OPRM1 Gene

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opioid receptor mu 1

genes

1. Introduction

The *OPRM1* gene provides instructions for making a protein called the mu (μ) opioid receptor. Opioid receptors are part of the endogenous opioid system, which is the body's internal system for regulating pain, reward, and addictive behaviors. It consists of opioid substances produced naturally within the body (called endogenous opioids) and their receptors, into which opioids fit like keys into locks. Opioid receptors are found in the nervous system, where they are embedded in the outer membrane of nerve cells (neurons). When opioids attach (bind) to the receptors, the interaction triggers a series of chemical changes within and between neurons that lead to feelings of pleasure and pain relief.

The μ opioid receptor was the first opioid receptor to be discovered. It is the primary receptor for endogenous opioids called beta-endorphin and enkephalins, which help regulate the body's response to pain, among other functions. The μ opioid receptor is also the binding site for many opioids introduced from outside the body (called exogenous opioids). These include commonly prescribed pain medications such as oxycodone, fentanyl, buprenorphine, methadone, oxymorphone, hydrocodone, codeine, and morphine, as well as illegal opioid drugs such as heroin.

When endogenous or exogenous opioids bind to the μ opioid receptor, the interaction triggers a cascade of chemical signals in the nervous system. These signals reduce the activity (excitability) of neurons in certain areas of the brain, which leads to pain relief and feelings of pleasure and intense happiness (euphoria). In addition, the chemical signaling ultimately increases the production of a chemical called dopamine. Dopamine is a chemical messenger (neurotransmitter) that helps regulate areas of the brain involved in reward-seeking behavior, attention, and mood.

2. Health Conditions Related to Genetic Changes

2.1. Alcohol use disorder

2.2. Opioid addiction

Common variations (polymorphisms) in the *OPRM1* gene have been studied as risk factors for opioid addiction. Opioid addiction is a long-lasting (chronic) disease characterized by a powerful, sometimes uncontrollable urge to use opioid drugs. Opioid addiction has major health, social, and economic effects.

The best-studied *OPRM1* gene polymorphism changes a single protein building block (amino acid) in a particular place in the μ opioid receptor protein. Specifically, it replaces the amino acid alanine (A) with the amino acid glycine (G) at position 118, written as Ala118Gly or A118G. (This polymorphism is also identified with a unique number, rs1799971.) The A118G polymorphism likely has an effect on the amount of μ opioid receptor present in the membrane surrounding neurons, and on the ability of the receptor to transmit chemical signals. Research into the association of this polymorphism with opioid addiction has had mixed results. Some studies suggest that having glycine (G) instead of alanine (A) increases the amount of an opioid medication needed to achieve pain relief and raises the risk of opioid addiction. However, other studies found no association between the polymorphism and opioid addiction, and still others reported a lower risk with the glycine (G) version of the polymorphism.

The glycine (G) version of the A118G polymorphism is much more common in certain populations, such as people of Asian or European ancestry, than in others, such as people of African or African American ancestry. These differences may help explain why the results of studies examining its role in opioid addiction have had conflicting results. Researchers suggest that studies with many more people would be needed to confirm an association between this polymorphism and the risk of opioid addiction in any particular population.

Common variations in the *OPRM1* gene other than A118G have also been associated with opioid addiction in specific populations, such as Han Chinese, European Americans, and African Americans. The A118G polymorphism and other common variations are among many suspected risk factors for opioid addiction. It is likely that a combination of health, social, economic, and lifestyle factors interact with genetic factors to determine an individual's risk of developing this complex disease.

2.3. Other disorders

Variations in the *OPRM1* gene have been associated with addiction to several additional substances. The μ opioid receptor appears to play a critical role in regulating the pleasure and reward that come from the use of alcohol, nicotine, and certain other drugs of abuse. Although these substances do not interact directly with the μ opioid receptor, they affect the levels of other neurotransmitters in the brain, triggering the body's own endogenous opioids to attach to the receptor. This interaction starts the cascade of chemical signaling in the brain that leads to pain relief and feelings of relaxation and pleasure.

As with opioid addiction (described above), most of the research on the connection between the μ opioid receptor and other addictions has focused on the A118G polymorphism. Studies of the effects of this polymorphism on nicotine and alcohol abuse have had inconsistent results, with different studies suggesting an increased risk, a decreased risk, or no effect of having glycine (G) versus alanine (A) at position 118. A person's geographic and

ethnic background may be important, and larger studies would be necessary to determine whether a true association exists.

Studies have also found associations between the A118G polymorphism and a variety of other traits, including perception of physical and psychological pain, sensitivity to social rejection, a preference for sweet and fatty foods, and how the body responds to stress. It is unclear how this genetic variation causes changes in the brain that influence these traits.

Another polymorphism in the OPRM1 gene, usually written as rs540825, is associated with the effectiveness of a drug called citalopram in people with major depressive disorder. This polymorphism changes a single amino acid near one end of the μ opioid receptor. People with major depressive disorder who have this polymorphism are more likely to experience periods without any symptoms (remission) when treated with citalopram than those who do not have the polymorphism.

3. Other Names for This Gene

- LMOR
- M-OR-1
- MOP
- MOR
- MOR-1
- MOR1
- mu opiate receptor
- mu opioid receptor hMOR-1a
- OPRM

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