MDMA AND CAFFEINE: A LETHAL COMBINATION

K.M. O'Boyle, K. Murphy and J.J. Callanan[1]. UCD Schools of Biomolecular and Biomedical Sciences and [1]Agriculture, Food Science and Veterinary Medicine, Conway Institute, University College Dublin, Belfield; Dublin 4, Ireland.

The ring-substituted amphetamine derivative 3,4-methylenedioxymethamphetamine (MDMA, ecstasy) is a widely used drug of abuse that causes acute hyperlocomotion and hyperthermia and long-term serotonergic neurotoxicity (Green et al., 1995). The aim of the present study was to investigate whether MDMA-induced toxicity was altered by co-administration of caffeine, a CNS stimulant frequently contained in impure ecstasy tablets and also in caffeine-laced high energy drinks.

Male Wistar rats (250-350 g) received two i.p. injections at 60 min intervals: saline or 20 mg/kg caffeine i.p. followed by saline or 20 mg/kg MDMA. Rats were assessed for (i) acute hyperthermic effects of drug treatments using a Braun Thermoscan infrared aural thermometer with digital readout, (ii) changes in blood biochemistry using a wet chemistry analyser (Randox Daytona) and (iii) post-mortem for changes to vital organs.

All rats that were treated with 20 mg/kg MDMA (n=25) survived; however, 4/4 rats co-treated with 20 mg/kg caffeine and 20 mg/kg MDMA collapsed lost their righting reflex and died within 4 hr of administration of MDMA ($p<0.0001$; χ^2 test). Thereafter, co-treated rats were euthansed 3 hr after administration of MDMA. MDMA increased rat aural temperature. The hyperthermic effect of MDMA was significantly enhanced by caffeine 1 hr after MDMA (Table 1). Administration of MDMA caused a significant increase in serum levels of urea and creatinine. These effects of MDMA were enhanced by co-administration of caffeine, which alone did not alter these parameters (Table 1). Both MDMA and caffeine increased serum potassium levels; however, serum levels of potassium in co-treated animals were similar to vehicle treated controls (Table 1).

Table 1. Effects of 20 mg/kg MDMA alone and in combination with 20 mg/kg caffeine

	Saline/Saline	Caffeine/Saline	Saline/MDMA	Caffeine/MDMA
Temperature °C	36.9 ± 0.5	36.8 ±0.4	37.3 ± 0.6	39.2 ± 0.4$^{\$\$\$}$
Urea mM	7.7 ± 0.2	8.1 ± 0.6	10.8 ± 2.6***	14.5 ± 0.8$^{\$\$}$
Creatinine µM	52.7 ± 4.9	67.5 ± 3.6	98.1 ± 17.9***	117.2 ± 3.8$^{\$}$
Potassium mM	8.3 ± 1.5	11.1 ± 1.2*	12.6 ± 1.8**	7.3 ± 0.4 $^{\$\$\$}$

Temperature measurements were made 1 hr after the second injection. Data are means ± SEM, n= 3-8. **p<0.01, ***p<0.001 vs saline/saline, $^{\$}$p<0.05, $^{\$\$}$p<0.01, $^{\$\$\$}$p<0.001 vs saline/MDMA, 1 way ANOVA followed by Bonferroni's test

These data demonstrate that doses of caffeine and MDMA that individually are well tolerated by rats are lethal when administered together. The cause of death mediated by the drug combination remains to be established. However, the increased rate of rise of body temperature, as well as the changes to serum urea and creatinine levels that are indicative of acute renal damage, may be contributing factors.

Green, R *et al*., 1995, *Psychopharmacology* **119**, 247-260

Supported by The Higher Education Authority of Ireland