Neuroplasticity in neurodegenerative diseases and stroke

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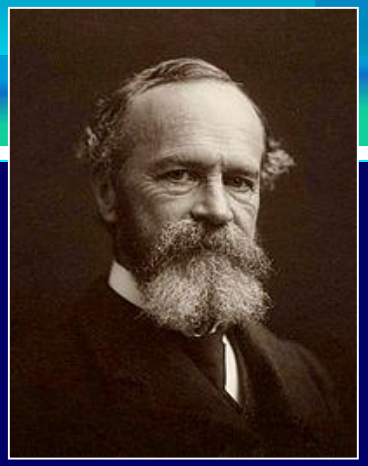
Neuroplasticity

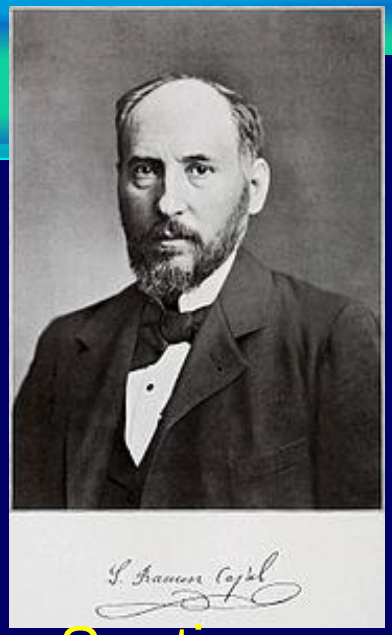
- Biological integral adaptive mechanism of nervous system that constantly modifies its own structural organization and functionality
- Requires neurochemical, synaptic and neuronal receptor and structural changes
- Plastic changes do not alter the original functional representation, but probably include unmasking of secondary roads and reorganization (re-mapping) and compensation and adaptation to brain lesion

Pascual-Leone A et al. Annu. Rev. Neurosci. 2005. 28:377–401



William James
(1890)

Jon
Kaas



Santiago
Ramon y Cajal
(1904)

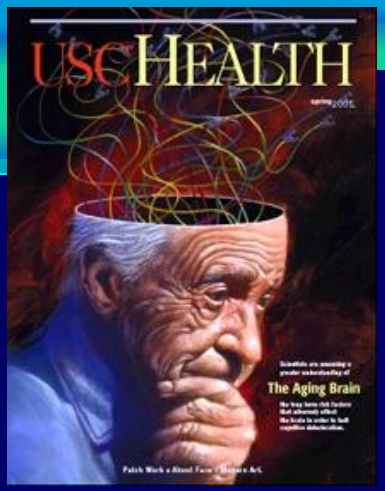
Edward Taub

Eric Richard
Kandel

Paul Bach-y-Rita

Michael M. Merzenich

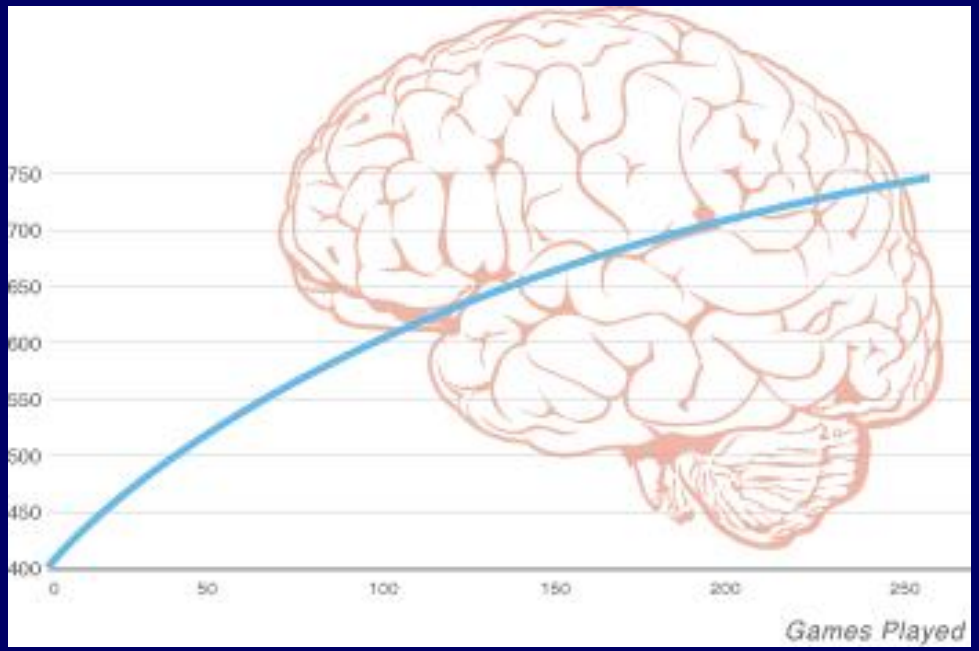
The Aging Brain

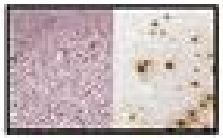


- **Cognitive abilities - processing speed, memory and reasoning start to decline in our late 20's.**
- **The brain's white matter begins to degrade around age 50.**
- **After the age of 60 brain shrinks - 0.5 – 1 % of its volume annually**
- **As we age we get better at dealing with the familiar, but worse at dealing with the new.**
- **It becomes more difficult to process and respond to information**

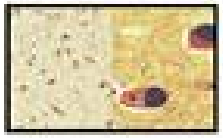
What contributes to the decline of our cognitive abilities?

- Normal aging process
- Stroke
- Dementia
- Alzheimer's
- Acquired brain trauma
- Neurodegenerative diseases

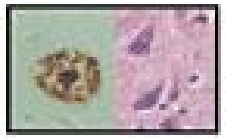




Prion disease
Location: diffuse cortical
Macro: cerebral atrophy
Micro: spongiosis, PrP-deposits



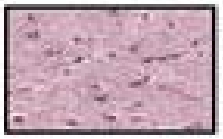
Frontotemporal Dementia
Location: fronto-temporal
Macro: cerebral atrophy
Micro: tau-deposits, Pick bodies



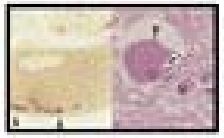
Alzheimer's disease
Location: temporo-parietal
Macro: cerebral atrophy
Micro: Aβ-plaques, tangles

Lewy-body dementia
Location: fronto-temporal
Macro: cerebral atrophy
Micro: Lewy-bodies

