ELSEVIER

Physiology & Behavior 84 (2005) 87–95

PHYSIOLOGY & BEHAVIOR

Social environment determines the long-term effects of social defeat

Jelly G. de Jong*, Bea J. van der Vegt, Bauke Buwalda, Jaap M. Koolhaas

Department of Animal Physiology, Biological Center, University of Groningen, P.O. Box 14, 9750 AA Haren, The Netherlands

Received 18 March 2004; received in revised form 18 October 2004; accepted 20 October 2004

Abstract

A single social defeat by a dominant conspecific induces long-term changes in several physiological and behavioral parameters in rats. These changes may represent an increased vulnerability to subsequent stress and stress-related pathology. Environmental factors, in particular possibilities for social interactions, could modulate these effects. Therefore, we assessed the influence of social environment on susceptibility for the long-term effects of social defeat. Socially housed males of an unselected strain of wild-type rats were equipped with radio-telemetry transmitters that recorded heart rate, temperature and activity. They were individually subjected to defeat and subsequently either housed alone or returned to their group. Behavioral and physiological responses to various novelty stressors were determined during a three-week period after the social defeat. Furthermore, changes in baseline behavior and physiology following defeat were studied in the rat's homecage. The results show a complex interaction between defeat and housing conditions. Depending on the parameters measured, effects were caused by both isolation alone, defeat alone or a combination of both defeat and isolation. Individual housing alone caused a characteristic hyperactive response to novelty stress. Though defeat did not affect behavioral responses, it amplified the physiological response to novelty and social housing did not attenuate this effect. However, social housing did reduce the effects of defeat on heart rate, temperature and activity in the home cage and completely prevented defeat-induced weight loss. Together these results indicate that social housing may indeed positively affect the animal's capacity to cope with stressors.

Keywords: Activity; Animal; Behavior; Body temperature; Exploratory behavior; Heart rate; Housing; Individual housing; Isolation; Long-term; Motor activity; Novelty; Physiology; Rat; Sensitization; Social defeat; Social housing; Social stress; Stress; Telemetry; Temperature; Wild-type

1. Introduction

Major life events appear to play an important role in the etiology of stress-related disorders, ranging from cardiovascular disease to psychopathologies such as depression and drug abuse [1–3]. One of the mechanisms underlying this phenomenon may be that the experience of a major stressor sensitizes an individual to subsequent stress and thereby increases their risk of developing such disorders [4].

Few animal studies have focused on the long-term effects of a single severe stressor. Most use repeated stress exposures or study changes observed relatively short (hours or days) after the inducing stressor. Furthermore, the stressors used, such as repeated footshock or restraint, often bear little or no resemblance to challenges an animal may encounter in its daily life [5]. Social defeat by an aggressive male rat is a natural stressor and induces a very strong acute stress response when measured by the amount of corticosterone and catecholamines released [6,7]. Following a single defeat, long-term changes in behavior and physiology develop, including changes in body growth, circadian rhythmicity, neuroendocrine functioning and behavioral responses to novel stressors [5,8–15]. These effects strongly differ in time-course and some of the changes suggest that the social defeat experience increases the susceptibility of animals to the effects of subsequent stress, i.e. the defeat induces stress-sensitization [5,6,16].

Because of their potential role in the development of stress pathology, it is of interest to know the conditions that influence the development of such enduring changes following a single stressful episode. Both human and animal

* Corresponding author. Tel.: +31 50 363 2337; fax: +31 50 363 2331.
E-mail address: jellydejong@home.nl (J.G. de Jong).

0031-9384/$ - see front matter © 2004 Elsevier Inc. All rights reserved.
doi:10.1016/j.physbeh.2004.10.013

studies suggest that the social environment may have a strong influence on the effects of stress on the organism [17–21]. Individuals with greater social support seem to be better protected against excessive neuroendocrine activation, thereby reducing the adverse effects of stress [22]. Community based studies also document an association between the extent and quality of an individual's social relationships and better health and longevity [17,19,23,24]. Animal studies likewise have reported that contact with others reduces physiological arousal in response to stressors and prevents many of the long-term effects of stress [9,21,25,26,28]. On the other hand, although supportive social relationships appear beneficial for health and are associated with reduced patterns of HPA and SNS activity, non-supportive social relationships and competition or aggression within a group are associated with enhanced reactivity to stress [22,24].

