Technology Development and Longitudinal Neuroimaging of children with HIV infection

Barbara Laughton, Stellenbosch University
Ernesta Meintjes, University of Cape Town
Andre van der Kouwe, MGH

Motivation

- Sub-Saharan Africa has 10% of the worlds' population, but 68% of HIV positive adults and 90% of HIV positive children.
- The highest absolute number of HIV-infected people in sub-Saharan Africa lives in South Africa.
- Most of the world's children born with HIV live in sub-Saharan Africa.
- Most infected children younger than 5 have acquired the virus through perinatal mother-to-child-transmission.
- With increased access to antiretroviral treatment (ART), these children are surviving longer with chronic HIV infection.
- There is a concomitant increase in cognitive deficits and impaired brain development by the time the children reach school age.

Specific Aims

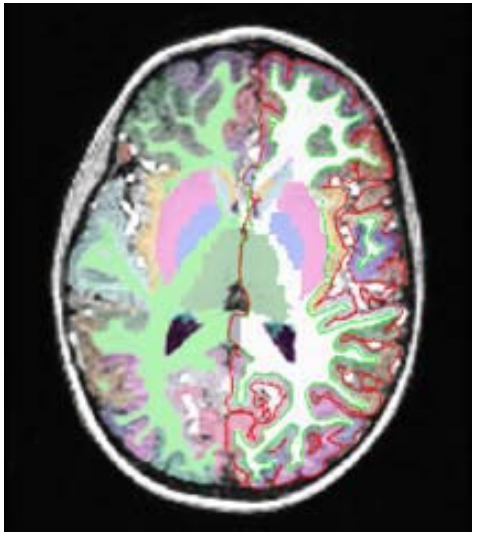
- Neuroimaging and neurodevelopmental assessment at 5, 7 and 9 years of 124 HIV infected children and controls that have been followed since birth
- 3 Treatment arms

Arm 1 - Deferred ART when needed 22	Arm 2 – Early (40 weeks) 32	Arm 3 – Early (96 weeks) 32

