EXERCISE ALTERS STRESS AND INFLAMMATORY RESPONSE IN LUNGS OF MICE

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The purpose of this experiment was to determine how different doses of exercise affect cellular stress responses and immune cell populations in the lungs.
Exercise and the J curve theory

Risk / severity of Infection

None  Moderate  Exhaustive
Exercise and exposure to virus

- Mice run on treadmill and infected with virus – intra-nasal route
- Control- mice above TM
- Moderate - mice run for 30 minutes
- Exhaustive - mice run until fatigue (3 hours)
AMOUNT OF VIRUS IN LUNGS
ACUTE EX AND CHRONIC EX

Log viral titer (Log scale)

Day 2: NON-EX (black), A-EX (red), C-EX (green)
Day 5: NON-EX (black), A-EX (red), C-EX (green)
Day 10: NON-EX (black), A-EX (red), C-EX (green)

Amount of virus in lungs: acute ex and chronic ex
We hypothesized that a single session of exercise would result in activation of cellular host defense pathways in a dose response manner, and that moderate exercise training over several weeks would result in an adaptation (modest down-regulation in gene expression).

We also hypothesized that immune cell populations would traffic toward the bronchoalveolar lavage fluid.
METHODS

• Chronic moderate exercise in BALB/c mice:
  - Mice exercised 5d/week for 10 weeks
  - Euthanized within 15 minutes after exercise session
  - BALF and lungs collected from euthanized mice
  - PCR on whole lung homogenates, Flow cytometry on lung cells and BALF cells

• Acute exercise (single session exercise):
  - 45 minutes
  - 90 minutes
  - 180 minutes
  - Euthanized within 15 minutes after exercise session
  - BALF and lungs collected from euthanized mice
  - PCR on whole lung homogenates, Flow cytometry on lung cells and BALF cells
Mice Treadmill Video
Total Live cells in BALF

Number of cells

No Ex
45 mins Ex
90 mins Ex
180 mins Ex

Live
SUMMARY – ACUTE EXERCISE

- As exercise duration increased, cellular stress measured by heat shock protein mRNA expression also increased. However, apoptosis was not induced in response to the stress, and no effect on anti-oxidant response was found.

- Activation of classic inflammatory markers did not occur as exercise duration increased.

- Moderate duration exercise (45-90 min) was associated with fewer leukocytes in the BAL, but at 180 min, total BAL cells increased (primarily macrophages).

- At 180 min, a decrease in the expression of the anti-microbial defense gene NOS2 (inducible nitric oxide) was found.
• In general, heat shock stress proteins were down-regulated with regular exercise training.

• Most genes showed little change in response to exercise training.

• A slight increase in lung leukocytes was observed in response to exercise training. The types of cells that increased included monocytes and neutrophils.
DISCUSSION

- The results suggested that as exercise duration increased, a greater stress response was induced in the lung. Although activation of stress proteins was present, cellular stress did not appear to be accompanied by apoptosis or activation of antioxidant genes. Studies have shown that heat shock proteins may inhibit apoptosis, and therefore the activation of heat shock proteins may have served a cellular protective effect (as exercise duration increased).

- An interesting observation was the reduction in NOS2 expression as exercise duration reached 180min. Nitric oxide has potent antimicrobial activities, and a significant reduction in nitric oxide may contribute to the increased susceptibility to infection known to occur with prolonged exercise. Also at 180 minutes, a greater number of leukocytes were present in the BALF, primarily macrophages. These cells serve an early host defense role, and the increase in MIP-1α may have played a role in trafficking of macrophages to the BALF. Additional studies are needed to establish how an exercise-induced change in nitric oxide and leukocyte populations contributes to susceptibility to infection.

- Adaptations to long-term exercise training may include a slight increase in the number of cells involved in early host defense (monocytes & neutrophils), perhaps contributing to increased protection against respiratory infection.