

Exercising Our Minds: Effects of Exercise on Brain Structure & Function

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**The Jack Brown and
Family Alzheimer
Research Foundation**

Changes

Time might change me, but I can't change time...

Sir David Bowie

- How we think about the brain
- Some of the people that have shaped our view of the brain.
- How the effects of exercise on the brain is changing our view of it again.

**We were taught the brain is like a
computer.**

We're all obsolete models!



=





**Our brains are dynamic.
Like skin and muscle, brains
change in response to their
environments**

The Brain is composed of billions of interconnected cells



Donald Hebb

1904 - 1984

CONNECTIONISM

Networks;
Cells that fire together,
wire together

Neurons

Glia

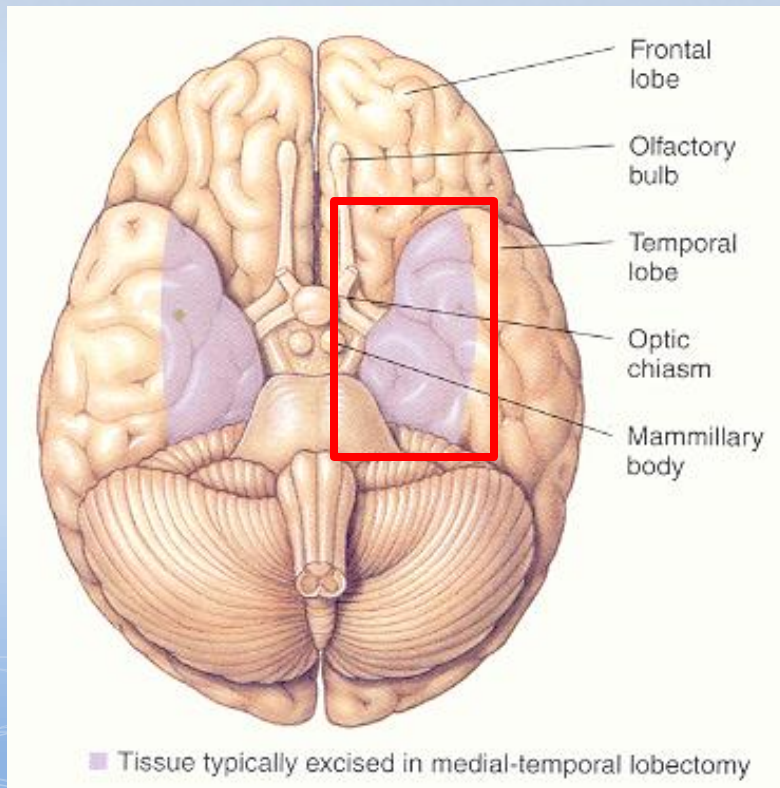
**Endothelial/
Vasculature**

Neural

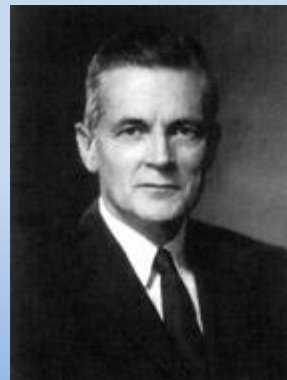
Stem Cells

Why Study the Hippocampus?

- ❑ Severe Epilepsy, bilateral initiation
- ❑ 1953 - Performed bilateral medial temporal lobectomy. H.M. was 27 yrs old.



Henry Gustav Molaison
Died December 2, 2008
Spent 55 yrs in a state of
permanent amnesia

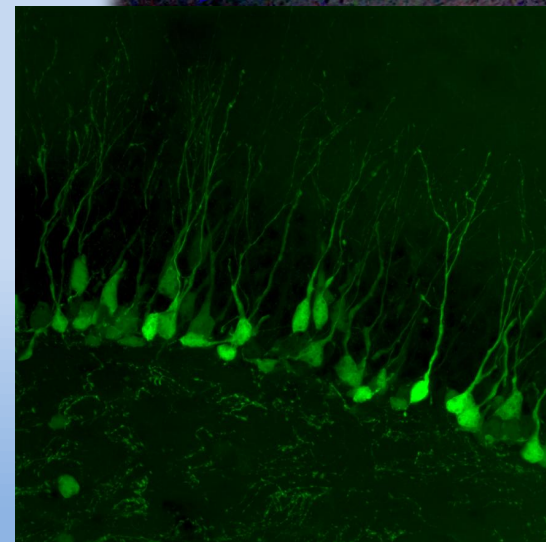
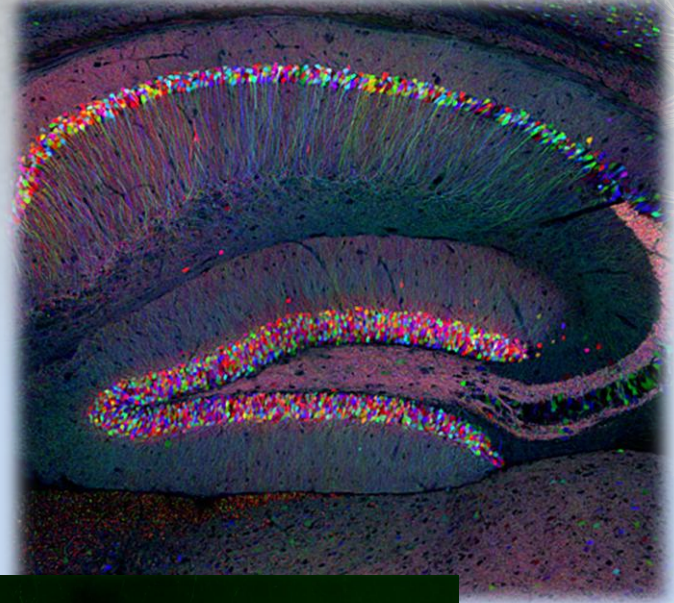
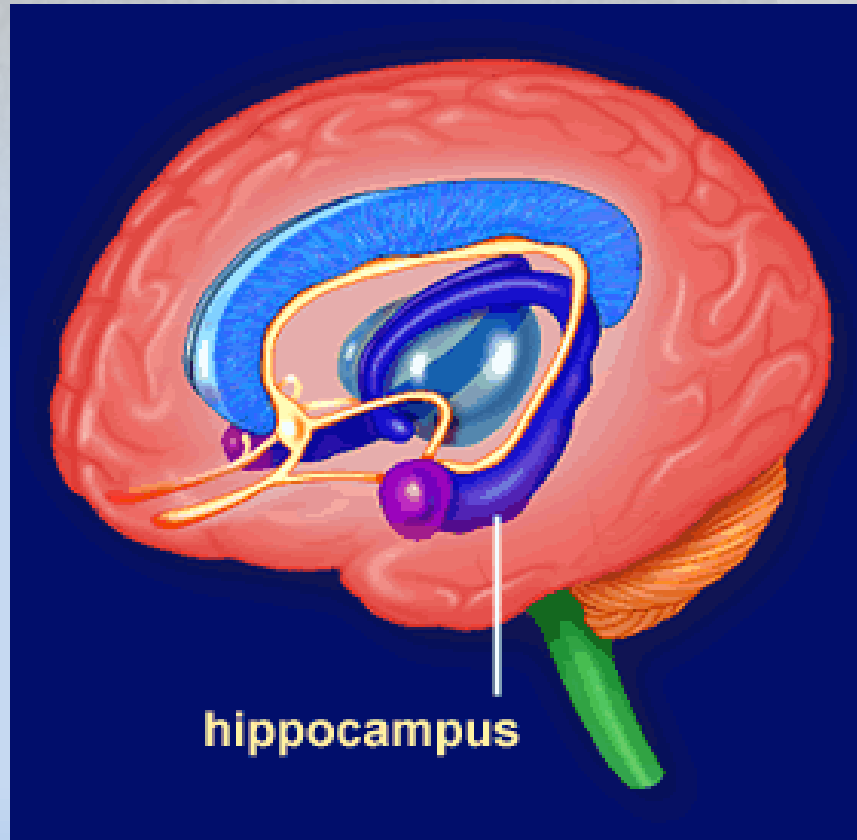


William Scoville, MD
Sept 1, 1953 performed
bilateral temporal lobe
removal



Brenda Milner, Ph.D.
-Showed working and procedural
memory intact.
-Couldn't form new explicit
memories.

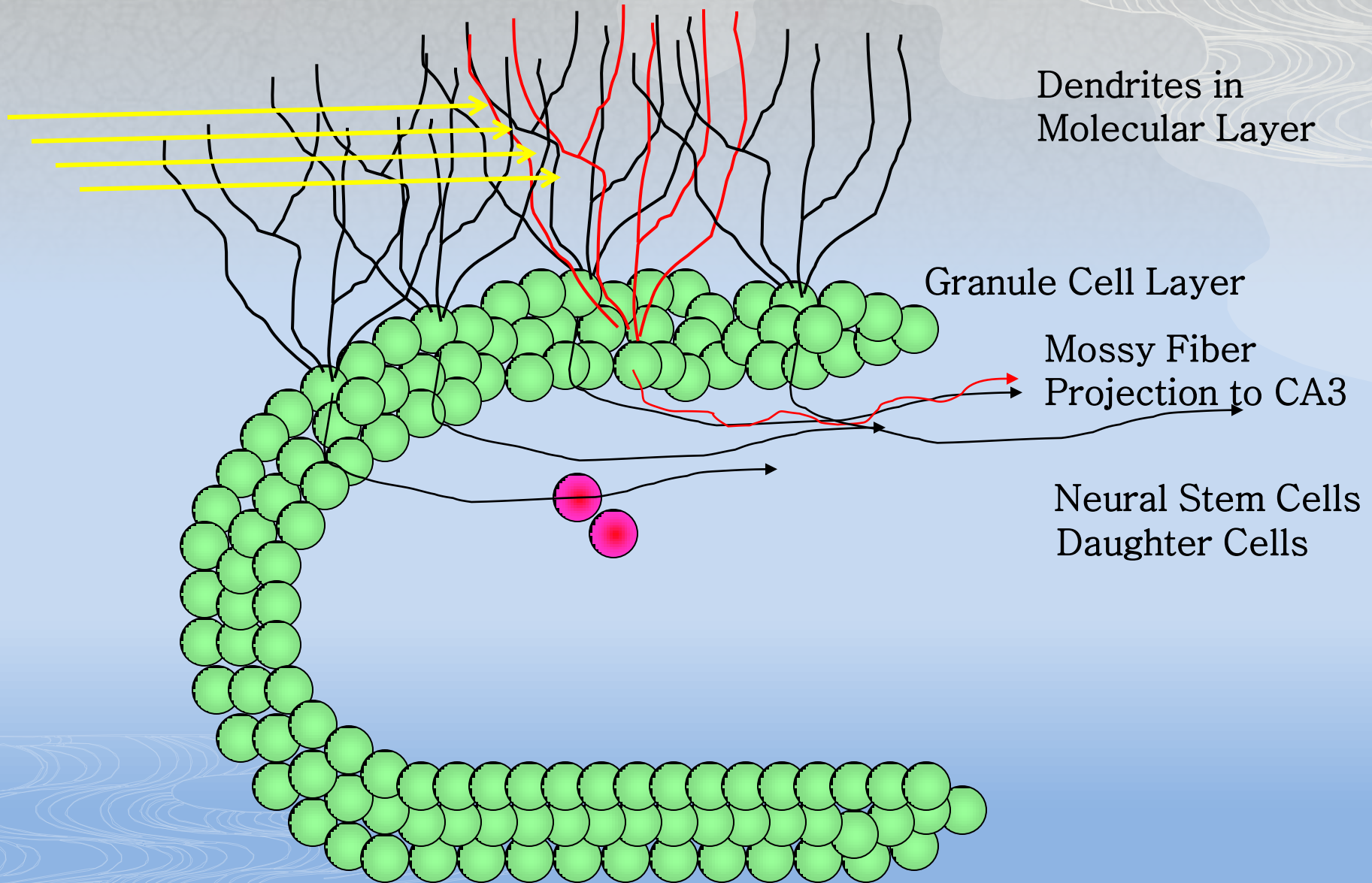
The Hippocampus contains neural stem cells

