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Research report

Sex differences in attentional processes in adult rats as measured by performance on the 5-choice serial reaction time task

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HIGHLIGHTS

- ► We examined attentional processing in adult male and female rats.
- ► Sex differences were revealed under challenging conditions.
- ► Males displayed greater vigilance than did females.
- ► Females exhibited greater inhibitory control than did males.

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ABSTRACT

The goal of the current study was to explore sex differences in attentional processes in adult rats using a test of attention shown to be dependent upon the prefrontal cortex. Male and female adult Long-Evans rats were trained on the 5-choice serial reaction time task. This task requires rats to identify the location of a brief light stimulus among five possible locations. Performance was assessed under baseline conditions and under behavioral challenge conditions during which task difficulty was increased. Behavioral challenge conditions included shortening the stimulus duration, shortening the time before the onset of the stimulus, lengthening the time before the onset of the stimulus, and presenting a distracting noise. Analyses across baseline and all challenge conditions revealed that vigilance or sustained attention was more disrupted in female rats than it was in male rats, as measured by percent correct and number of omissions. Analyses also revealed that inhibitory control was more disrupted in male rats than it was in female rats, as measured by number of premature responses. These differences were most prominent when the onset of the stimulus was unpredictably lengthened. There were no differences in reward collection latency or correct response latency indicating no differences in motivation or sensory processes between the sexes. These results indicate that under challenging conditions adult female rats are more prone to make errors of vigilance than are adult male rats, and adult male rats are more prone to make errors of inhibitory control than are adult female rats.

1. Introduction

Sex differences have been documented throughout the brain using techniques ranging from single-unit recordings to systems level brain imaging [For review, see 1]. In addition, basic behavioral research has generated support for the influence of sex and gonadal hormones on cognitive performance across a variety of tasks [For review, see 2]. In humans, males outperform females on tasks of mental rotation and navigation [3–6], and females outperform males on tasks of verbal memory [7–9]. Most behavioral research conducted using nonhuman animal models has focused on sex differences that arise during acquisition and performance of hippocampal dependent tasks [For review, see 2]. For example, male rodents outperform female rodents on tasks of spatial memory, as measured on the radial arm maze and Morris water maze tasks [10–15]. However, reports indicate that these results can vary with age, stress levels, and task demands [16–19]. Fewer animal studies have examined possible sex differences in tasks dependent upon other brain areas, including the prefrontal cortex [20–22], an important brain area for attentional processes [23–25].

Sex differences in the types of attentional problems displayed in certain neuropsychological disorders, including attention deficit hyperactivity disorder (ADHD) and schizophrenia, suggest that males and females may differ in the way that they process attentional information. For example, decreased vigilance, the ability to continuously allocate attentional resources in order to detect

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rare events [24], and decreased inhibitory control, the ability to refrain from making a premature or inappropriate response [25], are symptoms of ADHD [26]. The prevalence of ADHD is higher for males than it is for females. Males with ADHD display greater impulsive symptoms, and females with ADHD display greater inattentive symptoms [26,27]. Poor focus on tasks and excited, uncontrollable motor behavior are symptoms of schizophrenia [28]. The onset of schizophrenia is earlier in males than it is in females [29], and it has been suggested that estrogens may exert a protective effect against schizophrenia [30]. Whether these sex differences seen in pathological states are a function of differences in the general population is unclear.

Investigations of attentional processes using rodent models have typically focused on males [23–25,31]. The few studies that have directly compared male and female performance on attentional tasks have found mixed results. Some report a male advantage in vigilance and a female advantage in inhibitory control during attentional processing tasks [20]. Others report no or little effect of sex during attentional processing tasks [21,22]. The conflicting results of these studies could be due to differences in the demands of the tasks used in the studies or due to the relatively small amount of training before testing. Many sex differences disappear with extended training [2,18]. This disappearance could be due to differences in acquisition rate, but could also be due to the influence of sex on variables unrelated to task demands, such as anxiety or stress. Assessment of sex differences in attentional processes after extensive training decreases the influence of these variables on performance.

Circulating levels of testosterone and estradiol can affect attentional processing in male and female rats. For example, decreased levels of testosterone following gonadectomy impair the acquisition of an operant extradimensional set shifting task in male rats [32], and estradiol improves vigilance during performance of an attentional processing task in ovariectomized female rats [33]. The effect of testosterone and estradiol on attentional processing indicates that the different levels of gonadal hormones circulating in males and females could contribute to a sex difference in attentional processing.

