Hyperintensities in Mild Acute Focal Neurology
Supplementary File

Aims

1. Assess whether there was a difference in the total Scheltens score for patients with different final diagnoses (i.e. minor stroke, TIA, migraine, functional neurological disorder, other) and separately explore whether sex played a role.* A secondary aim was to ascertain the observed power, for this part of the analysis, to allow for appropriate interpretation of the results and also inform future study designs.
   *Note: The final diagnosis was made by the stroke consultant or senior registrar responsible for each patient.
2. Assess whether there was an association between the total Scheltens score and the following variables: sBP; dBP; pulse pressure; mRS; NIHSS; MoCA; cumulative score of five risk factors; age. A secondary aim was to assess whether there was an association between each individual component of the Scheltens scale (i.e. WMH, GMH, PVH, IFTH) and the above list of variables. The purpose of this was to explore whether statistically significant results in relation to the total Scheltens score (i.e. global changes) were also reflected at the regional level with the individual components of the Scheltens scale and identify any patterns of clinical relevance.

Methods

Ethical Approval

Approval for this study was granted by the North of Scotland Research Ethics Committee (reference number: 11/NS/0030). The study was also registered with the NHS Grampian Research and Development Department (reference number: 2011ST003). Written informed consent was obtained, from all study participants, prior to taking part in any research activity.

Study Design

This was a prospective neuroimaging study with patients referred from the NHS Grampian neurovascular clinic or the Acute Stroke Unit, between 2012 and 2014, with acute focal minor neurological symptoms consistent with a possible diagnosis of short duration ischemia (Easton *et al.*, 2009; Fischer *et al.*, 2010) for whom MRI would have been the investigation of choice. In terms of exclusion criteria, apart from standard MRI contraindications, the following also applied: i) < 18 years; ii) hemorrhagic stroke; iii) chronic mental health or neurodegenerative condition and brain tumours; and iv) moderate to severe carotid artery stenosis from doppler ultrasound. A detailed list of the inclusion and exclusion criteria is available by Varsou *et al.* (2014).

Scanning Protocol

Imaging data were acquired on the Aberdeen Biomedical Imaging Centre 3.0 Tesla Philips Achieva X-series MRI scanner (Philips Healthcare, Best, The Netherlands;

http://www.philips.com/global/index.page) with a Siemens 32-channel receive-only phased-array head coil (Siemens Medical Systems, Iselin, NJ; http://www.healthcare.siemens.co.uk). The structural sequences had the following parameters:

i) axial T_2-weighted short-τ inversion recovery spin echo structural sequence with a total acquisition time of 3 minutes and 6 seconds (repetition time of 3000 ms, echo time of 80 ms, inversion time τ of 100-150 ms, flip angle of 90˚, 230 × 184 × 129 mm^3 field of view, 0.8 × 0.8 mm^2 voxel size, and 26 slices);

ii) axial FLAIR spin echo structural sequence with a total acquisition time of 5 minutes and 52 seconds (repetition time of 11000 ms, echo time of 125 ms, refocusing angle of 120˚, 230 × 230 × 144 mm^3 field of view, 0.7 × 0.9 mm^2 voxel size, and 29 slices).

Scoring of Hyperintensities

The signal hyperintensities were assessed on axial T_2 and FLAIR MRI structural scans, provided by NHS Grampian PACS, using the Scheltens semiquantitative visual scoring scale by Murray *et al.* (2012). The WMH and PVH were assessed on FLAIR, whereas the GMH and IFTH were assessed on T_2. This method has a good interobserver and intraobserver reliability for total scores when compared to alternative scales (Murray, 2012). The Scheltens scale also quantifies the number and size of lesions within each of the different anatomical areas providing information not only at the global, but also the regional level (Scheltens *et al.*, 1993; Scheltens *et al.*, 1998). A trained assessor (OV), who was blinded to the patients' diagnosis at the time of the scoring, assessed the scans using the Scheltens scale. Additional information about the methodology is available in Murray *et al.* (2012) and Varsou *et al.* (2015).

Cumulative Risk Factors Score

A cumulative risk factors score was calculated from the following past medical history questions: i) hypertension; ii) hyperlipidemia; iii) diabetes mellitus; iv) ischemic heart disease; and v) previous TIA or stroke. A point was awarded for 'yes' answers to each of the above with the potential minimum to maximum range being 0 to 5.

