EDITORIAL

Contribution of Sympathetic Nervous System to High Blood Pressure in Salt Hypertensive Dahl Rats

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The important participation of sympathetic nervous system in various forms of experimental hypertension is well known. This is also true for salt hypertension elicited by excess salt intake in Dahl salt-sensitive rats (for review see Zicha *et al.* 2012). Two recent studies in Dahl rats (Zicha *et al.* 2019, Puleo *et al.* 2020) evaluated the hypothesis on the role of β-adrenergic WNK4-NCC pathway in salt-sensitive hypertension which has been proposed by Mu *et al.* (2011). Although these studies differed in many experimental details, both of them demonstrated a major importance of α_1- rather than β-adrenergic mechanisms for the development of salt hypertension in this rat strain.

Zicha *et al.* (2019) demonstrated that chronic β-adrenergic blockade by propranolol did not lower blood pressure (BP) in Dahl salt-sensitive rats developing salt hypertension. It also did not modify their sympathetic component or natriuretic response to acute hydrochlorothiazide administration which inhibited the activity of sodium-chloride cotransporter (NCC). Puleo *et al.* (2020) reported that chronic β-adrenergic blockade failed to affect salt hypertension development or to reduce renal WNK4-NCC pathway. On the other hand, their study demonstrated the important influence of α_1-adrenergic pathway on the activity, expression and phosphorylation of NCC. Chronic α_1-adrenergic antagonism by terazosin treatment in Dahl salt-sensitive rats, which started before the onset of high salt intake, considerably attenuated the development of salt hypertension. This treatment diminished BP difference between the salt-loaded Dahl salt-sensitive rats and their control groups by 70-75 %. However, terazosin-treated Dahl salt-sensitive animals fed a high-salt diet had not only suppressed renal NCC activity but they also did not respond to acute phenylephrine administration. This suggests that chronic α_1-adrenergic blockade affected both renal sodium retention mechanisms and α_1-adrenergic vasoconstriction (Puleo *et al.* 2020).

It remains to determine how these two mechanisms contribute to salt hypertension in Dahl rats. We found that the acute ganglionic blockade lowered substantially BP of salt hypertensive Dahl rats, abolishing 45-55 % of the BP difference between salt-loaded Dahl salt-sensitive rats and their control groups (Zicha *et al.* 2019). If we consider the results of both above studies, it seems that the renal contribution might be responsible for about 25 % of BP elevation seen in Dahl salt-sensitive rats developing salt hypertension, whereas α_1-adrenergic vasoconstriction contributes to this BP change by about 50 %.

Of course, this consideration is highly speculative. Nevertheless, it might stimulate further effort to distinguish the role of kidney and brain in the pathogenesis of salt hypertension. Perhaps even more promising could be the estimation of renal and extrarenal effects of central sympathoexcitation in Dahl rats (Mark 1991, Gabor and Leenen 2012, Fujita *et al.* 2009) which is related to central α_2-adrenergic mechanisms (Wainford *et al.* 2015). As far as the role of kidney in the pathogenesis of salt hypertension is concerned (Frame *et al.* 2019), some attention should also be paid to participation of renal vascular and tubular effects of increased sympathetic tone in these salt hypertensive animals.

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