Similar mechanisms and locations of white matter lesions in elderly healthy controls and asymptomatic carotid artery stenosis patients

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Background

- White matter lesions (WML) detected by T2w FLAIR hyperintensities
- WML indicate periventricular and deep white matter (WM) changes
- Individual watershed areas (iWSA)[1] most vulnerable to WML[2,3]
- WML commonly interpreted as microangiopathic changes, which can result in cognitive decline[4]
- Pathogenesis unclear[2], despite frequent findings in elderly subjects
- Potential causes are cerebrovascular dysregulation[5-7], small vessel damages and myelin sheath deformations[8]
- Microvascular[9] and microstructural[10,11] sensitive image promising
- Impact of internal carotid artery stenosis (ICAS) under debate[12-15]

Methods

- 59 participants: 29 asymptomatic, unilateral ICAS-patients, age = 70.1 ± 4.8 y and 30 age matched healthy controls (HC)
- 3T Philips (Best, Netherlands) Ingenia MRI, 16-ch head-neck-coil
- DSC-MRI for iWSA[16] and capillary transit-time heterogeneity (CTH)[9]
- DTI for fractional aniotropy (FA) and mean diffusivity (MD)[10,11]
- FLAIR WML mask segmentation by LST-toolbox[18]
- FLAIR scoring by Fazekas[19]
- Processing with SPM12,[20] FSL[21] and custom Matlab® programs
- Average parameter values compared inside vs. outside WML
- Two-sample t-tests considered statistically significant at p<0.05

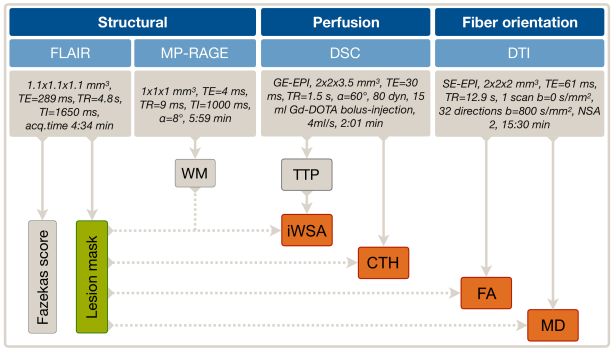

Figure 1: MRI protocol and derived parameters.

Aims

The aims of our study were to **investigate WMLs** in relation to **individual watershed areas**[16] and investigate **microvascular impairments** as well as **structural damage**, measured by CTH and DTI, respectively. Pathophysiologic and normal age-related WML effects[8] were compared between patients with **internal carotid artery stenosis** (ICAS) and elderly healthy controls (HC).

We hypothesize increased lesion loads inside iWSA. Furthermore, we hypothesize CTH increases and structural damage inside WML.

Conclusion

Lesion load was **increased** inside **iWSA** for both groups, which underlines the vulnerability of iWSA for structural damage in healthy ageing as well as disease. Furthermore, pronounced CTH elevations within WML imply an important role of **capillary dysfunction** in **WML pathogenesis**.

Interestingly, CTH and structural effects were largely comparable between ICAS and HC, strengthening the assumption of **WML formation** being not primarily caused by ICAS, but mainly **related to ageing effects**.

