Neuroinformatics

April 3, 2024

Lecture 6: Synaptic plasticity and Hebb's rule

Learning what is is?

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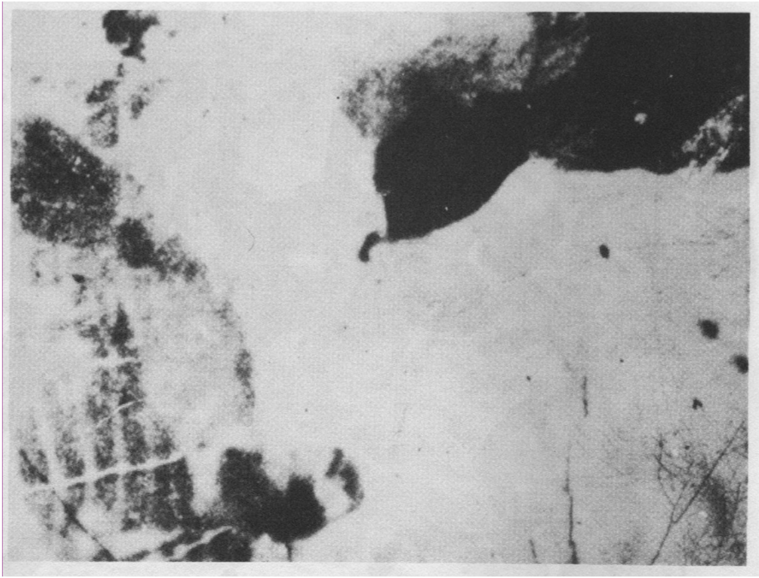
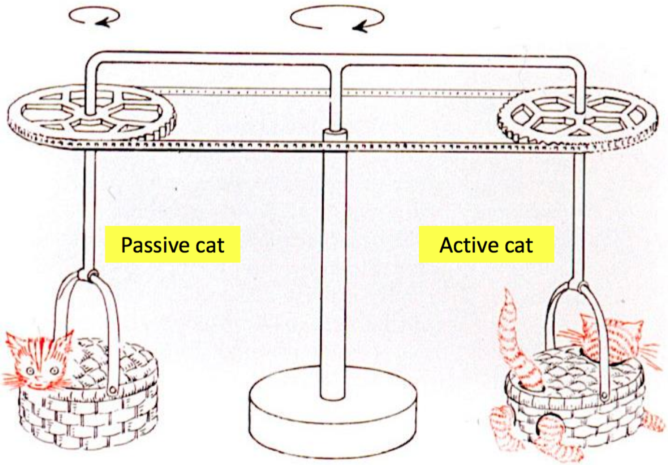


Action-perception loop



Held R, Hein A (1963)

Types of plasticity

- **Structural plasticity** is the mechanism describing the generation of new connections and thereby redefining the topology of the network.
- **Functional plasticity** is the mechanism of changing the strength values of existing connections.

Hebbian plasticity

”When an axon of a cell A is near enough to excite cell B or repeatedly or persistently takes part in firing it, some growth or metabolic change takes place in both cells such that A’s efficiency, as one of the cells firing B, is increased.”

Donald O. Hebb, **The organization of behavior**, 1949
See also Sigmund Freud, **Law of association by simultaneity**, 1888
Santiago Ramn y Cajal - memories might instead be formed by strengthening the connections between existing neurons to improve the effectiveness of their communication, 1894

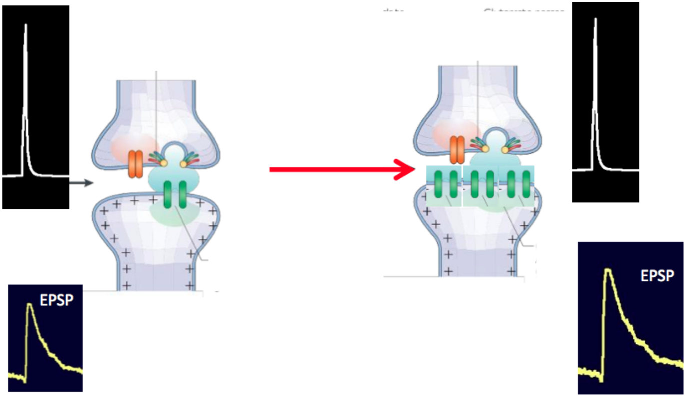
Possible neuronal mechanisms sub-serving learning and memory

New nerve cells grow - new functional neural networks are formed .1
for exhibiting new learned items- structural plasticity

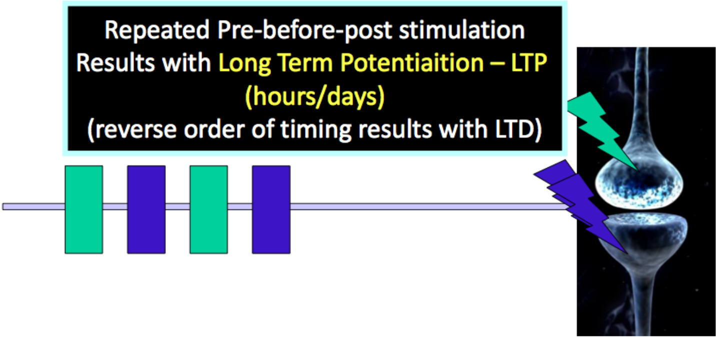
New synaptic connections (new functional neural networks) are .2
formed - structural plasticity - (*Ramon Y. Cajal)*

Strength of existing (synaptic) connections change - (new functional .3
neural networks) - functional plasticity (Donald Hebb)

Synaptic mechanism

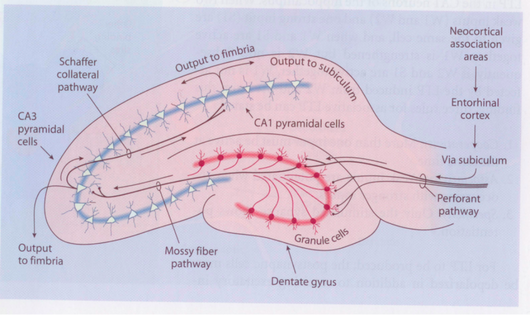


Long term potentiaition



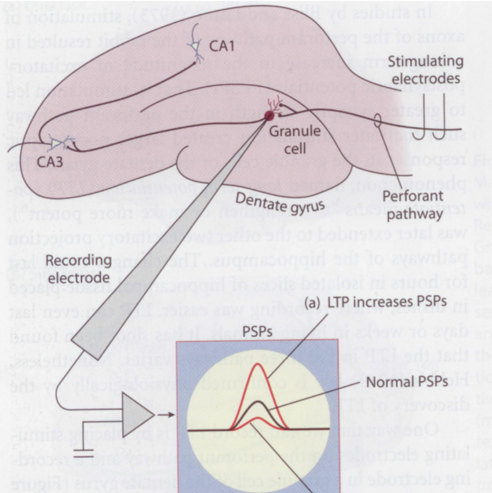
Hippocampus

- Hippocampus: centre of memory storage, The dentate gyrus is thought to contribute to the formation of new memories. It is notable as being one of a select few brainstructures currently known to have high rates of neurogenesis in adult rats
- Neurons must be plastic
- Experiment: isolated slices of hippocampal tissue placed in dishes



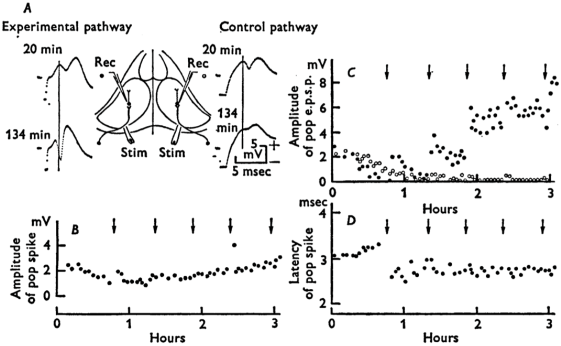
LTP experiment

- EXPERIMENTAL confirmation of Hebb's rule (1949)
- i) single pulse is presented ii) stimulation with burst of pulses: 100 pulses/sec ii) After LTP induced, single pulse stimulation
- Postsynaptic cells must be depolarized to LTP be produced AND receiving excitatory input - see Associative learning slide.

