Alcohol, substance use and smoking associations with lipoatrophy and lipohypertrophy

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Background

- Lipoatrophy (LA) and lipohypertrophy (LH) have been associated with antiretroviral therapy, HIV itself, and demographic and lifestyle factors
- Few studies have examined the role of behavioral factors such as substance use and physical activity
- Behavioral factors such as substance abuse, physical activity, and smoking are likely correlated with each other. Discerning unique contributions will require considering them simultaneously
- Prior studies have been small, yielded conflicting findings, and did not distinguish LA and LH
- We conducted this study to examine the independent association between alcohol and substance use with LA and LH among a large and diverse nationally distributed cohort

Methods

- **STUDY SUBJECTS**: Adults who completed a clinical assessment of patient reported outcomes (PROs) as part of a clinical care visit before 11/2013. The assessment was integrated into care between 2006 & 2012 at 6 CNICS sites across the US
- **DATA**: The CNICS data repository captures comprehensive longitudinal clinical data including demographic, clinical, laboratory, medication, and socioeconomic data
- Patients used tablet PCs with touch screens to complete the clinical assessment every 4-6 months including measures of LA and LH (based on the Fat Redistribution and Metabolic Change [FRAM] instrument), smoking status, alcohol use, illicit drug use, and physical activity
- BODY MORPHOLOGY: FRAM items for individual body regions were coded on a 7-point scale. A LH score was calculated using all positive responses and a LA score was calculated using all negative responses. LA and LH were also categorized as none (0 points), mild (1-12 points), and moderate-to-severe (>12 points)
- ALCOHOL: We used an AUDIT-C score of ≥4 for men and ≥3 for women to define at-risk alcohol consumption
- SUBSTANCE USE: We used the ASSIST to assess current, prior, or never use overall & for each of 4 drug classes: cocaine/crack, methamphetamine, opiates/heroin, marijuana
- **STATISTICAL ANALYSES**: We used generalized estimating equations with robust standard errors to assess differences in body morphology associated with alcohol, tobacco, and other substance use, while accounting for within-subject correlations between repeated measures
- We controlled for age, race, sex, site, currently on ART, total duration of stavudine/didanosine exposure, current and nadir CD4 cell count, viral load, hepatitis C & physical activity level
- We used ordinal logistic regression adjusting for repeated measures for categorical LA and LH
- Separate models were conducted for each outcome: LA and LH

Table 1. Demographic and clinical characteristics at initial assessment categorized by body morphology (N=7931)

Characteristic	Neither LA nor LH N=3156	Mild LA N=1664	Moderate LA N=244	*p* value	Mild LH N=2607	Moderate LH N=260	*p* value
	N (%)	N (%)	N (%)		N (%)	N (%)	
Sex							
Male	87	92	85	**<0.001**	86	68	**<0.001**
Race							
White	49	57	55		57	50	
Black	29	21	22		23	27	
Hispanic	17	18	18		15	20	
Other/Unknown	5	5	4	**<0.001**	5	4	**<0.001**
Age (years)							
<30	14	11	7		9	7	
30-39	25	21	13		21	17	
40-49	36	41	40		42	46	
≥50	24	28	40	**<0.001**	30	30	**<0.001**
HIV transmission risk factor							
MSM	63	67	52		63	52	
IDU	12	17	16		15	16	
Heterosexual	22	14	25		18	30	
Other	3	3	7	**<0.001**	3	2	**<0.001**
CD4$^+$ cell nadir (cells/mm^3)							
0-200	46	47	63		48	55	
201-350	28	25	20		27	19	
>350	25	27	17	**<0.001**	25	26	**0.02**
CD4$^+$ cell count current (cells/mm^3)							
0-200	14	16	34		12	13	
201-350	19	18	17		17	18	
>350	68	66	49	**<0.001**	71	69	0.3
Hepatitis C virus							
Yes	14	20	26	**<0.001**	20	19	**<0.001**
Physical activity level							
Very low	18	28	48		30	43	
Low	47	39	32		44	43	
Moderate	19	21	12		17	11	
High	15	12	7	**<0.001**	9	3	**<0.001**
Currently receiving ART							
Yes	74	81	75	**<0.001**	82	86	**<0.001**

