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Cell-type specific genetic effects and changes due to oxycodone exposure in RNA expression levels and co-expression networks in rat prefrontal cortex

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The US continues to experience an epidemic of opioid misuse and dependence, yet not enough is known about the contribution of neurogenetics. Using rat models, we can develop a better understanding of the role of genetics, the consequences of oxycodone exposure, and how these two elements interact to influence behavior. As part of our larger study of oxycodone self-administration behaviors in the Hybrid Rat Diversity Panel, we generated prefrontal cortex snRNA-Seq data from 4 rats (2 inbred strains with and without oxycodone exposure). The libraries were sequenced with ~200 million paired-end reads per sample and more than 2,500 high-quality nuclei per sample were captured. Cells were assigned to clusters using a standard Seurat protocol. For 20 out 25 clusters, we were able to confidently assign a single cell subtype because more than 80% of cells included in the cluster were predicted to be from a specific cell subtype according to the mouse motor cortex reference atlas and the distance between and location of the clusters in the UMAP projection reflected the anatomical structure of the cortex. In general, more genes were differentially expressed between strains than between oxycodone and saline exposure for all cell types examined. Within cell type co-expression analyses via hdWGCNA indicated both cell-type specific co-expression modules and co-expression modules shared across all cell types. RNA expression levels and co-expression networks at the single cell/nuclei and cell type specific levels provide additional resolution to important genetic differences in response to oxycodone. Supported by P30DA044223 and U01DA051937.