5.2: DIFFERENTIAL CHARACTERISTICS BETWEEN AORTIC PRESSURE AUGMENTATION AND CAROTID FLOW AUGMENTATION: CLINICAL IMPLICATIONS FOR CEREBRAL WHITE MATTER HYPERINTENSITIES

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Results: PE was associated with a higher placental MBG level (48.6 ± 7.0 vs. 13.6 ± 2.5 nmol/g; \( P < .01 \)), four-fold decrease of Fli1 and two-fold increase of collagen-1 in placenta (P < .01) vs. control. \( EC_50 \) was associated with fivefold decrease in Fli1 level and two-fold increase in collagen-1 level in the PE umbilical arteries vs. those from the normal subjects (P < .01). Isolated rings of umbilical arteries from the subjects with PE exhibited impaired response to the relaxant effect of sodium nitroprusside, vs. control vessels (EC_{50} = 141 nmol/L vs. EC_{50} = 0.9 nmol/L; \( P < .001 \)). In vitro 10 nmol MBG mimicked effect of PE, and monoclonal anti-MBG antibody reversed this effect.

Conclusion: These results demonstrate that elevated placental MBG level is implicated in the development of fibrosis umbilical arteries in PE.

Reference
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Oral Session V — Brain

5.1 STRESS-INDUCED SYMPATHETIC ACTIVITY AND THE RETINAL VASCULATURE: THE SAPBA PROSPECTIVE STUDY
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Objectives: Retinal vessels are part of the intracranial vasculature and analysis thereof complements behavioural and brain measures. Mental stress was related to downregulation of norepinephrine in Africans. Hence we continue by assessing prospective associations between sympathetic nervous system activity and retinal vessel calibres.

Methods: Black and Caucasian participants (n = 275; 45 ± 9 years) were stratified into tertiles according norepinephrine:creatinine (NE:Cr) ratio at baseline. Three year prospective % changes (Δ) for depression (PHQ-9), urinary NE:Cr, serum cortisol and High-Density-Lipoprotein (HDL), neuronal-membrane-integrity and ischemic stroke risk marker) were obtained. At 3yr-follow-up, retinal microvascular calibres were quantified from digital images in the mydriatic eye and salivary cortisol (sC) and \( \alpha \)-amylase (sAA), adrenergic activity marker were obtained.

Results: Only the low NE:Cr-tertile group (44% Black; 64% Men), showed chronic depression and hypertension prevalence. Over 3yrs, their NE:Cr increased whereas cortisol and HDL decreased. At 3yr-follow-up, wider venules (stroke risk marker) were apparent in the low- compared to the high-tertile group (Figure 1). In the low-tertile group, chronic depression was associated with stroke risk markers, wider venules [OR 1.7; \( P = 0.03 \)] and lower HDL [OR 4.8; \( P = 0.04 \)]. In this group, arteriolar narrowing was associated with \( \Delta NE:Cr \), \( \alpha \)-cortisol and sAA; whilst a wider venule was associated with \( \Delta NE:Cr \) and sC.

Conclusions: In reaction to depression and low NE:Cr levels, homeostatic reflexes facilitated upregulation of norepinephrine and concurrent downregulation of cortisol. Stress-induced sympathetic nervous system activity however disturbed myogenic tone, neuronal-membrane-integrity and retinal venular widening; increasing the susceptibility for ischemic stroke.

5.2 DIFFERENTIAL CHARACTERISTICS BETWEEN AORTIC PRESSURE AUGMENTATION AND CAROTID FLOW AUGMENTATION: CLINICAL IMPLICATIONS FOR CEREBRAL WHITE MATTER HYPERINTENSITIES

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Background: Aortic stiffness and pressure wave reflection have been found to be associated with age-related cerebral microvascular disease, but the underlying mechanism remains obscure. We hypothesized that cerebral (carotid) flow augmentation potentially mediates these associations.

Methods: Doppler waveforms were recorded in 286 patients with hypertension to measure the carotid flow augmentation index (FAIx) as the late/early systolic velocity amplitude ratio. Tonometric waveforms were recorded to estimate the aortic pressure augmentation index (PAIx), aortic compliance, and carotid-femoral and carotid-radial pulse wave velocities (PWVs). Additionally, white matter hyperintensities (WMHs) on brain MRI were evaluated using the Fazekas scale.

Results: With increasing age, the carotid late-systolic velocity increased whereas the early-systolic velocity decreased, although the aortic augmented pressure increased in parallel with the incident wave height (\( P < 0.001 \)). Both FAlx and PAIx increased with age, but the age-dependent curves were upwardly concave and convex, respectively. FAlx increased exponentially with increasing PAIx (\( r = -0.71 \)). Compared to PAIx, FAlx was more closely correlated (\( P < 0.001 \)) with the aortic PWV, aortic compliance, and aortic/peri- pheral PWV ratio. FAlx was associated with WMH scores independently of confounders including age, gender, diabetes, hypercholesterolemia and aortic PWV (\( P = 0.02 \)), and was more predictive of WMH presence than PAIx.

Conclusions: Carotid FAlx had closer associations with age, aortic stiffness and cerebral WMH than did aortic PAIx. These results indicate that carotid flow augmentation (enhanced by aortic stiffening and pressure wave reflection from the lower body) causes microcerebrovascular injury potentially through increasing cerebral flow pulsations, but this detrimental effect is even greater than that estimated from PAIx.

5.3 CAROTID ARTERY STIFFNESS INCREASES THE RISK OF INCIDENT DEPRESSIVE SYMPTOMS: THE PARIS PROSPECTIVE STUDY 3
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Background: Late-life depression is related to poor quality of life and increased risk of mortality and cardiovascular disease. Effective interventions for prevention and treatment of late-life depression need to be developed, which requires a better understanding of late-life depression risk factors. Arterial stiffness may contribute to late-life depression via cerebrovascular damage, but evidence is scarce. Aim: To investigate the association between carotid artery stiffness and incident depressive symptoms in a large community-based cohort study.

Methods: This longitudinal study included 7,013 participants (60 (SD 6) years; 36% women) free of depressive symptoms at baseline. Carotid stiffness (high-resolution echotracking) was determined at baseline. Presence of depressive symptoms was determined at baseline and at 4 and 6 years of follow-up and was defined as a score ≥ 7 on a validated 13-item questionnaire (Q20DA) and/or new use of antidepressants. Logistic regression and generalized estimating equations (GEE) were used.