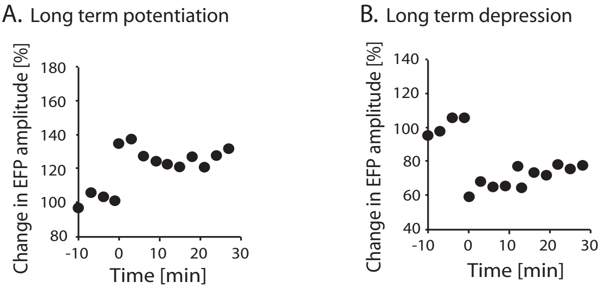


Original LTP by Bliss and Lomo, 1973

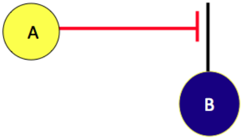
- Long-lasting changes of synaptic response characteristics
- High frequency-stimulus is applied (plasticity-induced tetanus) $\rightarrow$ long-term potentiation(to strengthen, make more potent) (LTP) average amplitude of EPSP increased
- Long frequency stimulus $\rightarrow$ long-term depression (LTD)



Classical LTP and LTD

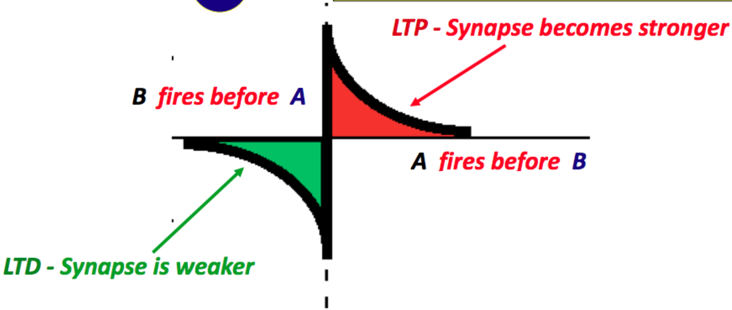


Hebbian model



$$\Delta w_+ = A_+ e^{\frac{-(t_{post} - t_{pre})}{\tau_+}} \quad when\left(t_{post} > t_{pre}\right)$$

$$\Delta w_- = A_- e^{\frac{-(t_{post} - t_{pre})}{\tau_-}} \quad when\left(t_{pre} > t_{post}\right)$$



Mathematical formulation of Hebbian plasticity - spiking models

$$w_{ij}(t+\Delta t) = w_{ij}(t) + \Delta w_{ij}(t_i^{\mathrm{f}}, t_j^{\mathrm{f}}, \Delta t; w_{ij}).$$

$$\Delta w_{ij}^{\pm} = \epsilon^{\pm}(w) K \pm (t^{\mathrm{post}} - t^{\mathrm{pre}})$$

Spike Timing Dependent Plasticity (SPDP)¿ (i) Exponential plasticity curve, (ii) Repeated spike pairings induced w UNBOUNDED growth $\rightarrow$ a weight dependent learning rate $\epsilon^{\pm}$

$$\Delta w_{ij}^{\pm} = \epsilon^{\pm}(w) \mathrm{e}^{\mp \frac{t^{\mathrm{post}} - t^{\mathrm{pre}}}{\tau^{\pm}}} \ \Theta(\pm[t^{\mathrm{post}} - t^{\mathrm{pre}}]).$$

Additive rule with hard (absorbing) boundaries:

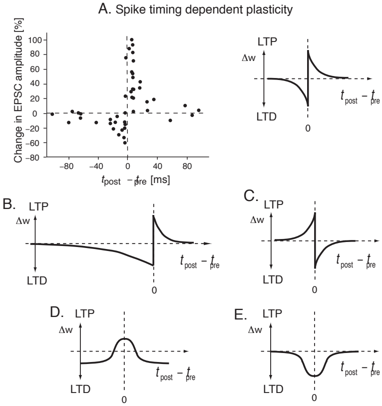
$$\epsilon^{\pm} = \begin{cases} a^{\pm} & \text{for } \ w_{ij}^{\min} \leq w_{ij} \leq w_{ij}^{\max} \\ 0 & \text{otherwise} \end{cases},$$

Multiplicative rule (soft boundaries):

$$\begin{aligned} \epsilon^{+} &= a^{+}(w^{\max} - w_{ij}) \\ \epsilon^{-} &= a^{-}(w_{ij} - w^{\min}). \end{aligned} \tag{1}$$

Spike timing dependent plasticity (STDP)

- Bi-Poo experiments: voltage clamp for hippocamal cells in vitro, $\rightarrow$ Excitatory PostSynaptic Current (EPSP) $\rightarrow$ critical time window $\Delta t = 40$ms
- critical window width is much larger, asymmetrical and symmetrical (for bursting neurons) form of Hebbian plasticity, inverse correlation in Purkinje cells (inhibitory) in the cerebellum

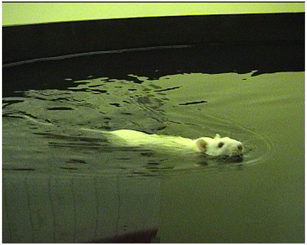


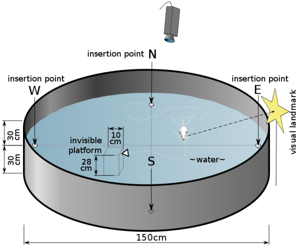
Features of associators and Hebbian learning

- Pattern completion and generalization, recall from partial input, overlap between input and trained pattern (recognition of noisy numbers)
- Prototypes and extraction of central tendencies, training on many similar but not equivalent examples (individual face, many common features in all faces)
- Graceful degradation and fault tolerance (loss of synapses or whole neurons)

Morris Water Maze - spatial memory

- i) mice training ii) Chemical blocking of LTP by AP5 impair spatial learning, keep control group iii) AP5-treated mice significantly impaired
- i) slices of the hippocampus were taken from both groups ii) LTP was easily induced in controls, but could not be induced in the brains of APV-treated rats
- Alzheimer's disease → cognitive decline seen in individuals with AD may result from impaired LTP ??

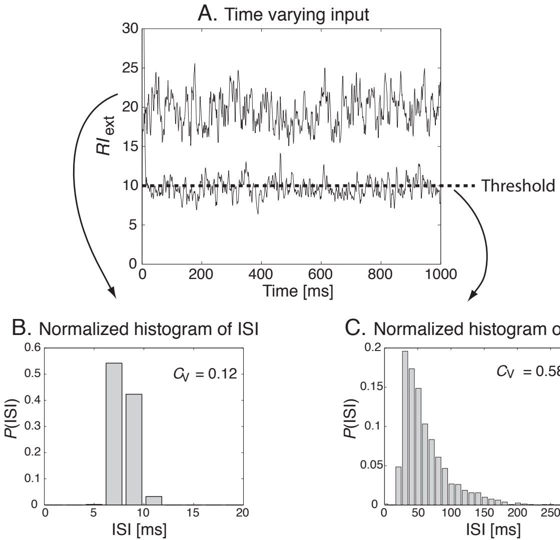




The LIF-neuron noise simulation I

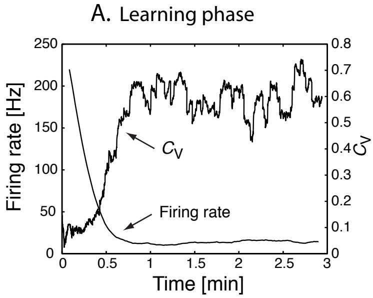
- real neuron with 5000 presynaptic neuron
- 10 % simulation $\rightarrow$ 500 Poisson-distributed spike trains with refractory corrections
- mean firing rate = 20 Hz, after correction 19.3 Hz, refractory constant 2 ms.
- each presynaptic spike $\rightarrow$ EPSP in form of α function
- $\omega = 0.5 \rightarrow$ regular firing, $C_V = 0.12$, average rate 118 Hz.
- $\omega = 0.25 \rightarrow$ irregular firing, $C_V = 0.58$, average rate 16 Hz. The $C_V >$ lower bound found in experiments

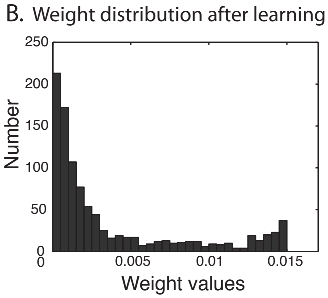
The LIF-neuron noise simulation II



Synaptic scaling and weight distributions

- IF neuron with 1000 excitatory synapses driven by presynaptic Poisson spike trains with average firing rate of 20 Hz, $\Delta w_{ij}^{\pm} = \epsilon^{\pm}(w)K\pm(t^{\mathrm{post}} - t^{\mathrm{pre}})$ applying additive rule and asymmetrical Gaussian plasticity windows
- (i) weights set to large values (ii) large frequency firing (see lec4) (iii) apply additive STDP rule with marginally stronger LTD than LTP
- increased CV, firing rate reduction, weight BINOMICAL distribution after 5 mins