Normality Test & Log Transformations

The Shapiro-Wilk test was used to assess normality for all numerical variables. Any variable, which was not normally distributed, was subsequently log transformed to base 10 (i.e. common log). The constant number '3' was also added to any variable that had values of 0, as it is not possible to take the log of 0. Details of the normality tests and log transformations are included in the table below.

Variable	Shapiro-Wilk	Log Transformation
Scheltens score	W (100) = 0.959, p=0.004	Lg10 (Scheltens score)
WMH	W (100) = 0.932, p<0.001	Lg10 (WMH)
GMH	W (100) = 0.971, p=0.028	Lg10 (GMH)
PVH	W (100) = 0.868, p<0.001	Lg10 (PVH)

IFTH	*W* (100) = 0.972, p=0.029	Lg10 (IFTH)
sBP	*W* (96) = 0.929, p<0.001	Lg10 (sBP)
dBP	*W* (96) = 0.926, p<0.001	Lg10 (dBP)
PP	*W* (96) = 0.945, p=0.001	Lg10 (PP)
mRS	*W* (100) = 0.525, p<0.001	Lg10 (mRS+3)
NIHSS	*W* (99) = 0.503, p<0.001	Lg10 (NIHSS+3)
MoCA	*W* (80) = 0.812, p<0.001	Lg10 (MoCA)
risk factors score	*W* (100) = 0.695, p<0.001	Lg10 (RF+3)
age	*W* (100) = 0.980, p=0.138	not log transformed

Statistical Analysis

A one-way ANOVA was used to assess for any significant differences between the total Scheltens scores and the different diagnoses. The observed power of this statistical test was also calculated. For the ANOVA, p values of < 0.05 were accepted as statistically significant. The Pearson's correlation coefficient was used to assess whether there was an association between the total/individual Scheltens scores and the various physical measurements/clinical assessments. The above analysis was performed in SPSS version 25 (IBM Corporation, Armonk, NY; http://www-01.ibm.com/software/analytics/spss/) by two independent researchers (OV & KT), who crosschecked all results to ensure no errors. To control for type I error (i.e. false positives) resulting from the multiple correlations, the Benjamini-Hochberg FDR procedure (Benjamini and Hochberg, 1995) was applied by an independent researcher (MS) as described in later parts of this supplementary file.

Descriptive Statistics

Descriptives

			Statistic	Std. Error
Age (years)	Mean		50.95	1.202
	95% Confidence Interval for Mean	Lower Bound	48.56	
		Upper Bound	53.34	
	5% Trimmed Mean		51.14	
	Median		51.50	
	Variance		144.533	
	Std. Deviation		12.022	
	Minimum		21	
	Maximum		82	
	Range		61	
	Interquartile Range		16	
	Skewness		-.287	.241
	Kurtosis		-.313	.478

Sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	55	55.0	55.0	55.0
	Female	45	45.0	45.0	100.0
	Total	100	100.0	100.0	

Final diagnosis

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	TIA	17	17.0	17.0	17.0
	Minor stroke	33	33.0	33.0	50.0
	Migraine	25	25.0	25.0	75.0
	Non-organic	7	7.0	7.0	82.0
	Other	18	18.0	18.0	100.0
	Total	100	100.0	100.0	

Clarification of final diagnosis if other

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid		82	82.0	82.0	82.0
	Acute vestibular neuronitis	1	1.0	1.0	83.0
	Anxiety	2	2.0	2.0	85.0
	Ballismus	1	1.0	1.0	86.0
	Global transient amnesia	1	1.0	1.0	87.0
	Left ulnar neuropathy	1	1.0	1.0	88.0
	Meniere's disease	1	1.0	1.0	89.0
	Minor contusion or focal seizure	1	1.0	1.0	90.0
	Neuropraxia	1	1.0	1.0	91.0
	Partial seizure	1	1.0	1.0	92.0
	Sporadic CJD	1	1.0	1.0	93.0
	Stress	2	2.0	2.0	95.0
	Subacute cerebellar infarct and migraine	1	1.0	1.0	96.0
	Unclear	4	4.0	4.0	100.0
	Total	100	100.0	100.0	

Descriptives

			Statistic	Std. Error
Sum of risk factors	Mean		.72	.109
	95% Confidence Interval for Mean	Lower Bound	.50	
		Upper Bound	.94	
	5% Trimmed Mean		.61	
	Median		.00	
	Variance		1.194	
	Std. Deviation		1.092	
	Minimum		0	
	Maximum		4	
	Range		4	
	Interquartile Range		1	
	Skewness		1.387	.241
	Kurtosis		.812	.478

