

Sex Differences in the Development of Abnormal Endothelium-Dependent Vasodilation in Aorta from Type 2 Diabetic Rats: Possible Role of Nitric Oxide

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Little is known about the interaction between diabetes and sex in vasculature. This study was designed to investigate whether there were sex differences in rat aortic endothelium-dependent vasodilation (EDV) in Zucker diabetic fatty (ZDF) rats, and the potential role of nitric oxide (NO). EDV to acetylcholine (ACh) was measured in aortic rings pre-contracted with phenylephrine (PE). Contractile responses to PE were generated before and after treatment with L-NAME (200 μ M), a NO synthase (NOS) inhibitor. In addition, the levels of endothelial NOS (eNOS) and NADPH oxidase (NOS, a potent source of superoxide) mRNA expression were determined using real-time RT-PCR. Type 2 diabetes significantly impaired EDV in aortic rings from female ZDF rats, however, potentiated the relaxation in males. Diabetes decreased the contractile responses to PE in aortic rings from rats, regardless of sex. Moreover, diabetes enhanced the extent of PE potentiation after blocking eNOS with L-NAME in females. Accordingly, the levels of eNOS mRNA expression were substantially enhanced in aorta of female ZDF rats compared to those in lean animals. In addition, Nox1 and Nox4 mRNA expression were substantially enhanced in aorta of female ZDF rats. These data suggest that the predisposition of the female aorta to injury in type 2 diabetes may be, in part, due to the alteration of NO production (supported by NIH/NIDCR).