

Ataxia & Autoimmune Encephalitis

Imagine you are at a playground with your friends playing hopscotch. It is your turn. You jump with both feet, hop on one foot, hop on the other, all just to get to the end. This type of motor control and balance is controlled by a particular brain structure called the cerebellum. The cerebellum (Latin for “little brain”) is traditionally known as the hub for motor coordination, balance, and posture, but recently has been recognized for its role in cognition (attention and language) and emotion regulation (like fear)¹.

Damage to the cerebellum results in a condition known as [Ataxia](#). Ataxia symptoms vary between each individual, but hallmark symptoms include trouble with coordination, walking, swallowing, speech, and on rare occasions, eye or heart problems^{2,3,6}. Anyone is susceptible to developing ataxia. It can be acquired through alcohol abuse, head trauma, stroke, vitamin deficiency, and/or autoimmunity². In some cases, ataxia is hereditary; someone can inherit either a dominant gene from one parent (autosomal dominant disorder), or a recessive gene from both parents (autosomal recessive disorder)^{2,3}. A common cause of ataxia and/or problems with balance and gait is due to the progressive loss and degeneration of cerebellar neurons, specifically Purkinje cells. Purkinje cells are one of the largest neurons in the brain and are the cerebellum’s main communicators with the rest of the brain⁸.

Once a patient is diagnosed with ataxia, physicians will try to identify the root cause by performing neurological examinations and laboratory tests⁵. While the neurological examination is used to determine the extent and severity of symptoms, the laboratory tests can help to ascertain if the ataxia is genetic, infectious, or immune related³. For instance, if a patient develops ataxia through a nutritional or immune-mediated cause, their abnormal vitamin or antibody levels would be detected during the laboratory tests⁵. A patient’s cerebrospinal fluid (CSF), the bodily fluid that surrounds the brain and spinal cord, can be examined to measure specific antibody levels and provide information about specific types of immune-mediated ataxia^{3,4}.

The cerebellum is particularly susceptible to damage and autoimmune attacks⁵. Autoimmune-related ataxias can encompass a spectrum of disorders including autoimmune encephalitis (AE), gluten ataxia, and Hashimoto's encephalopathy⁴. This type of ataxia can also be episodic - presenting as sudden and intense episodes of ataxia accompanied by vertigo and dizziness. These episodes are especially prevalent in a type of AE called anti-CASPR2 antibody-associated autoimmune encephalitis⁵⁻⁷.

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Is cerebellar degeneration observed in autoimmune-related ataxias? Not really³. For example, scientists who study anti-NMDA receptor (anti-NMDAR) encephalitis use magnetic resonance imaging (MRI) to produce detailed images of the cerebellum and found that 2 out of 15 patients exhibited cerebellar atrophy, which was a surprise because it has never been reported in this disease⁹. While it is not exactly clear why cerebellar atrophy is occurring in these anti-NMDAR encephalitis patients, one hypothesis posits that NMDAR antibodies act like NMDAR antagonists (blocking and inhibiting an NMDA receptor from turning on)⁹. NMDA receptors are critical for relaying signals between neurons and for a signal to be passed, the receptor must open. So, if an antibody is acting like an antagonist, the receptor can't open and the signal won't be relayed. In other words, if a cerebellar neuron (Purkinje cell) cannot receive or relay a signal to another neuron, then there is improper communication throughout the whole brain, resulting in impaired balance or coordination.

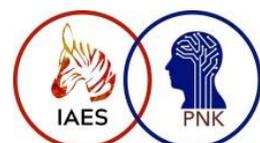
Above all, ataxia is an extremely rare condition and sometimes manifests with AE. Motor deficits are an early indicator that something is wrong and are typically the first thing doctors use to properly diagnose an autoimmune-related ataxia. Because there is no direct treatment, current methods focus on improving a patient's balance and gait, in addition to immunotherapy and/or medications that may ease a patient's symptoms like fatigue or muscle cramps². The cerebellum remains an enigma and everyday new research is coming to light. With new work, scientists are constantly able to develop new treatment options. For example, Dr. Beverly Davidson, a renowned scientist at the Children's Hospital of Philadelphia has dedicated over 20 years of her work towards developing genetic therapies for cerebellar ataxias, giving hope to the next generation of ataxia research!

References:

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To learn more about ataxia, read this [fact-sheet](#) provided by the National Ataxia Foundation.

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