Serotonin-Related Gene Polymorphisms and Asymptomatic Neurocognitive Impairment in HIV-Infected Alcohol Abusers

Objective: To determine whether genetic risk for neurocognitive impairment is associated with single-nucleotide polymorphisms, *SLC6A4* 5-HTTLPR, *TPH2* rs4570625 and *GALM* rs6741892 in HIV-infected adults.

Background: HIV-infected individuals continue to experience neurocognitive deterioration despite virologically successful treatments. While the cause remains unclear, evidence suggests that HIV-associated neurocognitive disorders (HAND) may be associated with neurobehavioral dysfunction. Genetic variants have been explored to identify risk markers to determine neuropathogenesis of neurocognitive deterioration. Memory deficits and executive dysfunction are highly prevalent among HIV-infected adults. These conditions can affect their quality of life and HIV risk-taking behaviors. Single nucleotide polymorphisms in the *SLC6A4, TPH2* and *GALM* genes affect the activity of serotonin and may increase the risk of HAND.

Methods: This cross-sectional study used baseline data collected as part of an adapted risk reduction intervention, the Holistic Health Recovery Program (HHRP-A), for HIV-infected alcohol abusers. Participants were randomly assigned to the HHRP-A or a Health Promotion Comparison (HPC) condition. Recruitment was from community-based organizations in Miami-Dade providing outpatient treatment services for alcohol and mental health problems to HIV-positive men and women. A total of 267 biologically unrelated individuals were genotyped for polymorphisms *SLC6A4* 5-HTTLPR, *TPH2* rs4570625 and *GALM* rs6741892. To assess neurocognitive functions, the Short Category and the Auditory Verbal Learning tests were used to measure executive function and memory.

Results: The sample was 65% male (mean age 45.1 SD=7.1) 34% female (mean age 45.3, SD=65.9), 76% African American, 16% Hispanic, and 8% Caucasian. *TPH2* rs4570625 showed a significant association with impaired executive function (odds ratio = 2.5, 95% CI, 1.1-4.9; p = .02). The risk increased in African American males (odds ratio = 4.8, 95% CI, 1.5-14.8; p = .005). *GALM* rs6741892 was associated with impaired memory (odds ratio = 1.9, 95% CI, 1.2 - 3.1; p = .006) and again the risk increased in African American males (odds ratio = 2.4, 95% CI, 1.2-4.9; p = .02). No significant association was found with polymorphism *SLC6A4* 5-HTTLPR.

Conclusions: These preliminary findings suggest that single nucleotide polymorphism in the *TPH2* and *GALM* genes increase the risk for neurocognitive deficits in memory and executive function. However, a more robust sample size is needed to confirm the results and determine the associations with race.

Remember: **Total word count for the *full* abstract is **no more than 350 words**.

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TPH2 rs4570625 and *GALM* rs6741892 polymorphisms in the serotonin system may influence cognitive control in HIV-infected alcohol abusers.