Cyclosporine adversely affects baroreflexes via inhibition of testosterone modulation of cardiac vagal control.

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Previous studies have shown that the immunosuppressant drug cyclosporine A attenuates arterial baroreceptor function. This study investigated whether the modulatory effect of cyclosporine on baroreceptor function involves inhibition of the baroreflex-facilitatory effect of testosterone. The role of cardiac autonomic control in cyclosporine-testosterone baroreflex interaction was also investigated. Baroreflex curves relating bradycardic responses to increments in blood pressure evoked by phenylephrine were constructed in conscious, sham-operated, castrated rats and in testosterone-replaced castrated (CAS + T) rats in the absence and presence of cyclosporine. The slopes of the curves were taken as an index of the baroreflex sensitivity (BRS). Short-term (11-13 days) cyclosporine treatment or castration reduced plasma testosterone levels and caused similar attenuation of the reflex bradycardia, as indicated by the significantly smaller BRS compared with sham-operated values (-0.97 +/- 0.07, -0.86 +/- 0.06, and -1.47 +/- 0.10 beats/min/mm Hg, respectively). The notion that androgens facilitate baroreflexes is further confirmed by the observation that testosterone replacement of castrated rats restored plasma testosterone and BRS to sham-operated levels. Cyclosporine had no effect on BRS in castrated rats but caused a significant reduction in CAS + T rats. Muscarinic blockade by atropine caused approximately 60% reduction in the BRS in sham-operated rats, an effect that was significantly and similarly diminished by castration, cyclosporine, or their combination. beta-Adrenergic blockade by propranolol caused no significant changes in BRS. These findings suggest that cyclosporine attenuates baroreflex responsiveness via, at least partly, inhibition of the testosterone-induced facilitation of cardiomotor vagal control.

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