POPPY

Pharmacokinetic and clinical observations in people over 50

Clinical Research Cerebral MRI findings in HIV-positive subjects and matched controls

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INTRODUCTION

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- Neurological conditions affecting the central nervous system, such as impairment in cognitive function and strokes, remain prevalent in people living with HIV (PLWH)[1,2]
- Cerebral magnetic resonance imaging (MRI) scans are commonly undertaken in PLWH as part of a full clinical work-up
- PLWH tend to have many non-specific abnormalities on clinical MRI scans[3]

[1]Winston A et al (2013) *PLoS One* [2]Benjamin LA et al (2016) *Neurol Neuroimmunol Neuroinflamm* [3]Haddow LJ et al (2014) *AIDS Patient Care STDS*

INTRODUCTION

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- A recent study has shown that PLWH are more likely to have cerebral MRI abnormalities than controls

HIV More Than Doubles Odds of Cerebral Small-Vessel Disease in French Study

Conference on Retroviruses and Opportunistic Infections (CROI), February 13-16, 2017, Seattle

  - Research imaging modalities
  - Control group not well matched

- We aimed to assess if these findings were reflected in clinical MRI scans

AIMS

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To describe and compare the clinical MRI report findings of PLWH and appropriately selected controls

To assess associations between MRI report findings and HIV status, demographic and lifestyle factors

To assess associations between clinical MRI reports and cognitive function

METHODS

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- POPPY is a multicenter, prospective observational study looking at the effects of advancing age on PLWH

- As part of a collaborative sub-study with the AGEhIV cohort in the Netherlands (called COBRA) we recruited older PLWH and older HIV-negative controls into a neuroimaging sub-study

METHODS

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Inclusion Criteria

PLWH	HIV-negative controls
Age > 50 years	
Informed Consent	
On antiretroviral therapy with viral load <50 copies/mL	Appropriately selected control population

Exclusion Criteria

- Current psychiatric or neurological disorders
- Contra-indication for MRI or Lumbar Puncture (LP)
- Daily recreational drug use (except cannabis)
- Excess alcohol (>48 units/week)

METHODS

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- 59 PLWH, 29 HIV-negative controls
- Information on demographic and lifestyle factors was collected from the POPPY study database
- Detailed cognitive test battery testing 6 different domains
  - Test scores were standardised to T-scores accounting for age and education
  - Global T-scores were obtained as average of individual domain T-scores

METHODS - MRI analysis

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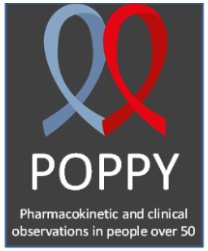
- Cerebral MRI scan at 3 Tesla
  - Reviewed by a neuroradiologist for reporting purposes and to ensure no contraindication for LP
  - Clinical MRI report generated

Description	Category
No abnormalities/ In-keeping with age	Normal
Abnormalities not in-keeping with age	Abnormal
Specific abnormality mentioned	Eg. WML
Aetiology	Microvascular disease (MVD) or non-specific

STATISTICAL METHODS



- Prevalence of common MRI abnormalities was compared between PLWH and controls using the Chi-square test or Fisher's exact test

- Demographic and lifestyle factors were added in a multivariable analysis to identify potential predictors of MRI abnormalities

- Global T scores were compared between individuals with and without MRI abnormalities using the Student's T-test

RESULTS – Demographic Factors

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		HIV-negative controls (n=29)	PLWH (n=59)
Age in years, mean (SD)		61 (7)	59 (7)
Gender, n (%)	**Males**	23 (79%)	50 (85%)
	Females	6 (21%)	9 (15%)
WCST Education, median (IQR)		16 (12,16)	15 (12,16)
Ethnicity, n (%)	**White**	28 (97%)	50 (85%)
	Black-African	1 (3%)	9 (15%)
Sexual Orientation, n (%)	**Heterosexual**	13 (45%)	14 (24%)
	MSM	16 (55%)	45 (76%)

SD – Standard Deviation, WCST – Wisconsin Card Sorting Test, IQR – Inter-quartile range, MSM – Men who have sex with men

