ACUTE RESTRAINT-STRESS INCREASED CONTEXTUAL CONDITIONED EMOTIONAL RESPONSE: INVOLVEMENT OF OXIDATIVE FACTORS

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Introduction: Stress is a risk factor for the development of affective disorders, such as anxiety and depression, and this response leads to neurochemical and behavioral changes that may be associated with oxidative stress. Recent evidences suggest that anxiolytic drugs may have antioxidant properties. However, the potential anxiolytic-like effect of antioxidants in rats exposed to acute stress has not been systematically investigated. Objective: The aims of the present study were evaluate the hypothesis that restraint-stress (RS) 1. may increase the conditioned emotional response (CER) and 2. induce oxidative / nitrosative damage in the Medial Prefrontal Cortex (MPCF) and hippocampus (HIP). In addition, 3. we investigated the efficacy of the antioxidant agent, 4-hydroxy-2, 2, 6, 6-tetramethylpiperidine 1-oxyl oxil (Tempol) on the attenuation of expression the fear-conditioned responses in rats re-exposed to the aversive context. Methods: The Institution’s Animal Ethics Committee approved housing conditions and experimental procedures (process number: 170-2011). Male Wistar rats (230-270 g) were separated in two groups: naive or restrained for 3 h (acute stress). These animals received an antioxidant, Tempol (1,5 or 20 mg/kg, i.p.), 30 minutes before the restraint-stress (RS). 24 h later animals were submitted to the contextual fear conditioning (3 electrical foot shocks, 0.8 mA, 2 s). After this, a polyethylene catheter was implanted in the femoral artery for cardiovascular recordings. 24h later the animals were re-exposed to the chamber previously paired with shock, but without shock presentation, and during this period the freezing behavior was manually counted and the cardiovascular activity was continuously acquired by a system. Results: The RS increased freezing behavior, medial arterial pressure (MAP, p<0.0001, MANOVA) and heart rate (HR, p<0.0001, MANOVA, n=5-6/group) during re-exposition to the aversive chamber (p<0.02, two-way ANOVA). Tempol attenuated both freezing behavior, MAP and HR in stressed rats (p<0.0001, Duncan, n=5-6/group). RS also increased carbonylated protein and lipid peroxidation in the MCPF and HIP and Tempol attenuated these effects (carbonyl protein, MPFC, p< 0.05 and HIP, p< 0.05; lipid peroxidation, MPFC, p < 0.001 and HIP, p<0.001). Conclusion: The present results showed
that RS increased oxidative stress in the MPFC and HIP and increased CER 24 h later. Moreover, the administration of an antioxidant agent before RS prevented these alterations. These results suggest that acute stressors could sensitize the animal to a subsequent aversive condition by increase oxidative state.

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