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An atlas of transcriptionally distinct cell populations within the rat ventral tegmental area

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The ventral tegmental area (VTA) is a complex brain region that is essential in reward function and substance abuse. While decades of research on VTA function has focused on the role of dopaminergic neurons, recent evidence has identified critical roles of VTA GABAergic and glutamatergic neurons in reward processes as well. Interestingly, molecular characterization of these cells has revealed that subsets of these neurons express genes involved in the transport of multiple neurotransmitters, providing evidence for the presence of co-release neurons. However, these studies have largely relied on low-throughput methods that do not provide comprehensive information on transcriptional diversity and heterogeneity within the VTA. Here, we performed single nucleus RNA-sequencing (snRNA-seq) on 21,600 cells from both male and female Sprague-Dawley rats. This resulted in the identification of 16 transcriptionally distinct cell types within the VTA, including 7 transcriptionally distinct neuronal populations. Subclustering of the 7 transcriptionally distinct neuronal populations identified multiple populations expressing genes required for either the synthesis (co-synthesis neurons) or release (co-release neurons) of multiple neurotransmitters. Furthermore, subclustering identified one population with high levels of expression for genes involved in the synthesis and transport of dopamine, glutamate, and GABA. Finally, snRNA-seq enabled the de novo identification of thousands of marker genes for each transcriptionally distinct population, revealing cluster-specific enrichment of genes implicated in neuropsychiatric and neurodevelopmental disorders. This dataset will be a useful tool to researchers performing cell-type specific manipulations within the VTA.