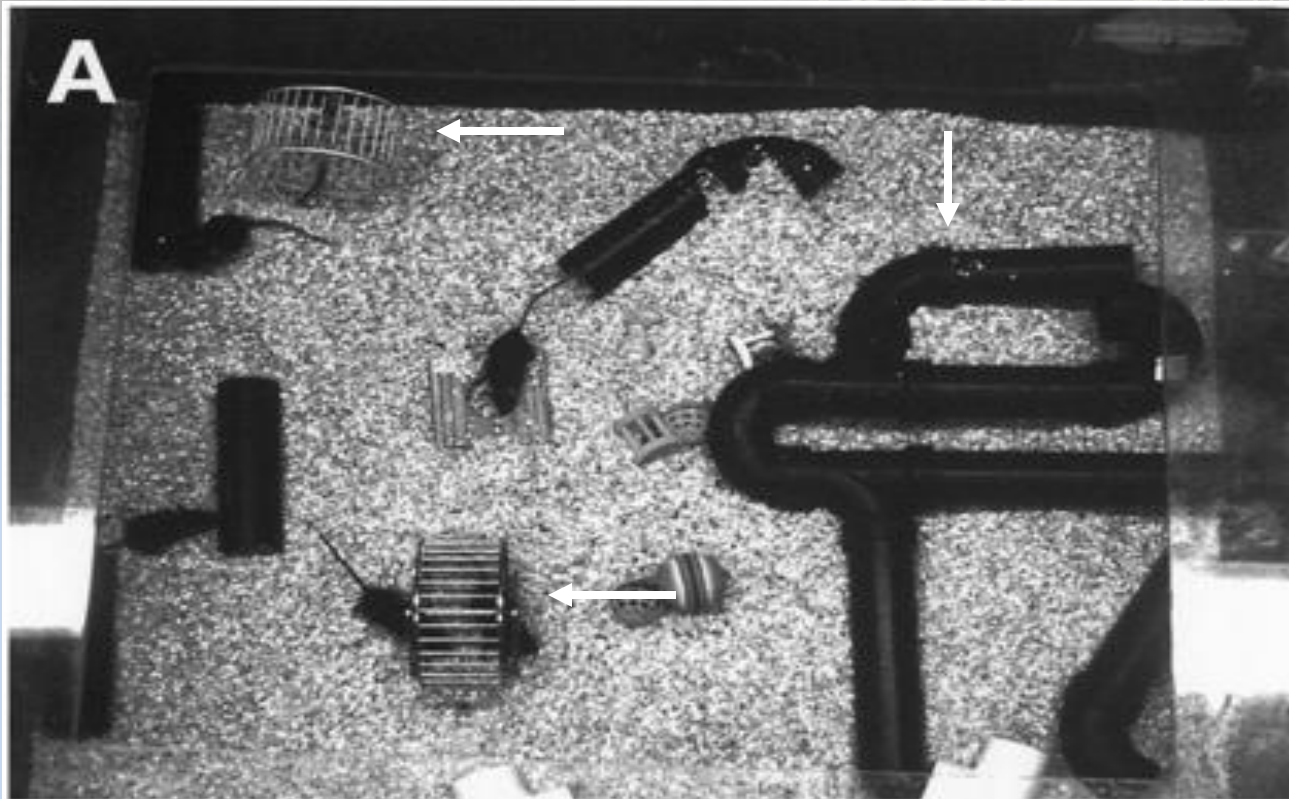


New Cells
expressing
GFP



Neurogenesis

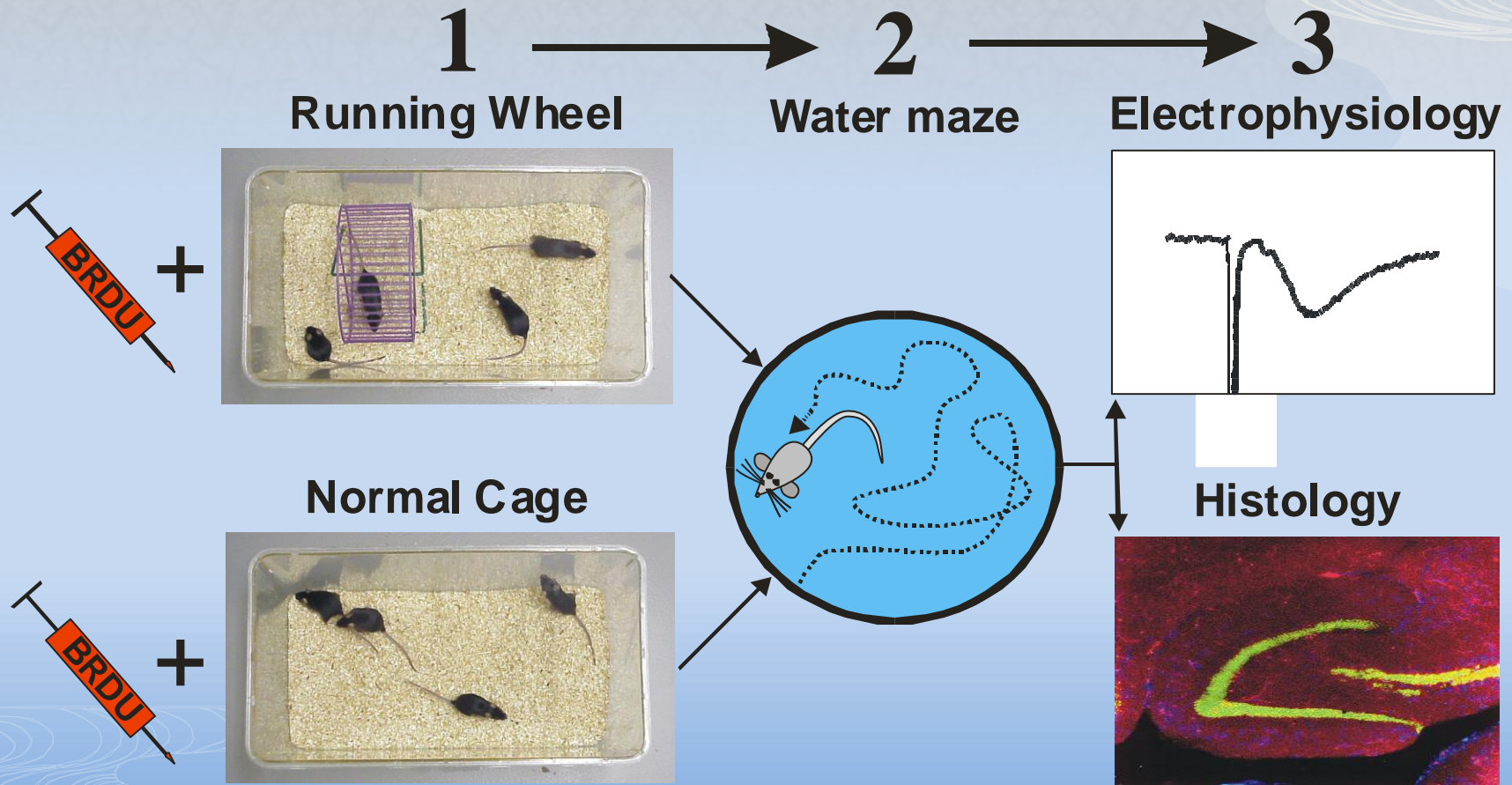




Donald Hebb showed enriched environments **improved learning** and memory in rats.

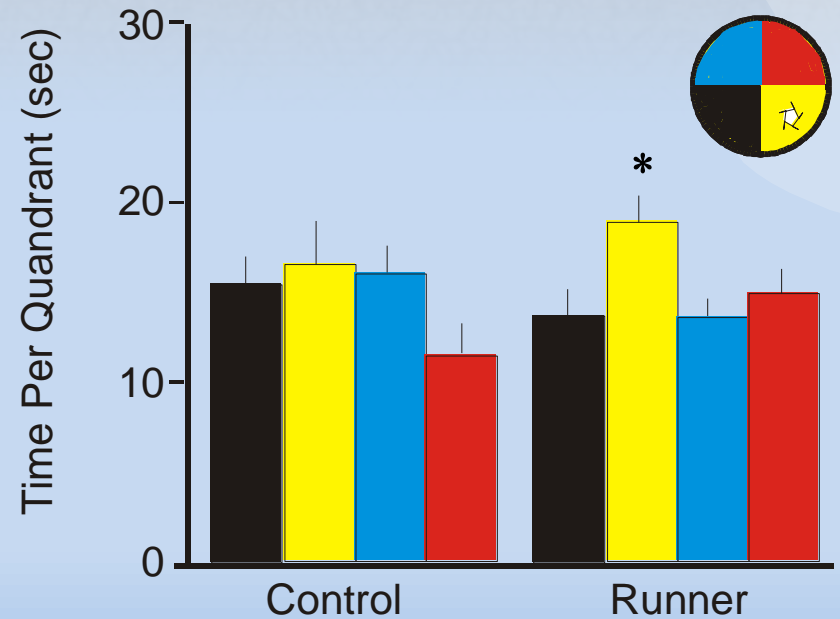
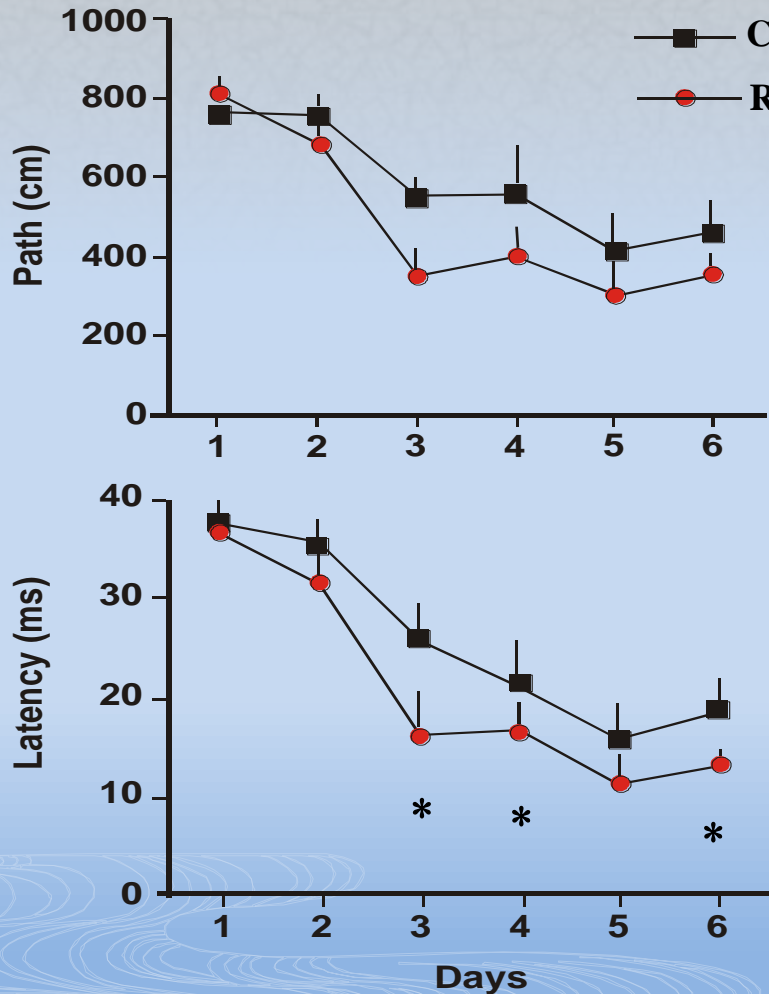
Kempermann and Gage showed enriched environments increased **neurogenesis** in the hippocampus.

