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Researchers identify key mechanism linked to neuropsychiatric lupus

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A breakthrough study by a SUNY Downstate Health Sciences University research team has identified a specific antibody target implicated in neuropsychiatric symptoms of lupus. These symptoms, including cognitive impairment, mood disorders, seizures, headaches and psychosis, are among the most prevalent manifestations of the disease and occur in as many as 80% of adults and 95% of children with lupus. The Lupus Foundation of America estimates that more than 1.5 million Americans and 5 million people worldwide suffer from some form of lupus, with 90% of cases affecting women.

The study, Neuronal BC RNA Transport Impairments Caused by Systemic Lupus Erythematosus Antibodies, was published today in the *Journal of Neuroscience*.

The study identified antibodies that are directed at regulatory brain cytoplasmic RNAs (BC ribonucleic acid) that are unique to lupus patients. In layman's terms, these antibodies disrupt these regulators of protein synthesis that allow synapses in the brain to control how they receive, store and recall information. Because these antibodies are unique in the brains of lupus patients, the study suggests that this is at the root of neuropsychiatric symptoms seen in these patients.

"Prior to this study, we poorly understood why lupus affects the brain in the way in which it does and causes neurocognitive symptoms," said Principle Investigator Henri Tiedge, Ph.D., Distinguished Professor, The Robert F. Furchgott Center for Neural and Behavioral Science at SUNY

Downstate. "Because we could not treat the cause, the only alternative was for physicians to treat the symptoms with anti-inflammatory drugs, immunosuppressives and other therapies, depending on the how the brain was being affected."

According to Dr. Tiedge, the discovery gives new insight into both how and why many lupus patients suffer from these symptoms, and, just as important, may well provide the basic understanding necessary for scientists to pursue effective treatments.

"Now that we appear to have an understanding of what is causing at least some of these neuropsychiatric affects, we can turn our attention to finding treatments that target the disease process itself and will block or repress these antibodies from causing the molecular disruptions."

"Women of color are three times more likely to be diagnosed with lupus and are much more likely to develop the disease at a younger age. Additionally, when diagnosed, women of color often have more serious complications and significantly higher death rates," said Wayne J. Riley, M.D., President of SUNY Downstate Health Sciences University. "Not only does this discovery by Dr. Tiedge and colleagues break new ground in our understanding of lupus, but it is also especially important to the diverse communities we serve here in Brooklyn."

In addition to Dr. Tiedge, other investigators include Ilham A. Muslimov, MD, Ph.D.; Anna Iacoangeli, Ph.D.; Taesun Eom, Ph.D.; Anne Ruiz, Ph.D.; Ellen M. Ginzler, MD; MPH, Stacy Stephenson, AAS; RLATg, and Madisen Lee, Volunteer. The study was a collaboration between both basic science and clinical researchers at SUNY Downstate Health Sciences University, including both The Robert F. Furchgott Center for Neural and Behavioral Science and the SUNY Downstate Division of Rheumatology.

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More information: Neuronal BC RNA transport impairments caused by systemic lupus erythematosus autoantibodies, *Journal of Neuroscience* (2019). DOI: 10.1523/JNEUROSCI.1657-18.2019

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