Cumulative exposure to CVD risk factors more adversely affects cognition in women than men with and without HIV

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BACKGROUND

- Cardiovascular disease (CVD) risk factors are common, modifiable contributors to cognitive impairment in people with and without HIV.
- In the general population, the adverse effect of CVD risk factors on cognitive health may be greater for women than men.
- Limited data from HIV cohorts suggest similar sex differences may be present in people with HIV (PWH).
- We evaluated if sex and HIV status modify the effect of CVD risk on cognition in the Women's Interagency HIV Study (WIHS) and the Multicenter AIDS Cohort Study (MACS).

METHODS

- PWH and people without HIV who underwent neuropsychological testing at least once beginning in 2005 in the MACS and in 2009 in the WIHS were eligible for the study.
- We examined performance on overlapping tests administered in both the cohorts: Trail Making Parts A and B, Symbol Digit Modalities, Stroop Color Word Trials 1-3, Grooved Pegboard
- We averaged demographically-adjusted T scores into a global summary score and within domains.
- We calculated cumulative years of exposure for binary CVD risk factors and the average cumulative level of continuous CVD risk factors at each follow-up visit
- We constructed adjusted mixed-effects linear regression models to estimate separate and interactive associations of each time-dependent CVD risk factor with sex and HIV on cognition.

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RESULTS

Table 1: Baseline demographics and clinical characteristics of participants from WIHS and MACS

N (%), unless indicated	WIHS HIV+ (n=2098)	WIHS HIV- (n=895)	MACS HIV+ (n=1477)	MACS HIV- (n=1225)	Total (n=5695)
Age (y), mean (SD)	38 (9)	36 (11)	37 (8)	38 (9)	37 (9)
Follow up (y), mean (SD)	4.2 (3.4)	4.7 (3.3)	5.5 (5.2)	9.6 (5.0)	6.6 (4.9)
Race					
Black	1278 (61)	520 (58)	496 (34)	272 (22)	2566 (45)
White	271 (13)	110 (12)	810 (55)	864 (71)	2055 (36)
Asian / Other	260 (12)	116 (13)	104 (7)	49 (4)	529 (9)
Multiracial	289 (14)	149 (17)	65 (4)	40 (3)	543 (10)
Hispanic ethnicity	346 (17)	173 (19)	231 (16)	113 (9)	863 (15)
BMI (kg/m^2), mean (SD)	29.9 (8.3)	30.5 (8.4)	25.5 (4.3)	25.4 (4.5)	27.8 (7.1)
LDL (mg/dL), mean (SD)	103 (31)	93 (28)	91 (28)	96 (31)	94 (30)
Statin use	91 (7)	39 (6)	81 (9)	12 (3)	223 (7)
Hypertension	683 (33)	276 (31)	322 (22)	280 (23)	1561 (27)
Anti-hypertensive use	395 (19)	124 (14)	116 (8)	48 (4)	683 (12)
Diabetes mellitus	96 (5)	49 (6)	31 (2)	17 (1)	193 (3)
Current smoking	987 (47)	497 (56)	586 (40)	415 (34)	2485 (44)
Current meth use	4 (0.3)	4 (1)	104 (8)	37 (3)	149 (3)
Current cocaine use	339 (16)	211 (24)	292 (20	161 (13)	1003 (17)
Antidepressant use	418 (20)	125 (14)	236 (16)	108 (9)	887 (16)
CD4 (/mm^3), mean (SD)	527 (301)	1070 (375)	623 (319)	996 (350)	738 (399)
Virally suppressed	1318 (67)	---	684 (64)	---	2002 (66)