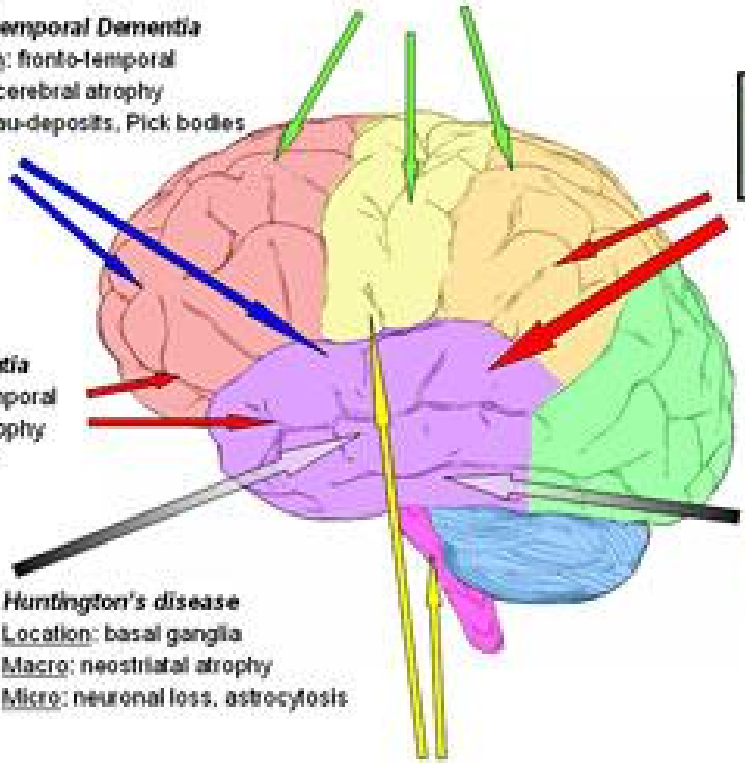
Parkinson's disease
Location: midbrain
Macro: pallor of substantia nigra
Micro: Lewy bodies



Huntington's disease
Location: basal ganglia
Macro: neostriatal atrophy
Micro: neuronal loss, astrocytosis



Amyotrophic Lateral Sclerosis
Location: motor cortex, brainstem, spinal cord
Macro: atrophy of motor neurons & muscles
Micro: inclusions (Bunina bodies, Lewy-body like)



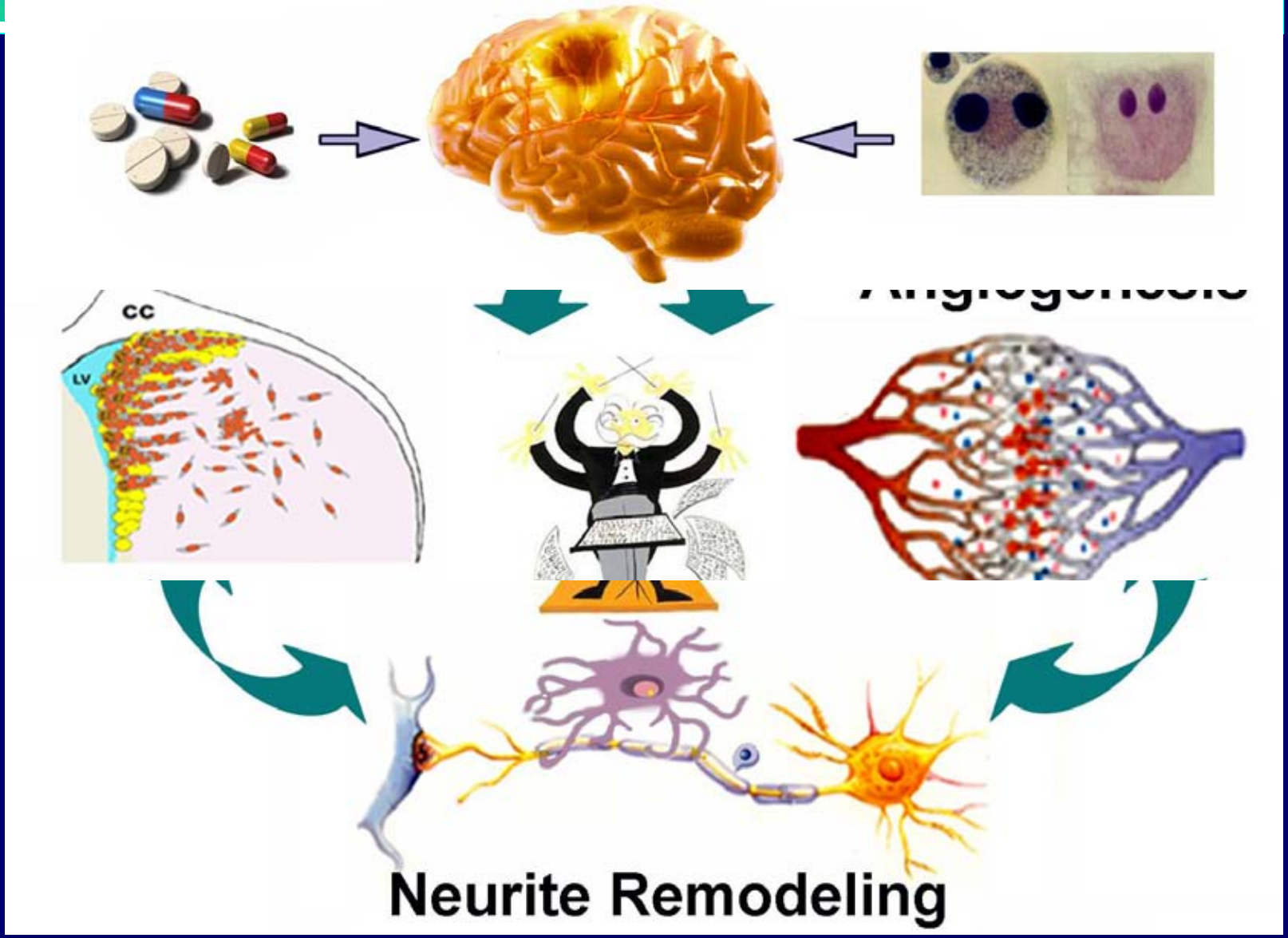
Bertram and Tanzi, *JCI*, 2005

- As early as 1868 Jules Cotard had shown that children with a diseased left frontal lobe could speak quite well without it
- Cases where someone is born with half a brain — only a right hemisphere. yet speaks normally, holds a job and has a normal life
- These findings amount to the discovery that the adult human brain, rather than being fixed or “hard-wired,” can not only change itself but works by changing itself

Neuroplasticity

- The brain is NOT hard-wired
- New brain cells and new neural pathways can form through the end of life
- Challenging your brain creates new brain cells which increase neural connections
- There is no age limit to changing our brain
- Intensive and challenging exercise leads to improvement in brain function.

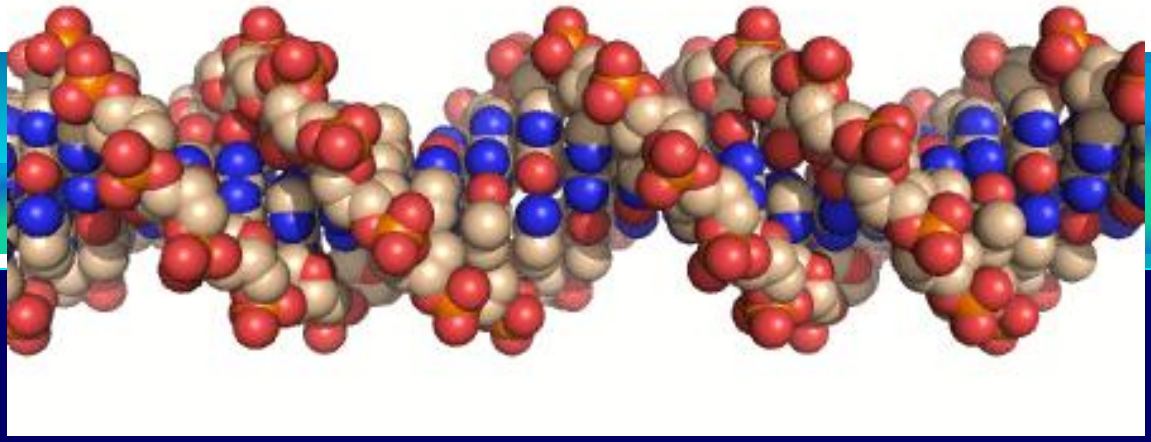
Astrocyte mediated remodeling of the brain after stroke and neural injury