RESULTS – Lifestyle Factors

		HIV-negative controls (n=29)	PLWH (n=59)
BMI [kg/m^2], median (IQR)		25 (23,30)	25 (23,29)
Hypertension*, n (%)		11 (39%)	30 (52%)
Smoking status, n (%)	Never smoked	13 (45%)	18 (31%)
	Ex-smoker	6 (21%)	25 (42%)
	Current smoker	10 (34%)	16 (27%)
Consume Alcohol*	Yes	25 (93%)	42 (82%)
	No	2 (7%)	9 (18%)
Anti-HCV Antibody Positive		NIL	9 (15%)

*Missing results of Hypertension (n=2), Alcohol intake (n=10). Hypertension defined as 3 measures of systolic blood pressure (BP) ≥ 140mmHg or 3 measures of diastolic BP ≥ 90mmHg or on antihypertensive

RESULTS – HIV Parameters

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	PLWH (n=59)
CD4 count [cells/µL], median (IQR)	600 (472, 752)
Nadir CD4 count [cells/µL], median (IQR)	160 (100, 235)
CD4:CD8 Ratio, median (IQR)	0.770 (0.523, 0.938)
Prior Clinical AIDS, n (%)	16 (27%)

RESULTS – MRI Findings

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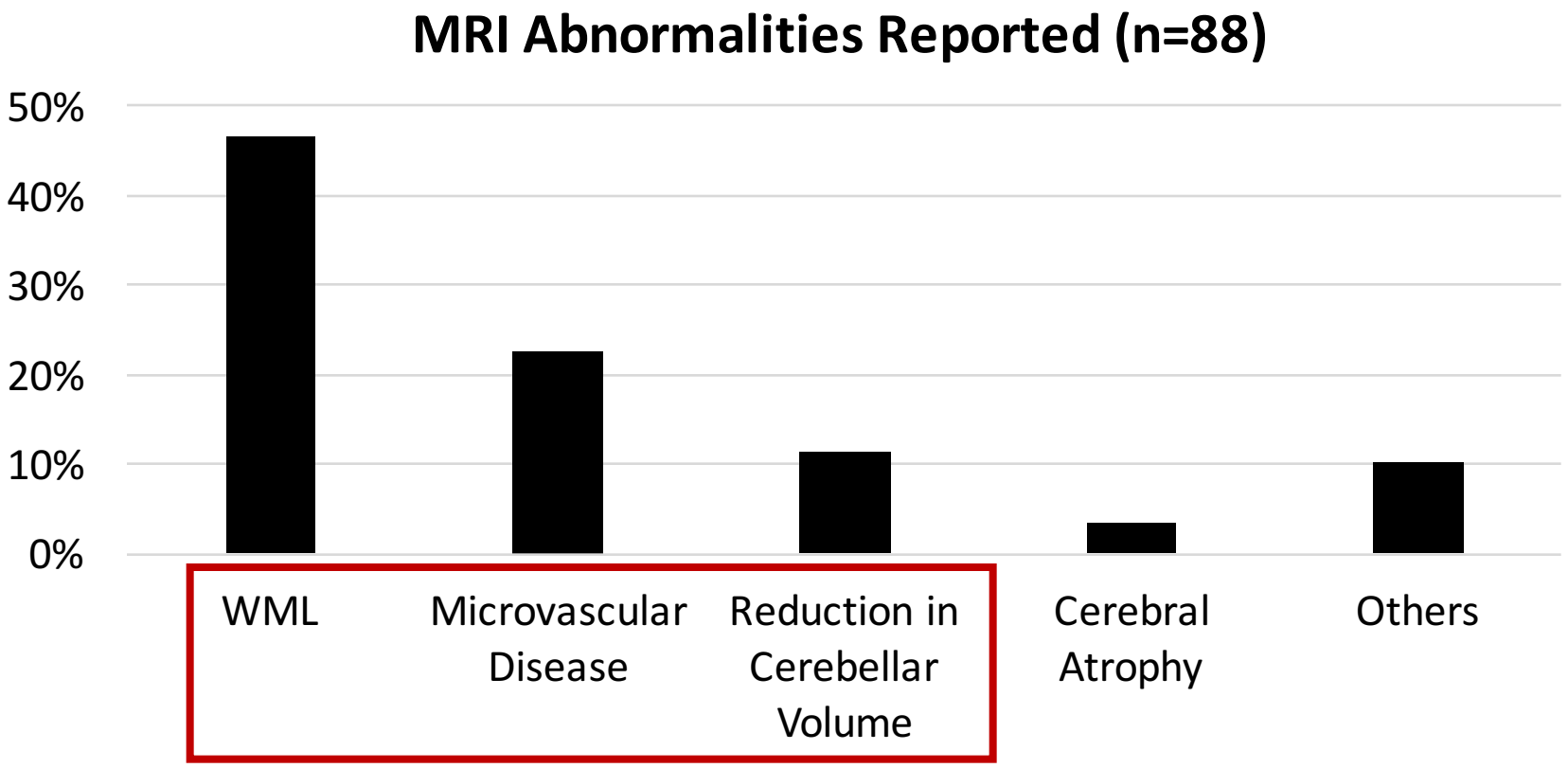
- 47.7% of the cohort had an abnormal MRI



