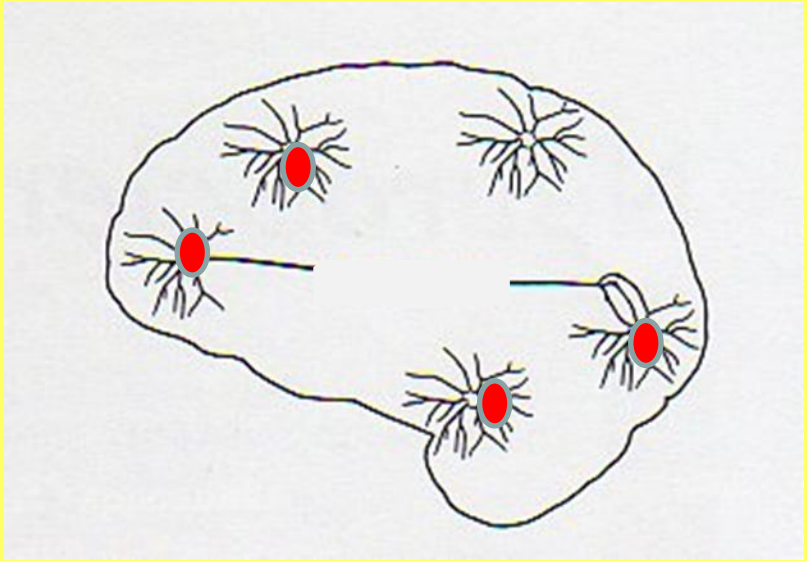
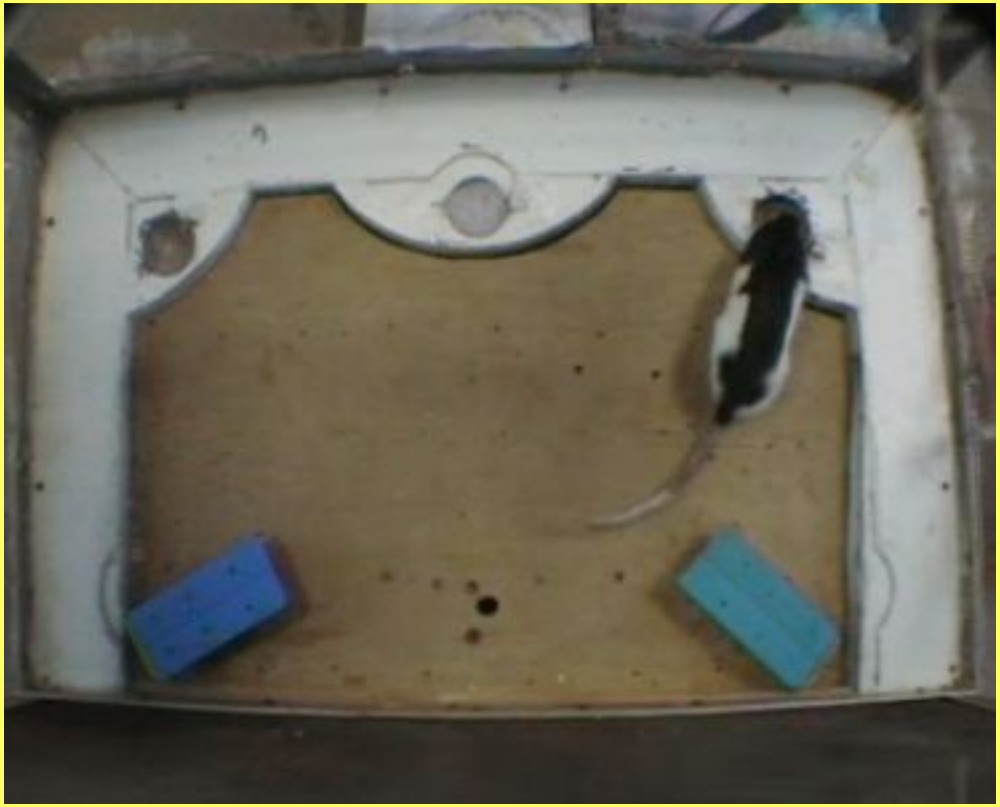
Психофизиология

Обучение



Поведенческий уровень



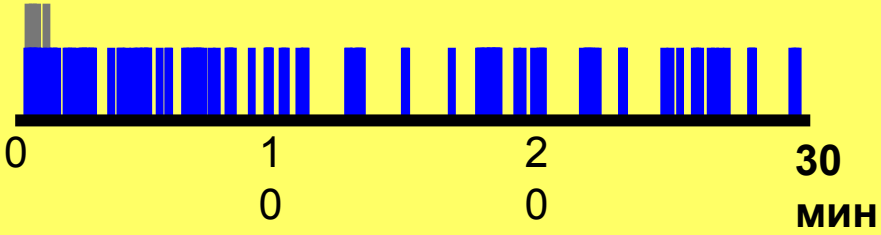
С чего начинается обучение?

- Старое НЕ РАБОТАЕТ (рассогласование)

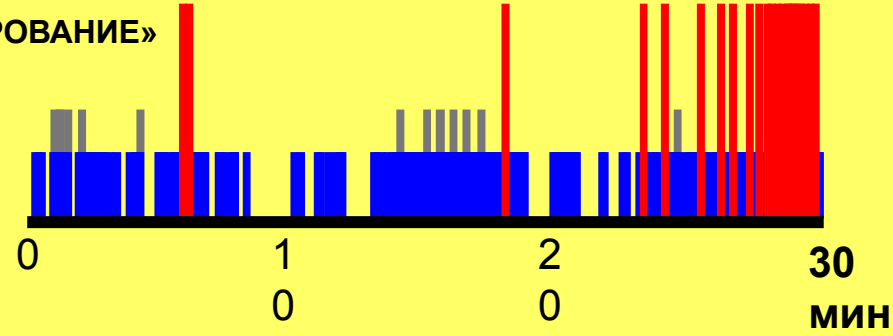
НАУЧЕНИЕ

ПОВЕДЕНЧЕСКИЙ УРОВЕНЬ

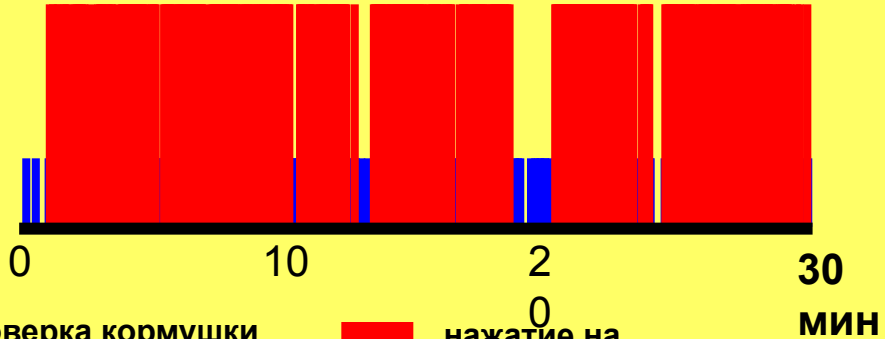
«РАССОГЛАСОВАНИЕ»



«ФОРМИРОВАНИЕ»



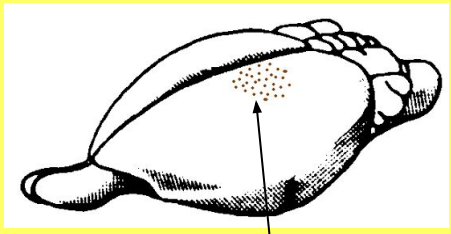
«РЕАЛИЗАЦИЯ»



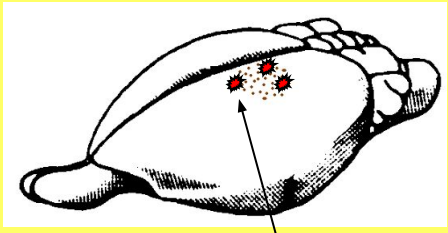
проверка кормушки

нажатие на педаль

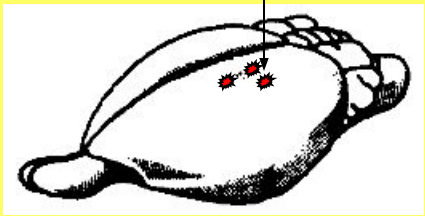
НЕЙРОНАЛЬНЫЙ УРОВЕНЬ



нейроны, экспрессирующие ген *c-fos*



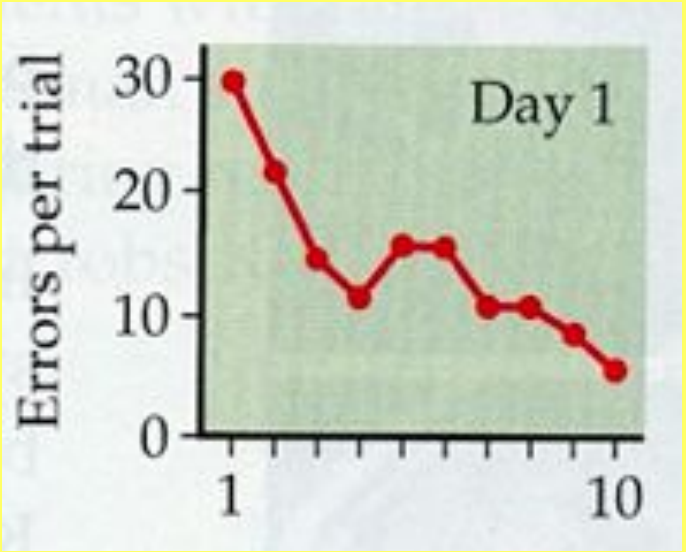
нейроны, специализированные относительно нажатия на педаль



Поведенческий уровень

- изменения поведения
  - ✔ являются следствием опыта
  - ✔ воспроизводятся, т.е. повторяются у данного индивида
  - ✔ имеют адаптивный характер
- «кривые обучения»

Кривые обучения

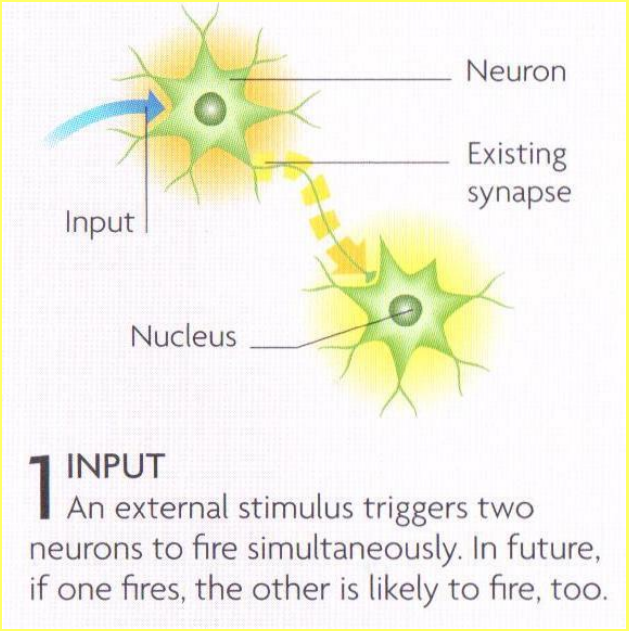


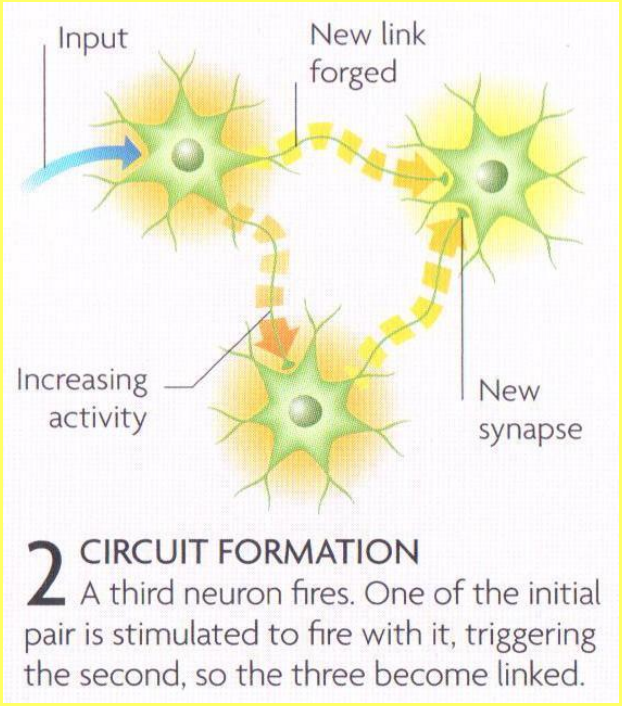
Воспоминание

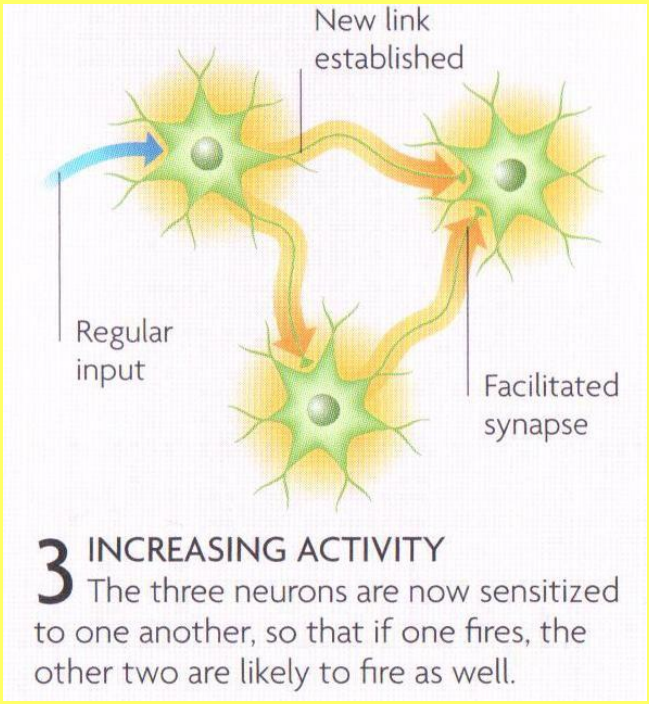
- Декарт: «Когда душа желает что-нибудь вспомнить ..., воля заставляет железу отклоняться то в одну, то в другую сторону, направляя дух в разные отделы мозга, пока он, наконец, не натолкнется в одном из них на следы, оставленные предметом, который мы хотим вспомнить. Такие следы существуют просто потому, что поры в мозгу, через которые дух проходил раньше при восприятии этого предмета, теперь более других склонны открываться, когда дух снова направляется к ним. И тогда дух легче входит в эти поры...»

Связанность (функциональная и структурная)

- Правило Хебба



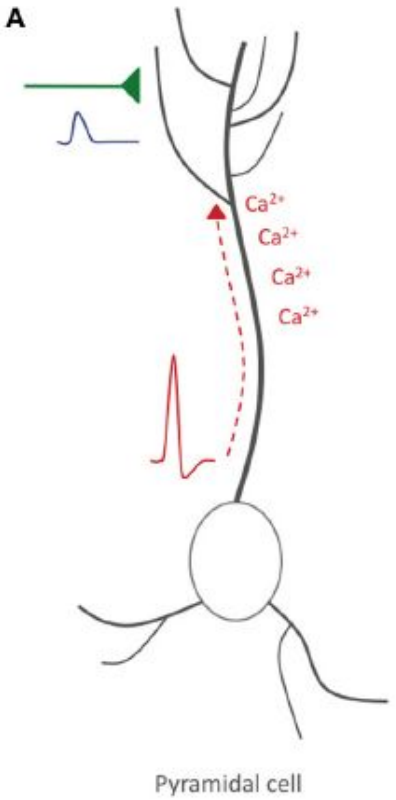




Hebb's postulate on synaptic modifications, which was formulated in 1949 in his book "*The Organization of Behavior,*" has laid the foundation for subsequent experimental work on memory storage by neuronal assemblies (Hebb, 1949):

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

1. Активность
2. Изменение метаболизма
3. Рост контактов



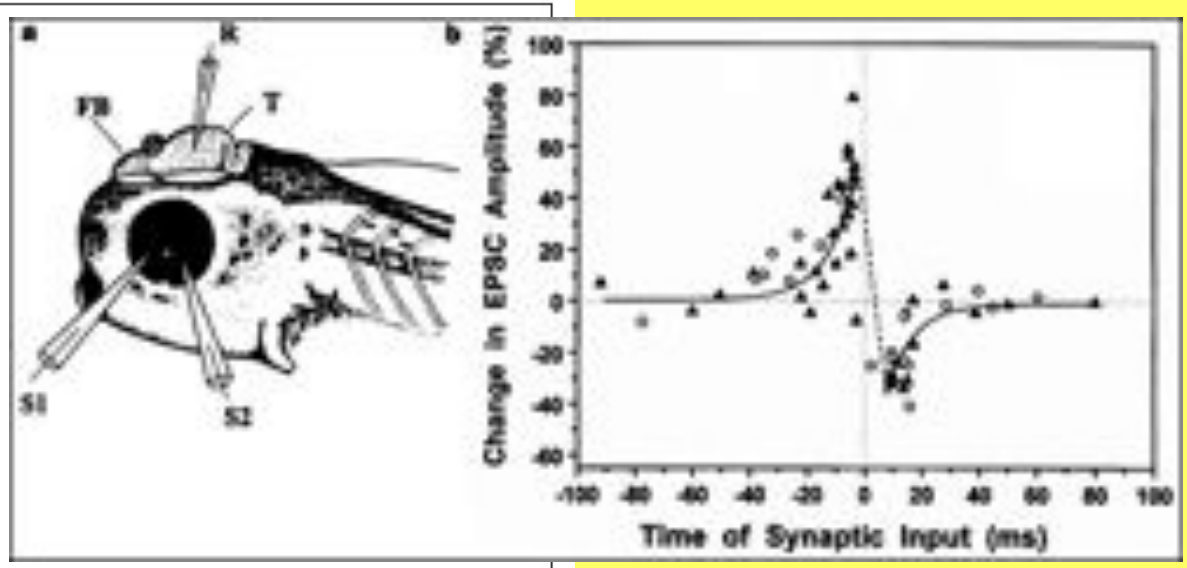


FIGURE 3 | Hebbian-style and non-Hebbian STDP. (A) Hebbian STDP in hippocampal and neocortical pyramidal cells. Action potentials are elicited near the soma and backpropagate into the dendrite, where the accompanying depolarization leads to calcium influx (red). The timing relative to incoming EPSPs (blue) evoked at glutamatergic synaptic inputs (green) determines whether LTP or LTD is induced.

