MRI With T2 Maps and Spectroscopy Show Chronic Progressive Brain Damage Despite HIV Suppression

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Bruce J. Brew[1 3], David Jakabek [1], Lauriane Juge[2 3], Kurt Lancaster[1 3], Caroline D. Rae[2 3], Lucette A Cysique[1 3]
[1]St. Vincent's Hospital, Sydney, NSW, Australia, [2]Insittution 2 Neuroscience Research Australia, Sydney, NSW, Australia, [3] The University of New South Wales, Sydney, Australia

BACKGROUND

- Multi-modal MRI and absolute concentration magnetic resonance spectroscopy (MRS) can assist in elucidating chronic HIV neuropathogenesis.

We used a 20-minute absolute single-voxel proton (^{1}H) MRS scan with relaxometry (T1 and T2 maps) to better quantify water as a reference for major brain metabolites in virally suppressed people living with HIV (PWH) who are aging and were assessed for HIV immune markers and cognitive functions.

METHODS

- 39 PWH, all male (mean age: 53 ± 14, 60+ years old: 35%, HIV duration: 18 years, 20% nadir CD4 <200 cp/mL) were enrolled into a prospective study investigating brain metabolites during long-term viral suppression.
- All completed a baseline and a two-year follow-up clinical visit for HIV biomarkers (CD4 and CD8 count, nadir CD4, HIV duration), a neuropsychological assessment, a structural brain MRI scan, and a 20-minute single-voxel ^{1}H MRS in the frontal white matter, right caudate, and posterior cingulate (**Fig. 1**) with whole brain T1 (**Fig. 2**) and T2 (**Fig. 3**) mapping to derive the absolute concentration of major brain metabolites. Imaging was acquired on a 3T Phillips Ingenia scan.
- ^{1}H MRS data were fitted with the spant R package and scaled using partial volumes (derived from Freesurfer and FSL MRS tools structural volumes). For absolute metabolite quantification we used formula from Near et al (2020, NMR In Biomedicine).
- Mixed effect models assessed associations and longitudinal changes to T1, T2, and metabolite concentrations with age, baseline HIV biomarkers, and HIV-associated neurocognitive disorder (HAND, Global Deficit Score (GDS)-based definition).

A 20-minute multi-modal MRI and absolute concentration MRS scan reveals slowly progressive atrophy and neuroinflammation, especially in the white matter, due to current (age, HAND, current CD4) and legacy factors (Nadir CD4).

RESULTS

Higher T2, but not T1 values, increased with age in white and grey matter ($p < 0.002$, **Fig. 4**). HAND (GDS-defined) was associated with higher T2 values over time ($p < 0.03$, **Fig. 5**). Older adults with HAND had higher T2 values than older adults without HAND ($p < 0.04$). *Myo*-Inositol concentration increased in all brain regions as a function of increased age ($p < 0.01$). There was a significant age-by-nadir CD4 interaction in frontal white matter for *Myo*-Inositol ($p < 0.001$, **Fig. 6**). Lower baseline CD4+ cell count, and HAND were associated with lower glutamate in the cingulate ($p = 0.04$) and caudate ($p = 0.003$) of older participants, respectively.

CONCLUSIONS

Our results confirm and expand the evidence for chronic and slowly progressive structural and neurometabolic abnormalities including age-related loss of brain tissue density, age and HAND-related inflammation/glial activation, legacy-related (nadir CD4) inflammation/glial activation, but also age, current immune function (baseline CD4) and HAND related excitotoxity in the cortex and basal ganglia. Our 20-minute absolute concentration MRI/S scan may be clinically scalable to monitor HAND stability or progression in virally suppressed PWH who are aging. Follow-up studies are needed.

ADDITIONAL KEY INFORMATION
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Bruce.brew@svha.org.au; lcysique@unsw.edu.au; djakabek@gmail.com

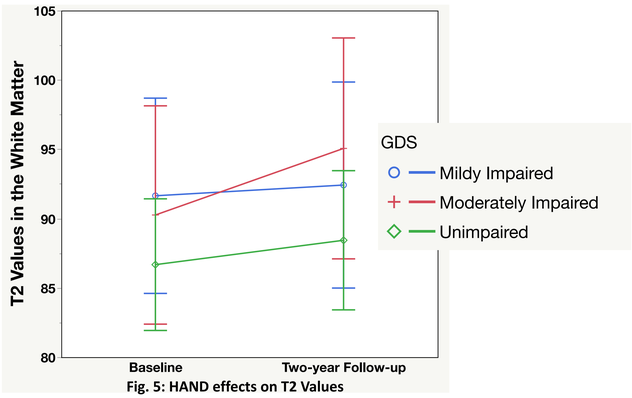


Fig. 5: HAND effects on T2 Values

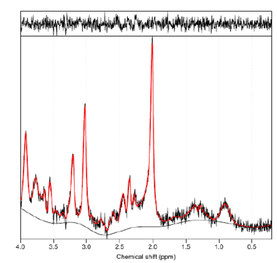
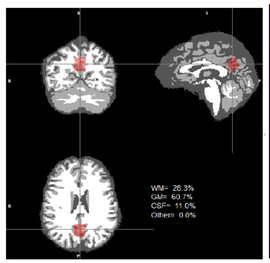
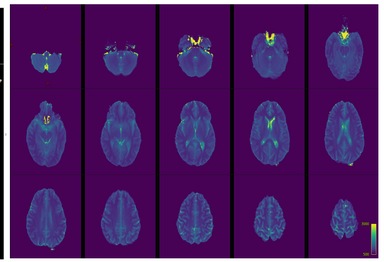
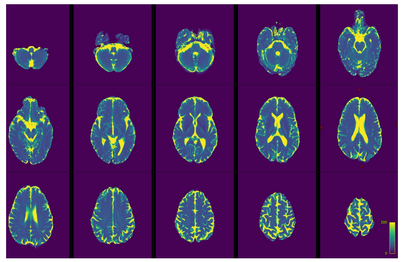


Fig. 1: Sample spectra
NAA, Choline, Creatine, Myo-inositol and Glx (glutamate and glutamine) were fitted




Fig. 2: Sample T1 map


Fig. 3: Sample T2 map

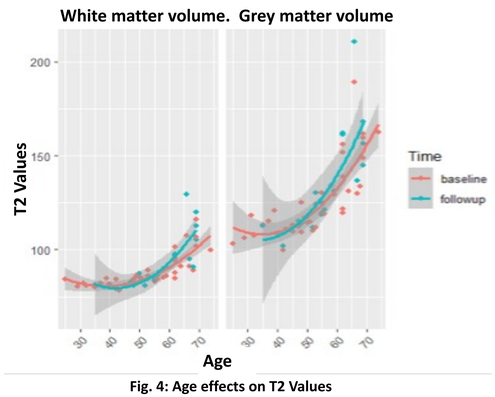


Fig. 4: Age effects on T2 Values

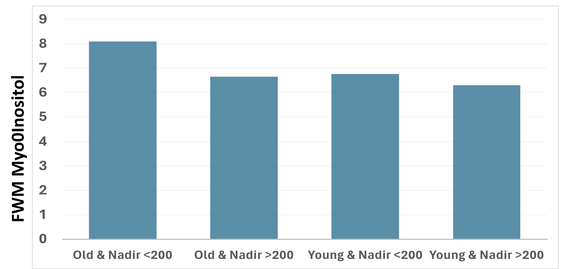


Fig. 6: Age and Nadir effect on Myo-Inositol concentrations ("main" effect baseline + Follow-up) (50yo was used as age cut-off for "Old" versus "Young".