## Învățarea și memoria

"Learning is the process by which we acquire knowledge about the world."

". . . memory is the process by which that knowledge of the world is <u>encoded</u>, <u>stored</u>, and later <u>retrieved</u>." Kandel 2000

-procese generate de interacțiunea dintre semnale/informație și sisteme

-învățarea-procesul prin care se achiziționează informația

-memoria este procesul prin care informația se codifică, stochează și actualizează

## Tipuri de memorie

Memorie innăscută

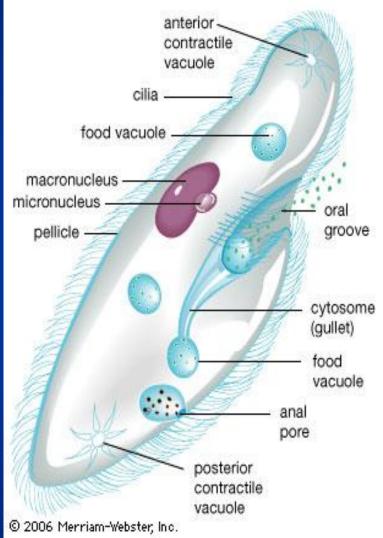
Memorie dobândită

Memoria ca fenomen

## Memorie innăscută













## Memorie innăscută







## Mean protein half-life:

- -budding yeast (cell cycle of ~1.5 hours) -
- ~43 minutes.
- -dividing mammalian cells (which have a cell cycle of ~24 hours) 0.5–35 hours and
- ~43 hours in non-dividing cells
- in mice brain, liver and blood 3-9 days
- -Nuclear pore proteins >1 month Lifetime

### Worm

- ->1 year Lifetime Rat
- Collagen- 117 years Half-life Human
- -mRNA Possibly indefinite Lifetime Plant seed

In trangenerational epigenetic inheritance, phenotypic information not encoded in DNA sequence is transmitted across generations. In germline-dependent mode, memory of environmental exposure in parental generation is transmitted through gametes, leading to appearance of phenotypes in the unexposed future generations. The memory is considered to be encoded in epigenetic factors like DNA methylation, histone modifications and regulatory RNAs

Environmental exposure may cause epigenetic modifications in the germline either directly or indirectly through primarily affecting the soma. The latter possibility is most intriguing because it contradicts the established dogma that hereditary information flows only from germline to soma, not in reverse. As such, identification of the factor(s) mediating soma to germline information transfer in transgenerational epigenetic inheritance would be pathbreaking

Factors such as RNAs and hormones, including neurohormones and europeptides, have previously been considered to potentially mediate soma to germline communication in epigenetic inheritance In last decade, small non-coding RNAs (sncRNAs) such as small interfering RNAs (siRNAs), microRNAs (miRNAs) and piwiinteracting RNAs (piRNAs) have emerged as master regulators of gene expression in eukaryotes

Transgenerational epigenetic inheritance: Focus on soma to germline information transfer. A. Sharma Progress in Biophysics and Molecular Biology (2012)

It is in this context that we would like to consider the genomic "darkmatter," one of the major mysteries of the postgenome era. Perhaps no other topic in contemporary genomics has inspired such diverse viewpoints as the 95+% of the genome, previously known as "junk DNA," that does not code for proteins.

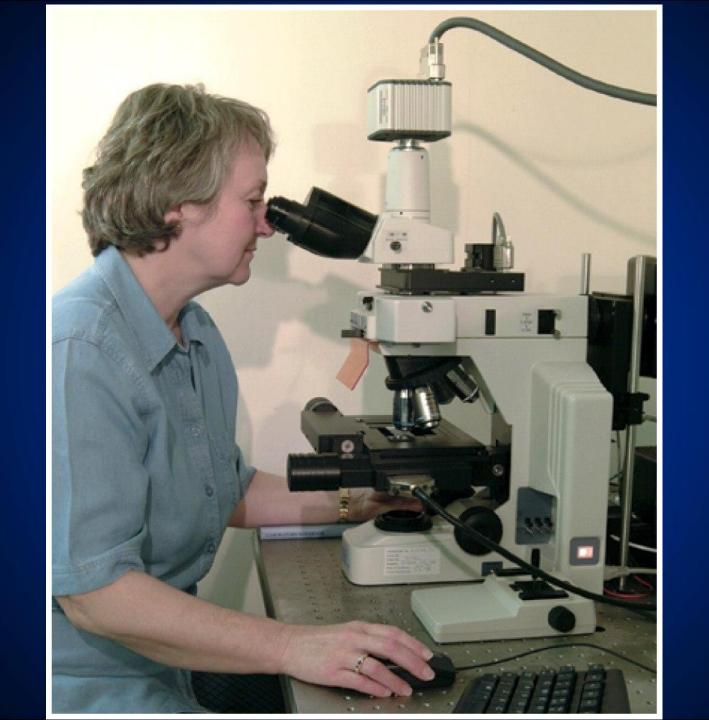
Considering only current knowledge of these networks, and without extrapolating to as yet undiscovered regulatory intricacies, their performance already gracefully exceeds that of systems biology models and mechanisms.

