Physiology & Behavior 142 (2015) 131–136

Contents lists available at ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb

Enduring effects of post-weaning rearing condition on depressive- and anxiety-like behaviors and motor activity in male rats

Belal Mosaferi [a], Shirin Babri [b], Hadi Ebrahimi [b], Gisou Mohaddes [b,*]

[a] Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
[b] Neuroscience Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

HIGHLIGHTS

- Environmental factors at critical periods could have long-lasting effects.
- Environmental enrichment led to an antidepressive-like response in later life.
- Environmental enrichment improved information processing ability in later life.
- Social interaction led to enhanced locomotor activity in later life.
- Anxiety state is sensitive to the post-weaning rearing conditions.

ARTICLE INFO

Article history:
Received 26 October 2014
Received in revised form 5 February 2015
Accepted 6 February 2015
Available online 7 February 2015

Keywords:
Critical period
Environmental enrichment
Depression
Anxiety
Motor activity

ABSTRACT

Environmental manipulation at early critical periods could have long-lasting effects. In spite of the great interest in the biological effects of the environmental condition so far, its long-lasting effects are less documented. This study looks at the enduring effects of rearing condition on tasks that measure affective responses and exploratory behavior in male Wistar rats. The animals were reared from weaning to adulthood in an enriched environment, standard laboratory condition, or isolated condition. Then, all rats were housed in standard laboratory cages to provide a common environment, and successively exposed to different tests between 0 and 11 weeks post-manipulation. The open field test indicated a more efficient exploratory behavior in the enriched group, and an enhanced spontaneous motor activity in both standard and isolated groups. In addition, rats reared in standard condition showed heightened motor activity in forced swimming test and elevated plus maze. Forced swimming test showed an antidepressive-like effect in the enriched environment group by increased climbing behavior. In respect to the anxiety behavior, environmental enrichment improved threat detection ability. It is concluded that rearing condition from weaning to adulthood has important and long-lasting effects on depressive- and anxiety-like and exploratory behaviors as well as motor activity.

1. Introduction

Particular experiences, often at particular critical periods during development, produce permanent alterations in behavior [14]. The simplest way to manipulate experience is to compare the animals placed in different environments [18]. Environmental enrichment (EE) represents one extreme of the environmental continuum (positive conditions) and isolation condition (IC) i.e., social isolation, is the other extreme of environmental continuum (negative conditions), with standard laboratory condition (SC) placed in the middle [31]. Environmental enrichment incorporates greater sensory, cognitive, and motor stimulation [23]. Early stimulation by an enriched environment exerts profound biological effects, most of which are beneficial [26], while social isolation interferes with adolescent brain development causing notable deleterious outcomes [22]. At the behavioral level, many have focused either on learning/memory in enriched reared animals, or on locomotor activity in isolated rodents [3]. The effects of environmental enrichment on emotionality are less documented, while developmental and social factors are known to play a role in the pathogenesis of affective disorders [4]. Less research has been conducted on the effect of environmental manipulation on depressive-like and anxiety-like behaviors.

In the open-field test (OFT), enriched condition has consistently led to less locomotor activity [2,8] and more rapid habituation [2,15,35] compared to SC and IC, which indicates greater information-processing of EE rats. On the other hand, a retarded novelty processing in isolated animals has been reported [8,15].

In the elevated plus maze (EPM), inconsistent effects of rearing condition have been reported. Some studies have reported that EE rearing

* Corresponding author.
E-mail address: mohaddesg@tbzmed.ac.ir (G. Mohaddes).

http://dx.doi.org/10.1016/j.physbeh.2015.02.015
0031-9384/

reduced anxiety [4,9,12], while others found no effect of EE on open arm time, thus indicating no anxiolytic effect [2,30]. Likewise, although social isolation increased anxiety in several paradigms [34], an anxiolytic [19] or no effect of isolation rearing [26] have been reported.

Early environmental life events could predispose adult depressive-like response [4]. Accordingly, in the forced swimming test (FST) – one of the most commonly used tests to assess depressive-like behavior in animal models – isolated rearing has been found to increase immobility time [3,17] and decrease swimming and climbing activity in rats whereas enriched rearing decreased immobility and increased swimming and climbing [3]. However, some studies found no effect of rearing condition on rats' FST behaviors [13,20,30].

In spite of great interest so far in the biological effects of the enriched condition [22], few studies have focused on the persistence of the effects caused by exposure to EE in a particular life period [26]. With regard to the stress-coping response and anxiety related behaviors, a long-lasting enhancement of exploratory activity in EE mice and rats [26,27], and enhanced locomotor activity in IC rats [15] have been reported. Nevertheless, EE was not able to induce any permanent effect on anxiety-like behavior [15,26]. To the best of our knowledge, no study has examined the long lasting effects of early rearing condition on depressive-like behavior.

The aim of this study is to investigate whether post weaning rearing condition exerts any long-lasting effect on stress-coping response and anxiety-like behavior in male rats.