Assessing the effects of exercise.



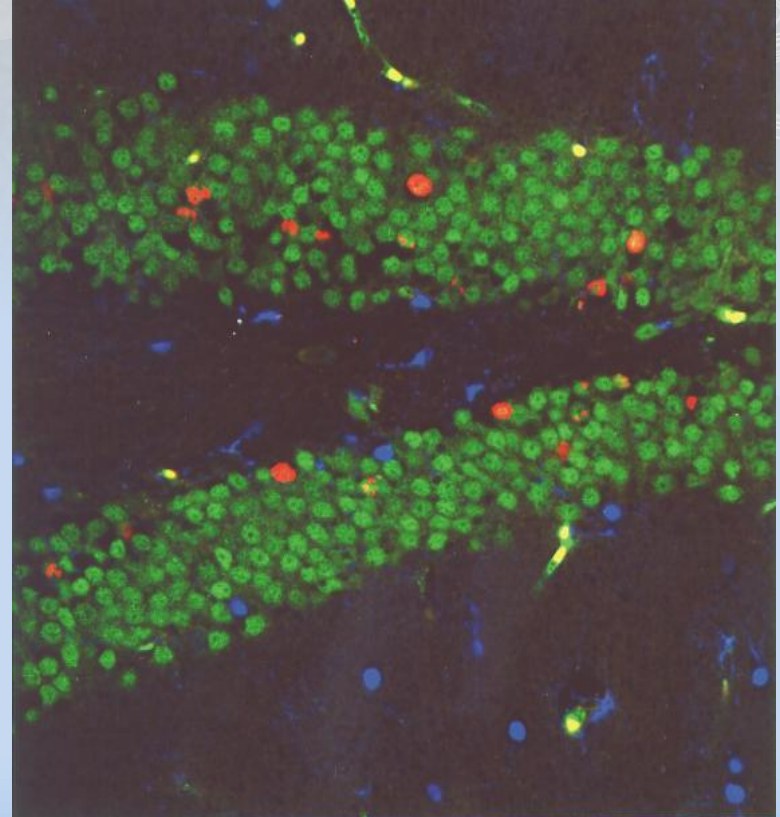
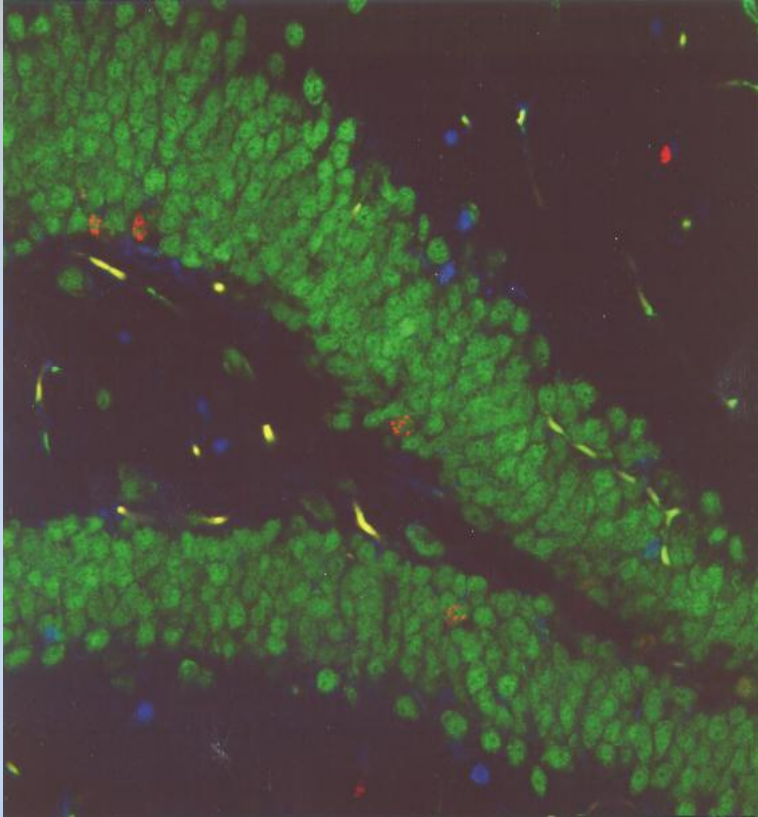
RESULTS

Exercise Improves Water Maze Learning



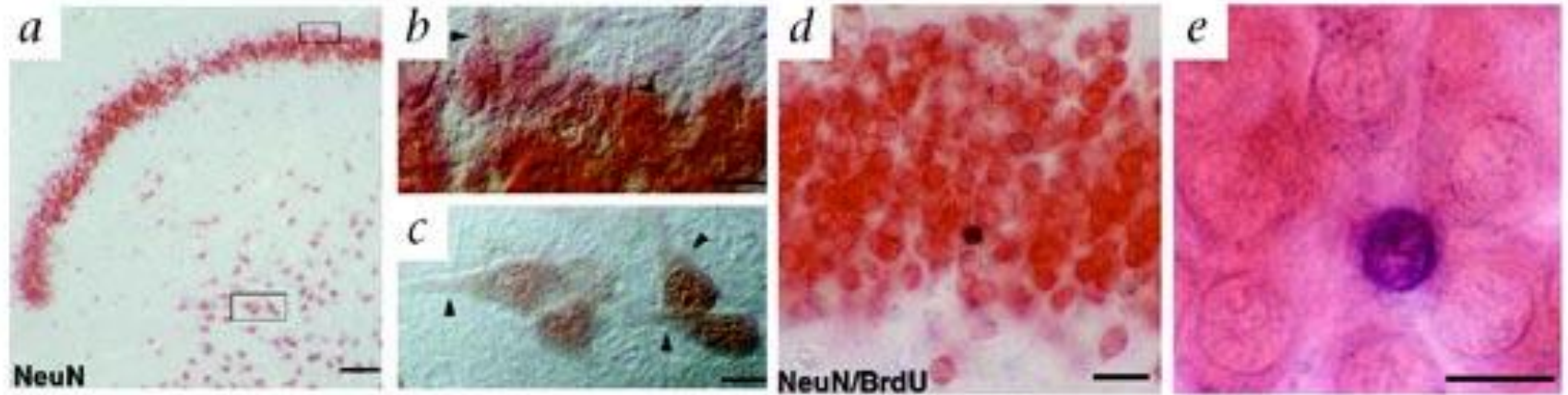
van Praag et al., 1999

Neurogenesis can be enhanced



Exercise increases hippocampal neurogenesis 2-3 times!

Neurogenesis in the adult human brain!

