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The Microbial community dynamics of cocaine sensitization in two behaviorally divergent Collaborative Cross strains.

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The role of the gut-brain axis in health and disease is becoming increasingly important. Microbial products produced in the murine gut exert effects on striatal gene expression and depletion of the microbiome by antibiotic treatment alters behavioral cocaine sensitization. Cocaine sensitization is correlated with drug self-administration behavior and is therefore a predictor of addiction vulnerability. The composition of the gut microbiome is altered by diet and age but is inherently under genetic control. We have previously mapped and identified QTL for microbial abundance in the Collaborative Cross (CC) and Diversity Outbred population. Here we profile the microbial dynamics in response to cocaine sensitization in two CC mouse strains, which display differentially extreme behavioral responses to cocaine sensitization. A principal coordinates analysis of the beta-diversity of the gut microbiome showed significant separation of the microbiomes by strain and cocaine effect. Analysis of Group Dissimilarity-Adonis based on microbial abundance matrix with Bray-Curtis distance shows significant difference between the naïve and cocaine exposure groups in the responsive strain. Barnesiella viscericola abundance was increased following the cocaine sensitization paradigm in the responsive strain but not in the unresponsive strain. The KEGG ontology pathways, represented by the responsive strain's microbiome post-sensitization were significantly increased in dopamine degradation components. Pathways related to the glutamine synthetase repressor and propionate metabolism were down regulated following sensitization. These findings are consistent with the host genetics controlling both the differential behavior observed within these two strains, their innate microbiome composition as well as the microbiomes response to repeated drug exposure.