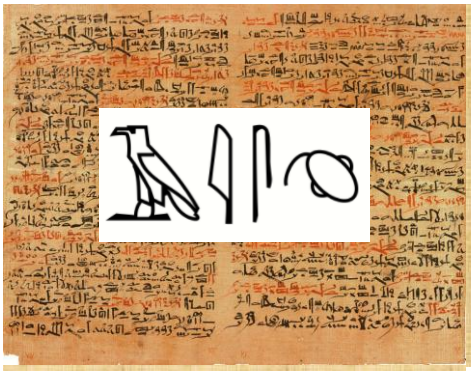
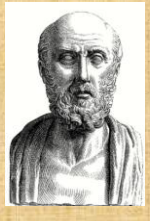


Un antico trattato medico egiziano scritto nel **XVII secolo a.C.** (Papiro Edwin Smith) contiene il primo geroglifico che indica il cervello. Il papiro descrive la superficie esterna del cervello, le meningi e il liquido cerebrospinale.

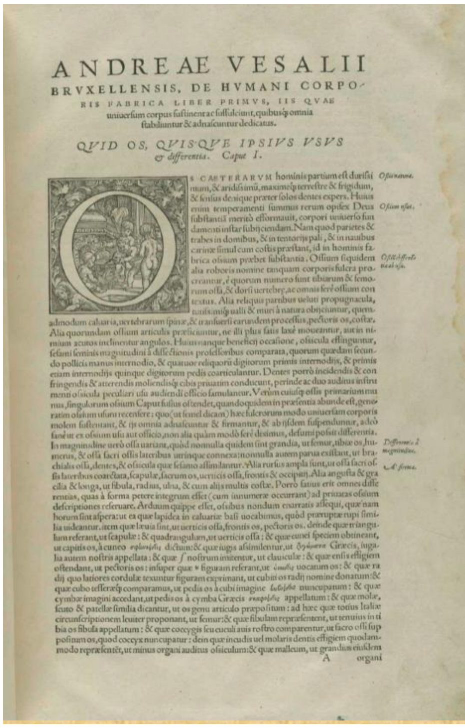
Nel **V secolo a.C.** nella **Magna Grecia**, **Alcmeone di Crotone**, considerò per la prima volta il cervello come sede della mente.: «l'uomo si distingue dagli altri animali perché capisce, mentre gli altri animali percepiscono ma non capiscono. Tutte le percezioni, dice, giungono al cervello e lì s'accordano»

Nello stesso secolo, ad Atene, **Ippocrate di Coo** riteneva che il cervello fosse la sede dell'intelligenza.



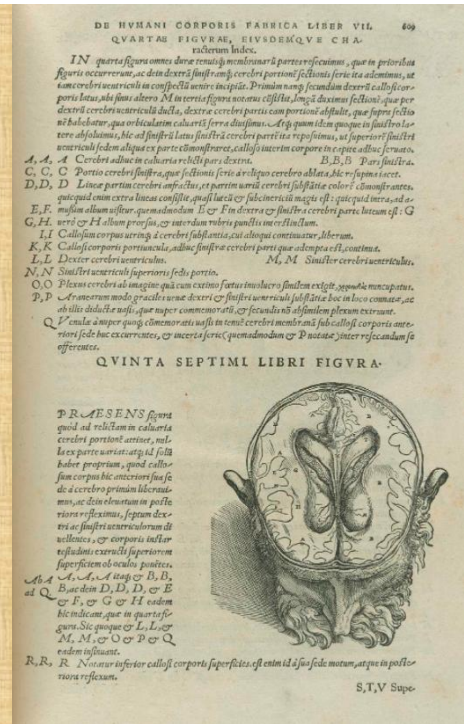
Aristotele descriveva le meningi e distingueva il cervello e il cervelletto

Erofilo di Calcedonia, tra il quarto e il terzo secolo a.C. distingueva il cervello e il cervelletto e forniva la prima chiara descrizione dei ventricoli cerebrali; con **Erasistrato di Ceos** compì esperimenti su cervelli animali viventi


ANDREAE VESALII BRVXELLENSIS, DE HVMANI CORPORIS FABRICA LIBER PRIMVS, IIS QVAE uniuersum corpus sustinent ac suffulciunt, quibusque omnia stabiliuntur & adnascuntur dedicatus.

QVID OS, QVISQVE IPSIVS VSVS & differentiae. Caput I.

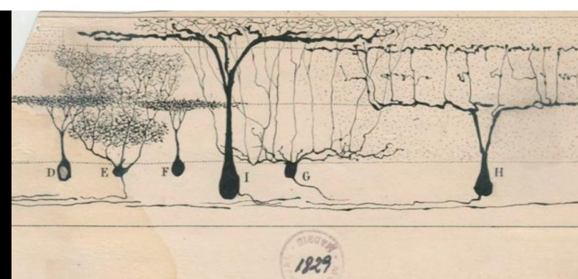
Vesalius, Andreas.
De corporis humani fabrica
(Basel,1543)


DE HVMANI CORPORIS FABRICA LIBER VII. 609

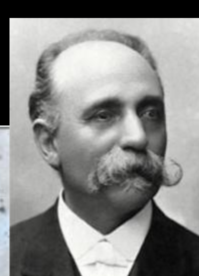
QVARTAE FIGVRAE, EIVSDEMQVE CHARACTERUM INDEX.

QVINTA SEPTIMI LIBRI FIGVRA.

«La colorazione nera»
reazione cromo - argentica



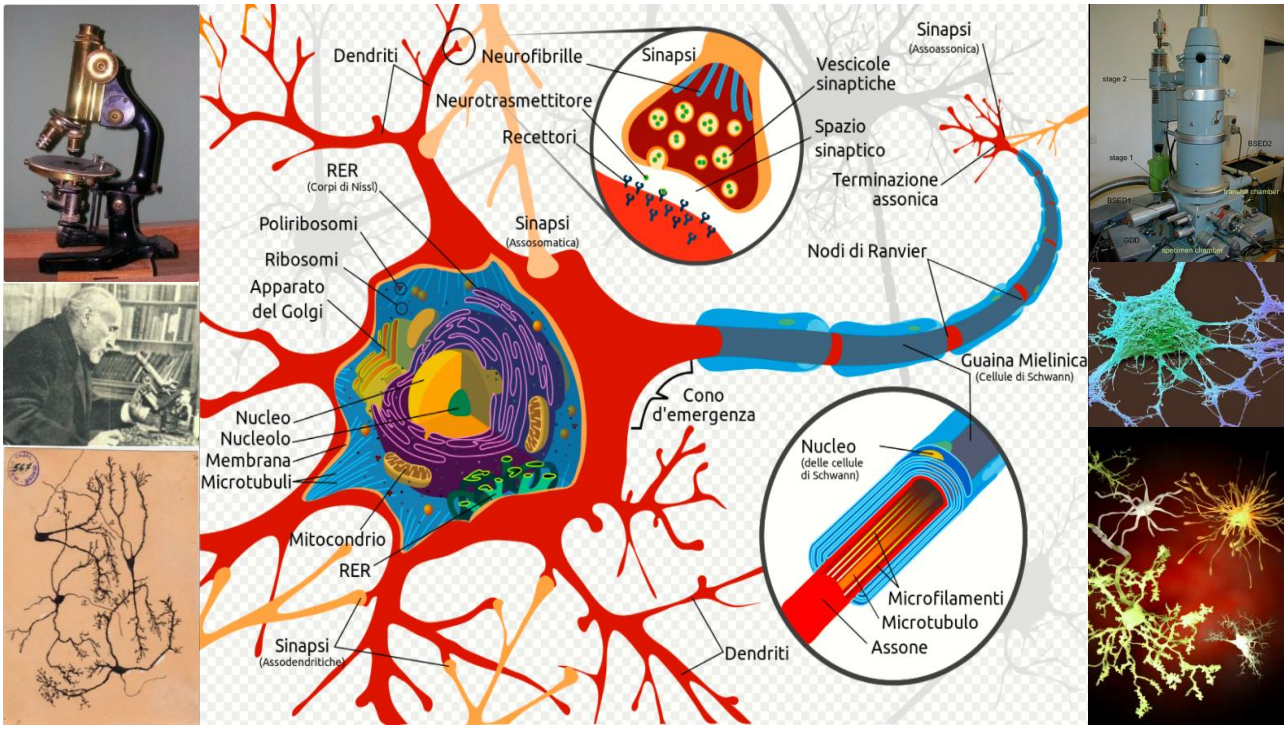
Camillo Golgi



1906 Premio Nobel
per la Fisiologia e la Medicina

Santiago Ramón y Cajal

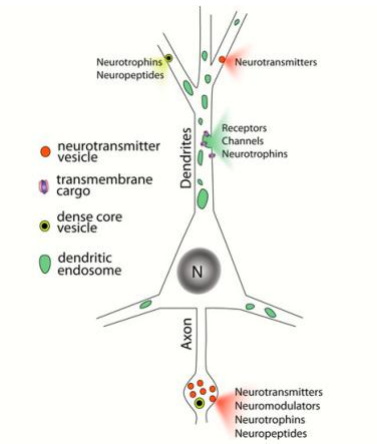
Che spettacolo inaspettato!
Filamenti neri sparsi, lisci e sottili,
oppure cellule nere spinose, spesse,
triangolari, stellate o fusiformi,
come disegni di inchiostro cinesi:
questo è il metodo di Golgi. (Cajal)



Dendritic trafficking for neuronal growth and plasticity

Michael D. Ehlers

Biochem. Soc. Trans. (2013) 41, 1365–1382



Neurons possess an **immense surface area** and intricate geometry: this morphological complexity is critical for the **neural circuit** formation in order to organize **cell–cell communication**.

