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Gene coexpression patterns predict opiate-induced brain-state transitions

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Opioid addiction is a chronic, relapsing disorder associated with persistent changes in brain plasticity. Reconfiguration of neuronal connectivity may explain heightened abuse liability in individuals with a history of chronic drug exposure. To characterize network-level changes in neuronal activity induced by chronic opiate exposure, we compared FOS expression in mice that are morphine-naïve, morphine-dependent, or have undergone 4 weeks of withdrawal from chronic morphine exposure, relative to saline-exposed controls. Pairwise interregional correlations in FOS expression data were used to construct network models that reveal a persistent reduction in connectivity strength following opiate dependence. Further, we demonstrate that basal gene expression patterns are predictive of changes in FOS correlation networks in the morphine-dependent state. Finally, we determine that regions of the hippocampus, striatum, and midbrain are most influential in driving transitions between opiate-naïve and opiate-dependent brain states using a control theoretic approach. This study provides a framework for predicting the influence of specific therapeutic interventions on the state of the opiate-dependent brain.