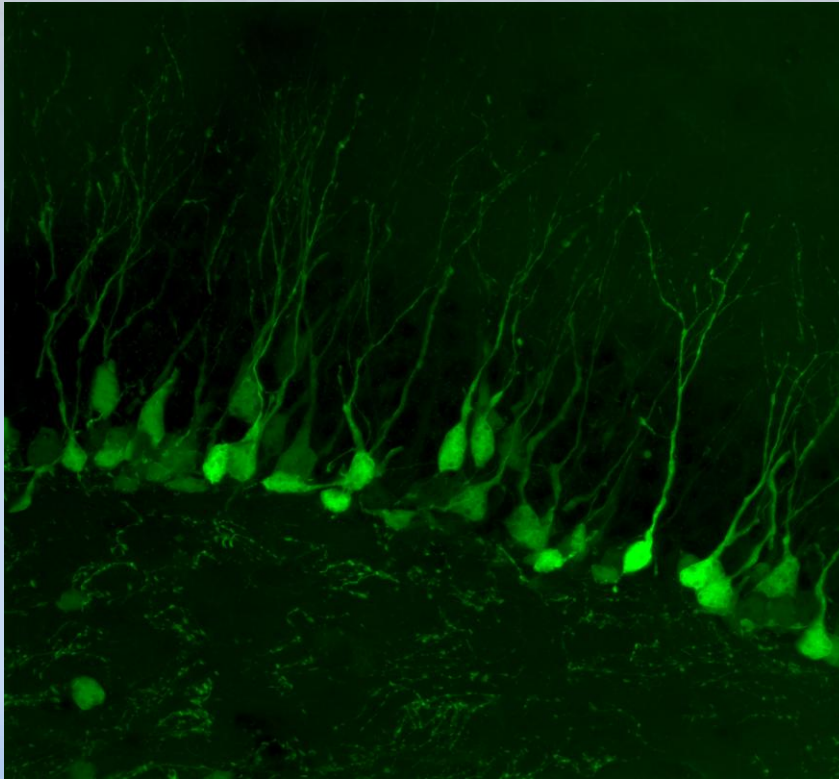


Human Cells

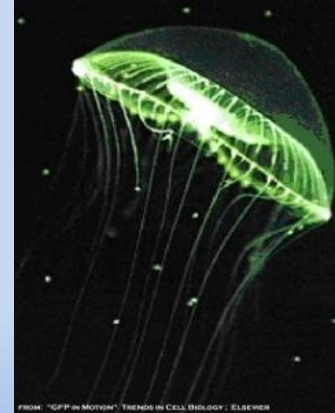


Animals that exercise produce a lot of new cells

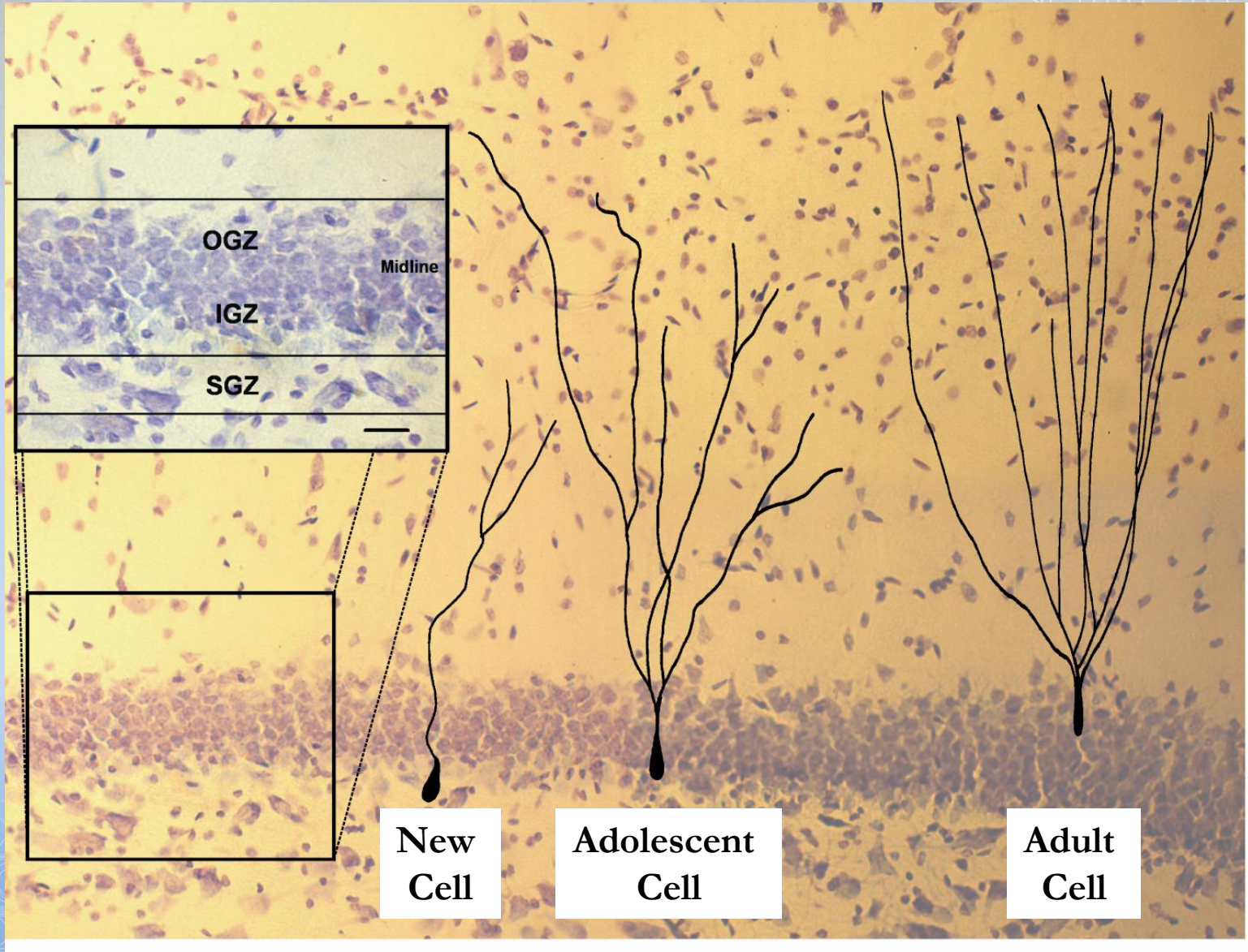
And we can identify them and study them!



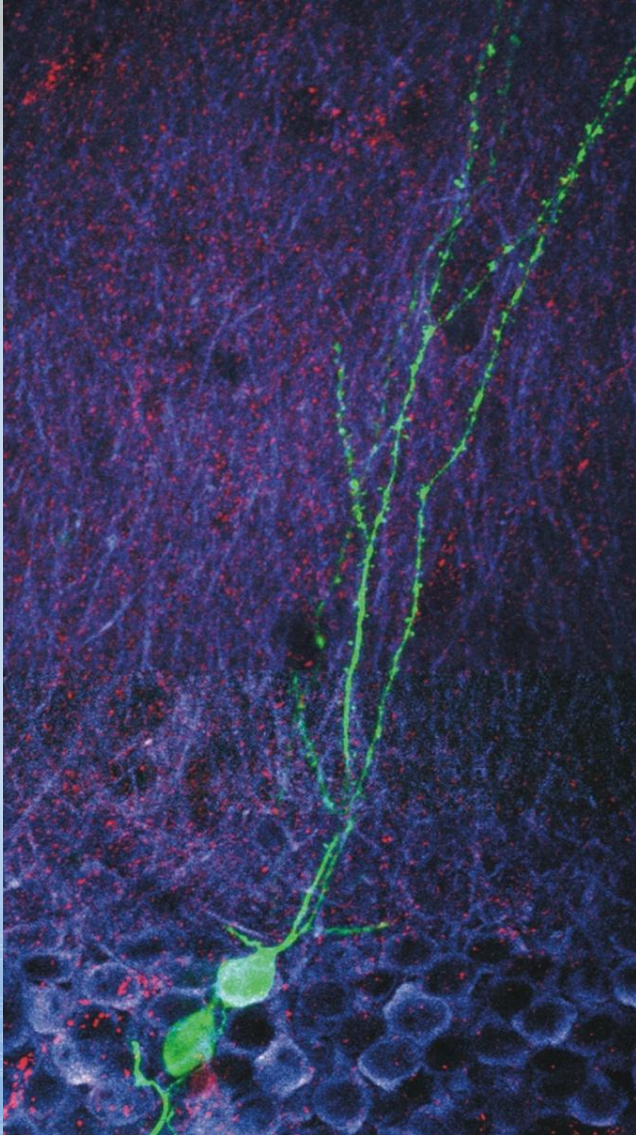
New Cells
expressing GFP



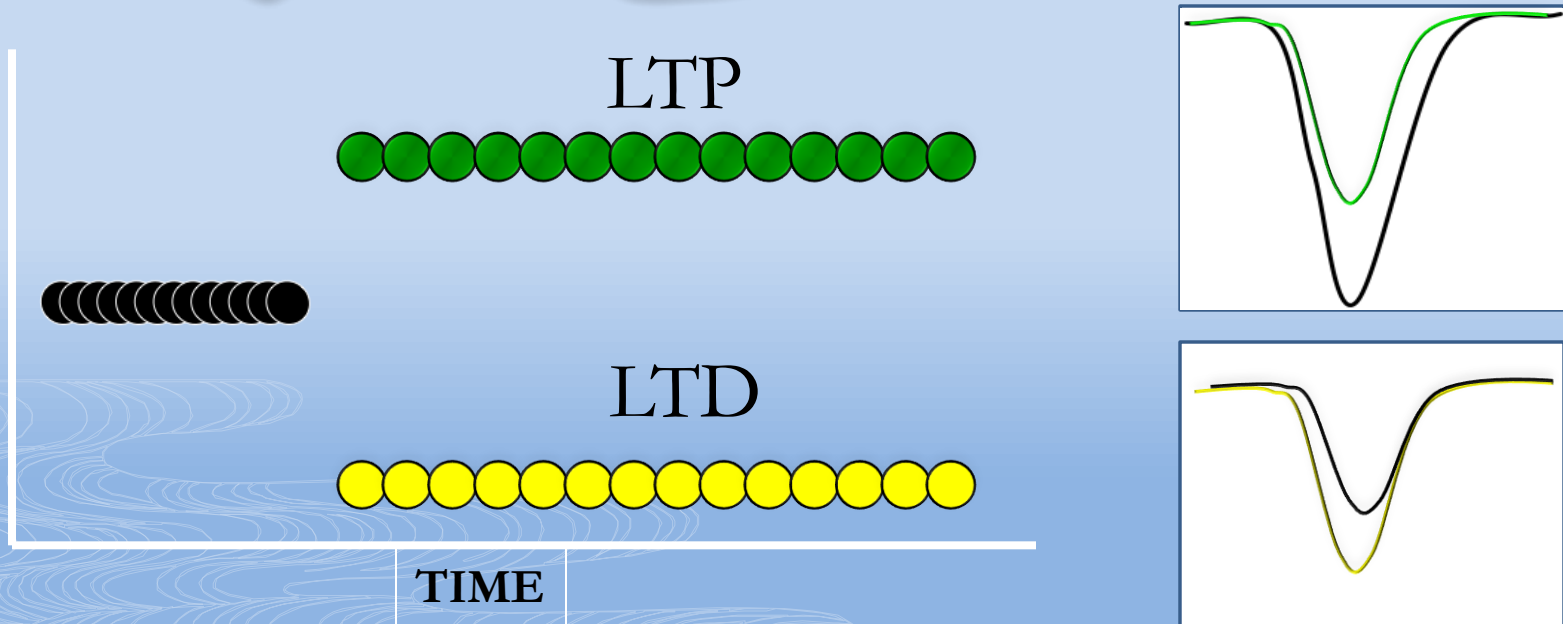
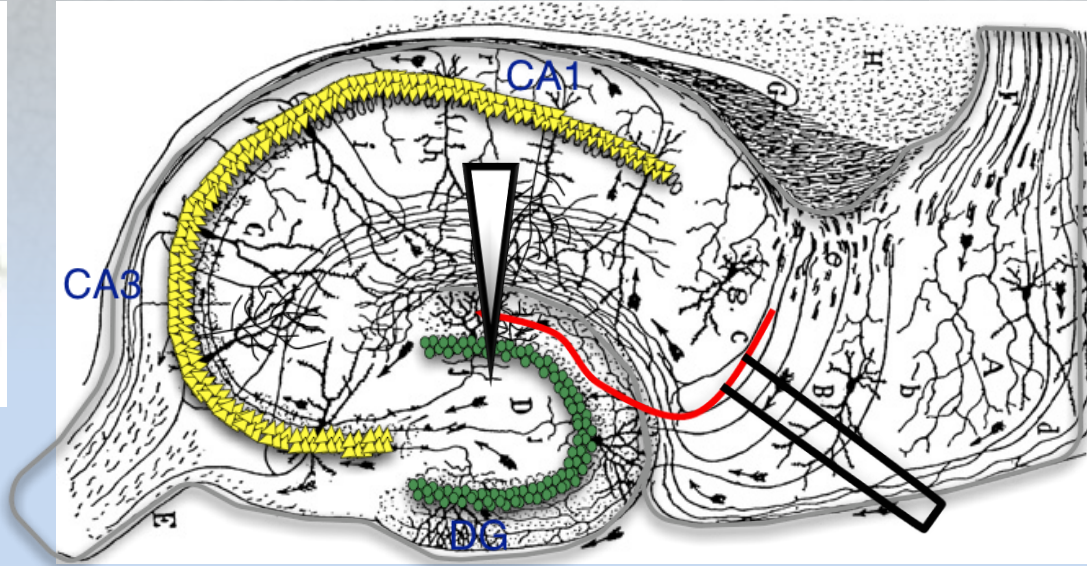
Exercise helps new cells grow and mature.



