

### Effects of MDMA and caffeine on serotonin uptake by rat whole brain synaptosomes

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3,4-Methylenedioxyamphetamine (MDMA, ecstasy) is a popular drug of abuse. Its main action is to evoke the presynaptic release of forebrain serotonin by altering the activity of the serotonin transporter (SERT). Recent reports indicate that the combination of MDMA with caffeine is lethal to rats (O'Boyle et al, 2005). This has implications for humans as caffeine is often a contaminant of ecstasy tablets and is found in coffee and high energy drinks. The aim of this study was to determine whether caffeine altered the effects of MDMA on SERT in rat brain synaptosomes.

The uptake of [<sup>3</sup>H]5-HT from rat whole brain minus cerebellum was measured as described by others (Rothman et al., 1993). Fresh synaptosomes were preincubated with GBR12935 and nomifensine to block uptake through dopamine and norepinephrine transporters, then incubated with 5 nM [<sup>3</sup>H]5-HT; non-specific uptake was measured in the additional presence of 10 µM paroxetine.

The uptake of [<sup>3</sup>H]5-HT by synaptosomes was time-dependent and potently inhibited by paroxetine (IC<sub>50</sub> = 1 nM). As shown in Table 1, MDMA inhibited the specific uptake of [<sup>3</sup>H]5-HT at 25°C and 41°C with IC<sub>50</sub> values in the high nM range. The effect of MDMA on uptake was independent of temperature and was not altered by 10<sup>-4</sup> M caffeine at either temperature. Caffeine alone did not inhibit uptake.

Table 1. Effect of MDMA in the absence and presence of caffeine on [<sup>3</sup>H]5-HT uptake

|                                   | 25°C      | 41°C      |
|-----------------------------------|-----------|-----------|
| MDMA pIC <sub>50</sub>            | 6.7 ± 0.2 | 6.6 ± 0.1 |
| MDMA + caffeine pIC <sub>50</sub> | 6.9 ± 0.3 | 6.7 ± 0.1 |

pIC<sub>50</sub> = -log IC<sub>50</sub>. Data are means ± S.E.M of n=3-4 experiments

These results suggest that MDMA and caffeine do not interact at the level of SERT.

O'Boyle KM et al, 2005 Proceedings of the British Pharmacological Society at [http://www.pa2online.org/abstracts/Vol3Issue4abst\\_069P.pdf](http://www.pa2online.org/abstracts/Vol3Issue4abst_069P.pdf)  
Rothman RB et al, 1993, Synapse 14, 34-39.