Professor Lisa Boulanger says studies suggest "that at least for some individuals, certain features of autism may result from the brain's inability to prune its network of connections."

NEUROSCIENCE

Brain Teaser

Understanding how an immune response may increase the risk of autism

Autism is thought to arise from a combination of factors, some genetic and others the result of environmental issues such as the mother's health during pregnancy, parental age, and exposure to pollutants. New research indicates that mouse pups born to mothers who had the flu during pregnancy show characteristics of autism and exhibit brain changes. So far, the work suggests that the link to autism likely is not the flu itself, but the response of the mother's immune system.

Lisa Boulanger, an assistant professor of molecular biology and neuroscience, studies the role of immune proteins called major histocompatibility complex class I (MHCI). These molecules are found on most cells in our body, where they help our immune cells find and attack cells infected by microorganisms. Until 15 years ago, these molecules were not thought to be present in the brain, but they now are known to play an important role in normal brain development.

Boulanger's work suggests a link between MHCI's function in the brain and autism. Her laboratory has shown that one job of MHCI is to trim the number of synapses, the connections between neurons that allow them to communicate. Mice without MHCI have more synapses in brain regions involved in higher cognitive functions, learning, and memory — too many, in fact. A similar synapse overabundance also is seen in the brains of children with autism and

Mouse pups born to mothers who had the flu during pregnancy show characteristics of autism.

in mice with autism-linked mutations. "More nerve connections might sound great, but actually, this causes a wide range of behavioral problems," Boulanger says. A drug, she found, can reverse the synapse number problems in mice with either autism-linked mutations or those deficient in MHCI.

Healthy babies are born with many connections, but these gradually are reduced throughout childhood. This pruning is crucial to the brain developing, Boulanger says, and problems with pruning may only become apparent years later. Both human and mouse studies "suggest that at least for some individuals, certain features of autism may result from the brain's inability to prune its network of connections," she says.

Boulanger's laboratory recently found mouse infections during pregnancy change MHCI levels in the developing pups' brains that persist as the mice grow into adulthood.

"These changes can affect synapse connections in the same way as some of the genetic mutations associated with autism," explains Boulanger. Individuals with autism-linked genetic mutations may be more vulnerable to the effects of an infection on the maternal immune system.

More work is necessary to better understand whether and how immune molecules are modified in the developing human brain following a maternal infection, and if this can contribute to autism. Currently, it is not clear what makes some women more vulnerable to these infections. The hope, says Boulanger, is to find ways to identify the subset of families who may be most vulnerable so they can reduce the risk of having a child with autism. "For those individuals," Boulanger says, "it might be worth it to take simple measures, like washing their hands more often and avoiding large public gatherings for a few months during pregnancy, to minimize their risk of catching colds or the flu."

*By Anna Azvolinsky *09*

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