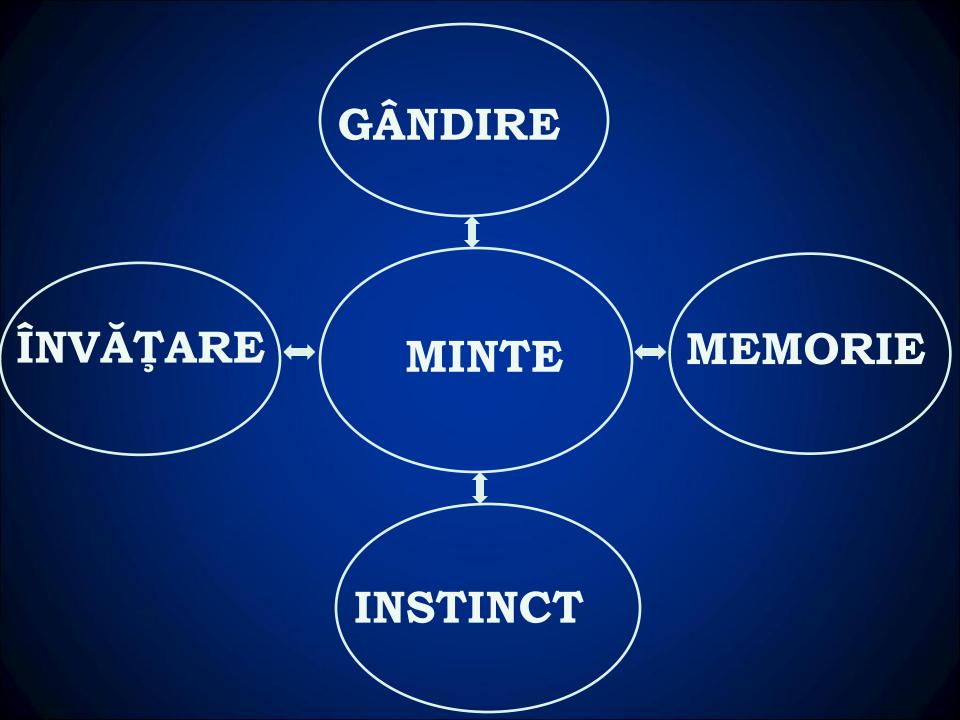
The observation that the percentage of "dark matter" genomic sequence correlates monotonically with organismal complexity, for every species sequenced to date, has inspired theories proposing a central role for these regions in the information processing of complex organisms

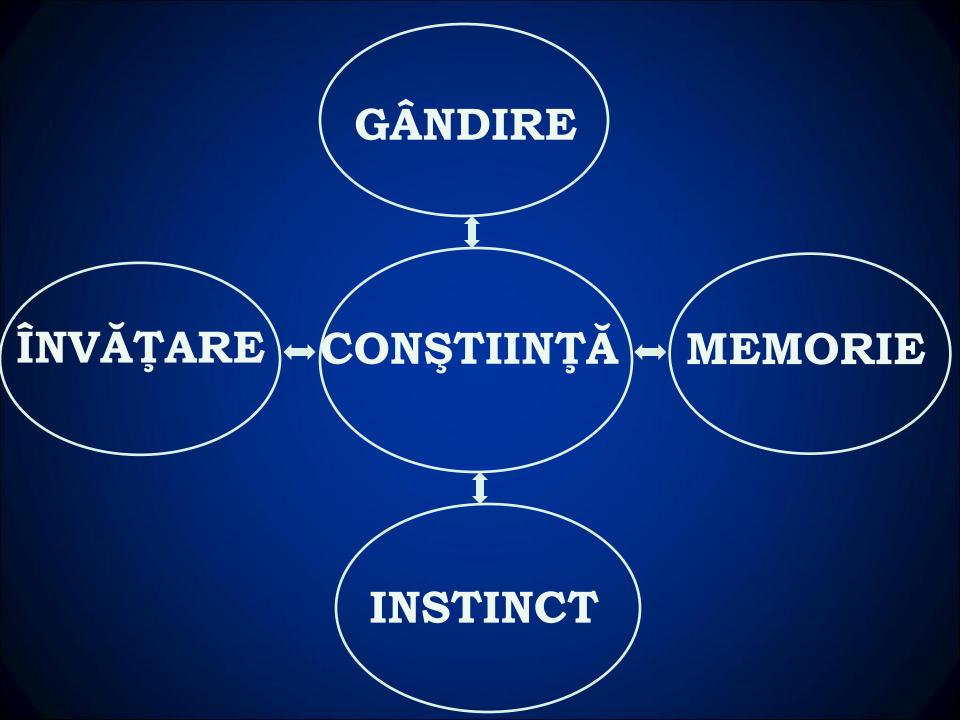
These lists of lncRNAs usually only cover a few percent of the genome, representing only a small fraction of the original pervasiveness of dark matter and typically, sample intergenic space as introns of known genes are usually assumed to represent pre-mRNAs. Partly due to this uncertainty, some authors have cast doubt on the importance of dark matter transcripts, labeling them transcriptional noise, or even arguing that they largely represent "fragments of known pre-mRNAs"

Dark matter RNA: an intelligent scaffold for the dynamic regulation of the nuclear information landscape. St.Laurent et al. Front. Genet. 2012.

