Clinical correlates of cognitive decline in HIV

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BACKGROUND

- ART has reduced HIV morbidity and LTC illness has emerged

- Cognitive impairment persists despite ART

- Estimated prevalence of HAND: 30-50% [1,2]

- Clinical factors that have been linked with HAND include CPE score, diabetes, age, survival duration, nadir CD4 T-cell counts, and baseline viral load [3,4]

- Evidence of detectable neuroimaging correlates in frontal and parietal lobes [5]

1. Heaton RK et al. Neurology. 2010;75(23):2087-96. 2. Sacktor N et al. J Neurovirol. 2002;8(2):136-42. 3. Cohen RA et al. J Neurovirol. 2010;16(1):25-32
4. Antinori A et al. Clin Infect Dis (2013) 56 (7): 1004-1017 5. Towgood KJ et al. Cortex. 2012;48(2):230-41.

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AIMS

To establish any correlation between cognitive deficits in PLHIV on stable ART and clinical factors including

- HIV related factors (nadir CD4 count, infection duration, time with and without HAART)
- Metabolic co-morbidities
- Alcohol and drug use

To correlate these with Diffusion Tensor Imaging (3T MRI)

METHODS

- Cross-sectional study

- 78 HIV positive MSM, 25-74 years, on ART with VL <50 for 6/12

- 48 HIV negative controls, 26-76 years

- Exclusions: history of CNS-AIDS defining illnesses, confounding neurological or psychiatric diagnoses, major head trauma, excess recreational drug or alcohol use, uncontrolled chronic medical condition.

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INVESTIGATIONS

- **Clinical evaluation**- structured clinical interview and medical records review, BDI, BAI, PRMQ

- **Neuropsychological assessments** (*tests selected were largely based on those used by the HIV Neurobehavioural Research Centre in San Diego*) - the following domains were assessed: memory, complex attention, executive function, perceptual motor function

- The cognitive scores for the HIV and control groups were compared using analysis of covariance. Regression models were run to investigate whether cognition correlated with key explanatory factors

- **DTI 3T MRI brain imaging**- Datasets were pre-processed and analysed using tools from the Oxford Centre for Functional MRI of the Brain Software Library

Demographic and clinical variables

	Control (n=48)	HIV (n=78)	*p*
Age	43.73 (13.51)	46.87 (12.38)	*.184*
Years in education	16.42 (1.76)	14.97 (2.46)	*<0.01*
NESB	10 (21%)	8 (10%)	*.099*
FSIQ	121.42 (11.57)	113.19 (13.42)	*.001*
Depression (BDI)	4.90 (3.39)	7.99 (7.36)	*.002*
Anxiety (BAI)	3.67 (3.26)	6.33 (7.16)	*.005*
PRMQ- prospective	56.81 (9.14)	51.27 (10.84)	*.004*
PRMQ- retrospective	58.62 (7.75)	54.53 (9.37)	*.013*
Alcohol units per week	11.59 (9.18)	11.48 (9.29)	*.948*
Drug use in past 3 months	8 (17%)	18 (23%)	*.388*
CD4 current		691.38 (280.58)	
CD4 nadir		210.09 (128.64)	
Infection duration (years)		11.22 (6.52)	
Treatment duration (years)		8.27 (5.05)	
Time without treatment (years)		2.95 (3.93)	
CPE score		6.73 (1.48)	
Metabolic comorbidities		18 (14%)	

Group difference analysis for neuropsychological assessment showed significant difference in cognitive function between HIV and control groups

	Control, n=48 mean (SD)	HIV, n=78 mean (SD)	*Group difference p value*
Global cognition	0.00 (0.49)	-0.46 (0.69)	*.003*
Executive function	-0.01 (0.60)	-0.44 (0.81)	*.030*
Complex attention	0.00 (0.61)	-0.47 (0.88)	*.040*
Memory	0.07 (0.63)	-0.42 (0.78)	*.014*
Perceptual motor function	0.00 (0.79)	-0.68 (1.13)	*.002*