The critical window for spike-timing dependent synaptic potentiation and depression. In vivo whole-cell recording from Xenopus tadpole retinotectal neurons. Synaptic inputs activated repetitively within 20 ms before spiking of the tectal neuron become potentiated, whereas inputs activated within 20 ms after spiking become depressed. (From Zhang et al., Nature, 395: 37-44, 1998)

Пластичность между нейронами зависит от очередности их активности

Piochon et al., 2013

INTRODUCTION

Hebb's postulate on synaptic modifications, which was formulated in 1949 in his book "*The Organization of Behavior,*" has laid the foundation for subsequent experimental work on memory storage by neuronal assemblies (Hebb, 1949):

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

A more popular version of this rule—assigned to neurobiologist Carla Shatz—says "neurons that fire together wire together." The discovery of long-term potentiation (LTP) in 1973 demonstrated that synaptic connections can indeed be strengthened in a use-dependent way, thus reflecting a key prediction of the Hebb postulate (Bliss and Lømo, 1973). LTP is now widely regarded as a potentiation mechanism involved in circuit development and adult learning. However, for more than 20 years, researchers did not dissociate the relative roles of synaptic input and action potential generation in the postsynaptic neuron in the induction of LTP (see Linden, 1999). The implication inherent to Hebb's postulate is that excitatory synapses that contribute to the initiation of action potentials in the target cell will be strengthened. This component of the Hebb rule was demonstrated by spike-timing-dependent plasticity (STDP) studies, in which the relative timing of presynaptic activity and postsynaptic spike firing determines the direction and amplitude of synaptic weight change. Excitatory postsynaptic potentials (EPSPs) preceding postsynaptic action potentials within a time window of up to tens of milliseconds cause LTP, while activation in the reverse order induces long-term depression (LTD) (Markram et al., 1997; Bi and Poo, 1998; Debanne et al., 1998). While Hebb did not explicitly discuss the weakening of synapses in his hypothesis, LTD was suggested in a complementary statement by Stent (Stent, 1973) based on studies by Hubel and Wiesel examining plasticity during the critical period in visual cortex (Hubel and Wiesel, 1965; Wiesel and Hubel, 1965). STDP has generated immense interest as a plasticity mechanism that not only obeys Hebb's rule, but also reconciled LTP

Piochon et al., 2013

Нейронный уровень

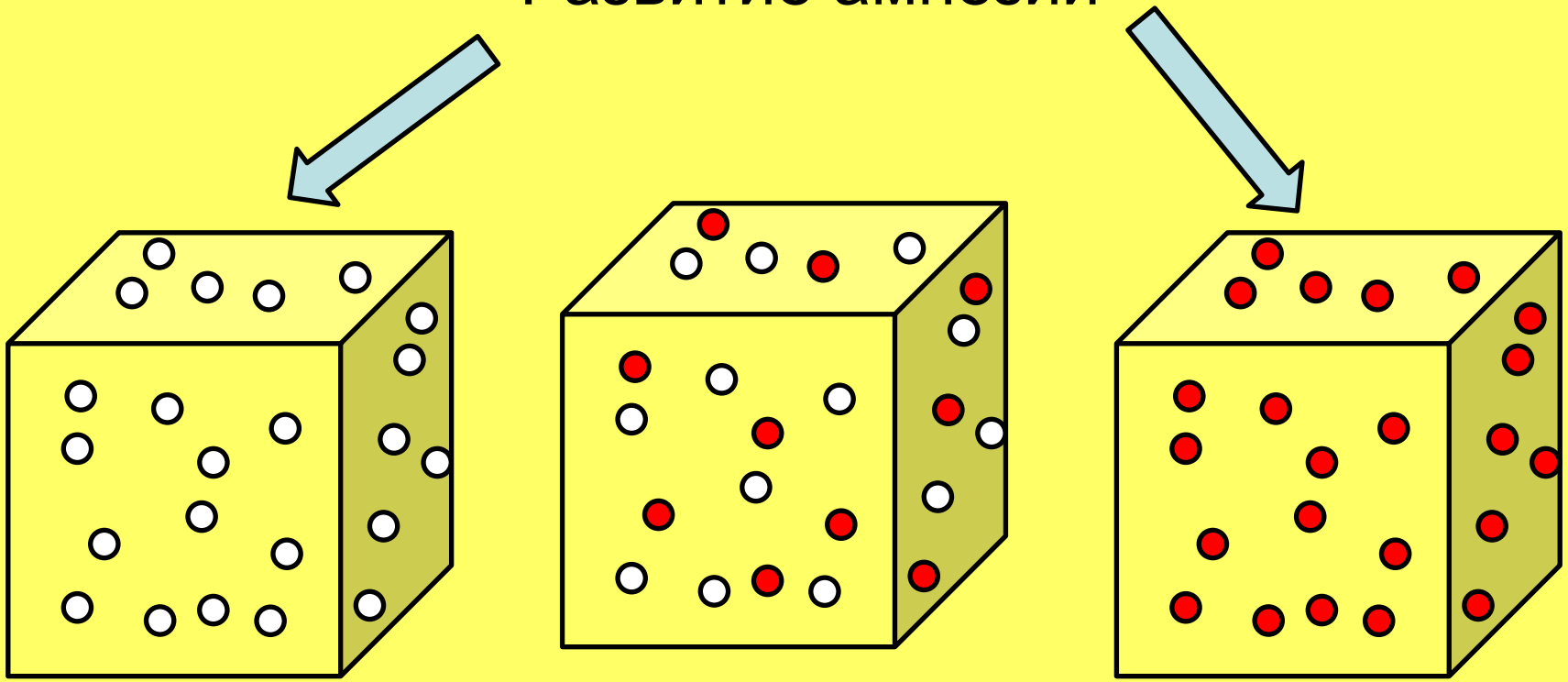
- травмы
- судороги

Развитие амнезии

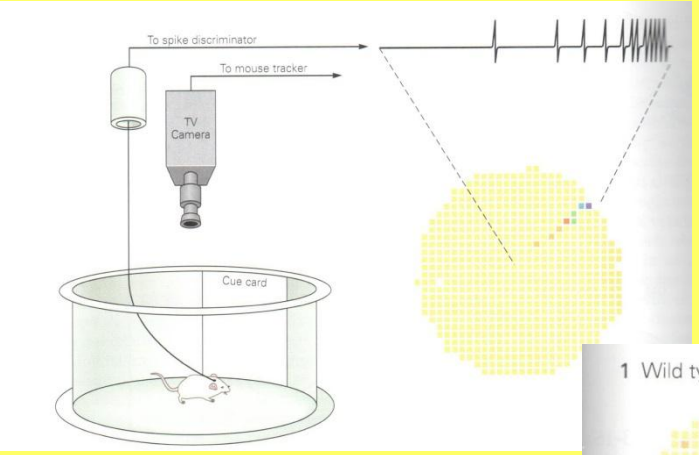
Нейронный уровень

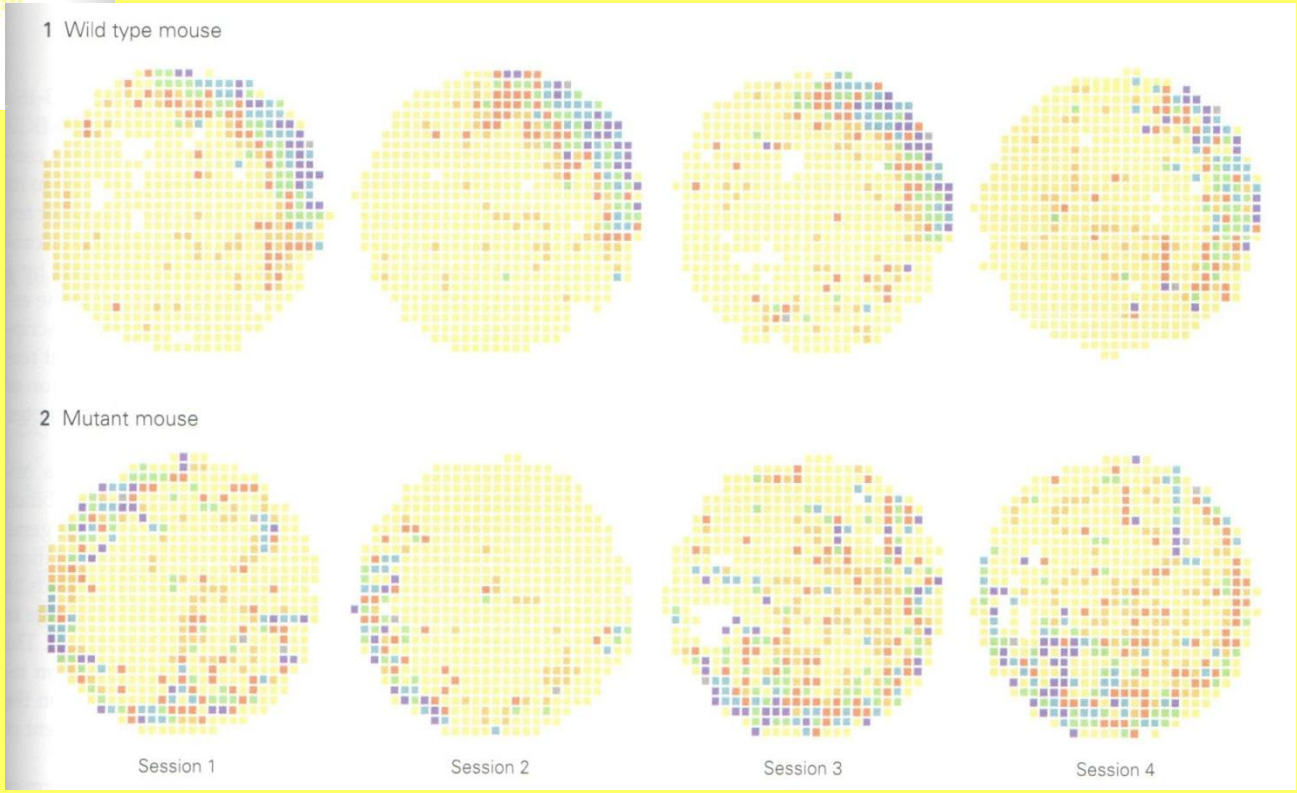
- травмы
- судороги

Развитие амнезии



Мутантные мыши не выучивают пространство





J Comp Physiol Psychol. 1949 Feb;42(1):32-44.

The retroactive effect of electroshock on learning.

DUNCAN CP.

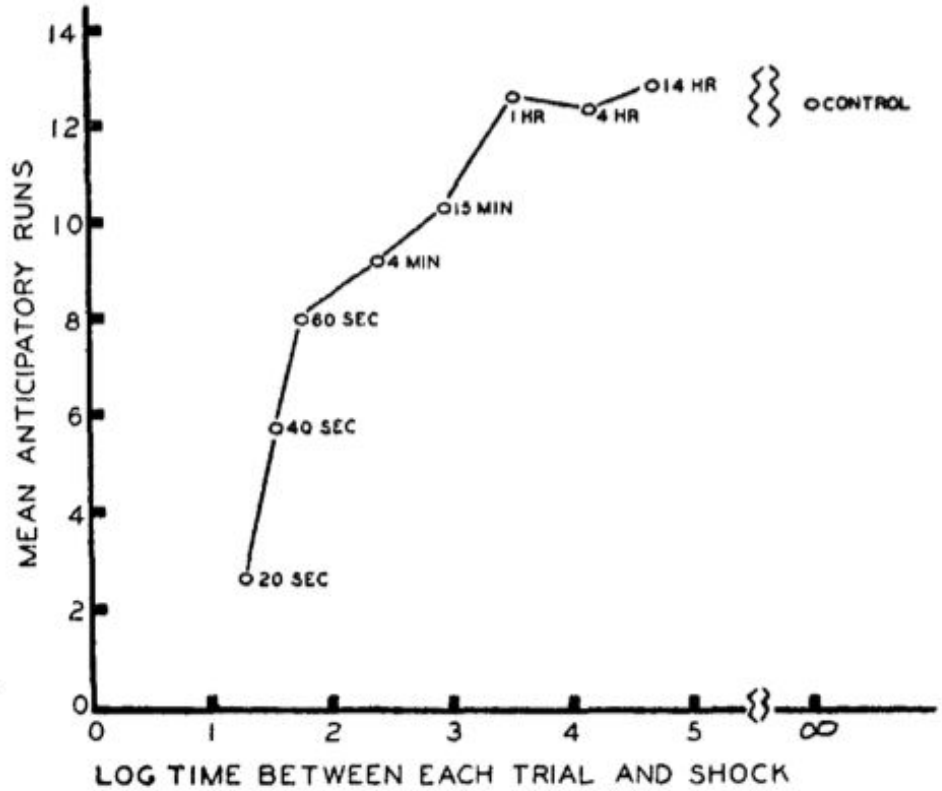


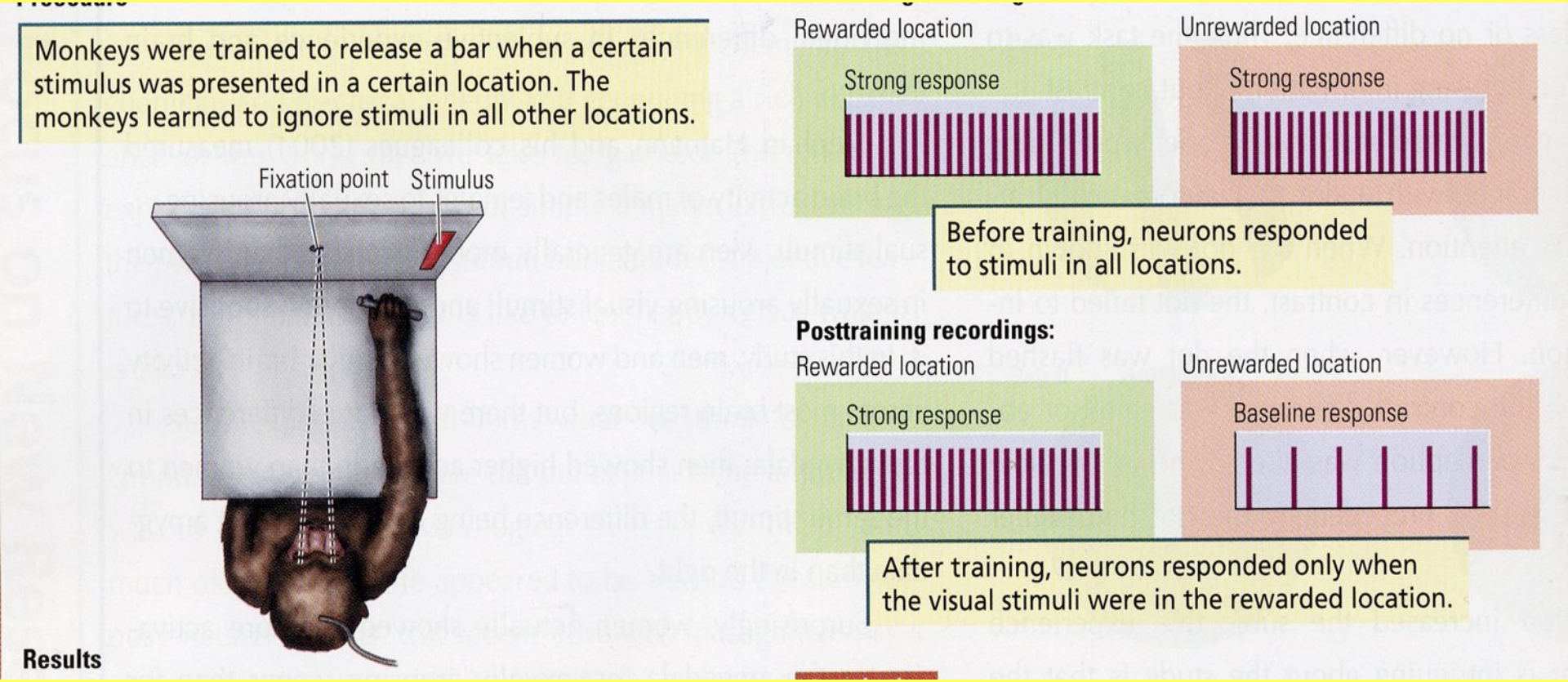
FIGURE 1. MEAN ANTICIPATORY RUNS FOR ALL 18 TRIALS AS A FUNCTION OF THE TRIAL-ELECTROSHOCK INTERVAL EXPRESSED IN LOGS

