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Cell-type Specific Impacts of Chronic Nicotine Vapor Exposure and Spontaneous Withdrawal on the Murine Hippocampus

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Hippocampal dysfunction contributes to nicotine withdrawal induced affective dysfunction and cognitive deficits. Both of these non-craving withdrawal symptomologies are major predictors of relapse to smoking behavior in humans. Therefore, we investigated the cell-type specific impacts of chronic nicotine exposure and spontaneous withdrawal on the murine hippocampus using a custom built La Jolla Alcohol Research, Inc. passive administration E-vape system in conjunction with the 10x Genomics single nucleus RNA sequencing (snRNA-seq) platform. We exposed adult mice to nicotine vapor or air for 14 sessions, with each session lasting 12hr from 2000 to 0800 the next morning. Mice marked for 24hr withdrawal did not receive nicotine vapor exposure during the 14th session. Mice were sacrificed 2 hours after the 14th exposure session and hippocampal tissues were collected. We performed snRNA-seq on the hippocampi of air control, chronic nicotine, and 24hr withdrawal mice (N=4) and profiled the transcriptomic changes due to nicotine exposure in Glutamatergic and GABAergic neuronal subtypes. The observed alterations in the transcriptomes of these neuronal subtypes demonstrate cell-type specific dysfunction in the hippocampus. These observations provide potential mechanistic insight into the contribution of the hippocampus to the non-craving nicotine withdrawal endophenotypes of affective dysfunction and cognitive deficits. Additionally, we are currently cross-referencing the transcriptomic changes observed in microglia from our experiment with previously published cell-type specific RNA-sequencing studies investigating the impact of substances of abuse on the brain. We aim to identify overlapping and unique microglial transcriptomic phenotypes associated with exposure to varying substances of abuse.