Dopamine mediates neuroinflammation and HIV infection of the CNS: critical roles in neuroAIDS

Tina Calderon1, Dionna Williams1, Lillie Lopez2, Eliseo Eugenia2, Peter Gaskell1, Mike Veenstra1, Kathryn Anastos3, Susan Morgello4 and Joan Berman1,*

1Department of Pathology, Albert Einstein College of Medicine, Bronx, NY, United States of America; 2Department of Microbiology, Biocemistry and Molecular Genetics, Rutgers State University of New Jersey, Newark, NJ, United States of America; 3Department of Medicine, Albert Einstein College of Medicine, Bronx, NY, United States of America; *Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY, United States of America

Substance abuse may accelerate the development and/or increase the severity of HIV-associated neurocognitive disorders (HAND). HIV neuropathogenesis in the drug-abusing infected population is not completely characterized. The percentage of peripheral blood CD14+CD16+ monocytes is increased with HIV infection. The transmigration of uninfected and infected CD14+CD16+ monocytes across the blood–brain barrier (BBB) contributes to HIV entry into the CNS and to the establishment and propagation of chronic neuroinflammation, which both mediate HAND. We demonstrate that the frequency of CD14+CD16+ monocytes in the periphery of HIV-infected substance abusers is increased when compared to those without active substance use. Dopamine, elevated in the brain in response to drug use, enhances the transmigration of CD14+CD16+ monocytes, but not T cells, across our in vitro model of the human BBB. Therefore, elevated extracellular CNS dopamine may be a novel mechanism by which active substance use increases CD14+CD16+ monocyte entry into the CNS of HIV-infected individuals. Transmigration is mediated by D1-like dopamine receptors as indicated by greater surface D1 and D5 dopamine receptor expression on CD14+CD16+ monocytes as compared to T cells, and the ability of the D1-like dopamine receptor agonist, SKF 38393, to increase CD14+CD16+ monocyte transmigration across the BBB. Pseudopod formation and active ADAM17 expression by CD14+CD16+ monocytes are increased by dopamine and may contribute to the ability of these cells to transmigrate. Thus, uninfected and HIV-infected CD14+CD16+ monocyte entry into the CNS may increase with active substance use and subsequent increased dopamine, contributing to CNS viral seeding, neuroinflammation, and HIV neuropathogenesis.

*Submitting author e-mail: joan.berman@einstein.yu.edu