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Using DREADD to Examine the Role of Infralimbic Gq-coupled Receptors in Fear Acquisition

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Using DREADD to Examine the Role of Infralimbic Gq-coupled Receptors in Fear Acquisition*

Héctor A. Haddock Martínez; James Porter, Ph.D.; and Anixa Hernández-López

Abstract

Post-Traumatic Stress Disorder (PTSD) can develop after a person experiences a very traumatic event that produces a strong and long-lasting aversive memory. During any given year, approximately 8 million adults will suffer from PTSD. Existing treatments often fail to achieve a full extinction of the traumatic fear the patients re-experience. Consequently, how the brain processes and modulates fear memories continues to be an active area of research. The excitability of the infralimbic cortex (IL), a sub-region of the medial prefrontal cortex, is important for fear extinction. Previous studies done in our lab found that Gq-coupled receptors located in this region of the brain, specifically muscarinic and mGluR5 receptors play a critical role in the consolidation of extinction memory. However, their effect on the acquisition of fear is still unknown.

Thus, the main purpose of this research is to determine whether the activation of Gq-coupled receptors in IL prior to the learning of fear affects fear memory. We hypothesized that stimulation of these receptors during fear conditioning would decrease acquired fear. To test this, we utilized a pharmacogenetic approach in the form of Designer Receptors Exclusively Activated by Designer Drugs (DREADD), which allow for controlled manipulation of the desired area in the brain using the selective agonist CNO. Adult male Sprague Dawley rats were surgically infused with a virus, which expressed a Gq-coupled DREADD. Three weeks later, the rats will be injected with CNO one hour prior to behavioral training and sacrificed for immunohistochemistry to examine neuronal activity.

KEYWORDS: PTSD; Gq; IL; DREADD; Fear conditioning

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ABSTRACT

Post-Traumatic Stress Disorder (PTSD) can develop after a person experiences a very traumatic event that produces a strong and long-lasting aversive memory. During any given year, approximately 8 million adults will suffer from PTSD. Existing treatments often fail to achieve a full extinction of the traumatic fear the patients re-experience. Consequently, how the brain processes and modulates fear memories continues to be an active area of research. The excitability of the infralimbic cortex (IL), a sub-region of the medial prefrontal cortex, is important for fear extinction. Previous studies done in our lab found that Gq-coupled receptors located in this region of the brain, specifically muscarinic and mGluR5 receptors play a critical role in the consolidation of extinction memory. However, their effect on the acquisition of fear is still unknown.

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