By courtesy of prof. Michael Chopp

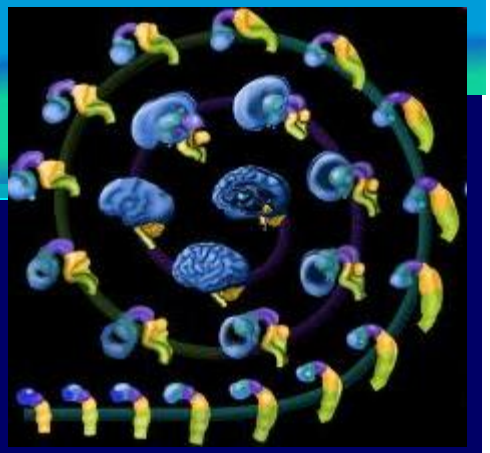
Mental Stimulation and Active Lifestyles

- Einstein's brain – 15% larger and had more connections
- London cab drivers have larger hippocampus – must learn complex maze of streets
- Studies on Bilingual people
- Nun Study



A big component of our lifelong brain health and development depends on what we do with our brains. Environment plays 80% of a role while genes are only 20% responsible

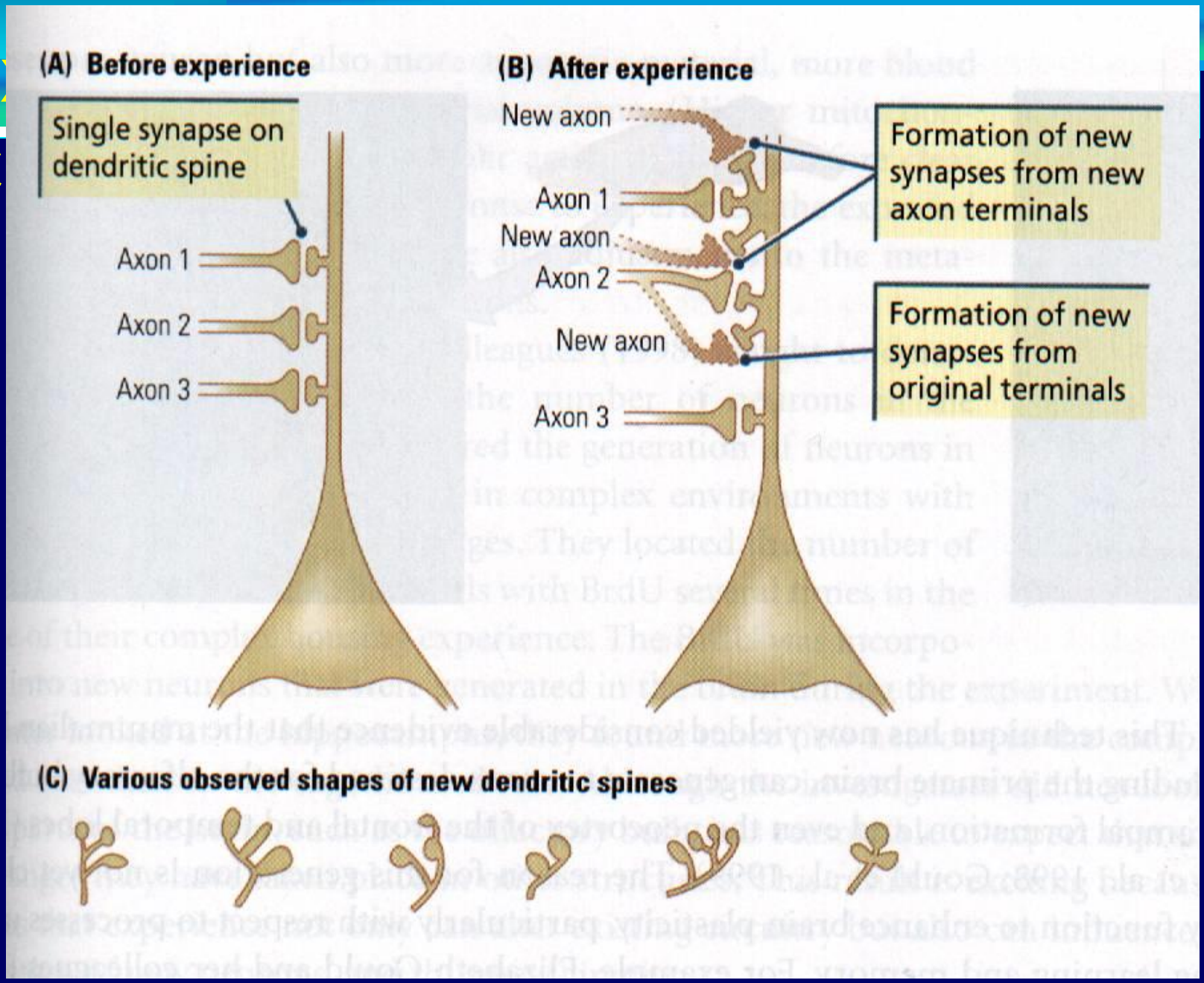
Individuals who lead mentally stimulating lives, through education, occupation and leisure activities, have reduced risk of developing Alzheimer’s. Studies suggest that they have 35-40% less risk of manifesting the disease”



How experience affects development

- Neural activity regulates gene expression that directs synthesis of cell adhesion molecules
- Neuronal activity regulates the release of neurotrophins (NGF) that are released from the dendrites; after synaptic connectivity
- Stimulates foundation of neuronal teminals and this promotes subsequent development

E
C


(A) Before experience
Single synapse on dendritic spine
Axon 1
Axon 2
Axon 3
(B) After experience
New axon
Axon 1
New axon
Axon 2
New axon
Axon 3
Formation of new synapses from new axon terminals
Formation of new synapses from original terminals
(C) Various observed shapes of new dendritic spines

