Adenosine A1 receptor-mediated haemodynamic responses in normal and lipopolysaccharide (LPS)-treated rats

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We hypothesised (Jolly *et al.*, this meeting) that reduced adenosine-mediated vasodilatation following LPS treatment could be explained by either enhanced A_1 receptor-mediated vasoconstrictor responses, or impaired A_2 receptor-mediated vasodilator responses. We have now assessed vascular responsiveness to the A_1 receptor agonist, 2-chloro-N^6-cyclopentyladenosine (CCPA) before and after treatment with LPS.

Anaesthetised (fentanyl and medetomidine 300µg kg^{-1} of each i.p.), male Sprague-Dawley rats (400-500g) had pulsed Doppler flow probes implanted to measure renal (R), mesenteric (M) and hindquarters (H) blood flows, and, at least 10 days later, catheters implanted in the jugular vein, peritoneal cavity and distal aorta. Experiments began at least 24h after catheter implantation. Cardiovascular responses to 3 min infusions of CCPA (1.4µg kg^{-1} min^{-1} i.v.) were assessed either 1.5h (n=8) or 6h (n=8) after saline (0.5 ml i.p.) on Day 1 and LPS (*E.coli* serotype 0127:B8, 1mg kg^{-1} i.p.) on Day 3.

In saline-treated rats CCPA caused significant ($P<0.05$, Friedman's test) bradycardia, hypotension, renal and mesenteric vasoconstriction and hindquarters vasodilatation (Table 1). At 1.5h after LPS treatment, CCPA caused greater bradycardia, smaller hypotension and no mesenteric vasoconstriction, whereas at 6h after LPS treatment, the bradycardic and renal and mesenteric vasoconstrictor responses to CCPA were greater than in the saline-treated condition (Table 1).

Table 1: Cardiovascular variables before (0) and changes (Δ) after 3 min CCPA infusions in saline- and LPS-treated rats. Values are mean ± s.e.m. Units are heart rate (HR) beats min^{-1}; mean arterial blood pressure (MAP) mmHg; vascular conductance (VC) (kHz $mmHg^{-1}$)10^3 at baseline (0) and % Δ. $^*P<0.05$ vs corresponding value in saline-treated rats (Wilcoxon Test).

	1.5h				6h			
	Saline		LPS		Saline		LPS	
	0	Δ	0	Δ	0	Δ	0	Δ
HR	336±6	-131±8	385±8*	172±12*	360±11	-75±11	416±6*	100±13*
MAP	110±2	-28±3	108±5	-16±3*	111±3	-7±1	99±3	-5±2
RVC	94±5	-45±4	109±7	-47±6	75±8	-29±3	98±11*	-35±4*
MVC	66±5	-19±5	50±9	+4±4*	70±8	-21±3	106±1*	-32±2*
HVC	45±5	+38±8	52±6	+28±6	42±5	+26±5	53±5*	+23±8

These results show that enhanced A_1 receptor-mediated vasoconstriction cannot explain the loss of adenosine-induced renal vasodilatation (at 1.5h after LPS) and hindquarters vasodilatation (at 6h after LPS) reported previously (Jolly *et al.,* this meeting). Whether or not these can be explained by changes in A_2 receptor-mediated vasodilatation remains to be determined.

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