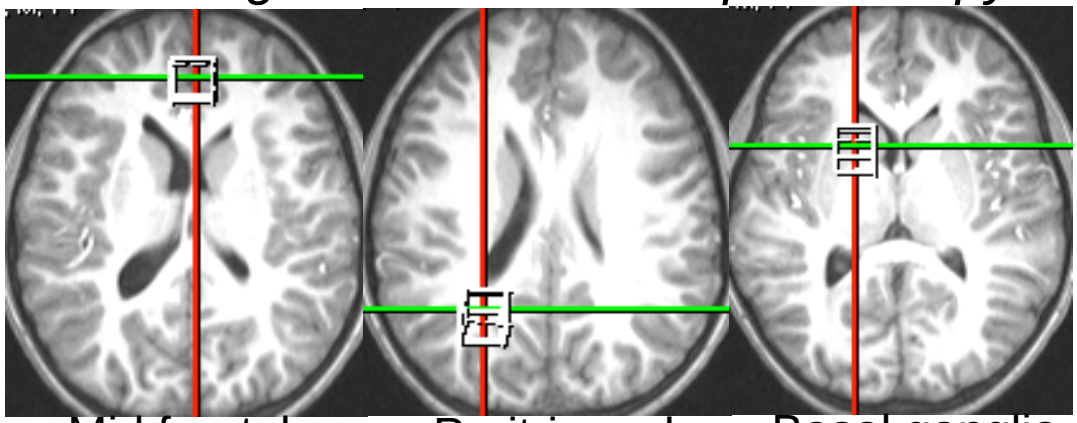
- 44 control children

Neuroimaging Protocol

Morphometry



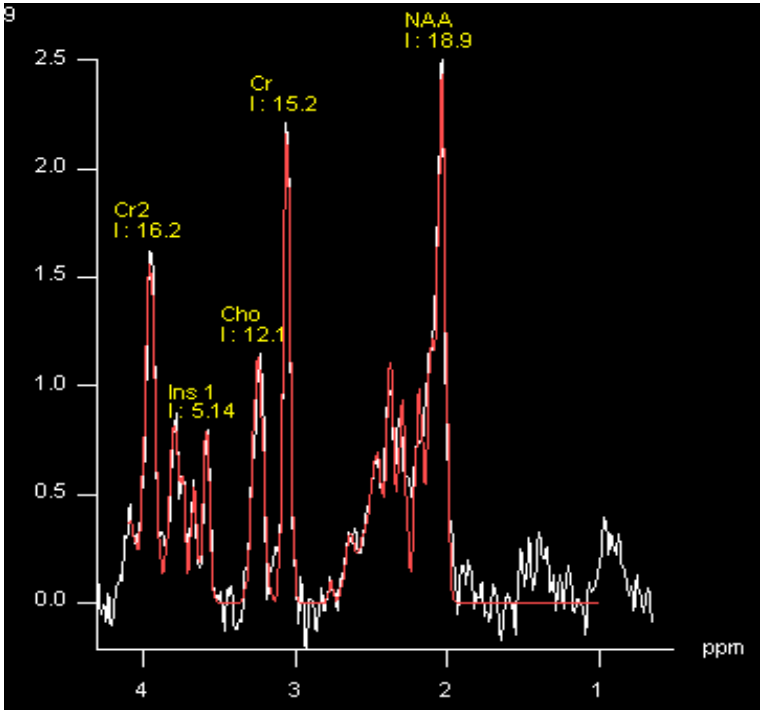
Magnetic Resonance Spectroscopy



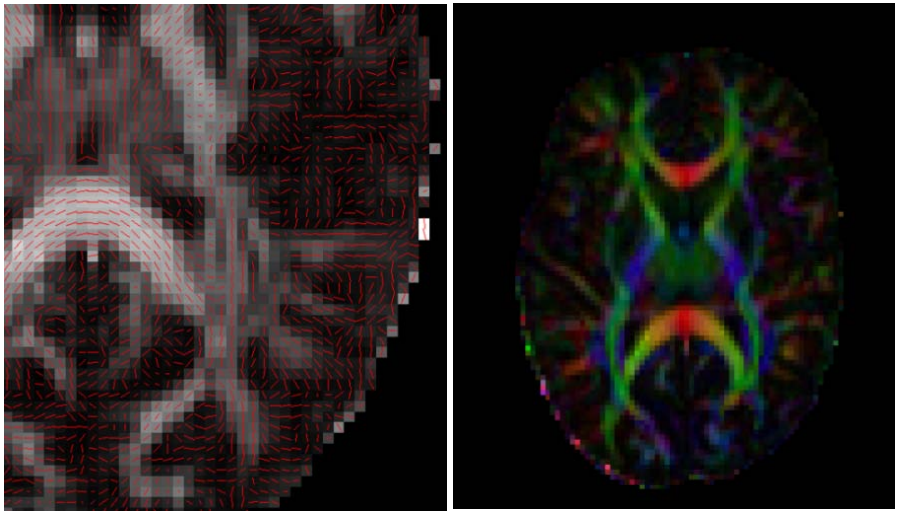
Mid frontal gray matter

Peritrigonal white matter

Basal ganglia



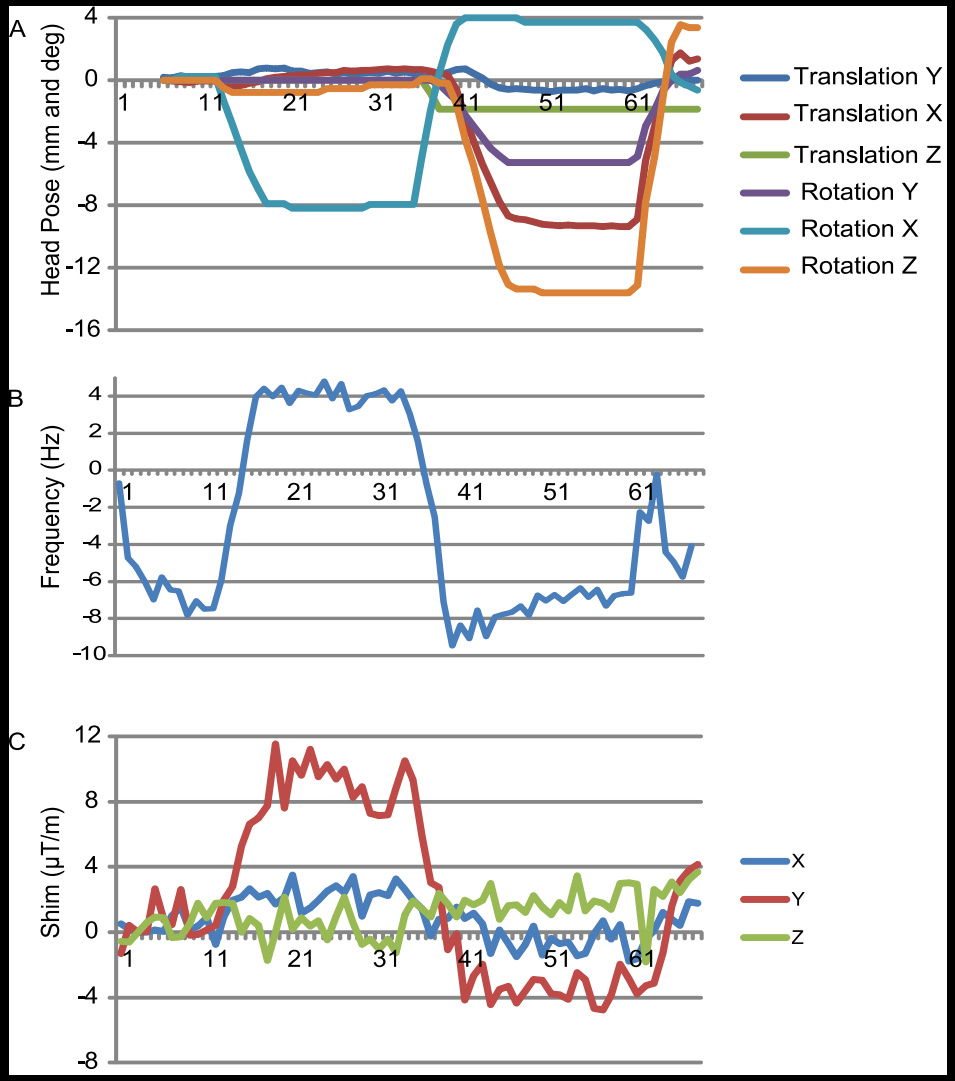
Diffusion Tensor Imaging

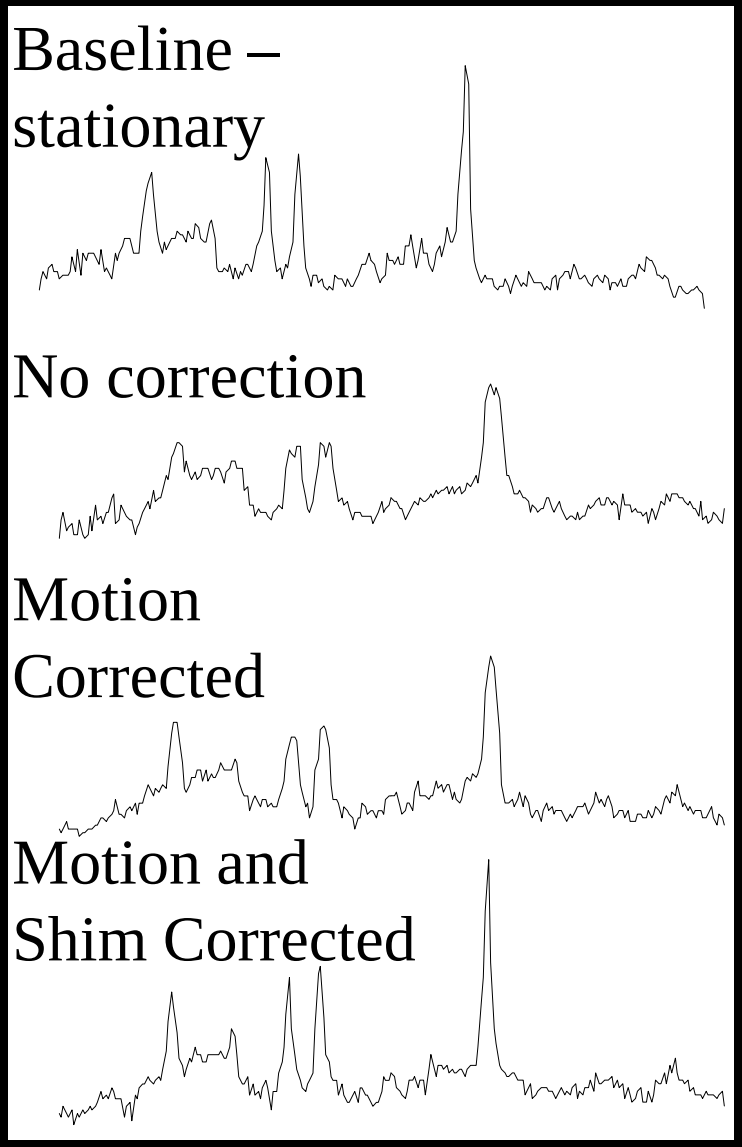


Progress to Date