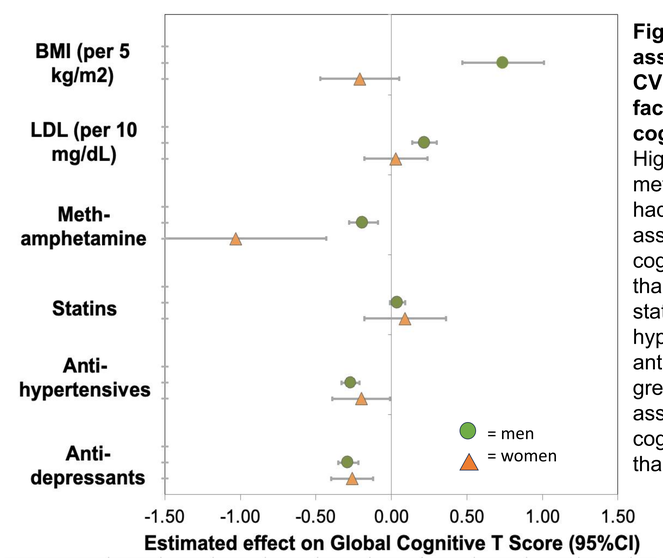


Figure 1: Differential association between CVD and other risk factors with cognition by sex. Higher BMI, LDL and methamphetamine use had a greater negative association with global cognition in women than men. Use of statins, anti-hypertensives and anti-depressants had a greater positive association with global cognition in women than men.

CONCLUSIONS

- Cumulative exposure to several CVD risk factors (e.g., BMI, LDL, and methamphetamine use) had a greater negative association with cognition in women, including women with HIV, than men, although the clinical significance of these modest differences is unclear.
- Future directions include evaluating interactive effects of sex and CVD risk factors on cognition in PWH, accounting for HIV-related factors including ART use and viral load, and investigating drivers of the greater negative association between CVD risk factors and cognition in women.

Table 2: Two and three-way interaction effects between risk factors and sex and between risk factors, sex, and HIV on cognition

	Interactive association[1] (95% CI)	P value
BMI*sex	-0.89 per 5 kg/m^2/yr (-1.27, -0.52)	<0.001
LDL*sex	-0.24 per 10 mg/dL/yr (-0.36, -0.11)	<0.001
Meth use*sex	-0.74 per yr exposure (-1.36, -0.12)	0.020
Statin use*sex	0.39/yr exposure (0.11, 0.67)	0.006
Anti-HTN use*sex	0.28/yr exposure (0.13, 0.43)	<0.001
Antidepressant use*sex	1.58/yr exposure (0.02, 3.13)	0.047
LDL*sex*HIV	-0.59 per 10 mg/dL/yr (-0.99, -0.19) on motor function -0.23 per 10 mg/dL/yr (-0.50, 0.04) on global cognition	0.004 0.09

[1]Association with global cognition unless noted

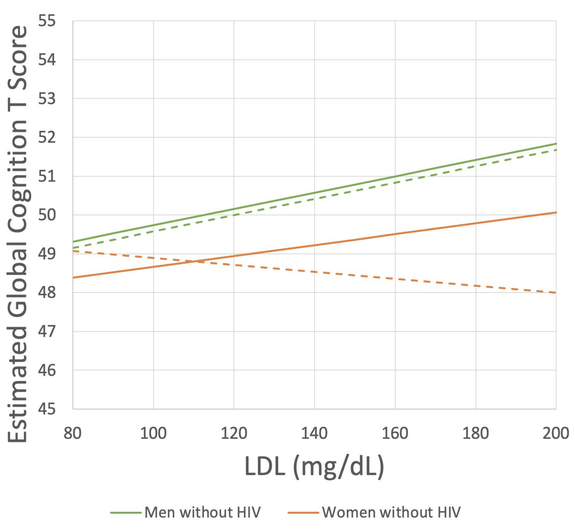


Figure 2: Association between LDL and global cognition by HIV and sex. The differential association between LDL and cognition by sex was more pronounced in PWH than people without HIV. *Models in Figures 1 and 2 adjusted for age, race/ethnicity, education, number of test administrations, BMI, diabetes, stroke, statin use, anti-hypertensives, hepatitis C, depression, smoking, alcohol/cocaine/meth-amphetamine/marijuana use.