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## **Linking Cannabis Use Disorder, Long-noncoding RNA and Olfactory Structure and Function**

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Cannabis use disorder, which is prevalent in trauma populations, has been linked to structural and functional changes in the olfactory neural system, but the mechanisms underlying these effects are incompletely understood. Long noncoding RNAs (lncRNA) play important roles in the modulation of olfactory brain development and structure by the environment and could represent one of the mechanisms by which cannabis influences olfactory functions and structure. The goal of this study was to examine cannabis use-associated lncRNA changes in non-invasively sampled olfactory neurons of adults who suffered severe psychosocial trauma during childhood study and to link these changes to structural changes in their primary and secondary olfactory brain cortices. This study included 46 African American female and male adults between the 18-55- years old, 23 of whom had a history of cannabis use disorders. All participants received one-time measurements of behavioral, social, and psychological constructs through multiple questionnaires focused on past and current experiences. Several clinical tasks were also completed such as salivary cortisol sampling, skin-conductance response sampling, Magnetic Resonance Imaging (MRI), and olfactory cell nasal sampling.

Nasal exfoliates collected were used for lncRNA-based epigenomic-transcriptomic analysis. Cannabis use disorder was independently associated with reduced grey volume in several structures in the primary olfactory cortex. Furthermore, cannabis use disorder was associated with differential expression of several lncRNA previously implicated in neurodevelopment, cortical brain volumes and cognitive impairments. This study provides preliminary insights into the possible roles of lncRNA in the relationship between cannabis use and changes in the olfactory neural system.