The Relationship of Cerebral Atrophy on 1.5T MRI to Subsequent Cognitive Decline in ART treated HIV+ Adults aged 50+ in Kilimanjaro, Tanzania

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1 Background

- The availability of combined antiretroviral therapy (c-ART) has improved life-expectancy for people living with HIV (PLWH) but chronic complications including HIV-associated neurocognitive disorders (HAND) are increasingly prevalent.
- HAND present as a spectrum of cognitive impairment typically involving executive function and working memory.
- HAND are not well understood, and neuroimaging data are limited, particularly in sub-Saharan Africa.
- In 2019, 91 PLWH aged 50 and older were clinically assessed for HAND and clinician rated 'gross atrophy' on 1.5T MRI in Kilimanjaro region, Tanzania.
- HAND prevalence was **56**% and gross cerebral atrophy was **66.7**%.
- There was no cross-sectional relationship between atrophy and HAND.

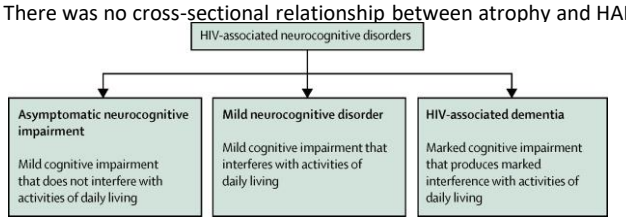


Figure 1: Classification of HAND subtypes[1]

2 Aim

To determine whether cerebral atrophy, defined as 'gross atrophy' by a clinician and quantitatively using brain parenchymal fraction, on 1.5T MRI predicts cognitive decline in HAND category in Tanzanian PLWH aged 50+ over four years of follow-up.

3 Method

- Longitudinal follow-up of n=91 PLWH aged 50+ systematically recruited in 2019 and with 1.5T MRI-brain.

Measures of Cerebral Atrophy

- Cerebral atrophy qualitatively defined as clinician rated 'gross atrophy'.
- Brain volumes were obtained using MATLAB with SPM12.
- Brain parenchymal fraction, the ratio of total brain volume to intracerebral volume, used as a quantitative measure.

HAND Diagnosis made using Frascati Criteria (Fig.2)

- Including a locally normed neuropsychological battery, clinical assessment and collateral history (fig.3).

Defining Cognitive Decline

- HAND diagnosis was compared in 2019 and 2023 to determine if there was a decline in HAND category (defined in figure 2)
- Cognitive decline was defined as a decline in HAND category.

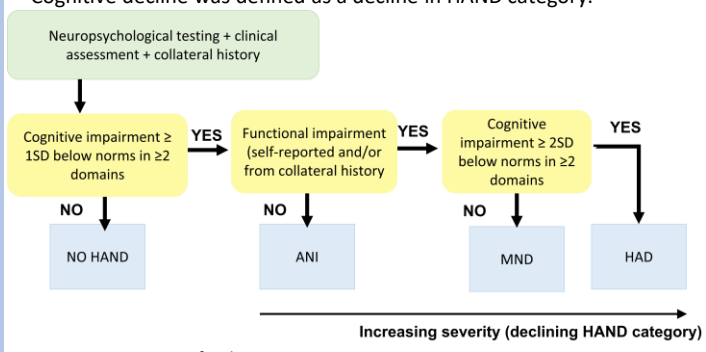


Figure 2: Frascati criteria for diagnosing HAND

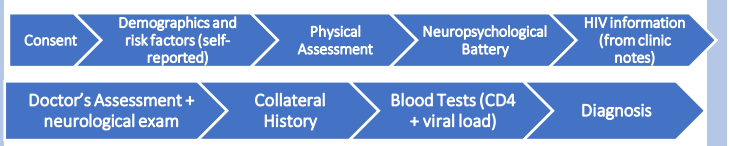
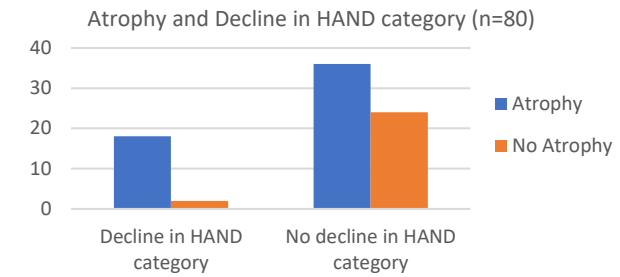
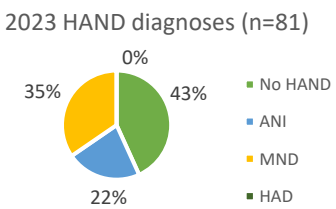


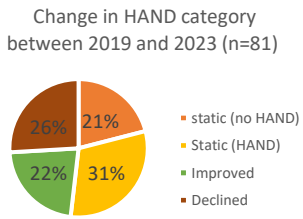
Figure 3: Summary of Methods

4 Results

- Of the 91 participants recruited in 2019, 81 were assessed in 2023 (3 died, 1 refused, 6 not-reachable).
- HAND prevalence was 57%, clinician rated 'gross atrophy' was 67.5%.
- 26% of participants declined HAND category.
- **Clinician rated gross atrophy** (yes/no) (p=0.019) and lower **brain parenchymal fraction** (p=0.007) were associated with a decline in HAND category.
- Lower **left frontal grey matter volume** (GMV) (p=0.047), **right frontal GMV** (p=0.024), **left temporal GMV** (p=0.008**), right temporal GMV** (p=0.031) and **left parietal GMV** (0.041) were also associated with a decline in HAND category.
- Co-variates associated with decline in HAND category: self-reported history of stroke (p=0.012), poor adherence to ARVs (p=0.003) and smoking (current or past) (p<0.001).







5 Discussion

Cognitive decline was associated with both qualitative and quantitative measures of cerebral atrophy

- This supports the hypothesis that HAND is the result of structural damage to brain regions associated with cognition.

Lower frontal and temporal GM volumes were associated with cognitive decline

- Reduced frontal and temporal volumes in HAND has been seen in other studies
- The frontal regions of the brain are involved in high-level executive function which is often impaired in HAND, so it follows that frontal atrophy is associated with cognitive decline.

Pre-existing structural changes seem to be more important in cognitive decline in HAND than HIV-disease/treatment factors

- Although there was a cross-sectional relationship between legacy effect and cerebral atrophy at baseline, age at diagnosis was not associated with cognitive decline.
- There was no association between detectable viral load or WHO HIV stage and cognitive decline.

6 Conclusions and Future Work

1. Cerebral atrophy (both quantitively measured as brain parenchymal fraction and qualitatively determined by a neuroradiologist) seem to predict decline in HAND.
2. MRI-brain may be useful to predict, and therefore follow-up more regularly, individuals at risk of cognitive decline.

Future research should identify an age-matched, HIV-negative Tanzanian normal cohort with MRI-brains for comparison.

References

1. Nightingale S, Winston A, Letendre S, Michael BD, McArthur JC, Khoo S, et al. Controversies in HIV-associated neurocognitive disorders. The Lancet Neurology. 2014;13(11):1139–51. doi:10.1016/s1474-4422(14)70137-1