Wild rats are a social species with a complex and flexible social structure [27], however, the social defeat model has been developed using individually housed rats. It may be hypothesized that returning animals after defeat to a familiar social group may serve as a buffer to the adverse effects of social stress. Indeed, social housing counteracts defeat-induced changes in reward and social behavior [26] and prevented changes in the dopaminergic system [25]. Previous experiments in our laboratory showed that animals housed alone following defeat reacted more strongly than socially housed animals to various behavioral tests and showed an increased HPA-axis reactivity in a combined dexamethasone (DEX)/corticotrophin-releasing factor (CRF) test [9]. Therefore, social housing may reduce or even prevent the long-term behavioral and physiological effects of social defeat and thereby reduce its sensitizing effects.

Other studies have shown that individually housed animals in general show larger responses to common laboratory procedures, such as a clean cage [28], and react with increased locomotor activity in novel environments [29,30]. Because social isolation alone may also induce hyper-responsiveness to relatively mild stressors, some of the effects of individual housing following social defeat may have been caused by an effect of the isolation as such.

The present experiment was designed to test the assumption that social housing attenuates the long-term effects of social defeat. We used males of an unselected strain of wild type rats (Wildtype Groningen, WTG) because of their high levels of social activity [31]. To avoid possible confounding effects of competition and aggression, groups consisted of siblings that were housed together since birth. Animals equipped with radio-telemetry transmitters that recorded heart rate, temperature and activity, were individually subjected to social defeat and subsequently either housed alone or returned to their original group. Behavioral and physiological responses to various novelty stressors were determined during a 3-week period after the social defeat. Furthermore, changes in baseline behavior and physiology following defeat were studied in the rat's homecage.

2. Materials and methods

2.1. Animals and housing conditions

All procedures in this study were approved by the Committee on Animal Bioethics of the University of Groningen, The Netherlands. For the experiment, we used 72 male wildtype rats (Wildtype Groningen, WTG), originating from 12 groups of six siblings. The wildtype strain was originally caught in the wild, but has been bred in our laboratory for 26 generations. The strain is known for its high levels of social activity [31].

Rats were divided into 24 groups of three siblings and subsequently assigned to one of four treatments: control/isolation, defeat/isolation, control/social housing, and defeat/social housing. To reduce the number of animals, we used all but two rats in the control/social housing groups for the experiments and combined the control/isolation and defeat/isolation groups before defeat. This resulted in a total of 40 experimental rats and 32 animals that were only used as companions. Experimental animals were equipped with a radiotelemetry (ECG/temperature/activity) transmitter for continuous registration of heart rate, temperature and activity (see below). Due to the limited availability of transmitters, the experiment was conducted in three cohorts, each consisting of eight groups of three rats.

The animals were 3 months of age at the start of the experiment and weighed 295±3.5 g (mean±SEM). They were housed in clear Plexiglas cages on a layer of wood shavings and remained socially housed until the social defeat procedure. Following defeat, they were either isolated or returned to their group (group cage: 55×35×20 cm and individual cage: 40×23×15 cm). The light/dark cycle was reversed and fixed at 12/12 h (lights on at 20:00 h) and room temperature was maintained at 21 °C. Food and water were available ad libitum. All experimental procedures were conducted between 10:00 and 16:00 h.

2.2. Data collection

The telemetry system consisted of a small ECG transmitter (model TA11CTA-F40, Data Sciences, St. Paul, MN, USA), which was implanted intraperitoneally under isoflurane/O_2/N_2O anesthesia. The two electrodes of the transmitter were attached to the dorsal surface of the xyphoid process and in the anterior mediastinum close to the right atrium respectively, as previously described by Ref. [32]. Following surgery, rats were briefly isolated to recover and then reintroduced into the same group. Experiments started no sooner than 2 weeks after regrouping. Data were collected via a receiver underneath the homecage (model RA1010, Data Sciences) and processed by a PC with a