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Poster presentation

Coxsackievirus B3 infection affects neurogenesis and hinders normal brain development

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Coxsackieviruses are significant human pathogens and the neonatal central nervous system (CNS) is a major target for infection. Despite the extreme susceptibility of newborn infants to coxsackievirus infection, tropism for the CNS, and a relatively high infection rate among infants, few studies have been aimed at determining the long-term consequences of infection on the developing CNS. We previously described a neonatal mouse model of coxsackievirus B3 (CVB3) infection, and discovered that proliferating stem cells in the CNS were preferentially targeted for infection. Since CVB3 is a cytolytic virus and therefore may damage target cells, we evaluated the later stages of infection, the ensuing inflammatory response, and subsequent developmental defects that may occur following the loss of neural stem cells. We infected 3 day-old mice (intra-cranially) with a recombinant CVB3 expressing eGFP (10^7 pfu) and characterized brain pathology (by histology and immunofluorescence for neural markers, viral protein, and apoptosis) and wet weight measurements of surviving mice. Intriguingly, CVB3 may persist in the CNS as a low level, non-cytolytic infection. A significant decrease was seen in wet weight measurements of brain in both young (1, 2, and 5 days post-infection – pi) and older (10, 30, and 90 days pi) mice, as compared to mock-infected mice. We also observed an inverse relationship between the amount of infectious virus present during acute infection and brain wet weight measurements: the more infectious virus present, the lower the brain wet weight values. This relationship became progressively stronger over time. At 10 days pi, infectious virus was no longer present. Despite the lack of infectious virus, a significant decrease in brain wet weight values was observed up to 90 days pi, as compared to mock infected control mice. Furthermore, apoptosis was observed in the subventricular zone of infected mice, which might indicate the early loss of proliferating ($Ki67^+$) neural stem cells. Hence, developmental defects induced by a relatively common infection during the neonatal period may be long-lasting, and the prognosis for newborn infants recovering from acute infection needs to be re-explored. With this in mind, long-term neurological sequelae might be expected following neonatal CVB3 infection.

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