Different points on the curve represent different groups

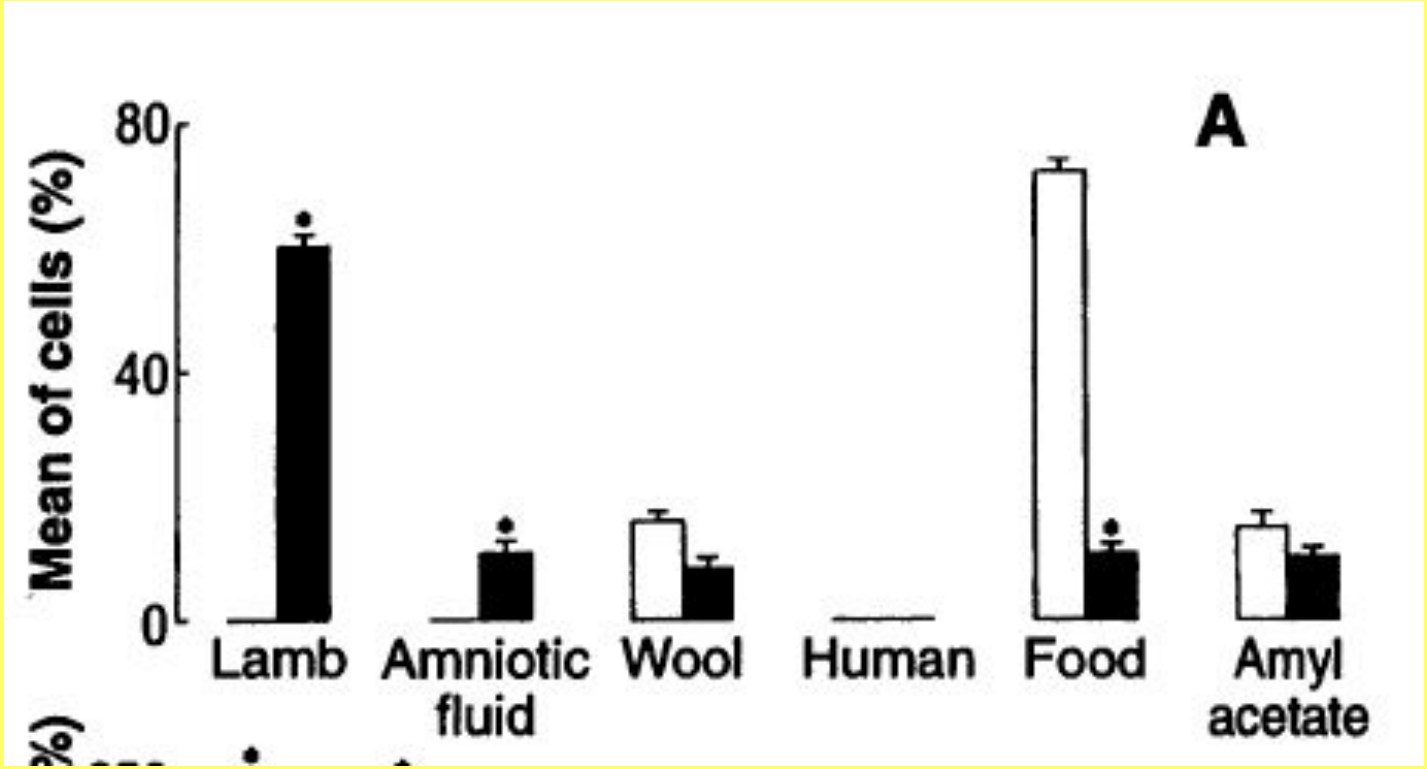
Память у экспериментальных животных нарушается при судорогах в те же временные интервалы, что и у людей

Нейронный уровень

- изменение активности нейронов (ПД)



Формирование нового поведения



Kendrick et al., 1992 (Science)

Как осуществляется научение

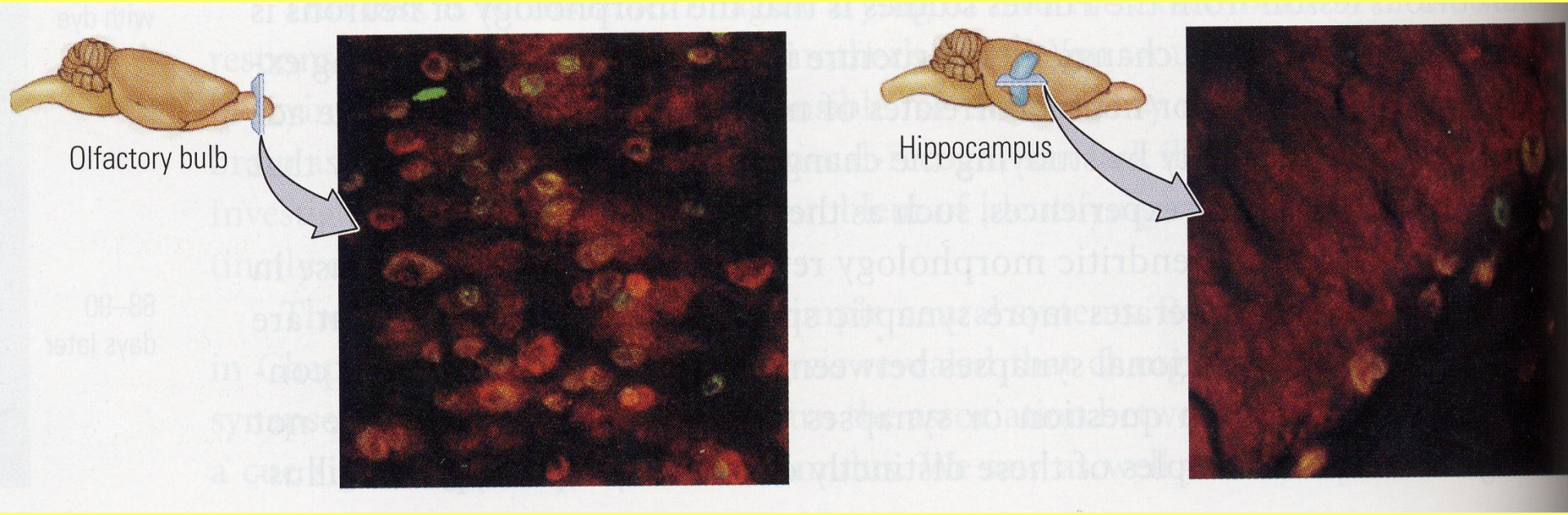
- нейроны, импульсная активность которых связана с новым элементом

откуда берутся эти нейроны? 4 варианта

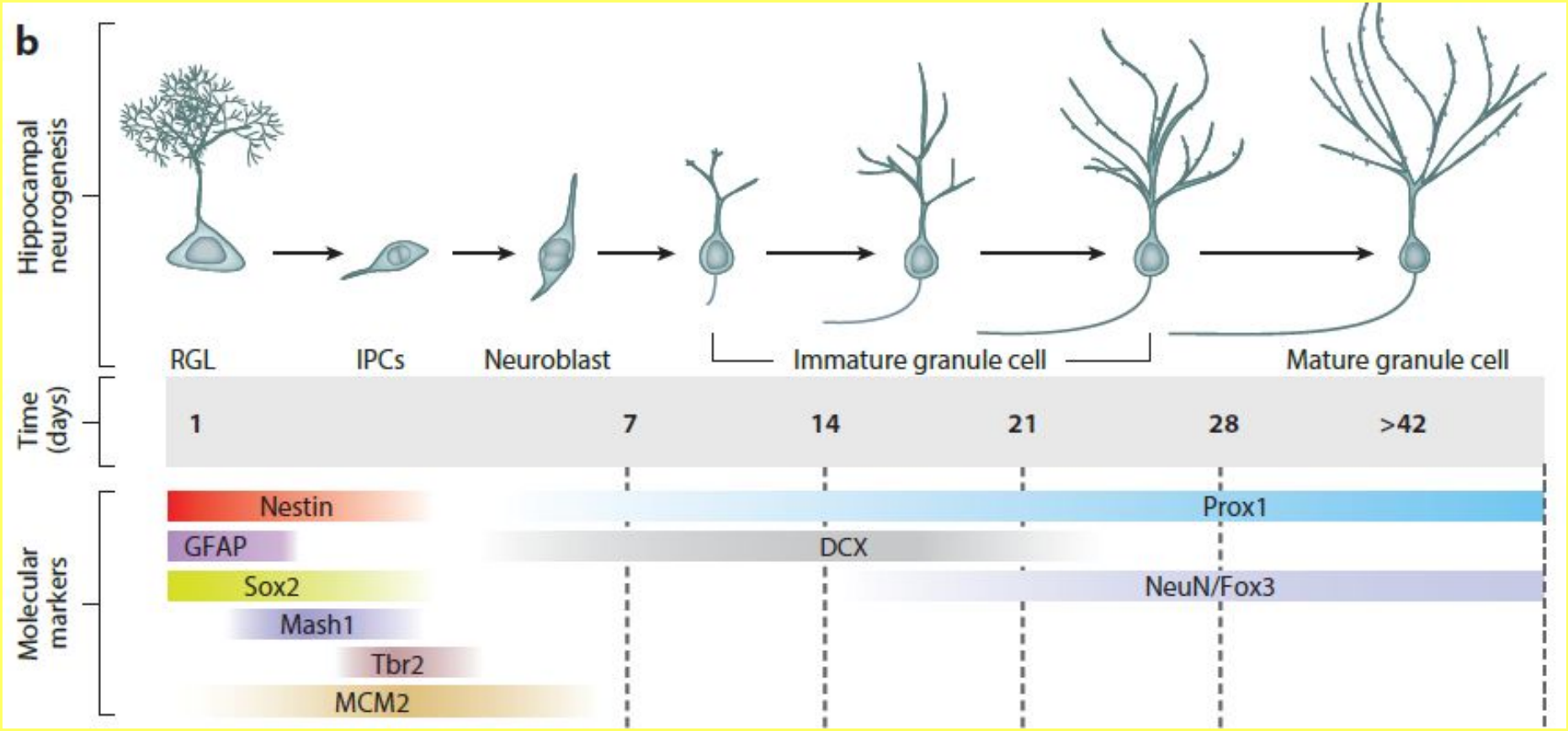
«Нейронные источники» обучения

- «молчащие» нейроны
- «новые» нейроны
- «изменение» специализации нейрона
- «уточнение» специализации нейрона

Нейрогенез



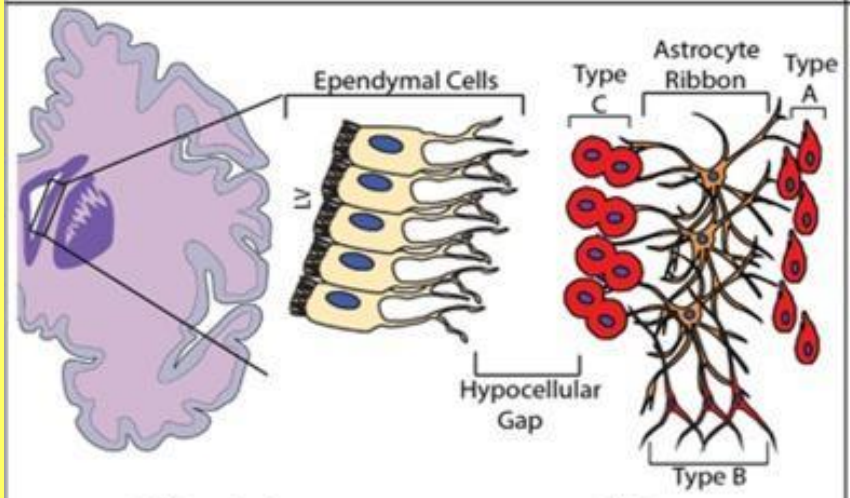
Нейрогенез



Christian et al 2014

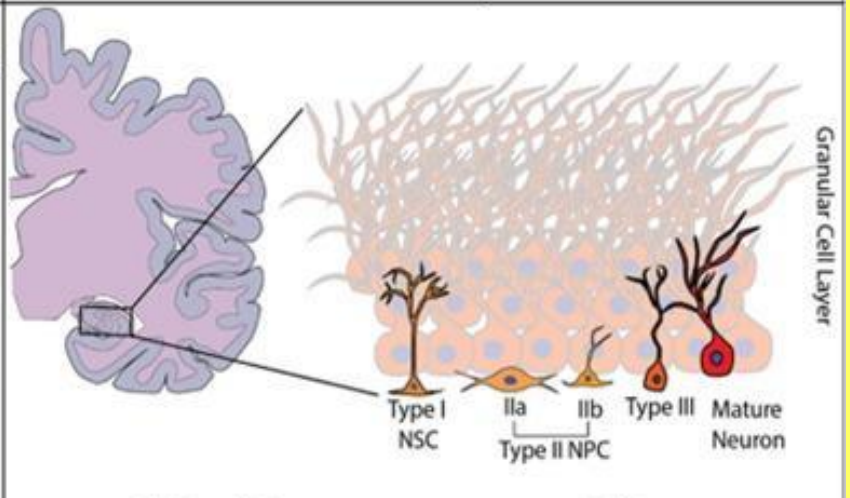
Нейрогенез

Subventricular Zone



Cell Population	Cell Fate
Type B NSC • Nestin⁺GFAP⁺Ki67⁺	• Quiescent neural stem cell
Type C Proliferating Neuroblasts • DCX⁺GFAP⁺Ki67⁺ • Nestin⁺PCNA⁺ • DCX⁺Tuj1⁺PSA-NCAM⁺	• Unknown fate or function of proliferating cells in the human SVZ
Type A Migrating Neuroblasts • PCNA⁺ • PSA-NCAM⁺ • Ki67⁺NeuroD1⁺ • DCX⁺Tuj1⁺PSA-NCAM⁺	• Migration away from SVZ in singlets or pairs. Reaching olfactory bulb?[6] • Migration to striatum[46]

Dentate Gyrus



Cell Population	Cell Fate
Type I NSC • Nestin⁺GFAP⁺Ki67⁺	• Quiescent neural stem cell
Type IIa NPC • Nestin⁺GFAP⁻Ki67⁺	• Proliferation in the SGL
Type IIb NPC • DCX⁺PSA-NCAM⁺	• Committed to neuronal fate
Type III Neuroblasts • DCX⁺PSA-NCAM⁺NeuN⁺	• Movement into the GCL, extension of processes into the molecular layer
Mature Neuron • NeuN⁺MAP2⁺	• Synaptic integration

Tobin et al 2014

Нейрогенез

Published in final edited form as:
Biol Psychiatry. 2008 April 1; 63(7): 650–655.

New Interneurons in the Adult Neocortex: Small, Sparse, but Significant?