## Memorie dobândită









**General Motors vs. Toyota** 

Using leading edge control, sensor and vision technologies, NASA and GM engineers and scientists came together at NASAs Johnson Space Center to build a new dexterous humanoid robot Robonaut2, capable of working side by side with people whether that means helping GM create safer cars and safer manufacturing plants or assisting NASA astronauts on dangerous space missions.

http://www.nasa.gov/mission\_pages/station/main/robonaut.html



The seat of the soul and the control of voluntary movement are to be sought in the HEART

The BRAIN is an organ of minor importance, perhaps necessary to cool the blood

Aristotel 384-322 î.c.- doctrina inexcitabilității cerebrale → 1870

Medicul regelui Filip cel frumos scrie "creierul este... rece și umed pt. a diminua extrema căldură și uscăciune a inimii, alb pt. a fi ca o tabula rasa și a primi orice imagine, lax și moderat de vâscos pt. ca lucrurile percepute să-l străbată ușor... 1300

Luigi Galvani (1791) - curentul
bioelectric
R. Caton (1875) primele cercetari
experimentale asupra curentilor
electrici cerebrali
Waldeyer (1891)-definește NEURONUL

Wilhelm His, August Forel Ramon y Cajal 1906 - TEORIA NEURONALĂ

Gh. Marinescu (1909) - La cellule nerveuse



Profesorul Dr. G. MARINESCU la vârsta de 60 ani.

#### LA

## CELLULE NERVEUSE

PAR

#### LE DR G. MARINESCO

Professeur de Clinique des Maladies nerveuses: à l'Université de Bucarest.

PRÉFACE DE M. LE Pr RAMON Y CAJAL (DE MADRID)

TOME PREMIER

Avec 90 figures dans le texte.

#### PARIS

OCTAVE DOIN ET FILS, ÉDITEURS

8, place de l'odéon, 8

1909

Tous droits réservés.

## Palay, De Robertis, Palade (1956) - confirmă teoria neuronală

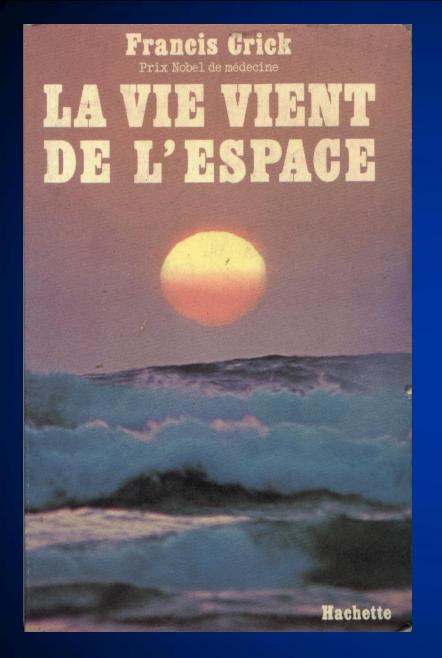
Erwin Neher, Bert Sakmann (1991) PN pentru tehnica de patch clamp

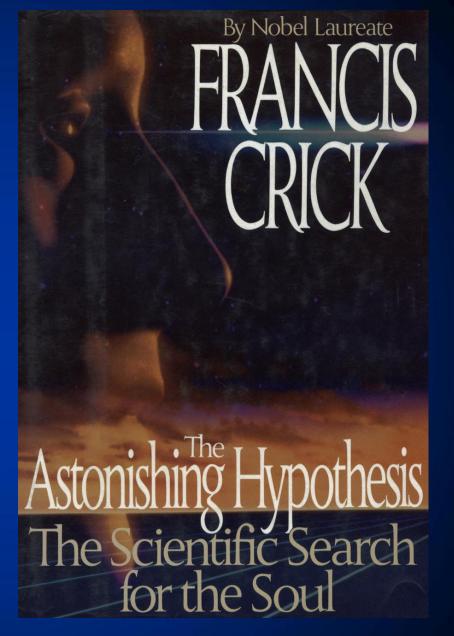
#### Nobel Prize laureates with research interests in neuroscience

- 1904 Ivan Pavlov "in recognition of his work on the physiology of digestion, through which knowledge on vital aspects of the subject has been transformed and enlarged"
- 1906 Camillo Golgi & Santiago Ramon y Cajal "in recognition of their work on the structure of the nervous system"
- 1911 Allvan Gullstrand "for his work on the dioptrics of the eye"
- 1914 Robert Bárány "for his work on the physiology and pathology of the vestibular apparatus"
- •1922 AV Hill for numerous precise measurements of the biophysics of nerves and muscles
- 1932 Sir Charles Sherrington & Edgar Adrian "for their discoveries regarding the functions of neurons"
- 1936 Sir Henry Dale & Otto Loewi "for their discoveries relating to chemical transmission of nerve impulses"
- 1944 Joseph Erlanger & Herbert Gasser "for their discoveries relating the highly differentiated functions of single nerve fibers"
- 1949 Walter Hess "for his discovery of the functional