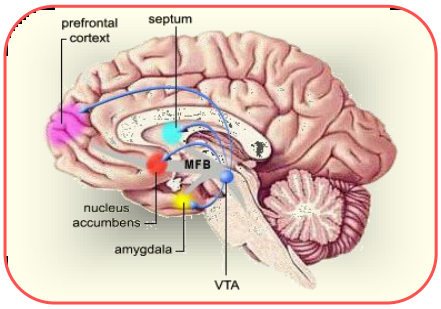
The adaptive plastic properties of neurons, synapses and circuits have been classically studied by measurement of **electrophysiological properties**, ionic conductances and excitability.

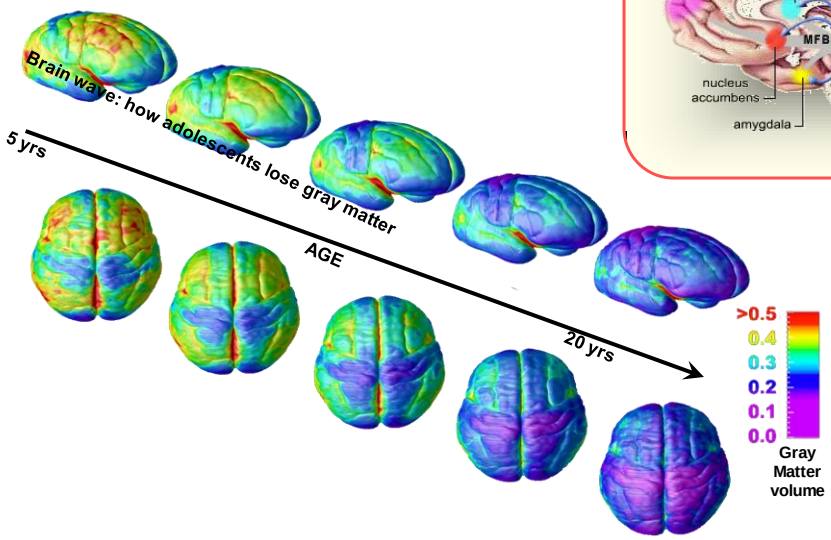
These highly differentiated cells utilize common eukaryotic **cellular machinery** to decode, integrate and propagate signals in the nervous system.

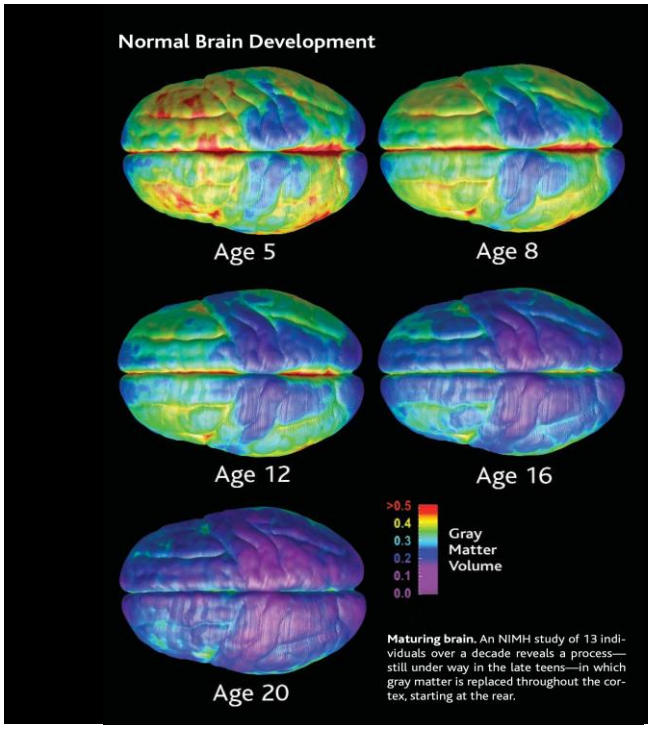
La plasticità dei neuroni

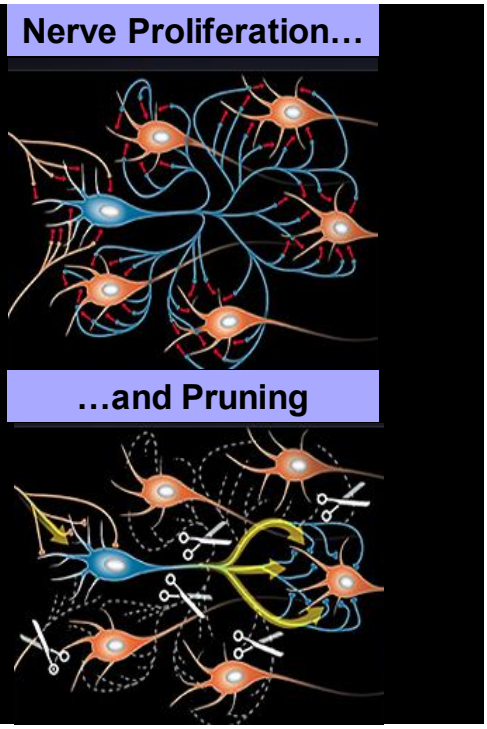
Earlier Development of the Accumbens Relative to Orbitofrontal Cortex Might Underlie Risk-Taking Behavior in Adolescents

A. Galvan et al., J. Neurosci, 2006









BIOCHEMISTRY (Moscow) Vol. 82 No. 3 2017

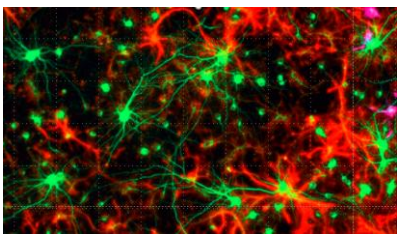
Molecular Mechanisms of Neuroplasticity: An Expanding Universe

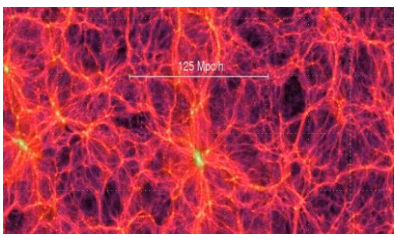
N. V. Gulyaeva

Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences,

Biochemical processes in synapses and other neuronal compartments underlie **neuroplasticity** (functional and structural alterations in the brain enabling adaptation to the environment, learning, memory, as well as rehabilitation after brain injury).

This basic molecular level of brain plasticity covers numerous specific proteins (enzymes, receptors, structural proteins, etc.) participating in many coordinated and interacting signal and metabolic processes, their modulation forming a molecular basis for brain plasticity.

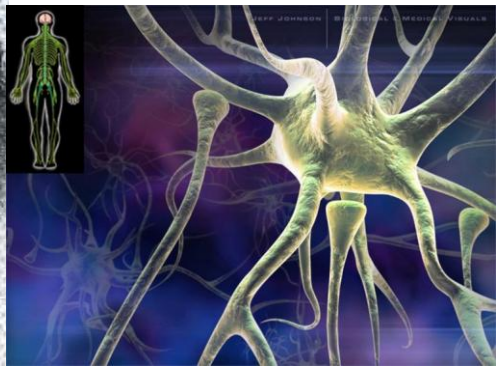




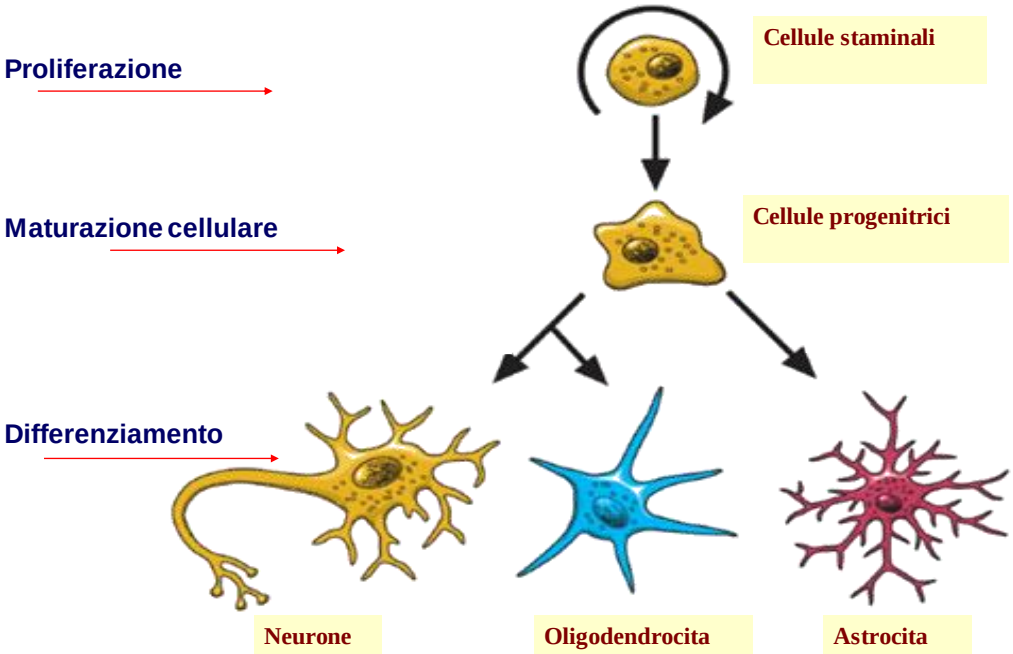
The Quantitative Comparison Between the Neuronal Network and the Cosmic Web

