Commentary on ‘Current computational models do not reveal the importance of the nervous system in long-term control of arterial pressure’

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In their review, Osborn et al. (2009) put forward many arguments in favour of an important role of the nervous system in long-term control of blood pressure (BP). However, the issue is not whether dysregulation of the autonomic nervous system can or cannot affect BP, but by which mechanisms such a dysregulation may affect BP.

As pointed out in our review (Montani & Van Vliet, 2009), there is considerable evidence for the role of the kidney and the pressure–natriuresis relationship (PNR) in long-term BP control. This viewpoint is challenged by Osborn et al. (2009), who argue: (1) that pressure natriuresis is important only under pathophysiological situations, as a 'back-up' to hormonal controllers of sodium balance; (2) that the kidney adapts to BP changes, and that sodium balance is controlled by hormonal systems independently of BP; (3) that Guyton’s model regulates BP via the control of blood volume, which is not well related to BP; (4) that Guyton’s model minimizes the role of the central nervous system (CNS) in long-term BP control; and (5) that an alternative mechanism of long-term BP control can be proposed with the sympathetic nervous system acting on blood volume distribution rather than via the kidney. The authors conclude that Guyton’s model cannot serve as a starting point and that new mathematical models should be developed based on different core concepts.

We will comment briefly, point by point. First, the acute PNR has been demonstrated in diverse situations, including isolated perfused kidneys, anaesthetized preparations and conscious animals. The relationship is continuous and operates over a wide range of physiological pressures without an apparent threshold. However, it is clear that other systems act to modify this relationship, altering the kidney’s ability to excrete salt and water at any given level of BP and thereby permitting salt balance to adjust even in the absence of a change in BP.

Second, there is strong experimental support for a sustained effect of BP per se on sodium excretion. In dogs instrumented for separate control of the perfusion pressure to each kidney, the acute PNR did not adapt during long-term (12 day) changes in arterial pressure (Mizelle et al. 1993).

Third, the authors misinterpret Guyton’s reliance on blood volume in regulating BP. Blood volume is an intermediary used to alter BP until sodium balance is again achieved. More importantly, BP is not a function of blood volume per se but of the ‘volume in excess’ in the vascular tree. Substances such as the vasoconstrictors angiotensin and noradrenaline, which decrease vascular capacitance at the same time as they promote sodium retention, thereby lead to hypertension in a volume-contracted state.

Fourth, Guyton’s analysis does not argue against the potential for the CNS to influence long-term BP control, it simply requires that the CNS modify the PNR so that salt balance can be achieved at the new BP level. Although the renal nerves are one pathway by which the CNS may modify the PNR, there are many other possibilities.

While improving what the authors call ‘the most widely accepted model for long-term control of arterial pressure’ is an ambitious task, there is no doubt that modelling the regulation of long-term BP is worthy of much further study. However, to be useful, mathematical models must be well rooted in empirical data to confirm the behaviour of the complete model and its components. With this in mind, it is our belief that mathematical models of long-term BP control should incorporate a pressure–natriuresis mechanism that does not adapt to pressure itself, but is sensitive to modulation by neurohumoral systems.

References