Exercise is Good for the Brain

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Experimental Model:
*Rhesus monkeys and Cynomolgus monkeys*
Exercise Training
Female Cynomolgus Monkeys

Two age groups
Middle aged (10-12 years)
Older age (15-17 years)

Three experimental groups
Runners (run 5 months)
Sedentary (sit 5 months)
Run-Stops (run 5 mo, sit 3 mo)

Running protocol
80% max heart rate
1 hr/day, 5 days/week
20 weeks
Cognitive Testing: WGTA
Monkeys that exercise are *more attentive*, and learn to use the testing apparatus *twice as fast*.
What is the affect of being more alert and attentive while you are in school??
Running Increases Vascular Volume in the Motor Cortex of Older Animals

BrdU-labeled endothelial cell
Running Increased Neurogenesis in the Hippocampus of Middle-aged Monkeys

**βIII tubulin**

**BrdU**

**Graph:**
- **Y-axis:** BrdU+ / βIII-Tubulin cells per 40 micron section
- **X-axis:** Middle age vs. Older age
- **Legend:**
  - Control
  - All Exercise
- **Middle age:**
  - Control: 6 cells
  - All Exercise: 10 cells
- **Older age:**
  - Control: 4 cells
  - All Exercise: 2 cells
- **Significance:**
  - * indicates a significant difference
Running Increased the Production of Astrocytes in the Motor Cortex

BrdU, S100β, NeuN

![Image of astrocyte production](image)

Graph showing increased production of BrdU/S100β in older age compared to middle age with exercise.
Conclusions:

- Exercise increases vascular volume in the cortex, neurogenesis in the hippocampus, and gliogenesis in many brain regions.

**Clinical Implications:** Exercise may counteract changes in the brain with aging, and protect against neurodegenerative diseases (i.e., PD, AD, & stroke)
Neuroprotective Effects of Exercise

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Michael Zigmond, Ph.D.

Rehana Leak, Ph.D.

Brian Lopresti, Ph.D.

Chet Mathis, Ph.D.

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Karoly Mirnics, Ph.D.

Vanderbilt Univ.

NINDS: R21 NS053471, P50 NS019608
Parkinson’s Disease

Substantia nigra

Braak et al., 2004

Lewy body
Experimental Design

- Adult, female Rhesus monkeys (15-20 yrs. old)
- MPTP (0.8 mg)
- Running (1 hr/day, 5 days/wk)
  [Sedentary, 60% max hr, 80% max hr]
- Running/Sedentary

3 months

1.5 months
Monkeys with Highest Levels of Physical Activity had the Least Damage to Nigrostriatal Dopamine Neurons
Monkeys with Highest Levels of Physical Activity had the Least Damage to Nigrostriatal Dopamine Neurons
Conclusions:

- Being more active, regardless of the quantity of aerobic exercise undertaken, can protect DA neurons in the striatum from neurotoxic damage.

Clinical Implications: Maintaining an active lifestyle may significantly protect the brain against neurodegenerative diseases (i.e., Parkinson’s Disease), or be useful in decreasing the rate of progression of Parkinson’s Disease. This is a health strategy that would be accessible to many people regardless of their baseline fitness.
Changes in the Brain with Normal Activity

Elinor Sullivan, Ph.D.
ONPRC
Karoly Mirnics, Ph.D.
Vanderbilt Univ.
Monkeys Have Been Fitted with Activity Monitors
There are LARGE individual differences in daily activity levels

Less Active Monkey

Very Active Monkey
Does General Activity Affect Health?
Monkeys put on a High Fat Diet Show Large Individual Differences in Weight Gain
Only Activity Predicts Body Weight Change in Adulthood

![Bar charts showing percent change in body weight for different activity levels with p-values: Activity p = 0.03, Food Intake p = 0.58, Metabolic Rate p = 0.14.](image)
Conclusion:

- Being more active is the best way to prevent adult weight gain.

*Clinical Implications:* Maintaining an active lifestyle is very important for preventing adult weight gain and obesity. With 60% of the adult population in the United States overweight, increasing activity is critically important for prevention of obesity-related diseases including heart attacks, strokes, and diabetes.
Current and Future Directions

• What are the intracellular mechanisms by which exercise modulates neuronal function?

• What are the differential effects of high activity vs. aerobic exercise?

• Will exercise be useful as a therapy or adjunct therapy in treating:
  – Substance abuse (smoking: Drs. Kupfer, Soreca and Monk)
  – Depression and Bipolar Disorder (Drs. Kupfer, Frank)
  – Neurodegenerative diseases (Drs. Zigmond, Zhang, Mirnics)
  – Normal aging (Drs. Zigmond, Mirnics)
Physiological Studies
Nathan Rockcastle
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Neuroanatomy
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Questions?