Descriptives

			Statistic	Std. Error
Systolic blood pressure (mmHg)	Mean		128.33	1.807
	95% Confidence Interval for Mean	Lower Bound	124.75	
		Upper Bound	131.92	
	5% Trimmed Mean		127.34	
	Median		125.00	
	Variance		313.467	
	Std. Deviation		17.705	
	Minimum		98	
	Maximum		200	
	Range		102	
	Interquartile Range		20	
	Skewness		1.103	.246
	Kurtosis		2.210	.488

Descriptives

			Statistic	Std. Error
Diastolic blood pressure (mmHg)	Mean		80.21	1.087
	95% Confidence Interval for Mean	Lower Bound	78.05	
		Upper Bound	82.37	
	5% Trimmed Mean		79.73	
	Median		80.00	
	Variance		113.367	
	Std. Deviation		10.647	
	Minimum		50	

	Maximum		119	
	Range		69	
	Interquartile Range		15	
	Skewness		.827	.246
	Kurtosis		2.541	.488

Descriptives

			Statistic	Std. Error
Pulse pressure (sBP-dBP; mmHg)	Mean		48.13	1.330
	95% Confidence Interval for Mean	Lower Bound	45.48	
		Upper Bound	50.77	
	5% Trimmed Mean		47.53	
	Median		45.00	
	Variance		169.816	
	Std. Deviation		13.031	
	Minimum		17	
	Maximum		94	
	Range		77	
	Interquartile Range		18	
	Skewness		.772	.246
	Kurtosis		1.190	.488

Descriptives

			Statistic	Std. Error
Modified Rankin Scale (0-6)	Mean		.30	.061
	95% Confidence Interval for Mean	Lower Bound	.18	
		Upper Bound	.42	
	5% Trimmed Mean		.22	
	Median		.00	
	Variance		.374	
	Std. Deviation		.611	
	Minimum		0	
	Maximum		4	
	Range		4	
	Interquartile Range		1	
	Skewness		2.977	.241
	Kurtosis		13.043	.478

Descriptives

			Statistic	Std. Error
NIHSS (/42)	Mean		.32	.073
	95% Confidence Interval for Mean	Lower Bound	.18	
		Upper Bound	.47	
	5% Trimmed Mean		.20	
	Median		.00	
	Variance		.527	
	Std. Deviation		.726	
	Minimum		0	
	Maximum		3	
	Range		3	
	Interquartile Range		0	
	Skewness		2.519	.243
	Kurtosis		5.998	.481

Descriptives

			Statistic	Std. Error
MoCA (/30)	Mean		28.61	.172
	95% Confidence Interval for Mean	Lower Bound	28.27	
		Upper Bound	28.95	
	5% Trimmed Mean		28.78	
	Median		29.00	
	Variance		2.367	
	Std. Deviation		1.538	
	Minimum		23	
	Maximum		30	
	Range		7	
	Interquartile Range		2	
	Skewness		-1.501	.269
	Kurtosis		2.324	.532

Descriptives

			Statistic	Std. Error
Total Scheltens score (/93)	Mean		28.49	1.193
	95% Confidence Interval for Mean	Lower Bound	26.12	
		Upper Bound	30.86	
	5% Trimmed Mean		27.93	
	Median		28.00	
	Variance		142.212	
	Std. Deviation		11.925	
	Minimum		6	

	Maximum	73	
	Range	67	
	Interquartile Range	13	
	Skewness	.755	.241
	Kurtosis	1.404	.478

Descriptives

			Statistic	Std. Error
White matter hyperintensities (/30)	Mean		9.44	.594
	95% Confidence Interval for Mean	Lower Bound	8.26	
		Upper Bound	10.62	
	5% Trimmed Mean		9.07	
	Median		8.00	
	Variance		35.299	
	Std. Deviation		5.941	
	Minimum		1	
	Maximum		30	
	Range		29	
	Interquartile Range		7	
	Skewness		.992	.241
	Kurtosis		.904	.478

Descriptives

			Statistic	Std. Error
Periventricular hyperintensities (/9)	Mean		4.41	.166
	95% Confidence Interval for Mean	Lower Bound	4.08	
		Upper Bound	4.74	
	5% Trimmed Mean		4.29	
	Median		4.00	
	Variance		2.749	
	Std. Deviation		1.658	
	Minimum		1	
	Maximum		9	
	Range		8	
	Interquartile Range		2	
	Skewness		1.111	.241
	Kurtosis		1.061	.478