- 1961 Georg von Békésy "for his discoveries of the physical mechanism of stimulation within the cochlea"
- 1963 Sir John Eccles, Alan Hodgkin & Andrew Huxley
- "for their discoveries concerning the ionic mechanisms involved in excitation and inhibition in the peripheral and central portions of the nerve cell membrane"
- 1967 Ragnar Granit, Haldan Hartline & George Wald "for their discoveries concerning the primary physiological and chemical visual processes in the eye"
- 1970 Sir Bernard Katz, Ulf von Euler & Julius Axelrod
- "for their discoveries concerning the humoral transmitters in the nerve terminals and the mechanism for their storage, release and inactivation"
- 1973 Karl von Frisch, Konrad Lorenz & Nikolass Tinbergen – "for their discoveries concerning organization and elicitation of individual and social behavior patterns"
- 1977 Roger Guilleman & Andrew Schally- "for their discoveries concerning the peptide hormone production in the brain"

- 1981 Roger Sperry "for his discoveries concerning the functional specialization of the cerebral hemispheres"
- 1981. David Hubel & Torsten Wiesel "for their discoveries concerning information processing in the visual system"
- 1986 Stanley Cohen & Rita Levi-Montalcini "for their discoveries of growth factors"
- 1991. Erwin Neher, Bert Sakmann "for their discoveries concerning the function of single ion channels in cells"
- 1997. Stanley Prusiner "for his discovery of Prions
- a new biological principle of infection"
- 2000 Arvid Carlsson, Paul Greengard & Eric Kandel "for their discoveries concerning signal transduction in the nervous system"
- 2003 Paul Lauterbur & Peter Mansfield "for their discoveries concerning magnetic resonance imaging"
- 2004 Richard Axel & Linda Buck "for their for their discoveries of odorant receptors and the organization of the olfactory system"





# Mecanisme moleculare ale învățării și memoriei

I had progressed from the naive notion of trying to find the ego, id, and superego in the brain to the slightly less vague idea that finding the biological basis of memory might be an effective approach to understanding higher mental processes.

In a large sense, learning and memory are central to our very identity. They make us who we are

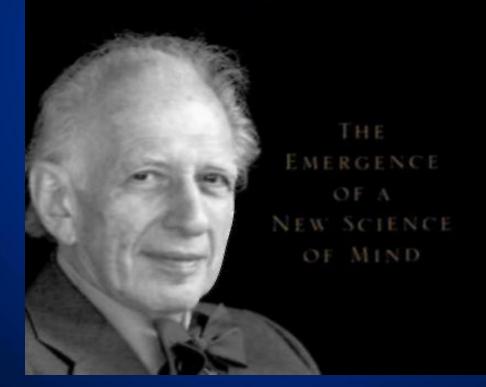
Understanding the human mind in biological terms has emerged as the central challenge for science in the twenty-first century. We want to understand the biological nature of perception, learning, memory, thought, consciousness, and the limits of free will. That biologists would be in a position to explore these mental processes was unthinkable even a few decades ago.

Until the middle of the twentieth century, the idea that mind, the most complex set of processes in the universe, might yield its deepest secrets to biological analysis, and perhaps do this on the molecular level, could not be entertained seriously.