Exercise can also help the cells we already have!

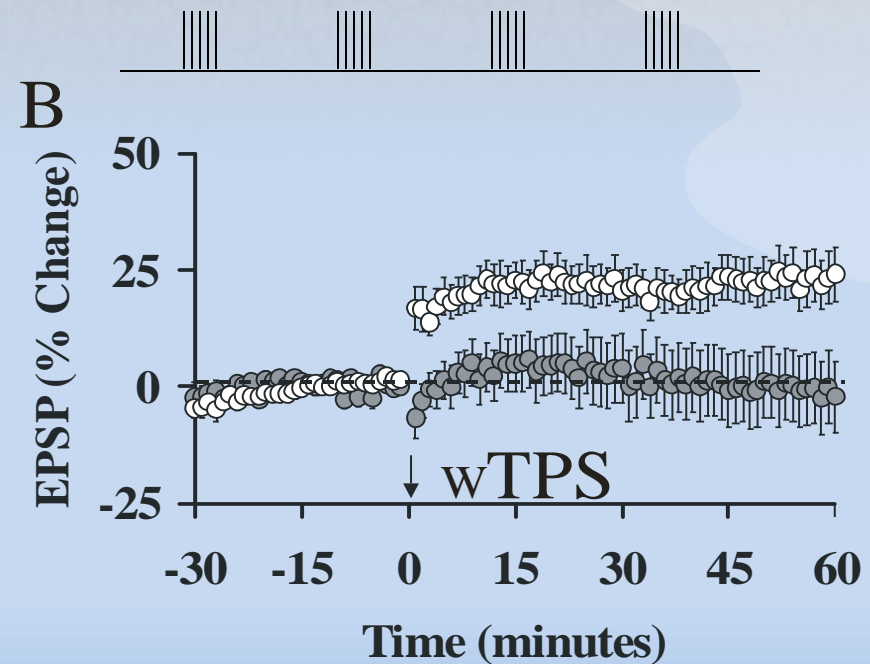
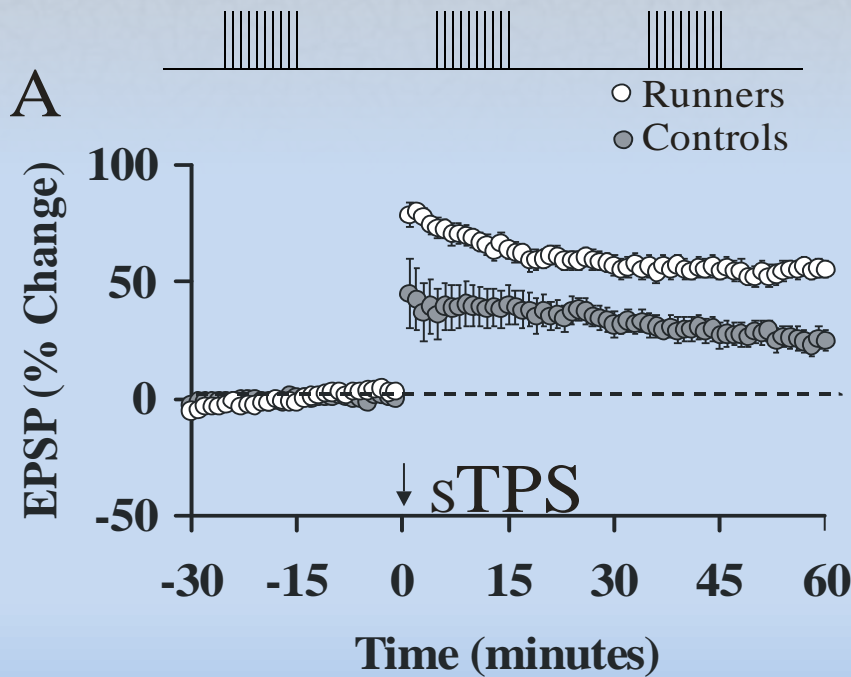


Hebb's Postulate: Synaptic Plasticity



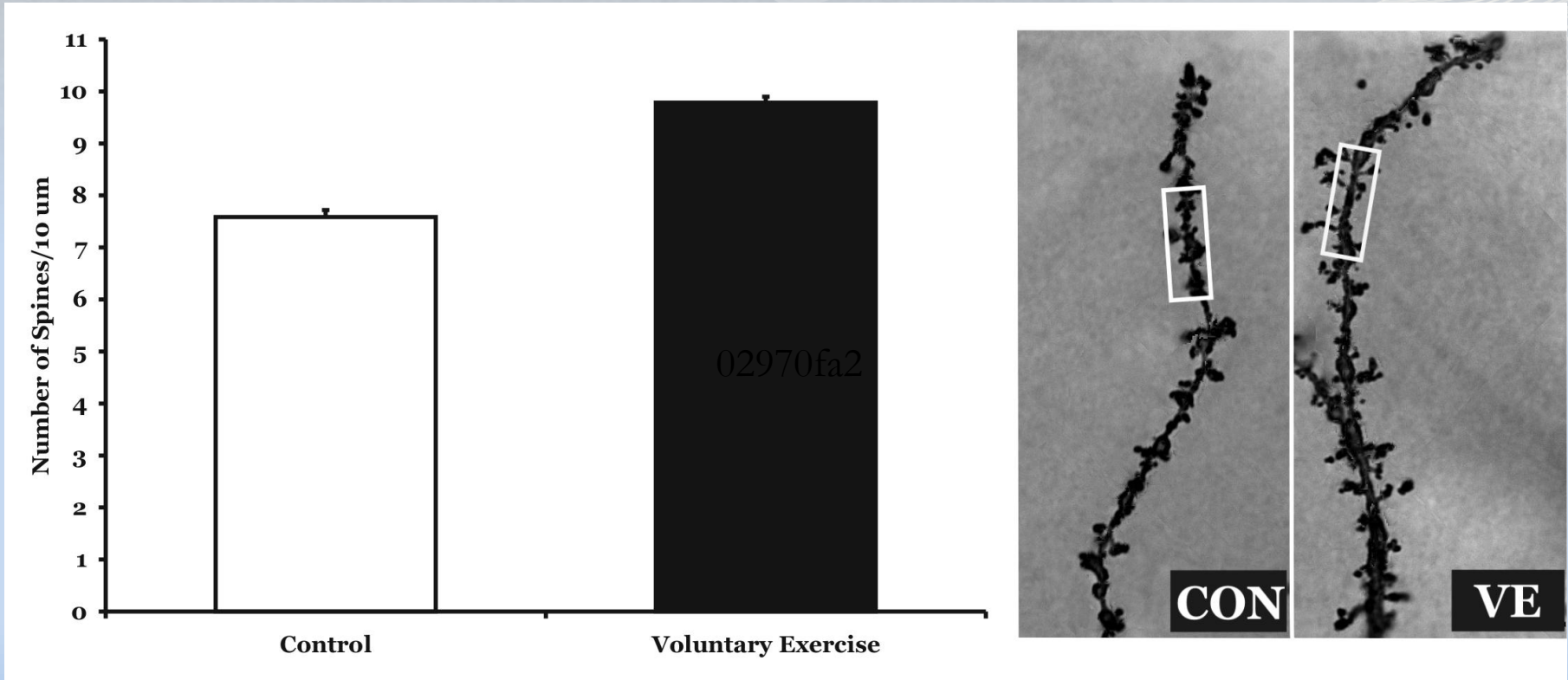
Exercise enhances LTP in the DG

RESULTS

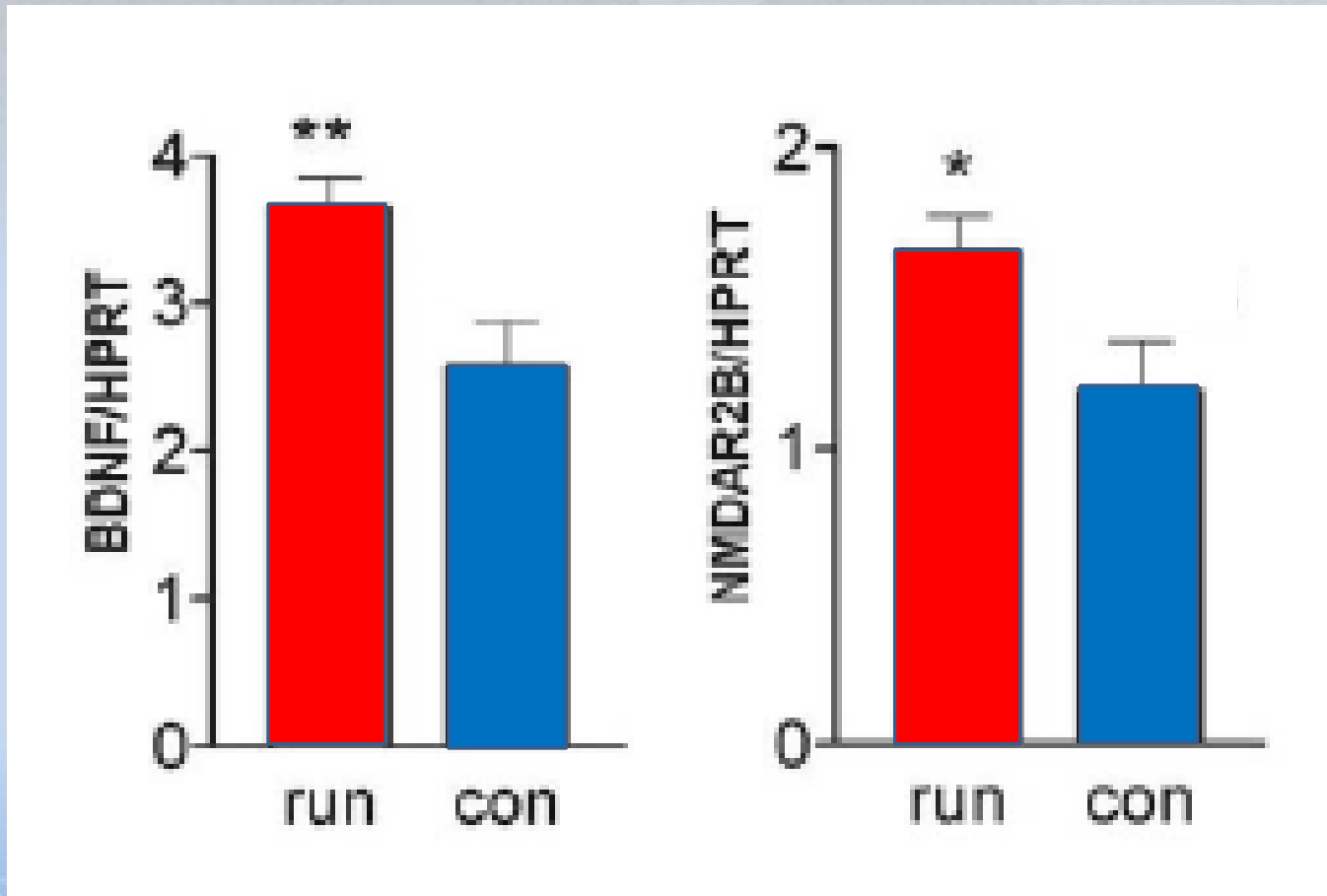


van Praag et al. 1999, PNAS. 96(23):13427-31.
Farmer et al., 2004, Neuroscience.

