Novel Treatment May Provide Relief for People with Schizophrenia

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DURHAM, N.C. – A compound that naturally occurs in the brain and other areas of the body may be a promising new treatment for the most severe and disruptive symptoms of schizophrenia, according to researchers from Durham Veterans Affairs Medical Center and Duke University Medical Center.

Researchers conducted a pilot study at the Durham VAMC that suggests the neurosteroid pregnenolone targets symptoms of schizophrenia for which no treatment options are available. The findings are published online in the journal Neuropsychopharmacology.

While antipsychotic medications can help reduce hallucinations and delusions associated with schizophrenia for some patients, the other two categories of symptoms often continue to significantly disable patients -- negative symptoms, such as apathy, lack of emotion and poor social functioning, and cognitive symptoms, which include memory impairment and difficulty concentrating and completing tasks.

“If replicated through further research, pregnenolone could provide a novel treatment for the cognitive and negative symptoms in schizophrenia, which severely impact the daily lives of patients,” says Christine Marx, M.D., M.A., lead author of the study and associate professor of psychiatry.

“Antipsychotic medications are the only FDA approved treatments for schizophrenia but the effects are typically modest and do not address the fundamental core of the disorder,” says Richard Keefe, Ph.D., study co-author and professor of medical psychology.

Prior research had found that pregnenolone enhanced learning and memory in rodents while also influencing the function of brain receptors associated with schizophrenia. Pregnenolone is present in varying levels in humans but not much was known about how it was regulated.

The new study included 21 people with schizophrenia or schizoaffective disorder who took a placebo for two weeks and were then randomly assigned to take pregnenolone or placebo for eight weeks in conjunction with a newer antipsychotic medication (aripiprazole, olanzapine, quetiapine or risperidone).

Compared to patients taking placebo, the pregnenolone group reported a significant reduction in negative symptoms. Increases in this neurosteroid also predicted improvement in cognitive symptoms in the group receiving pregnenolone. Patients taking pregnenolone had more than 20 percent improvement on a test used to calculate negative symptoms compared to the placebo group. Tests used to assess cognitive impairment point to improvements in the pregnenolone group. Patients with the lowest natural levels of the neurosteroid reported the most significant improvements on memory and concentration tasks.

“While pregnenolone is available as a dietary supplement, there have been extremely few studies of this compound in the last 50 years,” Marx explains. The researchers caution that the pregnenolone used in the study was carefully monitored and met FDA standards for purity, unlike supplements available over the counter.

“Further research is needed among a larger cohort of patients to confirm the findings we observed, but we are encouraged because pregnenolone was well tolerated and improved symptoms that we have not traditionally been able to treat,” Keefe adds.

“Drug development for mental health disorders has been moving at a glacial pace and we are in desperate need of new and novel treatments,” said Jeffrey A. Lieberman, M.D., study co-author and chair of the Department of Psychiatry at Columbia University Medical Center and director of the New York State Psychiatric Institute. “This small, proof of concept study represents a potentially major advance.”

Researchers said that larger studies are planned to further investigate pregnenolone's effects on schizophrenia, in addition to pilot studies in other conditions such as traumatic brain injury and post-traumatic stress disorder.

Study co-authors include Jason Kilts, Daniel Bradford, Jennifer Naylor, Victoria Payne, Lawrence Dunn and Lawrence Shampine of Duke and the Durham VAMC, Linda Leimone of the Durham VAMC, Robert Buchanan with the University of Maryland, Robert Hamer, Patrizia Porcu and A Leslie Morrow with the University of North Carolina at Chapel Hill and Adam Savitz of Weill Medical College of Cornell University.

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Marx is a co-applicant and Keefe is a contributor to a pending US patent application on the use of neurosteroids for the treatment of central nervous system disorders. Marx is an unpaid scientific advisor/board member of NeuroScience Pharmaceuticals, Inc. Keefe receives royalties for two of the cognitive test batteries used in this study, the BACS and the MATRICS Consensus Cognitive Battery.

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