

Role of leptin and insulin on renal sympathetic nerve activity in high fat fed rabbits

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Abstract

Using a rabbit model of obesity induced hypertension we have shown that a 3 week consumption of a high fat diet (HFD) induces elevated blood pressure (BP), heart rate, renal sympathetic nerve activity (RSNA) and plasma norepinephrine. Ganglion blockade completely abolishes the increase in blood pressure suggesting that this model of obesity hypertension is neurogenic. The changes are associated with elevation in plasma insulin and leptin which may be the basis for the development of long term obesity related hypertension. We found that 3 weeks of a HFD induces an increased sensitivity to the central sympatho-excitatory effects of leptin and also alpha-melanocyte stimulating hormone (MSH). We determined that the increase in BP and RSNA occur relatively quickly being detectable within 24 hours of commencing the diet. Also the main reason for the increases is the loss of pre-prandial reduction in cardiovascular measures. To determine the central mechanisms, we administered conscious rabbits with intracerebroventricularly (ICV) peptide antagonists of Leptin and Insulin. The insulin antagonist lowering BP slightly but had no effect on RSNA. By contrast leptin antagonist ICV abolished the hypertension and reduced RSNA. The antagonists had no effect in control rabbits. We conclude that increased RSNA associated with a HFD is due almost entirely to enhanced leptin signaling in the hypothalamus via MSH pathways.

Biography

Geoffrey Head is a Principal Research Fellow of the NH&MRC, Head of the Neuropharmacology Laboratory at the BakerIDI Heart and Diabetes Institute and adjunct Professor at Monash University. Research interests include, the understanding of mechanisms involved in the control of the heart and circulation by the central nervous system and its role in hypertension, heart failure and obesity. He has published over 200 scientific papers and is editor in chief of "Frontiers in Integrative Physiology". He was Secretary of the High Blood Pressure Research Council of Australia from 2005-10 and is treasurer for the International Society of Hypertension meeting in Sydney 2012.