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A PAST HISTORY OF SYPHILIS IS ASSOCIATED WITH POORER PERFORMANCE IN THE COGNITIVE DOMAINS OF MEMORY AND LEARNING IN HIV-1 INFECTED SUBJECTS ON STABLE cART

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BACKGROUND

- The pathogenic mechanisms underlying ongoing neurocognitive (NC) impairment in HIV-infected individuals on stable combination antiretroviral therapy (cART) are likely to be multifactorial and concomitant diseases affecting the central nervous system (CNS) such as syphilis infection may be one such factor.
- *Treponema pallidum (T. pallidum)*, the bacterium that causes syphilis, invades the CNS early in disease but little is known about the functional consequences of recent and past infection in HIV-infected individuals.

AIM

- The aim of this study was to examine if poorer neurocognitive performance was present in HIV-infected patients with and without a past history of syphilis.

METHODS

- HIV-1 infected subjects from our NC testing database, with a past history of syphilis were matched by age, gender, education and HIV risk acquisition to those without syphilis. All subjects were neurologically asymptomatic HIV- infected on stable cART with plasma HIV RNA<50 copies/mL.
- NC function was assessed with computerised tests (CogState). NC z-scores calculated were: overall (global); motor domains; memory and learning domains and executive function.
- NC scores were correlated with past history of treated syphilis confirmed by the presence of reactive serum *T. pallidum* enzyme-immunoassay (EIA); *T. pallidum* agglutination test (TPPA) and negative rapid plasma regain (RPR).
- Associations between NC scores and clinical parameters including CPE score, CD4 T-cell counts and stage of syphilis infection were evaluated using linear regression.

RESULTS

TABLE 1. Syphilis history of participants

Clinical parameter	Past Syphilis N=29
Years since last syphilis infection, median (range)	11(4-41)
Stage of last episode of syphilis infection, n (%)	
Early syphilis (primary or secondary)	20(69)
Late syphilis (>2 years)	5(17)
Neurosyphilis	0
Unknown	4(14%)
Recorded or self -reported history of treatment received n (%)	
Penicillins	24(85)
Doxycycline	2 (5)
Other or unknown	3(10)
Syphilis infection more than once n (%)	9(31)

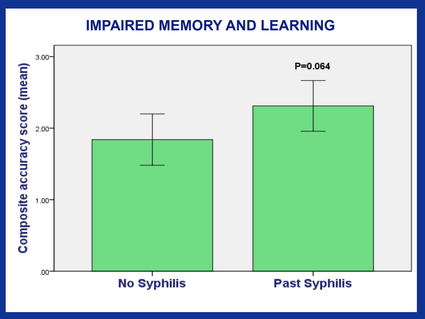
TABLE 2. Demographics of participants

Clinical parameter	Past syphilis N= 29	No past syphilis N=29	All N=58
Age, years	59 (24-77)	61(24-72)	62 (42-77)
Male gender	29 (100%)	24 (82.8%)	53 (91.4%)
CD4 cell count (cells/uL)	590(130-1170)	470(70-1320)	580(230-1320)
Nadir CD4 cell count (cells/uL)	210(10-430)	190(30-760)	190(10-760)
HIV RNA level <50 copies/mL	29(100%)	29(100%)	58(100%)
Chronic hepatitis C	7(24.1%)	12(41%)	19(32%)
Years of education	13(9-17)	14(6-20)	13(6-20)
CPE score	1.5(5-2.5)	1.5(1-2.5)	1.5 (1-2.5)

Data are expressed as N (%), median (IQR) and mean (SD)

RESULTS

- Subjects with prior syphilis :
  - 20 (89%) had past history of early syphilis infection.
  - 29 (100%) had either confirmed serological response or self-reported history of treated syphilis.
  - 26 (86%) had treatment with penicillin-based therapies.
- No statistically significant differences in global, motor or executive function NC parameters were observed between subjects with and without prior syphilis (p>0.1 all values, all observations).
- A trend towards poorer memory and learning scores (mean +/- SD) was observed in those with prior syphilis (1.40 +/- 0.406) vs no syphilis (1.2 +/-0.37), (p=0.064).
- Among those with syphilis, there was a significant association between poorer memory and learning domain scores and prior history of early syphilis infection (p=0.014).



- In a multivariate model, increasing age and past syphilis were significantly associated with poorer memory and learning domain scores (p= 0.001 and 0.045 respectably) whereas nadir CD4+ count , hepatitis C status, CPE score were not associated (p>0.10 all observations).

CONCLUSIONS

- In this study of neuro-asymptomatic HIV-infected adults on stable cART, prior history of syphilis was associated with poorer performance in learning and working memory.
- Among subjects with past syphilis, cognitive function was not related to type of syphilis treatment, years since last syphilis infection or reinfection.
- We hypothesize that a possible mechanism of injury could involve the persistence of treponemal antigens within the CNS following syphilis infection, that when followed by HIV-1 infection of the brain, could potentially cause an increase in levels of intrathecal inflammation, neuronal dysfunction and eventually NC impairment.
- Future research to investigate the relationship between syphilis stage and NC function in HIV-1 infected and uninfected individuals is warranted.