THE EFFECTS OF PIRACETAM ON MORPHINE-INDUCED AMNESIA AND ANALGESIA: THE POSSIBLE CONTRIBUTION OF CENTRAL OPIATERGIC MECHANISMS ON THE ANTIAMNESTIC EFFECT OF PIRACETAM

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ABSTRACT


The involvement of opiatergic mechanisms on the antiamnestic effects of piracetam was investigated in mice. First, the effects of piracetam and naloxone on the amnesia induced by scopolamine, electroconvulsive shock and morphine were evaluated by using elevated plus maze apparatus. Second, the effects of electroconvulsive shock and piracetam on the antinociceptive action of morphine were tested by means of radiant heat tail-flick experiment. Piracetam and naloxone reversed the drug- or electrically-induced amnestic effects. On the other hand, electroconvulsive shock treatment enhanced the antinociceptive effect of morphine while piracetam decreased the same activity. These results suggest an important role of the opiatergic system on the learning and memory process as well as on the antiamnestic effect of piracetam.

Keywords: electroconvulsive shock, morphine, naloxone, piracetam

INTRODUCTION

A nootropic drug, piracetam, which is known to have cognition-enhancing properties, is able to reverse the amnesia induced by electroconvulsive shock (ECS), scopolamine and hypoxia [1]. The mode of action of piracetam and related compounds, however, has not been clearly elucidated. They facilitate cholinergic transmission, a mechanism by which the enhancement of cognition may be produced [2,3]. The cholinergic system may play an important role in memory processes since cholinergic receptor antagonists, atropine and scopolamine, impair memory functions [4] and an acetylcholinesterase inhibitor, physostigmine, facilitates the same parameters [5]. Other transmitters, such as glutamergic, GABAergic, serotonergic, monoaminergic and opiatergic transmitters, may also participate in the cognition-enhancing action of nootropics. The indication for such possible mechanisms arises from the fact that ECS-induced amnesia, in which piracetam has memory-improving effect, can produce many biochemical changes in the central nervous system [6]. Among them, the release of opioid peptides after ECS treatment [7,8] seems to be interesting.
The present study was designed to assess whether the opiateergic system is involved in the effects exerted by piracetam on memory in mice. We employed morphine as an opioid agonist and examined the effects of piracetam and naloxone on scopolamine-, ECS- and morphine-induced amnesia. The effects of ECS treatment and piracetam on morphine-induced analgesia were also examined. In these experiments, the drugs were administered either alone or in combination to animals and the effects were evaluated by using the elevated plus maze apparatus. The tail-flick test was performed to investigate the analgesic activities, and the rota-rod test was also included to examine piracetam action on the motor functions of mice.

MATERIALS AND METHODS

Mice of either sex weighing 20-25 g were obtained from the Animal House of Çukurova University. They were housed in metal cages in a laboratory maintained at a room temperature of 22°C with a 12-h light–dark cycle. Each cage had five animals of the same sex. Food and water were provided ad libitum. The principles of laboratory animal care published by NIH were followed during the experiments.

Elevated plus maze experiments

The plus maze consisted of two open arms, 10 × 50 cm, and two enclosed arms, 10 × 50 × 50 cm [6]. The arms of each type, which were opposite each other, extended from a central platform (10 × 10 cm) raised 50 cm above the floor. The open arms and central platform were painted white and enclosed arms painted black. The principle in this experiment is based upon the aversive behaviour of rodents to open and high spaces. The animals dislike open and high spaces and move from them to an enclosed arm. The time before an animal enters an enclosed arm is termed the latency period (LP). Training (repeated exposure of animal to open arms) shortens this parameter, possibly as a consequence of learning acquisition and retention. In line with this observation, the measurements of LP values on the second day are significantly shorter compared with those on the first day and this continues over the subsequent days. Animals trained previously for two days were treated with scopolamine, ECS or morphine to produce amnesia. Piracetam and naloxone were used to test whether the amnestic situation is reversed by these agents.

Group I (control group)

The purpose of this experiment was to test whether training with the elevated plus maze of animals would cause the LP to shorten. Mice were individually placed at the end of one of the open arms facing the central platform and LP was recorded. Ten seconds after LP measurement, the animal was taken from the apparatus and put back in its own cage. The same test was repeated on subsequent days. One trial was