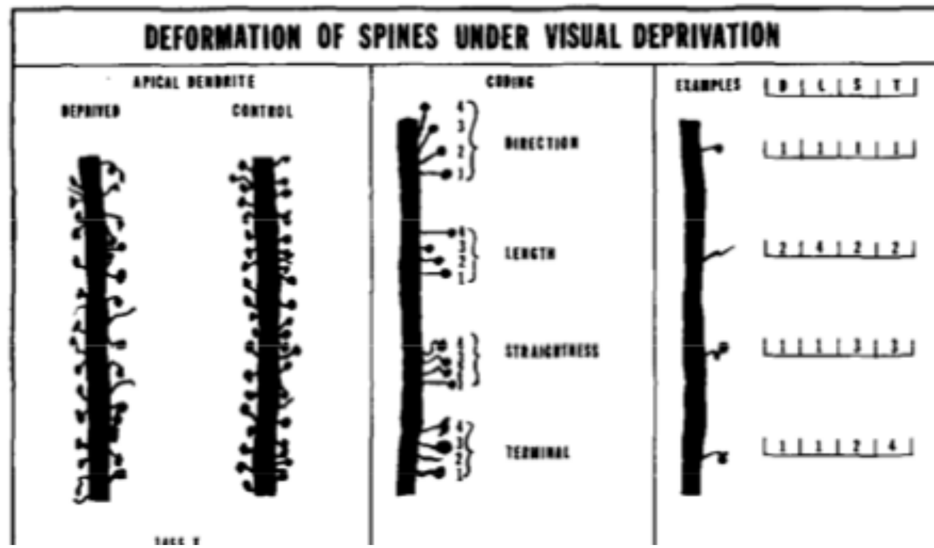
after Song, Miller and Abbott 2000

Structural plasticity

Morphological/anatomical changes that are correlated with learning

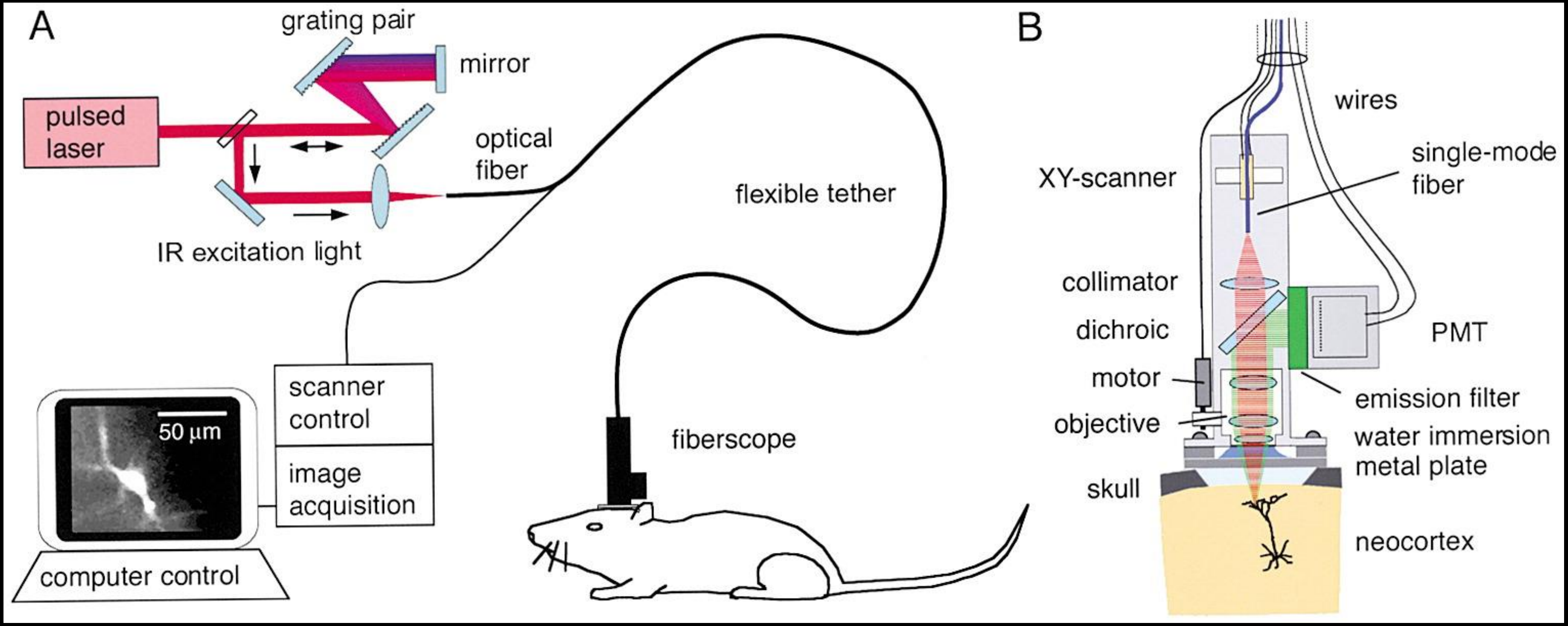
1967 – Globus & Scheibel

Sensory experience (visual deprivation) affects spine variation in rabbits

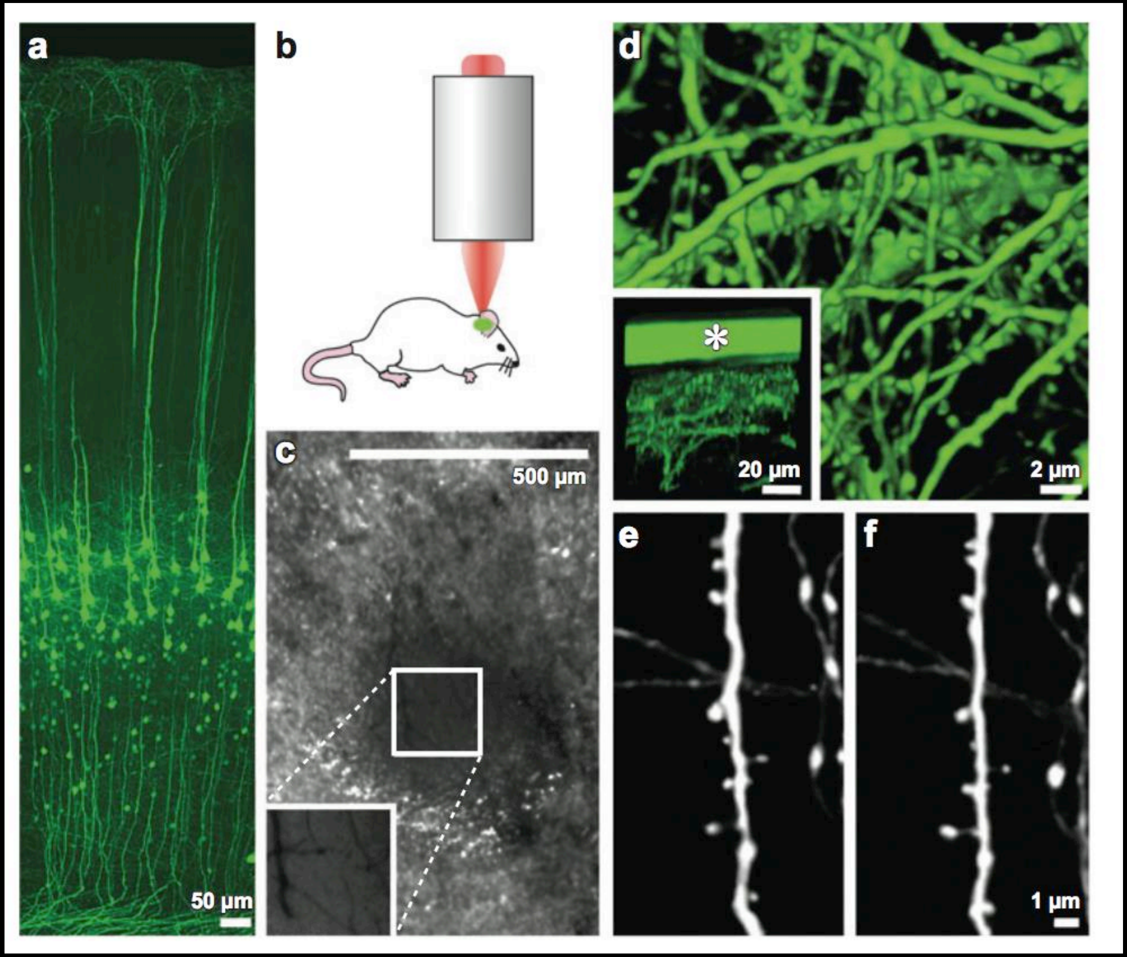


New optics + new anatomical methods

