

Modulation of recognition and temporal order memory retrieval by dopamine D₁ receptor in rats

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Abstract

The present study examines the effects of SKF 81297, a selective D₁ agonist, on information retrieval in recognition and temporal order memory for objects, using three different tasks. Separate groups of rats were trained in each task and then given an intraperitoneal injection of saline or the D₁ agonist (0.03, 0.3 mg/kg), before the memory testing trial in an object recognition, object location, and object temporal order memory tasks. We show that SKF 81297, at high dose (0.3 mg/kg), facilitates information retrieval after a long delay (4 h) in the three memory tasks whereas both high and low doses of D₁ agonist impair recognition memory after a short delay (15 min). These results indicate a significant role of dopamine D₁ receptors in recognition memory for both familiarity and place of objects in addition to object temporal order memory.

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1. Introduction

Dopamine is a key neurotransmitter that plays an important role in modulating learning and memory processes. Many aspects of learning function such as reward, attention, and fear have been shown to be influenced by the dopaminergic system (Beninger & Miller, 1998; Cole & Robbins, 1989; Granon et al., 2000; Nader & LeDoux, 1999; Schultz, 2002). Additionally, there is evidence that dopamine plays a major role in spatial-working memory functions in animals from rodents to primates with an activation of D₁ receptors that can exert both beneficial and detrimental effects on working memory performance (Cai & Arnsten, 1997; Chudasama & Robbins, 2004; Floresco & Phillips, 2001; Murphy, Arnsten, Jentsch, & Roth, 1996; Seamans, Floresco, & Phillips, 1998; Zahrt, Taylor, Mathew, & Arnsten, 1997).

Only a few studies have investigated the role of dopamine in recognition memory. This form of memory can be tested in rodents using the object recognition tasks that are based on spontaneous activity and the natural preference that rats display to explore a novel object more than a familiar one when the animal remembers previous exposure to the familiar object (Ennaceur & Delacour, 1988). Advantages associated with this class of measure include the fact that performance does not depend on the retention of a rule, and is not based on usual positive or negative reinforcers, such as food deprivation, immersion or application of an electric shock. In rats, administration of the selective D₁ antagonist SCH-23390 was previously shown to block preference for novel objects (Besheer, Jensen, & Bevins, 1999) and, recently, it has been proposed that the mesoprefrontal dopaminergic system could contribute to recognition memory (Morrow, Roth, & Elsworth, 2000). However, these later experiments were not designed to examine the direct effects of dopamine activation on recognition memory, but to study the consequences of an olfactory

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stress that was associated with activation of dopamine neurons and increased serum corticosterone. In mice, the lack of dopamine D₄ receptors has also been associated with a reduced exploration of a novel object (Dulawa, Grandy, Low, Paulus, & Geyer, 1999), whereas D₄ activation increases such exploration in normal mice (Powell, Paulus, Hartman, Godel, & Geyer, 2003).

The aim of the present study was to examine the effects of a selective D₁ agonist, SKF 81297, on the retention of object memory after a short and a long-term delay during three kinds of recognition memory tasks. Administration of the drug prior to the memory testing trial enabled selective assessment of its contribution to the retrieval of information. Experiment 1 consisted in testing the influence of the D₁ agonist on the ability of rats to distinguish the novel from the familiar object in the spontaneous object recognition task (Ennaceur & Delacour, 1988). Experiment 2 tested the D₁ agonist effects on the ability of rats to recognize the novel location of an object in the object location task (Dix & Aggleton, 1999; Ennaceur, Neave, & Aggleton, 1997; Warburton, Baird, Morgan, Muir, & Aggleton, 2000). These first two tasks of object and location discrimination are of interest since they involve nonspatial and spatial information processing, respectively. In Experiment 3, we also investigated the D₁ agonist effects in the object temporal order memory task. In this case, spontaneous exploratory activity of normal animals is to spend more time exploring the old familiar object than the recent familiar object. This task requires an assessment of the relative time presentation of object sequences, and not simply an evaluation of the relative familiarity between previously encountered objects (Hannesson, Howland, & Phillips, 2004; Mitchell & Laiacina, 1998).

2. Materials and methods

The study consisted of three experiments. Experiment 1: object recognition task; Experiment 2: object location task; and Experiment 3: object temporal order memory task.

2.1. Subjects

A total of 157 adult male Sprague–Dawley rats (300–350 g, Charles River, France) were used in these experiments. Rats were housed in pairs in a temperature controlled room with food and water ad lib. and under a 12L:12D cycle (lights on at 7:00 am). Forty-nine naive rats were used in Experiment 1, 72 naive animals were used in Experiment 2, and a cohort of 36 naive rats was used in Experiment 3. All procedures were performed in conformity with National (JO 887–848) and European (86/609/EEC) legislations on animal experimentation.

2.2. Drugs

The selective D₁ receptor agonist SKF 81297 (6-chloro-7,8-dihydroxy-1-phenyl-2,3,4,5-tetrahydro-3-benzazepine hydrobromide; Sigma, France) was stored as concentrated stock solutions. In all experiments, each rat was given an i.p. injection of either saline (NaCl 0.9%) or SKF 81297 (0.03, 0.3 mg/kg) 10 min prior to the testing trial.

2.3. Apparatus

The apparatus consisted of an open-box (100 × 100 × 60 cm) made of wood with the inside covered with green sticking paper. The objects to be discriminated (three geometrical forms: blue cylinder, green pyramid, and red cube; three animal forms: yellow duck, blue crocodile, and blue turtle) were made of plastic (all 5 cm height) and were available in four copies. The objects were fixed (Patafix) on the floor of the box, to ensure that they could not be displaced by the rats.

2.4. Handling and habituation

Rats were handled daily for 1 week prior to the study and then habituated to the apparatus and the test room. The first 2 days, rats were put together as a group of 4 to explore the empty arena for 10 min. On the third day, rats were put individually in the empty box for 3 min and on the next 2 days, in the presence of an object that was not later used in the tasks. For Experiments 1 and 2, testing began on day 7, and for Experiment 3, testing began on day 6.

2.5. Experiment 1: Object recognition task

Animals were tested in the object recognition task as described previously (Ennaceur & Delacour, 1988). The test session consisted of two trials with a duration of 3 min each on day 7. During the training trial, each rat was placed in the box with two identical objects placed in the far corners of the box arena each 10 cm from the side wall. After a delay of 15 min or 4 h, during which the animal was returned to its cage and both objects were replaced (one by its identical copy, the other by a new object in the same locations), the rat was returned to the box (testing trial). From rat to rat, the role (familiar or new object) as well as the relative position of the two objects were counterbalanced and randomly permuted.

On the first day, saline- and SKF 81297-treated rats (low dose) were tested on a 15 min or 4 h-delay and 48 h later, the same saline-treated rats were tested on a different delay (15 min or a 4 h) depending on which delay they were tested on before. The same procedure was applied to SKF 81297-treated rats (high dose). Some rats had to be excluded from the experiment because of their lack of exploratory behavior (exploration time = 0 for

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