F. Vazza and A. Feletti

"I neuroni sono cellule perenni"



Processo di Neurogenesi



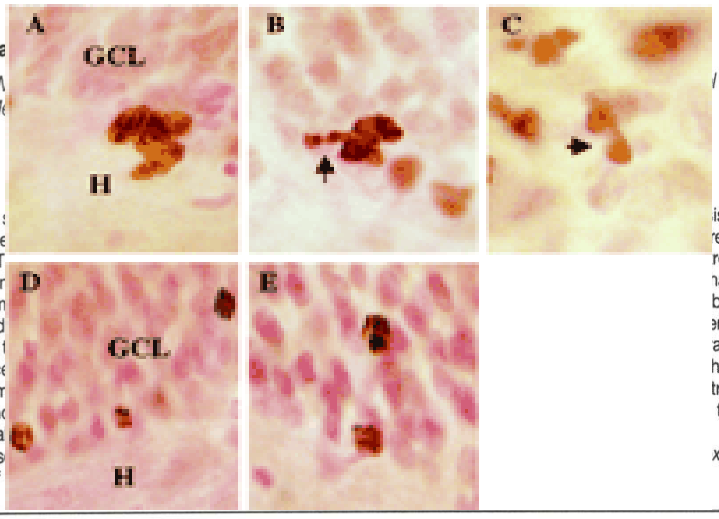
The Journal of Neuroscience, December 15, 2000, 20(24):9104–9110

Chronic Antidepressant Treatment Increases Neurogenesis in Adult Rat Hippocampus

Jessica E. Ma

Laboratory of M
Connecticut Me

l of Medicine,



Recent studies s
hippocampal ne
of depression. T
of antidepressar
using the thym
marker for divid
antidepressant t
BrdU-labeled ce
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upregulation of

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ers. These findings
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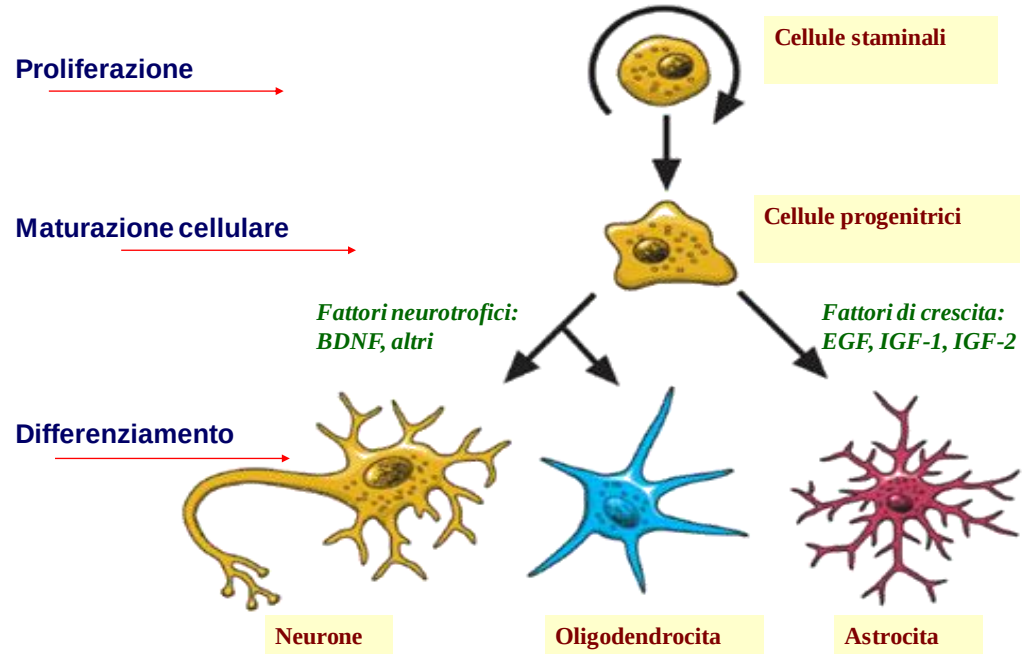
hich antidepressant
trophy and loss of
to the therapeutic

xetine; tranylcypro-

Processo di Neurogenesi

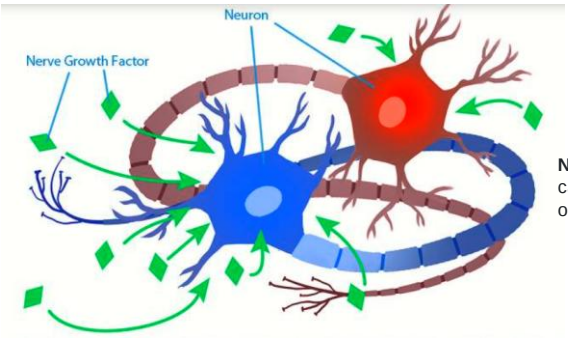


The Multiple Life of Nerve Growth Factor: Tribute to Rita Levi-Montalcini (1909-2012) Balkan Med J 2013; 30: 4-7

Luigi Aloe[1], George N. Chaldakov[2]

At the end of the 19th century, it was envisaged by **Santiago Ramon y Cajal,** but not proven, that life at the neuronal level requires trophic support.

The proof was obtained in the early 1950's by **Rita Levi-Montalcini** with the discovering the **nerve growth factor (NGF).**

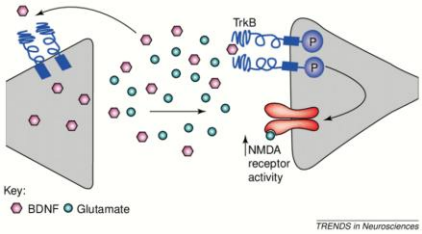


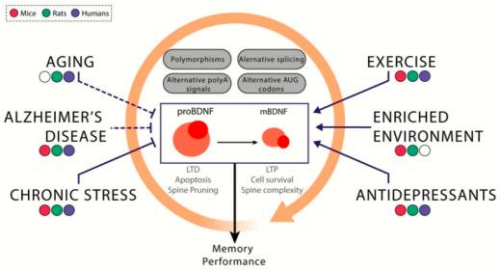
Nerve growth factor (NGF) is one of a group of small protein-like molecules called **neurotrophins** (BDNF is another) that are responsible for neurogenesis or the development of new neurons and for the maintenance of mature ones.

Role of BDNF epigenetics in activity-dependent neuronal plasticity

Nina N. Karpova Neuropharmacology 2013

Brain-derived neurotrophic factor (BDNF), is a protein that, in humans, is encoded by the BDNF gene. BDNF is a member of the neurotrophin family of growth factors, which are related to the canonical nerve growth factor.





Brain-derived neurotrophic factor (BDNF) is involved on neuronal development and plasticity.

Impaired control of neuronal activity-induced BDNF expression mediates various **neurological and psychiatric disorders**.

Environmental stimuli (pharmacological compounds, physical and learning exercises, stress exposure), lead to activation or inhibition of BDNF production.

Acta Medica Alanya
2021;5(1): 1-3

What is neuroplasticity? Why it is important?: Types and its basic mechanisms

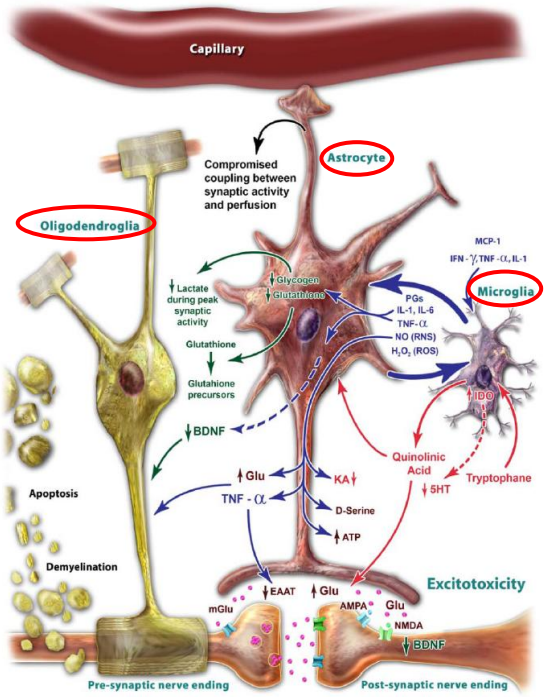
Burak Yulug , Ahmet Aslan

neuroplasticity shows at least three forms :

learning and post-trauma processes
that play an essential role during neurodevelopment and brain repair

activity-dependent plasticity,
related to hippocampal reorganization during the learning and memory process