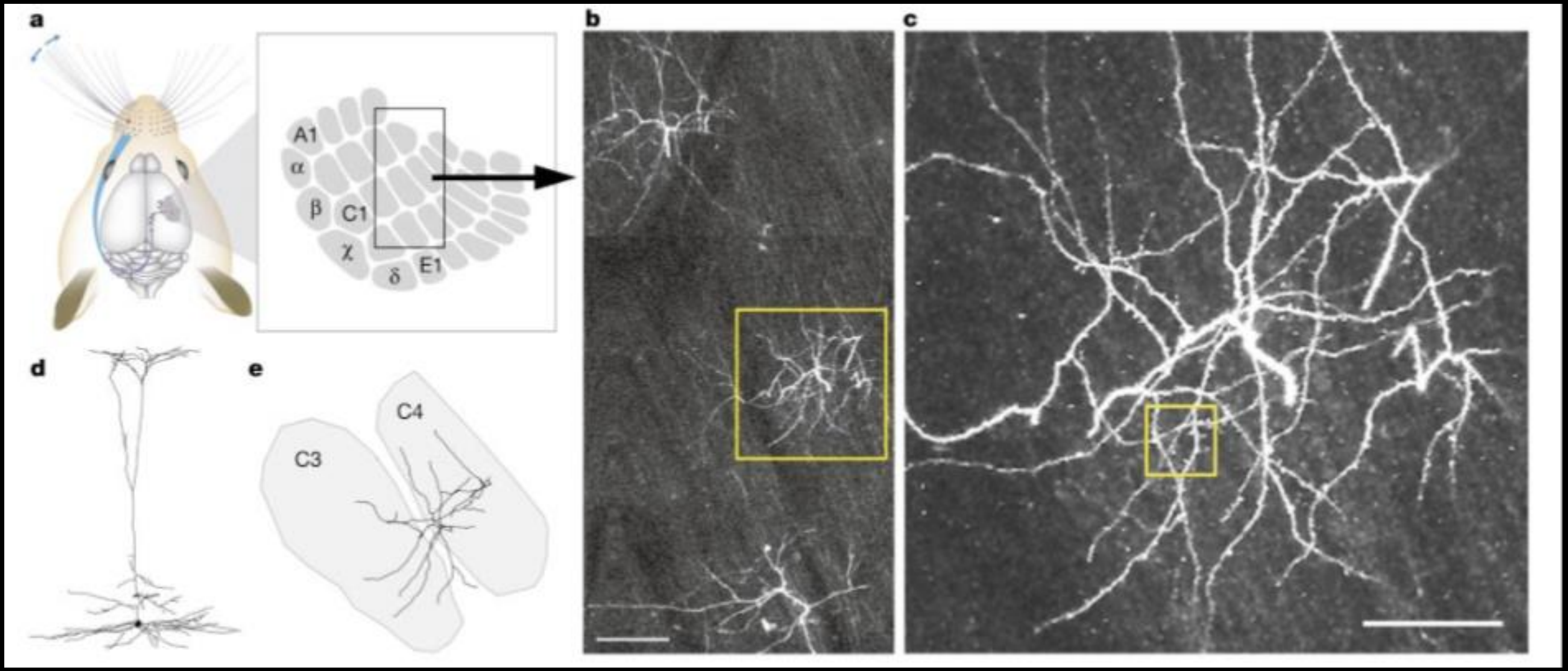
(the 2-photons microscope enable viewing spines in living brain tissue)



Recent studies: imaging dendritic spines in the *living brain*



Spines appear and disappear frequently in the adult cortex



(Trachtenberg et al. 2002)

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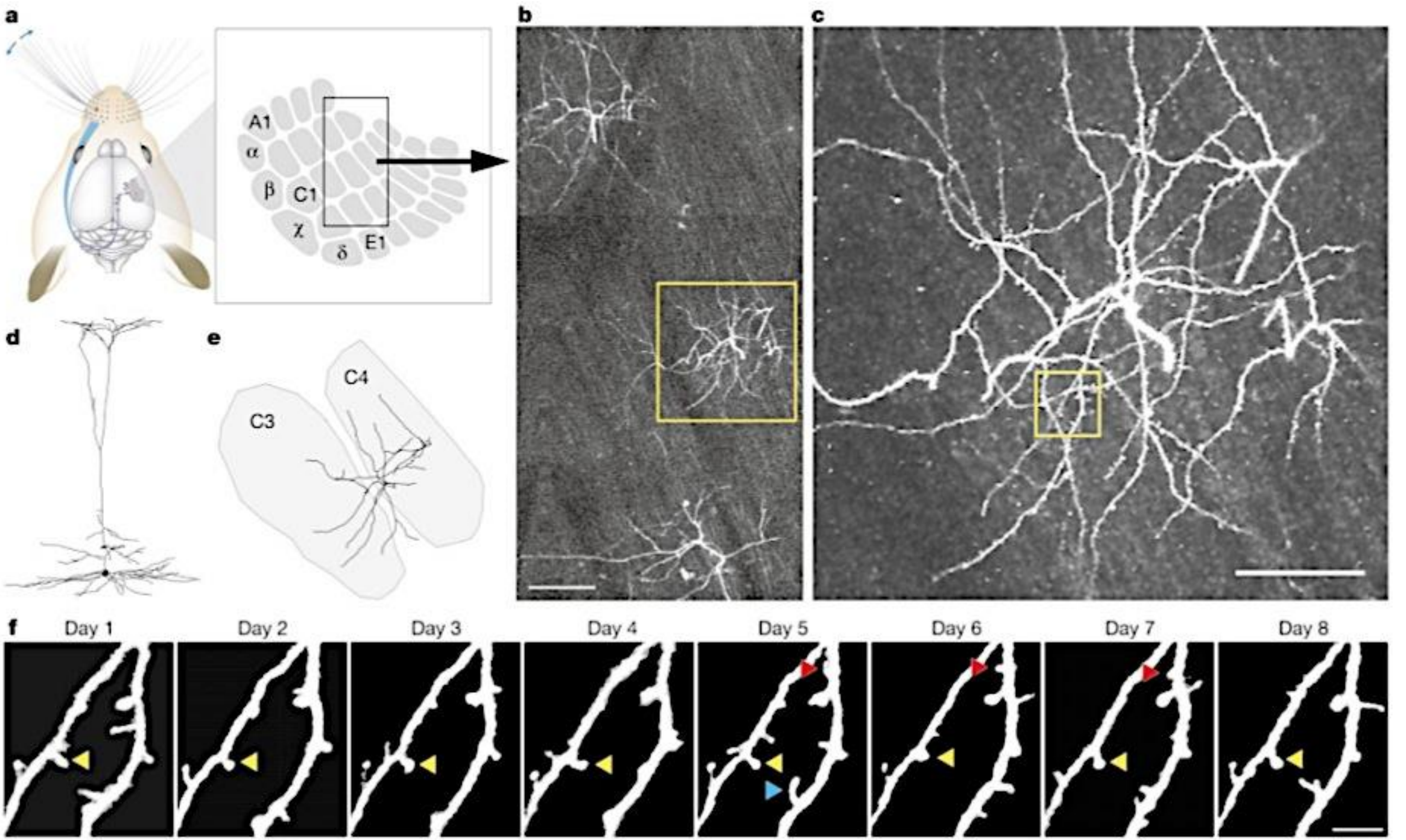
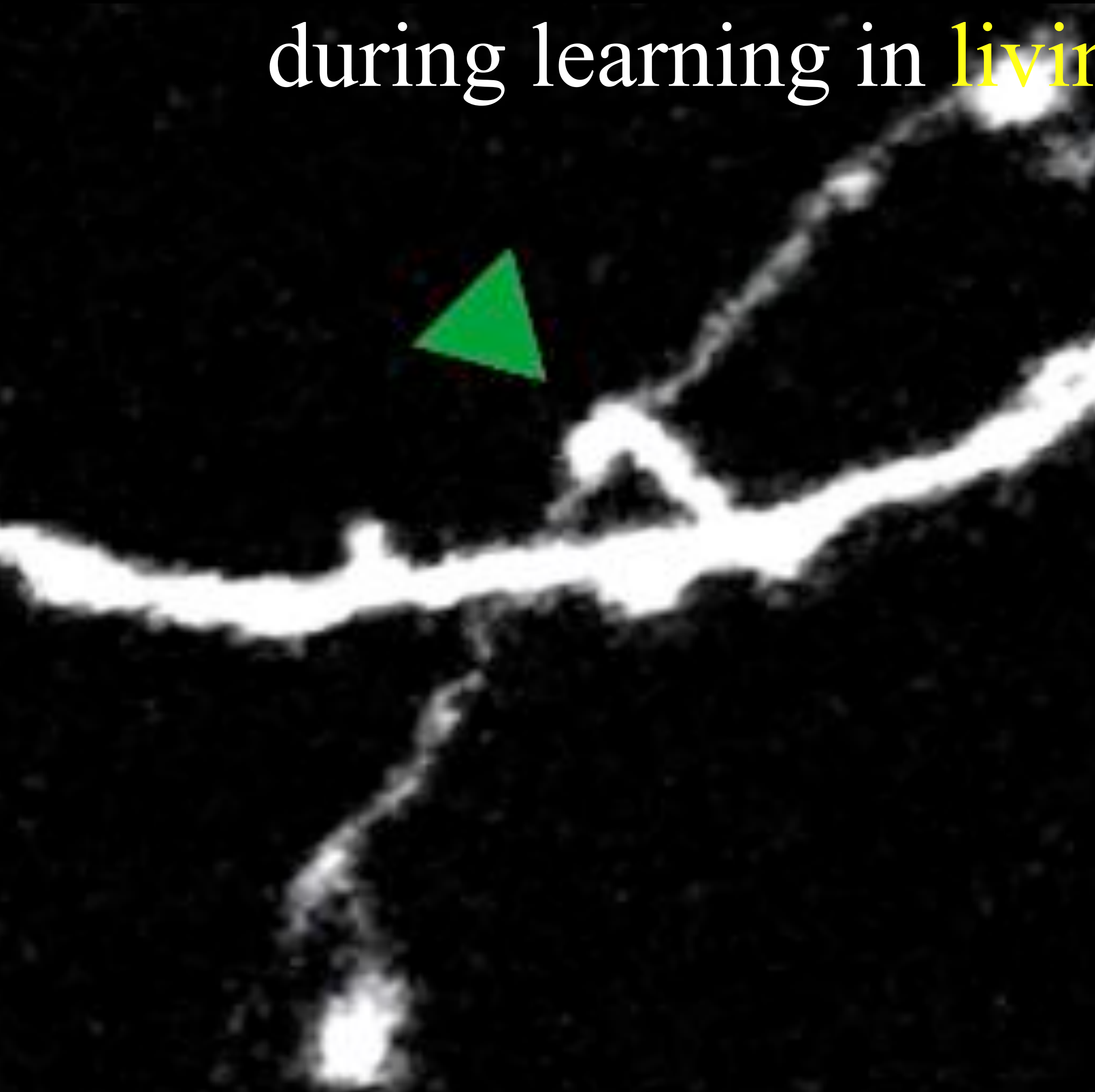


