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### **4.3: CAROTID HEMODYNAMICS DURING SYMPATHETIC NERVOUS SYSTEM STIMULATION VIA HANDGRIP AND COLD PRESSURE TESTING IN YOUNG HEALTHY SUBJECTS**

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**Background.** No longitudinal study addressed whether systolic blood pressure level (SBPL) or variability (SBPV) predict arterial properties or vice versa.

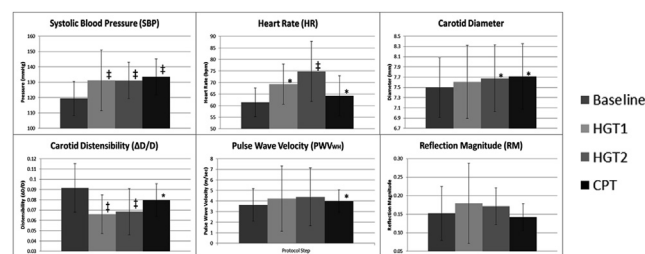
**Methods and Results.** In families randomly recruited from a Flemish population, we determined SBPL and SBPV from 5 consecutive blood pressure readings. The indexes of SBPV were variability independent of mean (VIM), the difference between maximum and minimum SBPL (MMD), and average real variability (ARV). We measured carotid intima-media thickness (cIMT) and distensibility (cD) by ultrasound and carotid-femoral pulse wave velocity (cfPWV) by tonometry (SphygmoCor, version 8.2). Effect sizes were computed for 1 SD increments in the predictors, while accounting for covariables and family clusters. Among 1171 participants (51.0% women; mean age, 39.8 years), followed up for 2.48 years (median), higher SBPL predicted ( $P \leq 0.036$ ) higher cIMT (+14  $\mu\text{m}$ ), lower cD (-1.57 10<sup>-3</sup>/kPa) and faster cfPWV (+0.298 m/s) at follow-up, whereas none of the SBPV indexes predicted the arterial traits at follow-up ( $P \geq 0.11$ ). In a subset of 749 participants, followed up for another 3.07 years, lower cD predicted ( $P \leq 0.026$ ) higher SBPL (+1.69 mm Hg), VIM (+0.304 units), MMD (+1.05 mm Hg) and ARV (+0.389). Higher cfPWV predicted a 1.06 mm Hg increase SBPL ( $P = 0.027$ ).

**Conclusions.** Temporality and effect size suggest that SBPL but not SBPV cause arterial stiffening and cIMT thickening. Carotid stiffening, independent of SBPL, predicts SBPV, possibly because baroreflexes originating from a stiffer carotid artery wall are impaired. Finally, stiffening of the aorta contributes to the age-related SBPL possibly because faster returning reflected waves augments SBPL.

**Methods.** A non-invasive protocol, consisting of two HGT (30% (HGT1) and 40% (HGT2) of maximal voluntary contraction) and CPT, was performed in 12 young healthy volunteers (6 males/6 females). Measurements included continuous finger blood pressure recordings (NexFin; non-dominant hand) and ultrasound measurement of common carotid diameter distension and flow velocity at discrete moments in time during the protocol (GE Vivid 7 system). Carotid distensibility ( $\dot{A}D/D$ ), local wave speed using the waterhammer equation ( $PWV_{WH}$ ) and reflection magnitude (RM; ratio of backward to forward diameter wave) were derived from the data.

**Results.** Consistent with the overall increase in blood pressure, carotid diameter increased while  $\dot{A}D/D$  decreased.  $PWV_{WH}$  and RM showed an increase during both HGT and a decrease during CPT (see Figure).

**Conclusion.** It is feasible to monitor the carotid hemodynamic response to a sympathetic nervous system stimulus. In this young, healthy population, the net result of the increased diameter and decreased distensibility on local  $PWV_{WH}$  was similar for all tests (increase) and on the magnitude of reflections was different for HGT (increase) and CPT (decrease).



The difference from baseline is indicated as significant \* ( $p < 0.05$ ) or highly significant ‡ ( $p < 0.001$ ).

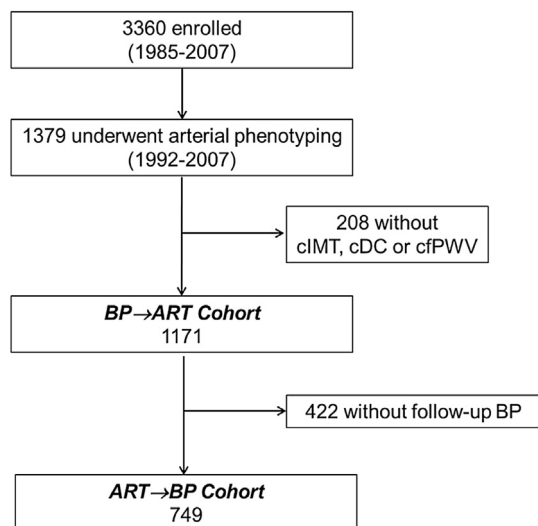


Figure 1 Flow chart of participants<sup>1</sup>.

#### 4.3 CAROTID HEMODYNAMICS DURING SYMPATHETIC NERVOUS SYSTEM STIMULATION VIA HANDGRIP AND COLD PRESSURE TESTING IN YOUNG HEALTHY SUBJECTS

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**Introduction.** Assessing arterial properties and hemodynamics in response to a physiological perturbation might provide additional information on an individual's "vascular health". The aim of this study was to assess the feasibility of measuring changes in carotid stiffness and hemodynamics in response to sympathetic nervous system stressors (Hand Grip Test (HGT) or Cold Pressor Test (CPT)).

#### 4.4

#### ASSOCIATIONS BETWEEN OBJECTIVELY MEASURED PHYSICAL ACTIVITY ENERGY EXPENDITURE AND CENTRAL HAEMODYNAMICS. THE ADDITION-PRO STUDY

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**Objective.** Physical activity (PA) has been associated with reduced cardiovascular disease (CVD). However, improvements in conventional risk factors do not explain the full benefit of PA on CVD risk. Therefore, we examined the association between PA and central haemodynamics to provide new insight into the link between PA and CVD.

**Methods.** We performed cross-sectional analyses of data from a health examination of 1,607 Danish adults at low to high diabetes risk. PA energy expenditure (PAEE) was measured by combined accelerometry and heart rate monitoring (ActiHeart®) expressed as kJ/kg/day. Aortic stiffness was assessed by applanation tonometry (SphygmoCor®), as aortic pulse wave velocity (aPWV), and central blood pressure was estimated from wave forms recorded at the radial artery. Associations between PAEE and central haemodynamics were examined by linear regression successively adjusted for sex, age, waist circumference, and smoking. Additionally, aPWV was adjusted for mean blood pressure. aPWV was logarithmically transformed. Individuals with previously myocardial or cerebral infarction were excluded ( $n = 183$ ). **Results.** Median age was 66 years (IQR: 61;71), 52% was men, median PAEE was 28 kJ/kg/day (IQR: 20;39), and median aPWV 8.0 m/s (IQR: 6.9;9.4). A higher PAEE of 10 kJ/kg/day was associated with a 1.0 % lower aPWV (CI: -0.17;-0.03). Associations with systolic blood pressure and pulse pressure were not statistically significant (-0.5 mmHg (CI: -0.11;0.01) and -0.02 mmHg (CI: -0.06;0.03)).