

Ask a Lurie Center Researcher: What is the “Neuroimmune Hypothesis” of Autism?

The neuroimmune hypothesis of autism is a scientific theory that suggests a connection between the body’s immune system and the development of autism spectrum disorder (ASD). This hypothesis proposes that activity of the immune system, particularly during the prenatal period and early development, may influence the development of some forms of ASD.

The term "neuroimmune" refers to the interaction between the nervous system (“neuro”) and the immune system (“immune”). During development these two body systems work together to shape themselves and each other. It may be that if this interaction doesn’t happen properly, in some cases, the individual may be born with the vulnerability to develop ASD.

The idea that autism is linked to the immune system is not new. In fact, over 80 years ago, a child and adolescent psychiatrist named Leo Kanner at Johns Hopkins University published a paper describing 11 children with autism, many of whom he noted had symptoms or diagnoses related to immune system issues. About 25 years later, an autistic child with an extensive family history of autoimmune disorders was described in the medical literature.¹ This prompted the researchers to speculate that familial autoimmune disorders could be involved in the development of ASD.

These early reports of a possible immune connection to ASD did not generate much attention in the scientific or medical communities at the time. However, in recent years many additional studies have found links between immune system functioning and ASD. Some of the most compelling findings are summarized here.

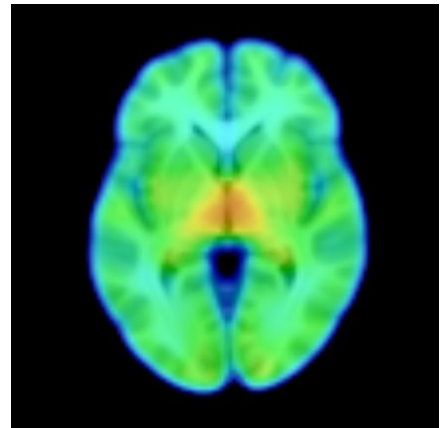
Immune system dysregulation in people with ASD: Many people with ASD have markers in their blood indicative of inflammation, and studies suggest there may be a subgroup of autistic individuals who have medical issues related to an inflammatory process, such as gastrointestinal disorders.² However, it is important to note that not all individuals with ASD show evidence of immune system abnormalities, and more research is needed to understand the specific mechanisms involved.

Neuroinflammation in the brain: Neuroinflammation is an immune system response in the brain. Evidence of neuroinflammation in the brains of autistic individuals includes altered activity of brain cells called glial cells. Glial cells support neurons in the brain and communicate with one another. Studies of deceased individuals with ASD have shown increased levels of inflammatory markers in the brain in some individuals, suggesting an altered immune response.^{3,4} In addition, brain imaging studies from scientists at the Lurie Center for Autism, have shown evidence of altered neuroinflammatory activity in the brains of living adults with ASD.⁵

Association with autoimmune disorders: Autoimmune disorders like multiple sclerosis (MS), lupus, Crohn’s disease, ulcerative colitis, rheumatoid arthritis, type 1 diabetes, eczema/psoriasis, and hypo- and hyperthyroidism occur when the body mistakenly attacks organs in the body. This causes inflammation throughout the body, including the brain. Studies have suggested that many individuals with ASD have a family history of autoimmune disorders.⁶⁻¹¹ This likely indicates some shared genetic vulnerability between familial autoimmune disorders and ASD.¹² In fact, some studies suggest that mothers who have an autoimmune disorder have a greater likelihood of having a child with ASD.^{13,14} In addition to ASD, researchers have found that autoimmune disorders may also occur more frequently in relatives of people with schizophrenia, major depression, bipolar disorder, and obsessive-compulsive disorder.

Maternal immune activation studies: The maternal immune system plays a crucial role in protecting a pregnant mother and her developing baby. However, under certain circumstances, the activation of the immune system during pregnancy can lead to an inflammatory response that may impact fetal brain development and increase the risk of neurodevelopmental disorders, including ASD.^{17,18} Many studies, both in animal models and humans, suggest that immune system activation during pregnancy is associated with an increased risk of ASD.^{15,16} This is referred to as “maternal immune activation.” Different triggers have been proposed to cause this activation such as infection, stress, having an autoimmune disorder before pregnancy or developing one during pregnancy, among others.

Taken together these findings lend support to the idea that immune factors could play a role in the development of ASD, at least in a subgroup of individuals. However, ASD is a complex and heterogeneous disorder likely with many causes. It is important to note that the neuroimmune hypothesis is just one of several theories attempting to explain the complex biology of ASD.



Position emission tomography (PET) imaging enables the study of neuroimmune markers in the brain. Image from Zurcher et al., 2021⁵.

In summary, the "neuroimmune hypothesis" of ASD refers to the interconnectedness of the nervous and immune systems and proposes that factors related to immune functioning impact the development of the brain in such a way as to lead to ASD. Researchers, including many at the Lurie Center, are trying to learn more about these connections and how to identify autistic individuals whose ASD may be particularly influenced by immune system abnormalities. This understanding could open new areas of targeted intervention with therapies designed to address immune system function.

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The Lurie Center for Autism is investigating the relationship between autoimmune disorders in first- and second-degree relatives and the presence of ASD in an individual. To learn more, click [here](#).