

Alphavirus Infection of the CNS: Entry, Dissemination, and Neurodegeneration

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Abstract

Alphaviruses most often associated with neuroinvasive disease are limited to the Americas and include strains of EEEV, VEEV, and WEEV. The process of alphavirus entry into the CNS of infected vertebrates following challenge is not well-understood. It is thought that virus entry into the CNS depends on the inoculation route. It is well-established that olfactory sensory neurons provide access to the CNS following challenge with airborne virus. However, less knowledge is available regarding virus entry into the CNS following peripheral, non-olfactory infection, which appears to rely on some form of hematogenous spread. We sought to determine the precise route of CNS entry following footpad inoculation by using a combination of *in vivo/ex vivo* bioluminescence imaging and traditional histological examination methods. We found a consistent pattern in the spatiotemporal distribution of virus among the imaged brains, none of which involved the olfactory bulb.

Keywords:

Extending these studies by performing histological analysis on the imaged tissues led to the finding that CNS entry by WEEV likely occurs in areas of the CNS where the blood brain barrier is naturally absent. These areas include the hypothalamus the subfornical organ the pineal gland and the area postrema. Importantly these results reveal a previously unrecognized method of alphavirus entry into the CNS