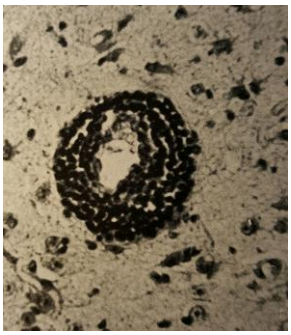
cross-modal plasticity
for example the visual cortex's compensatory potential
in overtaking the processing of tactile stimuli in blind people



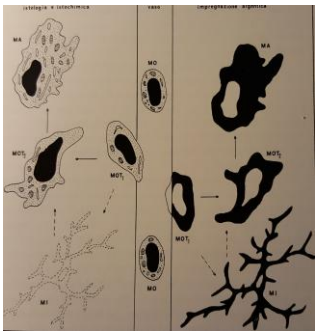
La glia non ha solamente funzioni
di **sostegno**
ma partecipa attivamente
al funzionamento delle **sinapsi**

Dal **neurone – neurone**
alla sinapsi **tripartita**

1983



manicotto di infiltrazione macrofagica perivasale

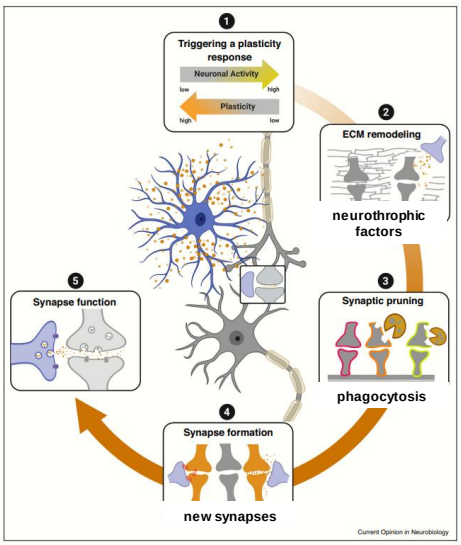


dai macrofagi alla microglia

Fabiani, Brignolio, Torta, 1983

Star power: the emerging role of astrocytes as neuronal partners during cortical plasticity **Current Opinion in Neurobiology 2021, 67:174–182**

Jerome Wahis, Maroussia Hennes, Lutgarde Arckens and Matthew G Holt



glial cells, in particular **astrocytes**,
are key regulators of neuronal plasticity.

The central panel shows a highly branched astrocyte (blue),
with processes enwrapping pre-synaptic and post-synaptic elements (grey),
forming a **tripartite synapse** (expanded view in box) that is a core unit of the plasticity response

Step 1: An initial decrease, or complete loss, of (inhibitory) neuronal activity (yellow),
leads to an **astrocyte response**,
which either initiates or enhances plasticity (orange).

Step 2: Extracellular matrix (ECM) is changed
through production of **neurothrophic factors** (orange dots),

Step 3: Inactive synapses show an '**eat-me-signal**' leads
to their phagocytosis by glial cells (orange pac man).

Step 4: Reactivation of deprived cortical regions depends
on the **formation of new synapses** (orange).

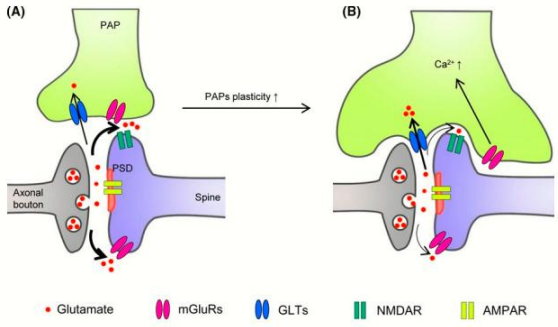
. Step 5: Astrocytes play key roles in **ongoing synaptic function**.
Through uptake and recycling of neurotransmitters,
provision of lactate to neurons for energy production, etc

Astrocytes can also monitor local synaptic activity through
the activation of cell surface receptors (in blue)

CNS Neurosci Ther. 2019;25:665–673.

Astrocyte morphology: Diversity, plasticity, and role in neurological diseases

Bin Zhou | Yun-Xia Zuo | Ruo-Tian Jiang

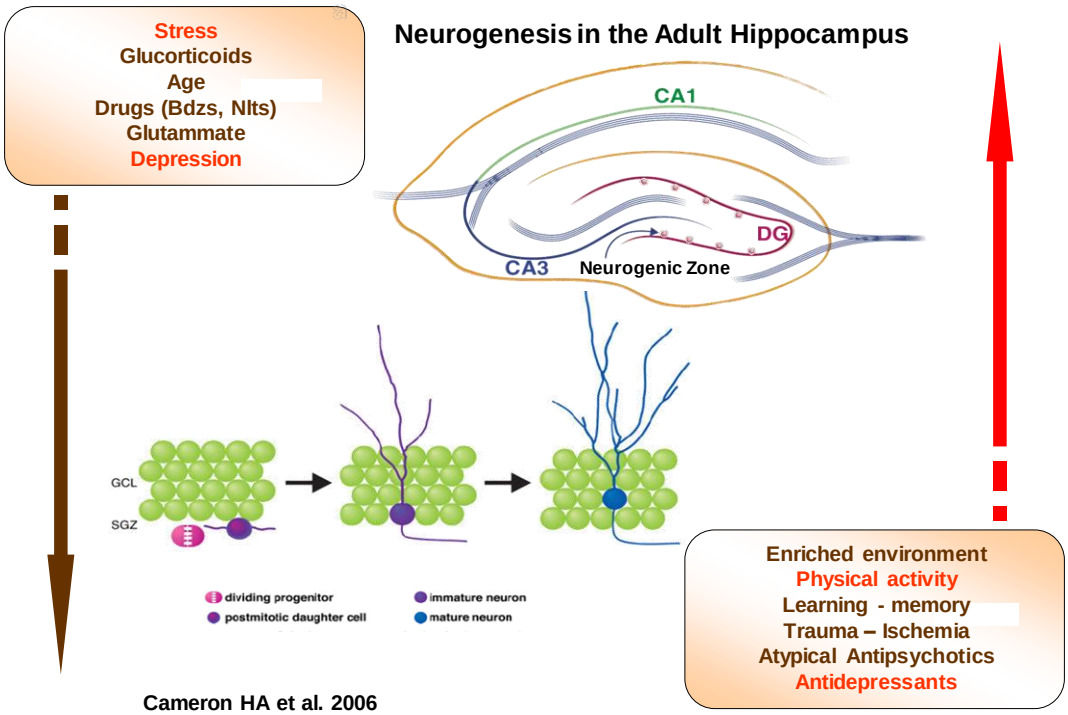


Astrocytes are the **most abundant glial cells in the central nervous system** (CNS) and participate in synaptic, circuit, and behavioral functions.

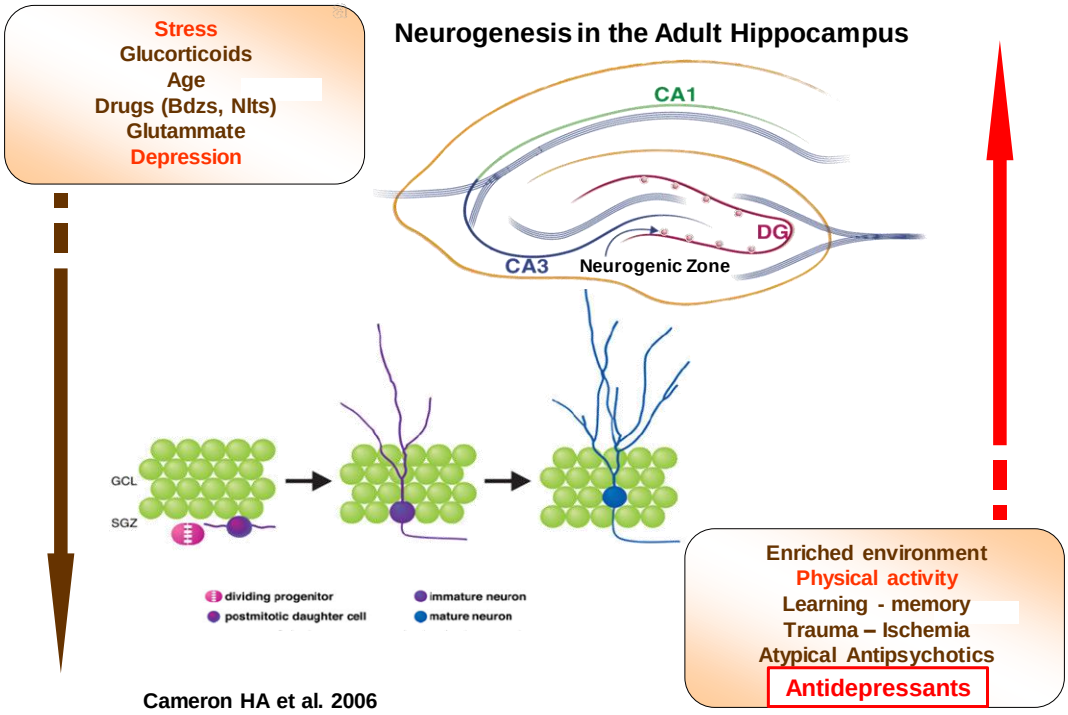
This highly complex morphology comes in contact with synapses, blood vessels, and other glial cells.

Perisynaptic astrocytes processes (PAPs) regulates the astrocytic coverage of synapse and synaptic transmission.