(Trachtenberg et al. 2002)

New synaptic connections are formed during learning in living brain

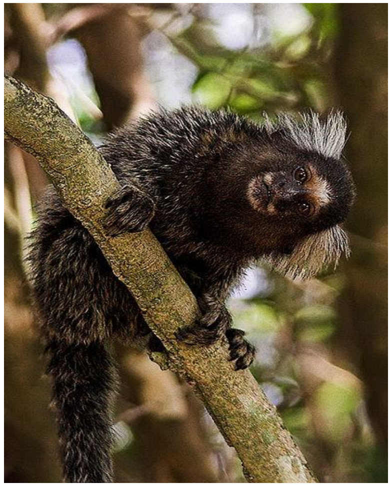


Are there new born cells (neurogenesis) in the adult Brain?

Rhesus macaque

asko Rakic found “not single heavily labelled ell with the orphological naracteristics of a euron in any brain of ny adult animal” and oncluded that “all eurons of the rhesus onkey brain are generated during prenatal and early postnatal life.” (1985)

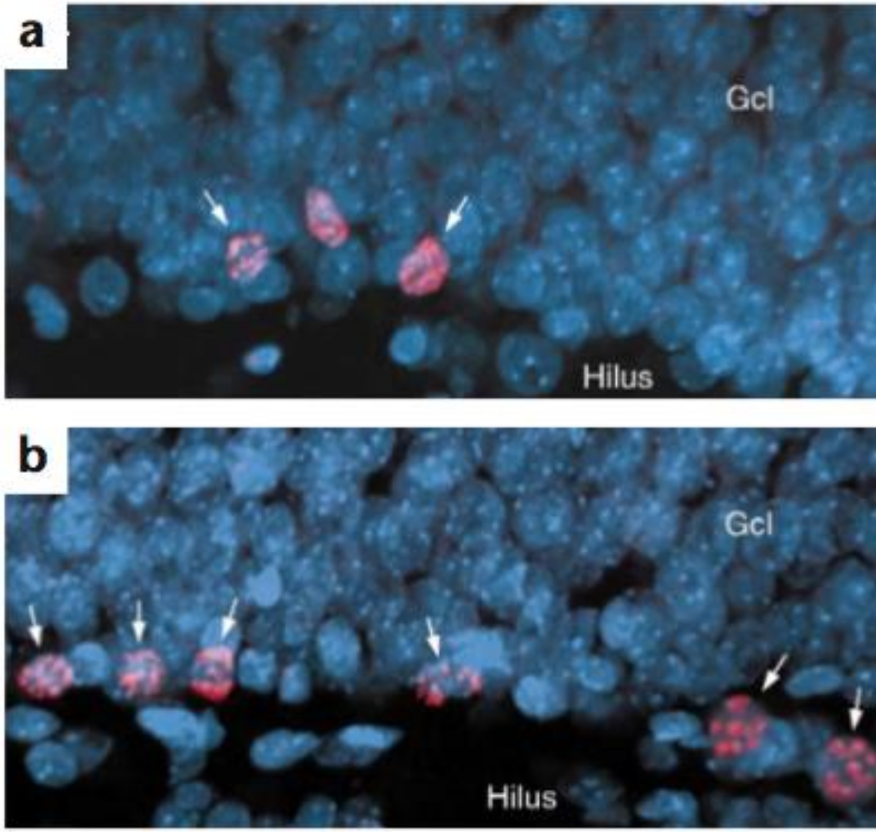
1997 –Elizabeth Gould, assistant professor of neuroscience at Princeton, and colleagues, showed neurogenesis in tree shrews

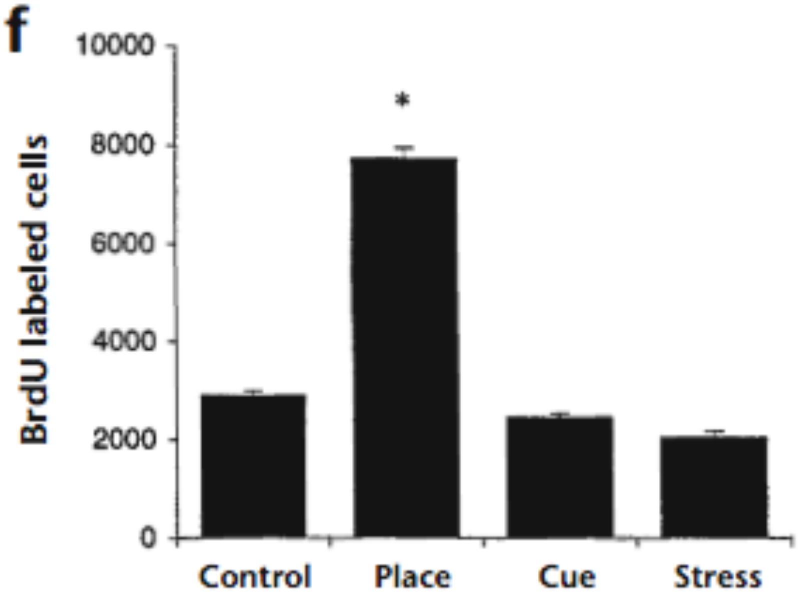


1998 – neurogenesis in marmoset monkeys (primate)

