

## CAROTID ARTERY WAVE INTENSITY MEASURED IN MID- TO LATE-LIFE PREDICTS FUTURE COGNITIVE DECLINE: THE WHITEHALL II STUDY

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**Introduction:** Accumulating evidence suggests that vascular risk factors may contribute to the development of dementia. Increased pulse pressure (PP) is hypothesized to impair cognitive function due to its damaging effect on the fragile cerebral microcirculation, but a direct relationship between the intensity of pulse waves travelling towards the brain and subsequent impairment in cognitive function has never been investigated. Wave intensity analysis allows the measurement of both the magnitude and direction of travel of waves within the common carotid artery, and may therefore represent a novel risk factor for future cognitive decline.

**Hypothesis:** We hypothesized that the intensity of carotid artery forward compression waves (FCW) measured during mid- to late-life would predict future cognitive decline during 11-14 year follow-up.

**Methods:** Duplex Doppler ultrasound was used to calculate net FCW in the common carotid artery of 3,192 individuals aged 58-74 years taking part in the Whitehall II Study. PP was measured in the brachial artery using an automated cuff sphygmomanometer. Cognitive function – assessed using a global z-score incorporating multiple cognitive domains – was measured at baseline (2002-2004) and then repeated a further three times until 2015-2016. To address possible confounding, all statistical models were adjusted for multiple sociodemographic variables, health-related risk factors, and health-related behaviors.

**Results:** Increased FCW were associated with a faster rate of overall cognitive decline ( $\beta = -0.020$  [-0.038, -0.002];  $p = 0.03$ ). Individuals with carotid FCW in the top quartile of the population distribution had a ~50% greater risk of experiencing accelerated cognitive decline (top 15% of decline in global cognitive score) than the rest of the cohort (Odds Ratio = 1.53 [1.17, 2.00]). Although brachial PP was positively associated with carotid artery FCW ( $p < 0.001$ ), there was no relationship between PP and change in cognitive function ( $\beta = -0.002$  [-0.018, 0.014];  $p = 0.78$ ).

**Conclusions:** Elevated carotid artery FCW in mid- to late-life are independently associated with a faster rate of cognitive decline. These findings support a link between cardiovascular disease and cognitive impairment in later life.