Neurotrophins

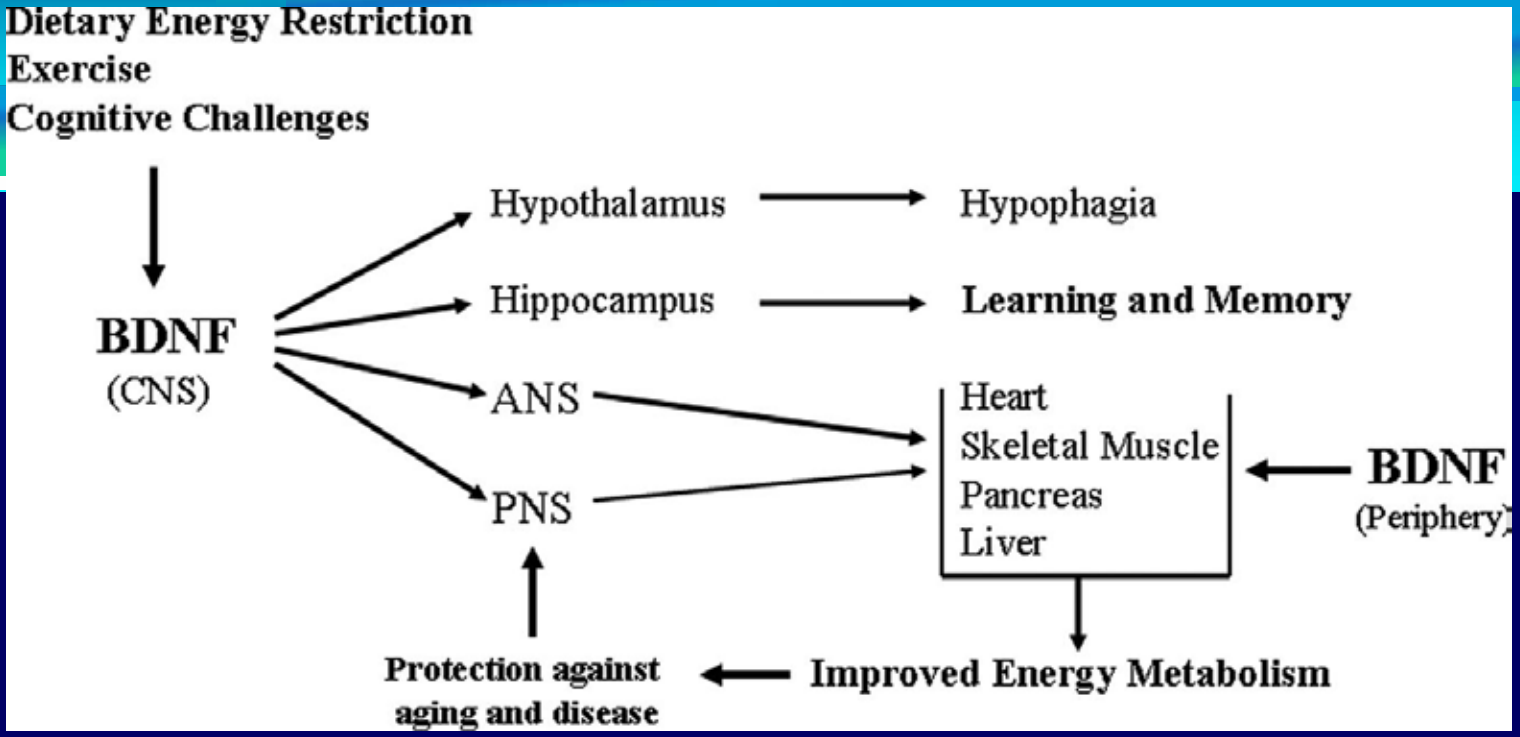
- In 1986 by Rita Levi-Montalcini and Stanley Cohen received the Nobel prize for identifying a set of proteins called nerve growth factor or NGF for short
- A neurotrophin is a type of protein that promotes the survival of neurons
- One type of neurotrophin, known as a "neurotrophic factor", is a growth factor that affects neurons in particular
- A growth factor is a protein that signals certain types of cells to survive, differentiate, or grow

J Physiol Pharmacol. 2010. 61(5):533-41.

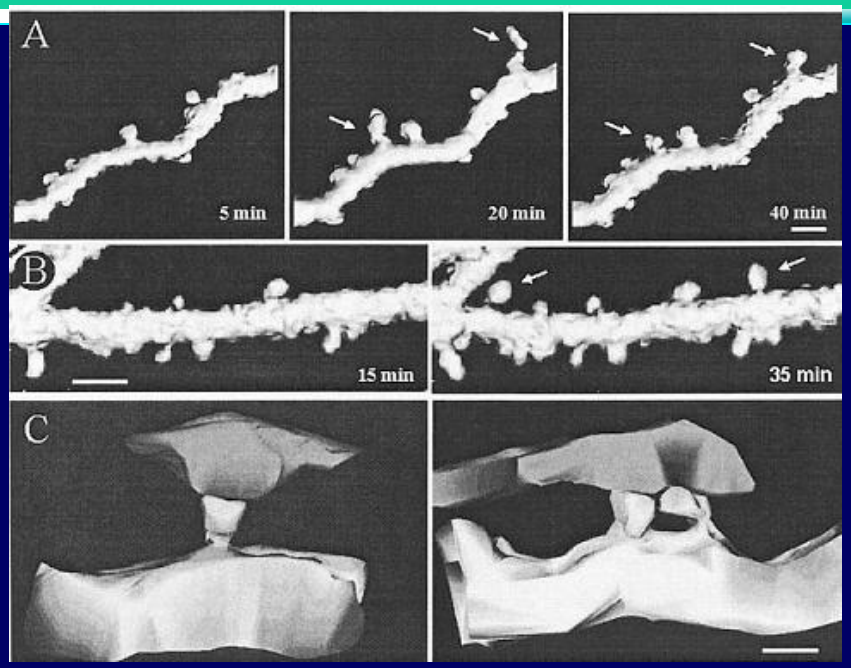
BDNF
(Brain Derived Neurotrophic Factor)

- was the second neurotrophic factor to be characterized after nerve growth factor (NGF). BDNF itself is important for long-term memory
- BDNF acts on certain neurons of the central nervous system and the peripheral nervous system, helping to support the survival of existing neurons and encourage the growth and differentiation of new neurons and synapses
- In the brain, it is active in the hippocampus, cortex, and basal forebrain—areas vital to learning, memory, and higher thinking
- Physical activity increases production of BDNF

- BDNF triggers the nucleus basalis (the brain's attention governor), keeping the brain constantly ready to absorb new memories and skills
- The nucleus basalis when turned on puts the brain in an extremely plastic state
- Henceforth the nucleus can be activated only when
  - Something is important,
  - Surprising, or novel occurs,
  - If we make the effort to pay close attention



- **Having adequate BDNF is essential for nerve and brain related health**
- **If your supplies run low then you cannot tolerate stress properly, you are more likely to be or become depressed, your brain is prone to excess inflammation, and you are set on a path of decline**
- **Conversely, adequate BDNF helps you keep up with the demands in your life**



Merzenich has shown that sensory and motor maps of the brain are not universal and unchanging, even for the same brain throughout life. They vary in their size and boundaries between individuals, but also in the same individual at different stages of life.

