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Low-input profiling of epigenomic dynamics in mouse brain to understand prolonged synaptic plasticity

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There has been increasing evidence that epigenetic mechanisms mediate the influence of environmental factors on gene activities in the CNS and therefore are likely involved in brain development and pathology of drug abuse. Profiling of brain epigenomes in a cell-type and brain-region specific manner requires use of low-input epigenomic technologies. We developed MOWChIP-seq for profiling histone modifications and TF bindings using as few as 100-1000 cells. We have applied this approach to study various histone marks in mouse brain tissues including repressive marks that contain information not reflected by open chromatin assay ATAC-seq. In one such study, we showed that administration of a single dose of psychedelic DOI produces changes in chromatin organization in mouse frontal cortex, particularly at enhancer regions of genes involved in synaptic assembly that stretch for days. In contrast to the much more transient transcriptomic changes, epigenomic dynamics are more likely to be associated with the prolonged synaptic plasticity caused by psychedelic exposure.