490

CNS Immunoactivation in HIV-patients on ART with HIV-associated Mild Neurocognitive Impairment

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Background

Although HIV-associated neurocognitive disorders (HAND) remains prevalent in patients on antiretroviral therapy (ART), it is unclear if neuronal damage continues despite effective suppression of HIV-1. The light subunit of the neurofilament protein (NFL) is a component of myelinated axons, and elevated concentrations in cerebrospinal fluid (CSF) are a sensitive marker of ongoing axonal injury in HIV-associated dementia (HAD).

Purpose

To investigate if milder forms of neurocognitive impairment – asymptomatic neurocognitive impairment (ANI) and minor neurocognitive disorder (MND) – are associated with ongoing neuronal damage, we analyzed CSF NFL in a well characterized cohort of virally suppressed subjects on ART with or without ANI/MND

Study design

In a cross-sectional analysis, subjects on ART with plasma HIV-1 RNA <50 c/mL without significant confounding conditions (e.g., current substance dependence) were identified from longitudinal studies (CHARTER and HNRC). Standardized neurocognitive performance (NP) testing was performed. Subjects were classified as NP-normal (NPN) or NP-impaired (ANI/MND) based upon demographically-adjusted norms. Subjects were selected to yield approximately equal samples of NPN, ANI, and MND.

Methods

CSF concentrations of NFL were measured by an enzymatic 2-site quantitative immunoassay (UmanDiagnostics, Umea, Sweden). CSF neopterin was measured by ELISA. Continuous variables were $\log^{10}$ transformed where appropriate. For two group comparisons, Mann-Whitney-U-test was used. Correlations were calculated using Pearson correlation coefficients test.

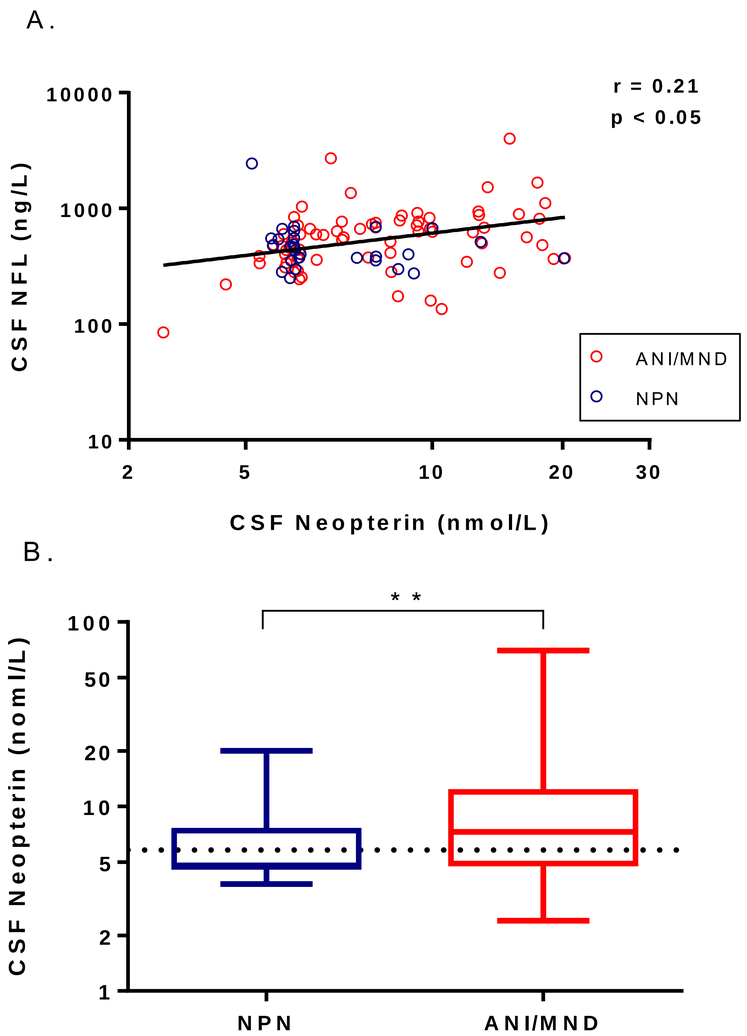


Figure 1

Values are $\log^{10}$ transformed for presentation. (**A**.) Correlation of CSF NFL and neopterin (**B**.) CSF neopterin in subjects with NPN (median 4.8, IQR 4.7-7.4 nmol/L) and ANI/MND (median 7.3, IQR 4.9-12 nmol/L). Dotted line represents upper normal reference for neopterin (5.8 nmol/L).

Results

100 (91% male) subjects were included in the analysis, 29 NPN and 71 with ANI/MND (ANI=38; MND=33). Median (IQR) age was 47 (41-54) years, with current CD4+ 524 (359-771) and nadir 72 (10-224) x10^6 cells/l. No statistically significant difference was found in NFL between the NPN and ANI/MND groups. CSF neopterin was significantly correlated to NFL in the whole study population (r=0.21; p=0.035). No significant correlation was found between CD4 cell count or CD4 nadir and NFL.

Conclusions

- **No difference in NFL was found in subjects with ANI/MND compared to subjects without neurocognitive impairment**
- **CSF neopterin was higher in the ANI/MND group indicating an association between increased intrathecal immunoactivation and neurocognitive impairment in patients on ART**
- **These findings indicate that virologic suppression is not sufficient to eliminate neuro-inflammation, which may reflect persisting viral reservoirs, elaboration of viral products from nonproductive infection, or other non-HIV mechanics**

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