LIPIDOME ALTERATIONS WITH EXERCISE AMONG PEOPLE WITH AND WITHOUT HIV

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ABSTRACT

Background: An increasing burden of age-related comorbidities and impairment of physical function in aging people with HIV (PWH) can be improved, in part, through exercise interventions. The effect of exercise and HIV serostatus on the mechanisms underlying these improvements, such as changes in lipidome composition, is not known.

Methods: Sedentary adults (50-75 years old) with (N=24) or without (N=25) HIV participated in supervised endurance/resistance exercise for 24 weeks. In this exploratory secondary analysis of The Exercise for Healthy Aging Study, concentrations of plasma lipids (~1200 lipid species from 13 lipid classes) at baseline and week 24 were measured by mass spectrometry. Changes in log10 lipid concentrations were compared by HIV serostatus using t-tests. P-values unadjusted for multiple comparisons (unadj-p) and Benjamini-Hochberg corrected (adj-p) are reported.

Results: Among PWH and controls, at baseline, there were no statistically significant differences in concentrations of total lipids. With the exercise intervention, changes in total triacylglycerol (TAG) levels significantly differed among people with and without HIV (unadj-p=0.006, adj-p=0.078): TAGs tended to decrease in PWH (% Change: -4.5 [-14.1, 6.2]), but significantly increased in controls after 24 weeks of exercise (% Change: 14.7 [6, 24.1]). Concentrations of TAG species (Table) composed of long chain fatty acids increased among uninfected controls but not PWH (unadj-p=0.001-0.036, adj-p =0.10-0.12) from baseline to week 24. Total diacylglycerols (DAGs) increased in PWH from baseline to week 24 (% Change: 6.1 [0, 12.5]), but decreased in controls (% Change: -5.1 [-12.7, 3.2]) (unadj-p=0.03, adj-p=0.2). Baseline to week 24 changes in specific DAGs composed of palmitic acid (16:0), palmitoleic acid (16:1), and stearic acid (18:0) varied by serostatus, with increases in PWH (unadj-p=0.009-0.03; adj-p 0.10-0.12) and non-significant decreases in controls (Table). The change in concentrations of lysophosphatidylcholine (LPC) species composed of saturated fatty acids (LPC FA(15:0;16:0;17:0)) also differed by serostatus, with increases in PWH and decreases among controls (unadj-p=0.02-0.05; adj-p=0.12-0.21); Table

Conclusions: Although exploratory, the effects of exercise on the plasma lipidome may differ among people with and without HIV, potentially due to underlying alterations in lipid processing and fatty acid oxidation in PWH.

Lipid Analysis

Lipid Class	Abbreviation	Species #
Cholesterol Ester	CE	26
Ceramide	CER	12
Diacylglycerol	DAG	60
Dihydroceramide	DCER	12
Free Fatty Acid	FFA	26
Hexosylceramide	HCER	12
Lactosylceramide	LCER	12
Lysophosphatidylcholine	LPC	26
Lysophosphatidylethanolamine	LPE	26
Phosphatidylcholine	PC	150
Phosphatidylethanolamine	PE	220
Sphingomyelin	SM	12
Triacylglycerol	TAG	520

Table 1. Plasma lipids were analyzed using the direct infusion-tandem mass spectrometry (DI-MS/MS) Lipidyzer platform. Results provided the concentration (uM) and fatty acid composition (mol%) of 13 lipid classes and ~1100 individual lipid species.

