Vasoconstriction of Porcine Coronary Artery by Amphetamines, Including MDMA

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Trace amine associated receptors (TAARs) bind amphetamines and structurally related molecules (Bunzow et al., 2001). This study aimed to determine whether 3,4-methylenedioxymethamphetamine ('Ecstasy', MDMA), D-amphetamine, (+)-methamphetamine ('crystal meth', (+)-MA) and (-)-methamphetamine ((-)-MA) cause vasoconstriction of isolated left anterior descending porcine coronary arteries via an indirect sympathomimetic action or whether the effect could be attributed to TAARs. Arterial rings were set up in Krebs solution (37 °C) gassed with 5% CO_2 in O_2 with an initial resting tension of 5g. Isometric tension was recorded on a PowerLab/4SP computer system and cumulative concentration–response curves for the amphetamines plotted as a percent of the constriction to KCl (60 mM). Statistical comparisons used one-way ANOVA and Dunnett post-test or unpaired t-tests. All amphetamines tested produced concentration-dependent vasoconstrictions that were not inhibited by the non-selective beta- and alpha 1-adrenoceptor antagonists DL-propranolol (3μM) and prazosin (1μM), respectively. The maximum responses and Log molar EC_{50} values to the amphetamines were not significantly different from that of MDMA in the presence of the adrenoceptor antagonists (Table 1). MDMA, D-amphetamine, (+)-MA and (-)-MA induce vasoconstriction via mechanisms other than sympathomimetic activity, probably via trace TAARs. However, the potencies are two-orders of magnitude less than for cloned TAAR1 in cell lines (Bunzow et al., 2001). Supported by the British Heart Foundation.

Table 1: Maximum responses to MDMA, D-amphetamine, (+)-MA and (-)-MA in the presence of DL-propranolol and prazosin in porcine coronary arteries. mean ± s.e.m.

	Maximum (%KCl)	**Log molar EC50**	**n**
MDMA	50.7± 5.9	-3.64 ± 0.10	4
D-amphetamine	38.5± 6.9	-4.09± 0.29	4
(+) - MA	49.8± 4.3	-3.49± 5.68	4
(-) - MA	36.5± 6.6	-3.05± 0.07	4

Bunzow, JR. *et al.* (2001). *Mol Pharmacol,* **60**, 1181-8.