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Chronic scream sound exposure alters memory and monoamine levels in female rat brain

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HIGHLIGHTS

- Scream sound impaired the spatial memory but did not affect the spatial learning.
- Scream sound decreased serum corticosterone level in female rats.
- Physiological parameters in females are inconsistent with males following scream sound stress.

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ABSTRACT

Chronic scream sound alters the cognitive performance of male rats and their brain monoamine levels, these stress-induced alterations are sexually dimorphic. To determine the effects of sound stress on female rats, we examined their serum corticosterone levels and their adrenal, splenic, and thymic weights, their cognitive performance and the levels of monoamine neurotransmitters and their metabolites in the brain. Adult female Sprague–Dawley rats, with and without exposure to scream sound (4 h/day for 21 day) were tested for spatial learning and memory using a Morris water maze. Stress decreased serum corticosterone levels, as well as splenic and adrenal weight. It also impaired spatial memory but did not affect the learning ability. Monoamines and metabolites were measured in the prefrontal cortex (PFC), striatum, hypothalamus, and hippocampus. The dopamine (DA) levels in the PFC decreased but the homovanillic acid/DA ratio increased. The decreased DA and the increased 5-hydroxyindoleacetic acid (5-HIAA) levels were observed in the striatum. Only the 5-HIAA level increased in the hypothalamus. In the hippocampus, stress did not affect the levels of monoamines and metabolites. The results suggest that scream sound stress influences most physiologic parameters, memory, and the levels of monoamine neurotransmitter and their metabolites in female rats.

1. Introduction

Stress usually refers to an event or succession of events that challenges homeostasis and causes a sequence of coordinated responses that maintain and/or restore homeostasis [1,2]. These stress-induced responses are mediated by the sympathetic–adrenal–medullary system and the hypothalamic–pituitary–adrenal (HPA) axis. The HPA axis exhibits sex differences under both basal and stress-induced conditions. For example, female rats have higher resting levels of corticosterone (CORT) compared with males. Furthermore, various stressors and delays (5 min to 24 h) induce higher stress-induced CORT levels in females than males [3–9].

Numerous studies demonstrate that sex differences are observed in HPA responses to stress, as well as in behavioral, morphologic, and neurochemical changes after stress exposure [10]. The majority of studies on the cognitive effects of chronic stress have focus on males. For

Abbreviations: ANOVA, analysis of variance; CORT, corticosterone; DOPAC, 3,4-Dihydroxyphenylacetic acid; DOPAC/DA, 3,4-Dihydroxyphenylacetic acid/dopamine;DA, dopamine; HPLC-ECD, high performance liquid chromatography with electrochemical detector; HVA/DA, homovaniilic acid/dopamine; HVA, homovaniilic acid; 5-HIAA, 5-hydroxyindoleacetic acid; 5-HT, 5-hydroxytryptamine; HPA, hypothalamus pituitary adrenal; NE (NA), norepinephrine, noradrenaline; ZG, zona glomerulosa; ZF, zona fasciculata; ZR, zona reticularis.

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example, 21 d of chronic restraint stress (6 h/d) impairs the performance of adult male rats in a variety of spatial tasks including the radial arm maze (RAM) [11], object placement [12,13], Y-maze [14], Morris Water maze (MWM) [15], and nonspatial object recognition tasks [2,16]. Interestingly, under the same stress conditions, females show better performance on the RAM [17,18], MWM [15], and Y-maze [19] but not on object placement [2,16]. Therefore, chronic stress induces sexually dimorphic effects on the learning and memory behavior of rats. Given that females are also part of the population, we aim to determine effects of stress on the performance of females.

The levels of central monoamine and neurotransmitter metabolites in the brain (prefrontal cortex (PFC), amygdala, hippocampus, and hypothalamus) also appear to be sexually dimorphic. Males exhibit decreased dopamine (DA) activity in the PFC and the amygdala after 21 d of restraint stress [20]. However, stress does not affect females in terms of DA activity in these areas [20]. In addition, stressed females show increased 5-hydroxytryptamine (5-HT) and norepinephrine levels in the CA3 region of the hippocampus, whereas stressed males exhibit no changes [10]. Moreover, the monoamine and metabolite neurotransmitters in brain areas are involved in learning and memory processes and are an essential part of normal synaptic neurotransmission and plasticity [18,21,22].

We have investigated the effects of chronic scream sound stress on male spatial memory performance by utilizing the MWM and the monoamine levels in various brain regions using high-performance liquid chromatography with electrochemical detector (HPLC-ECD) [23]. However, the responses of females to chronic scream sound stress remain unknown. Based on previously reported sex differences in spatial tasks, central monoamine levels, and neurotransmitter metabolite levels after chronic stress (21 days), we examined the effects of chronic scream sound stress on females. In this study, female rats were exposed to chronic scream sound, and then their capacity for spatial learning and memory, body weight, and the levels of CORT, central monoamines, and neurotransmitter metabolites in the brain were examined.