RESULTS

Figure 1. Study design

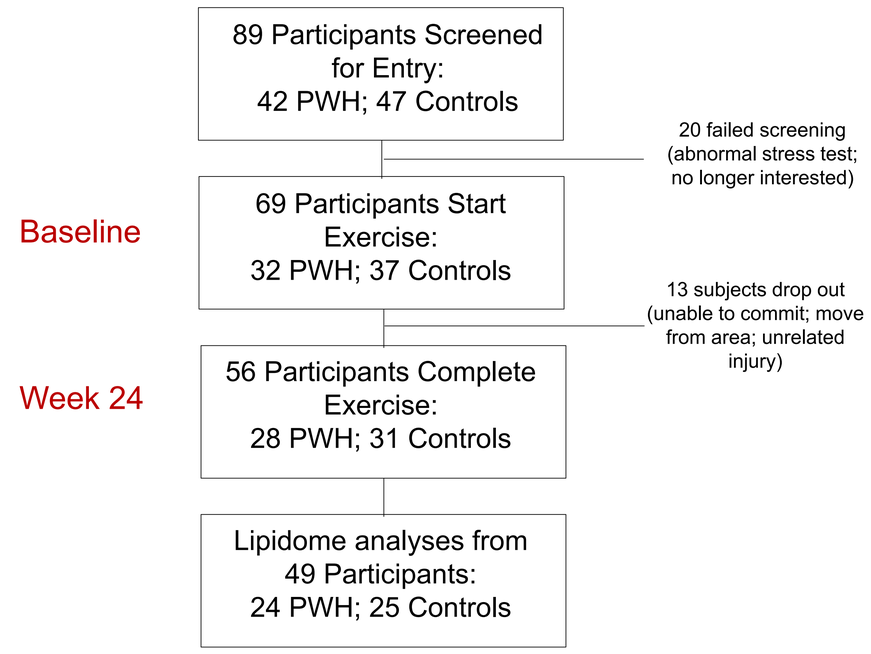


Figure 2. Lipid class concentrations at baseline among people with and without HIV

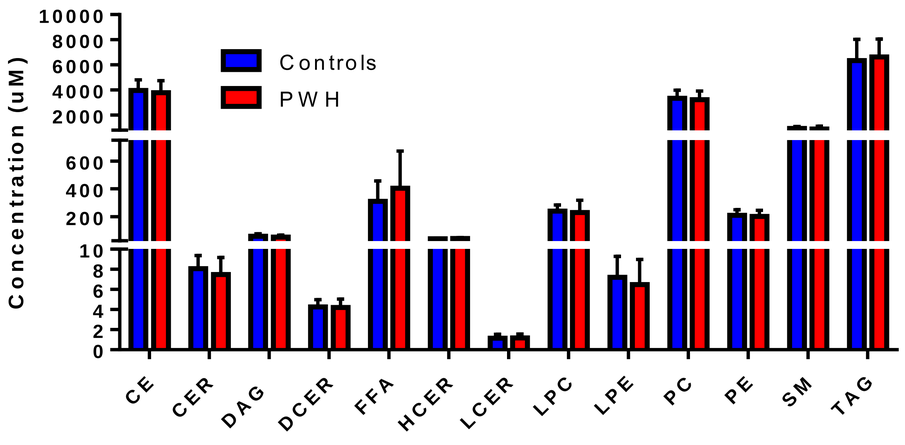


Figure 3. Lipid class concentrations following 24 weeks of exercise among people with and without HIV

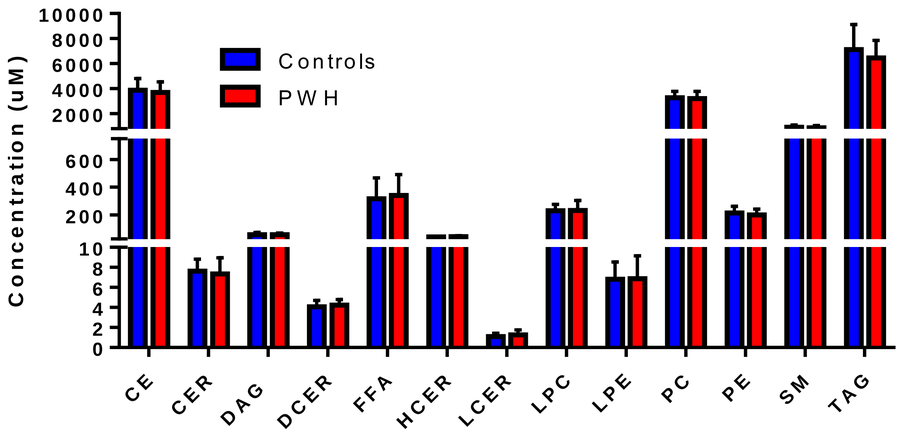


Table 2. Comparison of % change in lipid class concentrations after 24 weeks of exercise among PWH and controls

