# Increased Cerebral Arterial Transit Time in Obese Females with HIV and Metabolic Syndrome

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## BACKGROUND

- The prevalence of obesity, and subsequent metabolic syndrome (MetS), is increasing in persons with HIV (PWH) on antiretroviral therapy (ART), with nearly 1 in 4 meeting MetS criteria.[1]
- African females with HIV are at particular risk of developing obesity complicated by MetS.[2]
- Obesity increases the risk of cardiovascular and cerebrovascular disease.[3]
- Advanced MRI techniques can detect subtle vascular changes in the brain.[4]
- There are sparse data on the association of obesity and MetS in PWH with neuroimaging biomarkers of cerebrovascular hemodynamics and microcirculation.

## AIM

- **To assess the impact of obesity and metabolic syndrome on cerebrovascular function quantified using advanced MRI techniques of tissue perfusion and microvascular function.**

## METHODS

- **Population:** PWH from a primary care clinic in Cape Town, South Africa, suppressed on ART with newly diagnosed MetS using the Harmonized criteria enrolled in the SMART study (NCT05571319).
- **Study design:** All participants underwent cross-sectional clinical, laboratory, and brain MRI examination.
- **MRI Analysis:** Images processed and analyzed using the FSL, MATLAB and Python.
  - Cerebrovascular reactivity (CVR) was computed from resting-state functional MRI.
  - Cerebral blood flow (CBF), arterial transit time (ATT) and water exchange rate (Kw) were estimated via diffusion-prepared multi-delay arterial spin labelling.
  - Microcirculation was assessed with intravoxel incoherent motion (IVIM) via a 2-compartment model (diffusion, D; pseudo-diffusion, D*; perfusion fraction, f).

## Cerebral arterial transit time increased with body fat percentage

- **Statistical Analysis:**. Using linear regression, we correlated our imaging findings with a composite MetS severity z-score and body fat composition quantified using dual-energy X-ray absorptiometry (DXA).

## RESULTS

- 30 participants suppressed on dolutegravir-based ART were enrolled (Table 1).

| **Table 1. Baseline characteristics of study population (N=30)** | |
|---|---|
| Sex, n (%) | Female, 30 (100) |
| Age (years), mean ± SD | 48 ± 9.6 |
| CD4+ T cell count (cells/mm$^3$), median (IQR) | 639 (414 – 823) |
| Systolic blood pressure (mmHg), mean ± SD | 135 ± 11 |
| Hemoglobin A1C (%) | 5.8 ± 0.4 |
| High-sensitivity C-reactive protein (mg/L), median (IQR) | 6.6 (2.4 – 18.6) |
| Body mass index (kg/m$^2$), mean ± SD<br>range | 42.2 ± 8.0<br>28.4 – 56.9 |
| Body fat %, mean ± SD | 51.36 ± 5.1 |

- CBF, CVR, Kw were not associated with anthropometric measures, or MetS severity z-score or DXA measures.
- Body fat percentage was positively associated with ATT in the cortical, subcortical, and white matter regions and the whole brain (Table 2).
- BMI and gray matter D* were associated (R2 0.23; β 0.00002; p 0.02).
- Age, systolic blood pressure, glucose control and lipid profile were not significantly associated with ATT imaging findings. Age correlated with most IVIM metrics (except D*) and volumes in both white and matter gray matter.

| **Table 2. Anthropometric and DXA measures associated with ATT** | | | |
|---|---|---|---|
| | BMI | Body fat % | Android fat mass |
| **Gray matter** | | | |
| Cortical | $R^2$ 0.16; β 7.8; p 0.04 | $R^2$ 0.23; β 14.7; p 0.01 | $R^2$ 0.21; β 0.06; p 0.02 |
| Subcortical | $R^2$ 0.18; β 8.4; p 0.03 | $R^2$ 0.25; β 15.7; p 0.01 | $R^2$ 0.22; β 0.06; p 0.02 |
| **White matter** | $R^2$ 0.21; β 9.5; p 0.02 | $R^2$ 0.28; β 17.4; p 0.01 | $R^2$ 0.23; β 0.06; p 0.01 |
| **Whole brain** | $R^2$ 0.17; β 8.0; p 0.04 | $R^2$ 0.24; β 15.2; p 0.01 | $R^2$ 0.21; β 0.06; p 0.02 |

## CONCLUSIONS

- In obese African females with MetS and HIV suppressed on ART, ATT increased in all brain regions with increased body fat composition; most notably body fat percentage.
- This finding is also reflected in alterations of the microcirculation, as measured by the IVIM metric D*.
- ATT is an index of vascular resistance that increases in the presence of cerebrovascular disease.
- The population was homogenous with similar characteristics which controlled for known confounders of cerebral hemodynamics: sex, age, controlled chronic disease.

**Our data support that asymptomatic PWH suppressed on ART with metabolic syndrome have altered cerebral hemodynamics. The clinical implication of this finding should be established in future studies.**

## REFERENCES

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## ADDITIONAL INFORMATION

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