22) Neurotransmitter Release and Vascular Reactivity in Young and Adult Spontaneously Hypertensive Rats

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(Objective)

The change of the sympathetic nervous system have been implicated in the pathogenesis and maintenance of hypertension in spontaneously hypertensive rats. The objective of the present study was to measure neurotransmitter release from the sympathetic nerve endings around vascular beds of SHR and WKY at young and adult ages. And Ca-mediated control of neurotransmitter release as well as vascular reactivity were, also, investigated by using Ca-antagonist (verapamil).

(Materials and methods)

Isolated loop preparations of the mesenteric arteries in SHR (young; 7-8w, adult; 20-22w) and age-matched WKY, were perfused with Ringer-Locke solution. Pressor responses to electrical nerve simulation (5-15HZ) or exogenous noradrenaline (NA) were recorded. And the NA content in the perfusate was measured before and after the nerve stimulation, using high pressure liquid chromatography with electrochemical detector. The effects of Ca-antagonist on NA release and vascular reactivity were evaluated in the presence of various concentrations of verapamil in the perfusion fluid (5.0x10^-7M-2.5x10^-6M).

(Results)

(1) Pressor responses to electrical nerve stimulation were greater in SHR (at 15HZ stimulation; 7-8w 45.5±27.8mmHg, 20-22w 87.1±17.2mmHg, mean±SD) than WKY (7-8w 17.1±11.1mmHg, P<0.02; 20-22w 53.5±14.3mmHg, P<0.005).
(2) Similar results were also obtained for injections of exogenous NA (at 3.3ng of NA injections; 7-8w SHR 80.4±22.4mmHg, WKY 36.6±20.9mmHg, P<0.005; 20-22w SHR 125.0±16.3mmHg, WKY 93.3±9.3mmHg, P<0.005).
(3) The NA overflow from mesenteric vasculature was also greater in young SHR (5HZ; 0.61±0.35ng/g of tissue wet weight, 10HZ; 1.17±0.46ng, 15HZ; 1.63±0.69ng, mean±SD) than in age-matched WKY (5HZ; 0.34±0.30ng/g of tissue wet weight, 10HZ; 0.52±0.33ng, P<0.005, 15HZ; 0.65±0.62ng, P<0.05). On the contrary, in adult SHR, the NA overflow was reduced compared with WKY (at 15HZ stimulation, SHR 0.83±0.23ng/g of tissue wet weight, WKY 1.40±0.53ng, P<0.05).
(4) After infusion of verapamil (5.0x10^-7M-2.5x10^-6M), the suppression of pressor responses and NA overflow evoked by electrical nerve stimulation were greater in SHR than in WKY at both ages. Pressor responses to exogenous NA were also more inhibited in young SHR than in WKY. However, in adult SHR, the inhibition was similar to age-matched WKY.

(Conclusion)

These results suggest that NA release from the sympathetic nerve endings in SHR, which increases at young age and decreases at adult age, depends at least partly on Ca-influx, though vasoconstrictor reactivity is increased in SHR. Therefore, Ca-dependency in SHR at both pre- and post-synaptic sites of neurotransmission may contribute to the pathogenesis and maintenance of hypertension.