Increased grey matter transit times are associated with white matter hyper intensities

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Purpose: White matter hyper intensities of presumed vascular origin (WMH) are a common finding on brain magnetic resonance imaging (MRI) in the elderly.¹ They are associated with cognitive decline, neuropsychiatric symptoms and mortality. Neuropathologically they are characterised by changes resulting from low grade ischemia. Several small in-vivo studies have yielded inconclusive results regarding the relation between WMH load and cerebral blood flow (CBF).²,³ Transit time may play an important role in this ambiguity but until recently was difficult to assess in large cohorts.⁴,⁵ Developments in arterial spin labeling (ASL) have made assessment of CBF and transit time possible without the use of invasive contrast agents. The purpose of this study was to investigate whether CBF and transit time is correlated with WMH load, in a relatively large sample of elderly with hypertension.

Methods: 196 non-demented, community-dwelling elderly (72-80 years) with systolic hypertension were recruited from participants of the Prevention of Dementia by Intensive Vascular care trial (PreDIVA). Scanning was conducted on a 3T Philips-scanner (Intera). The protocol included a 1 mm³ isotropic 3D T1 for segmentation, a 3D FLAIR for WMH segmentation and two consecutive gradient-echo single shot EPI pCASL sequences (SENSE 2.5; TE/TR 14/4000 ms; FOV 240x240 mm; matrix 64x64; 17 slices, 7mm thick; no gap; background suppression; labeling duration 1650 ms; post-labeling delay 1525 ms; NSA 20 for each scan; duration 2x2 m), one with application of a vascular crusher (Venc 50mm/s; b 0.6 s/mm²). Transit time was estimated using FEAST.⁶ WMH were segmented using a fully automated technique.⁷ Univariate linear regression analyses were performed with WMH load (WMH volume/brain volume) as dependent and CBF, grey matter (GM) transit time, age and atrophy as predictors. Multivariate regression analyses were performed with significant predictors, correcting for cardiovascular risk factors (table 1). Using subject registered cerebral artery territorial masks, differences in associations between WMH load and ASL derived parameters in the different cerebral arterial territories were assessed.

Results: GM transit time was a significant predictor of WMH load, with and without correction for age, gender, intracranial volume and cardiovascular risk factors (Table 1). The association between WMH load and GM transit time was found to be strongest in the anterior (ACA, st.beta=0.200, p<0.007) and posterior (PCA, st.beta=0.229, p<0.002) cerebral artery territories. No significant association between GM or white matter CBF and WMH load was found (table 1).

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Conclusion: Increased WMH load was significantly associated with an increase in GM transit time in community-dwelling elderly with hypertension. This association was independent of atrophy, age and cardiovascular risk factors. These findings indicate that GM transit time may be a sensitive marker of SVD underlying WMH, in line with the hypothesis that WMH result from hypoperfusion of the deep white matter.