Brunner's Syndrome: The Overview

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Abstract

Brunner's Syndrome is a relatively unknown X-linked recessive gene mutation. This means that it requires both alleles to be present for this mutation to occur and they only exist on the X chromosome. This was discovered when all the males in a specific Dutch family had heightened impulsive behaviors and more violent/aggressive tendencies. This led to the discovery of Brunner's Syndrome and the start of a relatively undiagnosed syndrome. The mutations cause a deficit in the protein MAO-A which means that norepinephrine, dopamine, and serotonin degrade slower thus resulting in a higher concentration of all of these neurotransmitters. Leading to the increase in aggressive and impulsive behavior

Brunner's Syndrome: The Overview

A relatively new addition to the world of genetic disorders is Brunner Syndrome. Characterized by ADHD like tendencies, high impulsivity and aggressive or violent outbursts, difficulty sleeping rather through night tremors or insomnia. This recent discovery has also led to Brunner's argument that genetics rather than decision making process can lead to criminal activity or decisions. This is mostly defended by research done on mice with similar mutations and as a result Brunner believes that individuals cannot be held responsible for their genetics and should be dealt with differently in court hearings.

Discovery

Brunner's Syndrome was discovered in 1993 by H.G. Brunner and his colleagues. This disease was first discovered when all the men in a Dutch family shared a similar gene defect. This defect caused them all to react with aggression when they were either fearful or stressed. Brunner discovered later that MAO-A gene, which is responsible for managing fight or flight neurotransmitters, was completely inactive during all these male interactions. This meant that all the men had extremely heightened levels of norepinephrine, dopamine, and serotonin.

Clinical Symptoms

There are many ways that the MAO-A mutation causes complications in the body. Due to the increased norepinephrine those with Brunner's syndrome struggle to sleep or to stay asleep. Due to the increased dopamine those with Brunner's syndrome tend to be more impulsive as everything they do whether they think it through or work for it tend to send a large amount of positive stimulus to their brain leading to much more erratic decision making. The heightened amount of serotonin in their brain due to the lack of regulation also leads to muscle tremors and twitchiness. If left without treatment the disease progresses over time leading to more impulsivity and erratic behaviors, there isn't a mass deterioration of any functions unrelated to

the initial issues caused by Brunner's syndrome, just an exaggeration of the starting symptoms. The current prognosis of Brunner's syndrome is that if there is no treatment the impact on one's decision making, and violent behavior will only continue to worsen and become more extreme. There are very few current treatments, one of the most recently discovered treatments is cautious dosing of SSRI's as well as dietary change to help lower serotonin in the system and increase MAOA proteins to help promote the degradation of norepinephrine, serotonin, and dopamine.

Genetic Basis

Brunner's Syndrome is a genetic defect that affects the MAOA gene. The MAOA gene controls the production of the MAO-A protein. This protein is used to degrade neurotransmitters such as norepinephrine, serotonin, and dopamine. The absence of this protein leads to an excess of these neurotransmitters and in turn can cause more aggressive behavior, more impulsive behavior and trouble falling asleep or staying asleep. This gene is located on the X chromosome with a recessive pattern. This is why the first documented case of Brunner's Syndrome was a family where all the men were affected. The recessive X link means that it requires both alleles to be present for the mutation of the MAOA gene to be apparent. Meaning that men only need 2 of the alleles while women need 4 of the alleles. The location of the MAOA gene on the x chromosome is 11.3p. This means that it is on the shorter side of the X chromosome or on the p side of the chromosome. There are many different mutations in the MAOA gene that give rise to disease. There is GLN296TER, this is the mutation that was recorded with the first Dutch family that was diagnosed with Brunner's Syndrome. Another mutation that leads to Brunner's Syndrome is 1-BP INS which was recorded in two adult brothers from an Australian family. A third mutation that leads to Brunner's Syndrome is ARG45TRP this was also found from a different family with 2 adult brothers in Australia.

Intracellular Functions

The protein produced from the gene MAOA is the MAO-A protein. The normal cellular function for the MAO-A protein is the degradation of neurotransmitters, these neurotransmitters are norepinephrine, serotonin, and dopamine. When a person has Brunner's Syndrome the protein MAO-A is just produced in much smaller amounts meaning that they can't regulate the three affected neurotransmitters as effectively.

Unknown Still

This disease is only tested for when there is a family history of the disease or if someone shows extreme signs of clinical symptoms. This means that there has been very little research on Brunner's Syndrome. This extends to our lack of knowledge on how to treat Brunner's Syndrome. If researches want to learn more about this genetic defect there should be more genetic testing done if people are diagnosed with other syndromes that have similar symptoms in order to help more effectively find those with the syndrome so more effective research and treatment can be provided to those who need it.

Conclusion

Brunner's Syndrome is a new genetic disorder that leads to people being more erratic and aggressive. This in turn can lead to self-incrimination or more criminal activity and decisions. This means that if more research and broader sweeps are made by researchers, we can potentially help hundreds of people stay out of prison for genetic defects that they can't control. Since genetic research is always becoming more and more efficient and effective now is a better time than ever to over examine those who are willing to help find more and more genetic links to this syndrome so that researchers can learn how to treat it.