Post-training and pre-training chronic stressors have dramatically different effects on Pavlovian fear in mice

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Introduction

While fear is adaptive, dysfunction in the fear system is hypothesized to underlie clinical fear disorders. Stress enhancement of fear learning in the laboratory is a useful model for investigating the behavioral and neurobiological mechanisms of clinical anxiety disorders (Blesa et al., 2005).

The effects of chronic stress exposure have been studied extensively in rats. Chronic Restraint Stress enhances subsequent tone and context conditioning (Crescenzi et al., 1999) and can limit the effectiveness of extinction (Baus et al., 2006). Chronic Variable Stress enhances context fear conditioning (Zurita et al., 2006) but its effect on tone fear remains unknown.

There is (see Akirav & Maroun, 2007), the effects of stress on fear have been studied under designs in which stress exposure precedes fear acquisition. The study of the interaction of stress and fear is only beginning to find questions on conditioning with stress on declarative responding to.

The current set of studies seek to correct this by systematically applying chronic stress treatment either before or after fear acquisition.

Stress impacts the acquisition of fear, then pre-training stress should enhance fear while post-training stress should have little effect. If stress simply inflates fear responses, then both pre-training and post-training stress treatment should enhance fear.

Method

• Male C57BL/6 mice were subjected to 7 days of stress in each of three stress conditions: (1) Chronic Variable Stress inflates tone fear selectively. (2) Chronic Restraint Stress impairs context fear.

When applied for 7 days prior to conditioning,

(1) Chronic Variable Stress selectively inflates context fear. (2) Chronic Restraint Stress has no effect on either context or tone fear.

When applied for 7 days after conditioning,

(1) Chronic Variable Stress inflates tone fear selectively. (2) Chronic Restraint Stress impairs context fear.

Vertebrate Animals

All experimental procedures were conducted in accordance with the U.S. Public Health Service “Policy on Humane Care and Use of Laboratory Animals” and were approved by the Marquette University Institutional Animal Care and Use Committee.

Summary of Results

When 7 days of stressor exposure precede fear conditioning, repeated restraint hampers the unconditional response to footshock. Short-term freezing responses otherwise remain unaffected.

When 7 days of stressor exposure precede fear conditioning, context fear is inflated by variable stress but not by repeated restraint.

When 7 days of stressor exposure follow fear conditioning in mice, repeated restraint hampers the Conditional response to footshock.

When a 7-day interval intercedes between training and testing, baseline responding in a novel context is considerably among control animals and confined tone responding to a significant degree. When conditioning for baseline differences in responding, both repeated restraint and variable stress inflate tone responding when experienced after conditioning.

Limitations and Future Directions

• The designs used here do not allow a direct assessment of the impact of stressor timing, within each individual stressor, because the interval between training and testing is different for the pre- and post-training experiments.

• The designs also have slightly different stressor-testing intervals on, so the effects within each stress treatment are difficult to assess directly.

• Future effort should be made to assess the independent and factorial influences of stressor training interval, stress-testing interval, etc. The complexity of such an effect is multiplied further by any consequences of extinction processes within this theoretical framework.

• Nonetheless, it would appear that different stressor types have different effects upon fear acquisition and performance. These different stressor types will be engaged to design different behavioral paradigms and the acquisition and performance of different fear responses are known to rely upon different neural substrates. Future work should focus on relating these two sets of effects with one another.

References


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