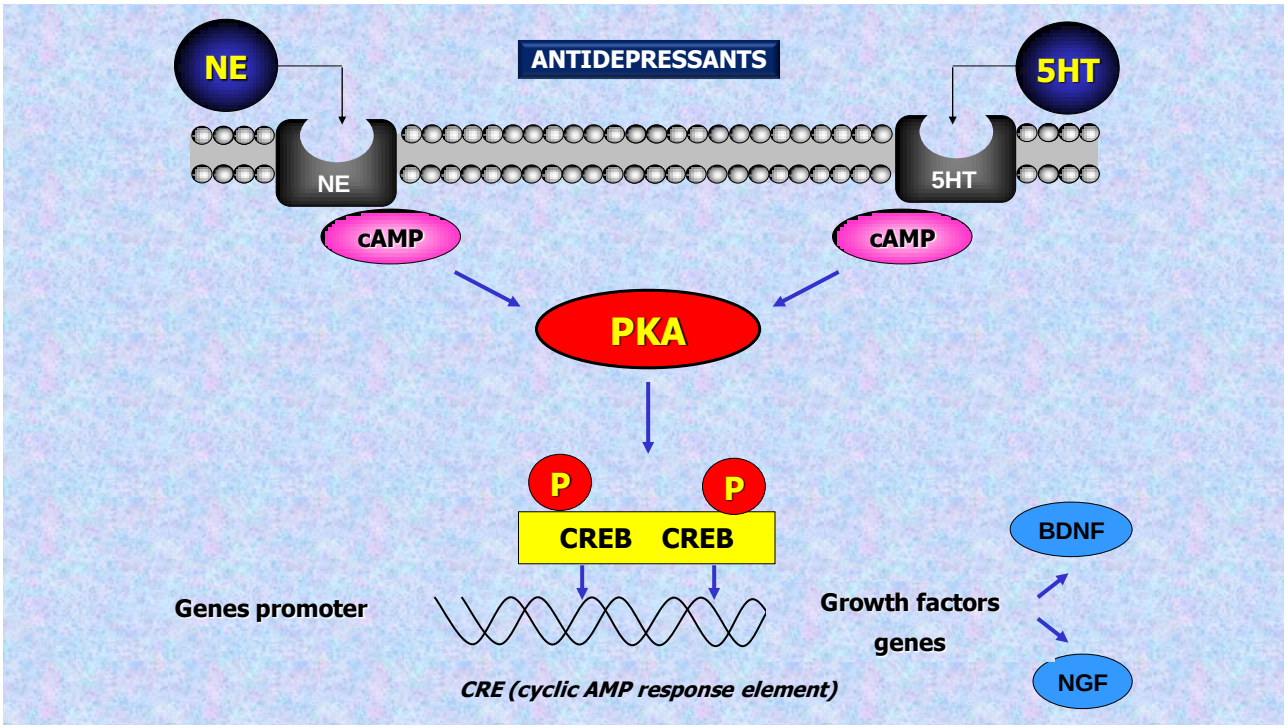
Increased PAPs plasticity, induced by mGluRs-mediated Ca2+ signals, enhances astrocytic coverage of synapse, with increased glutamate uptake



Cameron HA et al. 2006



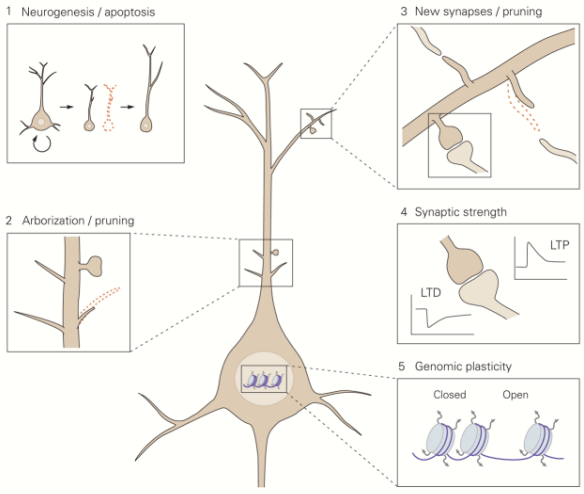
Cameron HA et al. 2006



Neuronal plasticity and antidepressant actions

Eero Castrén[1] and **René Hen**[2]

Trends Neurosci. 2013 May ; 36(5): 259–267.



Antidepressant treatments enhance plasticity and increase neurogenesis in the adult brain

1. Neurogenesis and selective apoptosis
induced by antidepressants and EE, leads to the increased survival of newborn neurons .Neurons that fail to functionally integrate into the hippocampal circuitry are eliminated through apoptosis.

1. Arborization and pruning of axonal and dendritic branches.
branches containing synapses that successfully work are stabilized
whereas arbors without active synapses remain short-lived and are pruned.

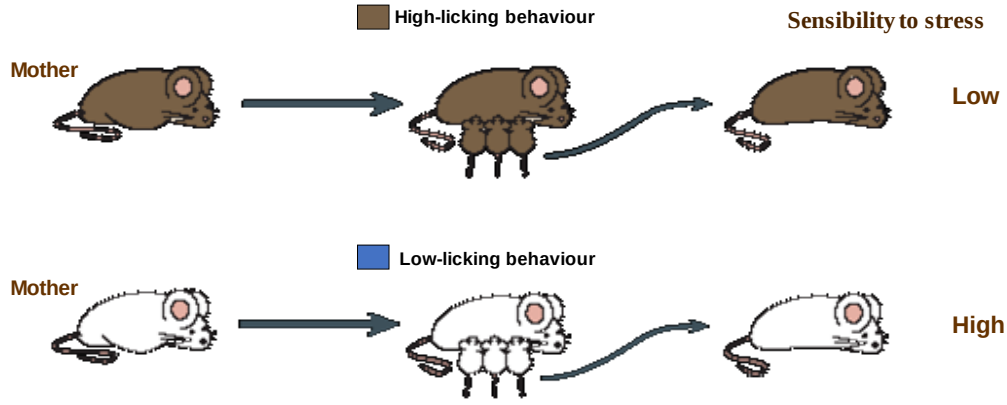
3. **Synaptogenesis and synaptic elimination**..
Synapses that are successfully activated are selected for stabilization, whereas contacts that fail to mediate activity collapse and are eliminated.

4. **Plastic regulation of synaptic strength**.
Information transfer through active synapses is potentiated through the process of **long-term potentiation** (LTP), whereas inactive or inappropriately active synapses are suppressed through **long-term depression** (LTD).

5. **Environmental activity** regulates the transcription and translation of effector genes involved in neuronal plasticity through transcriptional control and **epigenetic mechanisms**, such as remodeling of chromatin structure from a closed to an open state

Epigenetic programming by maternal behavior

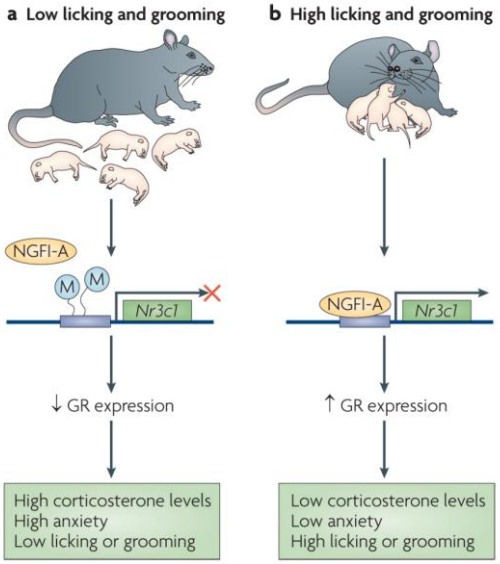
Ian C G Weaver[1,2], Nadia Cervoni[3], Frances A Champagne[1,2], Ana C D'Alessio[3], Shakti Sharma[1], Jonathan R Seckl[4], Sergiy Dymov[3], Moshe Szyf[2,3] & Michael J Meaney[1,2]

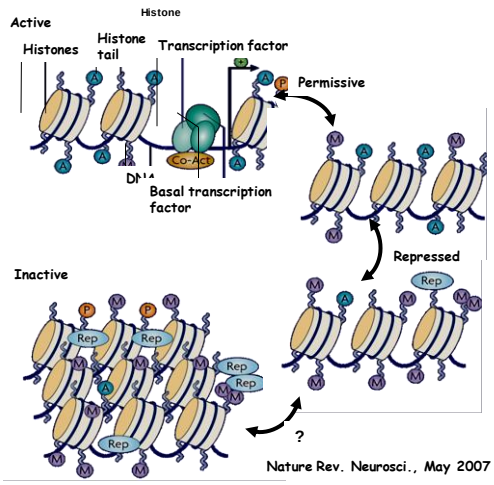


Modified by Nature Neuroscience, 2004

Epigenetic mechanisms of resilience

Epigenetics refers to stable changes in chromatin structure that underlie long-lasting alterations in gene expression and that are not associated with changes in DNA sequence

