Int. J. Devl Neuroscience 46 (2015) 108–114

Contents lists available at ScienceDirect

International Journal of Developmental Neuroscience

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

Post-weaning environmental enrichment improves BDNF response of adult male rats

Belal Mosaferi [a], Shirin Babri [b], Gisou Mohaddes [b,*], Saeed Khamnei [c], Mehran Mesgari [b]

[a] Neuroscience Research Center (NSRC), Tabriz University of Medical Sciences, Tabriz, Iran
[b] Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
[c] Department of Physiology, Tabriz Branch, Islamic Azad University, Tabriz, Iran

ARTICLE INFO

Article history:
Received 24 June 2015
Received in revised form 13 July 2015
Accepted 24 July 2015
Available online 18 August 2015

Keywords:
Developmental plasticity
Environmental enrichment
Brain-derived neurotrophic factor
Amygdala
Hippocampus

ABSTRACT

The environment could have long lasting effects on the individual phenotype through developmental plasticity. Early environmental enrichment exerts profound biological effects, most of which are quite beneficial ones. To explore the enduring effects of rearing condition quality on BDNF[1] responses, we reared male Wistar rats from weaning to young-adulthood in three different environmental conditions: 1. Enriched 2. Standard, and 3. Isolated. Then, at the age of 16 weeks, 10 rats from each group were randomly chosen and allocated to six common mix cages. They were kept together for 14 weeks. At the end of the experiment, each rat received ten inescapable foot-shocks. Twelve hours later, the BDNF contents of the amygdala and CA1 sub-region of the dorsal hippocampus were measured. The serum BDNF levels, hematocrit values as well as brain and testis weights were also measured. Results showed that the environmental enrichment led to stronger dorsal hippocampal BDNF response and higher serum BDNF levels, while rats from standard laboratory condition showed higher amygdala BDNF response. Also, enriched animals showed higher brain weight compared to isolation reared rats as well as higher testis weight and hematocrit value compared to animals reared in standard laboratory condition. Rats showed less body weights in isolated condition. In conclusion, the BDNF profile of enriched animals might represent the neurobiological correlate of resilience phenotype under a stressful situation.

1. Introduction

The environment could have long lasting effects on the individual phenotype through developmental plasticity (Macri et al., 2009). In mammals, the development continues into juvenile and early adulthood (Curley et al., 2011). Developing neural systems are highly plastic (Laviola et al., 2003), enabling them to respond better to changes in the environment. The environment is enriched to improve the animals' quality of life (Baroncelli et al., 2010). On the other hand, the IC[2] i.e., social isolation, is a negative condition, and SC[3] provides an intermediate environmental quality (Solinas et al., 2010). Early EC[4] exerts profound biological effects, most of which are seen to be quite beneficial (Pena et al., 2009), while an impoverished environmental condition during developmental periods could result in chronic neurological diseases (Fone and Porkess, 2008). The major focus of previous researches has mostly been on cognitive function, and the effects of environmental stimulation on emotional behaviors have been less documented (Brenes Saenz et al., 2006). Moreover, few studies have focused on the persistence of the effects caused by exposure to enriched environment in a particular life period (Pena et al., 2009). We have recently reported an enduring antidepressive-like effect in rats reared in an enriched environment compared to those reared in standard and isolated environments 11 weeks after the cessation of the manipulation period (Mosaferi et al., 2015).

Individual differences between rats in vulnerability to stress-related psychopathologies could be mediated by a differential

* Corresponding author. Fax: +98 41 33364664.
E-mail addresses: b.mosaferi82@gmail.com (B. Mosaferi), shirinb46@yahoo.com (S. Babri), mohaddesg@tbzmed.ac.ir, gmohades@yahoo.com (G. Mohaddes), Khamnei_s@yahoo.com (S. Khamnei), mehran1968@yahoo.com (M. Mesgari).

[1] BDNF: Brain-derived neurotrophic factor.
[2] IC: Isolation condition.
[3] SC: Standard laboratory condition.
[4] EC: Enriched condition.

http://dx.doi.org/10.1016/j.ijdevneu.2015.07.008
0736-5748/

activation of BDNF[5] signaling (Duclot and Kabbaj, 2013). BDNF is the most widely distributed neurotrophin in the brain (Timmusk et al., 1994) that is produced in a neuronal activity-dependent manner and is implicated in the growth, maintenance (Zacchigna et al., 2008) and plasticity (Gray et al., 2013) of the nervous systems. The enriched environment rescues vulnerable mice under stressful conditions by enhancing hippocampal BDNF[6] levels (Chourbaji et al., 2012). Enriched environment increases hippocampal plasticity in mice (Zhu et al., 2009). Nevertheless, neural plasticity, and possibly BDNF activity, leads to differential functional effects depending on the brain region: neural plasticity is diminished in depression, while anxiety disorders might be related to too much synaptic plasticity within the amygdala (Rattiner et al., 2005). Post-weaning environmental enrichment offered benefits for trait anxiety rats, which were associated whit increased BDNF levels in central amygdala and dorsal hippocampus (Ravenelle et al., 2014). The involvement of BDNF signaling pathway in susceptibility to stress is further emphasized by the fact that the expression of BDNF protein and its receptors changes over the course of development and in response to circulating gonadal hormones (Bath et al., 2013).

