HIV BRAIN LATENCY AS MEASURED BY CSF BCL11B IS LINKED TO DISRUPTED BRAIN CELLULAR ENERGY IN VIRALLY SUPPRESSED HIV INFECTION

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Background:
HIV brain latency may induce neuropathological events in virally suppressed HIV+ persons and persisting HIV-associated neurocognitive disorder (HAND). We investigated whether major brain metabolites that reflect slowly progressing HAND are impacted by a putative marker of brain HIV latency (CSF BcL11b, a microglia transcription factor that inhibits HIV transcription) in conjunction with CSF neopterin (neuroimmune marker), CSF Neurofilament Light-Chain (NFL, neuronal damage marker), and CSF HIV-Tat transcriptional protein.

Methods:
26 HIV+ men (mean: 57 years; 96% undetectable <50 cp/mL; 100% <100cp/mL) undertook a CSF lumbar puncture *at baseline*; a ^{1}H Magnetic Resonance Spectroscopy (MRS) scan, and a neuropsychological testing *at baseline and 18-months later*. ^{1}H MRS included measurements of *N*-acetyl aspartate (NAA), choline (Cho), creatine (Cr), *myo*-inositol (MI), glutamine/glutamate (Glx) in the frontal white matter (FWM), posterior cingulate cortex (PCC), and caudate nucleus area (CA). MR spectra were measured with reference to the unsuppressed water signal. HAND status was determined at baseline, and cognitive decline was corrected for practice effect.

Results:
Baseline adjusted regression models for neopterin, NFL and tat showed that a higher CSF BcL11b was consistently associated with lower FWM Cr (when adjusted for neopterin: Std beta=-.30; p=.15; when adjusted for NFL: Std beta=-.51; p=.03; and when adjusted for tat: Std beta=-.47; p=.02). In longitudinal analyses, we found no time effect, but a consistent BcL11b altering effect on FWM Cr. The effect reached a significant moderate effect size range when corrected for CSF NFL (β=-.36, *p*=.02) and CSF tat (β=-.34, *p*=.02), and clinical factors. Neurocognition was not a significant factor in the baseline and longitudinal analyses.

Conclusion:
Reduced FWM Cr may indicate subclinical HIV brain latency-related neuropathogenesis. ^{1}H MRS may offer a non-invasive option to measure HIV brain latency. This finding needs to be replicated in a larger sample.

Disclosure of interest statement:
This work was supported by the Peter Duncan Applied Neuroscience Unit at the St. Vincent's Hospital Applied Medical Research Centre, Sydney Australia (Head of Group. Prof. Bruce Brew) and the NHMRC CDF APP1045400 (CIA-Cysique). Merck

Sharpe and Dohme partially funded the current study but had no role in the study design, and data interpretation.