In mature mouse hippocampus

1. New born (stem) cells
2. More new-born cells following memory task in Morris Water Maze

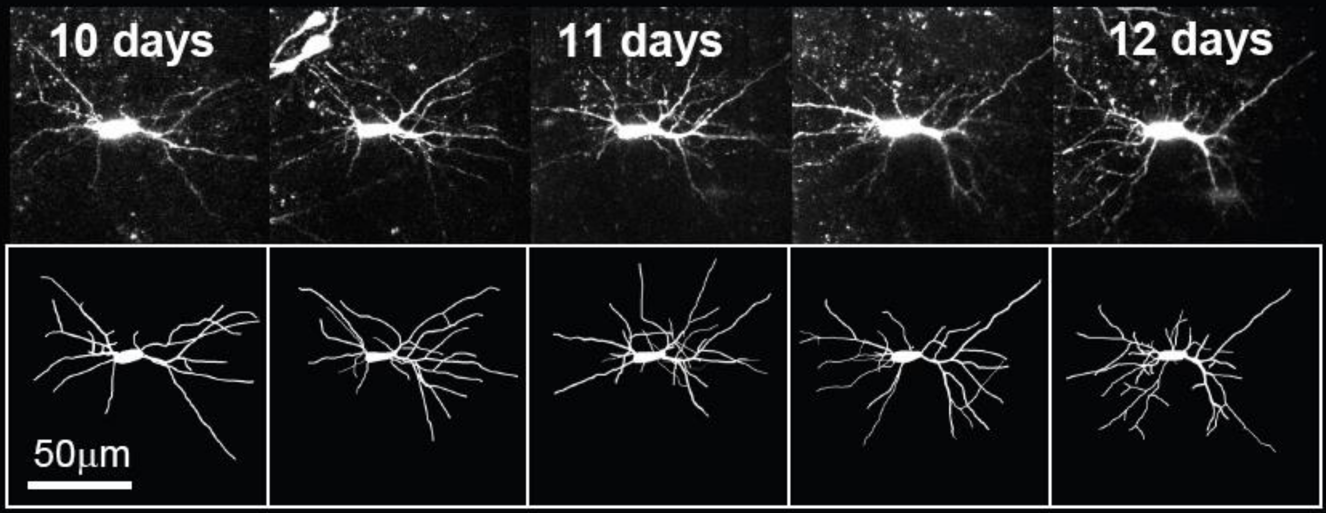




(Gould et al. 1999)

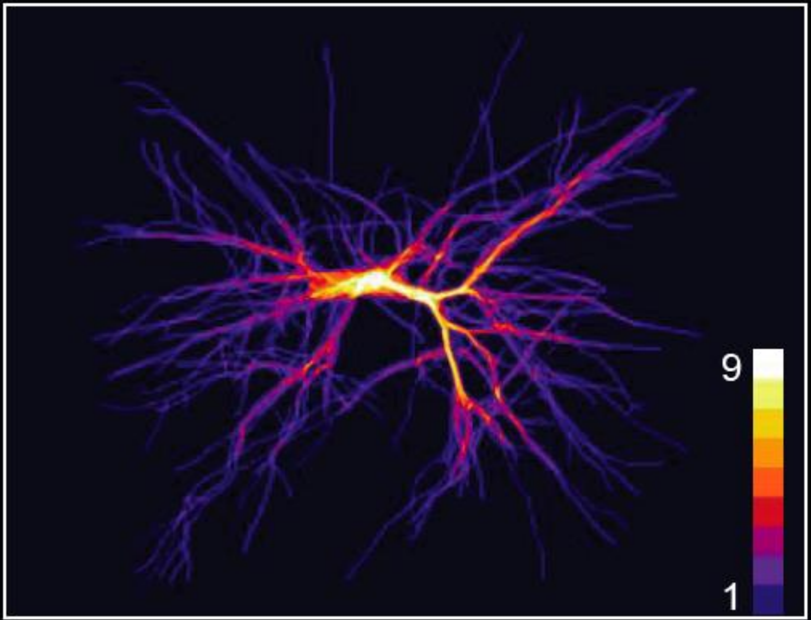
Prof. Adi Mizrahi Lab

Watching newborn (stem) cells growing in the adult brain



Top: In vivo images of a newborn neuron developing in the mouse brain over 3 days.

Right: projection image of 9 consecutive imaging sessions showing the remarkable dynamics of newborn neurons.



Neurogenesis

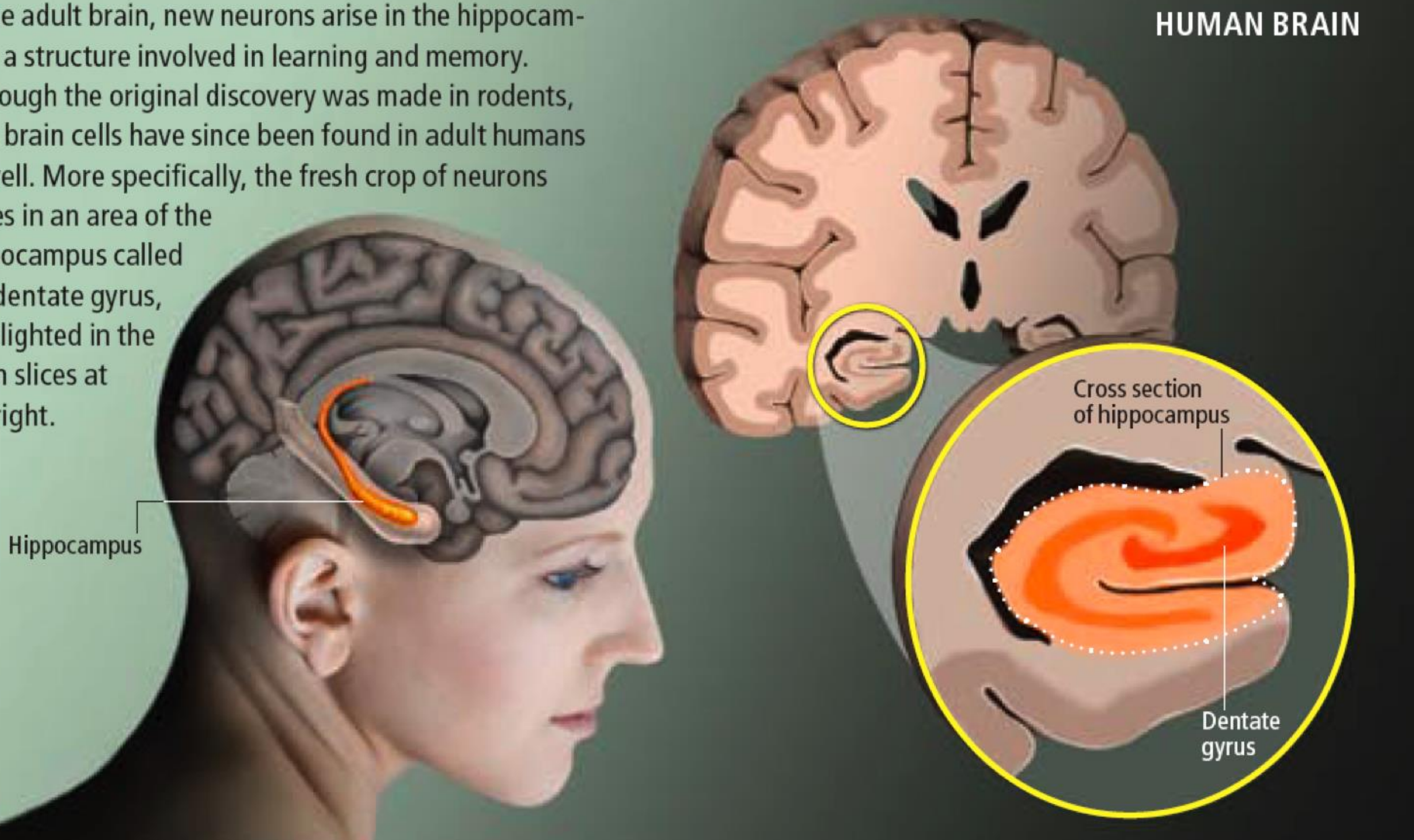
Saving NEW BRAIN CELLS

Fresh neurons arise in the adult brain every day. New research suggests that the cells ultimately help with learning complex tasks—and the more they are challenged, the more they flourish

BY TRACEY J. SHORS

WHERE NEW NEURONS FORM

In the adult brain, new neurons arise in the hippocampus, a structure involved in learning and memory. Although the original discovery was made in rodents, new brain cells have since been found in adult humans as well. More specifically, the fresh crop of neurons arises in an area of the hippocampus called the dentate gyrus, highlighted in the brain slices at the right.