Descriptives

			Statistic	Std. Error
Grey matter hyperintensities (/30)	Mean		8.27	.386
	95% Confidence Interval for Mean	Lower Bound	7.50	
		Upper Bound	9.04	
	5% Trimmed Mean		8.16	
	Median		8.50	
	Variance		14.906	
	Std. Deviation		3.861	
	Minimum		1	
	Maximum		21	
	Range		20	
	Interquartile Range		5	
	Skewness		.427	.241
	Kurtosis		.504	.478

Descriptives

			Statistic	Std. Error
Infra-tentorial foci of hyperintensity (/24)	Mean		6.36	.322
	95% Confidence Interval for Mean	Lower Bound	5.72	
		Upper Bound	7.00	
	5% Trimmed Mean		6.28	
	Median		6.00	
	Variance		10.354	
	Std. Deviation		3.218	
	Minimum		1	
	Maximum		15	
	Range		14	
	Interquartile Range		4	
	Skewness		.298	.241
	Kurtosis		-.347	.478

Statistical Analysis

ANOVA Total Scheltens Score

Between-Subjects Factors

		Value Label	N
Final diagnosis	1	TIA	17
	2	Minor stroke	33
	3	Migraine	25
	4	Non-organic	7

	5	Other	18

Descriptive Statistics

Dependent Variable: Lg10

Final diagnosis	Mean	Std. Deviation	N
TIA	1.4140	.16726	17
Minor stroke	1.4641	.23291	33
Migraine	1.3893	.17140	25
Non-organic	1.3029	.20734	7
Other	1.3936	.20664	18
Total	1.4129	.20262	100

Levene's Test of Equality of Error Variances[a,b]

		Levene Statistic	df1	df2	Sig.
Lg10	Based on Mean	.905	4	95	.464
	Based on Median	.838	4	95	.505
	Based on Median and with adjusted df	.838	4	89.570	.505
	Based on trimmed mean	.907	4	95	.463

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Dependent variable: Lg10

b. Design: Intercept + Final_diagnosis

Tests of Between-Subjects Effects

Dependent Variable: Lg10

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Noncent. Parameter	Observed Power[b]
Corrected Model	.192[a]	4	.048	1.177	.326	.047	4.709	.357
Intercept	148.060	1	148.060	3632.209	.000	.975	3632.209	1.000
Final_diagnosis	.192	4	.048	1.177	.326	.047	4.709	.357
Error	3.872	95	.041					
Total	203.693	100						
Corrected Total	4.064	99						

a. R Squared = .047 (Adjusted R Squared = .007)

b. Computed using alpha = .05

ANOVA Total Scheltens Scores by Gender

MALE

Between-Subjects Factors[a]

		Value Label	N
Final diagnosis	1	TIA	9
	2	Minor stroke	19
	3	Migraine	13
	4	Non-organic	2
	5	Other	12

a. Sex = Male

Descriptive Statistics[a]

Dependent Variable: Lg10

Final diagnosis	Mean	Std. Deviation	N
TIA	1.3721	.19460	9
Minor stroke	1.4587	.24027	19
Migraine	1.4245	.06442	13
Non-organic	1.4956	.06853	2
Other	1.3393	.22319	12
Total	1.4118	.19625	55

a. Sex = Male

Levene's Test of Equality of Error Variances[a,b,c]

		Levene Statistic	df1	df2	Sig.
Lg10	Based on Mean	3.301	4	50	.018
	Based on Median	2.539	4	50	.051
	Based on Median and with adjusted df	2.539	4	39.061	.055
	Based on trimmed mean	3.230	4	50	.020

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Sex = Male

b. Dependent variable: Lg10

c. Design: Intercept + Final_diagnosis

Tests of Between-Subjects Effects[a]

Dependent Variable: Lg10

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Noncent. Parameter	Observed Power[c]
Corrected Model	.135[b]	4	.034	.869	.489	.065	3.475	.257
Intercept	61.010	1	61.010	1568.756	.000	.969	1568.756	1.000
Final_diagnosis	.135	4	.034	.869	.489	.065	3.475	.257
Error	1.945	50	.039					
Total	111.697	55						
Corrected Total	2.080	54						

a. Sex = Male

b. R Squared = .065 (Adjusted R Squared = -.010)

c. Computed using alpha = .05

FEMALE

Between-Subjects Factors[a]