Baudry, Bi, Schreiber SINAPTIC PLASTICITY: BASIC MECHANISM TO CLINICAL APPLICATIONS, 2002

- **Mirror neurons** represent a specific subset of **visuomotor neurons**, originally discovered in area F5 of the rhesus monkey premotor cortex **that discharge both** when the monkey **performs** a particular action and **observes** another individual (monkey

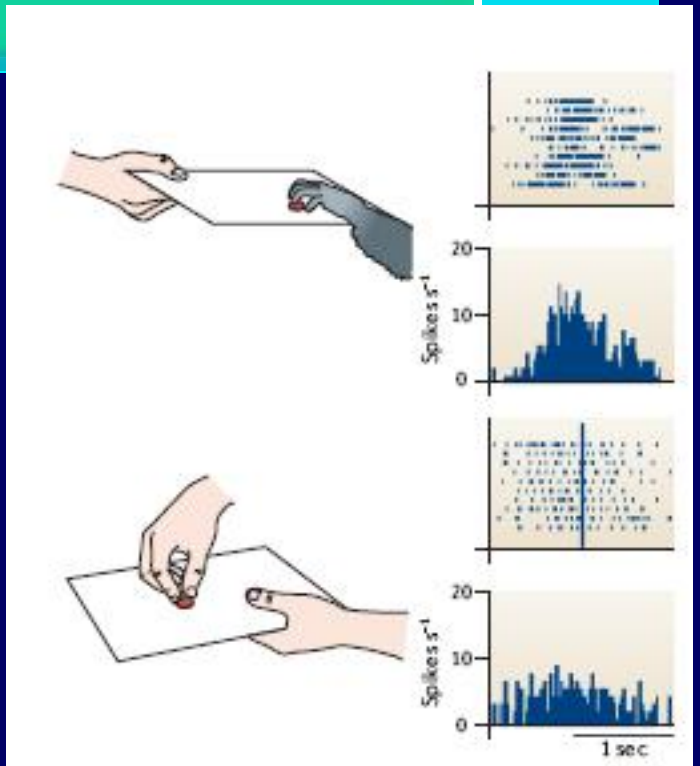
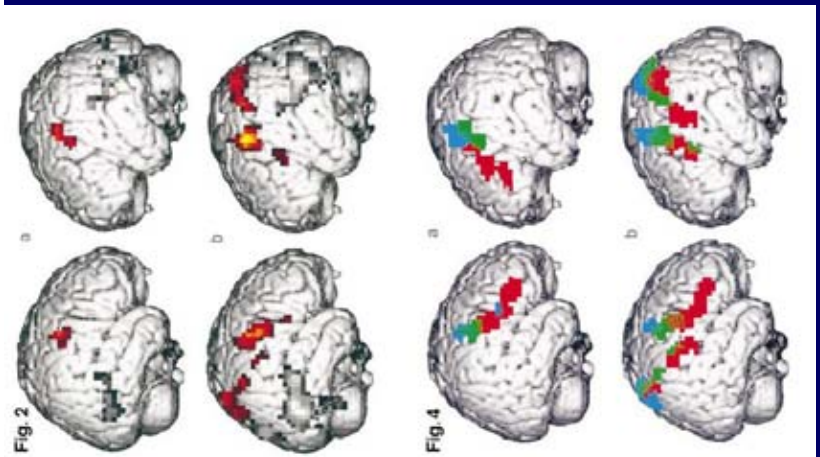


Figure 2 | Mirror neurons in area F5. The recordings show neural discharges of a mirror neuron in area F5 of the macaque inferior frontal cortex when the monkey grasps food (top) and when the monkey observes the experimenter grasping the food (bottom)[15]. Note that both tasks elicit strong neural responses in area F5. Modified, with permission, from REF. 115 © (2001) Macmillan Publishers Ltd.

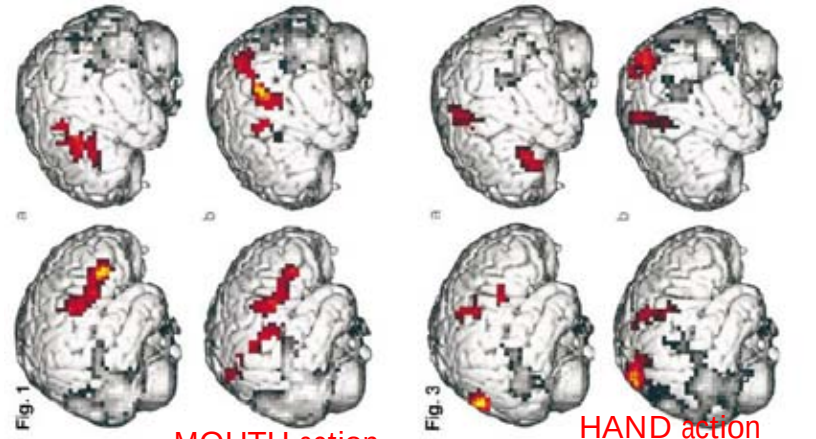
Gallese, V., Fadiga, L., Fogassi, L., & Rizzolatti, G. (1996). Action recognition in the premotor cortex. *Brain, 119*,593-609.