Exercise increases the number of spines on neurons



Exercise increases BDNF and NR2B receptor mRNA



Summary

- 1. Exercise increases the production of new neurons in the brain.**
- 2. Exercise enhances the growth of existing dendrites on neurons.**
- 3. Exercise enhances the number of spines on neurons.**
- 4. Exercise enhances synaptic plasticity**
- 5. Exercise enhances learning and memory processes.**

Can we use what we know about the effects of exercise for therapeutic purposes in neurological disorders?

Fetal Alcohol Syndrome

- Fetal Alcohol Syndrome (FAS) or Fetal Alcohol Spectrum Disorder (FASD) is caused by women drinking alcohol while pregnant.
 - FAS generally refers to the spectrum of morphological and cognitive disorders that are apparent in the offspring of “heavy” drinkers.
 - Many women don’t even know they are pregnant for months after conception and continue to drink until they find out they are pregnant. Their children are probably more at risk for FASD than FAS.
 - No amount of alcohol in pregnancy has been established as safe for the fetus.
-
- About 1% of North Americans suffer from FAS (Fetal Alcohol Syndrome) or FASD

Effects of Prenatal Ethanol Exposure are virtually the diametric opposite of those of exercise.



Dr. Joanne
Weinberg

1. There is cell loss in the Hippocampus of offspring following prenatal ethanol exposure.
2. Hippocampal cells do not appear to be fully mature.
3. Animals (including humans) exposed to ethanol prenatal exhibit impaired learning.
4. It's harder to show electrophysiological indices of learning and memory (LTP) in animals following PNEE.

Can exercise rescue animals from the deleterious effects of PNEE?

- These experiments require 3 groups of animals
 - 1. Ad Libitum Controls (AL)
 - 2. PNEE (35.5% ethanol derived calories)
 - 3. Pair-fed (PF) get the same number of calories as PNEE animals but have maltose-dextrin substituted for ethanol.

Ethanol Diet



Pair-fed, No Ethanol



Ad Libitum (no diet, no alcohol)



Gestation Day 1

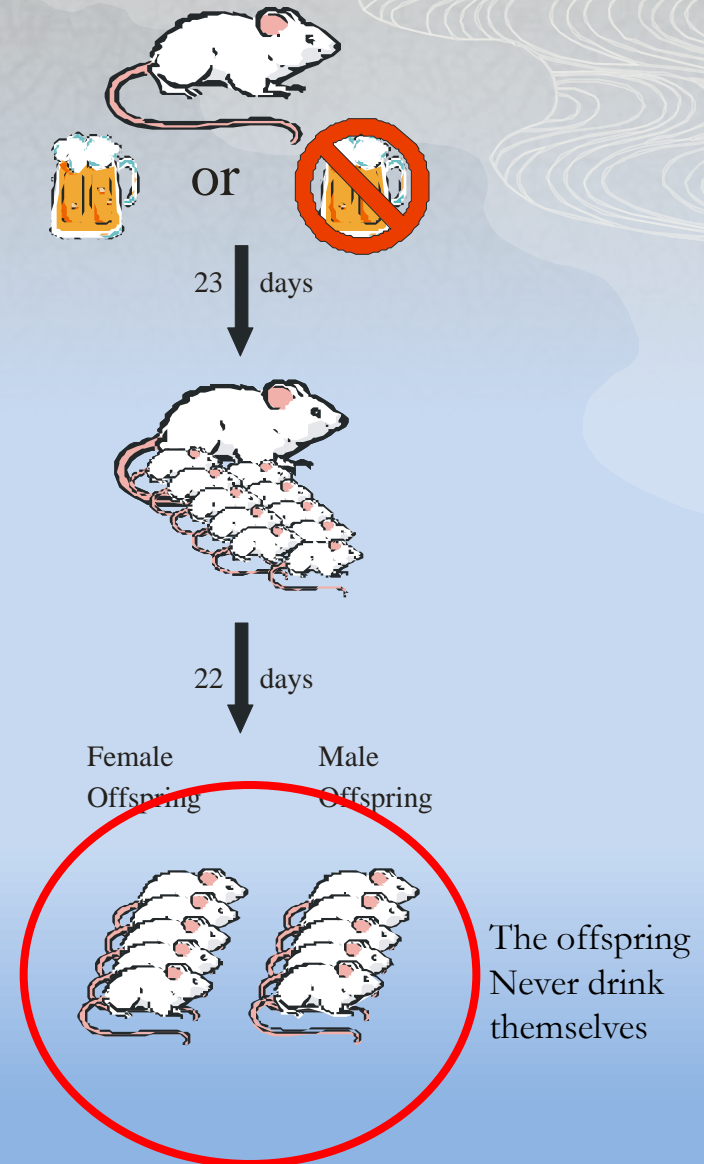
Female rats become pregnant and begin prenatal feeding (ethanol, pair-fed, or ad libitum diet).

Postnatal Day 1

Special diets end. Pups are born. Litters are culled to 10 (5 m and 5 f).

Postnatal Day 22

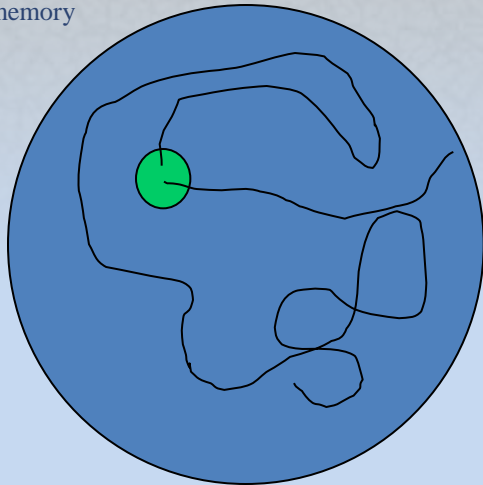
Pups are weaned and housed individually in either normal cages or cages containing an exercise wheel according to sex and prenatal diet.



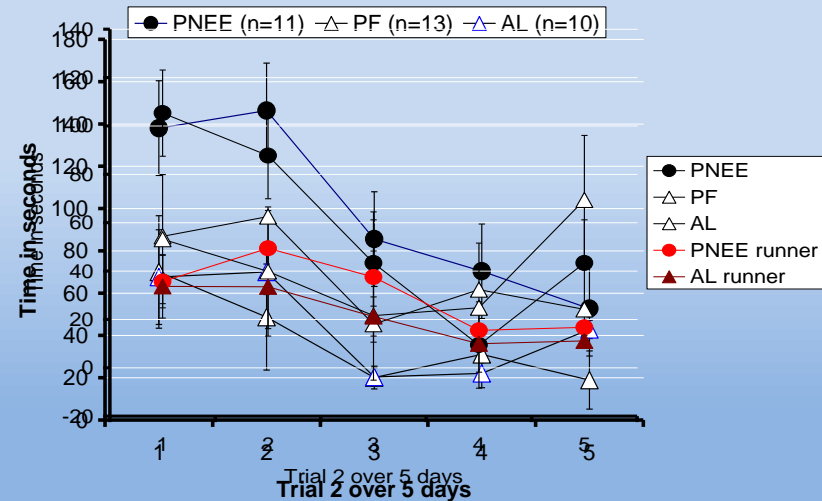
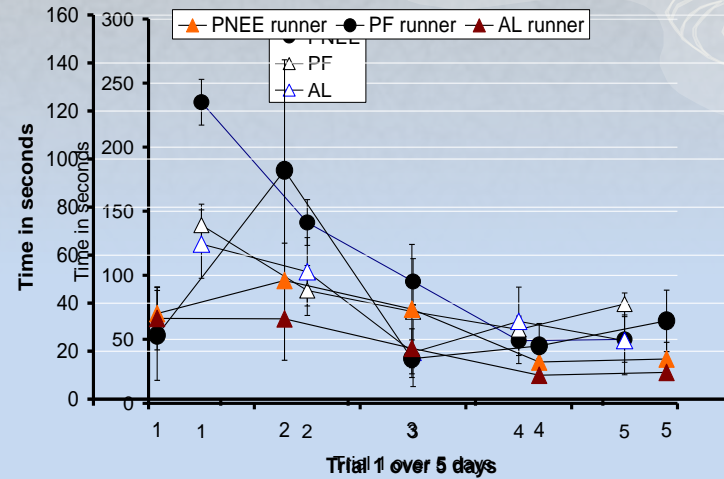
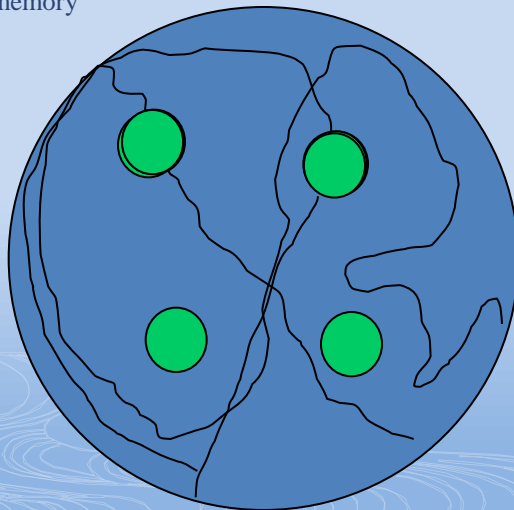
* Note this is the equivalent of drinking in G1 and G2 only.

Behavioural Testing in the offspring when they are adults (P50-60).