		Value Label	N
Final diagnosis	1	TIA	8
	2	Minor stroke	14
	3	Migraine	12
	4	Non-organic	5
	5	Other	6

a. Sex = Female

Descriptive Statistics[a]

Dependent Variable: Lg10

Final diagnosis	Mean	Std. Deviation	N
TIA	1.4611	.12600	8
Minor stroke	1.4715	.23130	14
Migraine	1.3510	.23770	12
Non-organic	1.2258	.19318	5
Other	1.5021	.11992	6
Total	1.4143	.21238	45

a. Sex = Female

Levene's Test of Equality of Error Variances[a,b,c]

		Levene Statistic	df1	df2	Sig.
Lg10	Based on Mean	.803	4	40	.530
	Based on Median	.595	4	40	.668
	Based on Median and with adjusted df	.595	4	29.468	.669
	Based on trimmed mean	.731	4	40	.576

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Sex = Female

b. Dependent variable: Lg10

c. Design: Intercept + Final_diagnosis

Tests of Between-Subjects Effects[a]

Dependent Variable: Lg10

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Noncent. Parameter	Observed Power[c]
Corrected Model	.335[b]	4	.084	2.033	.108	.169	8.131	.556
Intercept	76.052	1	76.052	1844.434	.000	.979	1844.434	1.000
Final_diagnosis	.335	4	.084	2.033	.108	.169	8.131	.556
Error	1.649	40	.041					
Total	91.997	45						
Corrected Total	1.985	44						

a. Sex = Female

b. R Squared = .169 (Adjusted R Squared = .086)

c. Computed using alpha = .05

Correlations Total Scheltens Score

Correlations

		Lg10Sceltens	Age
Lg10Scheltens	Pearson Correlation	1	.550**
	Sig. (2-tailed)		.000
	N	100	100
Age	Pearson Correlation	.550**	1

	Sig. (2-tailed)	.000	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Lg10Scheltns	Lg10MoCA
Lg10Scheltens	Pearson Correlation	1	-.280*
	Sig. (2-tailed)		.012
	N	100	80
Lg10MoCA	Pearson Correlation	-.280*	1
	Sig. (2-tailed)	.012	
	N	80	80

*. Correlation is significant at the 0.05 level (2-tailed).

Correlations

		Lg10Scheltens	Lg10sBP
Lg10Scheltens	Pearson Correlation	1	.340**
	Sig. (2-tailed)		.001
	N	100	96
Lg10sBP	Pearson Correlation	.340**	1
	Sig. (2-tailed)	.001	
	N	96	96

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Lg10Scheltens	Lg10dBP
Lg10Schletens	Pearson Correlation	1	.133
	Sig. (2-tailed)		.198
	N	100	96
Lg10dBP	Pearson Correlation	.133	1
	Sig. (2-tailed)	.198	
	N	96	96

Correlations

		Lg10Scheltens	Lg10PP
Lg10Scheltens	Pearson Correlation	1	.325**
	Sig. (2-tailed)		.001
	N	100	96
Lg10PP	Pearson Correlation	.325**	1
	Sig. (2-tailed)	.001	
	N	96	96

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Lg10Scheltes	Lg10 RF
Lg10Scheltens	Pearson Correlation	1	.228*
	Sig. (2-tailed)		.022
	N	100	100
Lg10RF	Pearson Correlation	.228*	1
	Sig. (2-tailed)	.022	
	N	100	100

*. Correlation is significant at the 0.05 level (2-tailed).

Correlations

		Lg10Scheltens	Lg10mRS
Lg10Scheltens	Pearson Correlation	1	.145
	Sig. (2-tailed)		.149
	N	100	100
Lg10mRS	Pearson Correlation	.145	1
	Sig. (2-tailed)	.149	
	N	100	100

Correlations

		Lg10Scheltens	Lg10NIHSS
Lg10Scheltens	Pearson Correlation	1	.210*
	Sig. (2-tailed)		.037

	N	100	99
Lg10NIHSS	Pearson Correlation	.210*	1
	Sig. (2-tailed)	.037	
	N	99	99

*. Correlation is significant at the 0.05 level (2-tailed).