- Completed neuroimaging of 76 children at age 5 years (25 controls, 51 HIV-infected – 16 arm 1 / 16 arm 2 / 19 arm 3).
- Performed neuroimaging of 28 children at age 7 years.
- Use motion and shim correction technology to obtain good quality spectra and images despite significant motion

Real-time motion and shim correction in MRS





Hess et al., MRM 2011, 66(2):314-23

Basal ganglia MRI: results summary

HIV-1 Infection diagnosed between 6 – 12 weeks of age and CD4 % > 25%.

Arm 1: ART treatment deferred until needed,
Arm 2: Short-course – 40 weeks of ART (12 weeks – 1 year),
Arm 3: Long-course – 96 weeks of ART (12 weeks – 2 years).

	Arm 1	Arm 2	Arm 3	Controls	F-statistic p-value
Age	5.4 ± 0.27	5.5 ± 0.32	5.4 ± 0.36	5.4 ± 0.37	0.86

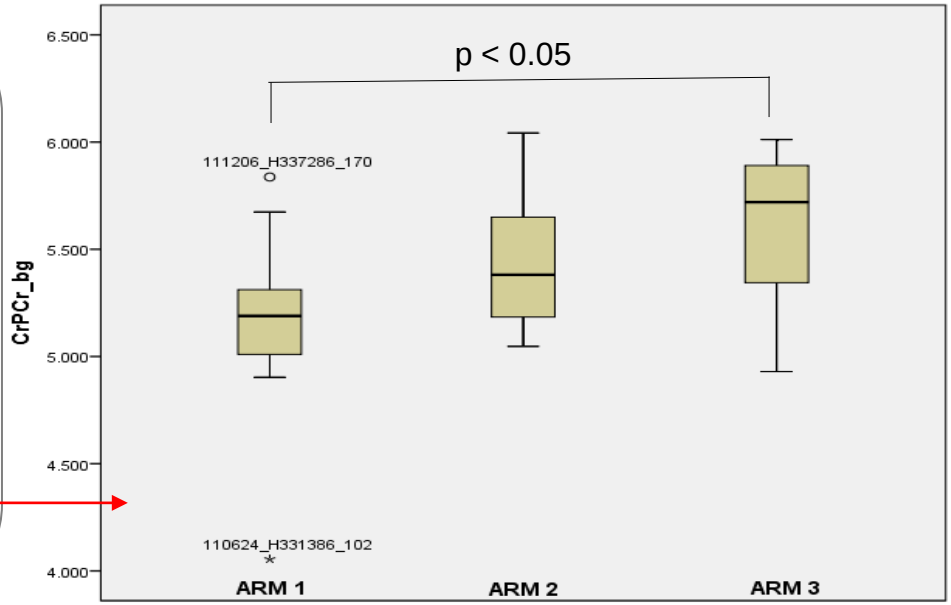
***Xhosa-speaking subjects only**

Comparison of metabolite values between 34 HIV-infected and 10 healthy 5-year old children.