Sex differences in vigilance and inhibitory control can be assessed using procedures that have been developed to model particular aspects of attention in rodents. The 5-choice serial reaction time task (5-CSRTT) was developed from the continuous performance task used to quantify attentional deficits in humans [24]. In the 5-CSRTT, rats must identify the location of a brief light stimulus presented randomly across five possible locations over a large number of independent trials [31]. The 5-CSRTT has been shown to be dependent upon the prefrontal cortex [24], and assesses both vigilance, the rats ability to sustain attention across the many trials, and inhibitory control, the rats ability to refrain from making a response until the appropriate time. To date, male and female performance on the 5-CSRTT has not been directly compared.

The goal of the current study was to use the 5-CSRTT to examine sex differences in attentional processes in adult rats. Performance was assessed under baseline conditions and under behavioral challenge conditions during which task difficulty was increased. Behavioral challenge conditions included shortening the stimulus duration, shortening the time before the onset of the stimulus, lengthening the time before the onset of the stimulus, and presenting a distracting noise.

2. Material and methods

2.1. Subjects

Fourteen male and fourteen female Long-Evans hooded rats, approximately 2 months of age, were purchased from Harlan Sprague Dawley Inc. (Indianapolis, IN). Animal care was in accordance with the guidelines set by the *National Institutes of Health Guide for the Care and Use of Laboratory Animals*, and all procedures were approved by the Institutional Animal Care and Use Committee of Tulane University. Animals were individually housed under a 12-h light/dark cycle and tested during the light phase of the cycle. All animals were weighed daily following behavioral training and food was provided in their home cages to maintain their weights at 85% of their free-feeding weights while allowing for growth of approximately 2% of their body weight each week.

2.2. Apparatus

Animals were trained and tested in one of four separate 25 cm × 25 cm aluminum chambers (Lafayette Instrument Co., Lafayette, IN). The rear wall of each chamber is convexly curved and contains five apertures, each 2.5 cm^2, 4 cm deep, and set 2 cm above floor level. Each hole can be illuminated with a 3 W light bulb located at the rear of the hole. Each hole has an infrared photocell beam monitoring the entrance. The four conditioning chambers are individually housed in sound attenuating cabinets. Each chamber is illuminated by a 3 W house light and equipped with a speaker that can deliver bursts of white noise. The front wall can be opened to place in and remove the animal from the chamber. On the front wall, 25 cm from each nose-poke hole, there is a food magazine where 45 mg food pellets (Test Diet, Richmond, IN) can be automatically dispensed. Each animal received one session of training per day throughout the experiment. House lights were on unless stated otherwise.

2.3. Behavioral training

First, animals were successively shaped to retrieve food rewards from the food tray and to poke any of the holes to receive food rewards. Then each animal was trained daily for 30 min on the 5-CSRTT by passing through several training stages of increasing difficulty. Each session terminated after 100 trials had been completed or 30 min had expired, whichever occurred first. An animal was moved to the next training stage once it performed at >80% correct and <20% omissions for two consecutive days. Percent correct reflects the percentage of correct responses, whereas omissions reflect the failure to respond to the stimulus. Each rat was always trained in the same conditioning chamber. Females were always trained in the same two chambers while males were always trained at the same time as the females in the other two chambers. Animals were trained at approximately the same time of the light phase each day.

For the initial training stage, animals were placed in the chamber and initiated the first trial by retrieving a single food pellet from the food tray. After a fixed 5 s inter-trial interval (ITI), one of the five horizontal lights was illuminated for a maximum of 60 s (cue duration) or until a response had been made. From the time the light first turned on, the animal had 60 s (limited hold period) to respond by making a nose poke into the previously lit aperture. Correct responses were immediately rewarded with delivery of a food pellet into the food magazine, and retrieval of the food restarted the next trial after a 5 s ITI. Several types of errors were recorded: (i) repeated nose pokes into the correct aperture were recorded as perseverative responses; (ii) responding into a non-lit aperture was recorded as an incorrect response; (iii) nose pokes during the ITI were recorded as premature responses; (iv) failure to respond within the limited hold period was recorded as an omission. All errors were punished by switching off the house light for a 5 s time-out period and no food was delivered. Responses to holes during this period would restart the time-out period.