

## ***Cocaine Inhibits the Central Nervous System Efficacy of HIV Antiretroviral Therapy***

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Antiretroviral therapy (ART) suppresses HIV replication to undetectable levels. However, ART does not quell virus in the brain to the same extent as the periphery. As a result, there are limitations in dosing of the brain that perpetuate a spectrum of cognitive disorders termed HIV Associated Neurocognitive Disorders (HAND) (Yuan and Kaul, 2019). HAND is a major consequence of HIV infection that affects between 30-70% of infected individuals and greatly impacts the survival and quality of life of those who are affected. Substance use commonly occurs among HIV infected individuals and may alter the incidence, severity, or progression of HAND. However, there is a paucity of data regarding the mechanisms by which substance abuse contributes to HAND (Chilunda, et al. 2019). The goal of this study was to characterize the mechanisms by which cocaine impacts the entry and efficacy of ART into the CNS.

**Methods:** To determine the localization of ART, brain was obtained from rhesus macaques infected with simian immunodeficiency virus and treated with ART. Following perfusion, the brain was cryosectioned and matrix assisted laser desorption ionization (MALDI) imaging mass spectrometry performed.

**Preliminary Results:** Two first line ART drugs, tenofovir (TFV) and emtricitabine (FTC), were imaged in five brain regions. Additionally, the pharmacologically active triphosphate metabolites capable of inhibiting HIV/SIV were also determined. TFV and FTC were present in brain to a significantly lower extent than the periphery. However, FTC was more abundant in brain than TFV. Metabolism into the pharmacologically active metabolites occurred in a heterogenous manner that was restricted to “hot spots”, where relatively high concentrations of ART were found.

**Discussion:** There is a limited penetrance of the pharmacologically active ART metabolites into brain, particularly in regions involved in the dopaminergic reward pathway. This suggests that the brain is undertreated during HIV infection which will perpetuate HAND, specifically in the context of substance abuse.

**References:** Yuan, NY. and Kaul, M. *Journal of Neuroimmune Pharmacology* (2019): 1-23; Chilunda, V, Calderon, TM, Martinez-Aguado, P, and Berman, JW. *Brain research* (2019): 146426.

*Funding was provided by NIH grants DA044838 (Williams), A1131306 (Clements), A1127142 (Clements), A1128781 (Bumpus), and GM103853 (Bumpus).*