Substance Use and Dysbiosis: Microbial Disruption in the Context of HIV

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Julie V. Sudovec-Somogyi[1,2], Leighanne Main[1,3], Yanis Bitar[2], Ashley Yoon[1,3], Samantha Horne[1,3], Tobi Taylor[1,3], Corrilynn O. Hileman[1,2], Adam Burgener[1,3], Ann Avery[1,2]

[1]Case Western Reserve University School of Medicine, Cleveland, OH, USA, [2] Infectious Disease Department, MetroHealth System, Cleveland, OH, USA,
[3] Center for Global Health and Diseases, Pathology Department, Case Western Reserve School of Medicine, Cleveland, OH, USA

BACKGROUND

- **Substance use** is associated with **impaired immune functioning** and **poorer health outcomes** in people with HIV (PWH).
- The **gut microbiome** plays and important role in overall health through its influence on **systemic inflammation**.
- Little is known about how substance use impacts the microbiome.

Hypothesis: marijuana and stimulants use affect gut microbial diversity and composition and lead to changes in inflammatory markers concentrations in PWH and people without HIV (PWoH).

Exclusive marijuana use is associated with higher gut microbial diversity in people with HIV and people without HIV.

METHODS

174 PWH and PWoH from the NIDA cohort who had 16S rRNA gut microbiome sequencing from rectal swabs and drug use data from hair toxicology

139 PWH and PWoH with inflammatory marker data (IL-6, TNF-R1, TNF-R2, CD14, CD163, LBP, FABP2)

Age, sex, sexual orientation, race, ethnicity, HIV status, annual income

- Analysis stratified by drug use and inflammatory marker tertiles
- Analysis stratified by sex and sexual orientation and drug use

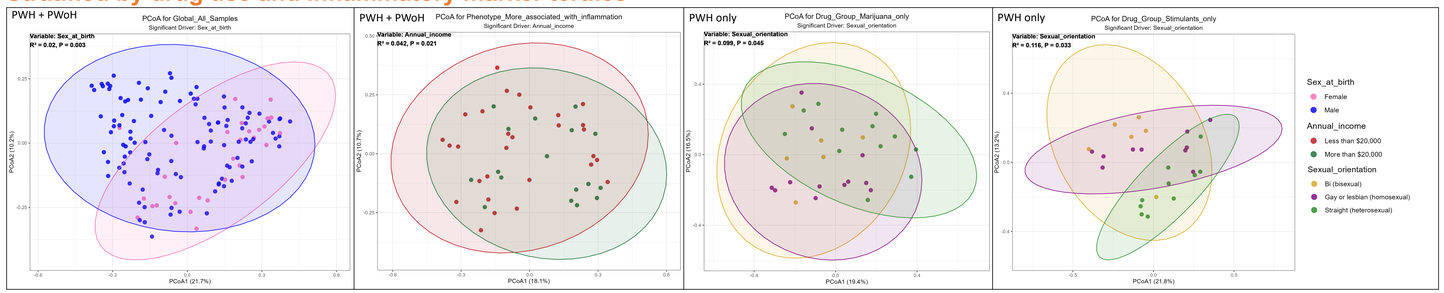
Beta-diversity with Bray-Curtis distance metric (PERMANOVA)
Alpha-diversity analysis with Shannon's diversity index
Generalized Linear Models
Linear regressions

RESULTS

49 years old | 77% male | 55% Black or African American
15% Hispanic or Latinx | 51% earn < $20k/year | 79% HIV+
108 different taxa



Stratified by drug use and inflammatory marker tertiles



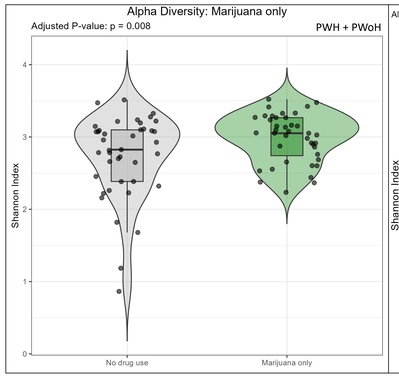
Covariates in beta-diversity analysis: all except Ethnicity