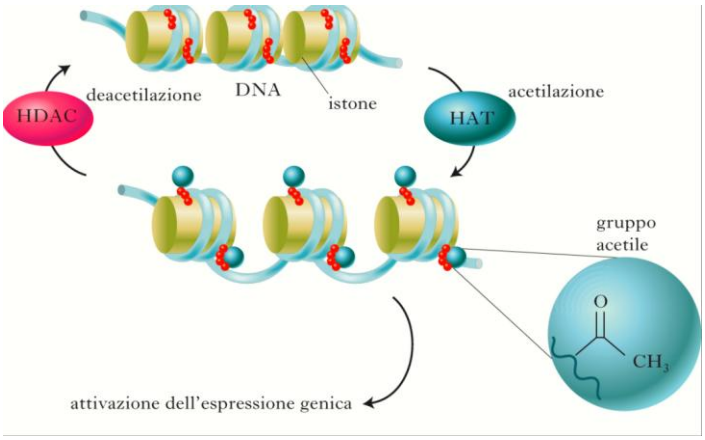




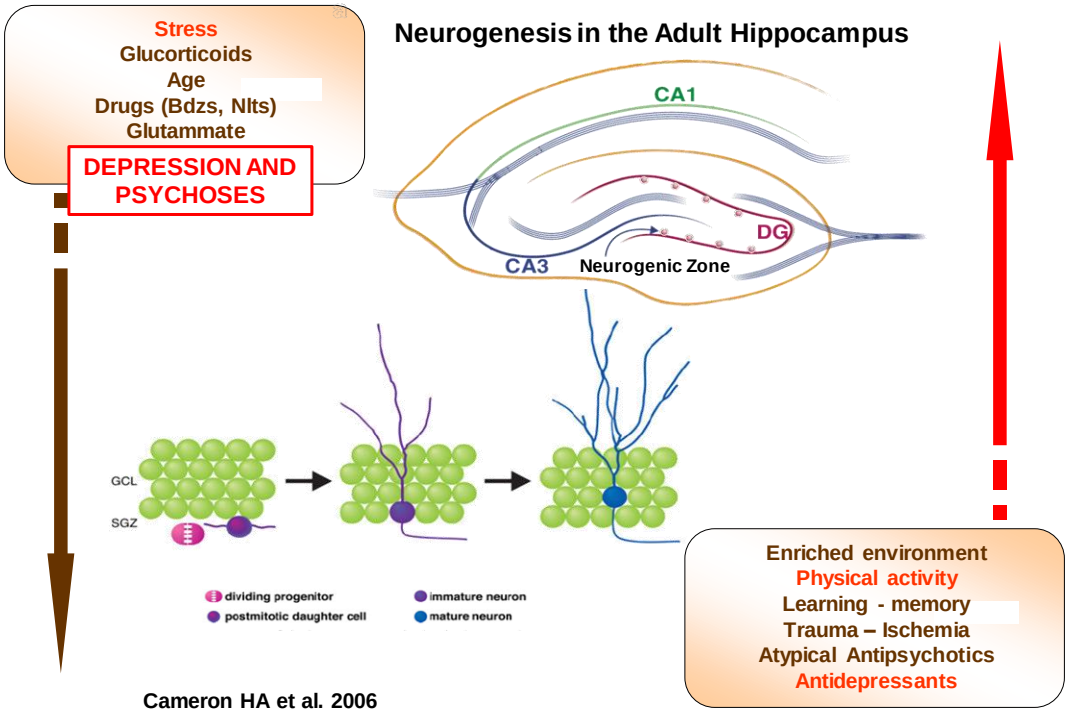
Histone Deacetylase (HDAC) Inhibitors - Emerging Roles in Neuronal Memory, Learning, Synaptic Plasticity and Neural Regeneration

Current Neuropharmacology, 2016, *14*, 55-71

Shabir Ahmad Ganai[†], Mahalakshmi Ramadoss[†] and Vijayalakshmi Mahadevan[*]

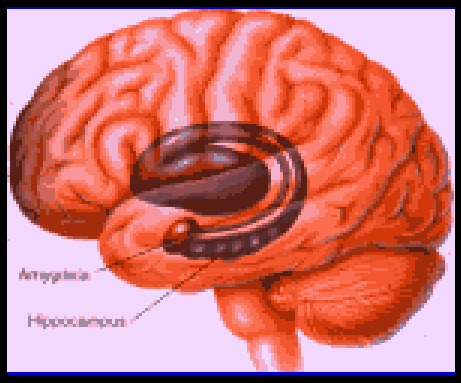


Histone Acetyl Transferases (HATs) and **Histone Deacetylases (HDACs)** are antagonistic enzymes that regulate gene expression through acetylation and deacetylation of histone proteins of DNA
HDAC inhibitors as potential drugs in neurological research and therapy.



Cameron HA et al. 2006

ATROPHY OF THE HUMAN HIPPOCAMPUS



- Cushing's disease
- Major Depression
- Bipolar Disease
- PTSD
- Schizophrenia
- Alzheimer Disease

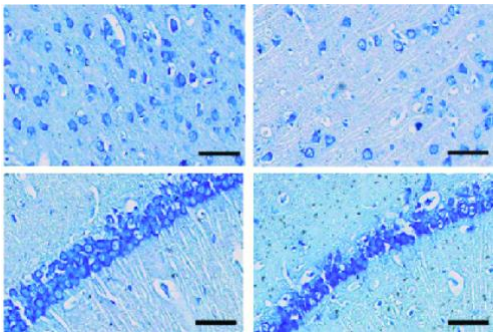
Psychosis is an extension of mood swings from the perspective of neuronal plasticity impairments

Medical Hypotheses 124 (2019) 37–39

T. Mizuno[a], H. Matsumoto[a,b], K. Mita[a], S. Kogauchi[a], Y. Kiyono[c], H. Kosaka[a], N. Omata[a,d,*]

depressive and manic states may be consecutive presentations of the same underlying neuronal plasticity, and that **moderate impairments** in neuronal plasticity **cause depressive states** while **further impairment** to neuronal plasticity **causes manic states.**

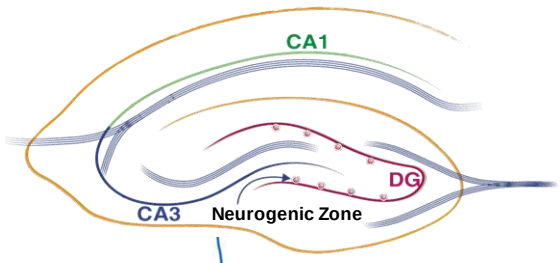
psychosis may also be considered a manifestation resulting from **additional impairments** to neuronal plasticity.



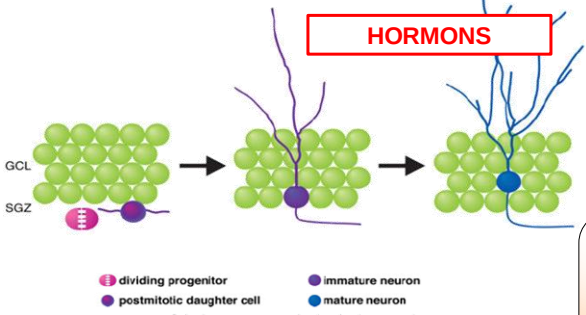
Normal neuronal plasticity → Normal Depressive Manic Psychotic → Impaired neuronal plasticity

Neurogenesis in the Adult Hippocampus

Stress
Glucorticoids
Age
Drugs (Bdzs, Nlts)
Glutammate
Depression



HORMONS



Enriched environment
Physical activity
Learning - memory
Trauma – Ischemia
Atypical Antipsychotics
Antidepressants

Cameron HA et al. 2006

Possible role of glial cells in the relationship between thyroid dysfunction and mental disorders

Mami Noda *

Frontiers in Cellular Neuroscience | June 2015

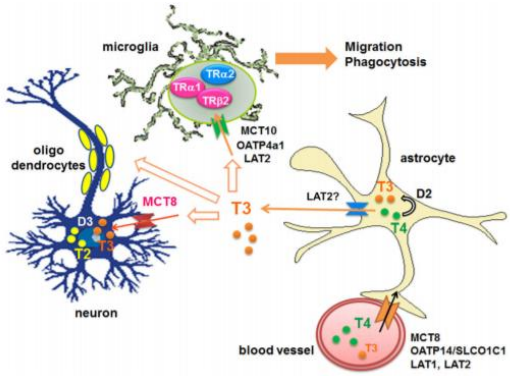
Thyroid Hormone in the CNS: Contribution of Neuron–Glia Interaction.

Mami Noda M.

Vitamins and Hormones, 2018

thyroid hormones (THs) are critical for the regulation of development and differentiation of neurons and neuroglia

T3 (3,3',5-triiodothyronine), an active form of TH, is important not only for neuronal development but also for differentiation of astrocytes and oligodendrocytes, and for microglial development



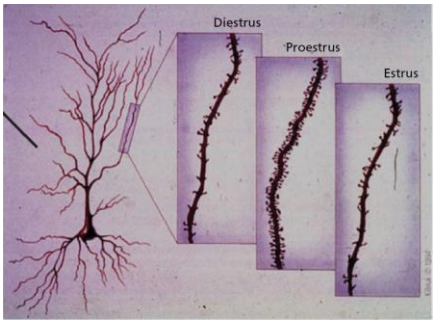
Therefore, dysfunction of THs may impair glial and neuronal function causing mental disorders.