Fmri studies:Action observation activate premotor and parietal cortex



FOOT action

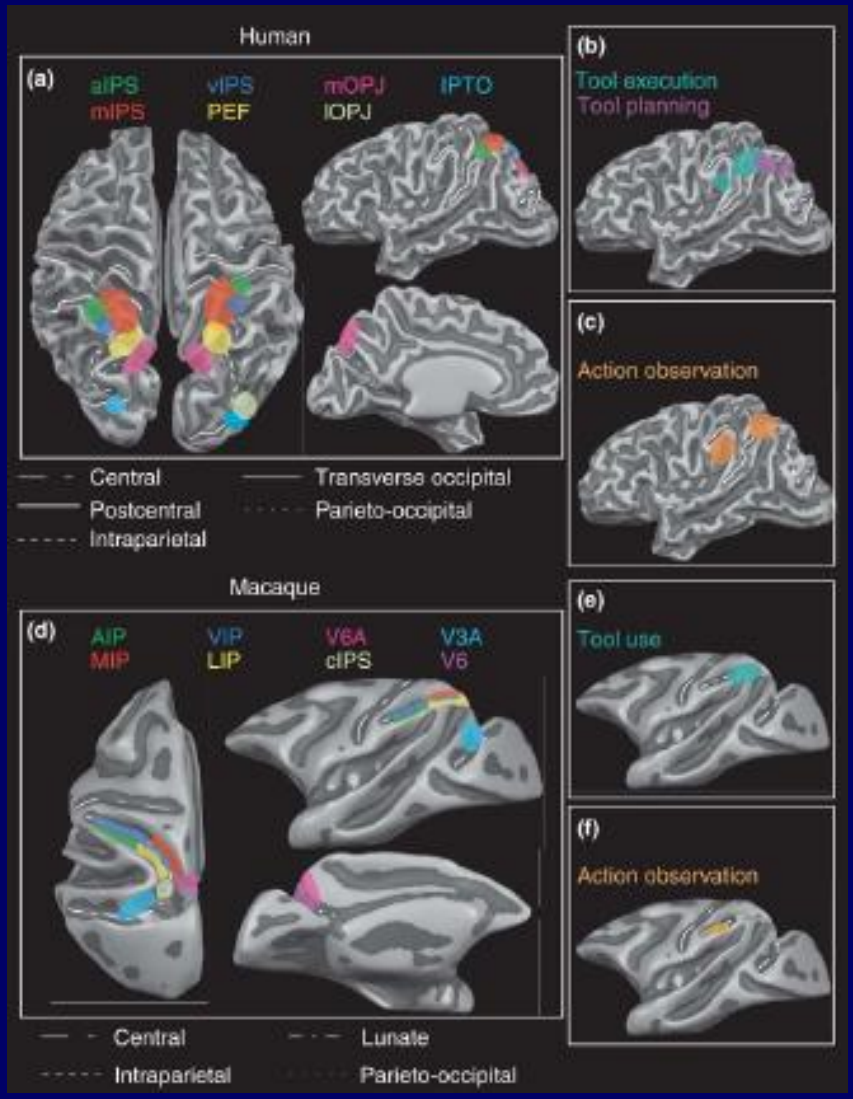
MOUTH+FOOT+HAND action



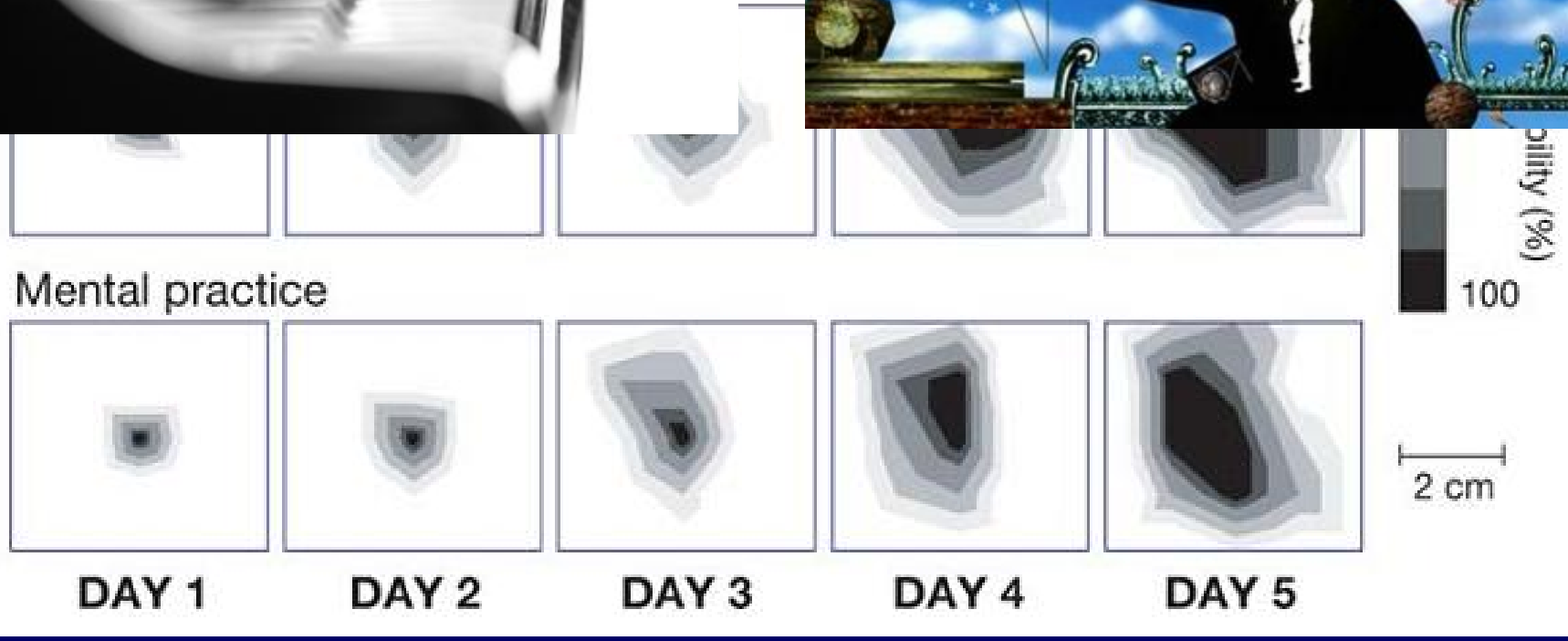
MOUTH action

HAND action

G. Buccino, F et al.Action observation activates premotor and parietal areasin a somatotopic manner: an fMRI study European Journal of Neuroscience, 2001Vol. 13, pp. 400-404



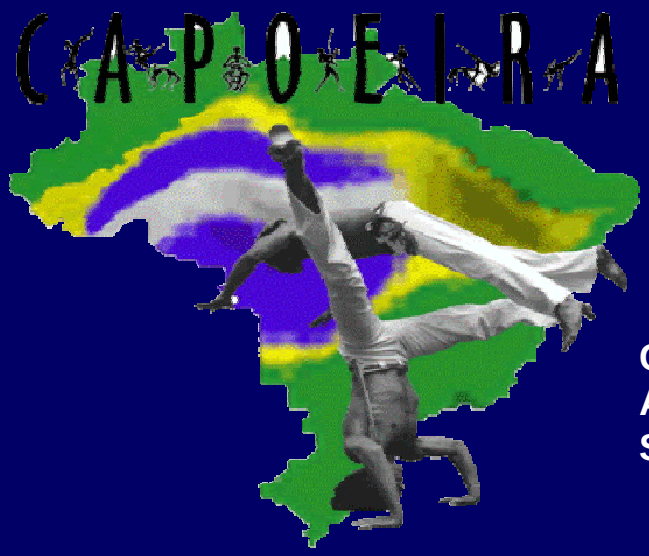
Jody C Culham Human parietal cortex in action Current Opinion in Neurobiology 2006, 16:205–212



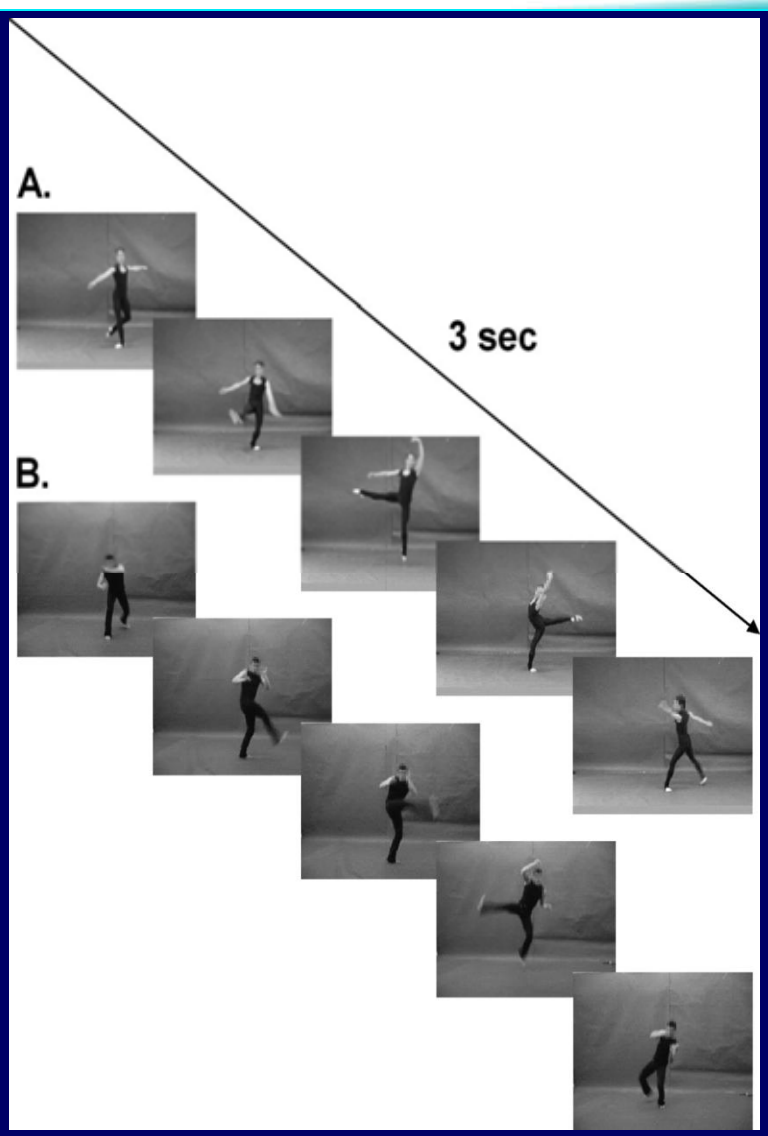
Pascal-Leone et al. THE PLASTIC HUMAN BRAIN Annu. Rev. Neurosci.2005. 28:377–401

