Carotid Artery Blood Flow Velocities and Cognitive Performance: Forecasting Cognitive Decline

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Cerebral blood flow and corresponding brain oxygenation were the earliest mechanisms posited as mediators of hypertension and cognitive deficit. While white and gray matter lesions became a major focus of interest as research grew, cerebral blood flow and brain perfusion continued to dominate the quest to discover the causal basis of relations between blood pressure extremes and cognition because inadequate brain perfusion plays a major role in the development of these brain lesions.

The article by Chuang et al. in this issue of the American Journal of Hypertension reminds us of the important role of blood flow and cerebral perfusion in hypertension-related cognitive decline. More importantly, it shifts our attention away from cerebral blood flow to the possible role of reduced carotid artery blood flow in early stages of cognitive decline. Chuang et al. examined cross-sectional associations between carotid flow velocities, blood pressure and cognitive function in 1,684 adults (63.4 ± 8.9 years of age). They used the Doppler ultrasound method and employed data from the I-LAN Longitudinal Aging Study. Systolic blood pressure (BP) was reported as the average of two BP measurements taken after resting with participants in a seated position. Carotid flow velocities were measured with participants in a supine position. The primary cognitive outcome measure was the Mini-Mental State Examination (MMSE), although additional tests of specific abilities were also employed: the Taylor Complex Figure Test, Chinese Version Verbal Learning Test, Boston Naming Test, Verbal Fluency Test, Digital Backward, and the Clock Drawing Test.

Peak systolic velocity and end-diastolic velocity were positively associated with MMSE score and systolic blood pressure was inversely associated with MMSE score after adjusting for age, sex, education, smoking habits (never, quit or current), nutrition (adequate or inadequate), hypertensive medicine (yes or vs. no) and fasting glucose (all \( P < 0.01 \)). Similar findings were reported for the Taylor Complex Figure Test with basic demographic adjustment (all \( P < 0.01 \)). Furthermore, the Boston Naming Test was associated with peak systolic volume with basic demographic adjustment (\( P < 0.001 \)).

These are interesting findings because the carotid arteries are often thought of as passive tributaries of blood to the cerebral arteries, which represent the final pathways to the various brain regions. We typically think of the cerebral arteries as the action vessels with regard to brain injury and cognitive dysfunction, but now we see that decreased internal carotid blood flow is related to lowered cognitive performance. In response to this finding, Chuang et al. raise a thought-proving hypothesis: “As carotid flow velocities are the origin of cerebral flow velocity and are significantly associated with MMSE, these may be involved in the early stage of cognitive dysfunction.” The unanswered question is: why might this be true?

The parsimonious explanation is that observed relations between carotid artery blood flow and cognitive function reflect parallel events taking place in the cerebral cortex. However, Chuang et al. seem to be suggesting that something unique is taking place at the level of the carotid artery complex and we learn something from these relations that we do not learn from focusing on cerebral blood flow and cognition. Certainly, blood flow simulation studies indicate that blood flow dynamics are different in the carotid arteries and the cerebral arteries; but these studies provide little in the way of insight as to how these differences translate into relations between blood flow and cognition.

Blood flow in the circle of Willis comes to mind as a source of variation in blood flow at the level of the carotid arteries. We learn the following from work by Tanaka et al. and Devault et al.: In the circle of Willis, under normal conditions, blood flow in the communicating arteries is of negligible importance, but blood flow is reduced when one of the communicating arteries is missing or in extreme cases...
when blood flow is completely occulted. This is no minor issue in terms of clinical significance. The circle of Willis is found to be incomplete or not fully developed in 50% of human brains defined as healthy and 80% of dysfunctional brains, and thus blood flow is affected by the integrity of this structure. Thus, the circle of Willis plays a role in blood flow dynamics at the level of the carotid arteries. It might, therefore, be useful to ask if blood flow dynamics in this vascular structure contribute something unique to the forecasting of the cognitive deficit from observed relations among blood pressure and blood flow in the carotid arteries.

As we read the article by Chaung et al., the question of how their findings would play out against individual differences in the autoregulation curve (Figure 1) come to mind. This question can be addressed with a focus on hypotension. This design requires multiple blood pressure assessments in the recumbent and standing positions rather than two sitting blood pressure assessments as in the study by Chaung et al. The fact that autoregulatory mechanisms play a central role in orthostatic hypotension translates into opportunity to examine interactions between autoregulation and carotid artery blood flow as they affect cognitive functioning. Work by Novak et al. suggests stratification based on three patterns of autoregulatory response for a study design employing hypotensive individuals: (i) impaired autoregulation with a flat blood flow curve; (ii) unimpaired autoregulation with an expansion of the range of autoregulation; (iii) failure of autoregulation with a steep blood flow-blood pressure curve. The latter group is characterized by Novak et al. as being at a substantial disadvantage in dealing with orthostatic hypotension. It is very likely that autoregulatory response will modify relations between carotid cerebral blood flow and cognition. This finding would come as no surprise, but how it modifies relations between carotid artery blood flow and cognition is an important question from a clinical point of view given the serious consequences of hypotension, including cognitive deficit, and difficulties in raising cerebral blood flow in hypotensive individuals.

As work stimulated by Chaung et al. continues, we can expect alterations in design that take two forms: (i) More extensive statistical models employing additional controls and; (ii) Improvements in the assessment of cognitive functioning, including longitudinal designs. The article by Chaung et al. includes a very basic set of demographic covariates and additional controls, including good nutrition (yes and no) and cigarette smoking (never, quit, or current). Obviously more extensive models can and should be built in the effort to uncover undetected sources of confounding and effect modification. The list of potential confounders is long and includes specific types of medication and caffeinated beverages. Furthermore, certain foods, chronic exercise, and select antihypertensive medications all offer possibilities for improving carotid artery and cerebral artery blood flow, a very important goal in the treatment of hypotension. For more information on potential confounders and effect modifiers, see work by: Joris et al., Fu et al., Fujishima et al., and Greene and Lee.

Improving cognitive assessment is a second important goal of future studies. The MMSE is a good instrument for evaluating general cognitive ability, but it is a low ceiling test. There are a variety of global measures of cognition that are more sensitive to existing cognitive deficits. In the study by Chaung et al., we see that executive functioning and naming skills, both important in the diagnosis of mild cognitive impairment and dementia, were related to carotid blood flow. The need for more comprehensive test batteries in future studies is very clear. Ideally, the following cognitive domains should be included in a comprehensive test battery: episodic, semantic and working memory, motor function, visual constructive abilities, visual perception, and executive function. Moreover, each domain should be indexed by one or more tests of abilities. Our group has written an article as to how these goals may be achieved, and several other articles offer good models for the evaluation of cerebral and carotid blood flow in relation to cognition: Elias et al., Pase et al., Nieboer et al., Poels et al. and Mitchell et al.

**SUMMARY**

The study Chaung et al. has implications for the potential importance of relations between carotid artery blood flow and cognition as an indicator of early decline in cognitive performance. It also raises an intriguing set of questions as to how carotid artery blood flow dynamics, separate from cerebral blood flow dynamics, may related to cognitive functioning. It sets us along an important path toward studies that can more fully address these questions.

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DISCLOSURE

The authors declared no conflict of interest.

REFERENCES