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It has been well documented that exercise is beneficial to human beings with regard to mental health, especially regarding the reduction of depression and anxiety. More recently, experiments have shown that exercise in wheel running mice is most beneficial as a preventative measure as opposed to a treatment for already present depressive/ anxious symptoms. This is demonstrated by the fact that wheel running following prior stress does not produce a reduction in anxious symptoms in mice (Hare et al., 2012). Stress is known to activate the HPA, and thus it is plausible that the HPA plays a role in the ability of stress to interfere with the anxiolytic effects of exercise (Hare et al., 2013). To explore this hypothesis further, RU-486, a glucocorticoid antagonist, or a vehicle solution, were administered to stressed and non-stressed C57BL/6J mice. They were then provided with running wheels. Both RU 486 and vehicle stress groups showed arrested weight gain, while non stressed animals gained weight as normal regardless of injection by RU 486 or vehicle. During mCPP augmented startle amplitude testing, which is used to measure anxiety-mimicking symptoms in mice, non-stressed mice injected with vehicle showed the lowest increase in startle amplitude [20%]. Both stress groups showed similar changes in startle amplitude [42%], demonstrating again that prior stress does interfere with the anxiolytic properties of exercise, and that RU-486, and consequently glucocoritoid transmission and negative feedback to the HPA, may not mediate the ability of stress to interfere with exercise. Paradoxically, non-stressed, RU-486 injected animals showed the highest increase in startle amplitude [59%], implying that RU-486 and glucocorticoid transmission do in fact have an effect on the ability of stress to interfere with exercise. Due to this inconsistency, the experiment must be repeated and expanded before significant conclusions can be drawn.