**Background**

- Although antiretroviral therapy (ART) has improved survival and morbidity, HIV-infected adults still have higher rates of non-AIDS disorders, such as neurocognitive impairment, than HIV-uninfected adults.
- (1-3)-b-D-glucan (BDG) is a fungal cell wall component which serves as a plasma biomarker for fungal infection and – in the absence of fungal infections – for gut barrier integrity failure and microbial translocation.

**Objective**

To determine whether higher plasma and cerebrospinal fluid (CSF) levels of BDG are associated with neurocognitive impairment [evaluated by global deficit score (GDS)] in HIV-infected adults

**Methods**

- **Setting:** This study included paired plasma and CSF samples from a cohort of 61 HIV+ adults on suppressive ART enrolled into the CNS HIV Antiretroviral Therapy Effects Research (CHARTER) study between 2005-2015.
  - All samples had been stored at -80°C on the day of collection.
  - The CHARTER study was funded in 2002 to explore the changing presentation of HIV neurological complications in the context of ART.
- **Dependent variables (collected as part of CHARTER):**
  - GDS, a score for neurocognitive impairment measured during CHARTER study visits.
- **Independent variables:**
  - BDG levels as well as levels of soluble urokinase plasminogen activator receptor (suPAR; a marker of monocyte activation and chronic inflammation that has previously been associated with non-AIDS disorders) were measured in paired plasma and CSF samples collected as part of the prospective CHARTER study between 2005-2015 at the University of California San Diego.
  - BDG testing of blood plasma and CSF supernatant was performed at the Associates of Cape Cod, Inc, Falmouth, MA.
- **Independent variables:**
  - suPAR was measured in the UCSD CFAR Research Laboratory using the suPARnostic ELISA assay.
  - Plasma CD4/CD8 ratio measured as part of CHARTER.

**Results**

- Median plasma BDG level was 18 pg/mL (range: 2-60 pg/mL), median CSF BDG level was 20 pg/mL (range: 0-830 pg/mL).
- Individuals with neurocognitive impairment (i.e., GDS>0.5, n=33) had higher plasma BDG levels compared to unimpaired individuals (median 21 pg/mL, range 5-60 versus median 16 pg/mL, range 2-30; p=0.027) and there was also a trend towards higher CSF BDG levels in impaired individuals (p=0.083).
- Higher levels of plasma BDG were associated with more severe cognitive impairment as measured by the GDS (Spearman r=0.35; p=0.006).
- Plasma levels of BDG and suPAR correlated significantly (r=0.31, p=0.016), while all other correlations were non-significant:
  - Plasma BDG and GDS (r=0.23)
  - plasma suPAR and GDS (r=0.19)
  - CSF suPAR and GDS (r=0.022)
  - CD4/CD8 ratio and GDS (r=0.028)

**Conclusions**

- Elevated plasma levels of BDG may be an indicator of gut barrier integrity failure and an independent biomarker associated with neurocognitive functioning in HIV+ adults on suppressive ART.

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