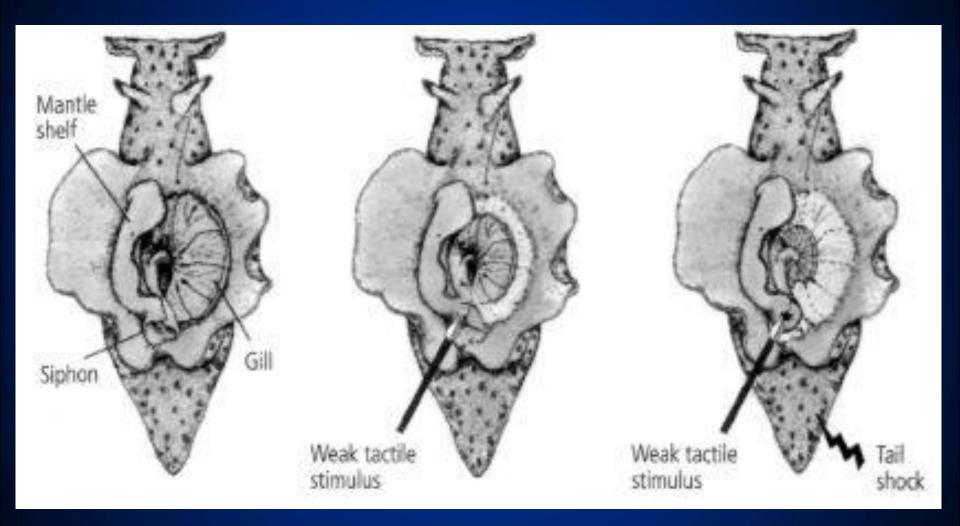


ERIC R. KANDEL

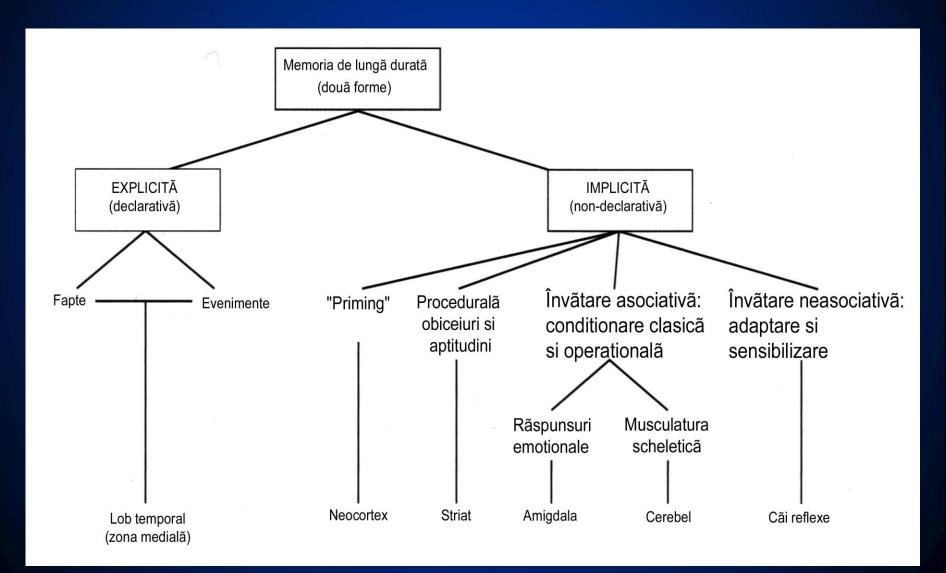
WINNER OF THE NOBEL PRIZE







#### Clasificarea memoriei



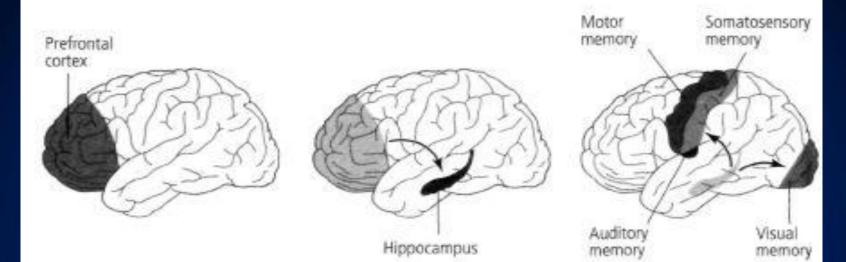
Explicit and implicit memories are processed and stored in different regions in the brain.

The explicit memory for people, objects, places, facts, and events is stored in the prefrontal cortex.

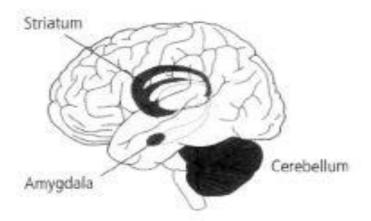
The implicit memories of skills, habits, and conditioning are stored in the cerebellum, striatum, and amygdala.

These memories are converted to longterm memories in the hippocampus and then stored in the parts of the cortex that correspond to the senses involved-that is, in the same areas that originally processed the information