Heather A. Cameron and **Alexandre G. Dayer**
From the Unit on Neuroplasticity, Mood and Anxiety Disorders Program, National Institute of Mental Health, National Institutes of Health, Bethesda, MD (HAC); and Department of Adult Psychiatry, Centre Médical Universitaire (CMU), Geneva, Switzerland (AGD)

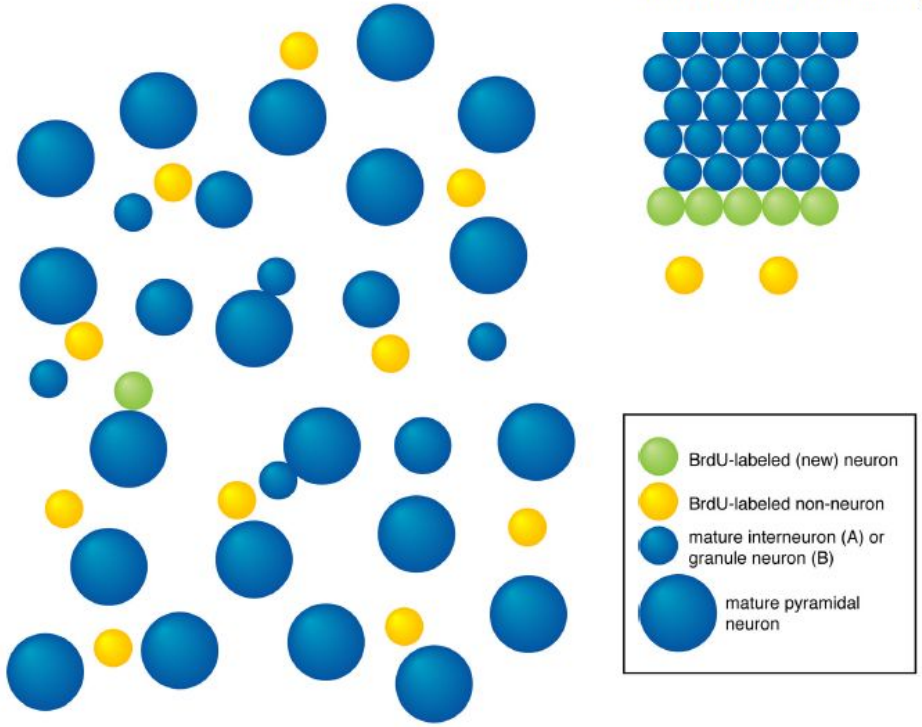
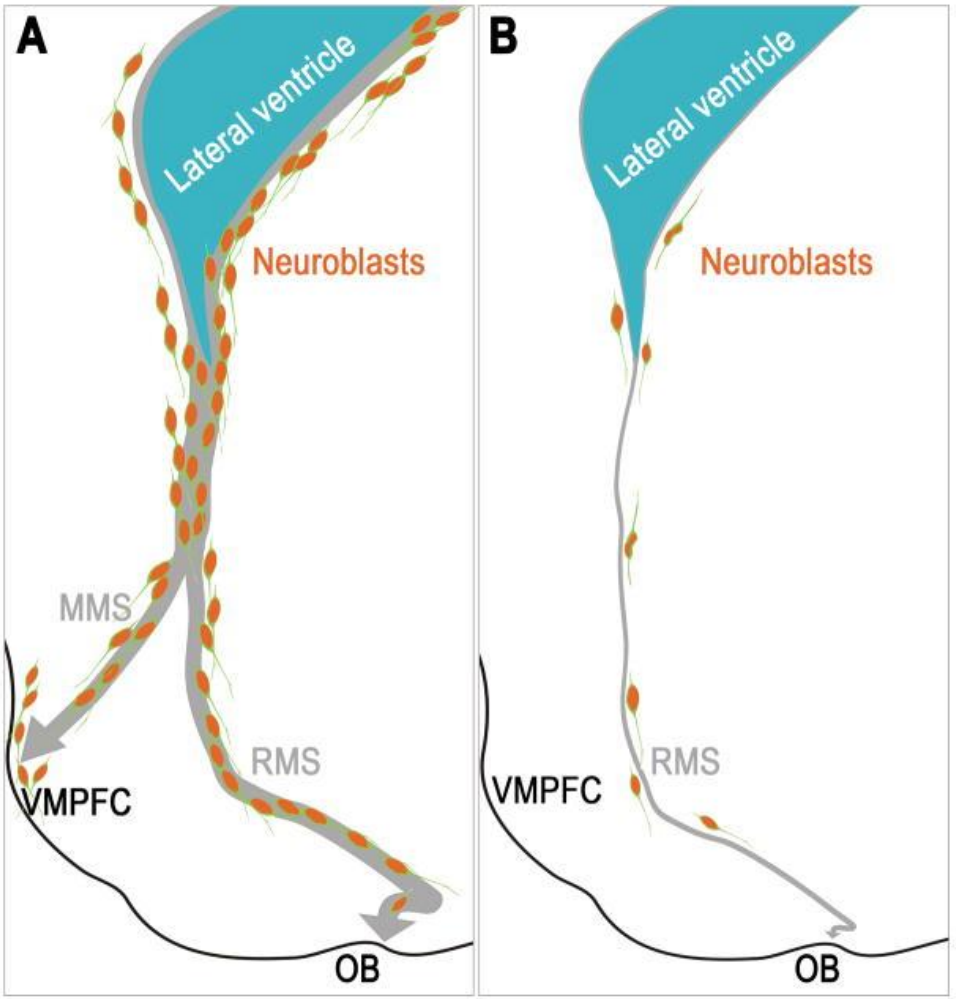


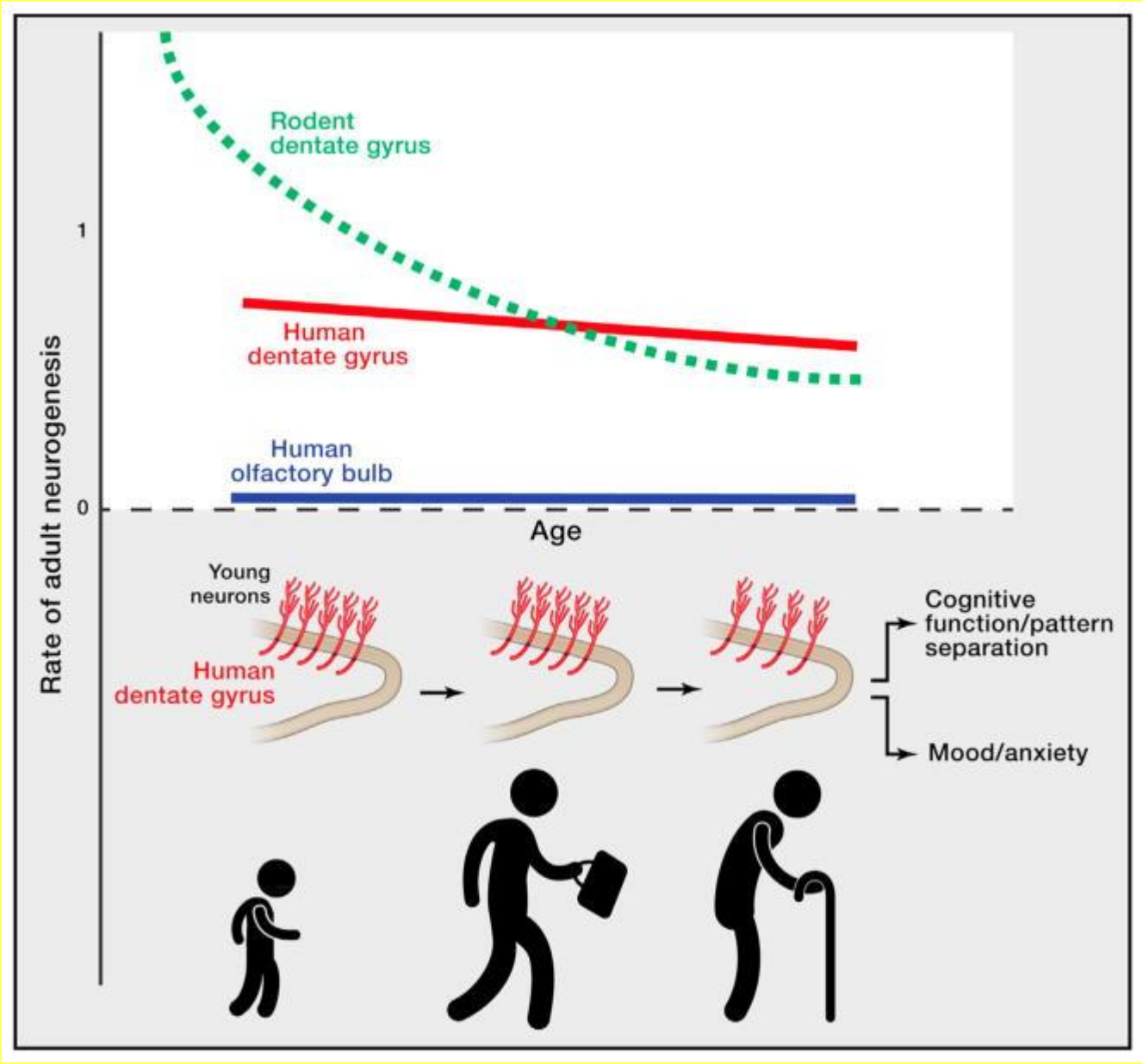
Figure 2.
Regional Differences Make New Neurons More Difficult to Find in Neocortex than in Dentate Gyrus. A. The large neocortical volume, large number of pyramidal neurons, and large number of BrdU-labeled non-neurons make new neocortical interneurons difficult to detect and recognize. B. The organization of newborn and mature granule cells in the dentate gyrus, small volume of the granule cell layer, and relatively small number of newborn non-neurons make it easier to detect the same relative number of new neurons (1 new neuron for every 5 mature neurons of the same type, in both A and B). This cartoon under-represents the differences between the two regions in at least two ways. First, the ratio of dentate gyrus new neuron density to neocortical new neuron density is 14:1 in the cartoon and greater than 1000:1 in the rodent brain (see Table 1). Second, the ratio of BrdU-labeled non-neurons to BrdU-labeled neurons is 10:1 in the cartoon (part A) and greater than 200:1 in the rodent neocortex.

Published in final edited form as:
Cell Stem Cell. 2011 November 4; 9(5): 385–386. doi:10.1016/j.stem.2011.10.007.

Postnatal neurogenesis in the human forebrain: from two migratory streams to dribbles

Zhengang Yang[1], **Guo-li Ming**[2,3,4], and **Hongjun Song**[2,3,4]





Kheirbek & Hen, 2013

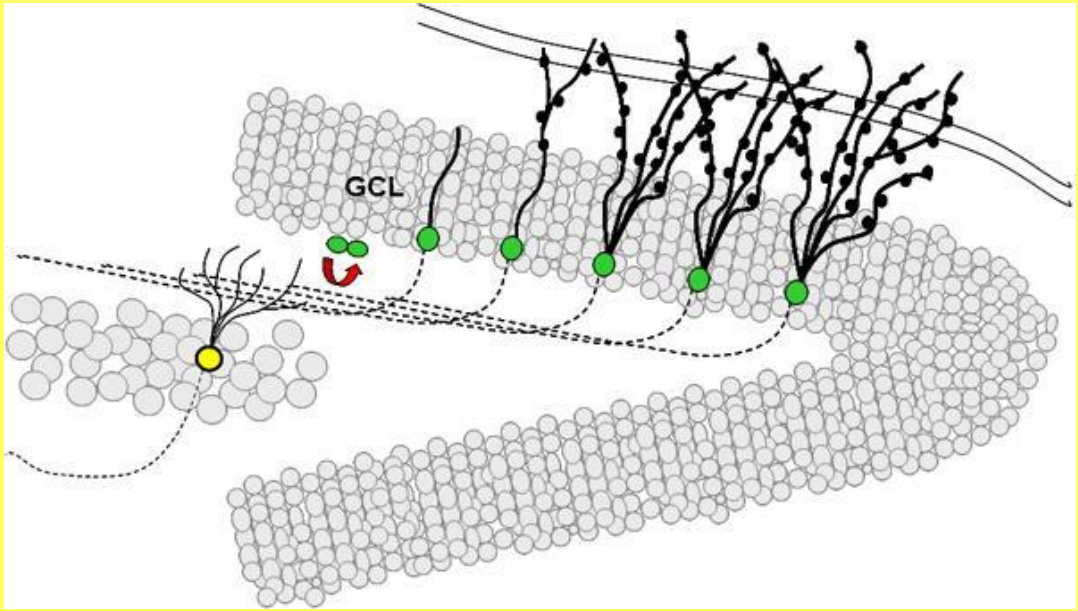
Нейрогенез

 БОЛЬШЕ НОВЫХ НЕЙРОНОВ

- ✔ обогащенная среда
- ✔ научение
- ✔ «спортивный образ жизни»

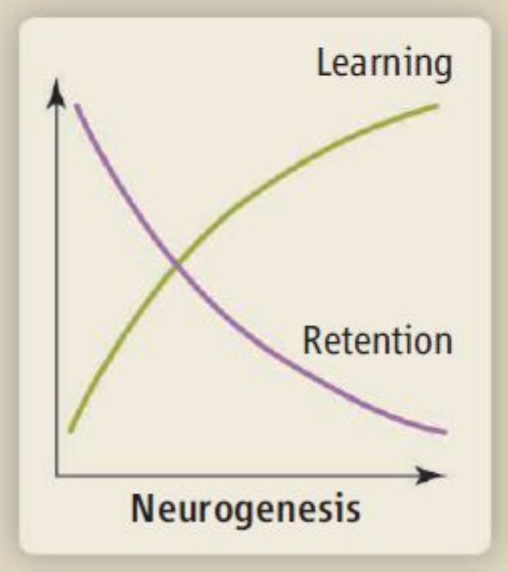
SYM 39 MOLECULAR AND BEHAVIOURAL MECHANISMS OF MEMORY RETRIEVAL AND RECONSOLIDATION (IBRO 2007, Australia)

✔ **Frankland (Canada): adult-generated cells incorporated into memory networks**



2 weeks of age - axon has extended into CA3 and dendritic processes have extended into the outer edge of the ML.
2.5 weeks - spines begin to develop
4-8 weeks - new neurons have lower threshold for LTP, LTD and are more excitable.

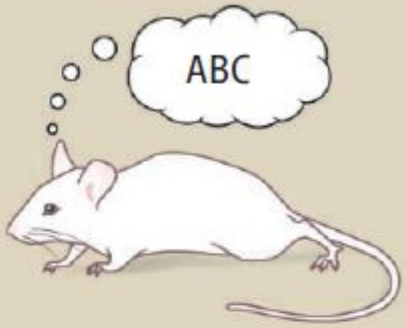
"By the time the cells are 4 or more weeks of age, they are more likely than existing granule cells to be recruited into circuits supporting spatial memory."



Learning

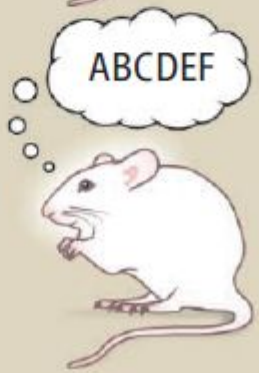
Retention

Too little neurogenesis



Too much neurogenesis

"Trade-off" neurogenesis



Консолидация

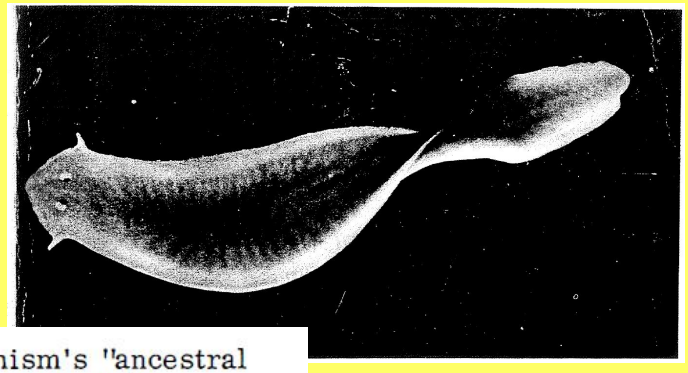
- «переход» кратковременной памяти в долговременную
  - Нужны повторные активации нейронной группы

Важность «шума» для обучения

https://www.youtube.com/watch?v=prfxjrz0_0k

Внутриклеточный уровень

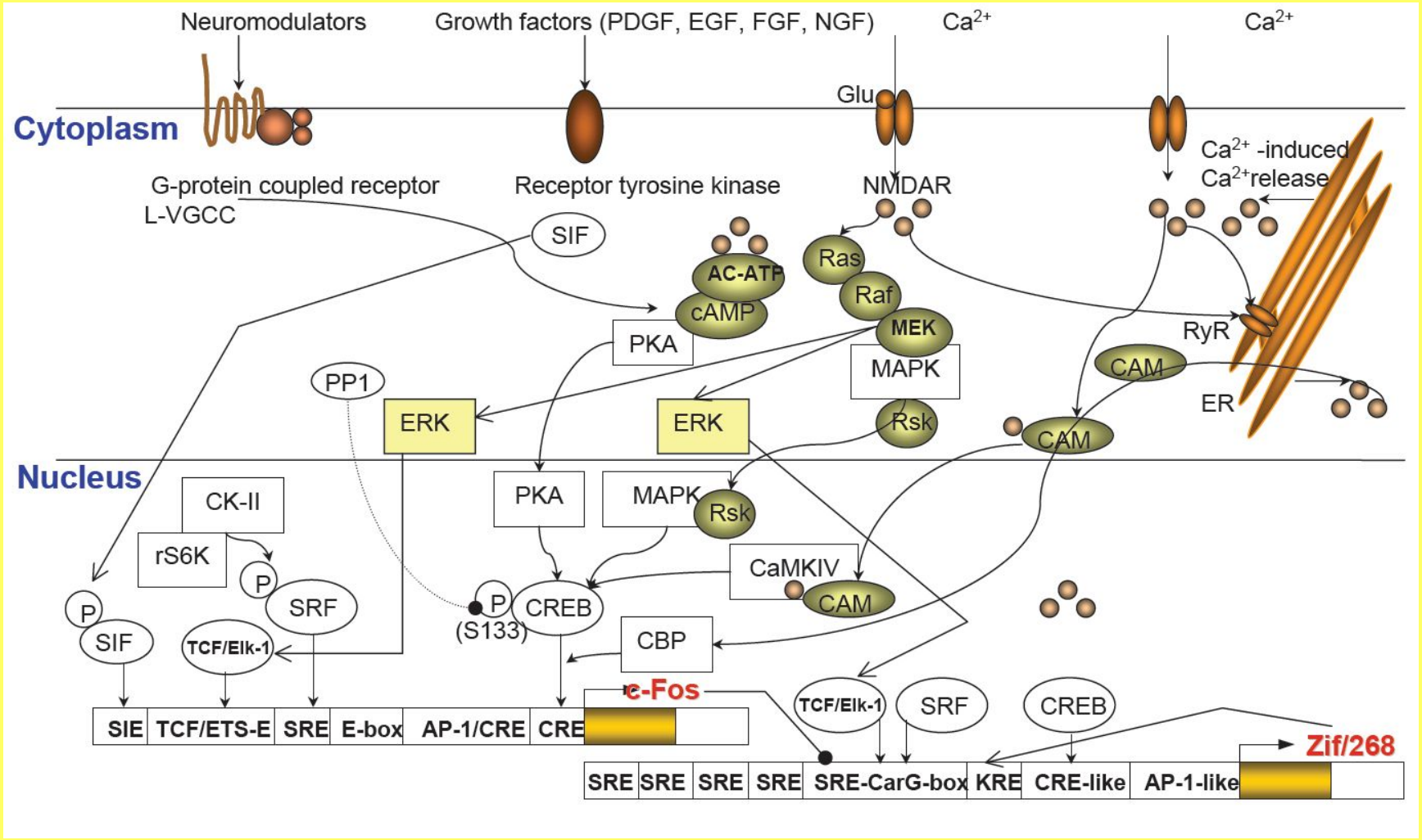
1962 - Hyden:
В это «временное окно» (1-2 часа) консолидации в мозге животных увеличивается синтез РНК и белка (планарии);