Metabolite	Total infected	Controls	*t*-test p-value
Glu	7.2 ± 0.97	7.1 ± 0.89	0.76
GPC	1.1 ± 0.11	1.1 ± 0.11	0.61
Ins	3.1 ± 0.51	3.1 ± 0.44	0.73
NAA	5.3 ± 0.42	5.0 ± 0.40	0.05
GPC+PCh	1.1 ± 0.12	1.1 ± 0.10	0.51
NAA+NAAG	5.6 ± 0.44	5.3 ± 0.34	0.06
Cr+PCr	5.4 ± 0.42	5.3 ± 0.42	0.72
Gln+Glu	9.3 ± 1.1	8.9 ± 1.3	0.30

Comparison of metabolite values in the basal ganglia among three groups (Arm 1, Arm 2, and Arm 3) of the 34 HIV-infected 5-year children

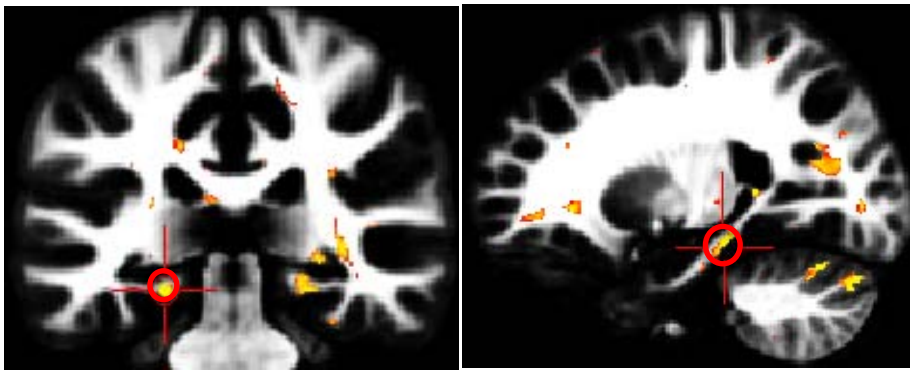
Metabolite	Arm 1 (12)	Arm 2 (11)	Arm 3 (11)	F-statistic p-value
Glu	6.8 ± 1.1	7.2 ± 0.8	7.6 ± 0.83	0.13
GPC	1.0 ± 0.13	1.1 ± 0.11	1.1 ± 0.060	0.14
Ins	3.0 ± 0.43	3.2 ± 0.71	3.2 ± 0.36	0.45
NAA	5.2 ± 0.46	5.4 ± 0.42	5.4 ± 0.39	0.51
GPC+PCh	1.0 ± 0.13	1.1 ± 0.14	1.1 ± 0.050	0.11
NAA+NAAG	5.5 ± 0.50	5.7 ± 0.38	5.7 ± 0.42	0.34
Cr+PCr	5.2 ± 0.44	5.5 ± 0.35	5.6 ± 0.36	0.03
Gln+Glu	8.7 ± 1.1	9.5 ± 1.2	9.7 ± 1.1	0.10

