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Cell-type specific gene expression changes associated with adolescence exposure to THC in mice

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There is substantial evidence of a statistical association between cannabis use and the development of psychoses. This association is predominantly found in daily users consuming high potency cannabis, and appears to be modulated by genetic factors. The implications of these findings are particularly relevant for adolescents. Adolescence is considered a vulnerable period for the development of mental disorders, because it is during this time that critical neural and behavioral changes occur in the brain. However, the precise mechanisms by which cannabis can alter the adolescent brain remain unknown. Our central hypothesis is that sustained changes in gene expression might be a critical mechanism by which cannabis induces long-term behavioral abnormalities linked to cannabis use. In an ongoing NIDA funded study (1DP1DA042232), we found that heavy, chronic administration of THC to adolescent mice is associated with long-term behavioral effects, including psychotic-like behaviors. By profiling the transcriptome of specific neuronal populations by RNAseq, we identified gene expression changes that are associated with a history of adolescent exposure to THC. Our preliminary analysis reveals that a history of THC is linked to changes in cell type specific genes implicated in synaptic functions and various metabolic pathways. Our current project is examining differences in chromatin accessibility linked to the history of THC. These findings will likely identify specific transcription factors involved in the regulation of relevant gene expression programs that are altered by cannabis use. Our results represent an important step in improving our understanding of the pathophysiological mechanisms involved in cannabis related disorders.