Role of Epithelial Sodium Channels in the Renal Myogenic Response?

To the Editor:

The recent publication by Guan et al1 and the accompanying editorial in a recent issue of Hypertension2 both state that the findings of Guan et al1 contradict the observations that we published previously concerning the effects of benzamil and amiloride on the myogenic response of the renal afferent arteriole.3 We argue that much of the data in the 2 studies are, in fact, complementary. In Guan et al1 and in our study, benzamil and amiloride did not inhibit the afferent arteriolar myogenic response at concentrations ≤1 μmol/L. We observed no affect of 3 μmol/L of amiloride, whereas Guan et al1 found 5 μmol/L of amiloride to fully block myogenic responses. It is important to note that the original studies implicating epithelial sodium channels (ENaCs) in myogenic signaling reported inhibition at concentrations >10 nmol/L. Studies directly evaluating the blockade of ENaC with amiloride analogues at such concentrations. We also observed marked effects of 10 μmol/L of benzamil on the afferent arteriole, but these actions were clearly not related to ENaC blockade (see Reference3 for discussion). Thus, our observations and those of Guan et al1 are quite similar. It is only our interpretations of these data that differ.

Finally, we could not consistently detect α, β, or γ ENaC mRNA in afferent arterioles.3 Using immunofluorescence, Guan et al1 report all 3 of the subunits to be expressed. Although the reasons underlying these apparently incompatible results await further investigation, it is noteworthy that the presence of the α subunit is suggested by Drummond et al4 to be incompatible with a role for the protein complex in mechanotransduction, because a constitutively active channel should be present if all 3 of the subunits are expressed. Direct electrophysiological approaches may ultimately resolve this issue and determine whether a channel with the functional and pharmacological properties of ENaC is observed in afferent arteriolar myocytes.

Disclosures

None.

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