What do you notice?
Adult Neurogenesis
the birth of new neurons in the adult brain

By Lara Rangel
COGS 1, February 23, 2016
The number of neurons in the brain is *constantly changing*

New estimates of the number of neurons in the human brain range from roughly **80 billion** to **120 billion**.

Herculano-Houzel 2009

We can **lose** neurons for many reasons such as disease, injury, stress, and normal aging.

We can also **increase** this number through a process called *adult neurogenesis*.
On the replacement of lost cells

**Question:**

If we could *gain* a neuron for every neuron that we *lose*, could the new neurons take over the job of the lost neurons?

Or are lost neurons irreplaceable?
There are two main neurogenic regions

The **subgranular zone**
of the dentate gyrus:

The **subventricular zone**
of the lateral ventricle:

www.BrainConnection.com,
Scientific Learning Corp., 1999

Huart, Rombaux, and Hummel, 2013

Eriksson et al., 1998
New neuron development:
from dividing radial glia to mature granule cell

This process is highly regulated

Aimone et al., 2014
Quantifying neuron proliferation (rate of division) and survival

**Doublecortin**: a microtubule-associated protein expressed in the first 2-3 weeks
Quantifying neuron proliferation (rate of division) and survival

5-bromo-2’-deoxyuridine (BrdU): a thymidine analog that is incorporated into the DNA of dividing cells during their S-phase

Mak et al., 2013
Quantifying neuron proliferation (rate of division) and survival

Measuring Proliferation

Control: BrdU, DCX, Ki67
- No manipulation
  - How many cells are dividing or are immature at this time?

Experimental: BrdU, DCX, Ki67
- Add manipulation
  - How many cells are dividing or are immature at this time?

Measuring Survival

Control: BrdU
- No manipulation
  - 1 week
  - No manipulation
  - How many adult-born cells survived 4 weeks later?

Experimental: BrdU
- No manipulation
  - 1 week
  - Add manipulation
  - How many adult-born cells survived 4 weeks later?

Less? More?
Many things can influence adult neurogenesis; proliferation is highly regulated.

**Proliferation (rate of division):**

- **Stress**
  
  Schoenfeld and Gould, 2012
  
  decreases

- **Physical Exercise**
  
  van Praag et al., 1999
  
  increases

- **Antidepressants**
  
  Boldrini et al., 2009
  
  increases

- **Aging**
  
  Kuhn et al., 1996
  
  decreases

- **Seizures**
  
  Jessberger and Parent., 2015
  
  increases
Many things can influence adult neurogenesis. Survival is highly regulated.

Survival:

- **Learning**
  Dupret et al., 2007

- **Alcohol**
  Crews and Nixon, 2004

- **Dietary Restriction**
  Kitamura et al., 2006

- **Enriching Environments**
  Tashiro et al., 2007
Many things can influence adult neurogenesis, and survival is highly regulated.

- Adult neurogenesis can be regulated at different stages of neuron development.

- Increased proliferation does not necessarily mean that there are more that survive.

- The fact that this process is highly regulated suggests that these cells may serve a special function.

- Is more neurogenesis a good thing?
Adult neurogenesis occurs in the hippocampus, a brain structure important for learning and memory.

The dentate gyrus (in the hippocampus) is important for being able to discriminate between similar experiences.

Rats require a dentate gyrus in order to discriminate between a new and old spatial location.

Gilbert et al., 2001
Aimone et al., 2011
Adult neurogenesis occurs in the hippocampus
a brain structure important for learning and memory

The dentate gyrus (in the hippocampus) is important for being able to discriminate between similar experiences.

Humans show stronger activation of dentate gyrus when presented with an object subtly different from another object seen previously.

Bakker et al., 2008
Adult neurogenesis occurs in the hippocampus—a brain structure important for learning and memory.

The rat hippocampus:

The time course of new neuron development may help us understand their role.

brainmaps.org

Aimone et al., 2006
What can activate adult-born cells?

How many of the adult-born neurons that survived by week 6 are **active during re-exposure** to the enriched environment?

Count the number of co-labeled cells

Tashiro et al., 2007
Adult-born neurons are active during re-exposure to experiences that occurred during their development.

**Experience** can influence the survival and future activity of immature cells. There is a **critical window** for this influence.

Tashiro et al., 2007
Adult neurogenesis occurs in the hippocampus, a brain structure important for learning and memory.

**Hypothesis:** Young cells may exhibit activity that is selective for experiences that occurred at a particular time point.

Events that occur far apart in time should engage different populations of adult-born neurons.

Adapted from Aimone et al., 2009
Adult neurogenesis occurs in the hippocampus, a brain structure important for **learning** and **memory**.

For experiences occurring weeks apart, granule cells exhibit activity selective to one experience.

Adapted from Aimone et al., 2009.

Testing for:

- Active
- Silent
- Silent

Experience 1 | Experience 2 | Experience 3 | Re-exposure

2 weeks | 2 weeks | 2 weeks |
Adult neurogenesis occurs in the hippocampus, a brain structure important for learning and memory.

For experiences occurring weeks apart, granule cells exhibit activity selective to one experience.

Testing for:
- silent
- active
- silent

<table>
<thead>
<tr>
<th>Events:</th>
<th>Time 1</th>
<th>Time 2</th>
<th>Time 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experience 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experience 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experience 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Re-exposure</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

= neuron spike
Adult neurogenesis occurs in the hippocampus, a brain structure important for learning and memory.

For experiences occurring weeks apart, granule cells exhibit activity selective to one experience. With neurogenesis, adult-born neurons may enable discrimination between temporally separated events through activity that is selective for experiences occurring at a particular time during their development.
Adult neurogenesis occurs in the hippocampus, a brain structure important for learning and memory.

- The dentate gyrus is important for helping us discriminate between similar experiences.
- Neurons in the dentate can detect differences between experiences by demonstrating highly selective and specialized activity.
- Adult-born neurons may facilitate the allocation of selective and dedicated activity for new experiences in the dentate gyrus.
On the replacement of lost cells...

**Question:**

If we could *gain* a neuron for every neuron that we *lose*, could the new neurons take over the job of the lost neurons? Or are lost neurons irreplaceable?
Thank You

My name:
Lara Rangel
lrangel@ucsd.edu