Researchers pursue red flag for schizophrenia relapse

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Blood levels of a protein that helps regulate inflammation may also serve as a red flag for relapse in some schizophrenia patients, according to research by Dr. Brian Miller, a psychiatrist specializing in schizophrenia at the Medical College of Georgia at Georgia Health Sciences University. Credit: Phil Jones, GHSU/GHS Campus Photographer

Blood levels of a protein that helps regulate inflammation may also serve as a red flag for relapse in some schizophrenia patients, researchers said.

"There are no good, objective measures of treatment efficacy or indicators for relapse," said Dr. Brian Miller, a psychiatrist specializing in schizophrenia at the Medical College of Georgia at Georgia Health

Sciences University.

Researchers hope monitoring levels of interleukin-6 can fill that gap for a population in which more than half of patients don't take their medications as prescribed, often because of side effects. The relapse rate is about 80 percent within two years in patients who don't take their medication properly and about half that in those who do, according to the National Institute of Mental Health.

"We hope the upshot of our studies will lead to new treatment approaches and strategies for care," Miller said, including the kind of personalized, multi-drug therapies that are becoming the standard for controlling other chronic conditions such as diabetes and hypertension. "We want to attack the disease from as many directions as possible."

To get a better handle on how IL-6 levels correspond to disease status, they are looking at levels in blood samples taken multiple times over several years in 305 patients enrolled in a study comparing injectable to oral medication. They also are taking one-time measurements in 80 healthy controls and comparing those to levels in 240 patients who are acutely ill, stable outpatients or stable outpatients who smoke marijuana, a drug commonly abused by patients. While many previous studies have excluded drug abusers, marijuana may increase inflammation, so they want to explore the relationship between IL-6 levels and its use, Miller said.

Miller received a five-year, $920,000 National Institute of Mental Health Mentored Patient-Oriented Research Career Development Award to measure IL-6 levels as a potential indicator of how well treatment is working to control disease in these vulnerable patients and whether they are headed to relapse.

Amazingly the contributions of "immune disturbances" to schizophrenia

have been debated for about 100 years yet anti-inflammatory drugs aren't routinely given to patients in addition to their antipsychotic medication, Miller said.

Part of the problem is physicians still have no idea what percentage of patients with this very heterogeneous disease have evidence of increased inflammation. In fact, no two patients have the exact constellation of symptoms considered disease hallmarks, such as hallucinations, delusions, disorganized speech and thinking, he said.

But mounting evidence suggests inflammation's impact in schizophrenia. A British study of 50 patients experiencing their first episode of schizophrenic behavior found a handful had indicators of an immune response to their brains, called autoantibodies, and no other conditions, such as a brain infection, to explain them. What amounts to a chronic low-grade flu has been found in some patients and rare immune system disorders such as Sjögren's syndrome, which attacks moisture-producing glands resulting in dry eyes and mouth, also tend to be more common in schizophrenics. Additionally, a handful of clinical trials has shown – not surprisingly – that patients with the highest levels of pro-inflammatory factors had the best response to anti-inflammatory drugs.

"It's likely we are talking about a subset of people with this illness who would be most likely to respond to anti-inflammatory therapy – in addition to standard anti-psychotics – so part of our work is to begin to piece out who those people are (and whether) they have a particular clinical picture," Miller said. "Even being able to predict relapse or improve therapy in 25 percent of patients would be a tremendous advance," he said, noting that the vast majority of schizophrenia drugs work essentially by the same mechanism.

Once patients can be identified, ideally with a blood test of their IL-6 levels, the next questions are which drugs to use and for how long.

Miller's primary mentor for the studies is Dr. Andrew Mellor, a molecular geneticist and immunologist who leads the Cancer Immunology, Inflammation Tolerance Program at the GHSU Cancer Center. Mellor also is Bradley-Turner & Georgia Research Alliance Eminent Scholar in Molecular Immunogenetics. Co-secondary mentors are schizophrenia experts Dr. Peter F. Buckley, Dean of the Medical College of Georgia at GHSU, and Dr. Mark Rapaport, Chair of the Department of Psychiatry and Behavioral Sciences at Emory University School of Medicine.

Schizophrenia affects about 1 percent of the population, or some 2.4 million American adults. Hallucinations are a disease hallmark: patients hear voices and can even see, touch and taste things that are not real. They can become depressed, reclusive and suicidal and have an increased risk of cardiovascular and other health conditions. Patients die on average15-20 years younger than the general population.

Miller, a recipient of the 2011 National Alliance on Mental Illness Exemplary Psychiatrist Award, said he felt a calling to psychiatry and specifically schizophrenia as a medical student at The Ohio State University. "The patients are wonderful and their stories are fascinating," he said, noting that the field is "wide open" to improve their care.

Provided by Georgia Health Sciences University

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