

Poster presentation

Effect of agmatine on mophine dependence in comparison with L-NAME: a microdialysis study in nucleus accumbens

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Background

Agmatine is an endogenous amine synthesized from L-arginine. It has several biological actions including NMDA receptor blockade and nitric oxide inhibition. It potentiates morphine analgesia, prevents tolerance and inhibits all symptoms of withdrawal. The aim of present study was to investigate effect of agmatine on L-citrulline levels during morphine dependence and withdrawal in nucleus accumbens.

Materials and methods

Three morphine pellets were implanted on successive days, namely one on the first and two on the third day, each containing 75 mg of base morphine, and the animals in control group were implanted with empty pellets. On the fourth day, stereotaxic surgery was performed to implant a concentric microdialysis probe into the NAcc of each rat. Twenty-four hours after stereotaxic surgery basal microdialysis samples were collected at 20 min intervals. After the collection of three basal samples, the rats were treated either with intraperitoneal saline or L-NAME (100 mg/kg) or agmatin (40 mg/kg). Forty minutes later, the rats were injected with naloxone (2 mg/kg) to elicit the signs of abstinence syndrome. The microdialysis samples were collected continuously during all these procedures. L-citrulline concentrations in the microdialysis samples were analyzed using HPLC with fluorescent detection. The change in L-citrulline levels was used as an indirect measure of NO production.

Results

The L-citrulline levels increased significantly in the first twenty minutes of naloxone induced morphine withdrawal period ($p < 0.01$), in saline treated morphine dependent rats. This increase was diminished by L-NAME and agmatine treatment in morphine dependent rats.

Agmatine found more potent than L-NAME on preventing withdrawal symptoms.

Discussion

These results may reveal that agmatine exerts its favorable effects during abstinence through some other mechanisms rather than its effect on NO synthase inhibition.