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Behavioural Processes 68 (2005) 135–144
BEHAVIOURAL PROCESSES
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Anxiety levels and wild running susceptibility in rats: assessment with elevated plus maze test and predator odor exposure

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Received 28 October 2003; received in revised form 26 July 2004; accepted 13 December 2004

Abstract

It is reported in the literature that nearly 20% of rats are susceptible to displays of wild running (WR) behavior when submitted to high intensity acoustic stimulation. Some characteristics of WR suggest that it can be viewed as a panic-like reaction. This work aimed to test whether WR-sensitive rats show higher levels of anxiety in elevated-plus-maze (EPM) and predator–odor exposure paradigms in comparison with WR-resistant ones. Male adult Wistar rats were submitted to two trials of acoustic stimulation (104 dB, 60 s) in order to assess WR susceptibility. Seven WR-sensitive and 15 WR-resistant rats were evaluated by the EPM test. Other 13 WR-sensitive and 18 WR-resistant animals were submitted to the predator–odor exposure test which consisted of a 10 min-session of free exploration in a specific apparatus containing two odoriferous stimuli: cotton swab imbedded with snake cloacal gland secretion or with iguana feces (control). WR-sensitive rats presented a significantly higher closed-to open-arm-entry ratio in the EPM test. All rats responded with anxiety-like behaviors to the predator odor exposure, although the WR-sensitive ones showed a marked behavioral inhibition regardless of the odor condition. We conclude that WR-sensitive rats present elevated levels of anxiety manifested by means of passive behavioral strategies.

Keywords: Anxiety; Elevated-plus maze; Panic; Predator odor; Rat; Wild running

1. Introduction

The study of defensive behavior of animals achieved great importance in scientific research, since it was considered useful to unfold the biological basis of emotions

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doi:10.1016/j.beproc.2004.12.003

(Ledoux, 1996). In mammals, it has been described that such behaviors are organized in a hierarchical structure that adjust the animal's reaction to the degree of danger in each situation (Hendrie et al., 1996). Based on that observation and supported by consistent experimental data, eminent authors propose that the initial steps of the hierarchical structure, which consist of behaviors related to risk assessment and coordinated escapes, are accompanied by anxiety (Graeff, 1994; see a discussion in Andreatini et al., 2001). Consequently, the final steps are motivated by the panic state, which is observed in animals by means of dramatic reactions to avoid hazards and, in rats is manifested by typical defensive fighting and vigorous flight (Blanchard et al., 1984; Hebert et al., 1999).

There has been additional interest in research concerning panic reactions because panic disorder is recognized as a very debilitating disease that affects 2–4% of the human population (Ballenger et al., 1998). In this connection, many animal models of panic have been developed based on different methodologies, such as electrical (Brandão et al., 1994) or chemical (Schenberg et al., 2001) stimulation of brain sites, exposure to elevated mazes (Teixeira et al., 2000), lactate infusions (Furlan and Hoshino, 2001) and social grouping after REM sleep deprivation (Sandrin and Hoshino, 1999). Although each specific experimental model is not essentially the panic disorder manifestation itself, the models have supplied a means to investigate many important questions about this anxiety disorder.

Audiogenic seizure paradigm is one animal model of generalized convulsion (Ross and Coleman, 2000) whose neural base involves a large number of coincident brain structures associated with panic reactions (Beckett et al., 1997; Lamprea et al., 2002; N'Guemo and Faingold, 1998; Garcia-Cairasco et al., 1993). Curiously, the tonic–clonic fit observed in this paradigm usually starts as a locomotor pattern called wild-running (WR) behavior, which closely resembles panic flight. Prior studies from our laboratory showed a direct correlation between the susceptibility to presenting defensive fighting induced by REM sleep deprivation and WR manifestation (de Paula and Hoshino, 2002). In addition, strychnine administered at a sub-convulsive dose exerts facilitatory action upon both defensive fights and WR (de Paula and Hoshino, 2004). Finally, WR can be reduced by anti-panic procedures such as dorsal periaqueductal gray lesion and imipramine treatment (de Paula and Hoshino, 2003). These findings suggest that WR may be considered a panic reaction, but additional evidence must be pursued.

In normal rat populations, nearly 20% are susceptible to displays of WR when submitted to high-intensity acoustic stimulation (Romanova et al., 1993). Also, it is already known that among colonies of rats, some of them show higher levels of anxiety (Ramos et al., 2002). So, given the possibility that WR is a panic reaction, it is reasonable to suppose that WR-sensitive rats could be more anxious than others. Aiming to test this hypothesis, the present work assessed the anxiety levels of rats with and without WR susceptibility by means of conventional elevated-plus-maze test and predator odor exposure.

2. Materials and methods

2.1. Subjects

Adult male Wistar albino rats, weighing 250–350 g at the beginning of the experiments, were used. They were bred at the UNESP Central Animal House in Botucatu (SP/Brazil) and maintained for at least 1 week before starting experiments in our laboratory conditions. During this period, they were housed in groups of five animals in conventional polypropylene cages (40 cm × 32 cm × 16 cm) containing wood shavings on the floor and having potable water and food (Labine chow) accessible ad libitum. Cages were kept at a temperature of 25 ± 3 °C in a light/dark-cycle controlled room and were regularly cleaned every 2 days. All recommendations for ethical usage of animals stated by the Colégio Brasileiro de Experimentação Animal (COBEA) were followed.

2.2. Determination of WR susceptibility

Wild-running susceptibility was assessed by means of the high-intensity acoustic stimulation trial routinely conducted in our laboratory. The trial started by placing the rat in a wire mesh cage (33 cm × 25 cm × 19 cm) located inside a sound-proof chamber (40 cm × 33 cm × 29 cm) containing a ringing bell, an incandescent lamp bulb (60 W), and a glass window through which complete visualization of the