and preventing pathological actions of endogenous dynorphin in response to injury.

Advantages

Experimental data demonstrate: 1) attenuation of motor activity deficits, flaccid paralysis and mechanical allodynia produced by dynorphin administration; 2) reduction of infarct size and locomotor deficits after cerebral ischemia; 3) the reduction of morphine tolerization; and 4) so far no visible side effects.

Institution

NIH - National Institutes of Health

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com