RESULTS – MRI Findings

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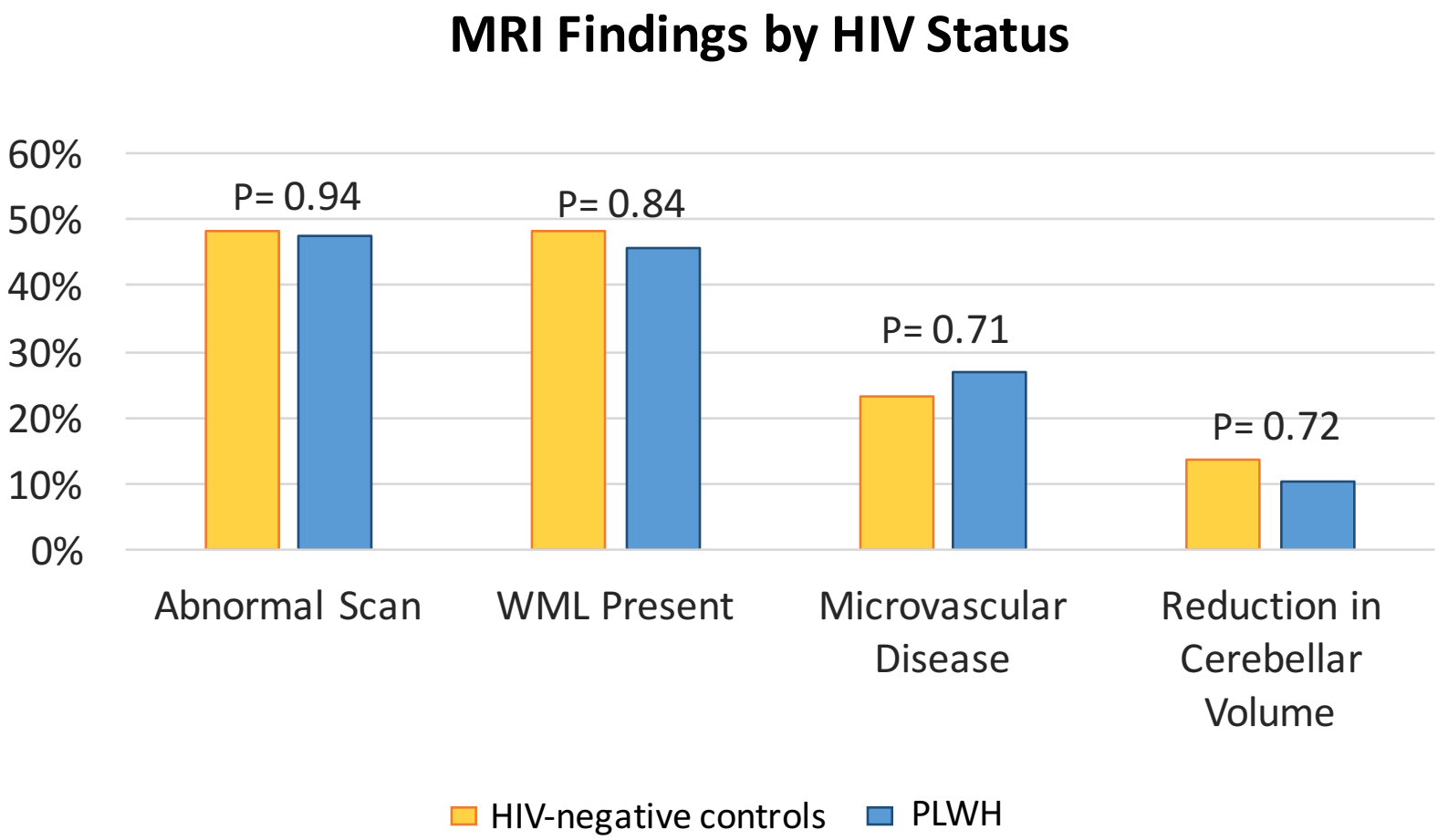

