

Schizophrenia linked with abnormal immune response to Epstein-Barr virus

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Functional magnetic resonance imaging (fMRI) and other brain imaging technologies allow for the study of differences in brain activity in people diagnosed with schizophrenia. The image shows two levels of the brain, with areas that were more active in healthy controls than in schizophrenia patients shown in orange, during an fMRI study of working memory. Credit: Kim J, Matthews NL, Park S./PLoS One.

New research from Johns Hopkins Medicine and Sheppard Pratt Health System shows that people in the study with schizophrenia also have higher levels of antibodies against the Epstein-Barr virus (EBV), a herpes virus that causes infectious mononucleosis, so-called mono.



Researchers proposed two explanations for the association of heightened immune responses in patients with <u>schizophrenia</u> and EBV infection: schizophrenia might alter the immune systems of these patients and make them more susceptible to EBV, or EBV infection might increase the risk of schizophrenia.

The article was published online Nov. 20 in Schizophrenia Bulletin.

"We are interested in the role of infectious agents such as Epstein-Barr virus in schizophrenia and other serious psychiatric disorders, so we did this study to look at the associations," said Robert Yolken, M.D., the Theodore and Vada Stanley Distinguished Professor of Neurovirology in pediatrics at Johns Hopkins Children's Center and senior author of the study. Yolken cautioned that the study wasn't designed to determine cause and effect.

Schizophrenia is a <u>mental disorder</u> where patients have distorted thinking, perception, emotions, language, sense of self and behavior. According to the World Health Organization, schizophrenia affects more than 21 million people worldwide.

While schizophrenia has some genetic associations, genes that have been found to date explain only a portion of the disease risk. Environmental exposures, including to some infectious agents, have also been identified in previous studies as increasing the risk for schizophrenia.

EBV initially causes fever and swollen lymph nodes, and is commonly transmitted through oral contact such as kissing. In severe cases, it can spread to the central nervous system and cause persistent infection. Researchers wanted to see the relationship between this EBV infection and schizophrenia.

The researchers conducted a study among 743 people—432 with a



schizophrenia diagnosis and 311 without a history of a psychiatric disorder to serve as a control group. Around 55 percent of the participants were men.

The researchers first measured levels of <u>antibodies</u> against components of EBV by comparing antibody levels in healthy people with those of people who have schizophrenia. They looked at the odds of having these antibodies in the 50th, 75th and 90th percentiles and found that people with schizophrenia were 1.7 to 2.3 times more likely to have increased levels of some EBV antibodies compared with people without schizophrenia.

Then they measured the antibodies to other related viruses such as varicella/chicken pox or herpes simplex type 1/cold sore virus, and didn't find an increase of antibodies against these viruses in people with schizophrenia. These findings suggest that only EBV was associated with increased risk of schizophrenia.

After that, the researchers sequenced a portion of the participants' DNA to determine their genetic risk for schizophrenia. Results from the analysis showed that people who had both evidence of increased genetic risk for schizophrenia and increased antibody levels to EBV had a more than eight times higher chance of being in the schizophrenia group as compared with controls. Approximately 10 percent of the individuals with schizophrenia had increased levels of both antibodies and genetic risk as compared with slightly more than 1 percent of the controls.

"We found that individuals with schizophrenia had an unusual response to Epstein-Barr virus," said Yolken. "This indicated that the prevention and treatment of Epstein-Barr virus might represent an approach for the prevention and treatment of serious psychiatric disorders such as schizophrenia."



Currently, there are no treatments available for EBV approved by the Food and Drug Administration, but a number of compounds that may prevent or treat replication of the virus are under investigation. The researchers considered the development of these approaches a high priority so that people with schizophrenia or other disorders associated with susceptibility to EBV could use them. In the meantime, researchers recommend preventing EBV transmission through good hygienic practices such as hand-washing and avoiding oral contact, such as kissing, with infected people.

More information: Faith Dickerson et al. Schizophrenia is Associated With an Aberrant Immune Response to Epstein–Barr Virus, *Schizophrenia Bulletin* (2018). DOI: 10.1093/schbul/sby164

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