#### **Explicit Memory Storage**



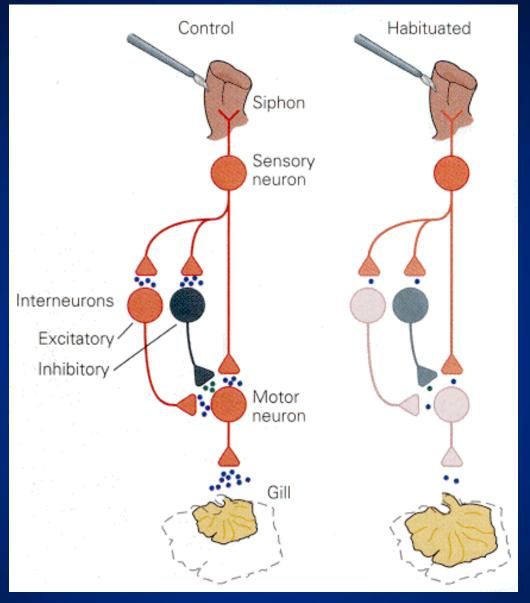
#### Implicit Memory Storage



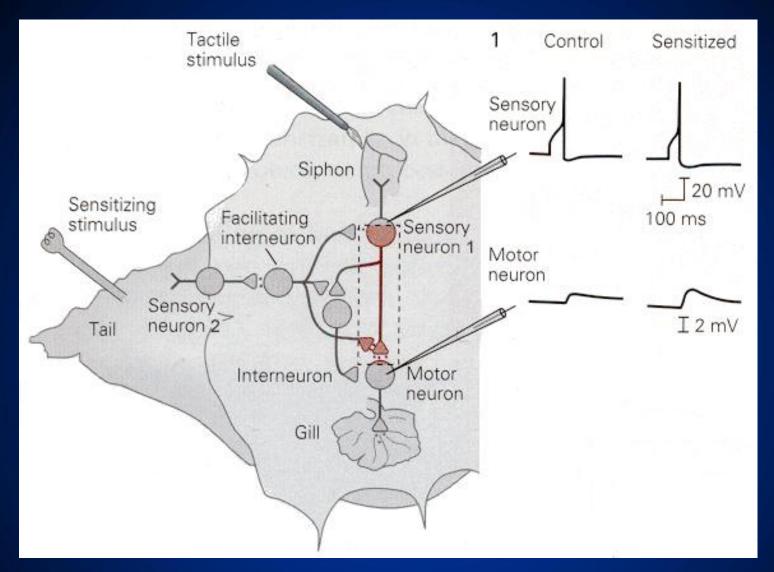
Mecanisme moleculare ale învățării și memoriei -declanșarea reflexului de retracție a sifonului și branhiei (siphon-and gill-withdrawal) poate fi obținută prin stimularea fie a sifonului fie a mantaleifiecare având inervație senzitivă diferită

### Mecanisme moleculare ale învățării și memeriei

-reflexul de retracție a sifonului și branhiei (siphon-and gill-withdrawal) poate fi îmbunătățit prin sensibilizare și condiționare clasică



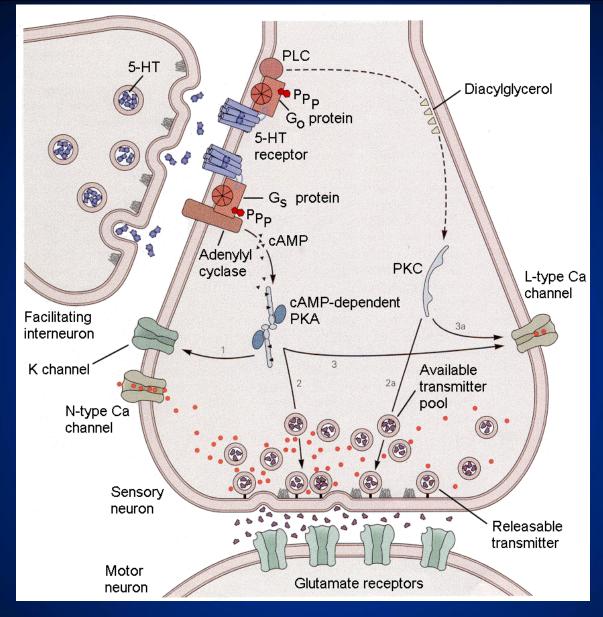
Habituarea implică neuroni senzitivi, motori și interneuroni



Sensibilizarea prin acțiunea unui stimul nociv

Condiționarea clasică -se obține prin asocierea stimulului condiționat (SC) acționând asupra oricărei zone cu un stimul necondiționat (SN) (nociv) acționând asupra cozii

-SC acționează cu 0,5 s înaintea SNe Mecanisme moleculare ale condiționării clasice -SN activează interneuronii modulatori (facilitatori)care vor activa neuronii senzitivi imediat după stimularea de către SC -Influxul de Ca<sup>2+</sup> indus de SC în neuronii presinaptici (facilitare) activează Ca-calmodulina



Facilitarea presinaptică implicată în senzitizarea de scurtă durată

## Mecanisme moleculare ale condiționării clasice

- Ca-calmodulina activată potențează răspunsul Ac din neuronii senzitivi la serotonină stimulând producerea de cAMP -Neuronul motor (postsinaptic) contine canale-receptor NMDA și non-NMDA

Mecanisme moleculare ale condiționării clasice -non-NMDA r sunt activați de SC în procesul de habituare și sensibilizare -NMDA r sunt activați de asocierea SC și SN? -asocierea SC și SN va crește eliberarea de glutamat inducând amplificarea depolarizării și dislocarea Mg din NMDAr

### Mecanisme moleculare ale condiționării clasice

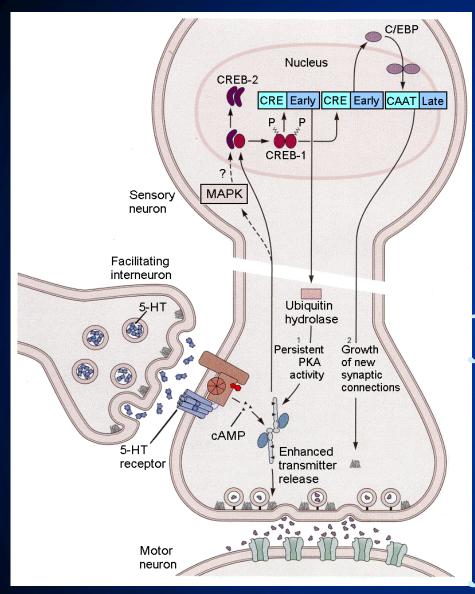
-creşterea Ca<sup>2+</sup> din neuronul motor va induce eliberarea unui mesager care va activa neuronul presinaptic

