Effects of Exercise on Immune Responses to Vaccination in Chronically Stressed Mice

Selena Wang, Julia Beck, Avani Patel, Yi Sun, Jeffrey A. Woods
Department of Kinesiology, College of Applied Health Sciences, University of Illinois at Urbana-Champaign

ABSTRACT

Methods:
C57BL/6 mice, aged 7 weeks old, were randomly assigned: control (CTRL, n=9), sedentary (SED, n=7), eccentric exercise (ECC, n=9), or voluntary wheel running (VWR, n=10) group. SED, ECC, and VWR mice received restraint stress for 6 hours/day, 5 days/week for 3 weeks. CTRL mice did not receive restraint stress. ECC mice exercised running downhill at -20% grade at 17m/min for 45 min. VWR mice voluntarily ran on a telemetered wheel. All groups received an OVA vaccination in two phases: first a sensitization phase with an intramuscular vaccination post 1-week of stress in the gastrocnemius muscle, a second intradermal vaccination in the ear post 3-weeks of stress. Swelling in the ear was measured to determine the proportional delayed-type hypersensitivity (DTH) reaction as part of the cell-mediated immune response (recruitment of memory T cells and effector cells) to the vaccine. Blood from the retro-orbital vein was collected pre-vaccination, 1wk, 2wk and 4wk post-vaccination for antibody responses.
Results:
In this study, there was a trend in increased humoral immunity, in regards to IgM and IgG antibody titers in the exercised groups. This study did not show any significant differences in cell-mediated immunity (indicated with delayed-type hypersensitivity (DTH)), with respect to the effect of exercise on chronic stress.
Conclusion:
Both acute eccentric exercise and voluntary wheel exercise training had a tendency to attenuate stress-induced reductions in antibody responses, but not cell-mediated responses. Further experiments are required to determine the precise significance of exercise's effects, as well as the determination of the underlying mechanisms.

INTRODUCTION

Vaccinations have greatly contributed to public health in the reduction of infectious diseases, but studies have shown that chronic stress reduces immune function, thus also reducing the efficacy of vaccination. Studies have also shown that chronic exercise increases the efficacy of vaccination, boosting immune response, in both humans and in aged mice. This study strives to determine whether or not exercise can alleviate the attenuation of vaccine response induced by chronic stress in an animal model, in young mice.

PURPOSE

To determine whether or not exercise can reduce chronic stress-induced attenuation of ovalbumin (OVA) vaccination responses.

RESULTS

Figure 1

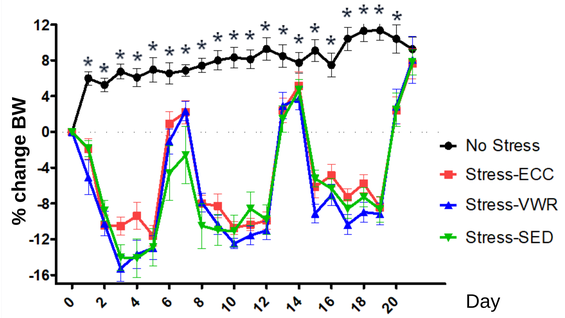


Figure 1. Percent change in mice's body weight (BW), over the course of the 21 days of restraint stress. *There was significant time main effect, ($F_{33,1023}$ =261.198, p<0.001), time x treatment effect ($F_{99,1023}$ =21.794, p<0.001), and treatment main effect, ($F_{3,31}$ =13.255, p<0.001). *signifies No stress group was found to be statistically higher than the other two stressed groups (p < 0.05).*

Figure 2

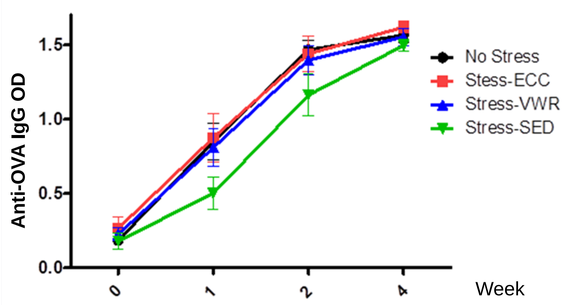


Figure 2. Change in optical density (OD), indicative of the mice's level of immunoglobulin G (IgG) antibodies, over the course of 4 weeks. *There was a significant time main effect, ($F_{3, 93}$ =257.816, p<0.001), but no time x treatment effect, ($F_{9, 93}$ =0.870, p=0.555), but a trend towards significance in treatment main effect, ($F_{3, 31}$ =1.842, p=0.16).*

Figure 3

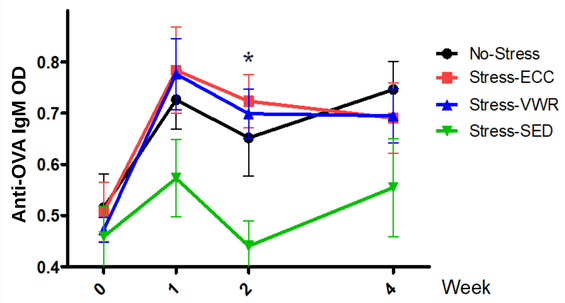


Figure 3. Change in optical density (OD), indicative of the mice's level of immunoglobulin M (IgM) antibodies, over the course of 4 weeks. *There was a significant time main effect, ($F_{3, 93}$ =16.532, p<0.001), but no time x treatment effect, ($F_{9, 93}$ =1.094, p=0.375), but a trend towards significance in treatment main effect, ($F_{3, 31}$ =2.421, p=0.085). Univariate analysis at week 2 shows significant treatment effect, ($F_{3, 31}$= 4.304, p=0.012). *signifies Stress-SED group's IgM antibody titers were statistically lower than the other groups' (p < 0.05).*

