Submitter Name: Brandon Baker
Submitter email: bb2@clemson.edu
PI name: Trudy Mackay
PI email: tmackay@clemson.edu

Single-cell transcriptional responses to cocaine exposure in the Drosophila brain.

Brandon Baker[1], Sneha Mokashi[1], Vijay Shankar[1], Rachel Hannah[1], Robert Anholt[1] and Trudy Mackay[1]

[1]Center for Human Genetics, Clemson University

Previous studies identified polymorphisms in candidate genes associated with variation in consumption of cocaine among lines of the Drosophila Genetic Reference Panel, and RNAi-mediated targeted gene disruption implicated dopaminergic projections to the mushroom bodies. To identify specific cell populations that respond to acute cocaine exposure, we analyzed single cell transcriptional responses in duplicate samples of flies that consumed fixed amounts of sucrose or sucrose supplemented with cocaine, sexes separately. After exposure, 20 brains for each sample were dissected, pooled and dissociated. Cells were separated and lysed, and cDNA was synthesized using Chromium 10x microfluidics followed by sequencing on an Illumina Novaseq. Integration of all eight samples distributed across sexes, conditions and replicates resulted in a dataset of 86,224 cells. Unsupervised clustering of this population yielded 36 distinct clusters. Annotation of clusters based on their gene markers revealed that all major cell types (neuronal and glial) as well as neurotransmitter types from most brain regions were represented (including the optic lobe and the mushroom body). Differential expression analysis within individual clusters indicated cluster-specific responses to cocaine. Specifically, clusters corresponding to glia, T1 and T4/T5 neurons of the optic lobe, Kenyon cells and photoreceptor cells showed dramatic transcriptional responses following cocaine exposure. Some clusters also showed significantly divergent responses across the sexes. Additionally, transcriptional responses to cocaine in most clusters were considerably more pronounced in male than in female brains. Thus, cocaine exposure elicits sexually dimorphic transcriptional responses in both glia and neurons in multiple compartments of the Drosophila brain.