In clinical depression, serum BDNF levels show a positive association with improved quality of life, and successful antidepressant treatment raises serum BDNF (Vinogradov et al., 2009). The basal levels of BDNF is increased by enriched housing in the brain (Ickes et al., 2000; Kuzumaki et al., 2011; Segovia et al., 2008). Preadolescent enriched environment presents high central BDNF levels in adulthood (Pietropaolo et al., 2004). On the other hand, neonatal stress combined whit young-adult glucocorticoid treatment caused learning deficiency in rats, which was accompanied by reduced BDNF expression in the CA1, CA3 and dentate gyrus sub-regions of the hippocampus (Choy et al., 2008). However, the BDNF response might be more determinant than absolute levels in mediating its effects (Duclot and Kabbaj, 2013).

It has been recently reported that foot-shocks induces a biphasic increase in BDNF levels of amygdala (Ou et al., 2010) and hippocampus (Bekinschtein et al., 2007). In both of which, the second peak occurring at 12 h after training is necessary for the persistence of the acquired memory (Bekinschtein et al., 2007; Ou et al., 2010). The reactivation of the CA1 neurons in dorsal hippocampus is crucial for the contextual fear memory (Shimizu et al., 2000; Tayler et al., 2011; Tayler et al., 2013). Phosphorylated BDNF receptor particularly shows a dense distribution in the CA1 sub region of the dorsal hippocampus (Gray et al., 2013). Therefore, to asses BDNF responses, one could measure BDNF levels in dorsal hippocampus and amygdala 12 after foot-shocks. The effect of rearing condition on BDNF response awaits further investigations.

We aimed at assessing the enduring effects of post-weaning environmental quality on BDNF responses in amygdala and dorsal hippocampus as well as serum BDNF levels 12 h after receiving inescapable foot-shocks.

2. Materials and methods

2.1. Animals

Forty-five male Wistar rats from nine different litters obtained from our own breeding colony were weaned at postnatal day 21 (Fig. 1) and semi-randomly assigned to one of three rearing conditions: EC, SC, and IC. The standard laboratory condition and isolated condition are used as control groups in assessing the effects of environmental enrichment (Simpson and Kelly, 2011). Equal numbers from each litter were allocated to each condition. Isolation condition composed of a singly-housed rat in a small plastic translucent cage (13.5 × 22.5 × 16.5 cm). SC rats were kept in standard plastic translucent laboratory cages (20 × 45 × 30 cm) under group housing (four rats per cage). Animals in the enriched condition lived in a group of five in a large cage (88 × 82 × 63 cm), furnished with a variety of objects (see Section 2.2). The cages in our laboratory (Mosaferi et al., 2015) were designed according to the previous studies (Simpson and Kelly, 2011). The rats were maintained in their respective cages 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 a week for all animals; IC rats received minimal contact. On young adulthood (PND[7] 112), ten animals were randomly obtained from each group and were randomly allocated to six standard laboratory cages to provide a common environment in mix cages: each cage contained one or two individuals from all three differential rearing conditions (the mix environment is similar to their natural status and closely mimics the complex environment that humans inhabit). Indeed, stressful life events are often social in nature (Schloesser et al., 2010){C}. When mixing, the aggressive animals were isolated for 1–2 days and then returned to their respective cages. They were kept in a common environment for 14 weeks. Body weight was measured weekly from week nine during the differential rearing period, and in 22 and 31 weeks of age. All procedures contributing to this work were approved by the Regional Ethics Committee of Tabriz University of Medical Sciences and are in accordance with the guide for the care and use of laboratory animals of the national institute of health (NIH; Publication No. 85-23, revised 1985). Minimal number of animals was used and particular care was taken to reduce their suffering.

2.2. Environmental enrichment

The EC cages were equipped with two running wheels, two food dispensers and two water bottles, and were enriched with a variety of toys (Mosaferi et al., 2015). 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 hard chewable plastic in addition to objects that they could chew such as ropes and paper nestles were provided and changed weekly; all EC cages received the same assortment of objects each time.

2.3. Inescapable foot-shock

At the end of the experiment (PND 211–213), each rat received ten inescapable foot-shocks in an acoustically isolated and dimly lit room (Fig. 1). Delivering the foot-shocks would put all animals in a similar stressful condition. The testing chamber was a rectangular acrylic box (21 × 25 × 26 cm) with a clear lid. The floor of the chamber consisted of a series of 6 mm caliber stainless steel bars spaced 1.5 cm apart. The grid was connected to a scrambled shocker to deliver the foot-shocks. The procedure was performed between 19:00 and 21:00 h on two consecutive days for each rat. On the first day, rats were picked up with support of their abdomen and thorax and were gently placed in the test chamber for 10 min acclimation period. Then they were put in their home cages and returned to the colony room. On the second day, each rat received ten foot-shocks: they were placed in the chamber and allowed a 25 s acclimation period (pre-shock period) and, then, they received one foot-shock (0.6 mA, 0.5 s duration) (Ou et al., 2010) and remained

[5] Brain derived neurotrophic factor.
[6] BDNF: Brain-derived neurotrophic factor.
[7] PND: Post natal day.