SLC6A3 Gene

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solute carrier family 6 member 3

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1. Normal Function

The *SLC6A3* gene provides instructions for making a protein called the dopamine transporter or DAT. This protein is embedded in the membrane of certain nerve cells (neurons) in the brain, where it transports a molecule called dopamine into the cell. Dopamine is a chemical messenger (neurotransmitter) that relays signals from one neuron to another. Dopamine has many important functions, including playing complex roles in thought (cognition), motivation, behavior, and control of movement.

To transmit signals, dopamine is released into the space between neurons (the synaptic cleft), where it attaches (binds) to receptors on the surface of neighboring neurons. The dopamine transporter brings dopamine from the synaptic cleft back into neurons for reuse. The activity of the transporter determines how much dopamine is present in the synaptic cleft and for how long. This activity makes the transporter a major controller of dopamine signaling in the brain.

2. Health Conditions Related to Genetic Changes

2.1. Dopamine transporter deficiency syndrome

At least 19 mutations in the *SLC6A3* gene have been identified in people with dopamine transporter deficiency syndrome, a rare movement disorder that worsens over time. Its signs and symptoms usually begin in infancy but can appear in childhood or later. Some of the mutations change single protein building blocks (amino acids) in the dopamine transporter protein. Others lead to the production of an abnormally short protein or prevent cells from producing any functional protein. All of these mutations impair the function of the dopamine transporter. Because the impaired transporter cannot carry dopamine out of the synaptic cleft and back into neurons, dopamine builds up in the spaces around neurons. The excess dopamine alters signaling between neurons and may suppress (inhibit) pathways that normally trigger the production of more dopamine. Although dopamine has a critical role in controlling movement, it is unclear how altered dopamine signaling causes the specific movement abnormalities found in people with dopamine transporter deficiency syndrome.

Studies suggest that the age at which signs and symptoms appear is related to how severely the function of the dopamine transporter is affected. Affected individuals who develop movement problems starting in infancy most often have transporter activity that is less than 5 percent of normal. Those whose movement problems appear in childhood or later tend to have somewhat higher levels of transporter activity, although they are still lower than normal. Researchers speculate that higher levels of transporter activity may delay the onset of the disease in these individuals.

2.2. Other disorders

Variations (polymorphisms) in the *SLC6A3* gene have been studied as possible risk factors for attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). ADHD, which typically begins in childhood, is characterized by overactivity, impulsive behavior, and difficulty paying attention. ASD represents a group of developmental conditions that affect communication and social interaction. Changes in dopamine signaling appear to play an important role in both ADHD and ASD. However, it is unclear how variations in the *SLC6A3* gene may be involved. Multiple genetic and environmental factors, most of which remain unknown, likely determine the risk of developing these complex conditions.

3. Other Names for This Gene

- DA transporter
- DAT
- DAT1
- dopamine transporter 1
- PKDYS
- sodium-dependent dopamine transporter
- solute carrier family 6 (neurotransmitter transporter), member 3
- solute carrier family 6 (neurotransmitter transporter, dopamine), member 3

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