



Review

Recognition memory tasks in neuroendocrine research



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HIGHLIGHTS

- The use of recognition memory tasks in neuroendocrine research is reviewed.
- Advantages of recognition tasks as compared to other memory tasks are discussed.
- Gonadal hormones enhance while adrenal hormones impair memory.
- Increases in dendritic spine density may contribute to enhancements of memory.

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ABSTRACT

The recognition memory tasks, novel object and novel object location, have been beneficial to neuroendocrine research concerning the effects of gonadal and adrenal hormones on cognitive function. This review discusses the advantages of these tasks in comparison with other learning and memory tasks. Experiments conducted across a number of laboratories show that gonadal hormones, both estradiol and testosterone, promote memory while the adrenal hormone, corticosterone, impairs memory. The effects of these steroid hormones on spine density in the prefrontal cortex and hippocampus are also briefly presented. Overall, results show that these steroid hormones are potent modulators of memory consolidation in rodent models.

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1. Introduction

Use of the recognition memory tasks, novel object and novel object location, have been beneficial to neuroendocrine research concerning effects of gonadal, adrenal and other hormones on cognitive function. Hormones, in comparison to most drugs, exert wide ranging effects in brain areas and can affect psychological performance parameters like affective state, sensory-perception and motor activity. Thus, delineating hormonal effects on performance parameters from mnemonic effects in cognitive tasks is often difficult. Since recognition tasks do not rely on either positive or negative reinforcements, the influence of psychological performance parameters is greatly lessened. In addition, the tasks can be applied in a post training paradigm which measures memory consolidation. The current review focuses on use of recognition memory tasks to demonstrate that gonadal and adrenal hormones are potent modulators of memory in rodent subjects and provides some information on the mechanisms for the changes.

2. Application of recognition memory tasks

2.1. Rational for use

In order to mitigate possible confounding influences of task requirements, experience, reinforcements and psychological performance variables in assessing hormonal effects on memory, our lab and others have adopted the use of recognition memory tasks to investigate hormonal effects on learning and memory [1–3]. Most memory tasks utilize positive (food or water) or negative (shock or fear of drowning) reinforcements which can influence performance. Hormones can influence performance parameters like affect (arousal, anxiety, mood motivation), regulatory mechanisms (thirst, hunger, body weight, composition, temperature), sensory-perception (vision, audition, olfaction, gustation, touch, attention, proprioception, nociception) and motor ability (activity, balance, skill) [4]. Thus, tasks with positive or negative reinforcements are sensitive to effects of psychological performance parameters. Recognition memory tasks instead utilize the curiosity, novelty seeking and exploratory nature of most rodents. Rats will readily explore new or novel objects and are more likely to explore a new object or an object in a new location than one previously explored previously. Instituting a delay period between the first exploration of an object and when subjects are presented the same, known object and a new object, allows for the assessment of memory for the known object. In addition, recognition memory tasks require minimal learning which allows for measuring hormone effects on memory without confounding effects of learning. However, possible changes in some performance parameters such as anxiety and motor activity cannot be ruled out in performance of recognition tasks. The contribution of these parameters can be assessed during the task itself (see below) and by use of other tasks such as open field and elevated plus maze to independently assess the effects of a specific treatment on anxiety and activity [5]. A further caveat is that hormones may increase the preference for novelty, not mnemonic processes. This possibility cannot be ruled out for chronic hormone treatments, but acute, post-training applications of estradiol, either subcutaneously or directly into the hippocampus, indicate that estrogens enhance memory consolidation (see Section 3.2).

2.2. Protocols

Variations in protocols for recognition memory tasks exist. We conduct recognition memory tests as shown schematically in Fig. 1.

Rats are allowed 3 min to explore two identical objects on an open field in the sampling or training trial (T1). After 1–4 h, subjects are returned to the field for testing in the recognition/retention trial (T2). As shown in the bottom portion of Fig. 1, one of the identical objects can be replaced with a new object, which is termed the object recognition (OR) task or one object can be moved to a new location, which is termed the object placement (OP) task. Object placement is a spatial memory task like radial arm maze and Morris water maze [6]. In both tasks, the time spent exploring at the new object/location and at the old object/location is recorded. Spending significantly more time exploring at the new object/location as compared to the old object/location indicates that the rat discriminates between old and new configurations, i.e. remembers the old object/location. If subjects spend similar amounts of time exploring the new object/location and old object/location, poor memory function is indicated. Recognition memory results can also be reported using an exploration ratio (time exploring new/time exploring old + new) where a ratio of 0.5 indicates chance (poor memory) and ratios higher than 0.5 indicate that subjects remember and significantly discriminate between the objects or locations. Ratios less than 0.5 indicate perseverative behavior, seeking the known. Perseveration is rare in young adult rats, but is present in aged rats and mice. We also utilize extensive habituation of subjects to the task before testing in order to eliminate effects of acute stress and anxiety. Subjects are first allowed to explore the field without objects for 5 min, and then objects are placed on the field and subjects receive object recognition trials with 1 min, 1 h and 2 h inter-trial delays. The following week, object placement tests with 1, 2 and 4 h delays are given. New objects are used in all trials, and we also give vehicle injections during some trials in order to habituate to this acute stress. Testing, with 4 h delays, begins either the day following the last habituation or three days later in order to account for weekends.

2.3. General performance on the tasks

It is our experience that most adult rats are able to readily discriminate in object recognition with a 4 h inter-trial delay [5,7–11], and others show significant discriminations up to 24 and 48 h [12,13]. Object placement, on the other hand, appears more difficult for rodents, and significant discriminations after delays longer than 4 h are not common [14]. Differences in task demands may account for performance differences between the two versions of the task. Cognitive load for spatial memory in object placement is greater than non-spatial object recognition [15,16]. Objects can be encoded and discriminated through multiple sensory modalities (e.g. vision and tactile) and using a variety of cues such as the size, shape, color and textures while discrimination of location of objects involves abstract categorizations and use of “cognitive maps.” The type of objects used and the size of the field may also impact on the ability of subjects to discriminate [7].

It should also be noted that sex differences are found in ability to perform object placement but not object recognition and should be taken into account in experimental designs. As shown in Fig. 2, males significantly discriminate between objects at old and new locations at 1, 2 and 4 h inter-trial delays while females can only typically significantly discriminate at a 1 h inter-trial delay. This observation is consistent with better performance of males as compared to females in other spatial memory tasks such as radial arm maze and water maze [4,17]. However, treatment of females with hormones such as estradiol (see Fig. 3) enables significant discriminations in object placement testing at 4 h inter-trial delays. It should also be noted that we sometimes find performance differences between cohorts of subjects such that some males may not discriminate at 4 h and some females may discriminate at 2 h. Thus,

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