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The Effects of Pharmacogenetic Activation or Inhibition of the Infralimbic Cortex on Fear Conditioning

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ABSTRACT

Post-Traumatic Stress Disorder (PTSD) can develop after experiencing a very traumatic event which produces a profound and lasting aversive memory in the affected person. Annually, about 8 million people suffer from PTSD. Current treatments are not optimal in achieving a full extinction of the traumatic fear the patients reexperience. Therefore, how the brain processes and modulates fear memories continue to be an active area of research. The excitability of the infralimbic cortex (IL), a sub-region of the medial prefrontal cortex (mPFC), is important for fear extinction, but the effects of IL on fear conditioning have not been extensively studied. Pharmacogenetic approaches, such as Designer Receptors Exclusively Activated by Designer Drugs (DREADD), currently allow for specific and controlled manipulation of different areas of the brain to study their respective functions. The main purpose of this research is to determine whether the excitability of IL affects fear conditioning. We hypothesized that activation of IL during fear conditioning would decrease the acquired fear. To test this, adult male Sprague Dawley rats were surgically infused with a virus that expressed a stimulatory DREADD. Three weeks later, the rats were exposed to fear conditioning, and sacrificed for immunohistochemistry to examine neuronal activity. Preliminary results show that activation of the DREADD receptor increased labeling of c-Fos, and pErk, which indicates increased neuronal activity. This suggests that stimulating the DREADD receptors is activating that brain structure. Next, we will examine whether activation of IL during fear conditioning will decrease acquired fear levels.

Key Words: Infralimbic Cortex, Fear Conditioning, DREADD, PTSD

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