Redox imbalances incite the hypertensive, baroreflex, and autonomic effects of cyclosporine in rats.

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Abstract

Previous studies including ours showed that cyclosporine (CSA) causes baroreflex dysfunction and hypertension. Here we tested the hypothesis that oxidative damage in central and peripheral tissues underlies the hypertensive, baroreflex and autonomic actions elicited by CSA in rats. We investigated the effects of individual and combined 7-day treatments with CSA (25 mg/kg/day, n=7) and 4-hydroxy-2,2,6,6-tetramethyl piperidinoxyl (tempol, superoxide dismutase mimetic, 100 mg/kg/day, n=7) on blood pressure, reflex heart rate responses to peripherally mediated pressor and depressor responses, and biomarkers of oxidative stress. CSA elevated blood pressure and reduced reflex bradycardic (phenylephrine) and tachycardic (sodium nitroprusside) responses. The ability of muscarinic (atropine, 1 mg/kg i.v.) or β-adrenoceptor blockade (propranolol, 1 mg/kg i.v.) to reduce reflex heart rate responses was reduced in CSA-treated rats, suggesting the impairment by CSA of reflex cardiac autonomic control. Concurrent administration of tempol abolished CSA-induced hypertension and normalized the associated impairment in baroreflex gain and cardiac autonomic control. Tempol also reversed the CSA-induced increases in aortic and brainstem nitrite/nitrate and malondialdehyde (MDA) and decreases in aortic superoxide dismutase (SOD). These findings implicate oxidative stress in peripheral and central cardiovascular sites in the deleterious actions of CSA on blood pressure and baroreceptor control of heart rate.