E-06

UNMASKING THE INDEPENDENT ROLE OF CSF HIVRNA DYNAMICS BY SINGLE COPY ASSAY IN NEUROBIOTYPES

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BACKGROUND

In the current study, we test whether low level HIV replication (by single Copy Assay-SCA in the plasma and CSF) is important in the pathogenesis of neurocognitive and neuroimaging biotypes, and independent of comorbidity and legacy effects.

METHODS

- **43 clinically stable men with HIV** (age 53±14 years, **plasma and CSF <20-50 cp/mL**) were included. **Neurocognition**, **CSF neopterin, plasma and CSF HIV RNA were measured (HIV RNA by single copy assay- SCA detection limit <0.3 cp/mL, RNA thereafter) at baseline, 6-, 12-, 18 and 24-month.**
- **Proton Magnetic Resonance Imaging/Spectroscopy (MRI/S) was conducted at baseline & 24-month.**
- Comprehensive lifetime, non-HIV medical, psychiatric, disability, and lifestyle history was integrated into a comorbidity score. Legacy effects were defined as historical HIV-associated neurocognitive disorder (HAND) and nadir CD4 <200. Our previous analyses had shown four neurobiotypes by neurocognitive and MRS changes. Here they are replicated with the following prevalence: **Fig. 1**.
- *Statistical analyses*: Mixed effect models tested main effect and time-association between the neurobiotypes and the CSF biomarkers with comorbidity or legacy as covariate.

Greater numbers of Single CSF HIVRNA Copies Independently Associate with Progressive & Stable Neurobiotypes, as well as CSF Neopterin across a 2-year period in virally suppressed people with HIV.

CONCLUSIONS

Partially compartmentalized CSF HIVRNA as measured by SCA links to neurobiotypes independently and despite comorbidities and legacy effects. Incident decline is the least common neurobiotype making the testing of predictors more challenging. Replication in larger and more diverse samples is needed.

ADDITIONAL KEY INFORMATION

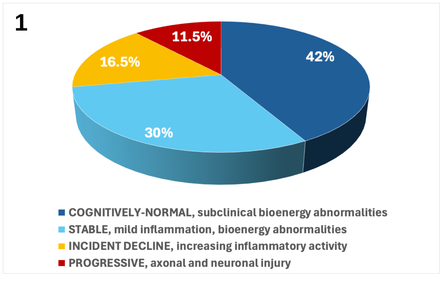
(E-06) CNS HIV Reservoirs on 12 March 2025 at 02:30 PM Pacific Time.

