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Long access heroin self-administration significantly alters gut microbiome diversity, structure and composition.

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It is well known that long-term opiate use disorder (OUD) is associated with alterations in gastrointestinal function (GI) to include constipation, reduced motility, increased absorption of fluids from the gut and inhibition of secretomotor neurons in the gut epithelium. These signs of disrupted GI function can be associated with alterations in the gut microbiome. However, it is not known if long-term opiate self-administration has effects on the gut microbiome. Therefore, we performed 16S rRNA gene sequencing on fecal samples from NIH Heterogeneous Stock rats collected before onset of heroin self-administration and after post-extinction reinstatement 48 days later. Community α-diversity (richness) was significantly decreased over the course of drug self-administration. Analyses of β-diversity (community structure) showed that pre- and post-self-administration groups clustered together within groups and significantly apart from each other. A significant effect of sex on β-diversity was noted. At the level of phylum, heroin self-administration decreased the relative abundance of Bacteroidetes while increasing that of Firmicutes. When rats were sorted into low- and high-consumption groups with regard to heroin intake, a significant difference in β-diversity was detected using both Bray-Curtis and Jaccard indices. High and low consumers also differed significantly in microbiome composition regarding the phyla Bacteroidetes and Firmicutes. In conclusion, long access heroin self-administration causes significant changes in the richness and composition of the gut microbiome. The detection of significantly different effects of sex- and high vs. low heroin intake on the gut microbial community suggests the possible existence of biomarkers for these variables.