Behavioural Brain Research 222 (2011) 246–264

Contents lists available at ScienceDirect

Behavioural Brain Research

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

Review

The impact of environmental enrichment in laboratory rats—Behavioural and neurochemical aspects☆

Joy Simpson*, John P. Kelly

Department of Pharmacology and Therapeutics, National University of Ireland, Galway, Ireland

ARTICLE INFO

Article history:
Received 11 November 2010
Received in revised form 28 March 2011
Accepted 3 April 2011
Available online 12 April 2011

Keywords:
Environmental enrichment
Housing conditions
Forced swim test
Elevated plus maze
Open field test
Morris water maze
Neurotransmitters
Neurogenesis
Brain injury

ABSTRACT

The provision of environmental enrichment (EE) for laboratory rats is recommended in European guidelines governing laboratory animal welfare. It is believed the EE implementation can improve animals' well-being and EE has been used to demonstrate learning and plasticity of the brain in response to the environment. This review suggests that the definition and duration of EE varies considerably across laboratories. Notwithstanding this, some EE protocols have revealed profound effects on brain neurochemistry and resulting behaviour, suggesting that EE can have the potential to significantly modify these parameters in rats. For this review, a literature search was conducted using PubMed and the search terms "Environmental Enrichment" and "rats". From the results of this search the most important variables for consideration in the implementation of EE are identified and summarised, and include cage size and housing density; rat age, sex and strain; duration of EE; the EE protocol and enrichment items employed; and the use of appropriate controls. The effects of EE in a number of behavioural tests and its effects on neurotransmitters, neurotrophic factors, stress hormones and neurogenesis and proliferation are outlined. The findings summarised in the present review show the range of EE protocols employed and their effects in tests of activity, learning and affect, as well neurochemical effects which mediate enhanced plasticity in the brain. EE, as is provided in many laboratories, may be of benefit to the animals, however it is important that future work aims to provide a better understanding of EE effects on research outcomes.

Contents

Abbreviations: EE, Environmental enrichment; OFT, Open field test; EPM, Elevated plus maze; FST, Forced swim test; MWM, Morris water maze; NOR, Novel object recognition; RAM, Radial arm maze; WM, Working memory; CNS, Central nervous system; PND, Post-natal day; EtOH, Ethanol; IC, Isolated condition; SC, Standard (group) condition; AMP, Amphetamine; SD, Sprague Dawley; WIS, Wistar; SHR, Spontaneously hypertensive; LE, Long-Evans; NO, Novel object; ADHD, Attention deficit/hyperactivity disorder; CPP, Conditioned place preference; WKY, Wistar Kyoto; NH, Neonatal handling; RHA, Roman high avoidance; RLA, Roman low avoidance; LIS, Lister-hooded; BPM, Behavioural pattern monitor; FH, Fawn-hooded; CORT, Corticosterone; COC, Cocaine; HPA axis, Hypothalamic-pituitary-adrenal axis; ACTH, Adrenocorticotrophic hormone; BDNF, Brain-derived neurotrophic factor; NGF, Nerve growth factor; 5HT, Serotonin; DA, Dopamine; NA, Noradrenalin; ACh, Acetylcholine; GABA, gamma-aminobutyric acid; PFC, Prefrontal cortex; DAT, Dopamine Transporter; 5HIAA, 5-Hydroxyindoleacetic acid; AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; NMDA, N-methyl-D-aspartic acid; EAAC, Excitatory Amino Acid Carrier; LTP, Long term potentiation; NT-3, Neurotrophin 3; TBI, Traumatic brain injury; SCI, Spinal cord injury; APS, Airpuff stressor.

☆ *Disclosure*: The following work has not been published previously, is not under consideration for publication elsewhere and its publication is approved by all authors. If accepted, it will not be published elsewhere including electronically, in English or in any other language, without the written consent of the copyright-holder.

* Corresponding author. Tel.: +35391495246; fax: +35391495586.
E-mail addresses: j.simpson1@nuigalway.ie (J. Simpson), john.kelly@nuigalway.ie (J.P. Kelly).