### Consolidarea memoriei implicite

- -transformarea memoriei de scurtă durată (MSD) în memorie de lungă durată (MLD)
- -traumatismele cerebrale și criza epileptică afectează MLD

## Consolidarea memoriei implicite

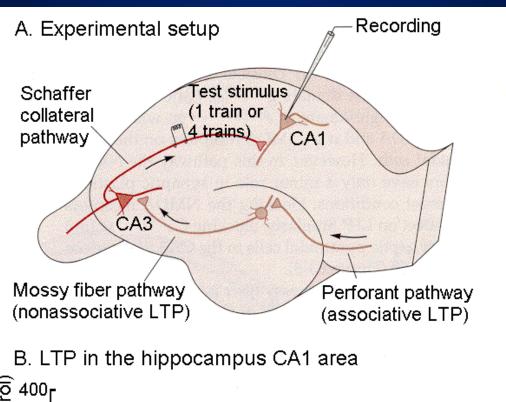
- -se realizeză prin trei mecanisme:
  - -exprimarea genică
  - -sinteza de noi proteine
  - -formarea de noi sinapse

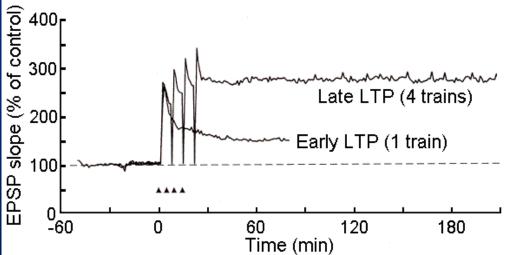


Facilitarea de lungă durată -MAPK-mitogen-activate kinase -CREB- cAMP-response element binding (CREB) protein -transcriptor factor -CRE-cAMP response element - promoter element C/EBP - trancription factor CAAT- DNA response

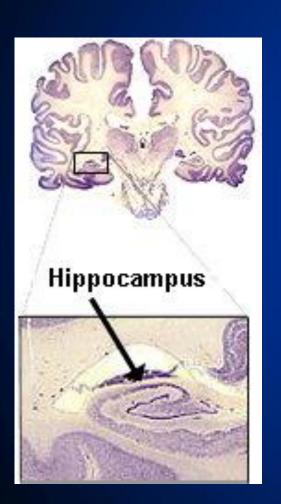
element

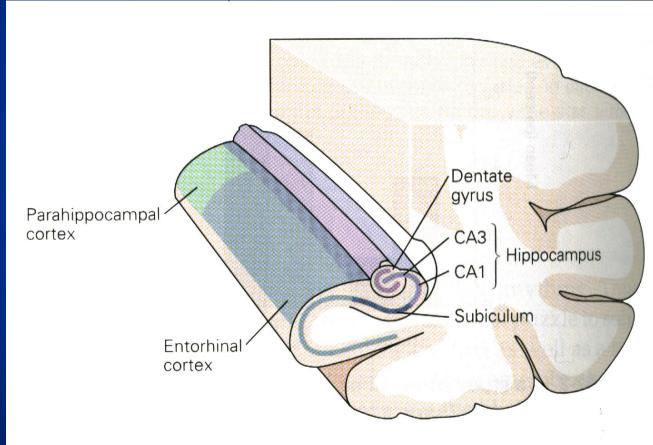
CREB 1/CREB 2 -?

