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"Effects of Alcohol on SIV Levels within the CNS of Rhesus Macaques"

Human Immunodeficiency Virus (HIV) infections are detrimental not only to the immune system, but also to the Central Nervous System (CNS). Despite effective combination antiretroviral therapy (cART), HIV persists in reservoirs within many tissues including the CNS. The CNS represents an immunologically privileged site where proviruses can be maintained in perivascular macrophages, microglia, and astrocytes. Neuronal injury is common, with approximately half of people living with HIV (PLWH) developing HIV-associated neurocognitive disorders. However, the exact mechanisms by which HIV effects neurocognitive dysfunction are not well-defined. Alcohol use disorders (AUD) have been associated with failure to control viremia, neurocognitive impairment, and worse disease outcomes in PLWH. We hypothesized that AUD will exacerbate the adverse neurocognitive deficits observed in PLWH by increasing viral levels in CNS tissues. To address this hypothesis, we utilized samples from a pilot study implementing modifications to a well-established animal model of HIV: rhesus macaques administered chronic binge alcohol (CBA) and infected with simian immunodeficiency virus (SIV). For this pilot study, five animals were fed a high fat or Western diet, infected with an SIV quasispecies that contained a neurotropic SIV strain (SIVmac251 and SIV17e), and treated with a three-drug cART regimen. As done with this model, three animals were administered CBA to achieve 50mM blood alcohol for five days per week via a gastric catheter prior to and throughout SIV infection, while two controls received water. Four of the animals were started on cART after 16 weeks of infection. Using quantitative PCR, viral loads were measured longitudinally in plasma and from CNS tissues taken at necropsy. The SIV envelope gene was sequenced to identify the specific strain present.

Prior to cART, plasma viral levels were slightly higher in the three CBA administered animals. After cART, plasma viral levels were significantly reduced in the four treated animals; however, plasma viremia remained detectable in the two CBA animals over the course of treatment, while viremia was undetectable in the controls. Additionally, virus was undetectable in the frontal cortex of the two control animals, but measurable SIV levels were observed in the frontal cortex of the two CBA animals. Although the neurotropic SIV17e strain was not the predominant genotype in the periphery, it was readily found in brain tissue and CSF of the CBA animals. The findings of this pilot study support the hypothesis that CBA increases viral reservoirs in the brain and demonstrates the efficacy of using this model to decipher the mechanisms of neurocognitive deficits seen in PLWH and those with AUD. Future studies will look at viral levels within other discrete regions of the CNS and evaluate if they harbor drug resistant mutations.