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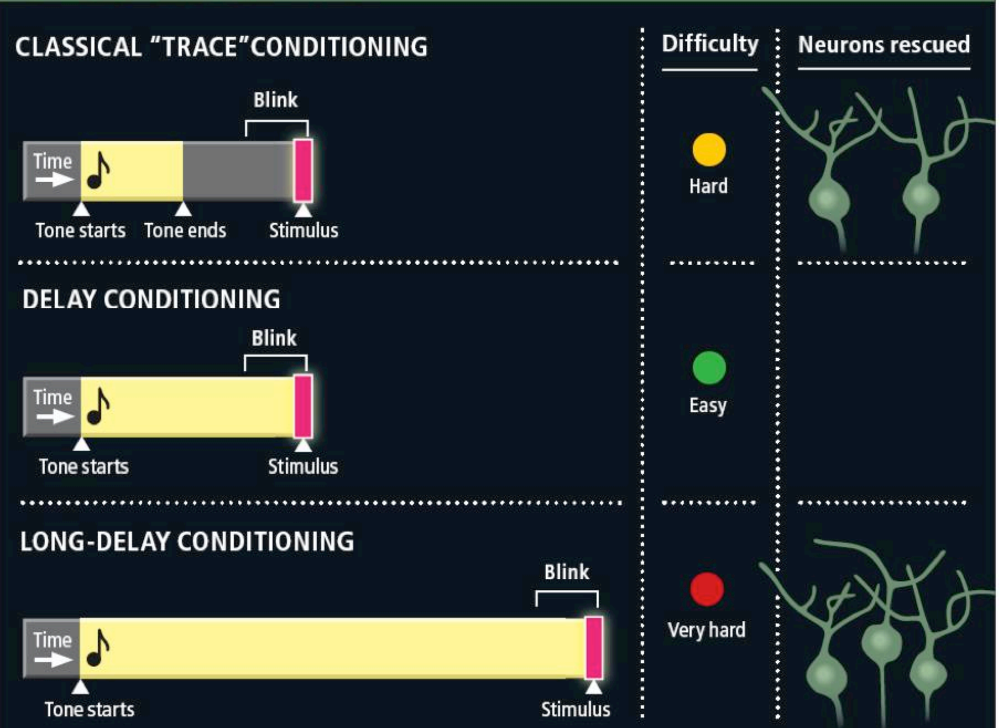
[LEARNING TESTS]

WHAT RAT STUDIES REVEALED

The author and her colleagues relied on "eyeblink conditioning" experiments to discover that working hard to learn something enhances the survival of new neurons. They began with a classical form of the experiment (*top*), in which an animal hears a tone that is followed half a second later by a stimulus that will make it blink. After several hundred trials, most animals learn to blink just before the stimulus arrives. Because the tone and the blink-inducing stimulus are separated in time, figuring out when to blink is difficult; this task rescues a large fraction of newborn neurons.

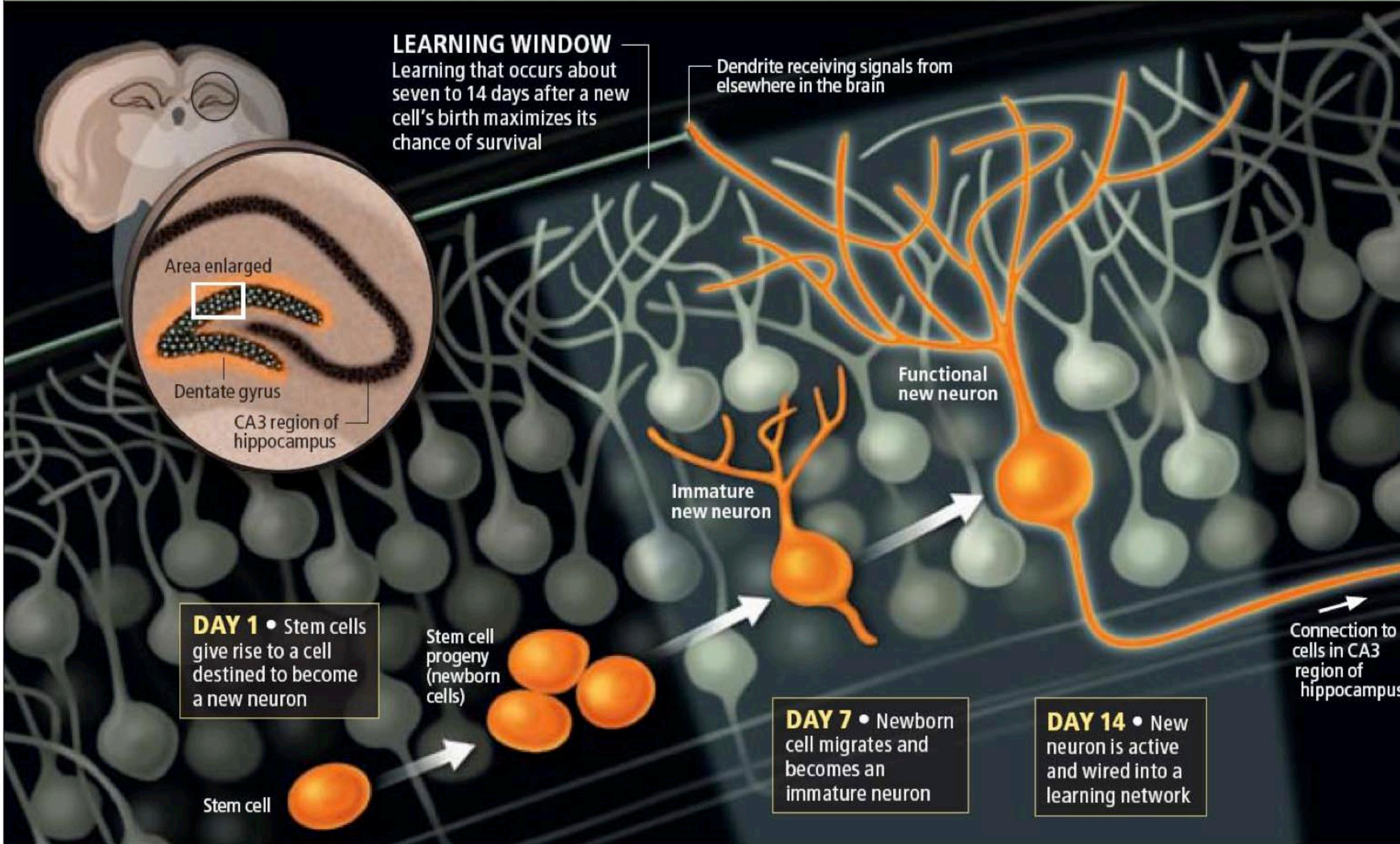
Rats master readily an easier version of the test—in which the blink stimulus overlaps with the tone (*middle*); this task does not enhance survival of new neurons. Making conditions more challenging—by having the rat wait much longer before the stimulus arrives (*bottom*)—rescues more neurons than even the classical approach does.