RESULTS – Predictors of Abnormalities

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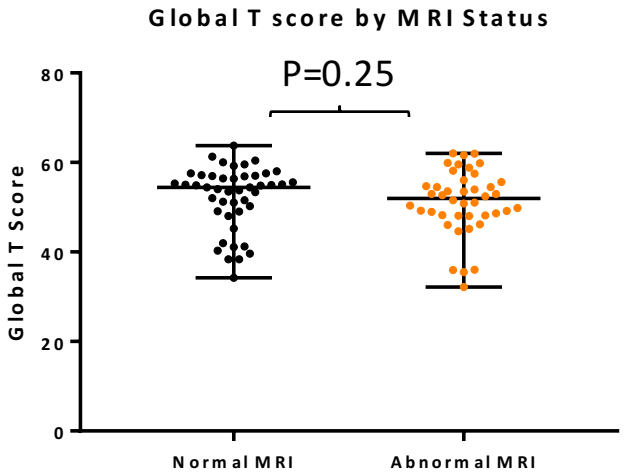
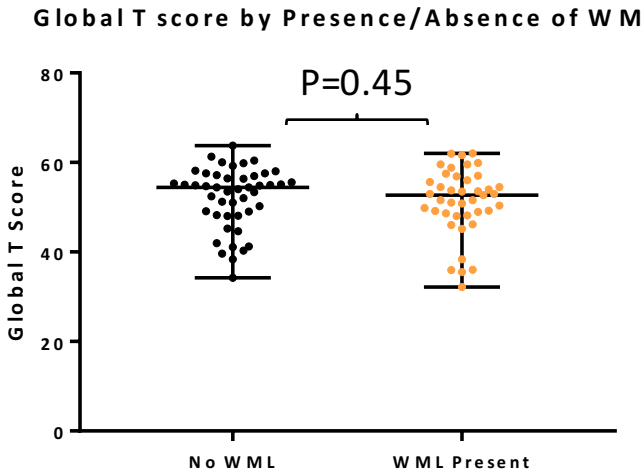
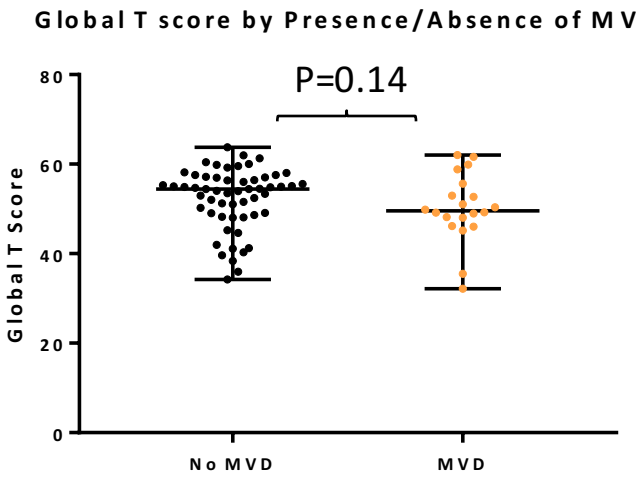
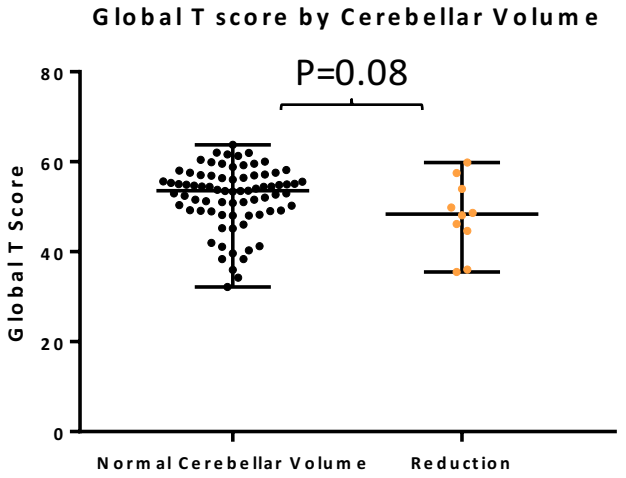
	Abnormal MRI Scan		WML		Microvascular Disease	
	Odds Ratio (95% CI)	P	Odds Ratio (95% CI)	P	Odds Ratio (95% CI)	P
Age/5 years	1.40 (1.00 – 1.99)	0.05	1.09 (0.79 – 1.09)	0.61	1.28 (0.88 – 1.88)	0.20
HIV Status	0.94 (0.36 – 2.45)	0.90	0.71 (0.27 – 1.88)	0.49	1.20 (0.36 – 4.03)	0.76
BMI/2kg/m²	-	-	-	-	1.21 (1.00 – 1.46)	0.05
Hypertension	1.48 (0.59 – 3.72)	0.41	3.05 (1.19 – 7.82)	0.02	2.03 (0.64 – 6.46)	0.23

