

Asymptomatic Langat virus infection-related impact on anxiety-dependent behavior and hippocampal neuron morphology and function.

Angela D.A. Cornelius^{1,7#}, Shirin Hosseini^{2,3,#}, Sarah Schreier^{4,#}, David Fritzscht^{4,#}, Loreen Weichert^{1,4,,}, Kristin Michaelsen-Preusse², Andrea Kröger^{1,4,5,6*}

¹Innate Immunity and Infection, Helmholtz Centre for Infection Research, Braunschweig, Germany

²Department of Cellular Neurobiology, Zoological Institute, TU Braunschweig, Braunschweig, Germany

³Neuroinflammation and Neurodegeneration Group, Helmholtz Centre for Infection Research, Braunschweig

⁴Institute for Medical Microbiology and Hospital Hygiene, Otto-von-Guericke University, 39120 Magdeburg

⁵Center for Behavioral Brain Sciences, Otto-von-Guericke University Magdeburg, Germany.

⁶Gesundheitscampus Immunologie, Infektiologie und Inflammation (GCI3), Medical Center, Otto-von-Guericke University, Magdeburg, Germany.

⁷Present address: Institute of Virology, Hannover Medical School, 30625 Hannover, Germany.

These authors contributed equally.

* Corresponding author: Andrea Kröger, Institute for Medical Microbiology and Hospital Hygiene, Otto-von-Guericke University Magdeburg, Leipziger Strasse 44, D-39120 Magdeburg, Germany.

Email: andrea.kroeger@med.ovgu.de

Tick-borne encephalitis virus is an important human pathogen and can cause the Tick-borne encephalitis (TBE), which is a serious illness. Patients with clinical symptoms can undergo severe meningo-encephalitis with sequelae including cognitive disorders and paralysis. Though, less than 30% of patients with clinical symptoms develop meningo-encephalitis. The number of seropositive humans in some regions indicates a much higher number of TBEV infections, either with no or subclinical symptoms. The functional relevance of these subclinical TBEV infections and their influence on brain functions, such as learning and memory, has not been investigated so far.

In the present study, we analyzed the phenotypic effect of a subclinical infection of Langat virus, a live-attenuated member of TBEV, on spatial memory and morphological changes in the hippocampus of mice. Viral replication in the olfactory bulb is associated with dendritic spine loss and activation of microglia and astrocytes in the hippocampus. Our data provide evidence that already subclinical infection affects hippocampus-dependent learning.