LONG-LASTING MEMORY ABNORMALITIES FOLLOWING EXPOSURE TO THE MOUSE DEFENSE TEST BATTERY

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Introduction

Dysfunctional memory processes are thought to play a crucial role in the development and maintenance of post traumatic stress disorder (PTSD). Patients persistently re-experience the traumatic event particularly on exposure to trauma-related cues leading to increased levels of physiological stress concentration and memory which are evident when they process neutral, non traumatic information [1]. In addition, clinical studies report differences in the way individuals with and without PTSD process and learn in the presence of trauma-related distractors in comparison to a neutral environment resulting in enhanced learning of trauma related as compared to neutral information in PTSD patients [2, 3].

In this context, the objective of the present study was to investigate the potential long-term effects of pre-shock stress exposure on behavior and on short-term episodic memory in mice by evaluating their cognitive performance following or not trauma context exposure.

The mouse defense test battery (MDTB) was used as stressful situation. This test has been designed to investigate defensive responses of mice confronted with a predator, i.e. a rat. It has the advantage of providing a precise delineation of defensive behaviors, including flight, avoidance, risk assessment, tonic vocalization, defensive threat and attack, and escape attempts [4].

Methods

ANIMALS

Experiments were conducted in male Swiss mice purchased from Charles River (France). They were maintained under a 12/12 Light/Dark cycle, and housed individually and used for experiments during the light period, in accordance with the “Guide and Care of Use of Laboratory Animals” (National Institute of Health) and were approved by the in-house Animal Ethics Committee.

Male Long Evans rats weighing approximately 150 g, at time of testing, were used as threat stimulus in the MDTB. They were killed by CO2 inhalation 10 min prior to the test session began in order to minimize their discomfort.

STRESS PROCEDURE

The test was performed in an oval runway. It involves a number of phases:

• Forced exploration test: Exploration and escape attempts during the pre-test period provided baseline activity data. The same measures, during the post-test period were compared to the pre-test period to provide an index of enhanced contextual defensive following rat exposure.

• Rat avoidance test. A dead rat is introduced at the opposite end of the apparatus and brought to the subject at a speed of approximately 0.5 m/s. If the mouse flees, avoidance distance is recorded. This is repeated five times.

• Chased flight test. The hand-held esthanized rat is brought up to the subject at a speed of approximately 2 m/s during 2 complete laps of the runway or 2 min. Stares, reversals and head orientations of the fleeing mouse were used as measures of risk assessment.

• Straight alley test. The runway is then converted to a straight alley of 80 cm long. The rat is placed at one end and while the mouse is at the other. Measures are taken for 2 min including freezing and the number of approaches/withdrawals (measures of withdrawal response).

• Forced contact test. The rat is brought up to contact the subject five times. Stares, vocalisations, upright postures and jump attacks by the rat are recorded and used as measures of defensive aggression.

RESULTS

Comparison of behaviors between the pre-test, the post-test and 14 days following predatory stress exposure.

CONCLUSION

These findings confirm that exposure to the MDTB induces behavioral alterations reminiscent of increased anxiety.

Re-exposure to the stress context shows that the increase of escape attempts from the runway, i.e. an area in which a danger has been previously encountered, is increased. The deficit in cognitive performance after stress exposure can be alleviated by prior exposure to the traumatic environment in the absence of stressor. It can be hypothesized that re-exposure to the context resulted in an increase of arousal, vigilance and/or attention, which subsequently led to an improvement in cognitive performance.

Together, this procedure reproduces some of the symptoms observed in patients suffering from PTSD and may thus be of interest for further studies on the complex interaction between emotion and memory and the mechanisms underlying memory abnormalities in PTSD.