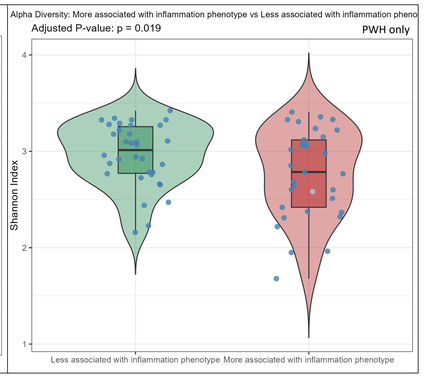
PLAIN LANGUAGE SUMMARY

People who use only marijuana – but not stimulants - have a more diverse gut bacteria composition, which is commonly associated with better gut health. People with HIV with higher inflammation have less diversity. Drug use can change gut bacteria in ways that affect inflammation.

Adjusted Generalized Linear Models: drug use as predictors, bacteria as outcomes (HIV + and -)

Drug use	Increase in	Decrease in
Marijuana	-	Roseburia faecis [-3.4 (CI -5; -1.8), p<0.01]
		Clostridium XIVa [-3.3 (CI -5.2; -1.4), p=0.01]
		Sutterella stercoricanis [-2.4 (CI -3.9; -0.9), p=0.02]
		Romboutsia [-2.7 (CI -4.4; -0.9), p=0.02]
		Staphylococcus [-3.1 (CI -5.5; -0.8), p=0.04]
Stimulants	Clostridiales [1.9 (CI 0.4; 3.3), p=0.04]	Lactobacillus iners [-3.1 (CI -5.4; -0.9), p=0.03]
		Streptophyta [-1.4 (CI -2.5; -0.3), p=0.04]





Covariates in alpha-diversity analysis: sex, inflammatory tertile

Stratified by sex and sexual orientation and drug use

Beta-diversity (with all covariates)

Group	Variable	R2	p-value
Males	Ethnicity	1.2%	0.04
Straight females	HIV status	4.5%	0.04
Bisexual males	Age	6.7%	0.03
	Marijuana use	8.9%	< 0.01

Alpha-diversity analysis (with all covariates): not significant.

Adjusted Linear Regression: bacteria that were associated with drug use in GLM as predictors, inflammatory markers as outcomes (HIV+ and -)

Bacteria	Increase in	Decrease in
Clostridiales	CD14 [0.06 (CI 0.02; 0.1), p<0.01]	-
	TNF-R2 [0.04 (CI 0.002; 0.08), p=0.04]	
Clostridium XIVa	TNF-R1 [0.05 (CI0.005; 0.09), p=0.02]	CD163 [-0.05 (CI -0.1; -0.003), p=0.03]
Roseburia faecis	-	CD14 [-0.04 (CI -0.09; -0.002), p=0.04]
		IL-6 [-0.04 (CI -0.09; -0.003), p=0.03]
		LBP [-0.07 (CI -0.1; -0.02), p<0.01]
Streptophyta	FABP2 [0.05 (CI 0.002; 0.1), p=0.04]	-
Romboutsia	IL-6 [0.05 (CI 0.01; 0.09), p<0.01]	-
Sutterella stercorincanis	LBP [0.04 (CI 0.001; 0.09), p=0.04]	-

CONCLUSIONS

- **Exclusive marijuana** use is associated with a **more diverse gut microbiome** in **PWH and PWoH**, which is commonly associated with **improved gut health.** This **effect is lost** in people who use **marijuana and stimulants**.
- Having **higher levels of inflammatory markers** ("more associated with inflammation" phenotype) is associated with a **less diverse** microbiome in **PWH** and therefore can have **negative implications**.
- **Marijuana and stimulant use** are associated to changes in **taxa** linked to **inflammatory markers**.

ADDITIONAL INFORMATION:
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