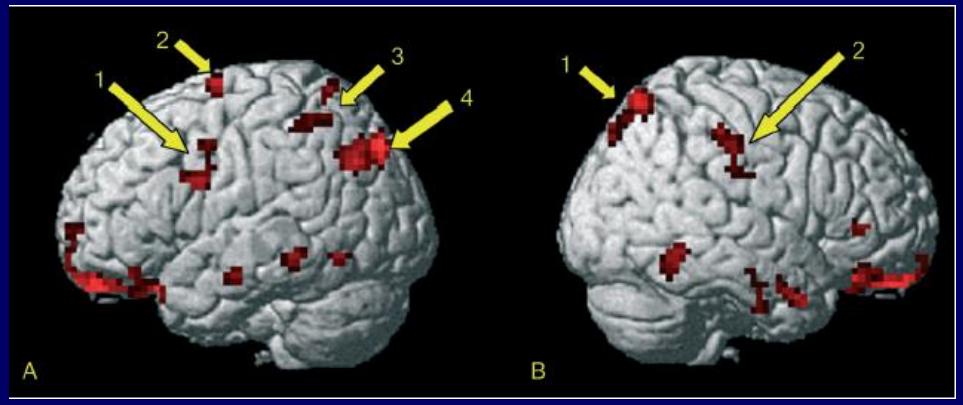
Calvo-Merino et al. (Calvo-Merino et al. 2005) detected differences in brain activity when participants observed the action which they learned to do and the action which they did not learn.

Experts in classical ballet, in capoeira and non-expert control subjects viewed videos of ballet or capoeira actions. Mirror neuron system displayed a greater activation in experts.



Calvo-Merino B et al.
Action Observation and Acquired Motor Skills: An fMRI Study with Expert Dancers
Cerebral Cortex 2005;15:1243-1249





Effects of motor expertise on brain responses to action observation

Mirror neuron system displayed a greater activation in experts.

Calvo-Merino B et al. Cereb. Cortex 2005;15:1243-1249

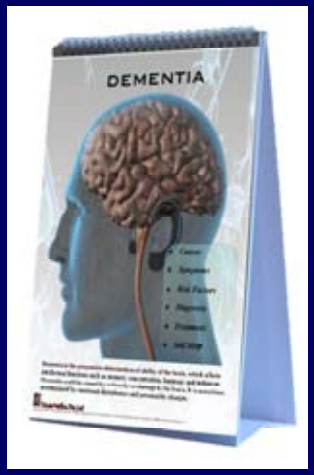
Pillars of Brain Health

1. Control of conventional cerebrovascular disease risk factors
2. Physical Exercise
3. Nutrition
4. Stress Relaxation
5. Mental Stimulation

Common risk factors for cerebrovascular disease

unmodifiable risk factors:

1. **Age**
2. **Gender**
3. **Race/ethnic**
4. **Genotype**
5. **Previous myocardial infarction, TIA or stroke**

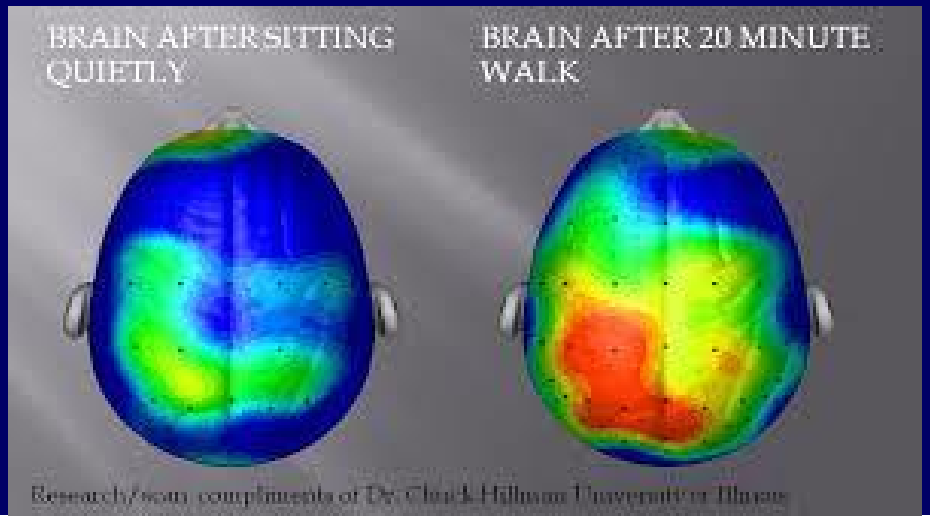


modifiable risk factors:

1. **Hyperlipidemia**
2. **Arterial hypertension**
3. **Atrial fibrillation**
4. **Coronary and or peripheral artery disease**
5. **Diabetes**
6. **Obesity**
7. **Physical inactivity**
8. **Stress**
9. **Alcohol**
10. **Smoking**

How does physical exercise help?

- **Slows down age-related shrinkage of the frontal cortex which is responsible for executive function**
- **Exercise improves blood flow, which improves the availability of energy to neurons**
- **Helps the body detoxify**
- **Helps improve cardiovascular health which in turn prevents heart attacks and strokes that can cause brain damage**
- **Exercise stimulates the production of proteins called “Growth factors”, which promote the formation and growth of brain cells and synapses**

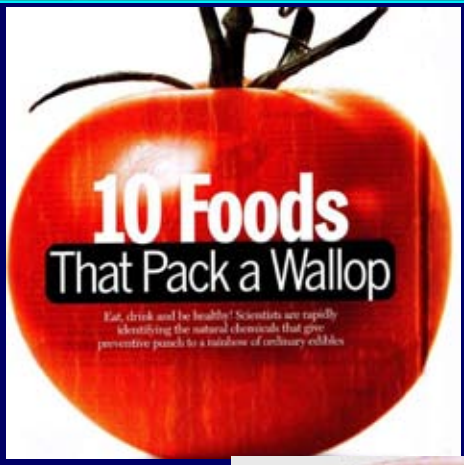


J Neurosci 2008;28(1):91-9.

