TACSM Abstract

Centrally Acting Perindopril Attenuates the Exercise Induced Increase in Muscle Sympathetic Nerve Activity during Heavy Dynamic Exercise

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ABSTRACT

Central angiotensin II (Ang II) linked free radical (FR) production scavenges nitric oxide (NO) enabling an increased central sympathetic neural outflow (SNA). The pathophysiological increase in Ang II linked FR production is recognized as a major mechanism involved in neurogenic hypertension. During exercise, there is a physiological increase in Ang II and muscle sympathetic nerve activity (MSNA) in direct relation to increasing exercise intensity. We tested the hypothesis that the exercise induced increase in Ang II linked FR production and MSNA activity during exercise is located within the brain. Six healthy subjects performed three randomly ordered trials of 70° upright back-supported dynamic leg cycling after ingestion of two different lipid soluble Angiotensin converting enzyme inhibitors ((ACEi) Perindopril (PER) - highly lipid soluble; Captopril (CAP) non-lipid soluble)) and/or placebo (PL). Repeated measurements of whole venous blood, MSNA, and mean arterial pressures (MAP) were obtained at rest and during steady-state heavy intensity exercise at heart rates (HR) of 120 bpm (e120). Peripheral venous superoxide concentrations as measured by electron paramagnetic resonance (EPR) were not significantly altered at rest ($P \geq 0.4$) and during E120 by the ACE inhibitors ($P \geq 0.07$). Likewise, baseline MSNA (PL, 25 ± 1.5 bust/min; CAP, 21 ± 0.7 bust/min; PER, 25 ± 0.7 bust/min) and MAP (PL, 86 ± 2.8 mmHg vs. CAP, 84 ± 2.6 mmHg; PER, 84 ± 0.7 mmHg) were unchanged at rest ($P \geq 0.1$; $P \geq 0.8$ respectively). However, during E120 central acting PER attenuated the increases in MSNA and MAP, increasing only 15±6% for MAP and 24±8% for MSNA when compared to PL (26 ± 6% MAP; 57±16% MSNA; $P<0.05$) and CAP (26±4%MAP; 69±13%MSNA $P<0.05$). From these data we conclude that centrally acting PER attenuated the central increase in the exercise induced Ang II linked free radical production resulting in an increased central NO activity induced reduction in MSNA during heavy intensity dynamic exercise.