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Candida yeast infections more common in men with schizophrenia or bipolar disorder

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In a study prompted in part by suggestions from people with mental illness, Johns Hopkins researchers found that a history of *Candida* yeast infections was more common in a group of men with schizophrenia or bipolar disorder than in those without these disorders, and that women with schizophrenia or bipolar disorder who tested positive for *Candida* performed worse on a standard memory test than women with schizophrenia or bipolar disorder who had no evidence of past infection.

The researchers caution that their findings, described online on May 4 in *npj Schizophrenia* -- a new publication from Nature Publishing Group -- do not establish a cause-and-effect relationship between mental illness and yeast infections but may support a more detailed examination into the role of lifestyle, immune system weaknesses and gut-brain connections as contributing factors to the risk of psychiatric disorders and memory impairment.

"It's far too early to single out *Candida* infection as a cause of mental illness or vice versa," says Emily Severance, Ph.D., assistant professor of pediatrics and member of the Stanley Division of Developmental Neurovirology at the Johns Hopkins University School of Medicine. "However, most *Candida* infections can be treated in their early stages, and clinicians should make it a point to look out for these infections in their patients with mental illness." She adds that *Candida* infections can also be prevented by decreased sugar intake and other dietary modifications, avoidance of unnecessary antibiotics, and improvement of hygiene.

Candida albicans is a yeastlike fungus naturally found in small amounts in human digestive tracts, but its overgrowth in warm, moist environments causes burning, itching symptoms, thrush (rashes in the throat or mouth) in infants and those with weakened immune systems, and sexually transmittable genital yeast infections in men and women. In its more serious forms, it can enter the bloodstream. In most people, the body's own healthy bacteria and functioning immune system prevent its overgrowth.

Severance says she and her team focused on a possible association between *Candida* susceptibility and mental illness in the wake of new evidence suggesting that schizophrenia may be related to problems with the immune system, and because some people with weakened immune systems are more susceptible to fungal infections.

Also, she says, patients and parents of patients had shared personal stories and testimonials with the researchers about their experience with yeast infections, and these discussions prompted the investigation into possible links between mental illness and the microbiome -- the body's natural collection of bacteria. The researchers, she adds, chose to focus on *Candida* because it is one of the most common types of yeast in the body.

For the study, colleagues from the Sheppard Pratt Health System took blood samples from a group of 808 people between the ages of 18 and 65. This group was composed of 277 controls without a history of mental disorder, 261 individuals with schizophrenia and 270 people with bipolar disorder. The researchers used the blood samples to quantify the amount of IgG class antibodies to *Candida*, which indicates a past infection with the yeast. After accounting for factors like age, race, medications and socioeconomic status, which could skew the results, they looked for patterns that suggested links between mental illness and infection rates.

Significantly, the team says, it found no connection between the presence of *Candida* antibodies and mental illness overall in the total group. But when the investigators looked only at men, they found 26 percent of those with schizophrenia had *Candida* antibodies, compared to 14 percent of the control males. There wasn't any difference found in infection rate between women with schizophrenia (31.3 percent) and controls (29.4 percent). The higher infection rate percentages in women over men likely reflects an increased susceptibility for this type of infection in all women.

Men with bipolar disorder had clear increases in *Candida* as well, with a 26.4 percent infection rate, compared to only 14 percent in male controls. But, after accounting for additional variables related to lifestyle, the researchers found that the association between men with bipolar disorder and *Candida* infection could likely be attributed to homelessness. However, the link between men with schizophrenia and *Candida* infection persisted and could not be explained by homelessness or other environmental factors. Many people who are homeless are subjected to

unpredictable changes in stress, sanitation and diet, which can lead to infections like those caused by *Candida*.

Severance says the data add support to the idea that environmental exposures related to lifestyle and immune system factors may be linked to schizophrenia and bipolar disorder, and that those factors may be different for each illness. Similarly, specific mental illnesses and related symptoms may be very different in men versus women.

This Johns Hopkins research group, led by Robert Yolken, M.D., director of the Stanley Division of Developmental Neurovirology, had previously shown that toxoplasmosis infection could trigger schizophrenia, and this could lead to neurocognitive problems. The organism that causes toxoplasmosis is a parasite that uses cats as its primary host, but it can also infect humans and other mammals.

To determine whether infection with *Candida* affected any neurological responses, all participants in the new study took a 30-minute assessment of cognitive tasks to measure immediate memory, delayed memory, attention skills, use of language and visual-spatial skills.

Each of the five skills tests are scored based on an adjusted 100-point system. Results showed that control men and women with and without prior *Candida* infection had no measureable differences in scores in the five neurological responses. However, the researchers noticed that women with schizophrenia and bipolar disorder who had a history of *Candida* infection had lower scores on the memory portions of this test compared to those women with no prior infection. For example, women with schizophrenia and the highest *Candida* antibody levels scored about an average of 11 points lower on the test for immediate memory than the controls, from a score of 68.5 without infection to 57.4 with infection. And the women with schizophrenia and the highest *Candida* antibody levels scored almost 15 points lower on the test for delayed memory, from a score of 71.4 without infection to 56.2 with infection. The effect of *Candida* infection in women with bipolar disorder on memory test scores was smaller than that seen in women with schizophrenia but was still measureable.

"Although we cannot demonstrate a direct link between *Candida* infection and physiological brain processes, our data show that some factor associated with *Candida* infection, and possibly the organism itself, plays a role in affecting the memory of women with schizophrenia and bipolar disorder, and this is an avenue that needs to be further explored," says Severance. "Because *Candida* is a natural component of the human body microbiome, yeast overgrowth or infection in the digestive tract, for example, may disrupt the gut-brain axis. This disruption in conjunction with an abnormally functioning immune system could collectively disturb those brain processes that are important for memory."

Severance says they plan to take their studies of the gut-brain connection into mouse models to test for a cause- and effect-relationship with *Candida* and memory deficits.

The researchers emphasized that the current study design had limitations. For example, they were unable to tell where in the body the infection was located and whether or not participants had a current or past infection of *Candida*. The researchers were also not able to account for every possible lifestyle variable that might contribute to these results.

The researchers in the Stanley Division of Developmental Neurovirology are investigating whether pathogens, such as bacteria or viruses, may contribute or trigger certain mental disorders.

According to the National Institute of Mental Health, about 1 percent of people in the U.S. have schizophrenia and about 2 percent have bipolar disorder. Although these diseases have a genetic component, there is evidence that they may also be triggered by environmental factors and stress.

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