



Research report

Role of cholinergic-muscarinic receptors in visual discrimination performance of rats: Importance of stimulus load

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HIGHLIGHTS

- ▶ Rats learned to discriminate two visual cues in a water maze apparatus.
- ▶ After acquisition, removal of one of the cues impaired performance.
- ▶ Scopolamine impaired performance when one visual cue was present.
- ▶ Scopolamine did not impair performance when both cues were available.
- ▶ Muscarinic receptors maintain performance when information availability is reduced.

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ABSTRACT

Central cholinergic transmission has long been implicated in various cognitive processes, including memory acquisition, consolidation, and attentional processes. Here, we examined the role of muscarinic receptors in visual discrimination performance under conditions of altered visual information availability. Adult rats were trained to discriminate two visual cues (indicating the presence and absence of a hidden escape platform, respectively) in a water maze-based, trapezoidal-shaped apparatus. Following task acquisition, testing continued with two types of trials: regular trials (RTs; both visual cues present, identical to training conditions) and probe trials (PTs; only one of the two cues present). In Experiment 1, removal of one visual cue on PTs impaired discrimination performance. Moreover, scopolamine administration (0.125–1.0 mg/kg, i.p.) tended to further suppress performance in a dose-dependent manner on PTs, while discriminations on RTs were left intact. In Experiment 2, these results were confirmed and extended by showing that PT (one visual cue) performance could improve with training in undrugged, but not in scopolamine-treated rats. Together, these experiments reveal that visual discrimination performance of rats benefits from the concurrent availability of two visual cues that provide complimentary and consistent information. Furthermore, muscarinic receptors are particularly important under conditions of reduced visual information availability, as well as in the adoption of new behavioral strategies, such as switching from two-cue to single-cue guided navigation.

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1. Introduction

A large body of research, conducted over several decades, has consistently implicated acetylcholine (ACh) in a number of cognitive processes. Pharmacological studies have been particularly useful in establishing a link between ACh and cognition by demonstrating that, in general, agents known to interfere with cholinergic functioning impair cognitive processes in humans and other animals, while drugs that augment ACh can enhance cognition [1–7].

Moreover, the well-documented cholinergic modulation of several forms of synaptic plasticity, including receptive fields plasticity and long-term potentiation (LTP) [8–13], provides additional evidence for a role of ACh in cognition and processes of learning and memory. Thus, despite the ongoing debate regarding the specific cognitive domains influenced by central cholinergic transmission (e.g., acquisition, consolidation, attention) [3,4,7,14–16], there is little doubt that ACh acts as a key modulator of forebrain activity and complex, cognitive capacities.

Many studies that have assessed a potential role of ACh in cognition have employed navigation-based behavioral tests, such as the Morris water maze [5,17–21]. This work has shown that ACh, acting on muscarinic receptors, plays a much greater role in performance of the spatial (i.e. hidden platform) version relative to

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the cued (i.e., visible platform) version of the task [17,22,23]. Further, blockade of muscarinic receptors exerts significantly greater effects on task acquisition in naive rats than on consolidation or retrieval processes, or on performance of rats that have experience with the procedural (non-spatial) aspects of the task [5,17,21–23], results that are consistent with data showing pronounced increases in ACh release during the acquisition of spatial tasks (see Ref. [21] for review).

Interestingly, recent investigations have revealed a surprising degree of overlap of brain systems subserving spatial, associational learning (i.e., hidden platform water maze) and some other forms of learning in rodents. Epp et al. [24], employed a novel, water-maze based visual discrimination task that required rats to discriminate between two visual images placed at the end of two goal arms, with one image consistently indicating the presence of a hidden escape platform, while the other indicated its absence. Lesions of the hippocampal formation, long thought to be critical for spatial and associational/configurational learning [25], resulted in a retrograde loss of visual information acquired prior to the lesion [24]. Additional support for a hippocampal role in visual memories has been obtained using a recognition memory task with different delays (seconds to minutes) between presentation of a visual image and a recognition test [26]. Thus, it appears that the mnemonic functions of the hippocampal formation include visual information acquired during non-spatial, non-configural training regimens [24]. Whether the same is true for the central cholinergic system has, to our knowledge, not been thoroughly assessed.

With the present experiments, we utilized the water-maze based discrimination task described by Epp et al. [24] to assess the role of cholinergic-muscarinic receptors in visual discrimination performance of rats. In addition, we tested the role of visual stimulus load (one vs. two stimuli present) on task performance. The results indicate that rats trained to discriminate two visual stimuli (indicating the presence and absence of an escape platform) show impaired performance when one of these stimuli is removed during test trials, a deficit exacerbated by scopolamine-induced muscarinic blockade. Further, while control rats readily learn to adopt a successful search strategy guided by a single visual cue, scopolamine-treated animal fail to do so. Importantly, scopolamine did not impair performance on regular trials, when both visual cues are available to guide the discrimination. These results highlight an important interaction of muscarinic receptors and the availability for visual information to guide discrimination performance, with ACh being particularly important under conditions of reduced information availability.

