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Physiology & Behavior 84 (2005) 97–104

PHYSIOLOGY & BEHAVIOR

Sexual behavior, neuroendocrine, and neurochemical aspects in male rats exposed prenatally to stress

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Received 3 June 2004; received in revised form 18 October 2004; accepted 20 October 2004

Abstract

The present study was designed to examine some short- and long-term effects of maternal restraint stress—during the period of sexual brain differentiation—on reproductive and endocrine systems, sexual behavior, and brain neurotransmitters in male rat descendants. Pregnant rats were exposed to restraint stress for 1 h/day from gestational days (GDs) 18 to 22. Prenatal stress did not influence the wet weight of sexual organs and the quantity of germ cells in adult male pups; however, these animals showed reduced testosterone levels, delayed latency to the first mount and first intromission, and also decreased number of ejaculations. Additionally, there was an increase in the dopamine and serotonin levels in the striatum. Our results indicate that prenatal stress had a long-term effect on neurotransmitter levels and sexual behavior. In this sense, reproductive problems caused by injuries during the fetal period can compromise the later success of mating as well as the capacity to generate descendants.

Keywords: Sexual differentiation; Prenatal stress; Testosterone; Sexual behavior; Neurochemistry; Rat

1. Introduction

In rats, the brain sexual differentiation occurs mainly during the last trimester of gestation (gestation days 14–21) and extends into the first 2 weeks of postnatal life [1]. In male rats, testosterone surges markedly on days 18–19 of gestation [2,3] and again during the first few hours following parturition [4–7]. During this period of brain sexual differentiation, testosterone or its metabolites are fundamental for masculinization and defeminization of sexual behavior, for the establishment of gonadotropin secretion patterns, and also for various morphological indices. In the absence of testosterone or its metabolites, sexually dimorphic structures and functions are feminized [8].

There is increasing evidence that variations in prenatal environment can influence the reproductive capability of the newborn [9]. For many years, the stress response induced by physical or emotional challenges has been recognized as a profound disruptive factor in reproductive function in both males and females [10–14]. It has been hypothesized that prenatal stress disrupts the normal maternal hormonal milieu and suppresses the fetal testosterone peak on gestational days (GD) 18 and 19, a peak necessary for later expression and maintenance of male sexual behavior [3]. This sexual behavior is controlled by the presence or absence of appropriate hormones and various central neurotransmitters [15]. Negative influence of maternal stress on the reproductive function of male pups has been demonstrated [3,10,15–17]. Based on the above consideration, different types of stressful events may sometimes produce qualitatively different patterns of effects on both behavior and physiology [18].

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0031-9384/$ - see front matter © 2004 Elsevier Inc. All rights reserved.
doi:10.1016/j.physbeh.2004.10.014

The present study was designed to examine sexual and neuroendocrine aspects in adult male pups that had been exposed to a single 1-h restraint stress session during the period of brain sexual differentiation (GD 18–22). Considering the paucity of data in the literature concerning neurotransmitter changes in prenatal stress, the neurochemical profiles of the hypothalamus and striatum, two brain regions widely involved in sexual behavior, were also evaluated.

2. Materials and methods

2.1. Animals, stress exposure, and experimental protocol

Wistar rats were used as the parent generation. They were kept in a controlled environment with temperature at 25±1 °C; humidity of 55±5%; 12-h light/dark cycle (lights on at 6:00 a.m.) and had free access to regular lab chow and tap water. Virgin female rats (200±10 g) were mated overnight. On pregnancy day 1 (determined by the presence of sperm in vaginal smears), 12 dams were randomly divided into two groups:

- control group: 6 dams not manipulated during gestation remained in their home cages during the stress period.
- stressed group: 6 dams restrained in a Plexiglas cylinder (with variable diameter and 16 cm length) for 1 h from gestational day (GD) 18 to 22. The removable restraining shield was readjusted to the tightest setting the expanding body size of the pregnant animals would allow.

On GD22, immediately after removal from the restraint, the dams were weighed, anaesthetized under ethyl ether inhalation, and laparotomized. The control dams were also weighed, anaesthetized under ethyl ether inhalation, and laparotomized. The pups of both groups were immediately culled to 8 pups per litter, keeping all the obtained males (females were kept just to complete the litter). The pups of both groups were fostered to recipient dams and were left with them until weaning (23 days of age). These recipient dams had not been manipulated during the gestation and had naturally delivered on the same day; at what time their pups were discarded.

The animals used in this study were maintained in accordance with Ethical Principles in Animal Research adopted by the Brazilian College of Animal Experimentation and approved by the Bioscience Institute/UNESP Ethical Committee for Animal Research (Protocol number: 065/03). The experimental protocol is diagramed in Fig. 1.

2.2. Maternal parameters of stress

On GD22, dams were weighed and submitted to the stress session. Immediately after, they were anaesthetized under ethyl ether and blood samples were collected from the abdominal aorta into heparin-coated syringes and centrifuged (2500 rpm for 20 min at 2 °C). Plasma corticosterone concentration was evaluated by radioimmunoassay using the kit COAT-A-COUNT (Rat Corticosterone, DPC, Los Angeles, CA). The test had an analytical sensitivity of 5.7 ng/ml.

Moreover, adrenal glands were collected from dams and from male pups (immediately after birth) for wet weight determination.

2.3. Body weight and anogenital distance during the preweaning period of male pups

At birth and on PND22, 10 male pups per group were weighed and the anogenital distance was obtained through a vernier-caliper.

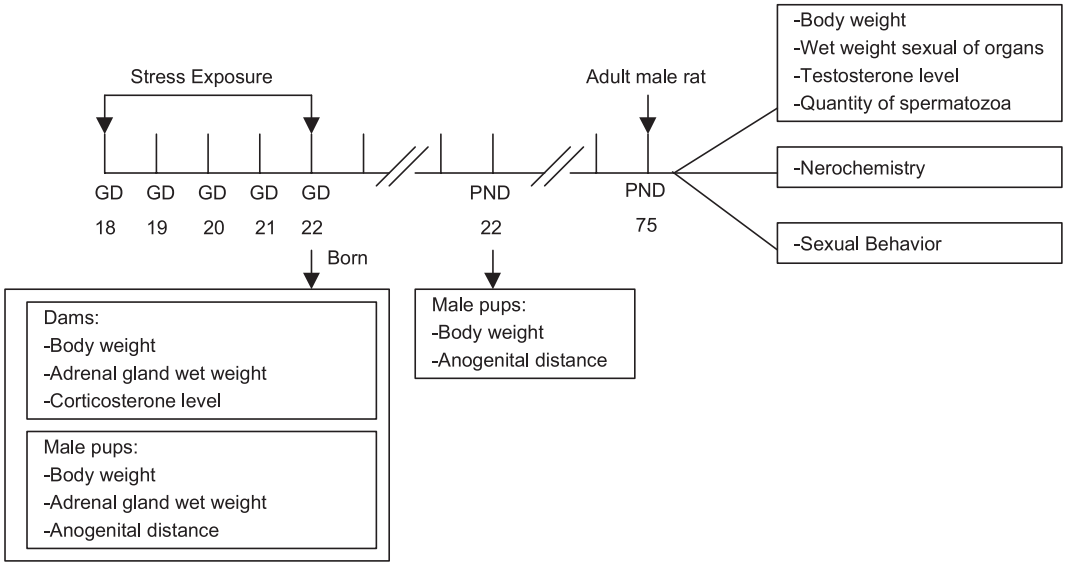

Fig. 1. Diagram of the experimental design. GD: gestational day; PND: postnatal day.