Associations between cognitive function and cardiovascular risk factors: differences between people with HIV and HIV-negative controls

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Background

- People living with HIV (PLWH) may report reduced cognitive function, even with effective and virologically suppressive therapy.

- The pathogenesis of this is not fully understood and likely involves, amongst other things, the impact of some age-associated comorbid conditions such as cardiovascular (CV) disease.

- A link between CV disease/CV risk factors and poorer cognitive performance has been reported in the general population - there is, however, little evidence on such a link in PLWH.
Aims

- To describe the associations of CV diseases and risk factors with cognitive performance among PLWH
- To compare associations to those found among HIV-negative individuals
The POPPY study

- Multicentre, prospective, observational study to examine the effects of ageing on the clinical outcomes of PLWH in UK and Ireland

- Cohorts of PLWH aged ≥50 and <50 years, and lifestyle-matched ≥50 HIV-negative individuals

**PLWH** (recruited/analysed = 1073/977)
- white/black African ethnicity
- acquired HIV via sexual routes
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**PLWH** (recruited/analysed = 1073/977)
- white/black African ethnicity
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**HIV- ≥50 yrs** (recruited/analysed = 304/276)
frequency matched on gender, ethnicity, sexual orientation and location (in/out London)
Cognitive function

- Assessment of cognitive function using CogState battery
- 11 tests grouped into six cognitive domains
  - Visual learning
  - Psychomotor function
  - Visual attention
  - Executive function
  - Verbal learning
  - Working memory and attention
- Test scores standardized into Z-scores (mean 0, SD 1)
- **Global Z-score**: average across the 11 individual tests
Cardiovascular risk factors

Modifiable risk factors:
- Past/Current smoking
- Weight
- BMI
- Waist circumference
- Overweight (BMI ≥25 kg/m²)
Cardiovascular risk factors

**Modifiable risk factors:**
- Past/Current smoking
- Weight
- BMI
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- Overweight (BMI ≥25 kg/m²)

**Self-reported history of:**
- Hypertension
- Type 2 diabetes
- Dyslipidaemia
- Myocardial infarction (MI)
- Angina pectoris
- Peripheral vascular disease
- Heart failure,
- Ischemic heart disease (IHD)
- Transient ischemic attack (TIA)/stroke
- Coronary artery bypass grafting
- Any cardiovascular disease (CVD)
- Any problem of the nervous system

**Use of:**
- Anti-hypertensive drugs
- Lipid-lowering drugs

**Family history of:**
- Hypertension
- MI
- High cholesterol
- Dementia
- TIA/Stroke
- Heart bypass
- Diabetes
- Angina pectoris
- Heart failure
- Other CVD
Cardiovascular risk factors

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- Angina pectoris
- Other CVD

Lipids:
- Total cholesterol
- High-density lipoproteins (HDL)
- Low-density lipoproteins (LDL)
- Triglycerides

Renal function:
- eGFR (CKD-EPI formula)
- Chronic kidney disease
  (CKD: eGFR ≤ 60)
- Creatinine clearance

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# Cardiovascular risk factors

## Modifiable risk factors:
- Past/Current smoking
- Weight
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- Waist circumference
- Overweight (BMI ≥ 25 kg/m²)

## Lipids:
- Total cholesterol
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- Low-density lipoproteins (LDL)
- Triglycerides

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- eGFR (CKD-EPI formula)
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- Creatinine clearance

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- Heart failure
- Other CVD

## Use of:
- Anti-hypertensive drugs
- Lipid-lowering drugs

## Other:
- Systolic blood pressure
- Diastolic blood pressure
- Haemoglobin
- Framingham risk score
- Serum albumin
Statistical methods

- Chi-square to compare CV risk factors between PLWH and HIV-negative individuals
- Multiple imputation with fully conditioned models
- Median regression models (accounting for socio-demographics) to investigate associations between CV risk factors and cognitive performance and the interaction with HIV-status
- Stepwise model selection to identify significant independent associations (sensitivity analyses with backward and forward model selection)
## Baseline characteristics