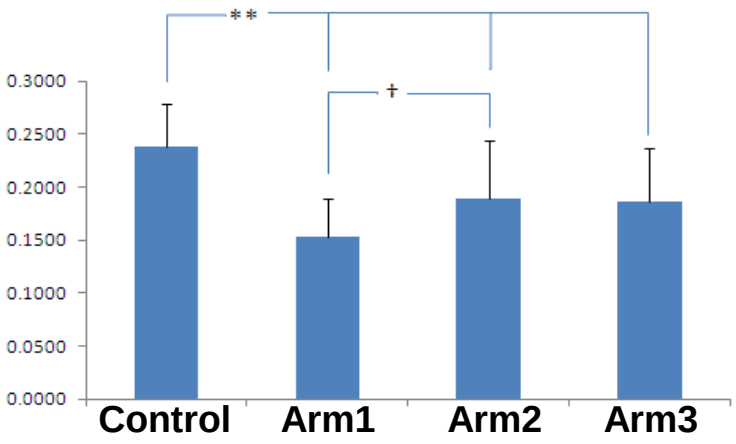


DTI: results summary

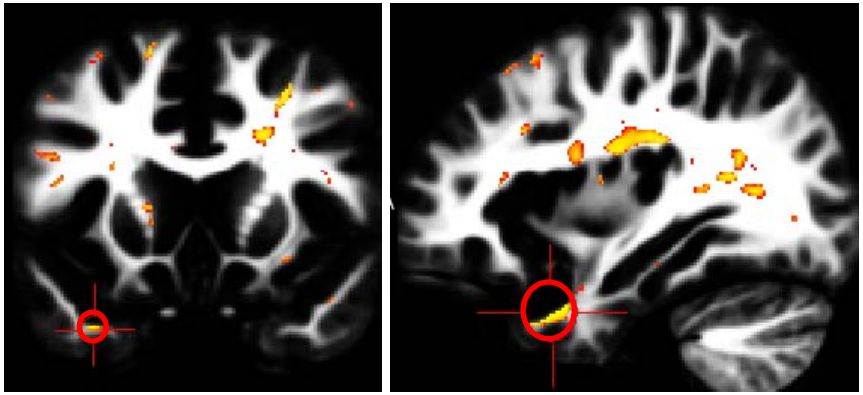
20 white matter regions where FA in HIV < Controls (p<0.01, cluster-size corrected)
Significant differences between arms in 2 of these regions

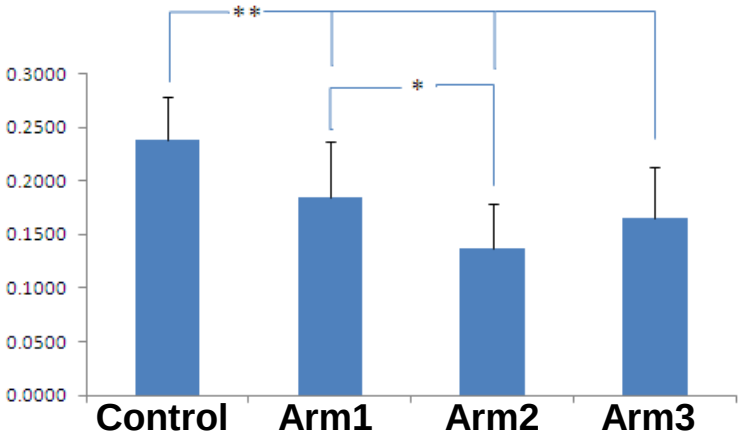
Left Parahippocampal Gyrus



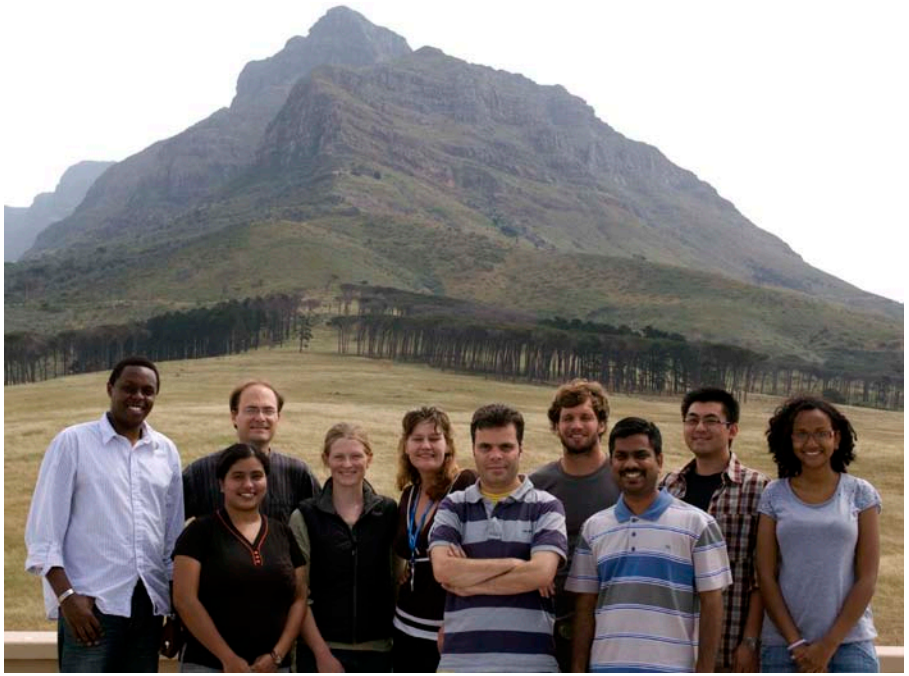


Left Superior Temporal Gyrus





Acknowledgements



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