Childhood virus infection linked to prolonged seizures with fever

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New research shows that human herpesviruses (HHV)-6B and HHV-7, commonly know as roseola virus), account for one third of febrile status epilepticus (FSE) cases. Results of the FEBSTAT prospective study now available in *Epilepsia*, a journal published by Wiley-Blackwell on behalf of the International League Against Epilepsy (ILAE), suggest that HHV-6B may be involved in the development of epilepsy and further research is urgently needed.

FEBSTAT is a multi-center study of the consequences of FSE, designed to identify the factors that increase the risk of injury to the hippocampus , an area of the brain responsible for long-term memory and implicated in the development of temporal lobe epilepsy. The FEBSTAT study is funded by the National Institute of Neurological Disorders and Stroke (NINDS) of the National Institutes of Health (NIH).

According to previous research, up to 5% of children under the age of five have febrile seizures, making it the most common type of seizure, with peak incidence at age 2. While brief or simple febrile seizures are most common, 5% - 8% of cases are prolonged and meet the criteria for status epilepticus (SE)—a critical condition where a persistent seizure lasts more than 30 minutes. Experts suggest that FSE accounts for 5% of FS; however, FSE accounts for 25% of all childhood SE and for more than 70% of SE cases that occur in the second year of life. FSE is associated with increased epilepsy risk, particularly temporal lobe epilepsy (TLE).

"One aim of the FEBSTAT study is to determine the frequency of HHV-6A, HHV-6B, and HHV-7 as a cause of FSE and whether infection with any of these herpesviruses increases the risk of brain injury and epilepsy," said lead author Dr. Leon Epstein a, pediatric neurologist at the Northwestern University Feinberg School of Medicine and Ann & Robert H. Lurie Children's Hospital of Chicago.

The team enrolled 199 children between the ages of 1 month and 5 years, who presented with FSE and received an assessment for herpesvirus infection within 72 hours of the episode. Viremia was detected using polymerase chain reaction (PCR) that identified the presence of HHV-6A, HHV-6B or HHV-7A DNA and RNA. In conjunction with PCR results, researchers used antibody titers to determine if the infection was a primary or reactivated herpesvirus.

Findings indicate that approximately one third of children with FSE had HHV-6 or HHV-7 viremia. HHV-6B viremia was detected in 32% of pediatric participants, with 38 and 16 children having primary and reactivated infection, respectively. Researchers found that 7% of children had HHV-7 viremia at baseline and 2 children had HHV-6/7 primary co-infection. There were no apparent differences in age, illness type, fever, seizure structures, or acute imagining abnormalities in children with or without one of the herpesviruses.

FEBSTAT researchers will continue to follow the 199 children involved in the study, expecting up to 40% of this pediatric population to develop TLE. The FEBSTAT study will determine whether there is an association between prolonged febrile seizures caused by HHV-6B viremia and the development of TLE. The current study adds to evidence from previous research by Donati et al. and by Fotheringham et al who detected HHV-6 in brain samples of patients with TLE.

"TLE could take 8 to 11 years to develop following an episode of FSE,

so more time is needed before the role of HHV-6B is fully understood," concludes Dr. Epstein. "If the FEBSTAT study finds that FSE caused by HHV-6B leads to TLE, this insight would provide a basis for clinical trials of antiviral and anti-inflammatory therapies to prevent TLE."

More information: "Human herpesvirus 6 and 7 in febrile status epilepticus: The FEBSTAT study." Leon G. Epstein, Shlomo Shinnar, Dale C. Hesdorffer, Douglas R. Nordli, Aaliyah Hamidullah, Emma K. T. Benn, John M. Pellock, L. Matthew Frank, Darrell V Lewis, Solomon L. Moshe, Ruth C. Shinnar, Shumei Sun and the FEBSTAT study team. *Epilepsia*; Published Online: June 14, 2012 (DOI: 10.1111/j.1528-1167.2012.03542.x).

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