Changes in nerve cells may contribute to the development of mental illness

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Reduced production of myelin, a type of protective nerve fiber that is lost in diseases like multiple sclerosis, may also play a role in the development of mental illness, according to researchers at the Graduate School of Biomedical Sciences at Mount Sinai School of Medicine. The study is published in the journal *Nature Neuroscience*.

Myelin is an insulating material that wraps around the axon, the threadlike part of a nerve cell through which the cell sends impulses to other nerve cells. New myelin is produced by nerve cells called oligodendrocytes both during development and in adulthood to repair damage in the brain of people with diseases such as multiple sclerosis (MS).

A new study led by Patrizia Casaccia, MD, PhD, Professor of Neuroscience, Genetics and Genomics; and Neurology at Mount Sinai, determined that depriving mice of social contact reduced myelin production, demonstrating that the formation of new oligodendrocytes is affected by environmental changes. This research provides further support to earlier evidence of abnormal myelin in a wide range of psychiatric disorders, including autism, anxiety, schizophrenia and depression.

"We knew that a lack of social interaction early in life impacted myelination in young animals but were unsure if these changes would persist in adulthood," said Dr. Casaccia, who is also Chief of the Center of Excellence for Myelin Repair at the Friedman Brain Institute at

Mount Sinai School of Medicine. "Social isolation of adult mice causes behavioral and structural changes in neurons, but this is the first study to show that it causes myelin dysfunction as well."

Dr. Casaccia's team isolated adult mice to determine whether new myelin formation was compromised. After eight weeks, they found that the isolated mice showed signs of social withdrawal. Subsequent brain tissue analyses indicated that the socially isolated mice had lower-than-normal levels of myelin-forming oligodendrocytes in the prefrontal cortex, but not in other areas of the brain. The prefrontal cortex controls complex emotional and cognitive behavior.

The researchers also found changes in chromatin, the packing material for DNA. As a result, the DNA from the new oligodendrocytes was unavailable for gene expression.

After observing the reduction in myelin production in socially-isolated mice, Dr. Casaccia's team then re-introduced these mice into a social group. After four weeks, the social withdrawal symptoms and the gene expression changes were reversed.

"Our study demonstrates that oligodendrocytes generate new myelin as a way to respond to environmental stimuli, and that myelin production is significantly reduced in social isolation," said Dr. Casaccia. "Abnormalities occur in people with psychiatric conditions characterized by social withdrawal. Other disorders characterized by myelin loss, such as MS, often are associated with depression. Our research emphasizes the importance of maintaining a socially stimulating environment in these instances."

At Mount Sinai, Dr. Casaccia's laboratory is studying oligodendrocyte formation to identify therapeutic targets for myelin repair. They are screening newly-developed pharmacological compounds in brain cells

from rodents and humans for their ability to form new myelin.

Dr. Casaccia is the recipient of the Neuroscience Javits Award by the National Institute of Neurological Disorders and Stroke, a division of the National Institutes of Health, who also funded this research (R37-NS42925-10) along with the National Multiple Sclerosis Society.

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