MIDLIFE ADIPOSITY PREDICTS COGNITIVE DECLINE IN THE MULTICENTER AIDS COHORT STUDY (MACS)

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Background

- Obesity, or excess adiposity, is a common, modifiable cardio- and cerebrovascular risk factor that may contribute to cognitive impairment in HIV
- Role of excess adiposity on cognition in HIV-uninfected adults:
  - Higher midlife body mass index (BMI) & central obesity (waist circumference, WC) is related to risk of late life, sporadic dementias (e.g., Alzheimer’s Disease).
  - Longer exposure to higher midlife adiposity is linked to memory loss in 60-64 years of age & higher midlife adiposity related to executive function 10 years later.
- Role of excess adiposity on cognition in HIV:
  - Obesity is related to global impairment & slower psychomotor speed cross-sectionally.

It is unknown whether midlife obesity predicts cognitive impairment or decline in HIV+ adults

Objectives

To examine BMI & WC associations with 10-year domain-specific cognition and change in cognition in HIV+ vs HIV- men

Hypothesis: Higher adult BMI & WC is associated with cognition and more pronounced cognitive change among HIV+ vs HIV- men

Participants

Multicenter AIDS Cohort Study (MACS): data analyzed from 1996-2015; HIV+ men included: ≥40 years of age at initial testing, testing ≥2 ART agents & HIV-1 RNA <400 copies/mL at ≥80% of visits. HIV- men included: ≥50 years of age at initial testing.

Measures

Primary predictors: BMI: normal/healthy weight (18.5-24.9 kg/m²), overweight (25.0-29.9 kg/m²), & obese (≥30 kg/m²); WC: obese (≥102 cm [40 inches]) vs not obese (<102 cm [40 inches])

Neuropsychological outcomes:

- Rey Auditory Verbal Learning (RAVLT); Rey Complex Figure
- Trail Making Test Part A & B; Stroop Test [color-word, interference trials]
- Symbol Digit Modalities Test
- Grooved Pegboard [dominant, non-dominant hand]
- WC: normal/healthy weight (18.5-24.9 kg/m²), overweight (25.0-29.9 kg/m²), & obese (≥30 kg/m²); WC: obese (≥102 cm [40 inches]) vs not obese (<102 cm [40 inches])

Statistical Analyses

Linear mixed-effects models stratified by HIV-serostatus where primary predictors were baseline BMI or WC and interactions with time (defined as participants’ age) on cognitive domains

Models adjusted for: cohort entry, baseline age, race/ethnicity, education level, number of visits/participant during follow-up period: tobacco, alcohol, marijuana, other drugs, & stimulants, depressive symptoms, hypertension; HIV-related factors: CD4+ T-cell count, history of AIDS defining illness, HIV RNA >400 copies/mL, current use of antiretroviral or stavudine

Results

Baseline characteristics of MACS men by BMI category

<table>
<thead>
<tr>
<th></th>
<th>HIV- (n=556)</th>
<th>HIV+ (n=316)</th>
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<tbody>
<tr>
<td>n (%)</td>
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<tr>
<td>Normal</td>
<td>245 (37)</td>
<td>149 (47)</td>
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<tr>
<td>Overweight</td>
<td>10.4 (4.9)</td>
<td>9.4 (4.5)</td>
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<tr>
<td>Obese</td>
<td>7.5 (4.9)</td>
<td>6.2 (3.7)</td>
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Time from baseline visits/participant

- % >60 years old: 10.6 (4.8); 10.2 (4.3); 10.1 (4.1)
- % White: 7.5 (4.9); 6.5 (3.6); 6.9 (4.0)

Sociodemographic

- Age, mean (SD): 51 (9); 52 (8); 52 (7)
- % <60 years old: 36 (15); 43 (15); 20 (15)
- % White: 184 (75); 224 (79); 89 (68)

Education

- High school or less: 27 (11); 36 (13); 20 (15)
- Some college: 51 (22); 49 (13); 60 (46)
- Graduate: 96 (39); 102 (36); 50 (38)

Behavioral factors

- Tobacco use: 67 (27); 58 (21); 33 (25)
- Alcohol use (vs no/weekly): 24 (10); 24 (8); 10 (8)
- Cannabis use: 75 (31); 74 (26); 24 (15)
- Stimulant use: 29 (12); 37 (13); 11 (8)
- Other drug use: 35 (14); 57 (20); 17 (13)
- Depression: 40 (16); 56 (20); 30 (23)
- Hypertension: 13 (5); 15 (5); 7 (5)
- Hepatitis C virus: 53 (22); 113 (40); 76 (58)

HIV-related factors

- CD4+ ≥200: 15 (10); 6 (5); 1 (3)
- Suppressed HIV-1 RNA: 140 (94); 119 (92); 33 (86)
- History of AIDS: 21 (14); 8 (6); 2 (5)
- Use of stavudine: 47 (31); 24 (19); 9 (24)
- Use of stavudine: 27 (18); 20 (15); 5 (13)

Higher body mass index (BMI) is associated with lower cognition cross-sectionally & greater cognitive decline, particularly in HIV- men

<table>
<thead>
<tr>
<th></th>
<th>Baseline BMI</th>
<th>normal/healthy weight</th>
<th>overweight</th>
<th>obese</th>
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</thead>
<tbody>
<tr>
<td>HIV-</td>
<td></td>
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<tr>
<td>HIV+</td>
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Higher waist circumference (WC) is associated with lower cognition cross-sectionally & greater cognitive decline, particularly in HIV- men

<table>
<thead>
<tr>
<th></th>
<th>Baseline WC</th>
<th>higher</th>
<th>lower</th>
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</thead>
<tbody>
<tr>
<td>HIV-</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>HIV+</td>
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Conclusions

- Total and central adiposity associated with baseline cognition in HIV & HIV- men. Specifically, adiposity associated with motor function in both groups & attention/working memory in HIV- men
- Although baseline adiposity-cognition associations were similar between HIV+ & HIV- men, longitudinal associations differed by HIV-serostatus (total adiposity greater decline in HIV-; adiposity protective in HIV+)
- Overweight & obesity, total & central, may be important predictors of neurological outcomes & avenues for prevention and intervention