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Mitochondrial Dysfunction and Oxidative Stress: Conserved Functional Phenotypes in Cocaine Addiction across Multiple Brain Regions

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Previous studies have reported widespread hippocampal gene expression changes in individuals with cocaine addiction and alcoholism, suggesting shared neuronal adaptations between these disorders (Zhifeng et al). Notably, long-term cocaine exposure uniquely induces functional alterations, such as impaired mitochondrial functions related to energy metabolism, similar to those observed in neurodegenerative diseases. To investigate whether this functional phenotype is conserved across other brain regions, we performed network analysis on the transcriptomes of various mouse brain regions, including the Prefrontal Cortex (PFC), Basolateral Amygdala (BLA), Ventral Hippocampus (VH), Dorsal Striatum (DS), and Ventral Tegmental Area (VTA).

Our network module preservation analysis identified significant modules, and gene ontology analysis with genes in these modules recapitulated previous observations, highlighting mitochondrial function and cellular stress (oxidative stress) as significant gene ontologies. To determine if these gene networks are preserved in other brain regions, we conducted network preservation analysis, assessing network similarity using modularity and silhouette scores and evaluating their significance with Z statistics.

Our findings revealed that mitochondrial function and oxidative stress-associated gene modules are highly conserved across five brain regions (BLA, DS, PFC, VH, NAC) with high significance and moderately conserved in the VTA, aligning with human postmortem brain cocaine transcriptome findings (Zhou et al.). This suggests that energy metabolism and cellular stress-mediated responses may be associated with cocaine addiction across multiple brain regions, providing valuable insights into potential therapeutic targets for intervention.