Results

- 7931 patients completed the clinical assessment 21,279 times
- Table 1 describes demographic and clinical characteristics at initial assessment by LA/LH
- Among all 21,279 assessments, no LA or LH was reported in 8,471 (40%), mild LA in 4301 (20%), mild LH in 7,123 (33%), moderate-to-severe LA was reported in 582 (3%), and moderate-to-severe LH was reported in 803 (4%) of assessments
- Older age, detectable viral load and high current CD4 cell counts were associated with more severe LA in adjusted analyses (Table 2)
- Current cigarette smoking, marijuana use, and opiate use were all associated with more severe LA in adjusted analyses
- Older age, male sex, and higher current CD4 count were all associated with more severe LH in adjusted analyses (Table 2)
- Prior methamphetamine use, prior and current cocaine use and prior marijuana use were all associated with more severe LH

Table 2. Association between demographic, clinical, and behavioral factors and body morphology in adjusted analyses

	LA (continuous)	LA (categorical)	LH (continuous)	LH (categorical)
Sex				
Male	Ref	Ref	Ref	Ref
Female	1.0; 0.8-1.2, 0.9	1.1 1.0-1.3, 0.1	0.2; 0.2-0.3, **<0.001**	0.6; 0.5-0.7, **<0.001**
Race				
White	Ref	Ref	Ref	Ref
Black	0.8; 0.7-0.9, **0.008**	0.8; 0.7-0.9, **<0.001**	1.1; 0.9-1.4, 0.4	0.9; 0.8-1.0, 0.06
Hispanic	1.2; 1.0-1.5, 0.05	1.1; 0.9-1.2, 0.3	1.2; 1.0-1.6, 0.08	1.0; 0.9-1.1, 0.9
Other	0.9; 0.6-1.2, 0.4	0.7 0.6-0.9, **0.008**	0.9; 0.6-1.4, 0.6	0.8; 0.6-1.0, **0.02**
Age (per year)	1.04; 1.03-1.04, **<0.001**	1.02; 1.02-1.02, **<0.001**	1.01; 1.01-1.03, **<0.001**	1.01; 1.00-1.01, **<0.001**
CD4$^+$ cell count nadir (cells/mm^3)				
0-200	Ref	Ref	Ref	Ref
201-350	1.0; 0.8-1.1, 0.6	1.0; 0.9-1.1, 0.5	0.6; 0.5-0.7, **<0.001**	0.8; 0.7-0.9, **<0.001**
351 or greater	1.0; 0.9-1.2, 0.7	1.1; 1.0-1.2, 0.2	0.8; 0.6-1.0, **0.02**	0.8; 0.8-0.9, **0.002**
Current CD4$^+$ cell count (cells/mm^3)				
0-200	Ref	Ref	Ref	Ref
201-350	0.4; 0.3-0.6, **<0.001**	0.8; 0.7-0.9, **<0.001**	1.3; 1.0-1.6, **0.03**	1.2; 1.0-1.3, **0.009**
351 or greater	0.4; 0.3-0.5, **0.003**	0.8; 0.7-0.9, **<0.001**	1.6; 1.3-2.0, **<0.001**	1.3; 1.2-1.5, **<0.001**
Current viral load				
Detectable	Ref	Ref	Ref	Ref
Undetectable	0.8; 0.6-0.9, **0.003**	0.8; 0.7-0.9, **<0.001**	1.5; 1.3-1.8, **<0.001**	1.2; 1.1-1.3, **0.002**
Current antiretroviral medications				
No	Ref	Ref	Ref	Ref
Yes	1.1; 0.9-1.3, 0.2	1.3; 1.1-1.5, **<0.001**	1.2; 1.0-1.5, 0.09	1.2; 1.1-1.4, **<0.001**
D4T or DDI use per year	1.1; 1.1-1.2, **0.001**	1.1; 1.0-1.1, **<0.001**	1.1; 1.0-1.1, **0.003**	1.03; 1.01-1.05, **0.001**
