HIV infection, even with antiretroviral therapy, appears to damage a growing child's brain

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HIV infection alters brain development in young children, even when they receive antiretroviral treatment early in life, shows a report in *Frontiers in Neuroanatomy*. Children exposed to, but not infected by, HIV also appear to have ongoing changes in their brain development.

Although advances in HIV therapy have enabled millions of people to live longer and healthier lives, the treatment of HIV-positive infants and children remains complex. HIV has been shown to cause abnormalities in a child's brain development, however therapeutic interventions can also harm a growing child. While children have always been eligible for treatment, it is only since 2008 that treatment for newborns became standard, after preliminary data from the Children with HIV Early Antiretroviral (CHER) clinical trial. Now, in the era of early treatment, researchers are working to better understand how HIV infection affects children's development—specifically their neurodevelopment.

"Despite early antiretroviral therapy, we continue to observe white matter damage at the age of 7 years, with new damage evident between the ages of 5 and 7," says Marcin Jankiewicz, a researcher at the University of Cape Town, South Africa and lead author of the study. "These observations in HIV-positive children point to ongoing disruptions in white matter development regardless of early antiretroviral therapy and viral suppression."

The researchers used an advanced magnetic resonance imaging technique, called diffusion tensor imaging, to look at differences in one type of brain tissue—called white matter—between groups of 65 HIV-positive and 46 uninfected 7-year-old children. White matter plays a critical role in transmitting information between distinct brain regions. The latest study confirmed ongoing microstructural differences in certain tracts between infected and uninfected children.

All the HIV-positive children had started antiretroviral treatment by the age of 18 months in the CHER trial, in Cape Town and Soweto, South Africa. This most recent study follows up on similar observations made when the children were 5 years old.

"The CHER cohort is one of the largest and best-documented trials of children receiving antiretroviral therapy within the first two years of life," says Jankiewicz. "Since age- and community-matched uninfected infants were enrolled in parallel, and our colleagues at Stellenbosch University had tracked brain development in these children throughout their early years in a neurodevelopmental sub-study, we had an amazing opportunity to add state-of-the-art neuroimaging assessments."

The neurodevelopmental sub-study also included children who were exposed to HIV, but who were not infected (for example when the mother was infected during pregnancy, but the infection did not transfer to the fetus or infant). These children formed a subset of the uninfected group in the current study, providing an opportunity to see if there were consequences of HIV and antiretroviral exposure in the absence of infection. Unfortunately, these children also appear to have ongoing changes in their white matter development.

While this was a small study and the future implications of such abnormalities are not yet clear, Jankiewicz hopes that these studies will contribute to a better understanding of brain development in HIV-

infected and exposed children, as well as the impact of long-term antiretroviral treatment.

"We hope that our work will eventually help identify the parts of the brain that are particularly vulnerable to HIV and/or antiretroviral therapy and clarify how the timing of therapy affects brain development," says Jankiewicz. "This could inform treatment policy, help improve drug combinations, and guide early intervention strategies."

More information: Marcin Jankiewicz et al, White Matter Abnormalities in Children with HIV Infection and Exposure, *Frontiers in Neuroanatomy* (2017). DOI: 10.3389/fnana.2017.00088

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