Reprinted (±)3,4-methylenedioxyamphetamine (MDMA) treatment enhances hippocampal long-term potentiation in Dark-Agouti rats
Gilda Baccini, Raffaella Morini, Boris Mlinar and Renato Corradetti
Dipartimento di Farmacologia, Università di Firenze, Italy

**Introduction:** Memory impairment is a frequently reported adverse neuropsychological consequence of MDMA use in humans. In regular users, MDMA is suspected to cause serotonin (5 HT) system damage, an effect clearly demonstrated in laboratory animals. Hippocampus is crucial in learning and memory and also a region sensitive to MDMA toxicity. Long-term potentiation (LTP) is widely considered the underlying mechanism of learning and memory as it is typically disrupted by pharmacological treatments or pathological processes that impair memory in laboratory animals.

**Aim:** We examined the relationship between 5-HT depletion, considered as an index of damage caused by MDMA administration *in vivo*, and the induction of LTP in the CA1 region *in vitro*.

**Methods**

**In vivo treatment of Dark-Agouti (D-A) rats**

- Multiple treatment (MT) [Week 1, Week 2, Week 3] → Experimental day
- Single treatment (ST) [Week 1] → Experimental day

**Extracellular recording in hippocampal slices**

Two independent synaptic inputs were alternatively activated by electrical stimulation of stratum radiatum. fEPSPs (set to ~40% of max in control) and population spikes (PSs) were recorded from area CA1. LTP was induced by theta rhythm-based patterns delivered to either input (Theta Bursts comprising of 5 or 10 trains of five pulses at 100 Hz, separated by 200 ms, thereby called TB5 and TB10, respectively). **Monoamine tissue content** was determined by HPLC in slices taken from the same animals. Statistical significance was assessed with Mann-Whitney test, two tails.

**Results and Conclusions**

Single MDMA treatment changed neither hippocampal monoamine content (5-HT, -10±2%; n=9) nor LTP induction (n=8, P=0.67). In contrast, repeated MDMA treatment reduced hippocampal 5-HT content by 55±3% (n=12; P<0.05) without affecting NA and dopamine level. TB5-induced LTP was significantly greater in MDMA-MT group compared to Sham-MT group (42.9±3.5%; n=12 vs. 29.2±3.2%; n=12; P<0.01). The magnitude of TB10-induced LTP in the same slices was not different (P=0.78), showing that near-maximal LTP was unaffected by multiple MDMA treatment.

These findings suggest that 5-HT depletion induced by MDMA interferes with learning and memory through functional saturation of hippocampal pathways rather than by disruption of synaptic plasticity.