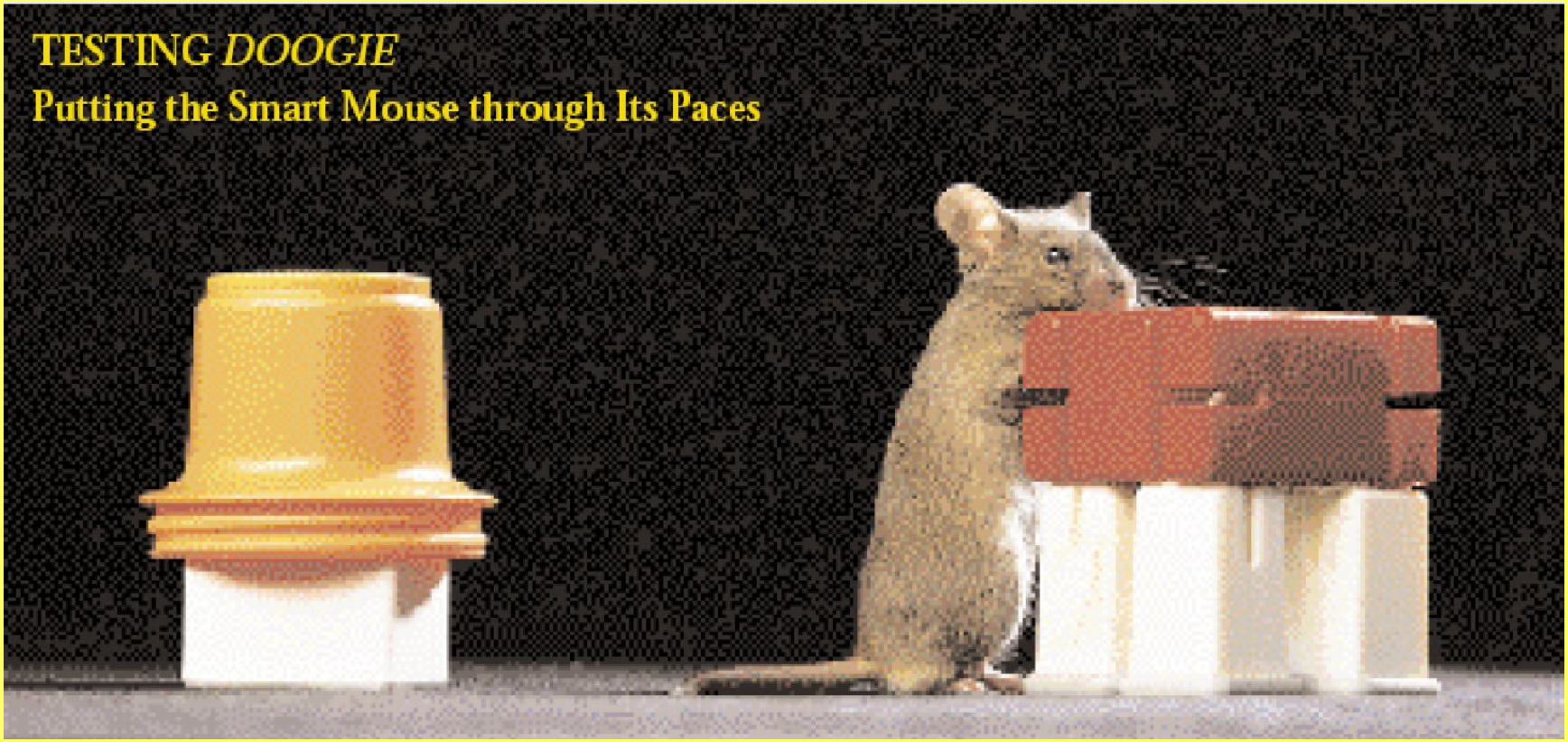
From one point of view, then, we may say that DNA stores an organism's "ancestral memories" in coded form; that is, DNA "remembers" what an organism's progenitors were like. Professor Hydén theorized that RNA might encode or "remember" an organism's own personal memories, that RNA might well be the "tablet" on which the fingers of experience wrote (by changing the chemical "code" carried by the RNA molecule). To test his theory, Hydén performed experiments with rats and rabbits. First, Hydén developed a beautiful technique for taking large single cells from the nervous system, cutting them open individually by hand with an incredibly tiny scapel and scraping out the protoplams inside each cell. With microanalytic techniques, he was then able to measure rather subtle changes in the RNA found in these cells. Then he took two groups of rats to work with. The first group was trained to balance on a taut wire in order to reach food; the second group was given passive exercise but did not learn the balancing trick. Hydén found that the gross amount of RNA increased markedly in cells taken from both groups of animals, but qualitative changes in the RNA (that is, apparent changes in the "code"

1963 - Flexner et al.:
Блокада синтеза белка во "временное окно" консолидации нарушает долговременную памяти;

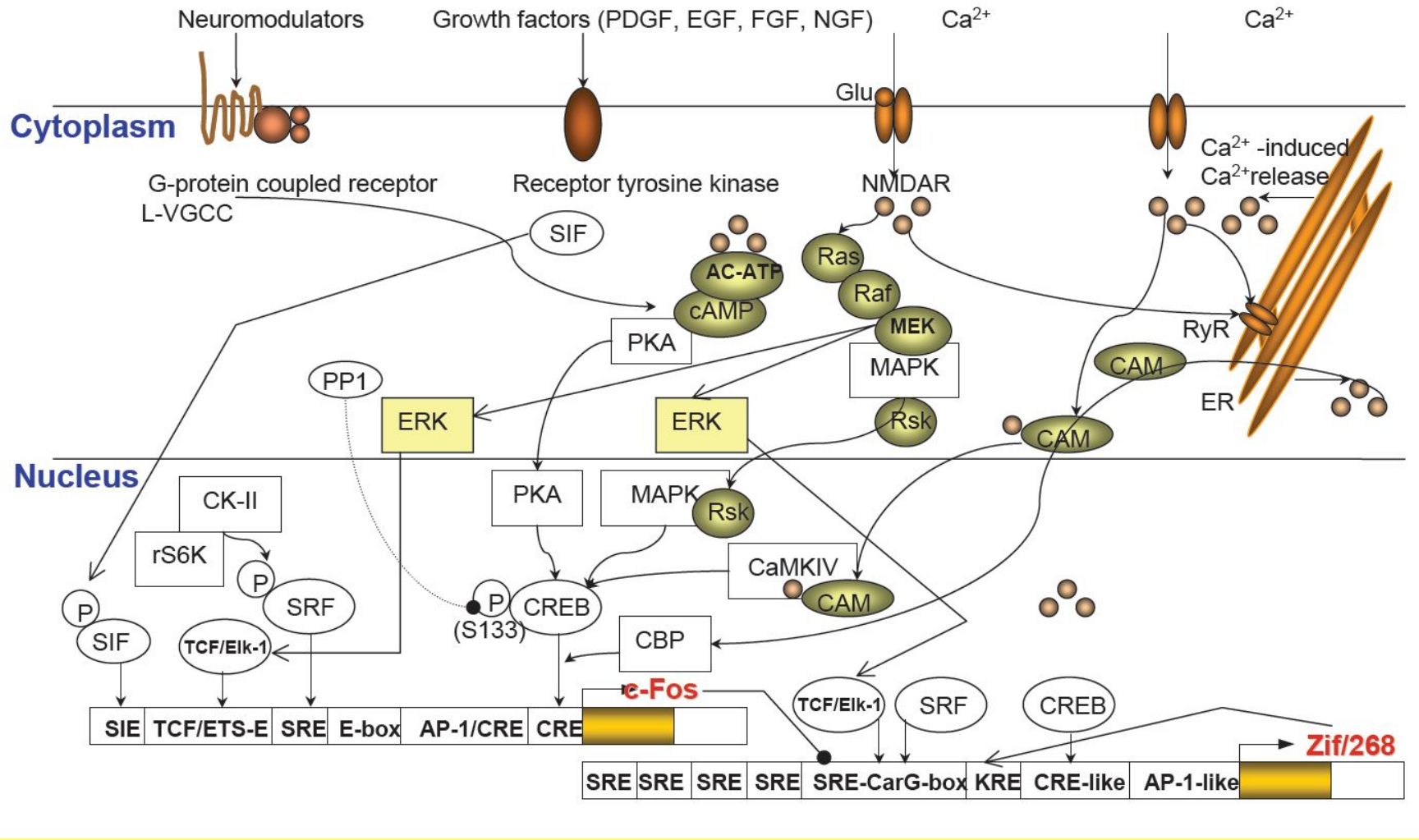
Каскады молекулярных событий при научении



“Умные” мыши (Tsien, 2000)

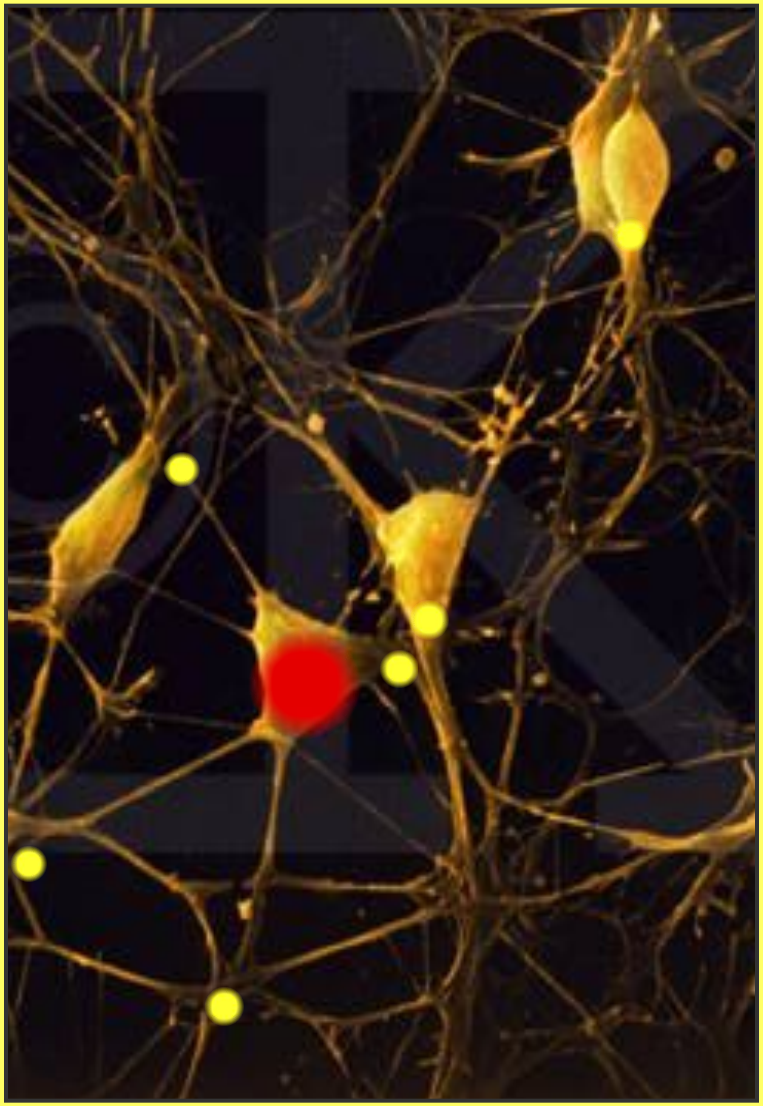


Каскады молекулярных событий



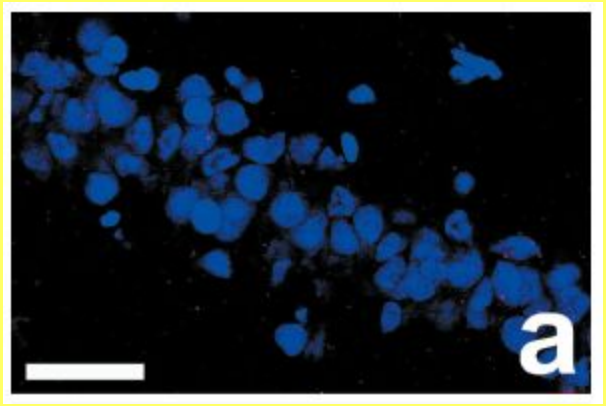
Экспрессия ранних генов

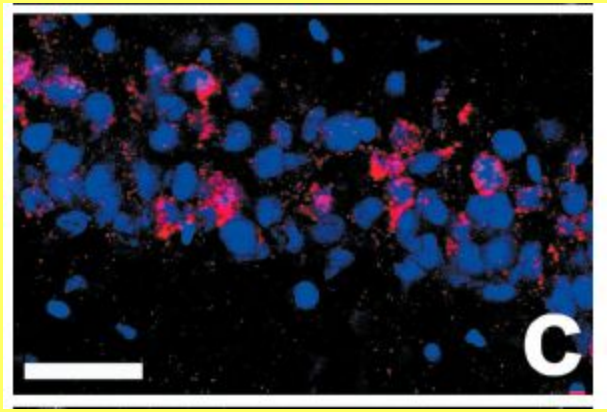
Низкий уровень в контроле
Происходит при обучении
Очень быстро (мин для мРНК)
Происходит в нейронах
Распределена по структурам мозга
Зависит от активности NMDA-R
Вовлечена в долговременные изменения функционирования
Требуется для консолидации долговременной памяти



Ген *arc*

- изменения активности генов

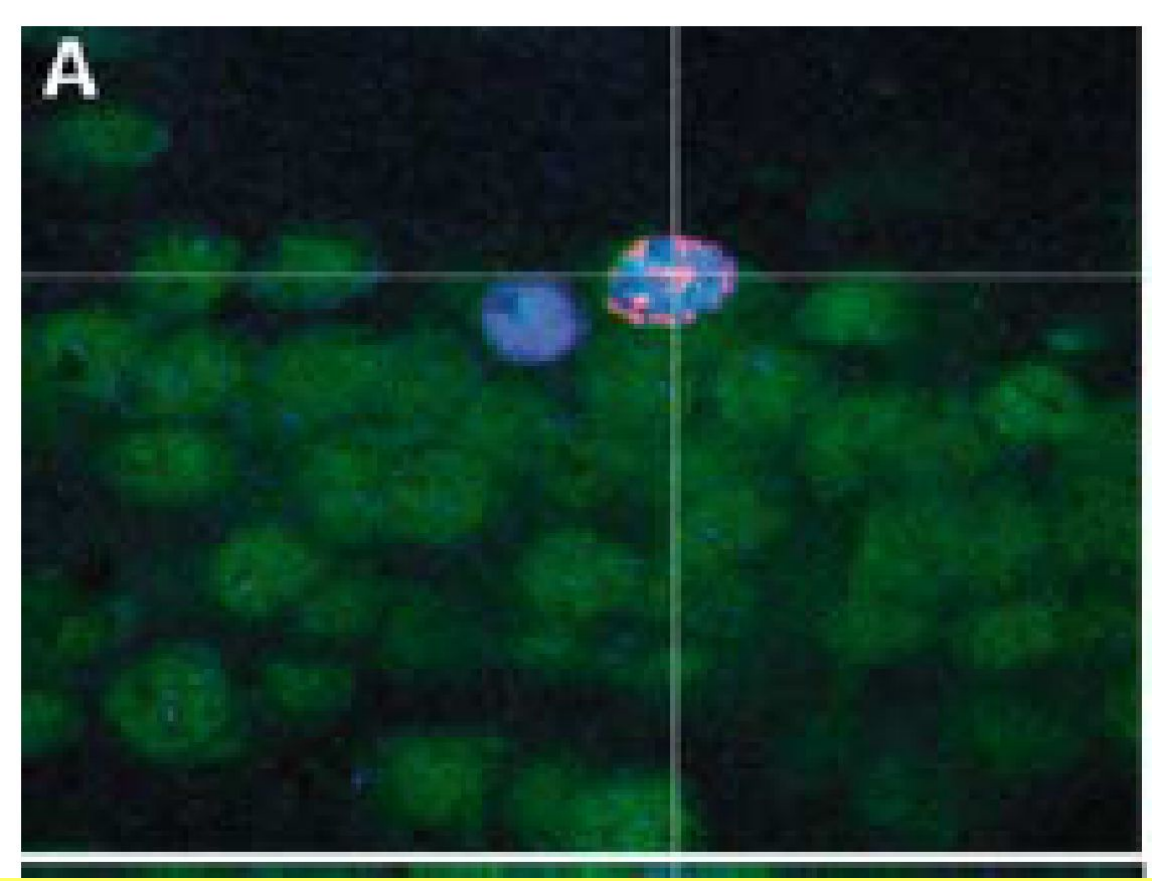




Guzowski et al.