	PWH % Diff	Controls % Diff	P-value
CE	-3.2 [-9, 3]	-1.1 [-7.7, 5.9]	0.638
CER	-2.2 [-7.4, 3.3]	-4.8 [-11.2, 2.1]	0.539
DAG	**6.1 [0, 12.5] ***	**-5.1 [-12.7, 3.2]**	**0.030**
DCER	1.4 [-9.5, 13.5]	-4.2 [-13.4, 6]	0.447
FFA	-11.6 [-28.4, 9]	0.7 [-20.6, 27.7]	0.397
HCER	-0.6 [-3.9, 2.9]	0.5 [-2, 3.2]	0.590
LCER	4.7 [-6.2, 16.9]	-3.8 [-13.6, 7.2]	0.261
LPC	2.8 [-12.5, 20.9]	-5.4 [-14.4, 4.7]	0.374
LPE	6.4 [-7.1, 22]	-4.6 [-14.3, 6.2]	0.199
PC	-0.4 [-4.6, 4]	-0.9 [-5.8, 4.2]	0.874
PE	-0.5 [-7.1, 6.5]	1.5 [-6.9, 10.6]	0.712
SM	-1.6 [-6.4, 3.3]	-1.1 [-6.7, 4.9]	0.874
TAG	**-4.5 [-14.1, 6.2]**	**14.7 [6, 24.1] ***	**0.006**

Percent change for each serostatus; reference = baseline

Table 3. Comparison of % Change in lipid species concentration after 24 weeks of exercise among PWH and controls

	PWH	Controls	P-value	Adjusted P-value#
TAG				
FA 18:0	-3.6 [-14.7, 8.9]	16.5 [6.9, 26.9] *	0.012	0.123
FA 18:1	-6.1 [-17.2, 6.5]	17.3 [7.4, 28.1] *	0.005	0.098
FA 18:2	-7.1 [-18.6, 6.1]	17.3 [7, 28.6] *	0.005	0.098
FA 18:3	-9.7 [-22.8, 5.6]	17.2 [5.9, 29.8] *	0.006	0.098
FA 20:1	-3.3 [-16.4, 11.8]	17.6 [7.2, 29] *	0.024	0.141
FA 20:2	-6.9 [-18.6, 6.4]	13.4 [3.4, 24.3] *	0.016	0.123
FA 20:3	-8.1 [-19, 4.2]	10.2 [1.1, 20.1] *	0.018	0.123
FA 20:4	-8.8 [-20.2, 4.2]	9.3 [0.5, 19] *	0.022	0.139
FA 20:5	-7.7 [-19.4, 5.6]	9.2 [0, 19.3] *	0.036	0.174
FA 22:1	-6.7 [-17.3, 5.2]	19.2 [9.1, 30.1] *	0.001	0.082
DAG				
FA 14:1	18.4 [-2.1, 43.2]	-9.6 [-23.6, 6.9]	0.033	0.169
FA 16:0	11.1 [0.9, 22.3]	-10.3 [-20, 0.7]	0.005	0.098
FA 16:1	10.5 [2, 19.8]	-6.8 [-15.8, 3.2]	0.009	0.117
FA 18:0	14.1 [3.2, 26.1]	-6.6 [-16.9, 5]	0.010	0.117
LPC				
FA 15:0	9.2 [-0.6, 20.0]	-5.9 [12.7, 1.5]	0.014	0.123
FA 16:0	4.7 [-1.6, 11.3]	-4.5 [-11.3, 2.8]	0.05	0.212
FA 17:0	7.1 [-3.3, 18.6]	-9.0 [-18.2, 1.2]	0.027	0.148
CER				
FA 18:1	5.2 [-5.2, 16.7]	-10.3 [-17.6, -2.4] *	0.017	0.123

Fold change comparison; Estimates are % difference (95% CI) from baseline value for each serostatus

CONCLUSIONS

- Effects of exercise on the plasma lipidome may differ among people with and without HIV
- Future studies comparing the consequences of exercise and altered lipid metabolism among people with and without HIV may be important