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Role of reactive oxygen species in salt-induced pressor and sympathoexcitatory responses

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Summary

High dietary sodium causes sympathetic hyperactivity and increases resting blood pressure (BP) in spontaneously hypertensive rats (SHR). Central nervous system mechanisms are thought to be involved in this response. Recent studies suggest that there is increased generation of reactive oxygen species (ROS) in the rostral ventrolateral medulla (RVLM) in SHR. The present study examined whether a high salt diet increases ROS in the RVLM of SHR and, if so, whether this is associated with BP elevation. Male SHR (6-week-old) and male WKY (6-week-old) were fed a high salt (8%: HS) or low salt diet (0.5%: LS) for 6 weeks. BP was measured using the tail-cuff method. Norepinephrine excretion was measured at 6 and 12 weeks of age. We evaluated ROS in the RVLM by measuring the levels of thiobarbituric acid-reactive substances (TBARs) at 12 weeks of age. To confirm the role of ROS in the RVLM in BP regulation, tempol (10 pmol, 100 pmol, and 1 nmol) was microinjected bilaterally into the RVLM of 12-week-old HS-SHR and LS-SHR. To determine whether basal sympathetic nerve activity is activated in HS-SHR, hexamethonium chloride was administered intravenously (40 mg/kg) at the end of the microinjection experiments. Systolic BP was significantly higher in HS-SHR than LS-SHR from 9 weeks of age on, but was not significantly different between HS-WKY and LS-WKY (211 ± 6 vs 170 ± 7 mmHg, $p<0.05$ at 9 weeks of age, n=5). Urinary norepinephrine excretion of HS-SHR was significantly higher than that of LS-SHR at 12 weeks of age (2.09 ± 0.97 vs 1.47 ± 0.51 μg/day, $p<0.05$ n=4). TBARs levels were significantly higher in the RVLM of HS-SHR than in the RVLM of LS-SHR (9.94 ± 0.46 vs 8.07 ± 0.61 μmol/g tissue, $p<0.05$, n=5), but were not significantly different between HS-WKY and LS-WKY. Bilateral microinjection of tempol into the RVLM tended to induce a greater depressor response in HS-SHR than in LS-SHR. These results suggest that a high salt diet increases ROS in the RVLM of SHR, which is associated with further increases in BP, at least in part via activation of the sympathetic nervous system.