2. Materials and methods

2.1. Animals

Adult female Sprague–Dawley rats weighing 185 g to 195 g were obtained from the Medical Experimental Animal Center of Shaanxi Province, China. All rats were housed in standard plexiglass cages (30 cm × 47 cm × 15 cm) at four rats per cage with sawdust, maintained at 23 °C ± 2 °C, and were given a standard rat diet (Laboratory Animal Centre, Xi'an Jiaotong University, China) as well as water ad libitum. Lighting was maintained on a 12 h light/dark cycle (lights on at 6:00 h and off at 18:00 h), and all tests were performed during the light phase of the cycle. Body weight was measured after the adaptation period. The experimental protocol was approved by the Institutional Animal Care Committee of Xi'an Jiaotong University and in accordance with the National Institutes of Health Guide for the Care and Use of Animals.

2.2. Scream sound stress procedure

Scream sound stress model was created as described previously [23,24]. Briefly, the model was performed as follows: One male rat was exposed to 49 s of electric foot shock, two were exposed for 28 s, and three were exposed for 41 s. Similarly, one female rat was exposed to 66 s of electric foot shock, two were exposed for 28 s, and three were exposed for 102 s. The scream sound of the rats during the electric foot shocks was recorded simultaneously in a professional recording room (Xi'an Yin Zhi Xuan).

After a 7 d acclimation period, 14 female rats were randomly assigned into the stress group (n = 7) and the background group (n = 7) to examine their physiologic parameters and monoamine levels. The remaining 12 female rats were randomly divided into the stress group (n = 6) and the background group (n = 6) for testing spatial learning and memory. Procedure of scream sound stress was carried out as described previously [23]. The rats in the stress group were exposed daily to the recorded scream sound for 2 h in the morning and 2 h in the afternoon for 3 weeks. The scream sound was programmed to play 22 times with 5 s pauses during the 2 h stress session. The loudspeaker (Panda CD-100 CD player) was placed 50 cm above the animal cages. The sound intensity ranged from 45 dB to 75 dB, as measured using a sound level meter (SL-5800). The background group was maintained in a quiet room and was exposed to background noise recorded at 40 dB to 45 dB [25].

2.3. Serum corticosterone concentration

After the female rats were sacrificed by decapitation 1 d after the stress period (21 d), blood samples were collected from 8:00 a.m. to 10:00 a.m. The blood was allowed to stand at room temperature for 1 h and centrifuged at 3000 rpm for 15 min to separate the serum, which was collected and stored at −80 °C for subsequent analysis. The serum CORT concentration was measured using radioimmunoassay (cort (HY-10063) RIA KIT, Beijing Sino-uk institute of Biological Technology).

2.4. Relative organ weight

The weights of the adrenal glands, thymus, and spleen relative to body weight were calculated [26]. The relative organ weight indicated the amount of stress received by rats [26].

2.5. Morphometric analysis of adrenals

The procedures for the morphometric analysis of adrenals are similar to those previously reported [23]. In general, adrenal glands were removed, fixed in 4% paraformaldehyde for 15 h at 4 °C, embedded in paraffin, cut into serial sections (7 μm) and stained with hematoxylin–eosin. LEICA Q550CW was used to record the morphology of adrenals.

2.6. MWM test

MWM test of the remaining 12 female rats was started one day after the stress period (22 d) during the light phase. The MWM consisted of a circular galvanized steel pool (diameter = 150 cm; wall height = 50 cm) filled with water at 23 °C ± 1 °C. A small round escape platform (8 cm diameter) was fixed at the center of one quadrant 1 cm beneath the water surface. The acquisition phase consisted of five training days, starting at four different positions in a random order. Eight trials were conducted daily, four trials in the morning and four trials in the afternoon. If a rat did not find the platform within 120 s, the experimenter guided the rat to the platform [27]. Then, the rat was allowed to stay on the platform for 15 s to memorize the location [28]. The water maze was surrounded with fixed clues. Moreover, the experimental room was kept invariable during MWM testing [29].

On the sixth day, the platform was removed from the maze. Spatial memory was assessed as the number of times the rats crossed the former platform location, time and distance, percentage of time and distance spent in the target quadrant within 120 s.

2.7. Measurement of monoamine levels and their metabolites

The brains of rats were rapidly collected under frozen conditions. The prefrontal cortex (PFC), hippocampus, hypothalamus, and striatum were removed from the brain, weighed, frozen in liquid nitrogen, and stored at −80 °C [30,31]. The monoamine levels and their metabolites