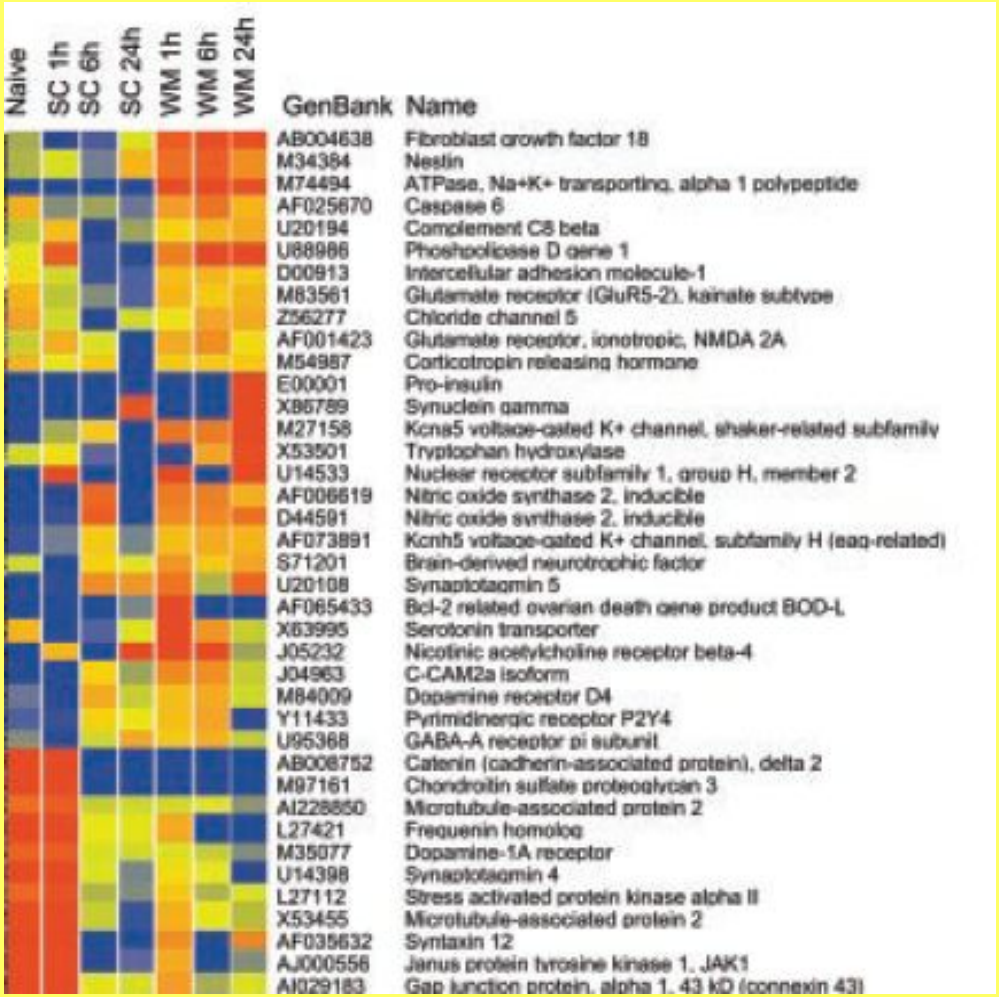
Arc в новых нейронах

- неонейрогенез



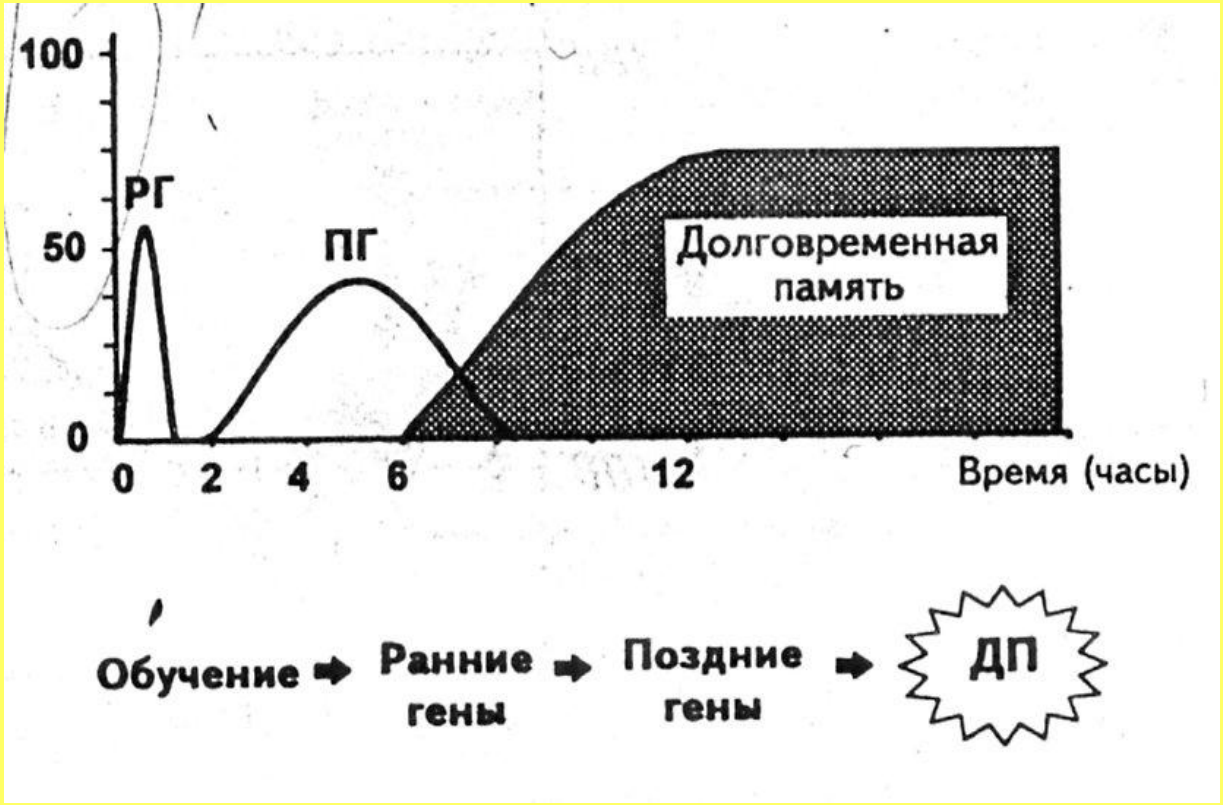
Jessberger & Kempermann, 2003

Изменения наборов экспрессирующихся генов



Временные периоды

- ранние гены
- поздние гены



Консолидация

- «переход» кратковременной памяти в долговременную
  - Нужны повторные активации нейронной группы
  - Нужны изменения внутри клеток данной нейронной группы

Структурный уровень

- структурные изменения
  - ✔ в синапсах (акт. зоны, пузырьки и др.)
  - ✔ число синапсов
  - ✔ отростки нейронов

Структурные изменения

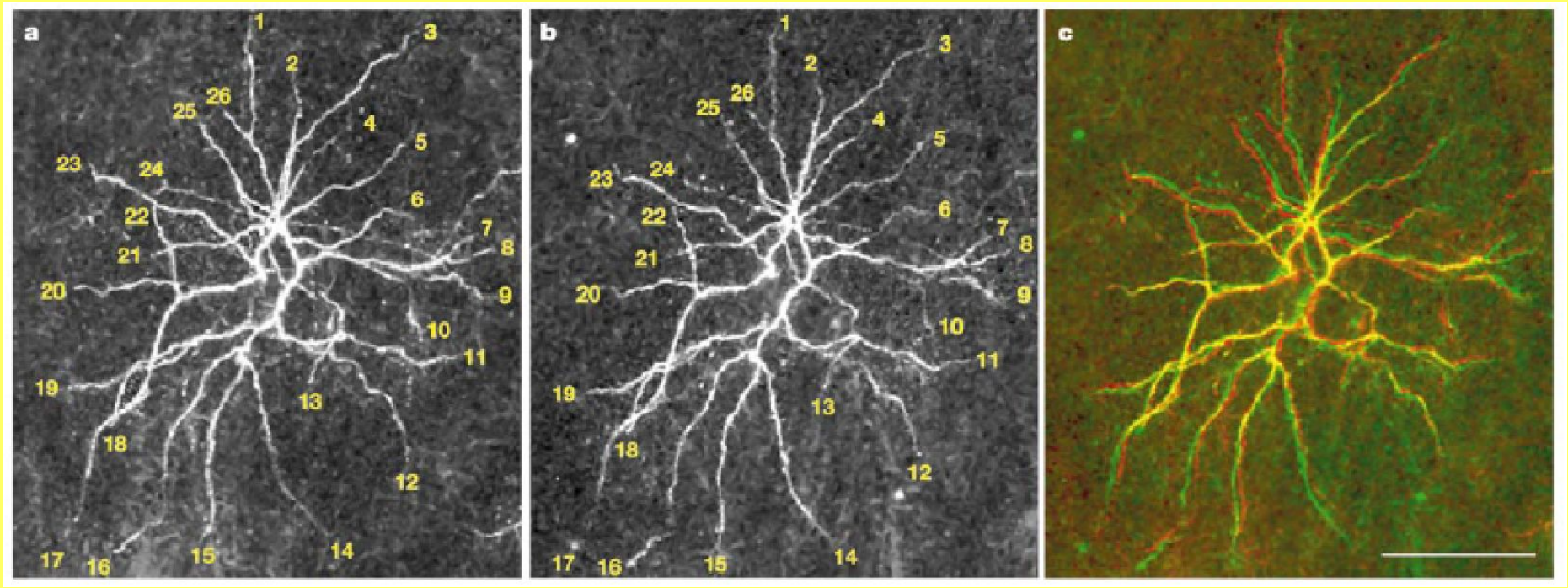
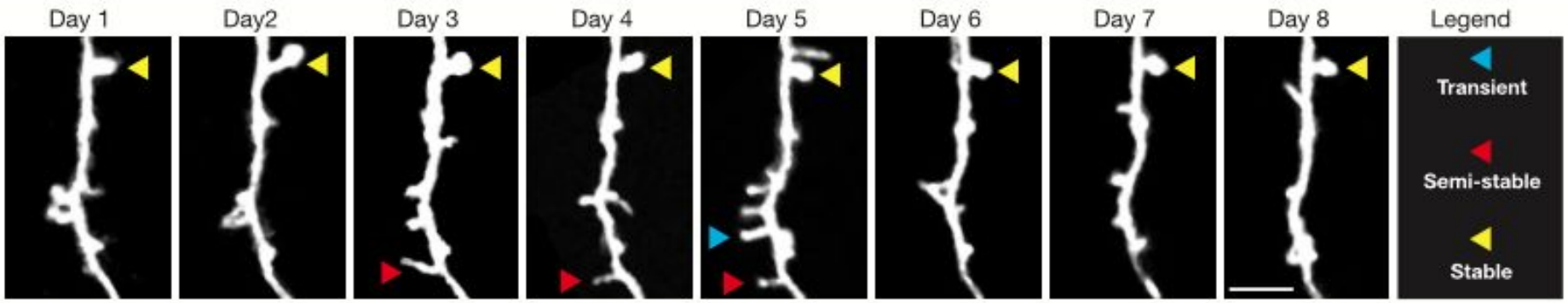


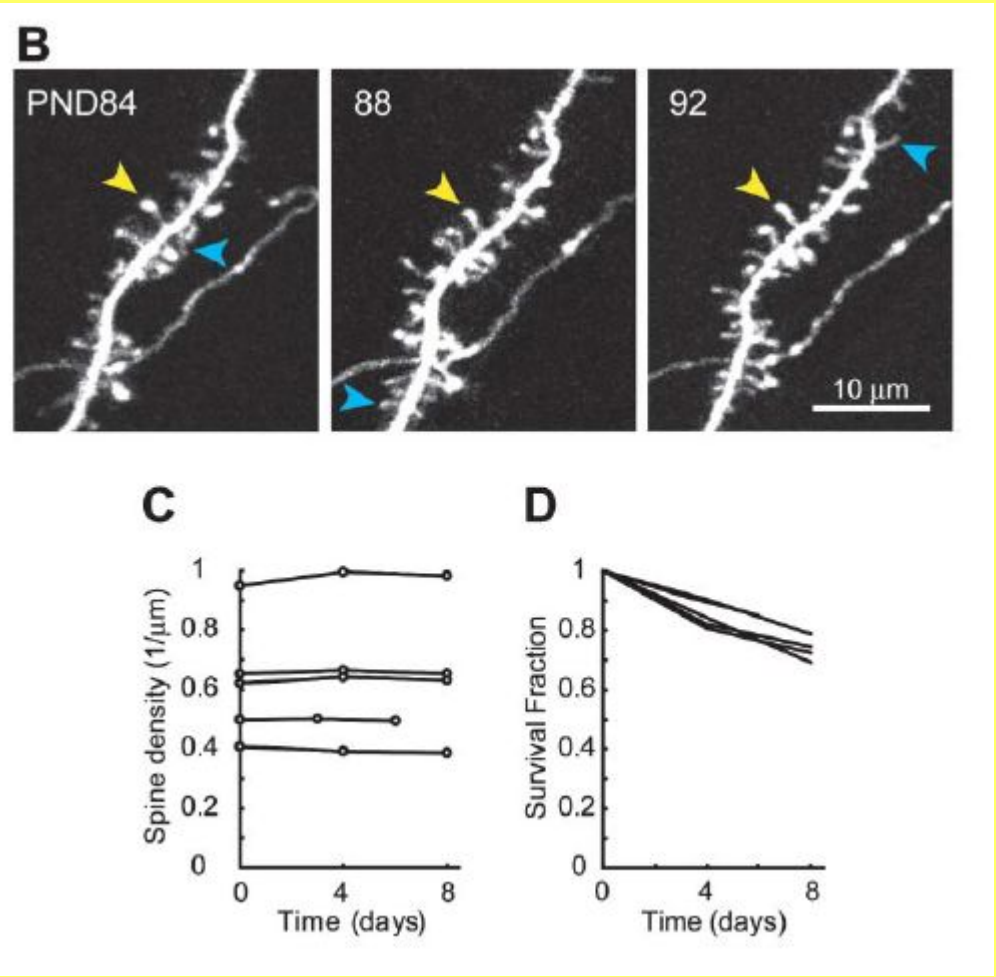
Figure 2 Dendritic branches are stable over weeks.

Trachtenberg et al., 2002



Trachtenberg et al., 2002

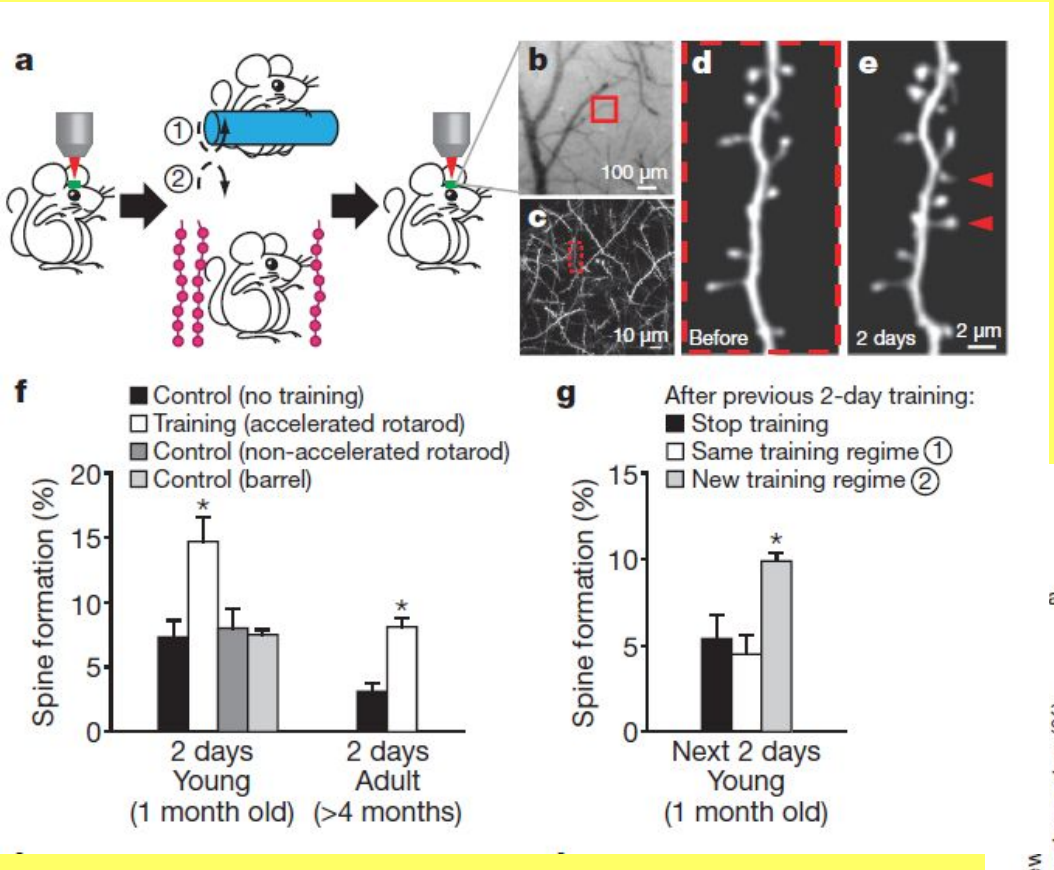
Изменение количества шипиков на дендритах