0166-4328/$ – see front matter
doi:10.1016/j.bbr.2011.04.002

1. Introduction

Environmental enrichment (EE) is a term for exposing laboratory animals to physical and/or social stimulation that is greater than they would receive under standard housing conditions [1]. EE can be divided into two types: physical and social enrichment. Physical enrichment strategies involve structural modifications, including increased floor space and the inclusion of features which allow exercise, play, exploration and permit animals some control over their environment [2]; these include (in the case of rats) bedding enhanced with natural materials (paper parchment, fibre-based bedding), plastic tunnels, wooden objects to gnaw, ropes, swings, running wheels, balls, ramps, ladders and other appropriately sized animal toys. Social enrichment on the other hand refers to housing social animals in groups wherever possible. Although social enrichment is probably easier to implement with cagemate(s) being a source of constant dynamic interaction and unpredictability, there are situations where animals must be housed alone and in such cases physical enrichment is particularly useful. Ideally, a combination of both social and physical enrichment elements are thought to be preferable [3].

Animals have been held in captivity for scientific purposes for almost 200 years [4]. However it was many years later before the impact of being held under such conditions on the animal's welfare became a concern. In the 1920s, the primatologist Robert Yerkes was a pioneering force behind improvements to the housing conditions of non-human primates in both zoos and laboratories. His lead was followed by many others as the century progressed. Increasing public pressure in the 1960s called for more naturalistic enclosures for zoo animals, which led to the issuing of guidelines and legislation to improve the welfare of all animals held in captivity, encompassing not just zoos, but also farms and research laboratories [5]. Sustained public concern and pressure has meant that there has been a growing obligation for the widespread implementation of EE policies in animal laboratories. Such concerns led, in 1997, to the EU Commission issuing a resolution on the accommodation and care of laboratory animals, which defined "enrichment" in terms of social interaction, activity-related use of the space and provision of appropriate stimuli and materials (Council of Europe, ETS 123 1997). In 2007, the Commission issued guidelines for the "Accommodation and Care of Animals used for Scientific and other Purposes", which included a section entitled "Housing, enrichment and care". As well as recommending the provision of social enrichment for rodents, the guidelines also encouraged that appropriate physical enrichment should be made available, such as wood sticks for gnawing, nesting materials, refuges, tubes, boxes and climbing racks (Council of Europe, 2007/526/EC).

The importance of enrichment for laboratory rodents was first formally recognised by Donald Hebb in the 1940s who found that laboratory rats given freedom to roam in his home as pets had superior problem-solving and learning abilities than rats housed in standard laboratory conditions [6]. In their natural environment, as in captivity, rats engage in nocturnal activity, nest building and burrowing, coprophagia (consumption of faeces), thigmotaxis (preference for the periphery of a novel environment), foraging and gnawing; however in captivity rodents exhibit maladaptive stereotyped behaviours, such as barbering (excessive grooming causing hair and whisker loss) and bar-biting [2]. One reason for a growing interest in EE is that such maladaptive behaviour repertoires can interfere with studies where the research aims to monitor ethologically an animal's natural behaviour; perseverance and stereotypies may affect learning and/or conditioning studies which depend on an animal's adaptability [7]. If one wishes to observe natural activity, inasmuch as possible, in behavioural experiments it is imperative to develop methods of biologically appropriate environmental complexity for animals and try to reduce such stereotypies. Another reason for the steady growth of EE as a discipline since the 1960s is the growing evidence that rodents reared in enriched conditions display a range of plastic responses in the brain including neurogenesis, increased dendritic branching, increased cell size and improvements in learning and memory [8–10], which have implications for recovery in animal models of neurodegenerative disease, brain injury and psychiatric disorders [11–15]. In such studies EE is introduced as an experimental variable and can contribute to assessing the external validity and robustness of various models as they are tested across a range of environmental conditions [16]. The use of EE as an experimental variable however requires standardisation of procedures and outcome measures if conclusions are to be valid and not simply an artefact of a particular laboratory [17].

A common theme in the area of EE is its inconsistent nature across scientific literature; furthermore the definitions of EE can vary greatly according to different authors, as some are vague and overly general [18]. The mandatory introduction of EE is generally