Correlations Individual Scheltens Scores

WMH

Correlations

		Lg10WMH	Age
Lg10WMH	Pearson Correlation	1	.585**
	Sig. (2-tailed)		.000
	N	100	100
Age	Pearson Correlation	.585**	1
	Sig. (2-tailed)	.000	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Lg10WMH	Lg10MoCA
Lg10WMH	Pearson Correlation	1	-.300**
	Sig. (2-tailed)		.007
	N	100	80
Lg10MoCA	Pearson Correlation	-.300**	1
	Sig. (2-tailed)	.007	
	N	80	80

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Lg10WMH	Lg10sBP
Lg10WMH	Pearson Correlation	1	.309**
	Sig. (2-tailed)		.002
	N	100	96

Lg10sBP	Pearson Correlation	.309**	1
	Sig. (2-tailed)	.002	
	N	96	96

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Lg10WMH	Lg10dBP
Lg10WMH	Pearson Correlation	1	.073
	Sig. (2-tailed)		.482
	N	100	96
Lg10dBP	Pearson Correlation	.073	1
	Sig. (2-tailed)	.482	
	N	96	96

Correlations

		Lg10WMH	Lg10PP
Lg10WMH	Pearson Correlation	1	.352**
	Sig. (2-tailed)		.000
	N	100	96
Lg10PP	Pearson Correlation	.352**	1
	Sig. (2-tailed)	.000	
	N	96	96

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Lg10WMH	Lg10RS
Lg10WMH	Pearson Correlation	1	.210*
	Sig. (2-tailed)		.036
	N	100	100
Lg10RS	Pearson Correlation	.210*	1
	Sig. (2-tailed)	.036	

N	100	100

*. Correlation is significant at the 0.05 level (2-tailed).

Correlations

		Lg10WMH	Lg10mRS
Lg10WMH	Pearson Correlation	1	.169
	Sig. (2-tailed)		.093
	N	100	100
Lg10mRS	Pearson Correlation	.169	1
	Sig. (2-tailed)	.093	
	N	100	100

Correlations

		Lg10WMH	Lg10NIHSS
Lg10WMH	Pearson Correlation	1	.155
	Sig. (2-tailed)		.127
	N	100	99
Lg10NIHSS	Pearson Correlation	.155	1
	Sig. (2-tailed)	.127	
	N	99	99

PVH

Correlations

		Lg10PVH	Age
Lg10PVH	Pearson Correlation	1	.467**
	Sig. (2-tailed)		.000
	N	100	100
Age	Pearson Correlation	.467**	1
	Sig. (2-tailed)	.000	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Lg10PVH	Lg10MoCA
Lg10PVH	Pearson Correlation	1	-.202
	Sig. (2-tailed)		.072
	N	100	80
Lg10MoCA	Pearson Correlation	-.202	1
	Sig. (2-tailed)	.072	
	N	80	80

Correlations

		Lg10PVH	Lg10sBP
Lg10PVH	Pearson Correlation	1	.188
	Sig. (2-tailed)		.066
	N	100	96
Lg10sBP	Pearson Correlation	.188	1
	Sig. (2-tailed)	.066	
	N	96	96

Correlations

		Lg10PVH	Lg10dBP
Lg10PVH	Pearson Correlation	1	-.033
	Sig. (2-tailed)		.753
	N	100	96
Lg10dBP	Pearson Correlation	-.033	1
	Sig. (2-tailed)	.753	
	N	96	96

Correlations

		Lg10PVH	Lg10PP
Lg10PVH	Pearson Correlation	1	.277**
	Sig. (2-tailed)		.006
	N	100	96

Lg10PP	Pearson Correlation	.277**	1
	Sig. (2-tailed)	.006	
	N	96	96

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Lg10PVH	Lg10RS
Lg10PVH	Pearson Correlation	1	.271**
	Sig. (2-tailed)		.006
	N	100	100
Lg10RS	Pearson Correlation	.271**	1
	Sig. (2-tailed)	.006	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Lg10PVH	Lg10mRS
Lg10PVH	Pearson Correlation	1	.150
	Sig. (2-tailed)		.138
	N	100	100
Lg10mRS	Pearson Correlation	.150	1
	Sig. (2-tailed)	.138	
	N	100	100

Correlations

		Lg10PVH	Lg10NIHSS
Lg10PVH	Pearson Correlation	1	.201*
	Sig. (2-tailed)		.046
	N	100	99
Lg10NIHSS	Pearson Correlation	.201*	1
	Sig. (2-tailed)	.046	

	N	99	99

*. Correlation is significant at the 0.05 level (2-tailed).

