Neurocognitive Outcomes Not Associated with Prior Syphilis or Number of Episodes of Syphilis in HIV+ Adults in Care in Ontario

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Background

Rationale

- Neurocognitive impairments observed in 40-60% of people living with HIV (PLWH), regardless of cART status
- Pathogenesis remains unclear
- Syphilis (*T. pallidum*) is a common STI in PLWH with incidence on the rise since 2000
- *T. pallidum* shown to invade CNS early in infection, putting PLWH at risk for neurosyphilis due to impairments in clearance of syphilis

Hypothesis

- We hypothesized that: 1) a history of syphilis (ever vs. never) and 2) the number of episodes of syphilis would be associated with worsened neurocognitive outcomes in PLWH
Methods

Study Design and Sample
- Retrospective study of PLHW in OHTN Cohort Study from 2008-2017 with neurocognitive testing data

Syphilis History
- Serology data obtained via data linkage to Public Health Ontario Laboratories
- Number of episodes based on:
  - New reactive RPR or treponemal test in someone previously non-reactive; or
  - a 4-fold rise in RPR 120 days after a previous episode; or
  - Chart review
- Each episode of syphilis preceded neurocognitive testing

Neurocognitive Outcomes
- Most recent MOS-HIV 4-item self reported cognitive scale
- Most recent Average T-score (ATS): based on formal neuropsychological testing of complex attention, speed of processing, and learning/memory
- Most recent Global deficit score (GDS): based on same neuropsychological testing, dichotomized into impaired (>0.5) or unimpaired (<0.5)

Analysis
- MOS-HIV and ATS: Wilcoxon Rank-Sum, Linear Regression Models
- GDS: Chi-Square, Logistic Regression Models
- Variables considered for adjustment in models were: age, education, income, race, years of HIV, nadir, most recent viral load, methamphetamine use, depression, and number of prior neurocognitive tests performed.
Results

Statistics

- Total 1288 participants with 366 episodes of syphilis across 271 people
- Median age 47 (IQR: 38,54), 53.5% were white, 78.0% were male
- Median CD4 count was 520 (IQR: 365,680) cells/mm³ and 80.5% had HIV viral load <50 copies/mL
- Comparing those with syphilis vs. without syphilis, no significant difference in:
  - Median MOS-HIV (85 vs. 80, p=0.80)
  - Median ATS (45.7 vs. 45.7, p=0.92)
  - Impairment on GDS (54.3% vs. 52.3%, p=0.72)
- Models: no significant relationship between syphilis or the number of episodes of syphilis and neurocognitive outcomes (Table)

### Table. Univariate and multivariable linear regression / logistic regression models

<table>
<thead>
<tr>
<th>Primary Predictor</th>
<th>Outcome</th>
<th>Univariate Model</th>
<th>Multivariable Model</th>
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<tbody>
<tr>
<td></td>
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<td>Regression</td>
<td>P-value</td>
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<td></td>
<td></td>
<td>Coefficient</td>
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<tr>
<td></td>
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<td>(95% C.I.)</td>
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<tr>
<td>Syphilis</td>
<td>MOS-HIV</td>
<td>-0.40 (-3.4,2.6)</td>
<td>0.79</td>
</tr>
<tr>
<td># of episodes of syphilis</td>
<td>MOS-HIV</td>
<td>-0.21 (-2.1,1.6)</td>
<td>0.82</td>
</tr>
<tr>
<td>Syphilis</td>
<td>ATS</td>
<td>-0.01 (-1.3,1.3)</td>
<td>0.99</td>
</tr>
<tr>
<td># of episodes of syphilis</td>
<td>ATS</td>
<td>-0.02 (-0.9,0.9)</td>
<td>0.97</td>
</tr>
<tr>
<td>Syphilis</td>
<td>GDS</td>
<td>1.08 (0.8,1.5)</td>
<td>0.65</td>
</tr>
<tr>
<td># of episodes of syphilis</td>
<td>GDS</td>
<td>1.04 (0.8,1.3)</td>
<td>0.76</td>
</tr>
</tbody>
</table>

a Odds ratio of the logistic regression (Confidence Interval)
b Adjusted for age, education, race, years of HIV, nadir CD4, most recent viral load, methamphetamine use, depression, and number of prior MOS-HIV performed
c Adjusted for income, years of HIV, nadir CD4, most recent viral load, methamphetamine use, and depression
Discussion

**Findings**
- Contrary to our hypothesis, we found no association between syphilis history and neurocognition on self-reported scales or formal neuropsychological testing in PLWH in care in Ontario
- Literature on effects of syphilis on neurocognition remain mixed\(^3\)-\(^5\)
- Continued study required to identify contributing factors to neurocognitive decline in PLWH

**Strengths**
- Large sample size in this area of study
- Serologic data available going back >20 years

**Limitations**
- Unable to adjust for neurologic or psychiatric confounders
- Assumptions around positive treponemal tests may have underestimated number of episodes of syphilis

**Future study**
- Effects of neurosyphilis vs. no syphilis

**References**