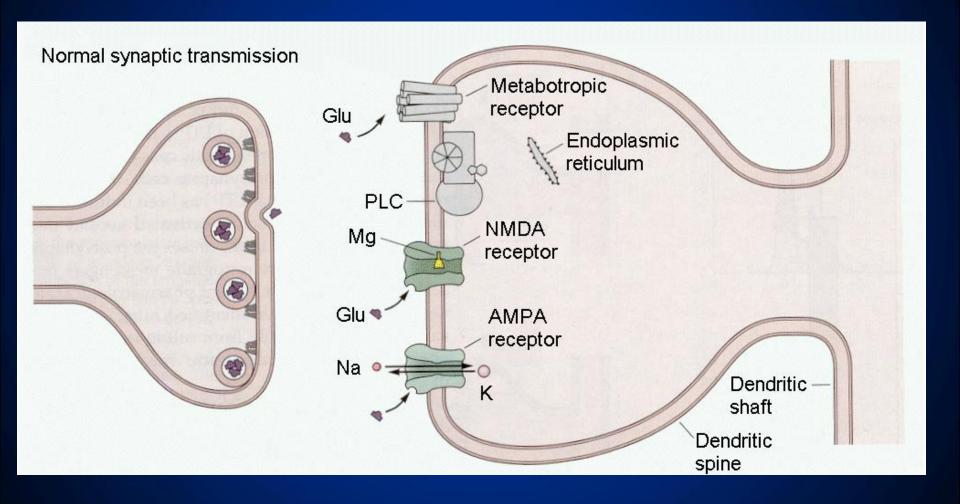


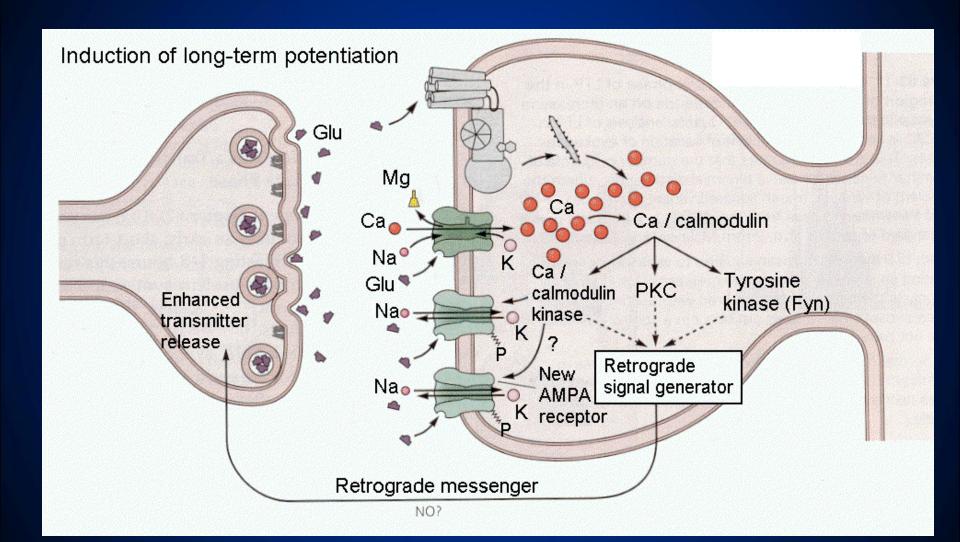


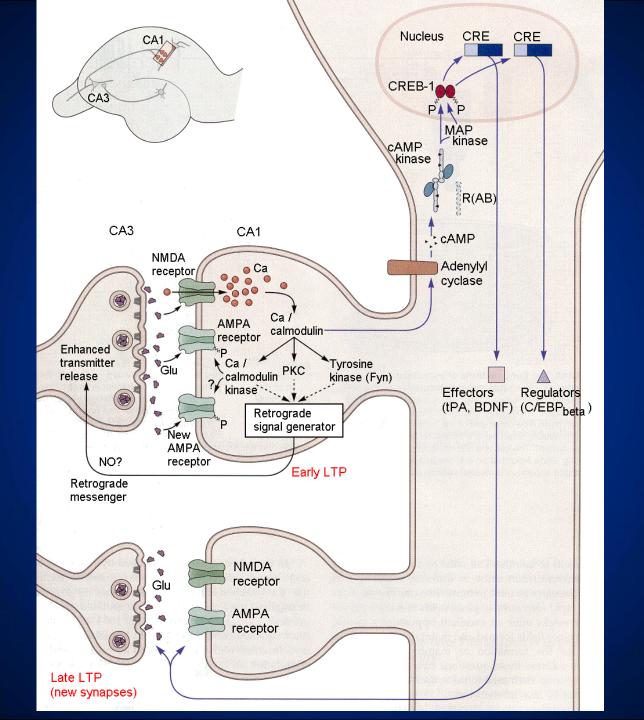
### Structura hipocampului

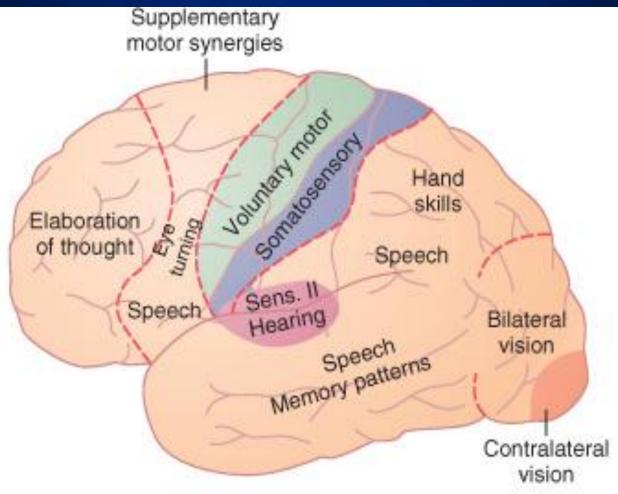












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#### Memoria ca fenomen

# HE EMPERAMENTAL HREAD

How genes,
culture,
time,
and luck
make us
who we are

Jerome Kagan

> Foreword by Richard J. Davidson