GMH

Correlations

		Lg10GMH	Age
Lg10GMH	Pearson Correlation	1	.399**
	Sig. (2-tailed)		.000
	N	100	100
Age	Pearson Correlation	.399**	1
	Sig. (2-tailed)	.000	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Lg10GMH	Lg10MoCA
Lg10GMH	Pearson Correlation	1	-.153
	Sig. (2-tailed)		.177
	N	100	80
Lg10MoCA	Pearson Correlation	-.153	1
	Sig. (2-tailed)	.177	
	N	80	80

Correlations

		Lg10GMH	Lg10sBP
Lg10GMH	Pearson Correlation	1	.355**
	Sig. (2-tailed)		.000
	N	100	96
Lg10sBP	Pearson Correlation	.355**	1
	Sig. (2-tailed)	.000	
	N	96	96

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Lg10GMH	Lg10dBP
Lg10GMH	Pearson Correlation	1	.243*
	Sig. (2-tailed)		.017
	N	100	96
Lg10dBP	Pearson Correlation	.243*	1
	Sig. (2-tailed)	.017	
	N	96	96

*. Correlation is significant at the 0.05 level (2-tailed).

Correlations

		Lg10GMH	Lg10PP
Lg10GMH	Pearson Correlation	1	.245*
	Sig. (2-tailed)		.016
	N	100	96
Lg10PP	Pearson Correlation	.245*	1
	Sig. (2-tailed)	.016	
	N	96	96

*. Correlation is significant at the 0.05 level (2-tailed).

Correlations

		Lg10GMH	Lg10RS
Lg10GMH	Pearson Correlation	1	.183
	Sig. (2-tailed)		.069
	N	100	100
Lg10RS	Pearson Correlation	.183	1
	Sig. (2-tailed)	.069	
	N	100	100

Correlations

		Lg10GMH	Lg10mRS
Lg10GMH	Pearson Correlation	1	.076
	Sig. (2-tailed)		.452
	N	100	100
Lg10mRS	Pearson Correlation	.076	1
	Sig. (2-tailed)	.452	
	N	100	100

Correlations

		Lg10GMH	Lg10NIHSS
Lg10GMH	Pearson Correlation	1	.207*
	Sig. (2-tailed)		.040
	N	100	99
Lg10NIHSS	Pearson Correlation	.207*	1
	Sig. (2-tailed)	.040	
	N	99	99

*. Correlation is significant at the 0.05 level (2-tailed).

IFTH

Correlations

		Lg10IFTH	Age
Lg10IFTH	Pearson Correlation	1	.229*
	Sig. (2-tailed)		.022
	N	100	100
Age	Pearson Correlation	.229*	1
	Sig. (2-tailed)	.022	
	N	100	100

*. Correlation is significant at the 0.05 level (2-tailed).

Correlations

		Lg10IFTH	Lg10MoCA
Lg10IFTH	Pearson Correlation	1	-.193
	Sig. (2-tailed)		.086
	N	100	80
Lg10MoCA	Pearson Correlation	-.193	1
	Sig. (2-tailed)	.086	
	N	80	80

Correlations

		Lg10IFTH	Lg10sBP
Lg10IFTH	Pearson Correlation	1	.171
	Sig. (2-tailed)		.095
	N	100	96
Lg10sBP	Pearson Correlation	.171	1
	Sig. (2-tailed)	.095	
	N	96	96

Correlations

		Lg10IFTH	Lg10dBP
Lg10IFTH	Pearson Correlation	1	.054
	Sig. (2-tailed)		.599
	N	100	96
Lg10dBP	Pearson Correlation	.054	1
	Sig. (2-tailed)	.599	
	N	96	96

Correlations

		Lg10IFTH	Lg10PP
Lg10IFTH	Pearson Correlation	1	.158
	Sig. (2-tailed)		.124
	N	100	96

Lg10PP	Pearson Correlation	.158	1
	Sig. (2-tailed)	.124	
	N	96	96

Correlations

		Lg10IFTH	Lg10RS
Lg10IFTH	Pearson Correlation	1	.102
	Sig. (2-tailed)		.314
	N	100	100
Lg10RS	Pearson Correlation	.102	1
	Sig. (2-tailed)	.314	
	N	100	100

Correlations

		Lg10IFTH	Lg10mRS
Lg10IFTH	Pearson Correlation	1	.048
	Sig. (2-tailed)		.633
	N	100	100
Lg10mRS	Pearson Correlation	.048	1
	Sig. (2-tailed)	.633	
	N	100	100

Correlations

		Lg10IFTH	Lg10NIHSS
Lg10IFTH	Pearson Correlation	1	.127
	Sig. (2-tailed)		.211
	N	100	99
Lg10NIHSS	Pearson Correlation	.127	1
	Sig. (2-tailed)	.211	
	N	99	99

