

## Interplay of Cardiac and Cognitive Function: How Much Do We Really Understand?

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In this issue of the *JAHA*, Launer et al report results of an association of cardiac function parameters with brain volume and function in an elderly population from the AGES-Reykjavik Study.<sup>1</sup> The authors found that left-ventricular stroke volume and cardiac output were related to brain volume and cognitive function. There are a number of limitations to this study. Medical information was largely based on self-reporting; the vast majority of participants suffered from arterial hypertension and a large proportion had diabetes; the indexed stroke volume and cardiac index are not reported. Yet, the data shed light from a different angle on the important yet under-appreciated relationship between the brain and the heart.

The results indicate that reduced left ventricular function may have a direct impact on the brain, which indeed has been suggested by previous animal studies. Unfortunately, due to the lack of follow-up data, the study does not prove more than an association. It is perfectly conceivable that a chronically lower oxygen turnover caused by inadequate cardiac output affects brain matter and thus cognitive function. In this sample, with a history or other evidence of arterial hypertension in >80%, chronically elevated arterial pressure may have caused hypertrophy (LV mass is not reported) with diastolic dysfunction, subsequently impaired ventricular filling, and thus reduced ventricular stroke volume. A frequently inadequate cardiac output could then have caused repetitive microscopic brain injury, leading to atrophy and cognitive dysfunction. In case of existing brain

tissue damage, congestion caused by an increased LV filling pressure could also directly induce reversible brain edema<sup>2</sup> with resulting cognitive dysfunction. Repetition of such events could result in chronic injury and atrophy. If confirmed, the consequences of such findings would be significant: Functional parameters of the heart would have to be considered important markers for neurologists and may represent important therapeutic targets for preventing cognitive dysfunction.

On the other hand, the association may just reflect two facets of the same problem: microvascular dysfunction, a hallmark of both hypertension and diabetes, leading to diffuse damage and dysfunction in the most sensitive tissues, which includes the heart<sup>3</sup> and the brain.<sup>4</sup> Both systems have a very high energy demand and thus may have a high sensitivity to inadequate blood supply, even in the absence of clinically overt ischemia. While the blood-brain barrier represents an important distinct feature of the brain, the response to injury on a microvascular and tissue level has many commonalities with that of the myocardium. Microvascular injury may not only be the result of a chronically increased glucose or blood pressure level but also of repeated mild toxic, inflammatory or mechanic injury, or acute stress events.<sup>5,6</sup>

The discussion reflects the knowledge gaps about the common pathophysiology and the interaction between the brain and the heart. For too long, clinical research ignored the impact of the heart on the brain and vice versa. How do brain and heart function interact on a vascular and neurological level in the presence of atherosclerotic risk factors? Can single bouts of severe mental stress lead to brain injury in the presence of normal cardiac output? How do repeated episodes of mental or vascular stress with associated variations in blood pressure affect short-term and long-term brain function? Given the societal relevance of cognitive dysfunction and the omnipresence of cardiovascular risk and disease, these questions require our attention.

The researchers of the AGES-Reykjavik Study are to be applauded for using precise MR methodology in a well-defined cohort. As such work often does, it provides new knowledge, yet also raises questions. As already suggested by the authors, longitudinal studies, including more

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population-based data, are required to clarify the impact and sequence of risk factors on cardiac and cognitive dysfunction. The brain and the heart are rightfully considered key players in our system, yet we have to learn more about how they play together.

## Disclosures

None.

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