Baroreflex, Cerebral Perfusion, and Stroke: Integrative Physiology at Its Best

To the Editor:

We wish to congratulate Sykora et al for their timely review on the potential role the arterial baroreflex plays in cerebrovascular disease outcomes. Although it may seem intuitive that both arterial baroreflex function and cerebral blood flow (CBF) regulation are important modulators of stroke outcome, clear and consistent evidence implicating the arterial baroreflex as an independent clinical predictor of stroke-related mortality is only emerging. The authors proffer several plausible hypotheses linking baroreflex dysfunction to the etiology of acute stroke and related clinical outcomes. Among them, the proposed “cross-linked” impairment of cerebrovascular autoregulation (CA) and altered autonomic drive as part of an underlying regulatory continuum in the context of stroke require further discussion.

According to classic dogma, CBF is autoregulated across a wide range of blood pressures (60 to 150 mm Hg). This concept suggests that the arterial baroreflex may be relatively unimportant for CBF control. Consistent with this notion, baroreflex-mediated changes in cerebral sympathetic nerve activity have been shown to play a limited role in regulating cerebrovascular tone, and animal studies using carotid baroreceptor stimulation or baroreceptor denervation protocols have failed to demonstrate any consistent baroreflex modulation of steady-state measures of CBF. However, although such experiments suggest that the baroreflex does not tonically modulate the static component of CA, which regulates CBF against gradual changes in blood pressure, they do not answer important questions that might be crucial to understanding why baroreflex dysfunction is an adverse prognostic indicator for stroke. For example, does the baroreflex modulate or interact with the dynamic component of CA, which is concerned with CBF regulation against rapidly changing blood pressures? And are there interactions between dynamic CA and baroreflex mechanisms taking place independent of baroreflex capacity to modulate cerebrovascular tone?

Searching for evidence of such interactions in humans, we recently showed that dynamic CA was significantly attenuated in healthy human volunteers after combined β1-adrenergic and muscarinic cholinergic blockade. The reduction in dynamic CA was related to the attenuated tachycardia after autonomic blockade, indicating that acute loss of the cardiac baroreflex compromises CBF homeostasis. Surprisingly, however, we subsequently observed that in otherwise healthy volunteers, dynamic CA was inversely correlated to cardiac–vagal baroreflex sensitivity and positively correlated to arterial blood pressure variability; that is, subjects with lower baroreflex sensitivity had greater blood pressure variability and better dynamic CA (and vice versa). These relationships have 2 main implications. First, they provide empirical support for the “cross-linked mechanism” hypothesis that CA and peripheral autonomic drive is part of the same underlying regulatory continuum. Second, they suggest that in the absence of stroke, dynamic CA may adjust over time to optimize CBF control depending on the prevailing level of baroreflex sensitivity or blood pressure variability. Such neuroplasticity could explain why spontaneously hypertensive persons with baroreflex impairment and elevated blood pressure variability have augmented dynamic CA compared with normotensive controls. However, more importantly, if such compensatory interactions were not able to take place, as might occur after a stroke with irreversible damage to the relevant neural networks responsible for CA–baroreflex integration, the brain would be rendered more vulnerable to excess variations in blood pressure. Therefore, we support the speculation that cross-link mechanisms governing the balance between baroreflex sensitivity and dynamic CA may be an important target in the development of new therapeutic interventions for stroke treatment and prevention. In this regard, the study of normal integrative physiology will no doubt continue to inform our understanding of cerebrovascular pathophysiology.

Disclosures

None.

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