THC supplementation results in weight loss and sex-dependent gut microbiota changes

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Introduction: Obesity and high-fat diets induce consistent alterations in gut microbiota composition, corroborating the relationship between microbiome with host physiology.[1] Observations from epidemiological reviews and experiments also illustrate weight regulation effects of delta(9)-tetrahydrocannabinol (THC) with microbiome shifts.[2,3] We aimed to examine associations connecting gut microbiome changes with THC-induced weight loss.

Methods: High-fat diet induced obese mice were treated with oral THC supplementation while maintaining diet. In addition to measuring weight, fecal samples were obtained at various timepoints, sequenced for bacterial 16s rRNA content and analyzed using QIIME2. Alpha and beta diversity were analyzed along with linear mixed effects (LME) models of bacterial relative abundance relationship to THC treatment and weight change.

Results: In both male and female mice, the THC group had significantly greater average weight loss than controls (-17.8% vs. -0.22%, p=0.00002 and -13.8% vs. +2.9%, p=0.00006 respectively). Male rats had 8 bacterial taxonomic features that were both significantly different in change of relative abundance between THC and controls and correlated with weight change. An LME model of three features explained 76% of the variance in weight change and accurately predicted weight change in a completely different male rat cohort (R=0.64, R^2=0.41, p=0.000001). Female mice had fewer significant predictive features and were difficult to model, but the 3-feature model still accurately predicted weight change (R=0.66, R^2=0.44, p=7e-9).

Conclusions: Our results indicate that gut microbiome composition changes play some role in THC-induced weight loss. Additionally, we proved the concept of a microbiome-based approach to predict weight loss utilizing statistical modeling.

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