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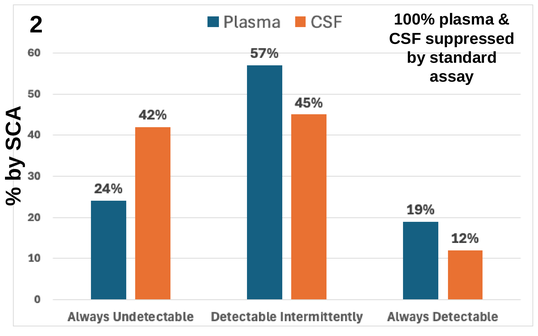
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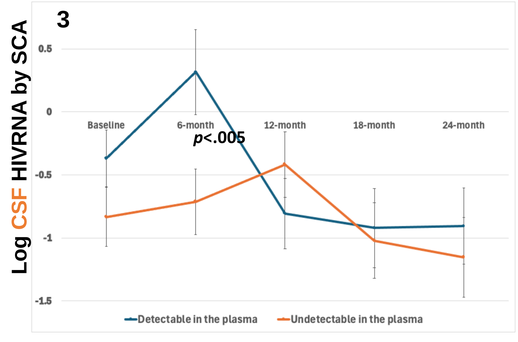
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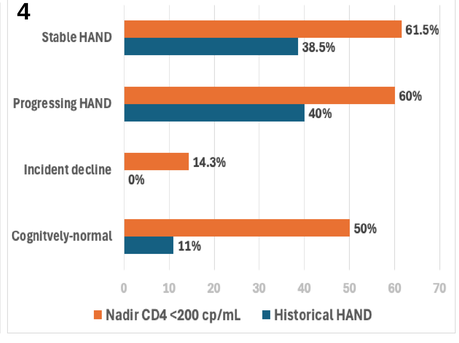
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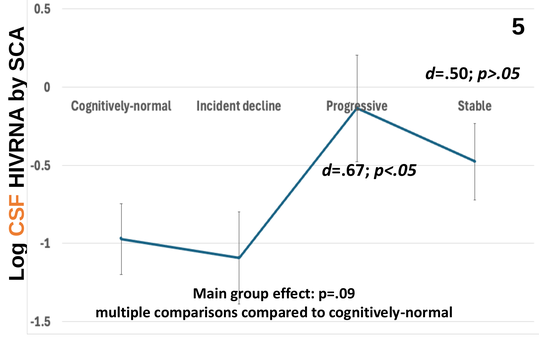
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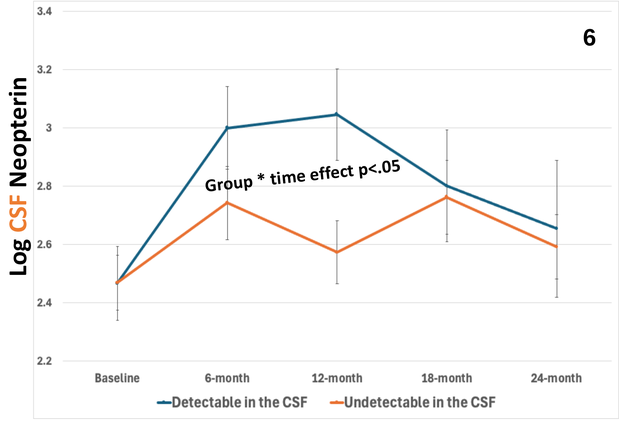
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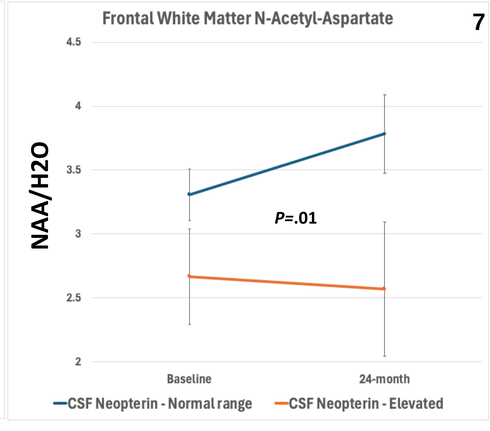
RESULTS

- A pattern of intermittent RNA or lack of detectable RNA was most common (**Fig. 2**).
- Plasma and CSF RNA showed a transient dissociation (p<.005) (**Fig. 3**).
- Relative to cognitively-normal cases (50%), nadir CD4<200 was less frequent in incident decline (14%, p=.005). Historical HAND was more frequent in progressing (60%, p<.04) and stable cases (61%, p=.02) versus cognitively-normal cases (11%).
- There were no nadir CD4 differences (**Fig. 4**). Comorbidities correlated modestly with baseline neurocognition (Rho=-.23;p<.08) but not with the neurobiotypes, although progressing cases had the greatest burden.
- Unlike plasma, CSF RNA was significantly increased in the progressive neurobiotype, and slightly in the stable neurobiotype (**Fig. 5**).
- CSF RNA was associated with CSF neopterin with time variations (**Fig. 6**).
- Only CSF neopterin was associated MRS abnormalities (axonal injury (**Fig. 7**) and neuroinflammation (**Fig. 8**)).
- The inclusion of comorbidities or legacy effects did not alter these results.

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