CEREBROSPINAL FLUID NFL DECREASES AFTER INITIATION OF ANTIRETROVIRAL TREATMENT, BUT SLOWER THAN INFLAMMATORY BIOMARKERS

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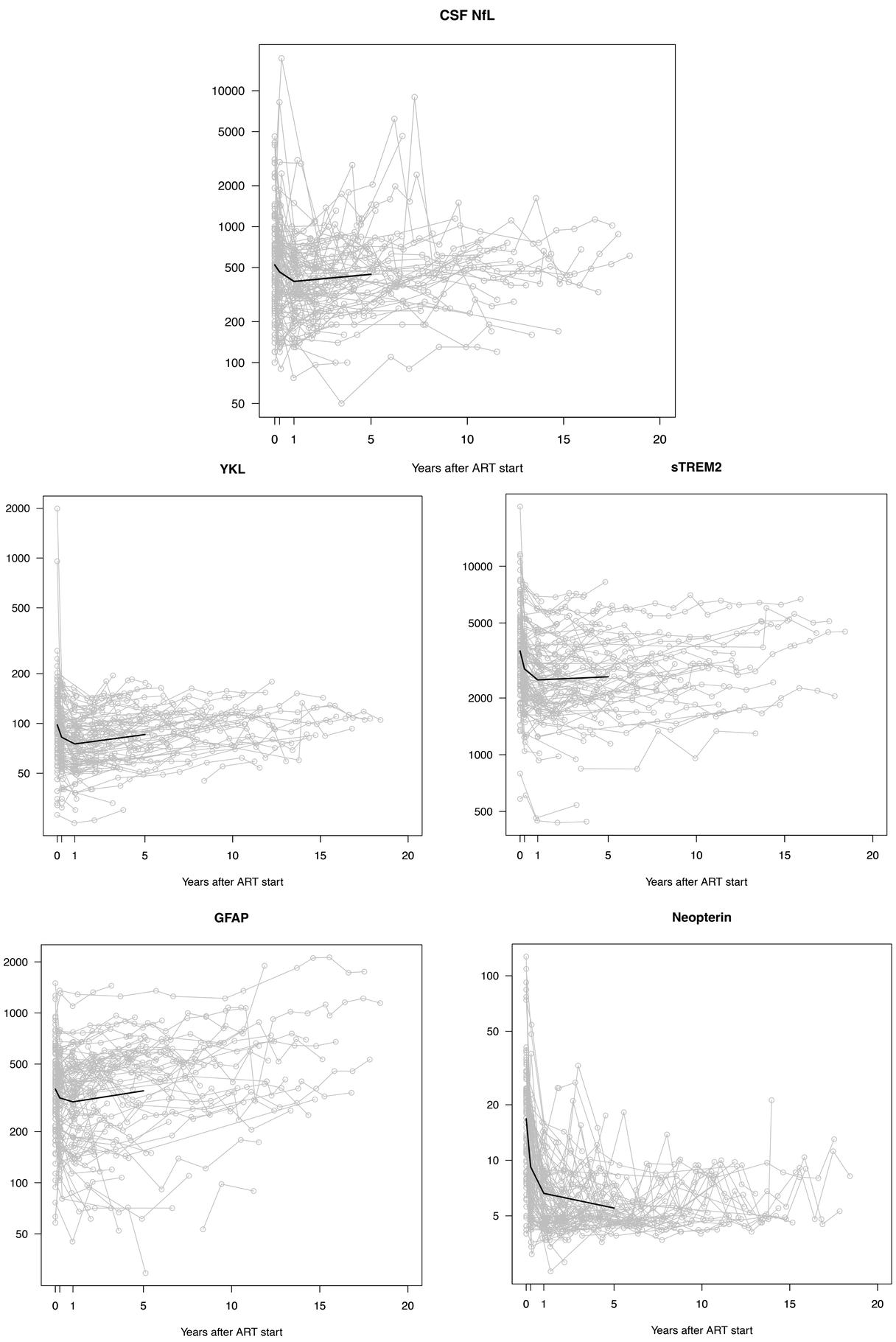

Figure 1. Spaghetti plots of longitudinal values of cerebrospinal fluid biomarkers. Black line marks mean values.

