The Role Of Reactive Oxygen Species And Oxidative Stress In The Development Of Endothelial Dysfunction And Hypertension In The Ageing Vasculature

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Excess cellular production of reactive oxygen species (ROS) (oxidative stress) has been found to play a major role in the pathogenesis of many cardiovascular diseases, such as atherosclerosis, hypertension and heart failure. Ageing is a primary risk factor of cardiovascular diseases. However, it is largely unknown about the role of oxidative stress in the development of endothelial dysfunction and vascular disorders found in the elderly. In this study, we used wild-type C57BL/6J mice, at young (3-4 m) and old age (20-24 m) (n=6) to investigate the potential role of ROS in age-related metabolic disorders and vascular dysfunction. All animal studies and procedures were approved by the Home Office and were performed in accordance with the Animals (Scientific Procedures) Act 1986. The body weight, heart weight and fasting glucose levels in the serum were recorded. There was no significant difference in the heart/body weight ratio (a measure of cardiac hypertrophy), and the levels of fasting glucose between the young and the ageing mice. The blood pressure was measured using volume pressure recording tail plethysmography, and there was a significant increase in blood pressure in ageing mice (141±2.5 mmHg) compared to their young controls (126±2.9 mmHg) (P<0.01). Vascular tone was examined using aortic rings isolated from the young and ageing mice in an organ bath. There was no significant difference in the vessel relaxation to a nitric oxide donor (sodium nitroprusside) between the young and ageing mice. However, there was a significant decrease in endothelium-dependent vessel relaxation to acetylcholine in ageing mice compared to their young controls, with maximum relaxations of 63±1.8 % (ageing) and 73±1.5 % (young) (P<0.01). Accompanied with the endothelium dysfunction found in the ageing mice, there was a significant increase (36%) in the levels of NADPH dependent superoxide production by the ageing vessels compared to the young controls as measured using lucigenin (5µM) chemiluminescence. In conclusion, there was a significant increase in the levels of ROS production in the vasculature of ageing mice (oxidative stress), which might contribute to the endothelial dysfunction and high blood pressure found in ageing mice.