Sex in the brain: hormones and sex differences

Jordan Marrocco, PhD; Bruce S. McEwen, PhD

Dialogues Clin Neurosci. 2016;18:.373-383

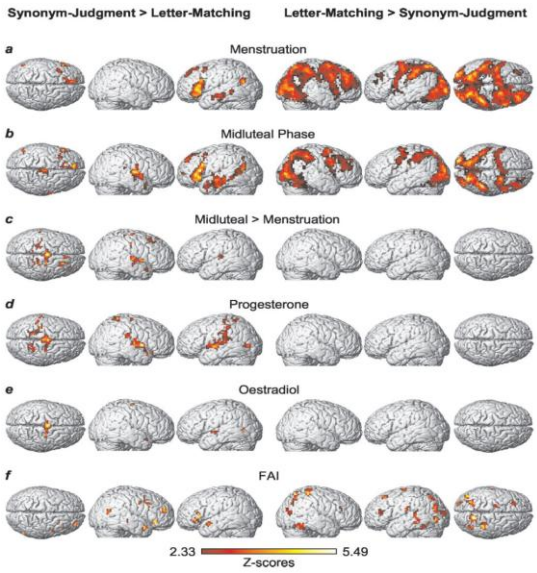
Many neural and behavioral functions are affected by estrogens, including mood, cognitive function, pain, and opioid sensitivity.

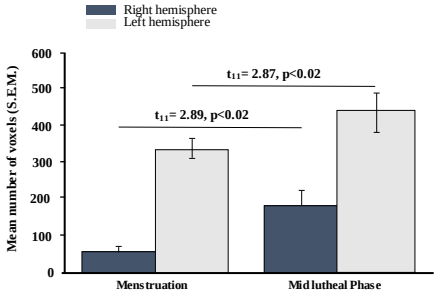


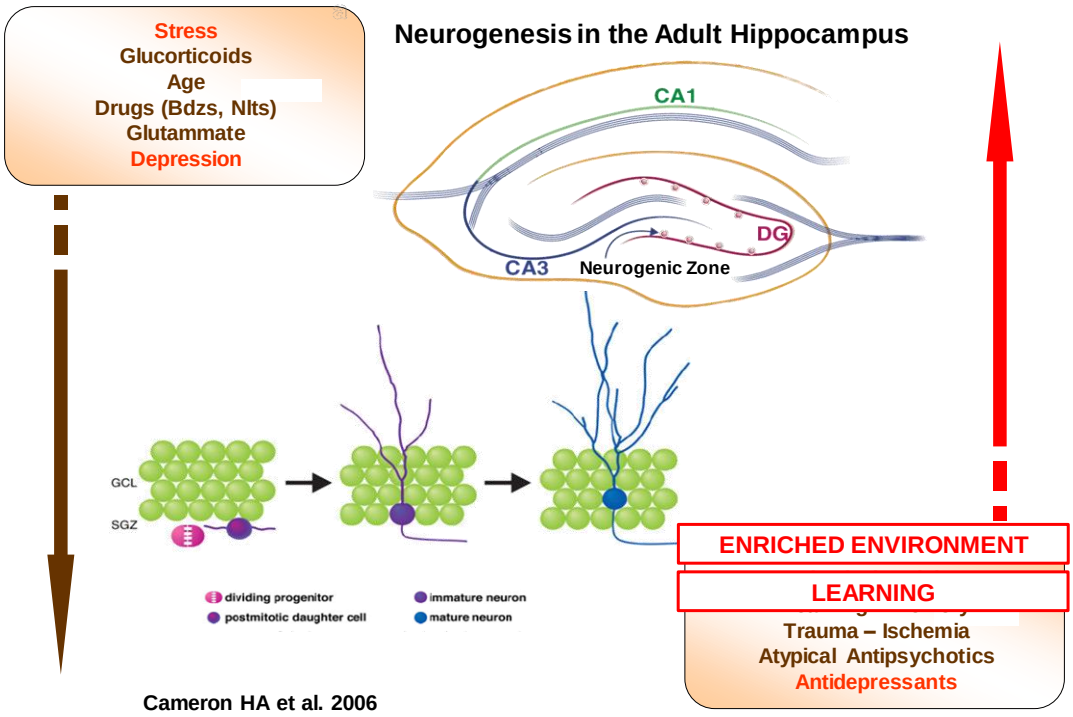
Estrogens play a key role in synapse remodeling in the hippocampus.

Dendritic spine density fluctuates over the estrus cycle.

"Menstrual cylcle-dependent neural plasticity in the adult human brain is hormone, task and region specific"
Fernandez G et al., *J Neurosci*, 2003





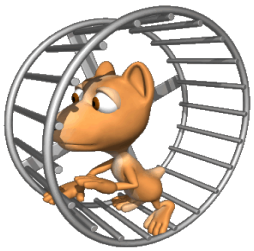


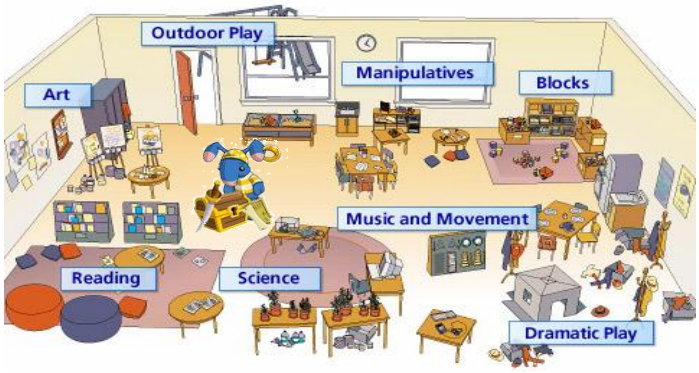
Cameron HA et al. 2006

Neuroscience, 2007

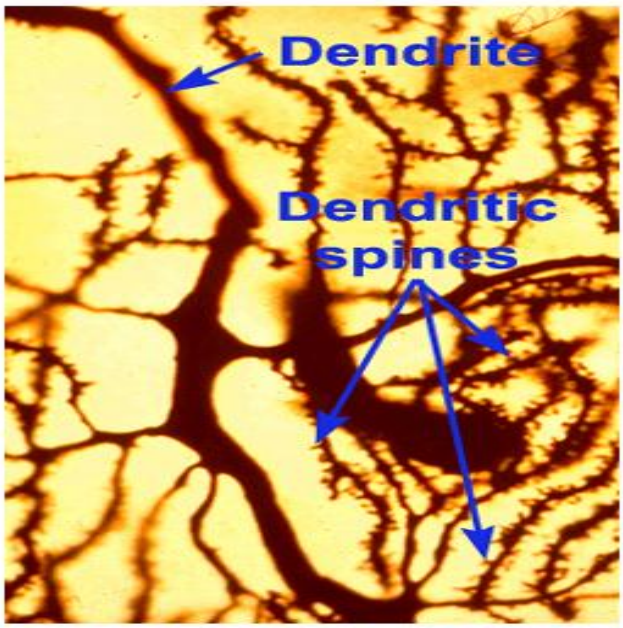
BDNF AND LEARNING: EVIDENCE THAT INSTRUMENTAL TRAINING PROMOTES LEARNING WITHIN THE SPINAL CORD BY UP-REGULATING BDNF EXPRESSION

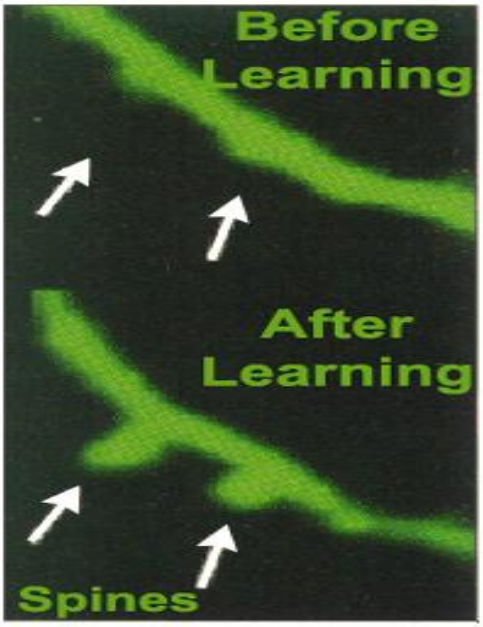
Gomez-Pinilla et al.





Dendritic Spines Increase with Learning





Exercise and cerebrovascular plasticity

T. Nishijima*,[1], I. Torres-Aleman†, H. Soya‡

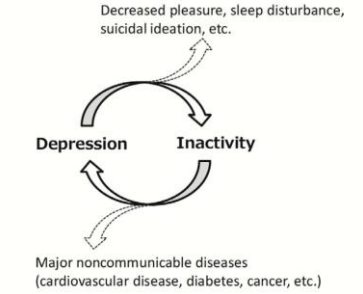
Progress in Brain Research (225) 2016

As Marcus Tullius Cicero (BC106–43) said that **"it is exercise alone that supports the spirits and keeps the mind in vigor"**, it has been empirically believed that **exercise, or higher levels of physical activity, can improve cognitive function and mental health**

Two decades of researches have successfully demonstrated that **exercise, or higher level of physical activity, is a powerful and nonpharmacological approach to improve brain function**.

Since the historical discovery that **exercise increases brain-derived neurotrophic factor (BDNF) gene expression in the rat hippocampus** (Neeper et al., 1995),

Exercise triggers improvements in neuronal plasticity, such as neurogenesis; however, exercise can improve cerebrovascular plasticity as well.