2. Materials and methods

2.1. Animals and rearing conditions

Forty-five male Wistar rats from nine different litters born in our own breeding colony were weaned at postnatal day (PND) 21 and semi-randomly assigned to three rearing conditions (n = 15 each). Equal numbers from each litter were allocated to the following conditions: SC, IC and EE. Standard condition group was kept in plastic translucent laboratory standard cage (20 × 45 × 30 cm) under group housing (four rats per cage). Rats in IC group were kept singly in plastic translucent small cages (13.5 × 22.5 × 16.5 cm). EE group was reared in an enriched environment in large plastic translucent cages (63 × 88 × 82 cm) with five rats per cage (see Section 2.1.1).

As shown in Table 1, the rats were kept in their respective home environments in a noise-isolated air-conditioned animal room with constant temperature (22 ± 2 °C) under a regular 12 h light/dark cycle (lights on at 0700 h). Bedding was changed once in a week for all animals; IC rats received minimal contact. On PND 94, ten animals were randomly obtained from each group, and were randomly allocated to six standard laboratory cages to provide a common condition for all rats, as well as to provide a condition similar to the complex environment that humans inhabit. The animals were successively exposed to different tests between 0 and 11 weeks post-manipulation. It should be noted that the first behavioral test was conducted before transferring animals to the common condition. All procedures were approved by the Regional Ethics Committee of Tabriz University of Medical Sciences. A minimum number of animals were used and particular care was taken to reduce their suffering.

Table 1
Experimental design.

Tests[a]	W/RC	EPM[I]/CE	EPM[II]	OFT	FST
Weeks	0	10	14	16	21
PND	21	93–94	123	137	152

[a] W: weaning; RC: rearing conditions; CE: common environment; EPM: elevated plus maze; OFT: open field test; FST: forced swimming test; and PND: postnatal day.

2.1.1. Environmental enrichment

EE cages were equipped with two running wheels, two food dispensers, two water bottles, and were enriched with a variety of toys. The internal configuration of the cages was changed every week, creating different spaces with several types of stairs and PVC tubes that the rats could move into or climb over. Novel objects (balls, rings and a block of plate with predrilled holes) made of non-chewable plastic in addition to objects that they could chew on such as ropes and paper nestles were provided and changed weekly All cages received the same assortment of objects each time.

2.2. Behavioral testing

Behavioral tests were performed in sufficient time intervals, and in an order that moved from least to most-stressful paradigms to reduce interfering effects (Table 1). All behavioral tests were conducted in a brightly lit room. The animals were transported to the experimental room 1 h prior to testing. All test procedures were performed during the light cycle, between 13:00 and 18:00 h. Both OF and EPM were placed in the center of the room to provide similar levels of illumination to all parts of the apparatus. Behavioral activities were recorded and subsequently analyzed by an observer blind to the experimental condition.

2.2.1. Open-field test

The open field was a 50 cm high, 50 cm wide, and 40 cm deep arena with black plywood walls and a brown floor divided into nine squares by black lines. Two earthen pots (10 cm diameter at the open end), each having a handle, were fixed at adjacent corners. Each rat was gently placed in the center of the arena and was allowed to freely explore the novel environment for 5 min. Whole locomotion (number of squares crossed with the four paws), locomotion for the first minute, number of rearing (posture sustained with hind paws on the floor), time of grooming (licking and washing movements as well as genital cleaning), number of central area crossing and time spent in the center were assessed to typify exploratory behavior, habituation and anxiety. Between each rat, the arena was cleaned with 70% ethanol and dried.

2.2.2. Elevated plus-maze

To evaluate the anxiety state, animals were exposed to an elevated plus maze. The apparatus consisted of a wooden maze covered with black Formica with two enclosed arms (50 × 10 × 40 cm) and two open arms (50 × 10 × 1 cm) that extended from a central platform (10 × 10 cm) to form a plus sign. The maze was elevated 50 cm above the floor. Upon testing, rats were placed in the middle compartment facing the same open arm opposite to the experimenter. The entire 5 minute session was videotaped with a camera located approximately 1.5 m above the maze. The parameters of interest were the total number of entries into the four arms, the number of entries and the time spent in the open arms. Entry into an arm was considered valid only when all four paws of the rat were inside the arm. The apparatus was cleaned with 70% ethanol after each trial and dried. As illustrated in Table 1, the EPM was run at two time points: PNDs 93–94 and 123.

2.2.3. Forced-swimming test

The FST procedure consisted of a 10-minute test. During the test, individual rats were placed in a glass cylinder (50 cm tall, 25 cm diameter), filled with water (23–25 °C) to the depth of 30 cm. The entire test session was videotaped with a camera located approximately 50 cm above the maze. The parameters of interest were time spent climbing, swimming, diving (animal submerges its entire body towards the bottom of the cylinder) and immobile (animal makes only necessary movements to keep its nose above water). However, diving behavior occurred infrequently and was placed within the swimming categories in the analysis. After each session the rats were removed from water, dried with a towel and placed in a warmed arena.