

Chronic pain, defined as pain lasting more than 3-6 months, affects approximately 20% of the global population and has a profound socioeconomic effect, inducing a severe drop in the quality of life of patients with few effective treatment and management options available. Relaxin-3, a neuropeptide, has been shown to diminish the sensation of pain in a chronic pain mouse model, and as such has been identified as a potential target for pain management therapies treating chronic pain. However, in order to be an effective treatment, Relaxin-3 must also affect the emotional aspect of pain. This project sought to determine whether Relaxin-3 is able of doing so via a Conditioned Place Preference paradigm utilizing pain relief as a rewarding incentive. We found that Relaxin-3-induced pain relief is able to create a preference for the associated chamber in an inflammatory chronic pain mouse model, but not in their painless counterparts, indicating that Relaxin-3 is indeed able to affect the emotional aspect of pain. Via pharmacogenetic manipulation of the Relaxin-3 circuits of the Bilateral Amygdala, we additionally found evidence that Relaxin-3 induces pain relief via the inhibition of Bilateral Amygdala Somatostatin Neurons. Finally, we generated a continuous activation of the Relaxin-3 pathway in the Anterior Cingulate Cortex by virally inducing the production of R3/I5, analyzing its effects on the development of chronic pain. We found no apparent abnormalities in regards to the behavior of the mice or their development of chronic pain; however we determined that the effects of R3/I5 expression are functionally identical to those of Relaxin-3 injection, and thus determined that it is a potential alternative to these injections.