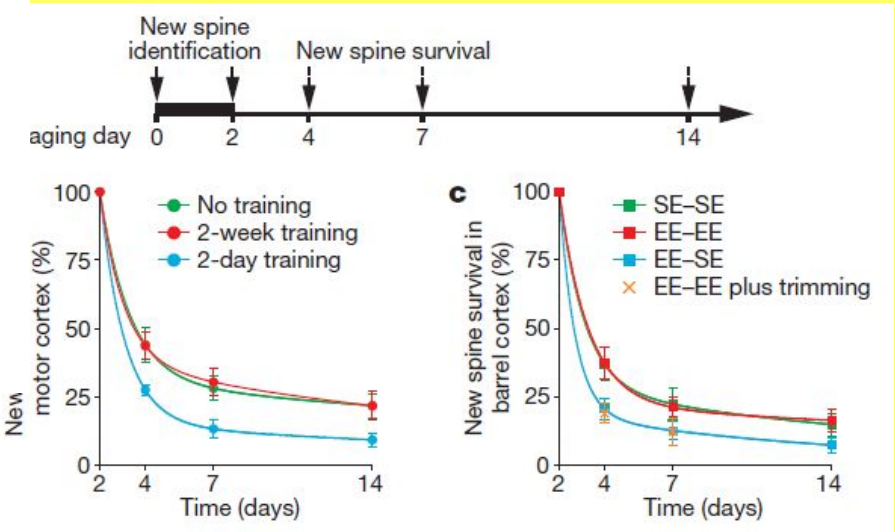


Persistent and Transient Spines in the Neocortex
Spines are motile structures. They can undergo morphological changes on timescales of seconds and minutes (Bonhoeffer and Yuste, 2002; Dailey and Smith, 1996; Fischer et al., 1998; Lendvai et al., 2000). Complete re-

Holtmaat et al., 2005

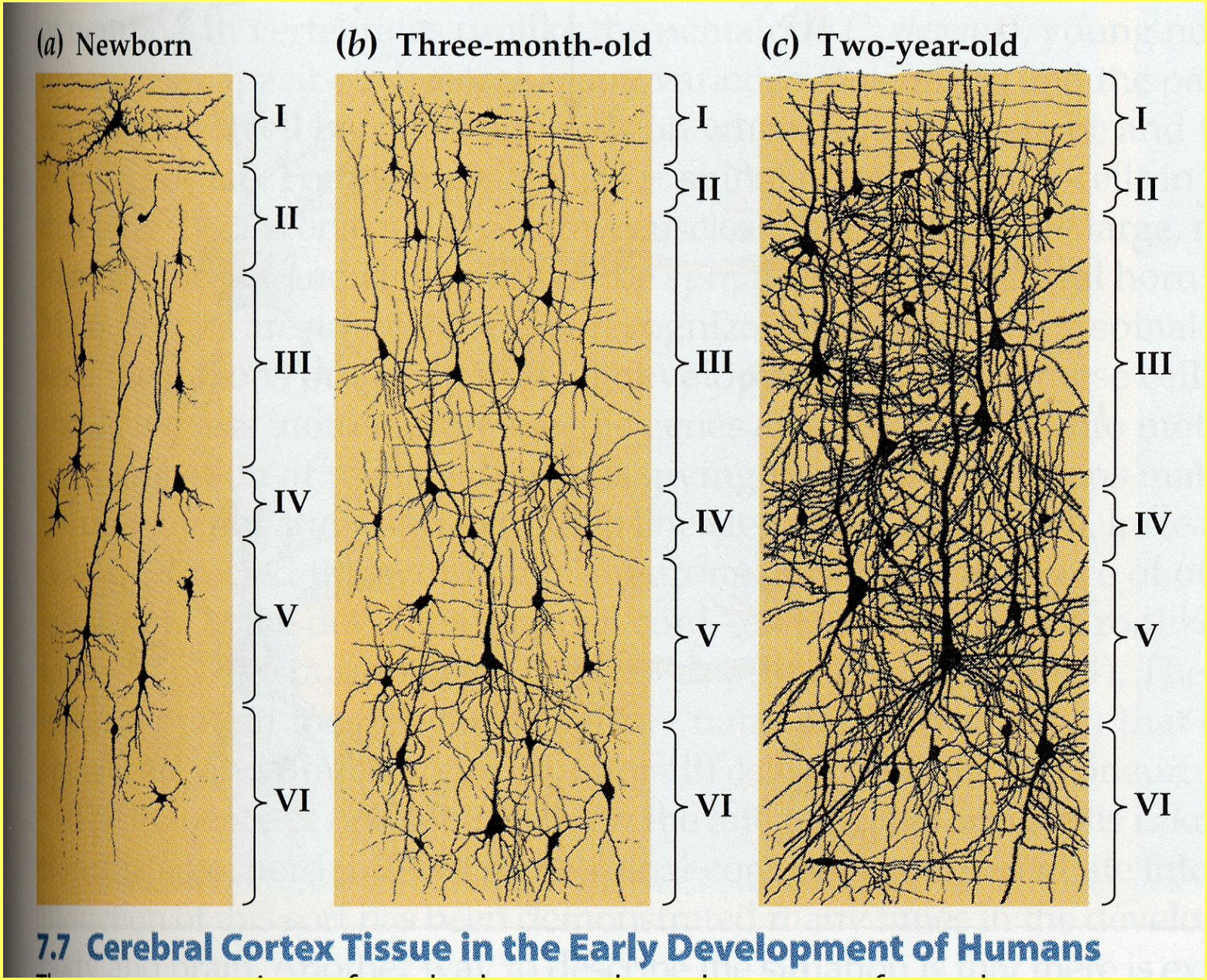
Изменение количества шипиков на дендритах при обучении





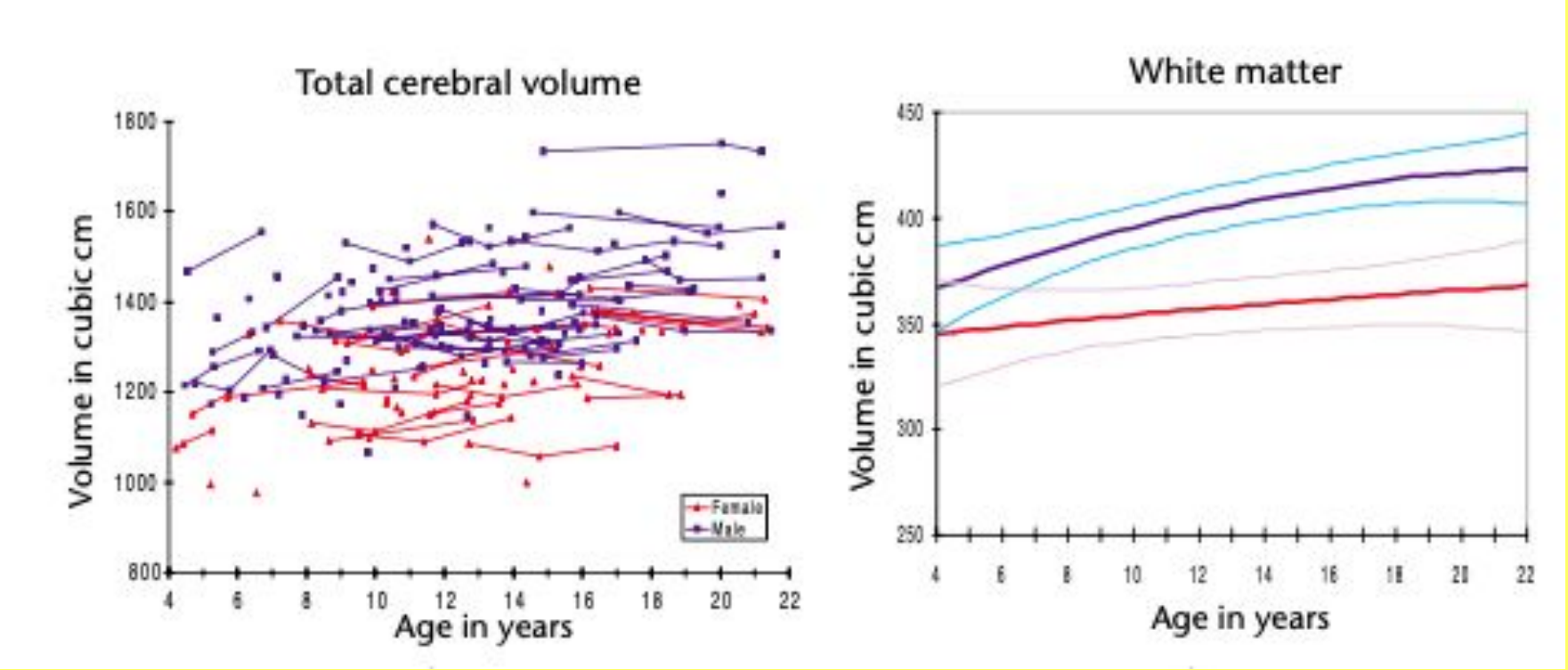
Stably maintained dendritic spines are associated with lifelong memories

Yang et al., 2009

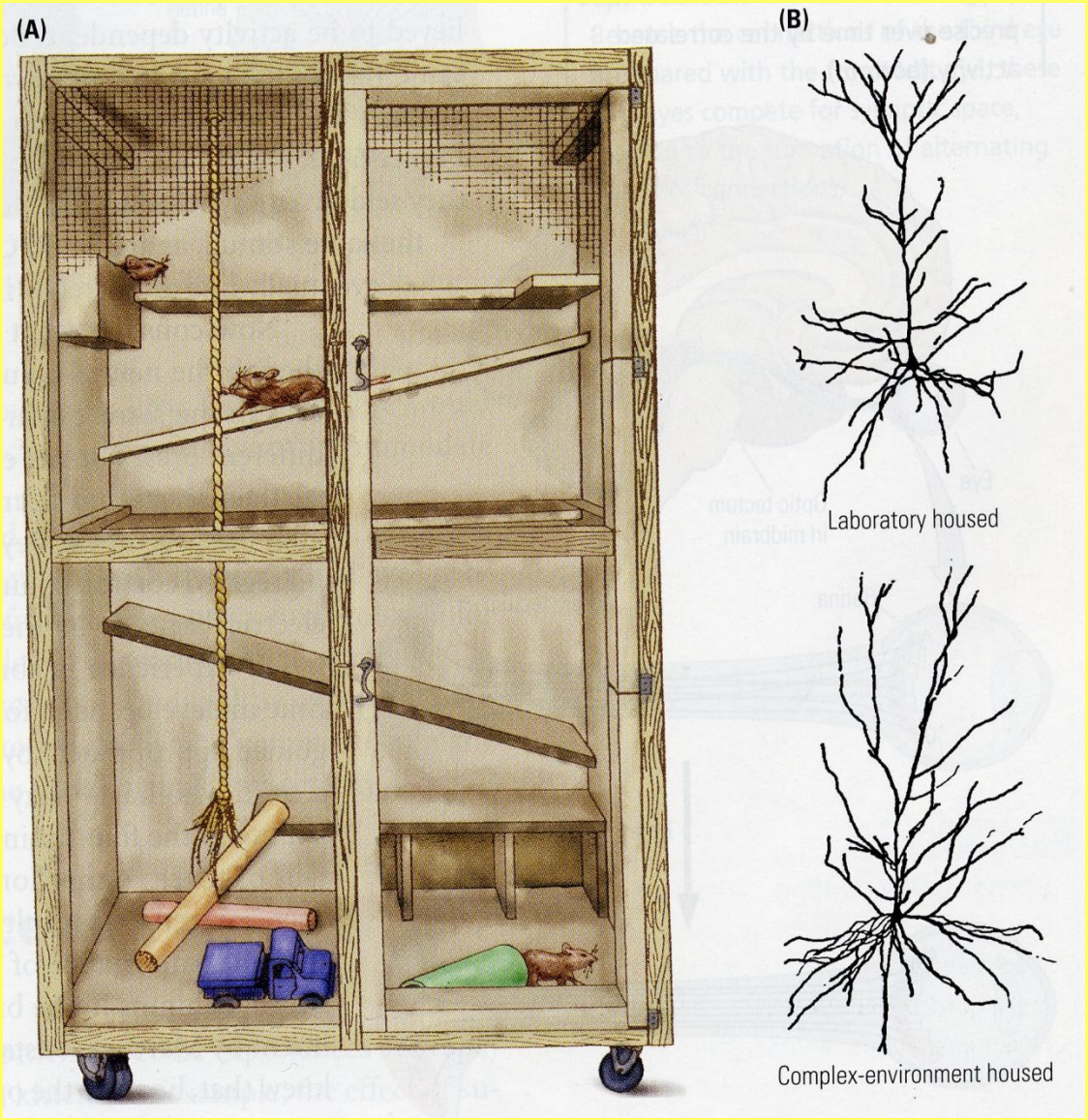


7.7 Cerebral Cortex Tissue in the Early Development of Humans

- РОСТ МОЗГА (клеточные тела и отростки)