<table>
<thead>
<tr>
<th>n (%) or median (IQR)</th>
<th>HIV- (N=276)</th>
<th>PLWH &lt;50 (N=340)</th>
<th>PLWH ≥50 (N=637)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male gender</strong></td>
<td>180 (65.2%)</td>
<td>275 (80.9%)</td>
<td>564 (88.5%)</td>
</tr>
<tr>
<td><strong>White ethnicity</strong></td>
<td>252 (94.3%)</td>
<td>274 (80.6%)</td>
<td>560 (87.9%)</td>
</tr>
<tr>
<td><strong>Age [years]</strong></td>
<td>58 (53, 63)</td>
<td>43 (37, 47)</td>
<td>56 (53, 62)</td>
</tr>
<tr>
<td><strong>Man having sex with men (MSM)</strong></td>
<td>138 (50.0%)</td>
<td>246 (72.4%)</td>
<td>509 (79.9%)</td>
</tr>
<tr>
<td><strong>PHQ-9 score</strong></td>
<td>1 (0, 3)</td>
<td>4 (1, 8)</td>
<td>4 (1, 10)</td>
</tr>
<tr>
<td><strong>Current/past ID use</strong></td>
<td>6 (2.2%)</td>
<td>46 (13.6%)</td>
<td>59 (9.3%)</td>
</tr>
<tr>
<td><strong>Recreational drugs use 6 months before visit</strong></td>
<td>42 (15.2%)</td>
<td>116 (34.1%)</td>
<td>164 (25.8%)</td>
</tr>
<tr>
<td><strong>Viral load &lt;50 copies/mL</strong></td>
<td>N/A</td>
<td>290 (85.8%)</td>
<td>586 (92.3%)</td>
</tr>
<tr>
<td><strong>CD4 count [cells/µL]</strong></td>
<td>N/A</td>
<td>654 (490, 833)</td>
<td>620 (470, 799)</td>
</tr>
</tbody>
</table>
CV risk factors

- Overweight: 56%
- Current smoking: 25%
- MI: 4%
- Hypertension: 21%
- Dyslipidaemia: 28%
- Type 2 diabetes: 4%

PLWH (people living with HIV)
CV risk factors

- Overweight: 56%
- Current smoking: 25%
- MI: 4%
- Hypertension: 21%
- Dyslipidaemia: 28%
- Type 2 diabetes: 4%

On anti-hypertensive drugs: 15%
On lipid-lowering drugs: 18%
Family history of hypertension: 46%
Family history of diabetes: 21%
Framingham risk ≥ 20%: 6%
CKD: 21%
Aims

- To describe the associations of CV disease and risk factors with cognitive performance among PLWH

- To compare associations to those found among HIV-negative individuals
Associations with cognitive scores

Model: one factor at the time

**significant associations** (p≤0.05)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Difference in Median Global Z-score</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>-0.10 (-0.19, -0.01)</td>
<td>p=0.04</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>-0.35 (-0.66, -0.04)</td>
<td>p=0.03</td>
</tr>
<tr>
<td>Heart failure</td>
<td>-0.33 (-0.57, -0.09)</td>
<td>p=0.01</td>
</tr>
<tr>
<td>IHD</td>
<td>-0.49 (-0.97, -0.01)</td>
<td>p=0.05</td>
</tr>
<tr>
<td>On anti-hypertensive drugs</td>
<td>-0.16 (-0.26, -0.06)</td>
<td>p=0.002</td>
</tr>
<tr>
<td>Overweight</td>
<td>-0.07 (-0.15, -0.01)</td>
<td>p=0.05</td>
</tr>
<tr>
<td>Albumin ≤40g/l</td>
<td>-0.08 (-0.15, -0.01)</td>
<td>p=0.04</td>
</tr>
<tr>
<td>Haemoglobin &lt;13 g/dl</td>
<td>-0.15 (-0.28, -0.03)</td>
<td>p=0.01</td>
</tr>
</tbody>
</table>

* Adjusted for age, gender, ethnicity, education and depressive symptoms
Associations with cognitive scores

Model: one factor at the time

**significant associations** (p≤0.05)
- Hypertension
- Peripheral vascular disease
- Heart failure
- IHD
- On anti-hypertensive drugs
- Overweight
- Albumin ≤40g/l
- Haemoglobin <13 g/dl

**non-significant associations** (p>0.05)
- Past/Current smoking
- Weight, BMI, waist circumference
- History of dyslipidaemia, MI, angina pectoris, TIA/stroke, CABG, any CVD, type 2 diabetes
- Family history of CVD
- Lipid-lowering medication
- Lipids
- BP and Framingham risk score
- CKD, eGFR and creatinine clearance

* Adjusted for age, gender, ethnicity, education and depressive symptoms
Associations with cognitive scores

