

Dopamine release in vivo by trazodone: studies with microdialysis in rats

G. Santo, F. Zitarelli, S. De Santi, B. Garrone and L. Durando

ACRAF – Angelini Research Center, S.Palomba – Pomezia (RM) - Italy

Addiction is a complex disorder characterized by compulsive drug use. The nucleus accumbens is considered a key target of the action of abuse drugs. Several studies have shown a role for mesolimbic dopamine in mediating the behavioural effects of positive reinforcers. Drugs abused by humans (e.g., opiates, ethanol, nicotine, amphetamine, and cocaine) increase extracellular dopamine concentrations in nucleus accumbens whereas non-addictive drugs fail to modify synaptic dopamine concentrations.

The aim of the present study was to evaluate the effect of trazodone on extracellular dopamine levels in the nucleus accumbens in freely moving rats using microdialysis technique coupled to high performance liquid chromatography (HPLC) detection method.

For the microdialysis experiments stereotaxic surgery was performed. Animals were anaesthetized and placed in a Kopf stereotaxic frame. A guide cannula was then implanted in the nucleus accumbens. Briefly, twenty-four hours after surgery, each rat was placed in a plexiglas cage. After a 1 hour equilibrating period, a total of ten dialysate samples, at 30 min interval each, were collected. Dopamine levels in dialysate samples were quantified using HPLC detection method.

Drugs were administered after the collection of the first three samples (baseline). Animals received a single intraperitoneal (ip) injection of trazodone (10 and 100 mg/kg) or morphine (20 mg/kg). Control animals received only the vehicle.

Changes in dopamine levels were expressed as percent variations over the mean of the samples collected before drug administration (baseline). Drugs effect was also expressed as area under the curve (AUC).

In agreement with previous literature data, ip administration of morphine at the dose of 20 mg/kg induced a time-dependent increase in extracellular dopamine level peaking after 2.5 h. Conversely, single administration of trazodone at the dose of 10 and 100 mg/kg did not induce changes in dopamine levels respect to the control group. These results were confirmed by AUC analysis.

Our study demonstrated that trazodone does not induce changes in extracellular dopamine levels in the nucleus accumbens, while an increasing effect was observed after treatment with the reference drug morphine. Our experimental results suggest a low abuse potential for trazodone.

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