Multiple Comparison Correction

To control for type I error (i.e. false positives) resulting from multiple comparisons during the above correlations, the FDR method described by Benjamini and Hochberg *et al.* (1995) was applied to all p values by an independent researcher (MS). In the Benjamini-Hochberg procedure, all p values are arranged in ascending order and their critical values are calculated using the formula below:

$$\left(\frac{i}{m}\right)Q$$

i= rank
m=total number of tests
Q=FDR threshold

The next step involves identification of the highest p value that is smaller than its corresponding critical value. All p values above this point (i.e. lower p values) are considered as significant. The table below summarizes this method as applied to our dataset with the point from which p values and above (i.e. lower p values) should be considered as significant highlighted in grey for two different thresholds.

				FDR=0.05	**FDR=0.1**
	Variable	**p value**	**Rank**	**(i/m)Q**	**(i/m)Q**
Scheltens	Age	0	1	0.00125	0.0025
PVH	Age	0	2	0.0025	0.005
WMH	Age	0	3	0.00375	0.0075
WMH	PP	0	4	0.005	0.01
GMH	Age	0	5	0.00625	0.0125
GMH	sBP	0	6	0.0075	0.015
Scheltens	sBP	0.001	7	0.00875	0.0175
Scheltens	PP	0.001	8	0.01	0.02
WMH	sBP	0.002	9	0.01125	0.0225
PVH	PP	0.006	10	0.0125	0.025
PVH	RS	0.006	11	0.01375	0.0275
WMH	MoCA	0.007	12	0.015	0.03
Scheltens	MoCA	0.012	13	0.01625	0.0325
GMH	PP	0.016	14	0.0175	0.035
GMH	dBP	0.017	15	0.01875	0.0375
Scheltens	RF	0.022	16	0.02	0.04
IFTH	Age	0.022	17	0.02125	0.0425
WMH	RS	0.036	18	0.0225	0.045
Scheltens	NIHSS	0.037	19	0.02375	0.0475
GMH	NIHSS	0.04	20	0.025	0.05
PVH	NIHSS	0.046	21	0.02625	0.0525
PVH	sBP	0.066	22	0.0275	0.055
GMH	RS	0.069	23	0.02875	0.0575

PVH	MoCA	0.072	24	0.03	0.06
IFTH	MoCA	0.086	25	0.03125	0.0625
WMH	mRS	0.093	26	0.0325	0.065
IFTH	sBP	0.095	27	0.03375	0.0675
IFTH	PP	0.124	28	0.035	0.07
WMH	NIHSS	0.127	29	0.03625	0.0725
PVH	mRS	0.138	30	0.0375	0.075
Scheltens	mRS	0.149	31	0.03875	0.0775
GMH	MoCA	0.177	32	0.04	0.08
Scheltens	dBP	0.198	33	0.04125	0.0825
IFTH	NIHSS	0.211	34	0.0425	0.085
IFTH	RS	0.314	35	0.04375	0.0875
GMH	mRS	0.452	36	0.045	0.09
WMH	dBP	0.482	37	0.04625	0.0925
IFTH	dBP	0.599	38	0.0475	0.095
IFTH	mRS	0.633	39	0.04875	0.0975
PVH	dBP	0.753	40	0.05	0.1

List of Abbreviations

TIA: transient ischemic attack
dBP: diastolic blood pressure
sBP: systolic blood pressure
PP: pulse pressure
mRS: modified Rankin score
MoCA: Montreal cognitive assessment
NIHSS: national institutes of health stroke scale
WMH: white matter hyperintensities
GMH: grey matter hyperintensities
PVH: periventricular hyperintensities
IFTH: infratentorial hyperintensities
MRI: magnetic resonance imaging
PACS: picture archiving and communication system
ANOVA: analysis of variance
FDR: false discovery rate

Contributions

OV: Study design; Participant assessment; Hyperintensities scoring; Statistical analysis; Manuscript write up; Manuscript review.
KT: Statistical analysis; Manuscript write up; Manuscript review.
MS: Study design; Post-hoc statistical analysis; Manuscript review.
CDF: Study design; Post-hoc statistical analysis; Manuscript review.
ADM: Training for hyperintensities scoring; Manuscript review.
CS: Study design; Manuscript review; co-PI.
MJM: Study design; Patient recruitment; Final diagnosis; Manuscript review; PI.

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