CHRNA2 Gene

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cholinergic receptor nicotinic alpha 2 subunit

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1. Normal Function

The *CHRNA2* gene provides instructions for making one part (subunit) of a larger protein called a neuronal nicotinic acetylcholine receptor (nAChR). Each nAChR protein is made up of a combination of five subunits, usually two alpha (α) and three beta (β) subunits. Many different combinations are possible, and the characteristics of each nAChR protein depend on which subunits it contains. The *CHRNA2* gene is responsible for producing a subunit known as α2. Little is known about the specific function of nAChR proteins made with this subunit.

In the brain, nAChR proteins are widely distributed and play an important role in chemical signaling between nerve cells (neurons). The proteins act as channels, allowing charged atoms (ions) including calcium, sodium, and potassium to cross the cell membrane. These channels open when attached to a brain chemical (neurotransmitter) called acetylcholine. The channels also open in response to nicotine, the addictive substance in tobacco.

Communication between neurons depends on neurotransmitters, which are released from one neuron and taken up by neighboring neurons. The release and uptake of these chemicals are tightly regulated to ensure that signals are passed efficiently and accurately between neurons. Researchers believe that nAChR channels play an important role in controlling the normal release and uptake of neurotransmitters.

A wide range of brain functions depend on nAChR channels, including sleep and arousal, fatigue, anxiety, attention, pain perception, and memory. The channels are also active before birth, which suggests that they are involved in early brain development. At least one drug that targets nAChR channels in the brain has been developed to help people quit smoking; other medications targeting these channels are under study for the treatment of schizophrenia, Alzheimer disease, and pain.

2. Health Conditions Related to Genetic Changes

2.1. Autosomal Dominant Nocturnal Frontal Lobe Epilepsy

At least one mutation in the *CHRNA2* gene has been found to cause autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE). It appears that changes in this gene are a very rare cause of ADNFLE. Some researchers suspect that the known mutation actually causes a separate form of epilepsy with features similar to ADNFLE.

The identified *CHRNA2* mutation changes a single protein building block (amino acid) in the α2 subunit of nAChR channels. Specifically, it replaces the amino acid isoleucine with the amino acid asparagine at protein position 279 (written as Ile279Asn or I279N). This mutation makes the channels more sensitive to the neurotransmitter acetylcholine, allowing them to open more easily than usual. The resulting increase in ion flow across the cell membrane alters the release of neurotransmitters, which changes signaling between neurons. Researchers believe that the overexcitement of certain neurons in the brain triggers the abnormal brain activity associated with seizures. It is unclear why the seizures seen in ADNFLE start in the frontal lobes of the brain and occur most often during sleep.

3. Other Names for This Gene

- Acetylcholine receptor, neuronal nicotonic, alpha-2 subunit
- ACHA2_HUMAN
- Cholinergic receptor, neuronal nicotinic, alpha polypeptide 2

- cholinergic receptor, nicotinic alpha 2
- cholinergic receptor, nicotinic, alpha 2
- cholinergic receptor, nicotinic, alpha 2 (neuronal)
- cholinergic receptor, nicotinic, alpha polypeptide 2 (neuronal)

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