Behavioral validation of a novel animal model that capture both the emotional and cognitive features of Post-Traumatic Stress Disorder

A. Berardi[1], M.G. Coseglia[1], V. Trezza[2], P. Campolongo[1], V. Cuomo[1]

[1]Department of Physiology and Pharmacology, Sapienza University of Rome, P.le A. Moro 5, 00185 Rome, Italy
[2]Department of Sciences, Section of Biomedical Sciences and Technologies, University 'Roma Tre', Rome, Italy

Posttraumatic stress disorder (PTSD) is a psychiatric disorder of significant prevalence and morbidity. Even if anxiety is a common symptom of PTSD patients, the pathogenesis of the disorder relies on paradoxical changes of emotional memory processing. Cognitive features involve the re-experiencing of the trauma through different modalities, i.e. nightmares, intrusive recollections, intense fear responses to trauma-related reminders. Anxious symptoms include a persistent hyper-arousal, numbing of general responsiveness, irritability, hyper-vigilance. Since current animal models of PTSD often endorse only one of the two characteristics of the disorder, the aim of the present work was to develop an animal model of PTSD able to mimic, at least in part, both the cognitive and anxiety features of the pathology at the same time. To this aim, we exposed different cohorts of Sprague-Dawely rats to two different sources of stress, namely either a small piece of cat collar placed in a Plexiglas arena for 20 minutes or a series of 5 inescapable footshocks given in the black compartment of an inhibitory avoidance apparatus (0.8 mA, 2 sec each). Rats were re-exposed to the stressor-paired context at different time intervals and the cognitive responses were evaluated by scoring freezing behavior. Rats were then subsequently tested in the elevated plus maze and social interaction tests to investigate the emotional sequelae induced by stress exposure. We found that rats expressing intense fear responses during the cat odor exposure session failed to show any conditioned response when re-exposed to the same context after 7 and 14 days from stressor exposure. Conversely, rats that received the series of footshocks displayed significantly higher contextual freezing rates than unexposed controls 1, 7, 14 and 21 days after stressor exposure, thus showing a strong memory retention of the stressful experience. Footshock exposed animals did not show any anxious phenotype when tested in the elevated plus maze test 1, 7, 14 and 21 days after footshock experience. However, they made significantly less entries into the closed arms of the maze than unexposed controls, thus making this paradigm not suitable to evaluate anxiety profile due to a reduced locomotory activity of the exposed rats. When tested in the social interaction test, footshock exposed animals spent significantly less time interacting with a social partner than unexposed controls at every tested interval, thus showing, in the absence of any effect on locomotor activity, a robust anxiogenic-like profile correlated to the experience of the aversive event. Taken together, our results indicate that the footshock experience led the exposed rats to express a persistent fear memory for the traumatic event accompanied with a long-lasting anxious phenotype, both easily detectable with already well validated behavioral paradigms. Thus, although there is no animal model capable of mimicking all the facets of human diseases, by capturing both the cognitive and emotional features of the pathology, we believe that the present model could represent a useful tool in preclinical research oriented toward the discovery of novel pharmacological aids for PTSD prevention and treatment. Moreover it might be of great help in complementing clinical studies and in elucidating issues in ways that are not practicable in the clinical setting.