2. Methods

2.1. Subjects

The experiments were conducted on adult, male Long-Evans rats ($n=42$; 300–500 g; Charles River, Quebec). All procedures followed the guidelines set by the Canadian Council on Animal Care and were approved by the Queen's University Animal Care Committee. Subjects were housed as pairs in polycarbonate cages in a colony room maintained on 12:12 h reversed light–dark cycle with free access to food and water. Behavioral procedures were carried out during the dark phase (7:00–19:00 h) of the light–dark cycle.

2.2. Visual discrimination apparatus

Visual discrimination training took place in a trapezoidal-shaped, Plexiglas insert (Fig. 1A), placed in a circular Morris water maze (180 cm diameter, 60 cm height). The water maze was filled with water ($22 \pm 2^\circ\text{C}$, made opaque by adding non-toxic, white paint) to a depth of 40 cm. The trapezoidal insert (140 cm length, 61 cm height; 81 and 51 cm width at the goal arm and release end, respectively) contained two goal arms, separated by a black Plexiglas divider (50 cm length). During training and regular test trials, a rectangular (36 cm \times 12 cm; 38 cm height) escape platform, constructed from clear Plexiglas, was placed 5 cm from the end of one of the two goal arms. The platform was submerged 2 cm below the water surface to remain hidden from view.

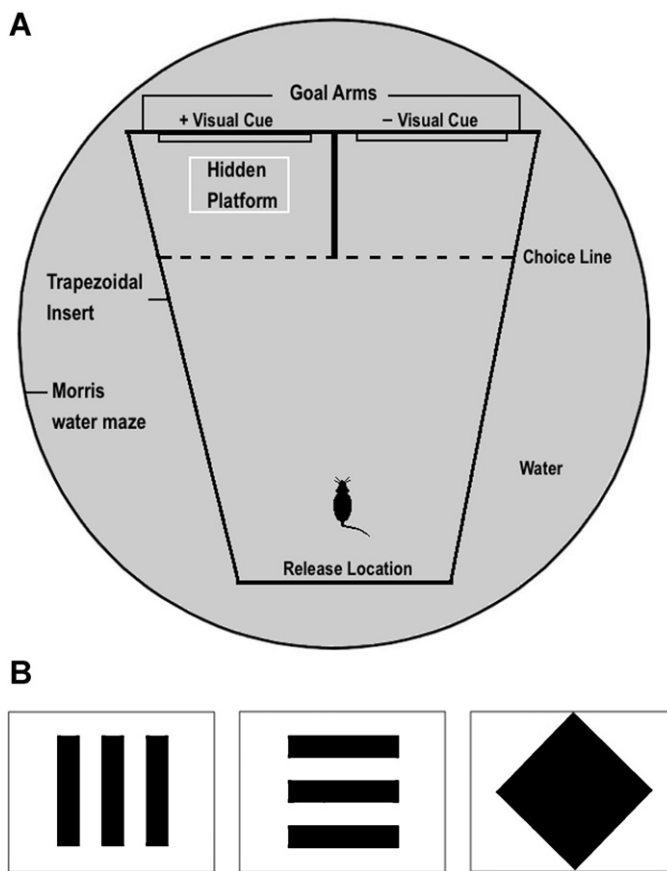


Fig. 1. A schematic representation of the test apparatus and visual stimuli used for visual discrimination training. (A) The major components of the apparatus include the circular Morris water maze, trapezoidal-shaped insert with the release end and two goal arms separated by a black divider, the location of the visual stimuli, and an example of the positioning of the hidden escape platform. (B) Visual stimuli used for discrimination training. For each rat, two of the cues were selected to serve as the CS+ (platform presence) and CS– (platform absence). The usage of cues was counterbalanced among subjects.

Three distinct geometric patterns, printed on laminated pieces of white paper (21.6 cm \times 28 cm), served as visual cues during training (Fig. 1B). The cues were designed as follows: (a) three solid black vertical bars (2.9 cm \times 14.5 cm) 2.9 cm apart; (b) three horizontal black bars (14.5 \times 2.9 cm) 2.9 cm apart; and (c) a solid black diamond (14.5 \times 14.5 cm). For each rat, two of the three visual cues were randomly assigned to act as the positive conditioned stimulus (CS+, indicating the presence of the escape platform) and negative conditioned stimulus (CS–, indicating the absence of the platform), with cues counterbalanced across animals. During training, rats learned to discriminate between the two cues, based on their respective association with the hidden escape platform.

2.3. Visual discrimination: training

Training procedures were similar to those described previously [27]. All subjects underwent three training phases, carried out over successive days. For all phases, a trial commenced when the rat was released into the pool facing the wall opposite to the goal arms. Rats then turned and swam toward the goal arms in order to locate the hidden escape platform. An experimenter recorded the first goal arm entered by the rat, defined by about half of the rat's body entering the arm. A correct response was scored when the rat entered the correct goal arm and mounted the hidden escape platform.

Phase 1: Habituation (Day 1): For one day, rats were habituated to swimming in the maze and climbing onto the platform in the absence of visual cues indicating platform location. Each rat received a maximum of 20 trials, administered as two blocks of 10 trials each. The escape platform remained in the same goal arm during each block, but was switched to the opposite arm between block 1 and 2. At the onset of each trial, the rat was released into the pool and allowed 60 s of swimming to find the hidden platform. If 60 s elapsed without successful localization of the platform, the experimenter manually guided the rat to it. Once the platform was mounted, the rat remained there for 15 s, until the start of the next trial. This procedure was

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