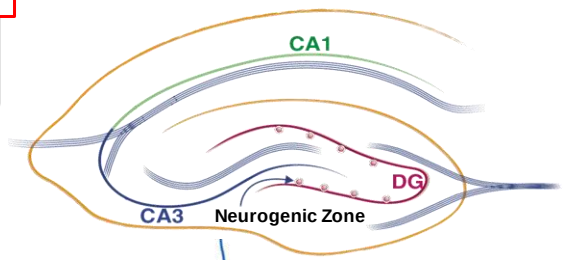


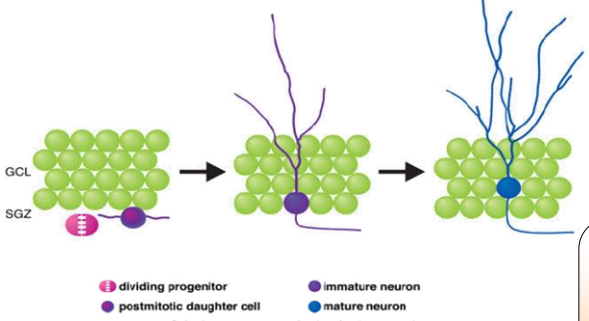
Epidemiological studies have demonstrated that **physical inactivity and depression are bidirectional**, which strongly suggests that these two form a negative chain reaction.

STRESS AND GLUCOCORTICOIDS

Age
Drugs (Bdzs, Nlts)
Glutammate
Depression

Neurogenesis in the Adult Hippocampus





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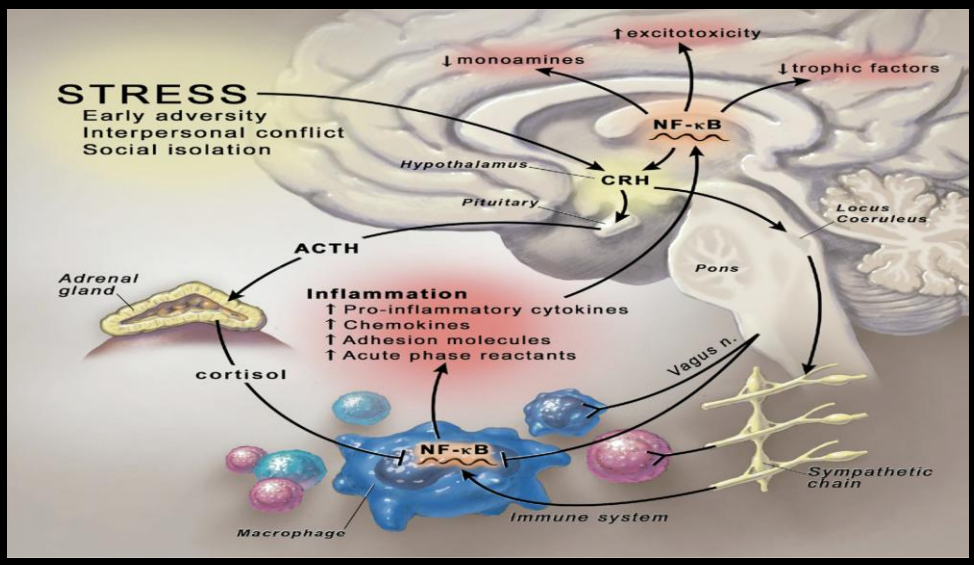
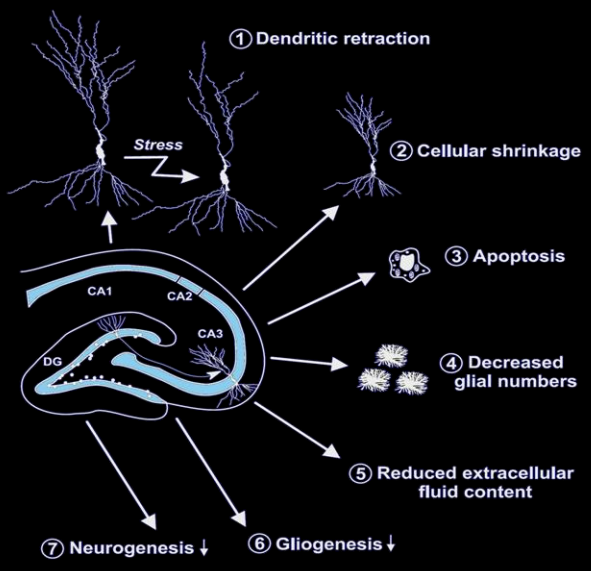
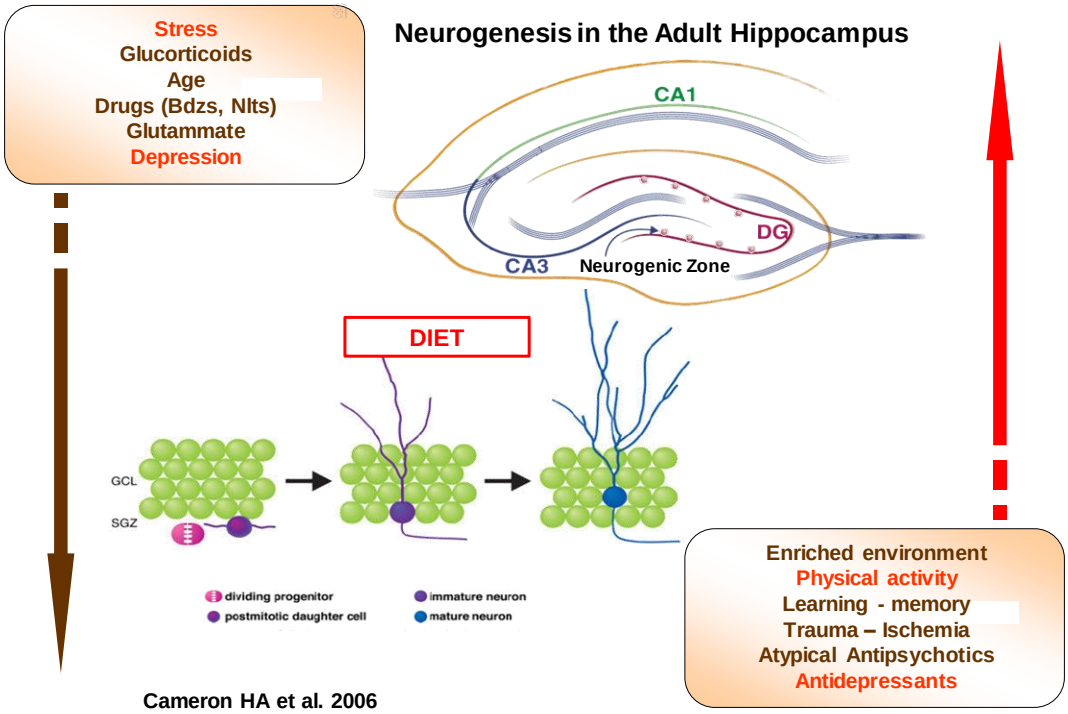


What may cause hippocampal volume loss as a consequence of stress?



these changes can be reversed by recovery or antidepressant treatment

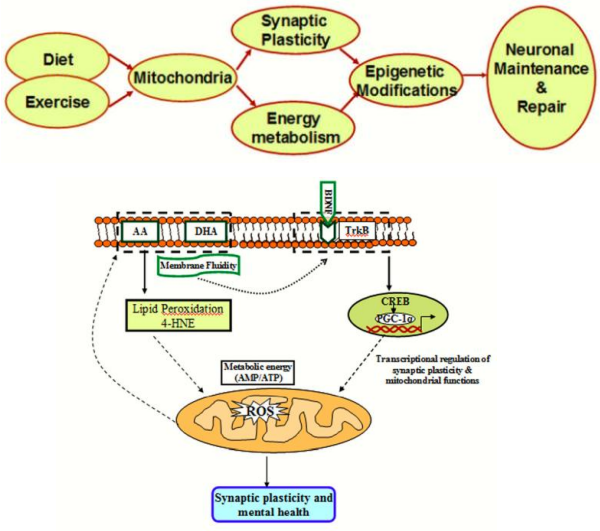


Cameron HA et al. 2006

Diet and cognition: interplay between cell metabolism and neuronal plasticity

Fernando Gomez-Pinilla and Ethika Tyagi

Curr Opin Clin Nutr Metab Care. 2013



Foods have the ability to benefit the brain:

Epigenetic regulation of neuronal plasticity appears as an important mechanism by which foods can prolong their effects on long term neuronal plasticity.

Oxidative stress promotes damage to phospholipids present in the plasma membrane such as the omega-3 fatty acid DHA, disrupting neuronal signaling.

Thus, **dietary DHA** seems crucial for supporting plasma membrane function, interneuronal signaling, and cognition. .

Dietary factors can affect neuronal signaling and energy metabolism.
The omega-3 fatty acid docosahexaenoic acid (DHA) can influence neuronal signaling by altering plasma membrane biodynamic or fluidity at synaptic regions

DHA is essential for maintaining **membrane integrity**, which can affect neuronal signaling through receptors embedded in the plasma membrane., i.e., BDNF receptor TrKB) via CREB.

Appius Claudius Caecus
(350 aC - 271 ac)

homo faber ipsius fortunae