Figure 4

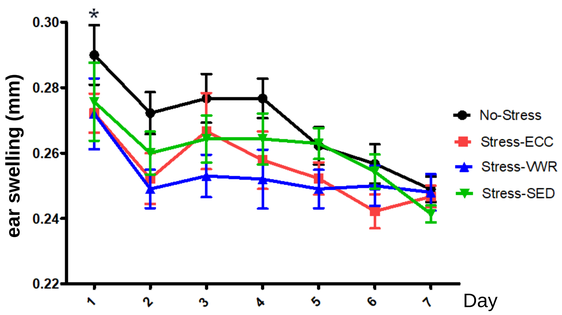


Figure 4. Delayed-type hypersensitivity (DTH) of the mice, over the course of 7 days. *There was a significant time main effect, ($F_{6, 186}$=9.061, p<0.001), and a significant treatment main effect ($F_{3, 31}$=4.111, p=0.014), but no significant time x treatment, ($F_{18, 186}$=0.559, p=0.925). *signifies that the No-stress group was significantly different from the three stressed groups at day1 (p < 0.05).*

Figure 5

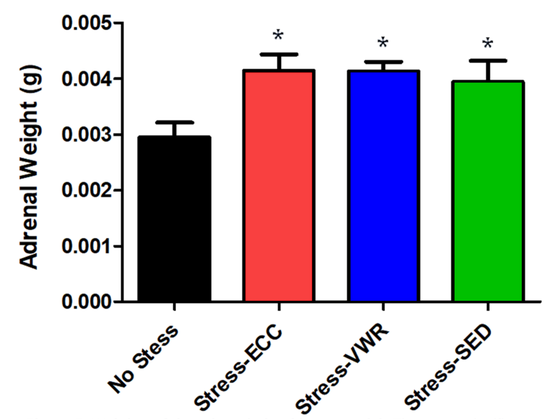


Figure 5. Weights of the adrenal gland in grams (g). *There was significant treatment effect, ($F_{3, 31}$ =4.343, p=0.011). *signifies that the No-stress group had an adrenal weight significantly lower than the three stressed groups (p < 0.05).*

Figure 6

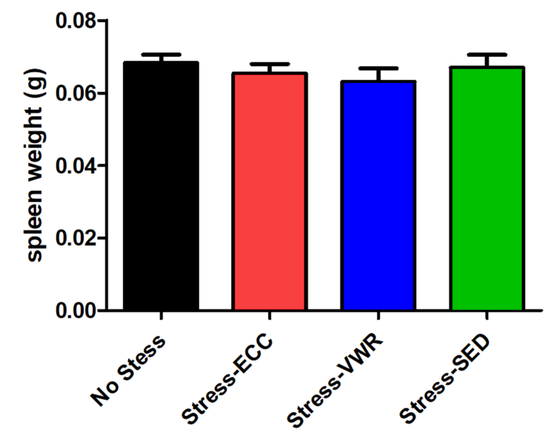
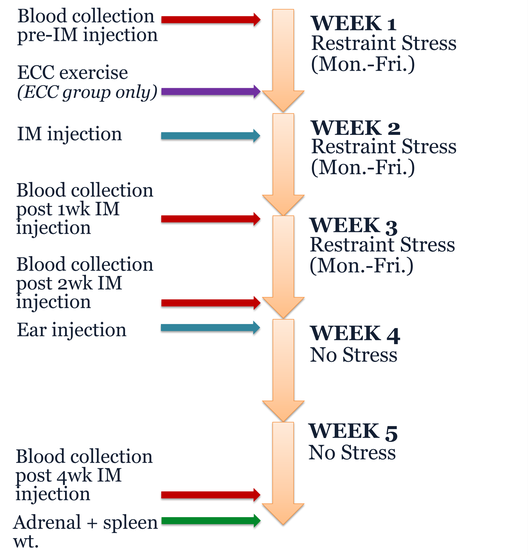


Figure 6. Weights of the spleen in grams (g). *There was no significant treatment effect, ($F_{3, 31}$ = 0.530, p=0.665).*

METHODS



CONCLUSIONS

Our study investigated cell-mediated immunity via delayed-type hypersensitivity (DTH), humoral immunity via immunoglobulin G (IgG) and immunoglobulin M (IgM) levels, relative activity of the adrenal gland via adrenal gland weights, stress levels via body weight (BW), and leukocyte storage via spleen weights, all in response to chronic stress and vaccine responses.
We can conclude that exercise has a tendency to alleviate chronic stress-induced attenuation of vaccine response, particularly in humoral immunity (IgM antibody levels) in an animal model.
Further studies are required to elicit the underlying mechanisms of exercise's alleviation of chronic stress-induced attenuation in vaccine response.

ACKNOWLEDGEMENTS

Thank you to Yi Sun and Jeffrey A. Woods' support for making this poster presentation possible.

ILLINOIS