Table 2: Mean (SD) z-scores for cognitive performance

Diffusion Tensor Imaging 3T MRI
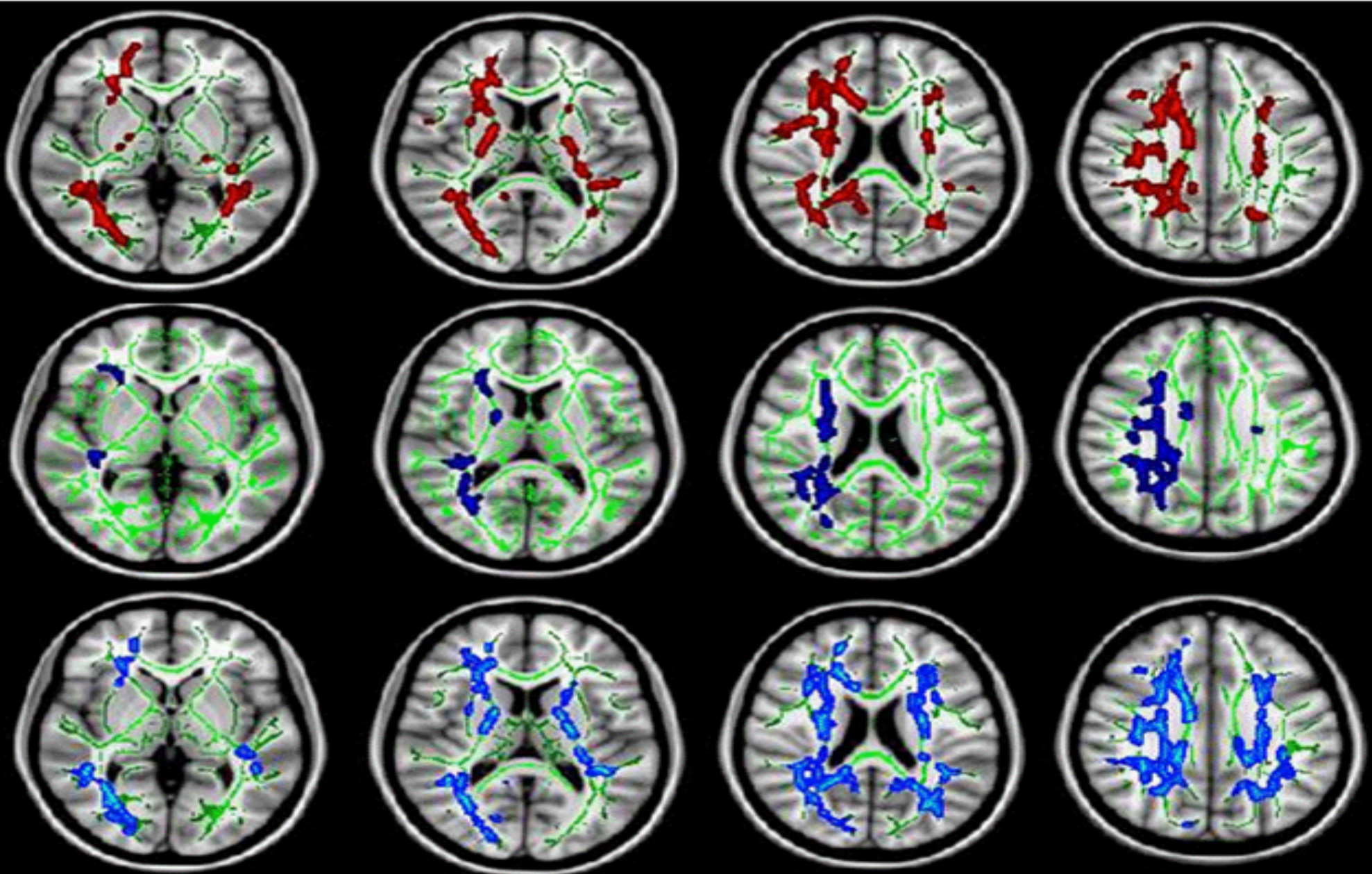
Analysis of effect of clinical, psychiatric and lifestyle variables with cognitive function

	Memory p	Complex attention p	Executive function p	Perceptual motor function p
Current CD4	.256	.552	.440	.128
Nadir CD4	.350	.119	.378	.601
Infection duration	.053	.842	.452	.965
Treatment duration	.319	.600	.601	.266
Time without treatment	.704	.773	.654	.512
CPE score	.048	.558	.659	.900
Metabolic co-morbidities	.236	.771	.639	.836
Depression (BDI)	.814	.144	.061	.967
Anxiety (BAI)	.005	**<.001**	**<.001**	.078
Weekly alcohol units	.891	.397	.499	.361
Drug use in past 3 months	.717	.716	.652	.979

Notes: All models controlled for age, years in education and ESB and alpha was set at p=.001 to correct for running multiple analyses.

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CONCLUSIONS

- There was a significant **difference in cognition** between the HIV and control groups

- There were **white matter changes in HIV on DTI** (MD and FA measures)

- **Anxiety** correlated significantly with complex attention and executive function

- HIV duration and ART duration correlated with perceptual motor function, but not when we adjusted for age.

- No correlation was found between cognitive function and CD4, nadir CD4, CPE score or metabolic factors.

ACKNOWLEDGMENTS

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