Radiofrequency renal denervation attenuates kidney fibrosis in spontaneously hypertensive rats
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OBJECTIVES/SPECIFIC AIMS: The goal of this study was to investigate whether RF-RDN attenuates renal fibrosis and inflammation in SHR with established hypertension. METHODS/STUDY POPULATION: Twenty-two-week-old SHR received bilateral RF-RDN or Sham-RDN (Biosensor Webster Stockert 70 generator and RF-probe). Four weeks later, SHR were sacrificed and paraffin sections of kidneys were stained for fibrosis by Masson's trichrome staining. Kidney tissue were homogenized for measurement of cytokines levels by ELISA. RESULTS/ANTICIPATED RESULTS: The results showed that Sham-RDN treated SHR had extensive fibrosis as demonstrated by moderate thickening of Bowman's capsule, collagen deposition in glomerulus, extensive tubulointerstitial fibrosis, and segmental glomerulosclerosis. In contrast, RF-RDN significantly reduced each of these pathological components of fibrosis in kidney cortex and medulla as compared with Sham-RDN treated kidneys. In addition, RF-RDN decreased CD4+ T cells and CD68+ T cells in the kidney of SHR as measured by flow cytometry. Meanwhile, kidney tissue levels of IL-17, INF-γ, MIP-3α, TNF-α, and TGF-β were decreased as compared with respective levels in Sham-RDN. DISCUSSION/SIGNIFICANCE OF IMPACT: Together, these findings demonstrate that removal of the influence of heightened renal sympathetic activity by RF-RDN decreases kidney inflammatory markers and attenuates renal fibrosis in hypertensive SHR.

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Regulation of retinal protein O-GlcNAcylation by angiotensin-(1-7) and cAMP
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OBJECTIVES/SPECIFIC AIMS: Increased retinal protein O-GlcNAcylation occurs in response to hyperglycemia and contributes to diabetic retinopathy. Renin-angiotensin system (RAS) blockers reduce the incidence of diabetic retinopathy. Beneficial effects of RAS blockers are often attributed to production of angiotensin-(1-7) (Ang1-7). The objective here is to determine the impact of Ang1-7 on retinal protein O-GlcNAcylation. METHODS/STUDY POPULATION: C57/B6J mice were fed a high-fat diet for 8 weeks and then treated for 3 weeks with either a vehicle control, the RAS blocker captopril, or captopril and the Ang1-7 receptor antagonist A779. R28 cells were used to assess levels of O-GlcNAcylated proteins in response to Ang1-7, and the role of cAMP was investigated with addition of forskolin, 6-Bnz-cAMP-AM, and 8-pCPT-2-O-Me-cAMP-AM to cell culture medium. RESULTS/ANTICIPATED RESULTS: Captopril attenuated retinal protein O-GlcNAcylation in mice fed a high-fat diet. This effect was reversed by A779. Ang1-7 attenuated protein O-GlcNAcylation and increased cAMP levels. Forskolin and the EPAC selective cAMP analog 8-pCPT-2-O-Me-cAMP-AM, but not the PKA selective cAMP analog 6-Bnz-cAMP-AM, attenuated O-GlcNAcylation. Inhibiting EPAC blocked the effect of forskolin, whereas inhibiting PKA did not. DISCUSSION/SIGNIFICANCE OF IMPACT: This study demonstrates a novel role for Ang1-7 in the retina and identifies a potential EPAC-dependent mechanism that regulates protein O-GlcNAcylation. Thus, future therapeutics targeted at an Ang1-7/EPAC axis in retina may be used to address Diabetic Retinopathy.

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Relationship power imbalance and history of male partner HIV testing among pregnant women in central Uganda
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