- In 1999, researchers at the University of Illinois found that older people who started exercising showed faster reaction times, better ability to focus.
- In 2006, the same team found that aerobic exercisers actually increased their brain size by about 3 percent.
- In 2007, Columbia University researchers found that when people exercised regularly for three months, blood flow increased to a part of the hippocampus which is important for memory.
- New US study (University Illinois, Pitsburgh, Ohio) confirmed previous results

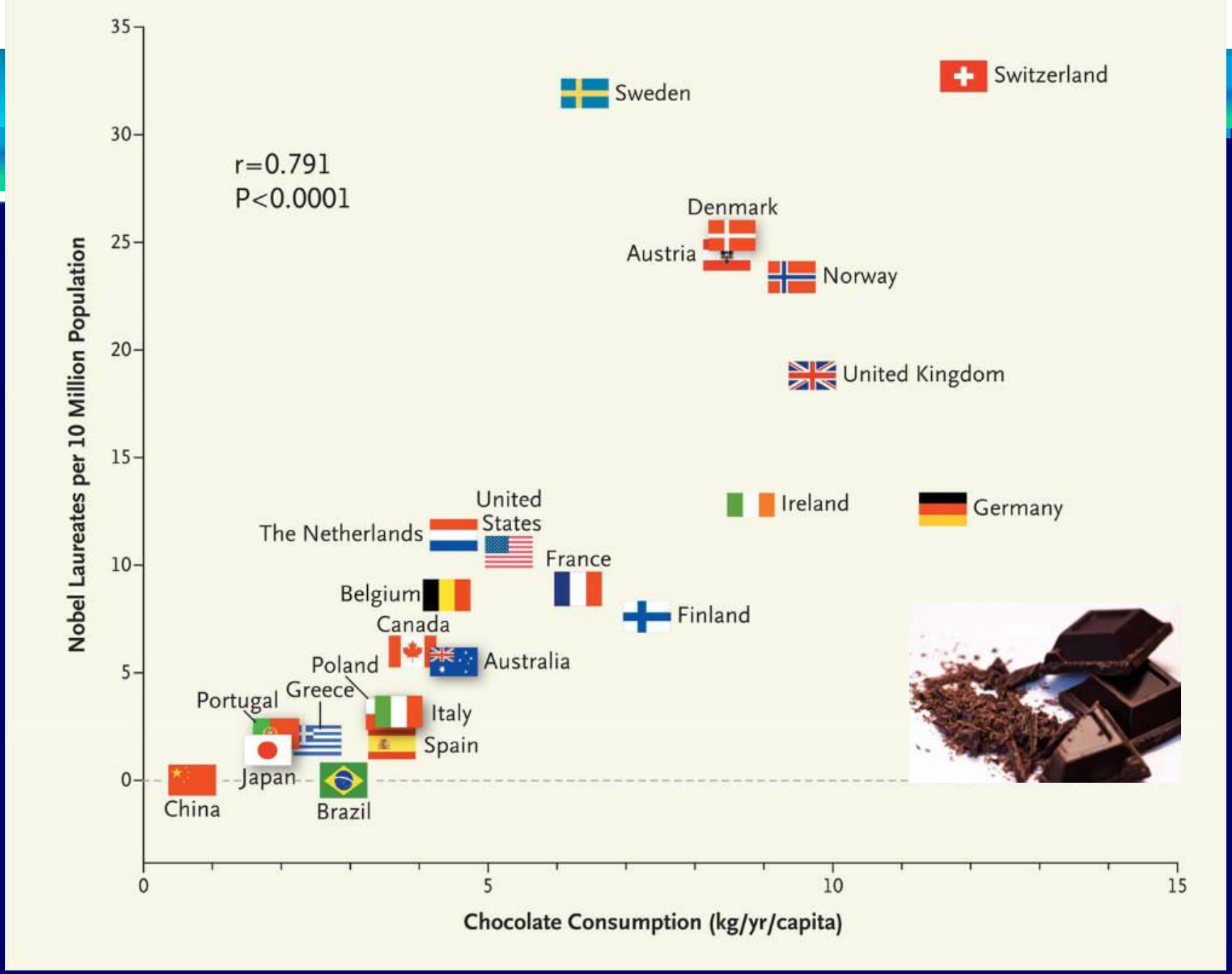
Front Hum Neurosci 2011;14(4):229

WALK, DON`T RUN!



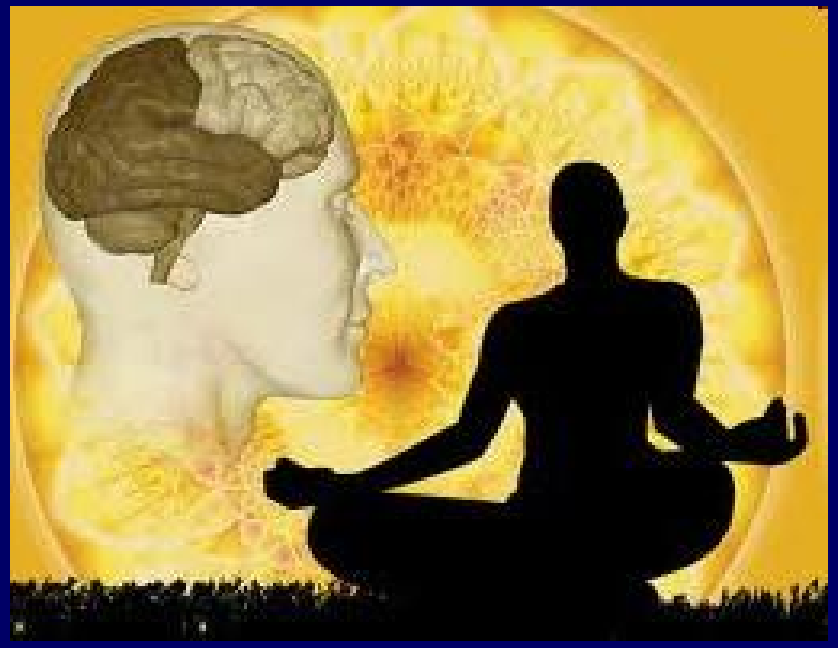

Assiette crétoise
Herbes, légumes
(et, secondairement, les fruits frais). Parmi les herbes, le persil frais, très utilisé en Crète, est l'une des plus riches en vitamine C. Il renferme en effet 170 mg de vitamine C pour 100 g, ainsi que du bêta-carotène et des vitamines E et B.
Vin rouge
Consommé avec modération, le vin rouge a des propriétés anti-inflammatoires et de fluidifiant sanguin, qui
Huile d'olive
Renfermant 80 % d'acide oléique, un acide gras insaturé, elle contribue à la diminution du taux de cholestérol total et du taux de triglycérides.

Assiette nordique



NEJM October 2012., Chocolate Consumption, Cognitive Function, and Nobel Laureates, Franz H. Messerli, M.D

Reduce Stress



Stress management is important - stress has been shown to actually kill neurons and reduces the rate of creation of new ones.

Prolonged elevation in stress hormones damages the hippocampus (involves memory and learning)

Brain Exercise – Mental Stimulation

- **Improve Memory**
- **Improve Attention**
- **Improve Auditory Processing (listening skills)**
- **Improve Visual-Spatial**
- **Improve Word retrieval skills**
- **Improve Speed of Processing**
- **Improve Concentration**
- **Improve Reasoning skills**

Brain protection

- Antioxidants
- NADH
- Q-10
- Omega -3
- Curcumin (BDNF)
- Coconut oil
- Vitamins B, C, D, E

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June, 9 – 13, 2014

www.croatianstrokesociety.org

Thank you!