RESULTS – Cognitive Tests









Lines indicating median, maximum and minimum scores

SUMMARY

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High rates of MRI abnormalities were observed but there were no differences associated with HIV serostatus

MRI abnormalities are associated with hypertension and BMI but are not associated with HIV status

Clinical MRI findings are not associated with cognitive function

DISCUSSION

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Strengths

- Appropriate control group
- All PLWH in our study were virally suppressed which is clinically relevant[4]

Limitations

- This was undertaken in a cohort which did not present with cognitive complaints
- Study was not powered to determine associations between MRI findings and cognitive results

[4]Skingsley A (2015) HIV New Diagnoses, Treatment and Care in the UK 2015 report.

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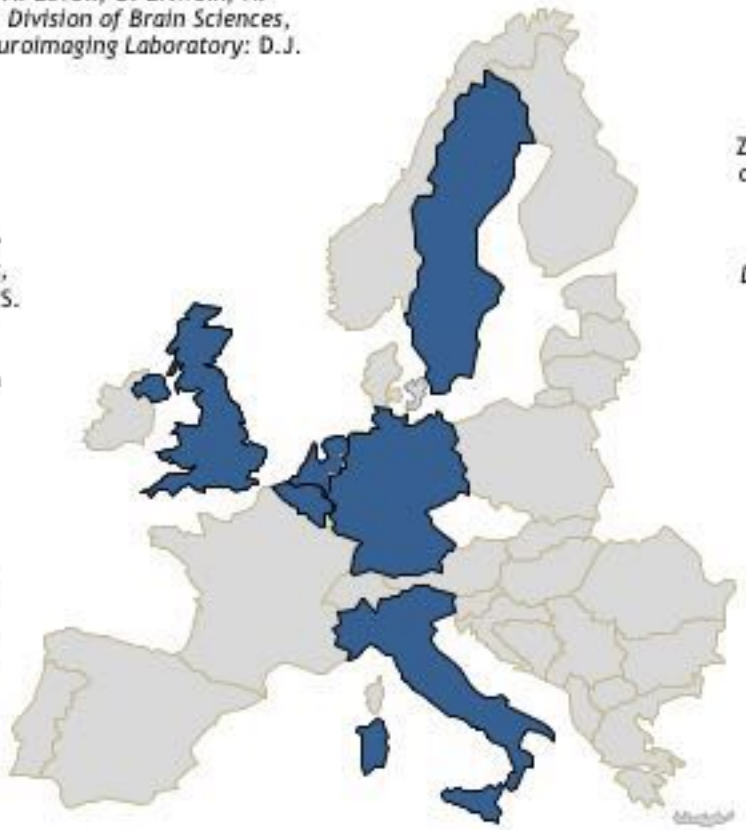

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