Evidence for the role of $a_1A$-adrenoceptor subtype in the control of renal haemodynamics in fructose-fed Sprague–Dawley rat

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Abstract
Aim To explore the hypothesis that high fructose intake results in a higher functional contribution of $a_1A$-adrenoceptors and thereby blunts the adrenergically and angiotensin II (Ang II)-induced renal vasoconstriction.
Methods Twelve Sprague–Dawley rats received either 20% fructose solution (FPR) or tap water (C) to drink ad libitum for 8 weeks. The renal vasoconstrictor response to noradrenaline (NA), phenylephrine (PE), methoxamine (ME) and Ang II was determined in the presence and absence of 5-methylurapidil (5-MU) ($a_1A$-adrenoceptor antagonist) in a three-phase experiment (pre-drug, low- and high-dose 5-MU). Data, mean ± SEM were analysed by ANOVA or Student’s unpaired t-test with significance at $P < 0.05$.
Results FPR exhibited insulin resistance (HOMA index), hypertension and significant increases in plasma levels of glucose and insulin. All agonists caused dose-related reductions in cortical blood perfusion that were larger in C than in FPR while the magnitudes of the responses were progressively reduced with increasing doses of 5-MU in both C and FPR. The degree of 5-MU attenuation of the renal cortical vasoconstriction due to NA, ME and Ang II was significantly greater in the FPR compared to C.
Conclusions Fructose intake for 8 weeks results in smaller vasoreactive response to adrenergic agonists and Ang II. The $a_1A$-adrenoceptor subtype is the functional subtype that mediates renal cortical vasoconstriction in control rats, and this contribution becomes higher due to fructose feeding.
Keywords Renal vasoconstriction · Noradrenaline · 5-methylurapidil, fructose, $a_1A$-adrenoceptors

Introduction
Fructose intake produces an elevation in blood pressure [1], hypertriglyceridaemia [2] and hyperinsulinaemia [3]. Insulin resistance and hyperinsulinaemia in fructose-fed rats impair endothelial function and thereby contribute to the elevated blood pressure in this model [4]. Furthermore, an activation of the sympathetic nervous system due to fructose intake in the rat [5] has been associated with insulin resistance and may contribute to the onset and maintenance of cardiovascular and renal complications [6].

$\alpha_1$-Adrenoceptors have been suggested to be the functionally relevant adrenoceptor subtype in the renal vasculature of the rat [7, 8]. Three $\alpha_1$-adrenoceptor subtypes have been identified ($\alpha_1A$, $\alpha_1D$ and $\alpha_1E$), all from the G protein-coupled receptor family [9–11]. The $\alpha_1A$-adrenoceptor subtype has been reported to be the major functional subtype mediating adrenergically induced vasoconstriction in the kidney [12–14], and there is a shift in the functional contribution of $\alpha_1A$-adrenoceptor subtypes in certain