Reference memory

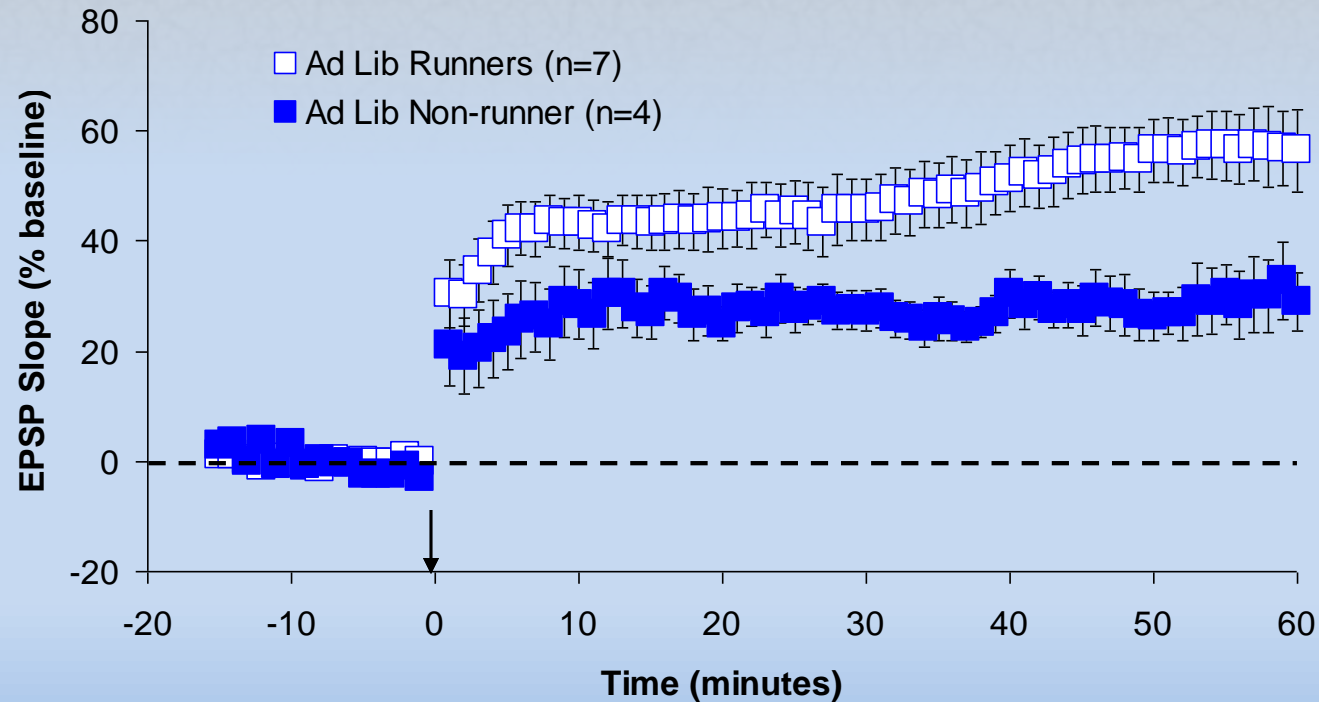


Working memory

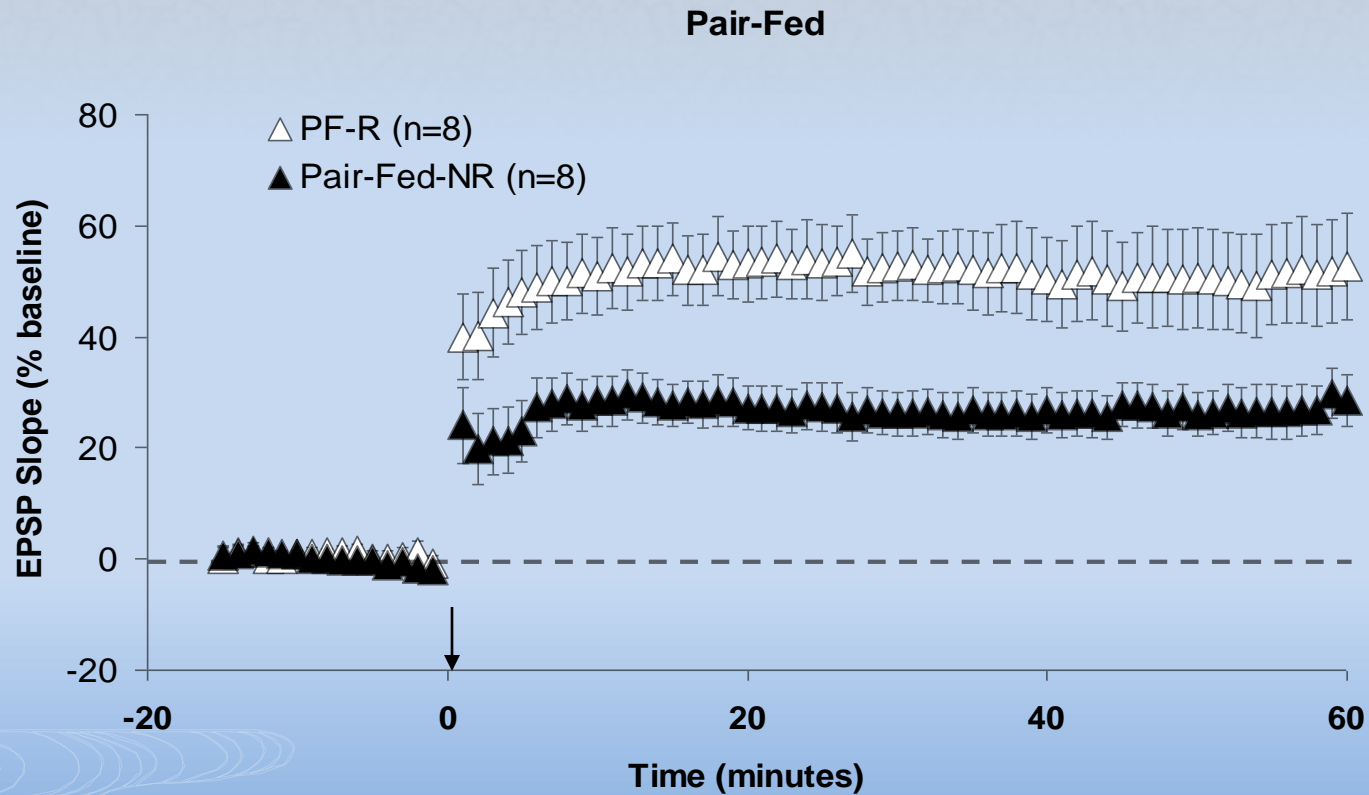


Normal adult animals show more LTP when they are allowed to exercise.

Ad Libitum

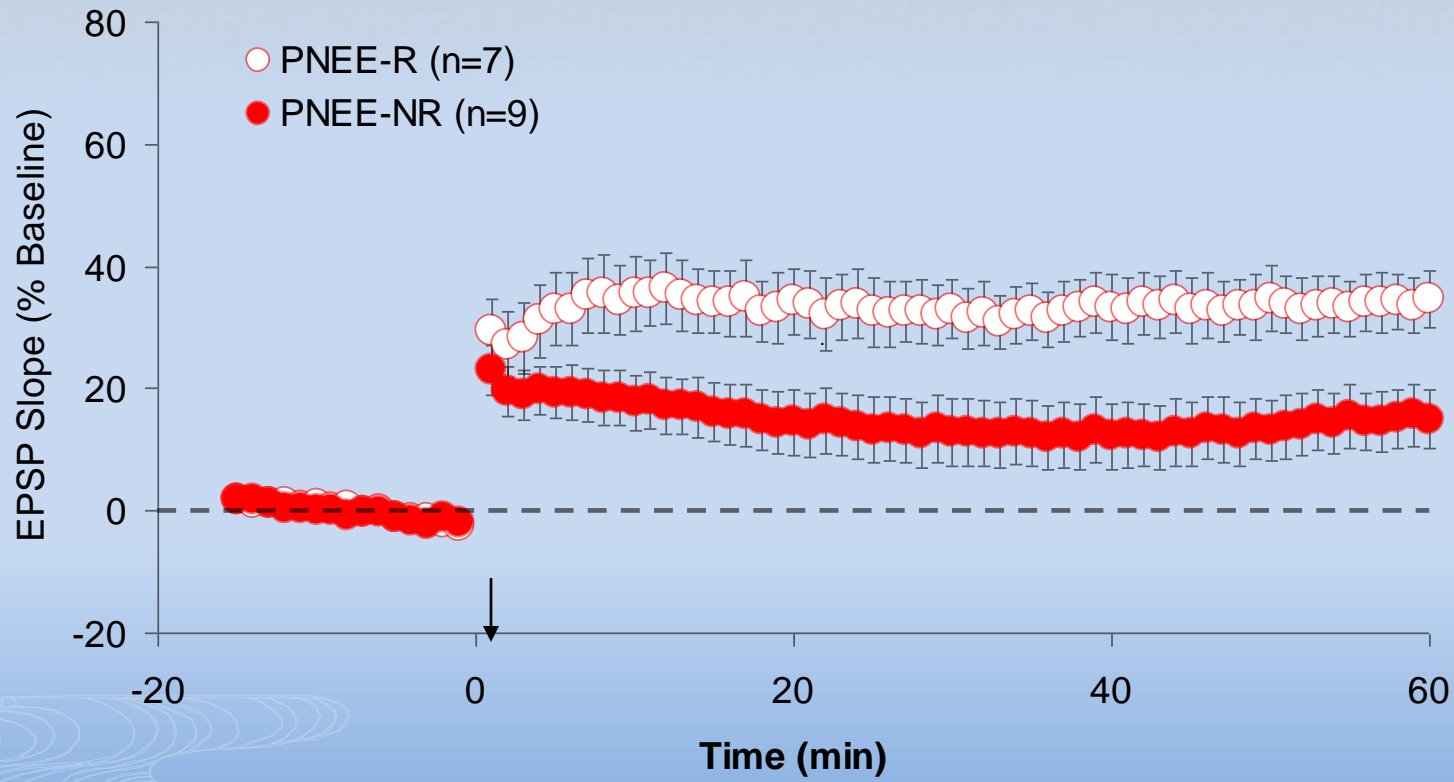


Pair-fed animals also show more LTP when they are allowed to exercise.