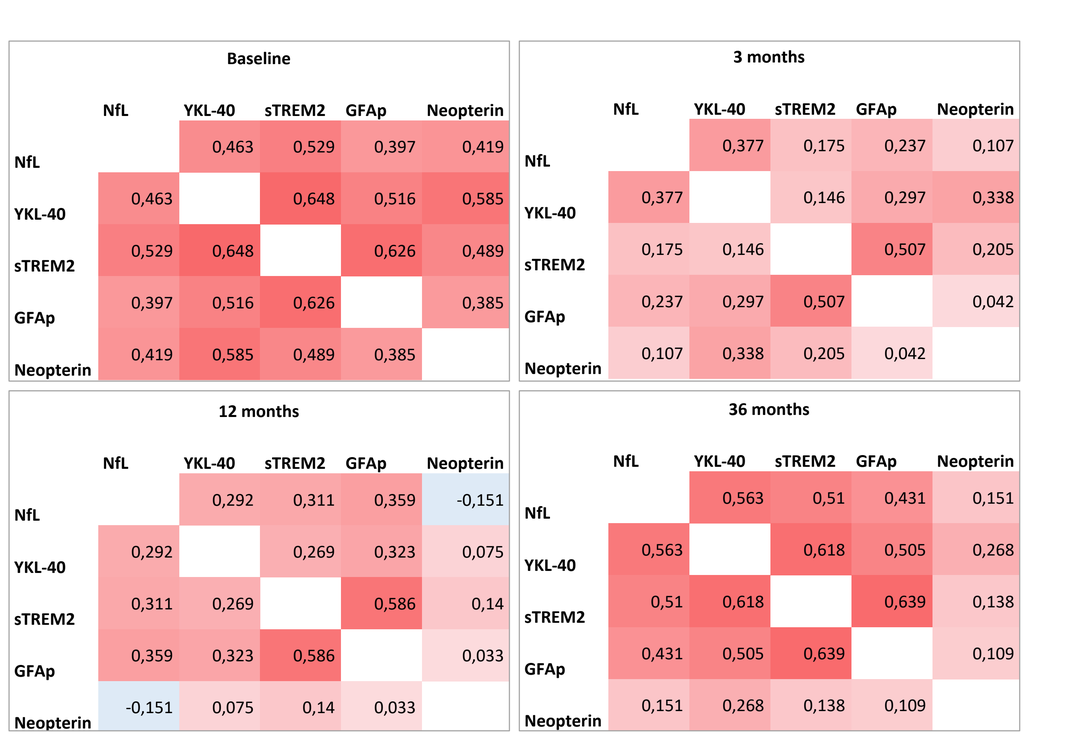

Figure 2. Heatmaps of correlations between cerebrospinal fluid biomarkers, calculated adjusting for age

Background

Persistent intrathecal immune activation and signs of neuronal disturbances are present in many HIV-infected individuals despite effective antiretroviral treatment (ART). We have studied the decay characteristics of neurofilament light (NfL) protein, a marker of neuronal injury, in cerebrospinal fluid (CSF) after initiation of ART in a large cohort of HIV-infected individuals.

Method

In this longitudinal study, we assessed the levels of NfL, and a panel of neuroinflammatory biomarkers, including YKL-40, sTREM-2, neopterin and GFAp, in consecutive archived CSF samples from 99 people with HIV (PWH) who had achieved viral suppression. Participants were followed from before treatment initiation and up to at least one year on ART. Comparison of means was performed using t-test and partial correlations were calculated adjusting for age.

Results

Twenty-five percent of the study participants had CSF NfL levels above normal reference limits prior to initiation of ART. Following 12 months of ART, a significant reduction in mean NfL levels was observed (-27 %, $p < 0.005$); however, no significant decline was noted after three months of treatment (-12 %, $p > 0.05$) (figure 1). No further change in NfL levels was observed after 24 or 36 months of ART. CSF levels of YKL-40, sTREM2 and neopterin significantly declined after both 3 and 12 months while GFAp did not decline significantly at neither 3 nor 12 months. Notably, strong correlations were observed between all evaluated biomarkers at baseline and all except neopterin at 12 months.

Conclusion

The decrease of NfL as well as biomarkers of immune activation suggests that ART significantly reduces axonal injury as well as neuroinflammation within one year of treatment initiation. The significant decrease of inflammatory biomarkers, but not NfL, after three months indicate that reduction of neuroinflammation precedes reduction of neuronal harm.

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