Figures

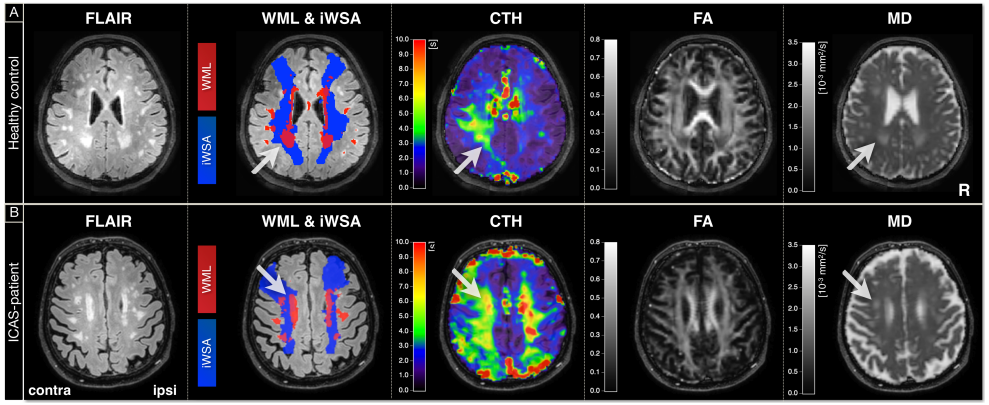

Figure 2: Exemplary healthy control and right-sided ICAS-patient data. Compared are FLAIR images, overlays of white matter lesions (WML, red) and individual watershed areas (iWSA, blue), capillary transit-time heterogeneity (CTH), fractional anisotropy (FA) and mean diffusivity (MD). (A) The HC's lesion volume was 22206 mm³ with Fazekas 3 and (B) 14635 mm³ for the ICAS-patient, also with Fazekas 3. In both cases, the lesion load was increased inside iWSAs. Arrows indicate similar WML locations and parameter alterations.

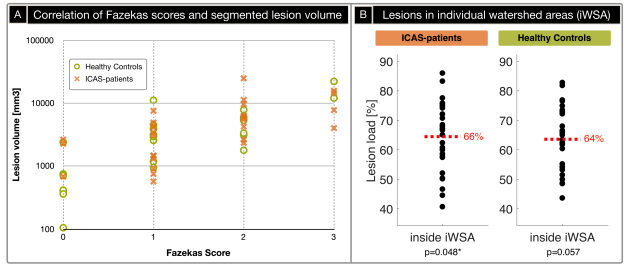

Figure 3: WML volume and localizations. (A) Fazekas scores were compared to WML volumes in semi-logarithmic scaling. Markers represent lesions of HC (green circles) and ICAS-patients (orange crosses). Pearson correlation revealed R_{HC}=0.74 and R_{ICAS}=0.56. (B) Spatial analysis showed that about 2/3 of all WML are located in iWSAs, similarly for HCs and ICAS-patients.

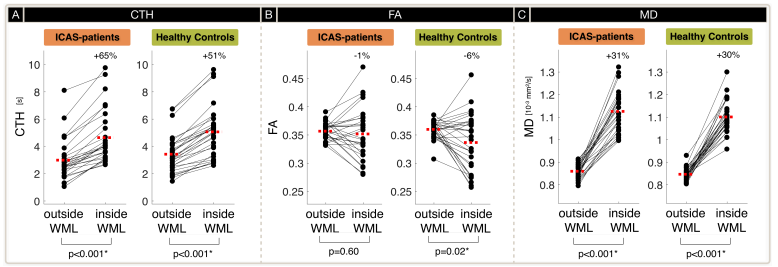

Figure 4: WML effects on capillary function and structural parameters. Comparison of (A) CTH, (B) FA and (C) MD outside vs. inside WML for ICAS-patients and HCs. Dots represent average parameter values of each subject outside vs. inside WML. Black lines connect same subject's values. Red dotted lines show average parameter values. Mean changes inside WML are noted in percent. Asterisks mark significant differences.

Results

- Locations of WML, iWSA and CTH elevations are similar (Fig. 2)
- No hemispheric WML lateralization in ICAS (p=0.54)
- Similar Fazekas-scores in ICAS and HC (1.4 vs. 1.0)
- Fazekas-scores and WML volume correlate reasonably well (Fig. 3A)
- Increased WML load inside iWSA in ICAS (p=0.048) and also HC (p=0.057)
- WML load in iWSA similar for both groups (Fig. 3B)
- Average WML load non-significantly increased in ICAS (p=0.19) with mean±std=5533±5421 mm³ compared to HC with 3812±4599 mm³
- Elevated CTH inside WML for both groups (p<0.001, Fig.4A)
- Similar structural effects for both groups (Fig.4B,C)

Discussion

- Increased lesion load in iWSA (65%) comparable in ICAS and HC, in agreement with previous CT-MRI study in tumor patients[3]
- No significant hemispherical lateralization in unilateral ICAS in agreement with the literatre[15]
- Fazekas-score correlations in agreement with the literature[23]
- WML volumes and Fazekas-scores non-significantly elevated in ICAS compared to HC
- Possible influencing factor in known multifactorial WML pathogenesis[2,8] is increased hypertension[22] with 79% in our ICAS-patients vs. 53% in our HC
- Findings agree with previous study in asymptomatic ICAS, which proposed no causal role of ICAS in the WML development[14]
- Strong impairments of CTH inside WML indicate important role of capillary dysfunction in lesion formation
- Microstructural DTI showed increased MD inside WML for every participant indicating axonal degeneration[11,24]
- Those findings indicate similar WML locations of WML in healthy ageing and different pathologies

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