HIV-associated Neurocognitive Disorder: an Investigation using Structural Neuroimaging in a c-ART Treated Tanzanian Cohort

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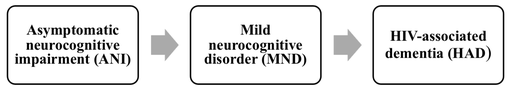
Introduction

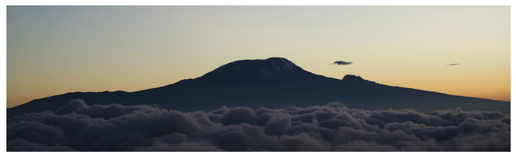
- Newly emergent ageing population of people living with HIV (PLWH) in Africa
- Subsequent increase in chronic complications such as HIV-associated neurocognitive disorder (HAND), defined by the 2007 AAN criteria[1] as..



- Existing research suggests HAND is prevalent, however the aetiology remains unclear
- Structural measures such as cerebral atrophy offer an objective method of measuring HAND
- No pre-existing structural imaging data for HAND in Sub-Saharan Africa
- Vital to understand why people with controlled HIV are developing cognitive impairment

Aim

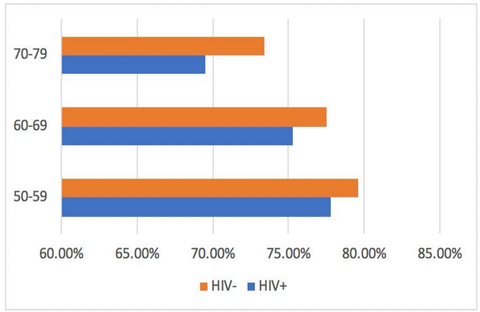
1. Explore whether substantial atrophy is present on clinical MRI reports and quantitative analysis of people with optimally managed HIV in Northern Tanzania
2. Explore the aetiology of HAND by assessing whether cerebral atrophy is associated with demographic risk factors, HIV-related factor and/or comorbidities



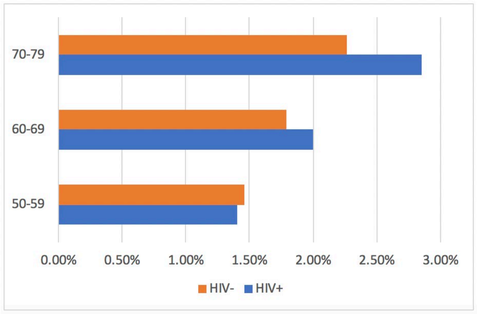
Method

- A systematic sample aged ≥50 years were recruited from a HIV clinic in Kilimanjaro, Northern Tanzania
- Demographic data, HIV-disease severity measures (viral load, CD4) and comorbidities were recorded
- HAND were diagnosed by consensus AAN criteria based on detailed locally-normed neurocognitive battery, neurological examination and informant history
- 1.5T MRI brain were clinically reported
- Quantitative analysis using SPM-12 and in-house code produced measures of brain volume (ml) and ventricle volume (ml)
- Both measures analysed as ratios of intracerebral volume

Graph 1: Comparison of brain volume in age ranges 50-59, 60-69 and 70-79 in a Tanzanian HIV+ and an English HIV- cohort



Graph 2: Comparison of ventricle volume in age ranges 50-59, 60-69 and 70-79 in a Tanzanian HIV+ and an English HIV- cohort



Results

- 91 participants were included in the final analysis (64.8% female, median age 58 years, age range 50-79 years)
- HIV disease control was good:
  - Viral load suppression (<50 copies/ml) in 75.9% (n=66)
  - Median load 0 copies/ml
  - Median CD4 count 507 cells/ul
- 100% (n=90) were on c-ART, 80% (n=72) first line regimes
- 63.7% were diagnosed with HAND according to AAN criteria
- Comorbid opportunistic infections:
  - 1.1% (n=1) Tb; 18.8% (n=15) syphilis; 5% (n=4) Hepatitis B; 1.3% (n=1) Hepatitis C
- Atrophy prevalence: 66.7% had gross atrophy on clinical MRI report
  - 66.1% (n=27) 50-59 years
  - 67.9% (n=19) 60-69 years
  - 66.7% (n=4) 70-79 years
- In comparison to a HIV negative control group from a UK-based study[2]:
  - Brain volume was smaller for all ages in the HIV+ cohort (Graph 1)
  - Ventricle volume was larger from 60+ years in the HIV+ cohort (Graph 2)

Table 1: Independent predictors in multivariate linear regression models

Structural Measure	Variable	B	Confidence Interval (lower, upper)	Sig
Brain Volume	Age at diagnosis	-.018	-.028, -.008	.001
Ventricle Volume	Gender	-.153	-.218, -.089	<.0001
	Age	.013	.008, .018	<.0001
	Frailty	.026	.013, .040	<.0001

Discussion

- Comorbid opportunistic infections were minimal
- Compared to a "normal" ageing population, there was increased cerebral atrophy
- Neurological damage was objectively present
- Age was an anticipated predictor of cerebral atrophy
- It was not possible to determine whether ageing was accelerated or accentuated by HIV due to study design
- Older age at diagnosis and male gender are associated with a later presentation to HIV services, and increased neuronal damage before the initiation of c-ART
- Frailty was a significant predictor of cerebral atrophy, supporting the hypothesis that age and comorbidities contribute to HAND

Conclusion

- First MRI study of older c-ART treated PLWH in Africa
- Despite c-ART and good disease management, HAND and cerebral atrophy were both highly prevalent
- The high rate of atrophy supports the high rate of cognitive impairment identified on clinical assessment
- Cerebral atrophy was unrelated to measures of HIV
- HIV legacy effect was associated with both measures of cerebral atrophy
- Increased age was independently associated with cerebral atrophy
- MRI is a useful and objective tool in investigating HAND

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References

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2. Yarnall A, Breen D, Duncan G. Characterizing mild cognitive impairment in incident Parkinson disease: The ICICLE-PD Study. Neurology. 2014;82(4):308-316