Multivariable model (stepwise selection)

On anti-hypertensive drugs: -0.11 (-0.21, -0.01) - p=0.03

Overweight: -0.09 (-0.15, -0.02) - p=0.02

Haemoglobin <13 g/dl: -0.13 (-0.24, -0.02) - p=0.02

* Adjusted for age, gender, ethnicity, education and depressive symptoms
Aims

- To describe the associations of CV diseases and CV risk factors with cognitive performance among PLWH

- To compare associations with those found among HIV-negative individuals
CV risk factors: PLWH ≥50 vs HIV-negative

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>PLWH ≥50</th>
<th>HIV- ≥50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current smoking</td>
<td>15%</td>
<td>23%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>21%</td>
<td>28%</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>20%</td>
<td>36%</td>
</tr>
<tr>
<td>On lipid-lowering drugs</td>
<td>12%</td>
<td>24%</td>
</tr>
<tr>
<td>CKD</td>
<td>4%</td>
<td>9%</td>
</tr>
</tbody>
</table>

Notes: p-values: Current smoking p=0.01, Hypertension p=0.04, Dyslipidaemia p<0.001, On lipid-lowering drugs p<0.001, CKD p=0.05.
CV risk factors: PLWH ≥50 vs HIV-negative

- Current smoking: PLWH ≥50 15%, HIV- ≥50 23%, p=0.01
- Hypertension: PLWH ≥50 21%, HIV- ≥50 28%, p=0.04
- Dyslipidaemia: PLWH ≥50 20%, HIV- ≥50 36%, p<0.001
- On lipid-lowering drugs: PLWH ≥50 12%, HIV- ≥50 24%, p<0.001
- CKD: PLWH ≥50 4%, HIV- ≥50 9%, p=0.05

- CABG: PLWH ≥50 2%, HIV- ≥50 4%, p=0.35
- Type 2 diabetes: PLWH ≥50 3%, HIV- ≥50 5%, p=0.18
- On anti-hypertensives: PLWH ≥50 16%, HIV- ≥50 21%, p=0.09
- Framingham risk ≥20%: PLWH ≥50 26%, HIV- ≥50 31%, p=0.29
- Overweight: PLWH ≥50 66%, HIV- ≥50 59%, p=0.04
Associations with cognitive scores /2

one factor at the time – PLWH ≥50 only

- Smoking
- Overweight
- Any CVD
- Hypertension
- Dyslipidaemia
- Type 2 diabetes
  - On antihypertensive drugs
  - Use of lipid-lowering drugs
- CKD
- Albumin (per 10 g/l)
- Haemoglobin (per 10 g/dl)

* Adjusted for age, gender, ethnicity, education and depressive symptoms
Associations with cognitive scores /2

one factor at the time

- Smoking
- Overweight
- Any CVD
- Hypertension
- Dyslipidaemia
- Type 2 diabetes
  - On anti-hypertensive drugs
  - Use of lipid-lowering drugs
- CKD
- Albumin (per 10 g/l)
- Haemoglobin (per 10 g/dl)

HIV-negative ≥50
PLWH ≥50

*p interaction

- p=0.04
- p=0.16
- p=0.40
- p=0.11
- p=0.82
- p=0.43
- p=0.23
- p=0.05
- p=0.45
- p=0.11
- p=0.79

* Adjusted for age, gender, ethnicity, education and depressive symptoms
Associations with cognitive scores /2

one factor at the time

- Smoking
- Overweight
- Any CVD
- Hypertension
- Dyslipidaemia
- Type 2 diabetes
- On anti-hypertensive drugs
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- CKD
- Albumin (per 10 g/l)
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HIV-negative ≥50

PLWH ≥50

p interaction

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- p=0.05
- p=0.45
- p=0.11
- p=0.79

* Adjusted for age, gender, ethnicity, education and depressive symptoms
Conclusions

- Some CV risk factors appear to correlate with cognitive health in virally suppressed PLWH
- On the whole, associations are similar to those seen in comparable HIV-negative individuals
- Given the higher burden of CV disease in PLWH, prevention and active management of CV disease and its risk factors may reduce the risk of cognitive disorders
Acknowledgments

POPPY Management Team: Daphne Babalis, Marta Boffito, Laura Burgess, Paddy Mallon, Frank Post, Caroline Sabin, Memory Sachikonye, Alan Winston

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