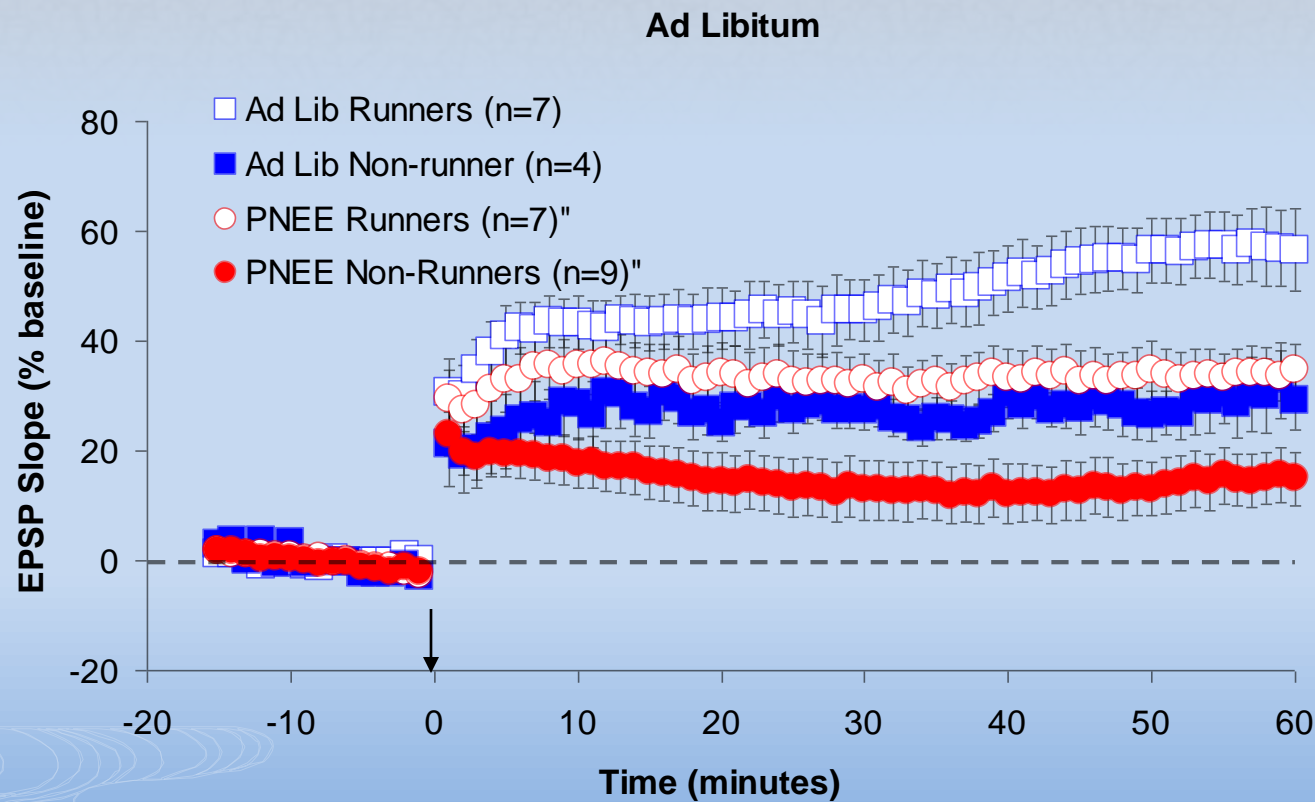


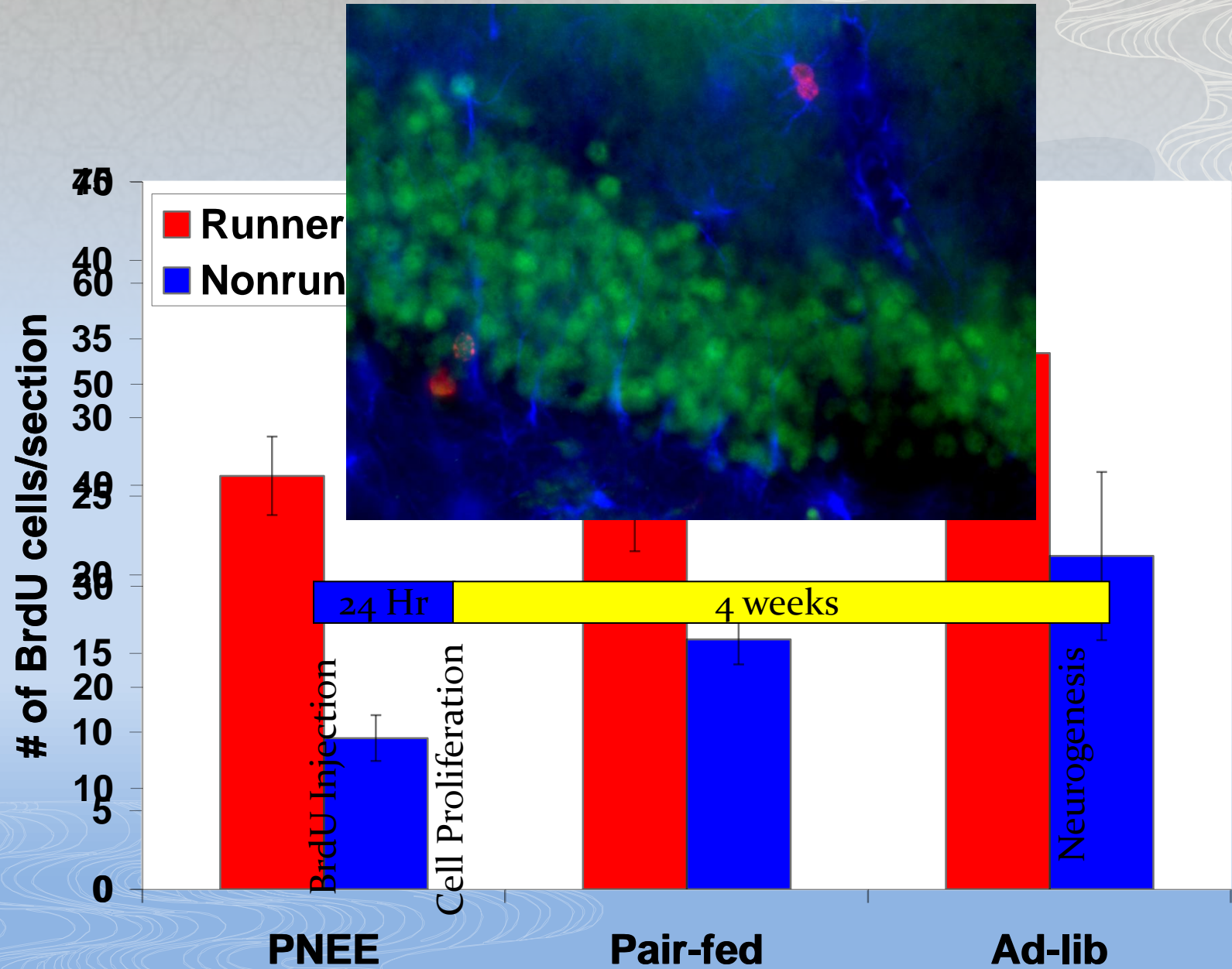
PNEE animals also show more LTP when they are allowed to exercise!

PNEE

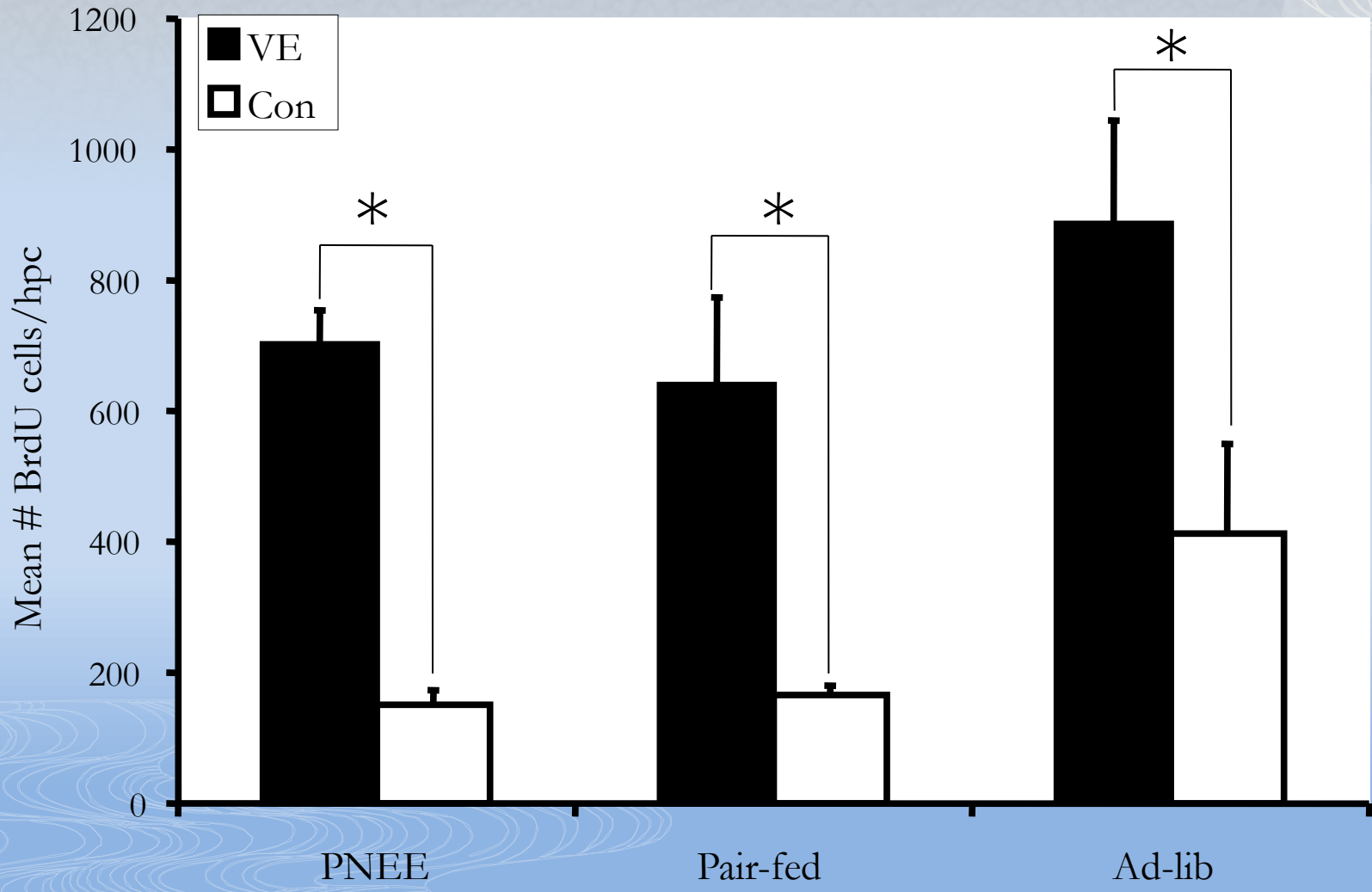


After exercising, PNEE animals do slightly better than normal “non-exercising” animals.





DG Neurogenesis



Take Home Messages

1. Exercise enhances neurogenesis in the DG.
2. Exercise enhances synaptic plasticity in the DG.
3. Exercise increases dendritic complexity in the DG.
4. Exercise enhances learning in behaviors that seem to involve the DG.
5. Early teratogen exposure can reduce neurogenesis, synaptic plasticity, and learning.
6. **Exercise may help to alleviate these deficits.**



PDF



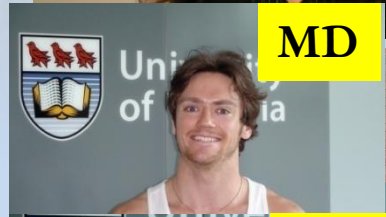
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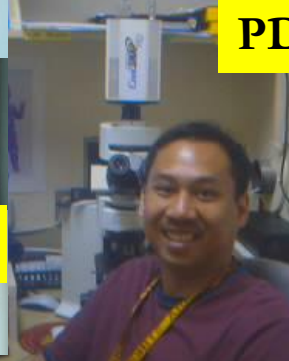
MSc



MD



Nursing



PhD



The Ups and Downs of Neurogenesis

Physical Activity

Enriched Environments

Anti-depressants

Anti-Oxidant Rich Foods?

Omega-3 Fatty Acids?

Mental Exercise?

Social Interactions?

Inactivity

Isolation

Depression

Brain Irradiation

Alcoholism

Drug use

Stress

Poor Sleep

Working for the government