Angelman syndrome

Description

Angelman Syndrome (AS) is a severe neurological disorder characterised by profound developmental delays, problems with motor coordination and balance, and epilepsy. The estimated frequency is 1/15000 – 1/20000, affecting all races and both genders equally. Individuals with AS rarely develop basic functional speech. Feeding disorders in infancy are common and some persist throughout childhood. Sleeping difficulties are commonly noted in individuals with AS. Individuals with AS tend to have a happy demeanor, characterised by frequent laughing, smiling and excitability. Many individuals with AS are attracted to water and enjoy activities like swimming and bathing.

The symptoms of AS are principally due to a lack of the UBE3A gene. This gene regulates the function and recycling of many proteins in brain cells. Without UBE3A, brain cells fail to mature, integrate and function efficiently. In about 70% of patients with Angelman syndrome, lack of UBE3A is due to deletion of a region on the maternally-inherited chromosome 15. A similar deletion affecting the paternally-inherited chromosome 15 results in Prader-Willi syndrome, a clinically distinct condition. Other inherited and sporadic mechanisms can affect the UBE3A gene or its function. The severity of the disorder principally depends on the type of genetic change occurring.

A neighbouring gene, GABRB3, is often missing along with UBE3A. The absence of this second gene means that brain cells are unable to respond to their chemical signals properly, leading to epilepsy.

Treatment

There is no current treatment for AS. Most epilepsies associated with AS are not treatable with current anti-epileptic drugs. Of those that have been trialed, sodium valproate in combination with benzodiazepines has had some success. Based on biomedical research in mouse models of AS, clinical trials are underway with minocycline to normalise behavioural features.

Prognosis

Most individuals with AS will have severe developmental delays, speech limitations, and motor difficulties. Some improvement in epilepsy severity and frequency is seen as individuals get older. Individuals with AS generally do not show developmental regression as they age and can expect normal life spans. Feeding disorders can lead to obesity in some individuals. Hyperactivity and ataxia leads to bruises, cuts and abrasions. Fascination with water and poor motor coordination leads to an increased risk of drowning.

Support services

People living with AS require life-long care, intensive therapies to help develop functional skills and improve their quality of life. Multiple medical interventions are required.

Link to latest Australian research papers (within last 5 years) (PubMed database):

- Click here for the latest Australian research papers on Angelman syndrome.

Links to other websites for further information:

- Click here for the Foundation for Angelman Syndrome Therapeutics. An international organization advocating and working towards treatments.
- Click here for the minocycline clinical trial listing

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