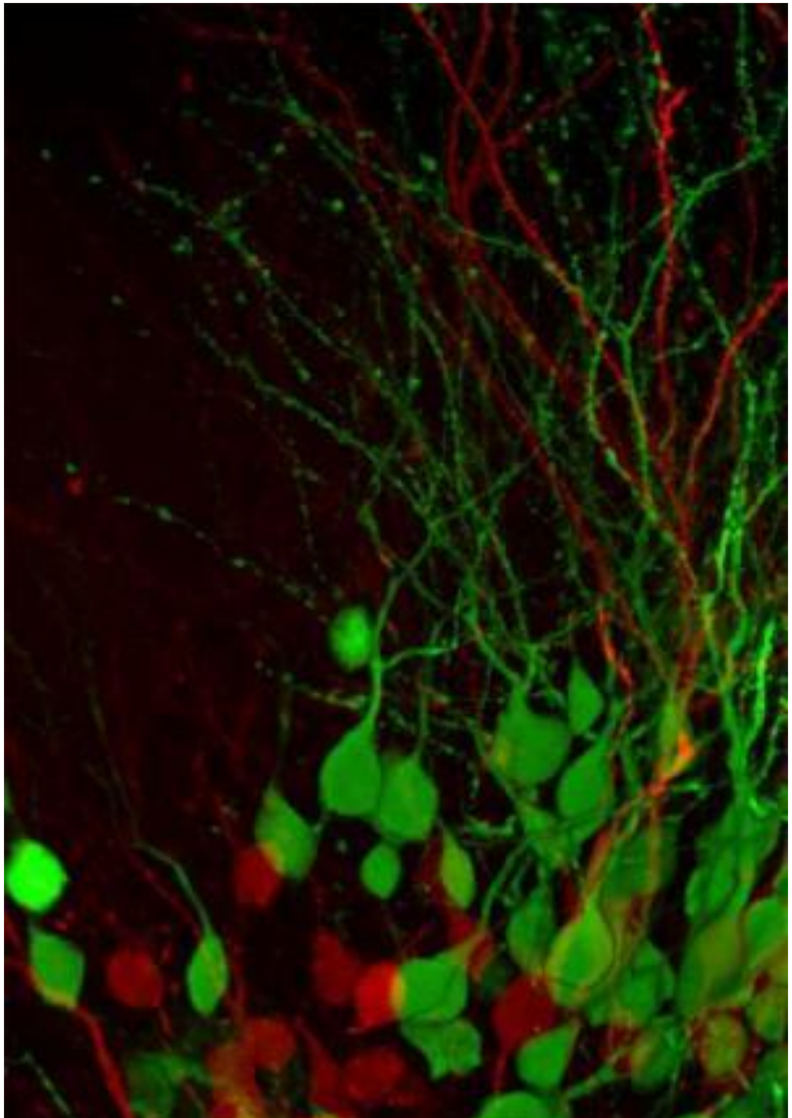
NIGEL CATTLIN *Photo Researchers, Inc.* (*rat*); JEN CHRISTIANSEN (*illustrations*)

HOW LEARNING HELPS TO SAVE NEW NEURONS

During their first week of life, newborn hippocampal cells migrate from the edge of the dentate gyrus in to a deeper area, where they mature and become wired into a network of neurons. Learning that occurs when the cells are between about one to two weeks old enhances their survival—perhaps exerting this effect by stimulating existing neurons, which in turn release signals that foster maturation of young cells. In the absence of learning during the maturation period, most new hippocampal cells will die.

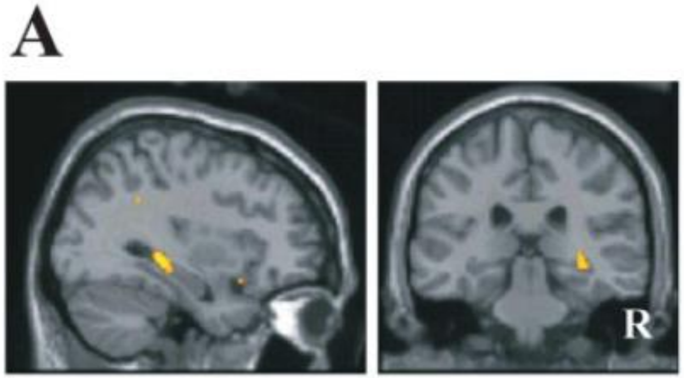


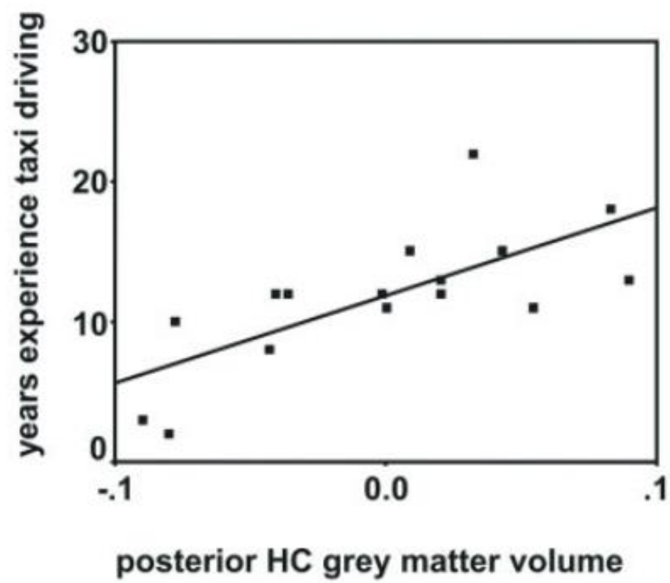
Implications: disease



Neurogenesis: provides hope for therapies for neurodegenerative diseases such as Parkinson's and Alzheimer's… as well as for rehabilitation from stroke and brain injury

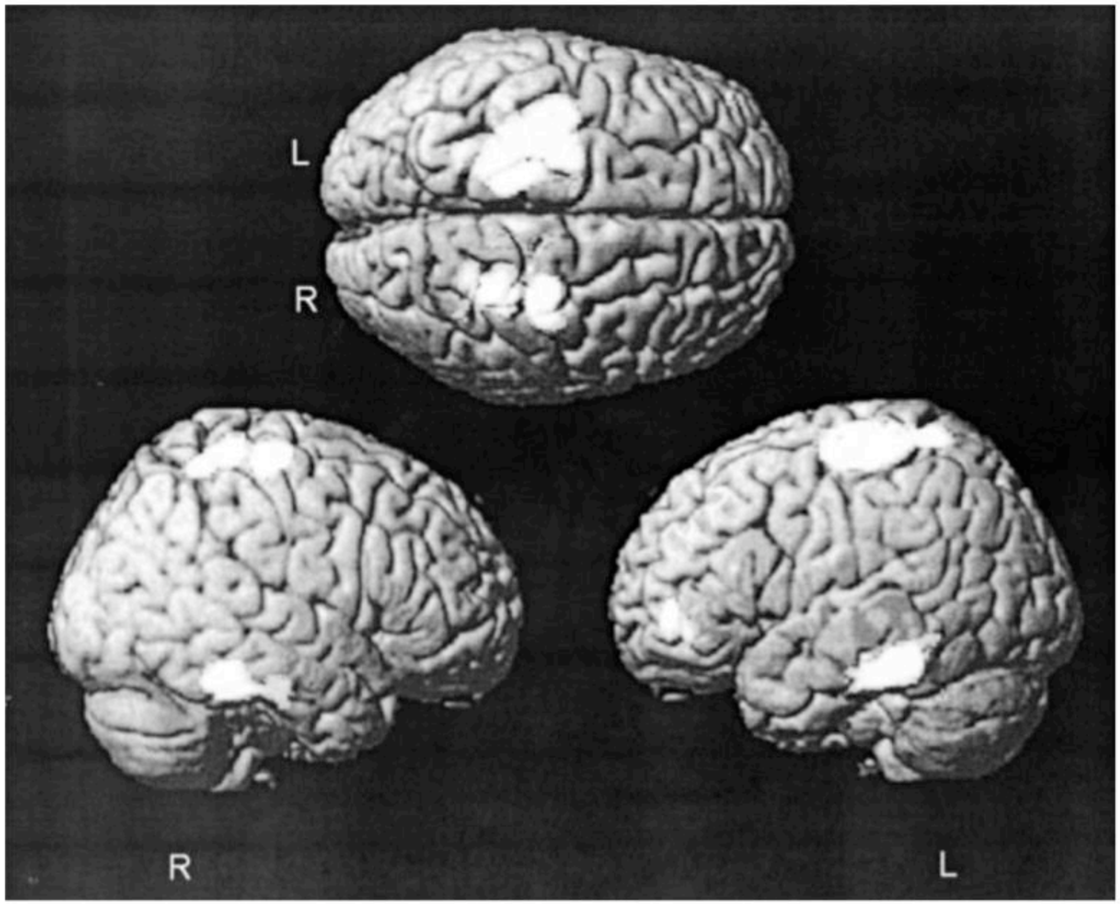
Hippocampus of London Taxi Drivers





(Maguire et al. 2006)

Whole brain structural differences between musicians and non-musicians



(Gaser & Shlaug 2003)