The Effect of Exercise and Heart Rate Variability on the Antibody Response to Influenza Vaccination: A Pilot Randomized Controlled Trial

Master thesis in Medicine

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Abstract/Summary

Objective: Evidence suggests that chronic aerobic exercise acts as a behavioral adjuvant to vaccination mainly in the elderly although the mechanisms are uncertain. Aging is associated with immunosenescence largely attributed to low-grade chronic inflammation. Efferent vagal signaling has anti-inflammatory effects. High frequency heart rate variability (HF-HRV) is a noninvasive measure of vagal activity. In this pilot randomized control trial (RCT), we examine whether exercise training, cardiorespiratory fitness, measured as maximal oxygen uptake (VO2max) from exercise test, and HF-HRV relate to the antibody response to influenza vaccination.

Method: Twenty-six healthy, sedentary adults (23-56 years, mean age 36.8 SD=9.9) were randomly assigned to an exercise group (n=13) or waitlist control group (n=13). Subjects assigned to exercise group exercised at 65-80% of their maximum heart rate for 30 minutes, 4 days/week for 12 weeks prior to trivalent influenza vaccination and for 4 weeks after vaccination. Controls did not change activity and were also immunized at 12 weeks. HF-HRV, VO2max, and antibody titers were measured before intervention, at the time of vaccination, and 4 weeks later.

Results: Antibody titer values were log transformed and antibody-response was calculated as increase relative to pre-vaccination titers. Exercisers significantly increased their mean VO2max values compared to controls (6.24 to 1.13 ml/kg/min, p=0.0274) after 16 weeks, but there was no group effect on HF-HRV. Titers increased significantly (all 3 strains) post-vaccination, but no group difference was observed in antibody response or seroprotection (hemagglutination inhibition titer, HAI, ≥40). Regression analysis showed neither higher levels of VO2max nor HF-HRV at time of immunization predicted a greater antibody response. Similarly, greater increases of
VO2max and HF-HRV, measured at both 12-week pre-vaccination period and 4-week post-vaccination period, did not predict a greater antibody response.

**Conclusion:** A 16-week exercise intervention did not enhance the antibody response to the flu vaccine in healthy sedentary young adults. Higher levels and greater increases of VO2max and HF-HRV were not predictive of a greater antibody response. In addition to small sample size, this trial is limited by studying mainly younger participants, in whom exercise may not further enhance antibody responses due to a possible ceiling effect. Future studies, preferably in older individuals, are needed to assess if greater exercise-induced HF-HRV as an index of vagal regulation is associated with the antibody response to immunization.

**Keywords:** Exercise; Influenza; Vaccination; Heart rate variability; Immunity