Methamphetamine use				
None	Ref	Ref	Ref	Ref
Prior	1.1; 0.9-1.3, 0.2	1.0; 0.9-1.2, 0.5	1.4; 1.1-1.6, **0.001**	1.2; 1.1-1.3, **<0.001**
Current	1.1; 0.9-1.4, 0.5	1.2; 1.1-1.4, **0.003**	0.9; 0.7-1.2, 0.6	1.0; 0.9-1.2, 0.7
Cocaine/crack use				
None	Ref	Ref	Ref	Ref
Prior	1.0; 0.9-1.2, 0.8	1.0; 0.9-1.1, 0.8	1.5; 1.3-1.8, **<0.001**	1.2; 1.1-1.3, **<0.001**
Current	1.3; 1.0-1.6, 0.08	1.1; 0.9-1.3, 0.4	1.5; 1.1-1.9, **0.009**	**1.2; 1.0-1.4, 0.04**
Opiate/heroin use				
None	Ref	Ref	Ref	Ref
Prior	1.1; 0.9-1.3, 0.5	1.1; 1.0-1.2, 0.2	1.1; 0.9-1.4, 0.4	1.1; 0.9-1.2, 0.4
Current	1.6; 1.0-2.4, **0.03**	1.4; 1.1-1.7, **0.01**	1.1; 0.7-1.6, 0.7	1.1; 0.8-1.3, 0.6
Marijuana use				
None	Ref	Ref	Ref	Ref
Prior	1.1; 0.9-1.2, 0.4	1.1; 1.0-1.2, **0.04**	1.4; 1.2-1.7, **<0.001**	1.3; 1.1-1.4, **<0.001**
Current	1.5; 1.2-1.8, **<0.001**	1.6; 1.4-1.8, **<0.001**	1.0; 0.9-1.2, 0.7	1.1; 1.0-1.3, 0.2
Cigarette smoking				
Never	Ref	Ref	Ref	Ref
Prior	1.2; 1.1-1.5, **0.009**	1.2; 1.0-1.3, **0.008**	1.1; 0.9-1.4, 0.2	1.1; 1.0-1.3, **0.01**
Current	1.5; 1.2-1.7, **<0.001**	1.2; 1.1-1.4, **<0.001**	0.8; 0.7-1.0, **0.05**	0.9; 0.8-1.0, 0.08
Alcohol use				
Not at-risk	Ref	Ref	Ref	Ref
At-risk	0.8; 0.7-0.9, **0.002**	0.8; 0.8-0.9, **0.001**	1.0; 0.9-1.2, 0.7	1.0; 0.9-1.1, 0.5
Physical activity				
Very low	Ref	Ref	Ref	Ref
Low	0.4; 0.4-0.5, **<0.001**	0.7; 0.6-0.8, **<0.001**	0.4; 0.3-0.4, **<0.001**	0.6; 0.6-0.7, **<0.001**
Moderate	0.5; 0.4-0.6, **<0.001**	0.8; 0.7-0.9, **<0.001**	0.3; 0.3-0.4, **<0.001**	0.6; 0.5-0.6, **<0.001**
High	0.5; 0.4-0.6, **<0.001**	0.8; 0.7-0.9, **<0.001**	0.2; 0.2-0.3, **<0.001**	0.4; 0.3-0.4, **<0.001**

Discussion/Conclusions

- We found a high prevalence of body morphology abnormalities: 60% of 7391 patients had at least some LA or LH
- Most abnormalities were mild, with only a small percentage reporting moderate-to-severe LA (3%) or LH (4%)
- Behavioral factors differed in their associations with LA and LH. Current opiate, marijuana, and current and past tobacco use were all associated with more severe LA. Prior methamphetamine, cocaine, and marijuana use and current cocaine use were associated with more severe LH
- These results support the conclusion that LA and LH are distinct. While lack of physical activity and higher CD4 counts are associated with both, associations with substance use and other clinical characteristics differed
- These results may prove useful in counseling patients who wish to avoid body morphology changes and further our understanding of associations with these conditions and their possible mechanisms