

07 EFFECTS OF ANGIOTENSIN II AND TUMOR NECROSIS FACTOR- α ON CARDIAC APOPTOSIS AND NOSII EXPRESSION

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ABSTRACT

Angiotensin II (AngII) and tumor necrosis factor (TNF) have been shown to promote reactive oxygen species, including superoxide anion and nitric oxide (NO), and induce apoptosis in vitro. These agents are implicated in cardiovascular disease, but few studies have evaluated their interactions in vivo. We tested the hypothesis that AngII, TNF, or their combination promotes cardiac cell apoptosis and that NOSII is a participant in these events. Osmotic mini-pumps were implanted in rats to deliver continuous infusion of AngII (288 μ g/kg/day), TNF (22 μ g/kg/day), or their combination, for 3 days. These treatments did not alter blood pressure or heart rate when compared to vehicle control (tail cuff measurements). At sacrifice on day 3 cardiac tissues were fixed in formalin for TUNEL staining and immunohistochemistry. AngII or TNF alone induced significant increases in cardiac cell apoptosis (nuclei/mm² = 18.7 \pm 8.4, 18.2 \pm 8.8) relative to vehicle control (7.5 \pm 2.2, p<0.05), but combined infusion resulted in no change (4.7 \pm 2.9). Apoptotic nuclei included both cardiac myocytes and non-myocytes. Prevalence of NOSII was slightly detectable in control tissues; no significant differences were observed in any treatment group (NS, digital image analysis). These results demonstrate that AngII and TNF alone promote cardiac apoptosis in vivo independent of hemodynamic changes, but their combined administration does not. This is apparently not related to NOSII induction, but suggest that important interactions exist between these agents in vivo.

tyrosine tyrosinase inhibitor.
pt pheochromocytoma 5-HT_{2A}
1. 5-HT_{2A}
2. 5-HT_{2A} antagonist α -blocker.