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[1-2]

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 ($\geq$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/mm^3 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

		Univariate Model		Multivariable Model	
Primary Predictor	Outcome	Regression Coefficient (95% C.I.)	P-value	Regression Coefficient (95% C.I.)	P-value
Syphilis	MOS-HIV	-0.40 (-3.4,2.6)	0.79	0.22 (-2.4, 2.9)[b]	0.87
# of episodes of syphilis	MOS-HIV	-0.21 (-2.1, 1.6)	0.82	-0.11 (-1.8, 1.6)[b]	0.90
Syphilis	ATS	-0.01 (-1.3, 1.3)	0.99	-0.16 (-1.5, 1.2)[c]	0.82
# of episodes of syphilis	ATS	-0.02 (-0.9, 0.9)	0.97	-0.19 (-1.1, 0.8)[c]	0.70
Syphilis	GDS	1.08 (0.8,1.5)[a]	0.65	1.13 (0.8,1.7)[a,c]	0.53
# of episodes of syphilis	GDS	1.04 (0.8, 1.3)[a]	0.76	1.08 (0.8, 1.4)[a,c]	0.55

[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

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