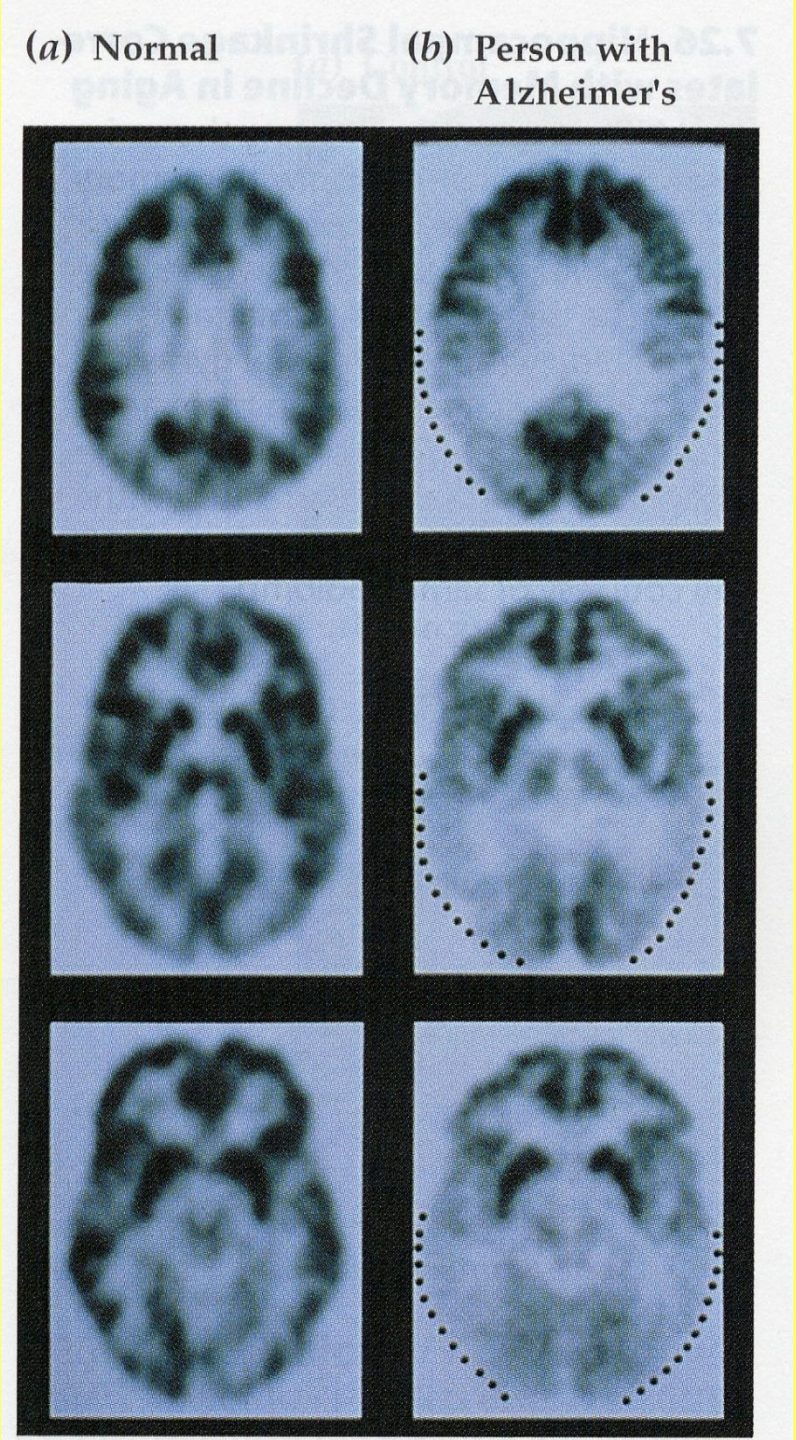
Ранний онтогенез



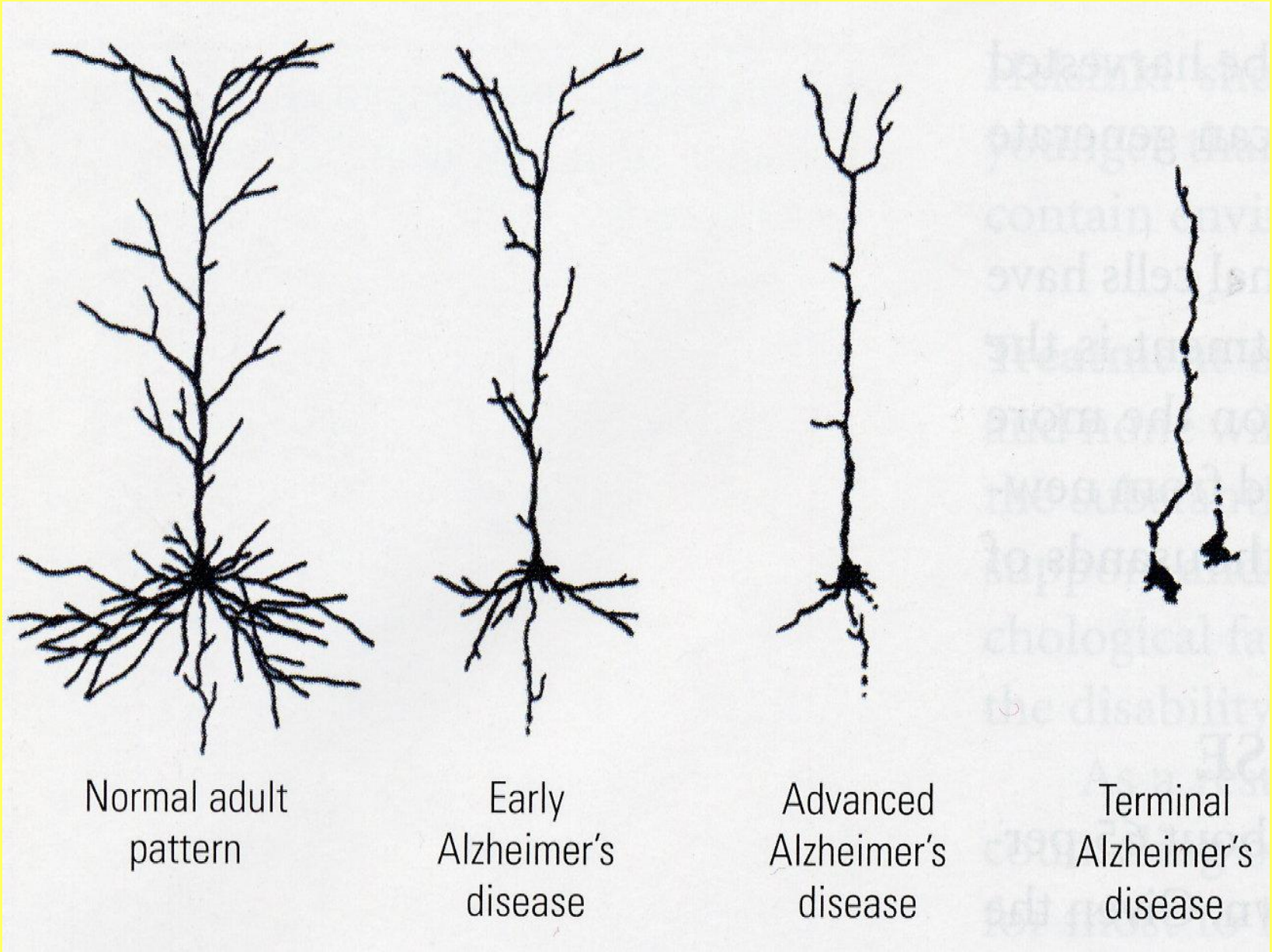
Реювенилизация – реактивация процессов развития при обучении

- модификация функциональных свойств нейронов
- регуляция экспрессии генов
- структурные изменения

Болезнь Альцгеймера



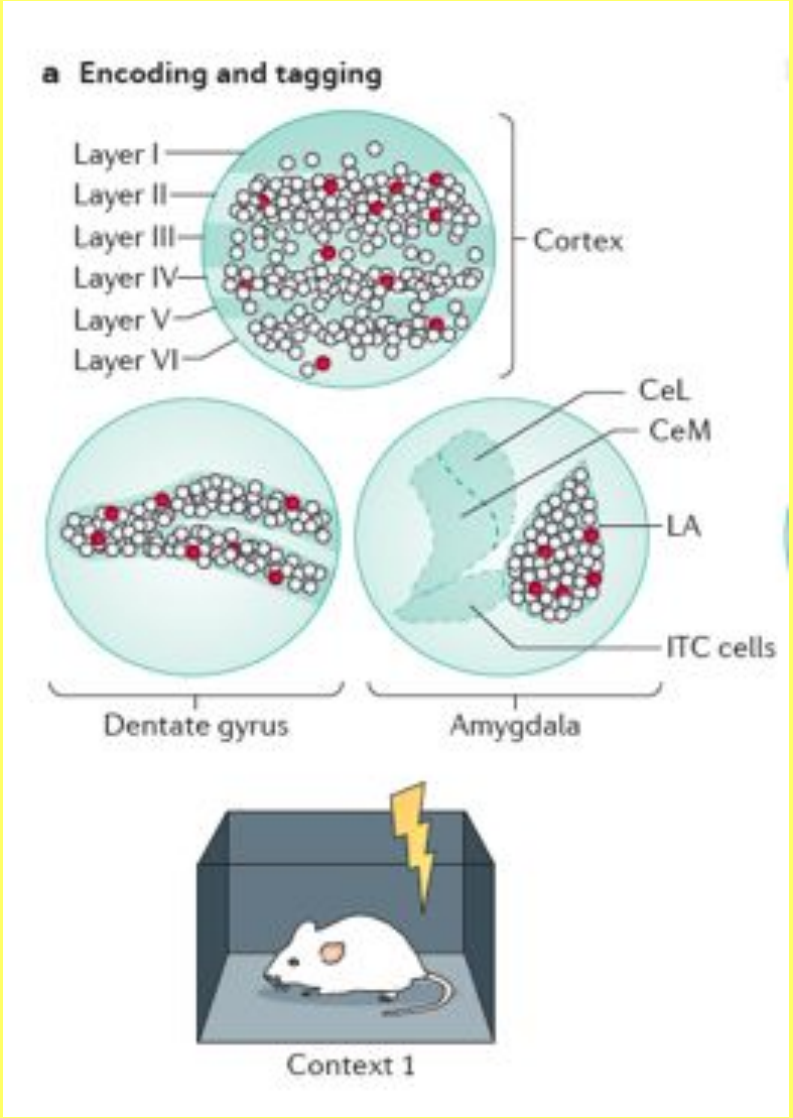
Болезнь Альцгеймера

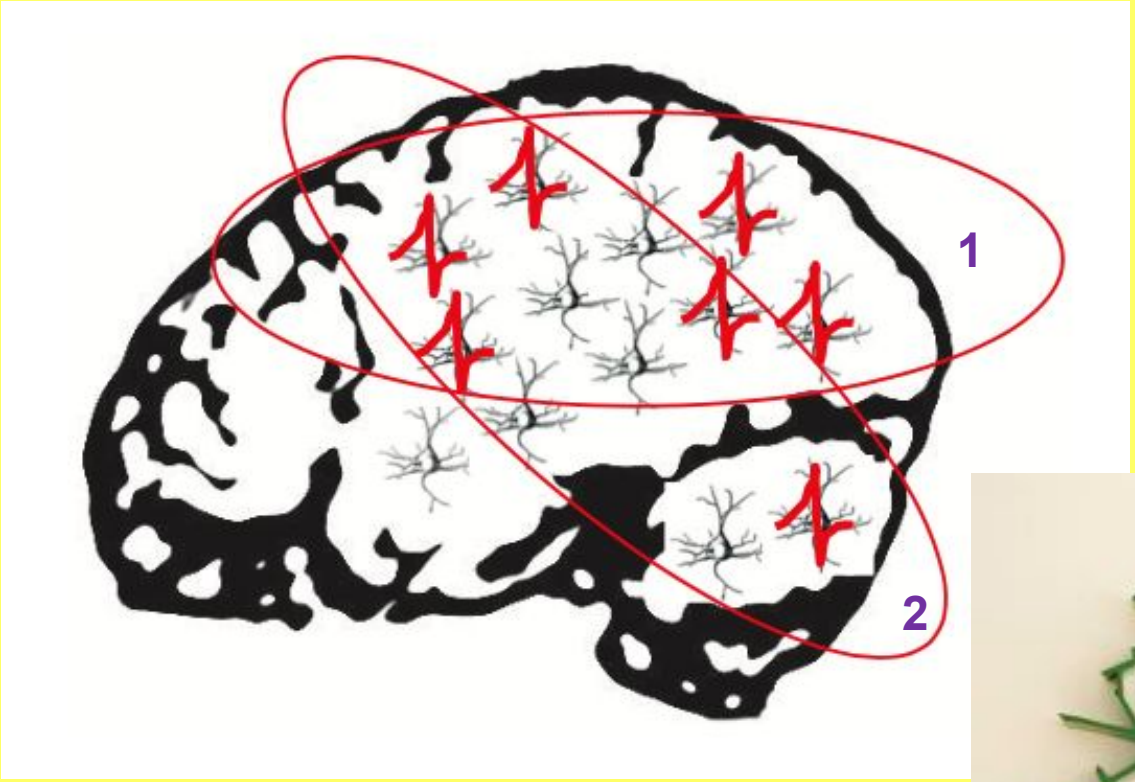


Консолидация

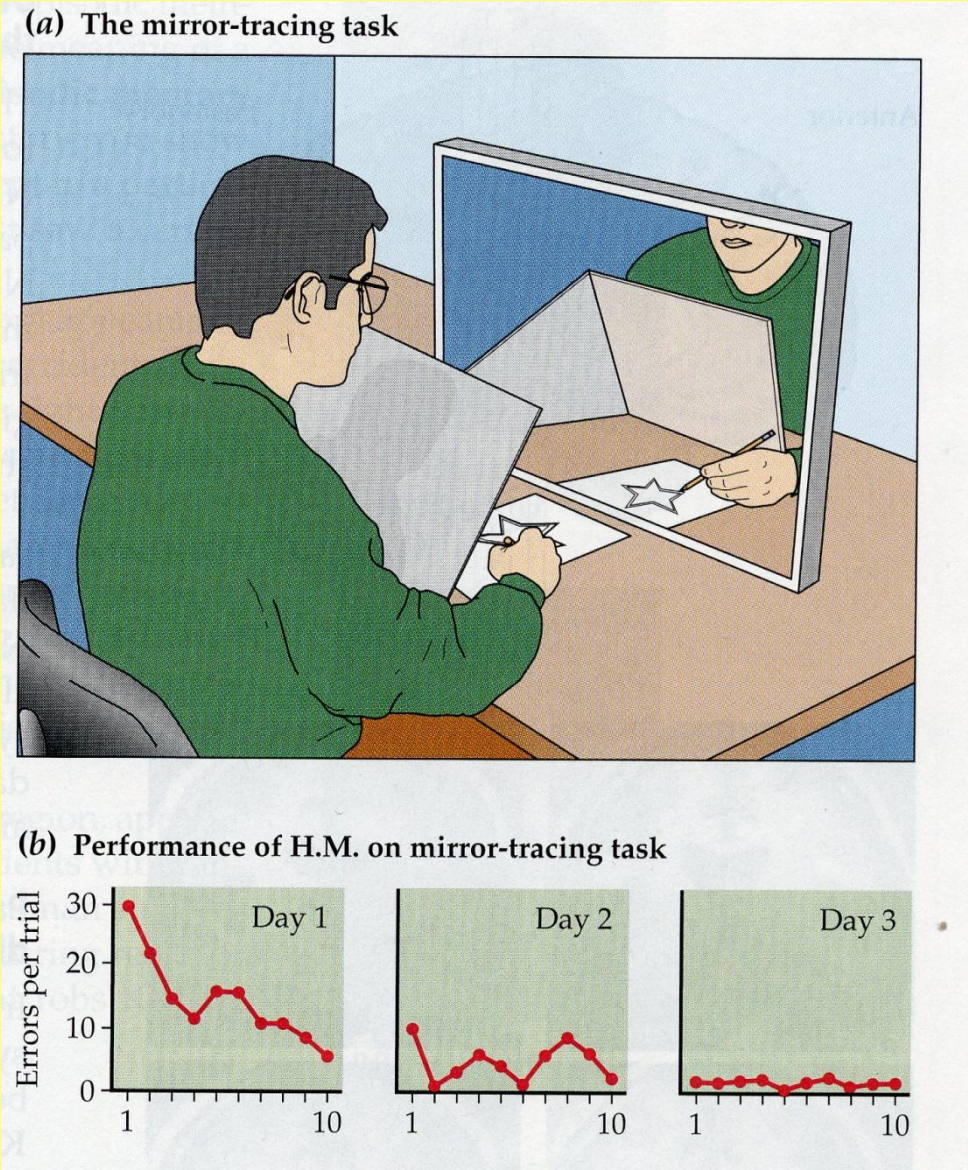
- «переход» кратковременной памяти в долговременную
  - Нужны повторные активации нейронной группы
  - Нужны изменения внутри клеток данной нейронной группы
  - Нужны изменения структуры связей между нейронами

ОБУЧЕНИЕ – формирование нейронной группы, активность которой связана с этой деятельностью




1
2

Обучение без сознательного отчета



Brooks, D.N. & Baddeley, A.D. (1976). What can amnesic patients learn? Neuropsychologia, 14, 111–122.

Article PubMed Google Scholar

Claparède, E. (1911). Recognition et moitié. Archives of Psychology Genève, 11, 79–90.

Google Scholar

The Claparède phenomenon: A further example in amnesics, a demonstration of a similar effect in normal people with attenuated memory, and a reinterpretation

Peter Meudell & A. Mayes

Current Psychology **1**, 75–88(1981) | Cite this article

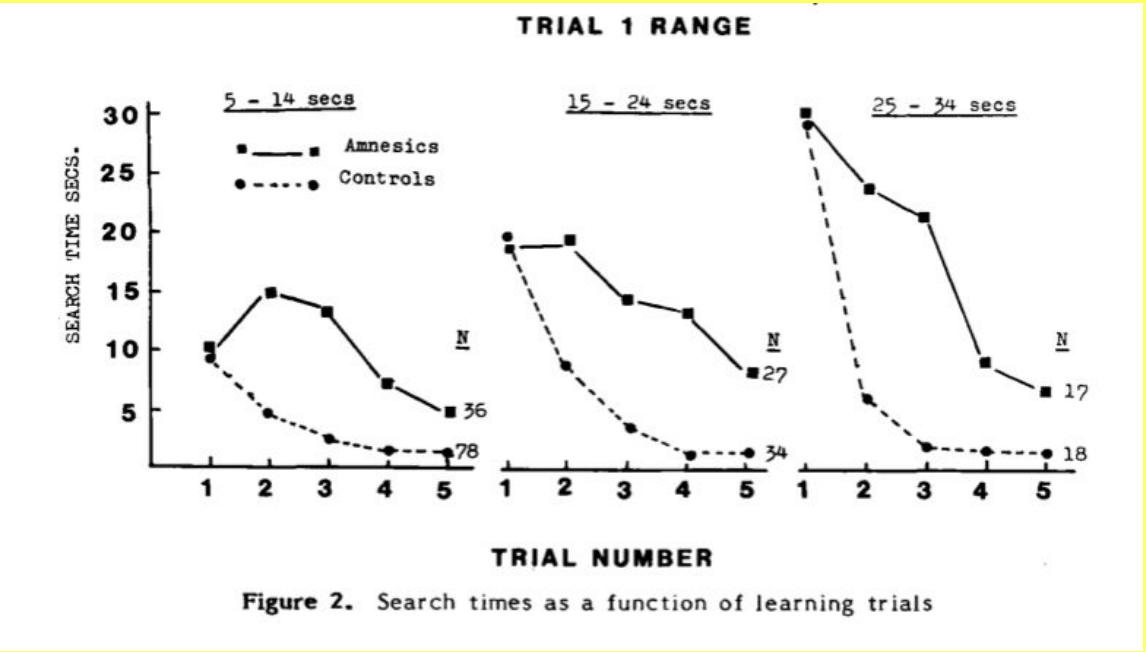
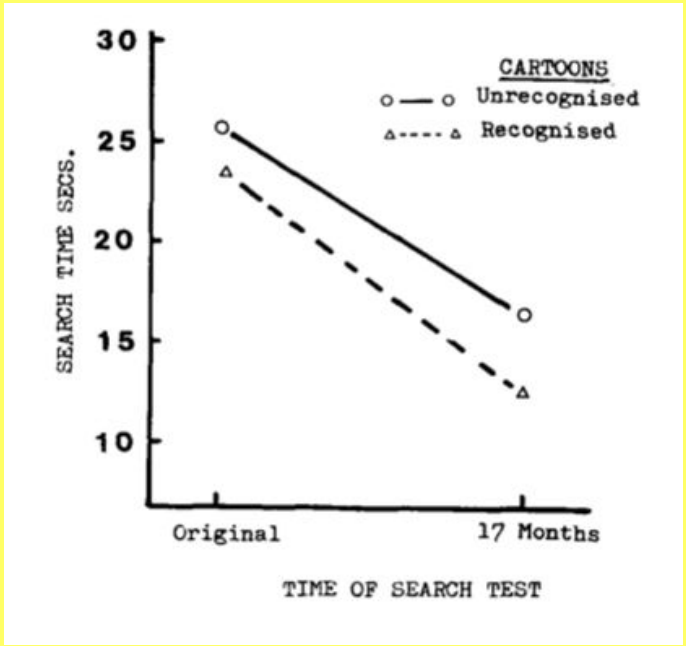


Figure 2. Search times as a function of learning trials




UNKNOWN
НЕИЗВЕСТНЫЙ


THE LONG
KISS
GOODNIGHT