Joint Effects of HIV and Obesity on the Microbiome of Young Men who have Sex with Men

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Background

- The prevalence of obesity is rising among people living with HIV
- Both obesity and HIV infection are associated with immune dysregulation and may work synergistically to increase the risk of inflammation-associated sequelae.
- Disruption of gut bacterial communities may be one of the key drivers of this inflammation; however, the combined effects of HIV and obesity on the microbiome have not been explored.

Materials & Methods

- Participants (N=381) with archived rectal swabs collected between 2014 and 2017 were selected from an ongoing cohort of diverse young men who have sex with men (The mSTUDY, NIDA U01 DA036267).
- Thirty-nine participants were HIV+ and obese (H+O+), 143 were HIV+ and non-obese (H+O−), 64 were HIV- and obese (H−O+), and 135 were HIV- and non-obese (H−O−).
- Microbiome composition was assessed by targeted sequencing of the V4 region of the 16S rRNA gene followed by exact sequence inference with DADA2.
- Analyses included permutational multivariate ANOVA (PERMANOVA) with Bray-Curtis distance to test for differences in overall composition and zero-inflated negative binomial (ZINB) models to test for differential abundance of specific genera.
- All analyses utilized inverse probability of treatment weighting to control for a large set of clinical and behavioral factors including demographics, ART use, sexual behavior, positive rectal STI test by PCR, smoking, and self-reports of methamphetamine, marijuana, and alcohol use.

Results

- Men averaged 31 years old, 49% were Hispanic and 39% were non-Hispanic Black (Table 1).
- Significant variability in microbial composition was explained by the combination of HIV and obesity (R² for the marginal contribution of the H+O+ group = .008, p = .001; Figure 1B).
- HIV+ individuals generally showed higher diversity than HIV−, with little difference by obesity (Figure 1C).
- H+O+ participants had the highest ratios of Prevotella to Bacteroides, a pro-inflammatory enterotype that has been described in HIV and obesity independently (Figure 2B).
- H+O+ participants had lower levels of Bacteroides and Veillonella than all other groups, suggesting a synergistic effect of HIV and obesity on these genera (Figure 3).
- Dietzia and Finegoldia were reduced and Faecalibacterium was enriched in H+O+ compared to H+O− and H−O+, but not compared to H−O− controls, suggesting that HIV and obesity may have some antagonistic effects on these genera (Figure 3).

Conclusions

- In a diverse sample of young men who have sex with men, microbial composition was altered by the combination of HIV and obesity over and above the contributions of each condition alone.
- Our findings may help explain higher levels of generalized inflammation among people living with both HIV and obesity.
- Interactions between conditions altering the microbiome, such as HIV and obesity, should be taken into consideration when designing interventions to address dysbiosis and reduce its inflammatory consequences.