Preceptorship on rehabilitation in multiple sclerosis

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Biological bases of recovery processes

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- Clinical observation indicate that acute damage in the Central Nervous System is frequently followed by some degree of spontaneous recovery

nevertheless

- The traditional view in neurosciences was that the mature Central Nervous System has no possibility to regenerate and has little capacity to reorganize and repair itself in response to injury

- Beginning in the 1970s, basic and electrophysiological researches from many laboratories revealed that CNS does have the ability to reorganize itself after injury, mostly at the level of the cerebral cortex (cortical reorganization)

- More recently it became evident that neurogenesis do occur in the CNS and may have a role in the mechanisms of repair

- The relative contribution of brain plasticity and neurogenesis to the spontaneous recovery is not clear

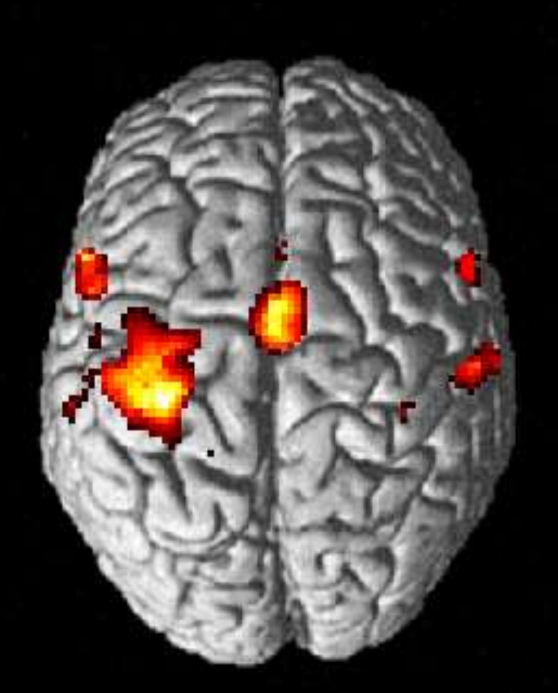
however

- The possibility to manipulate these processes could produce relevant advantages to patient with neurological injury

In the last 20 years two techniques have provided fundamental evidences of the brain plasticity

TMS

fMRI



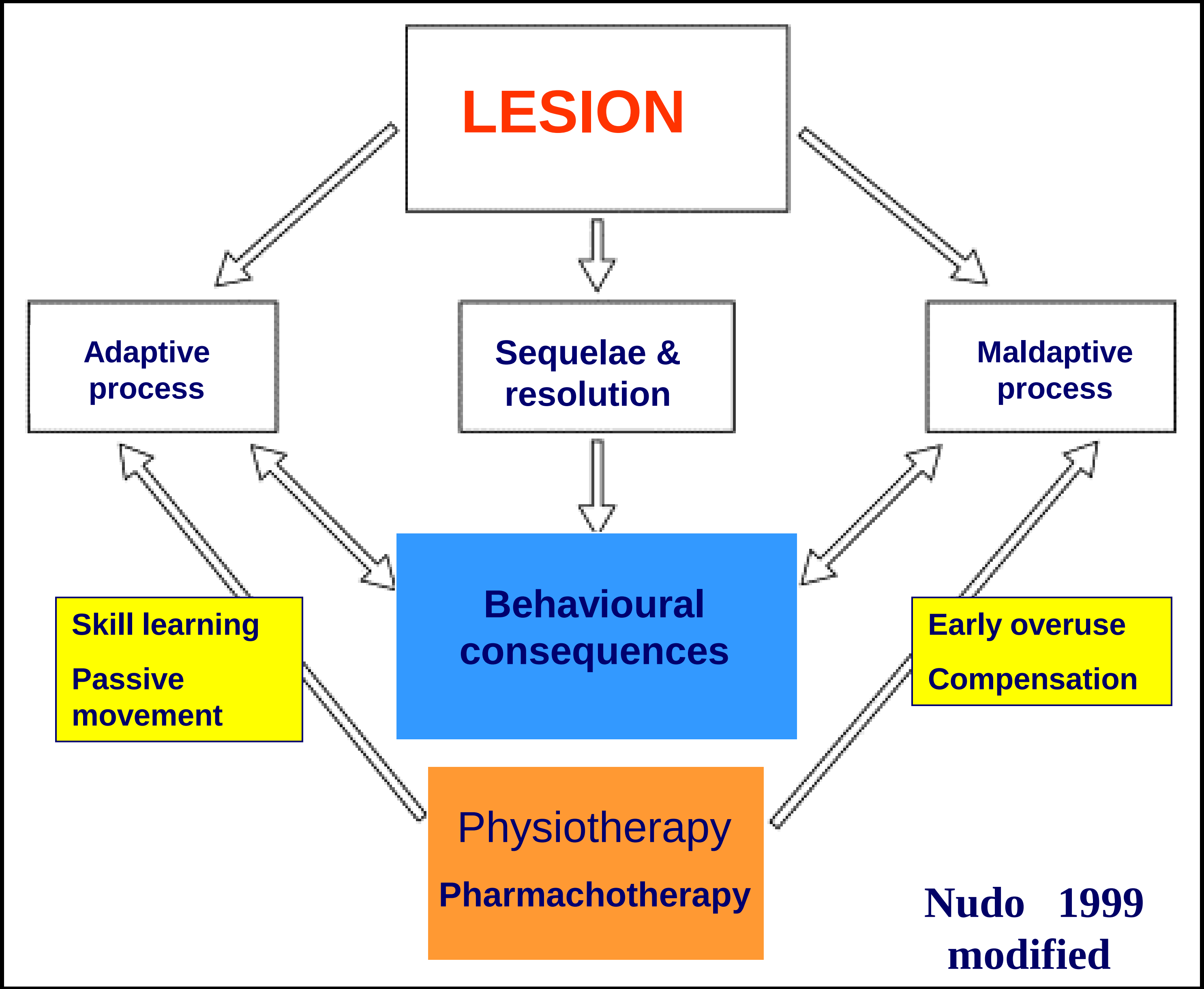
Plasticity

- Brain plasticity is a broad term for the property of the human brain to adapt to environmental pressure, experiences, and challenges.
- "Any enduring change in the cortical properties either morphological or **functional**" (Donoghue, 1996) .
- It play a major role in development and learning and it is variably reactivated when central and peripheral nervous system damage occurs.

Plasticity

- At the molecular level plasticity is modulated by genetic and epigenetic mechanisms
- At the synaptic level, plasticity refers to changes in the efficacy of synapses
- At the systems level, plasticity refers to changes of the neural connectivity resulting in changes in the neuronal networks that carry cognitive and behavioral implications

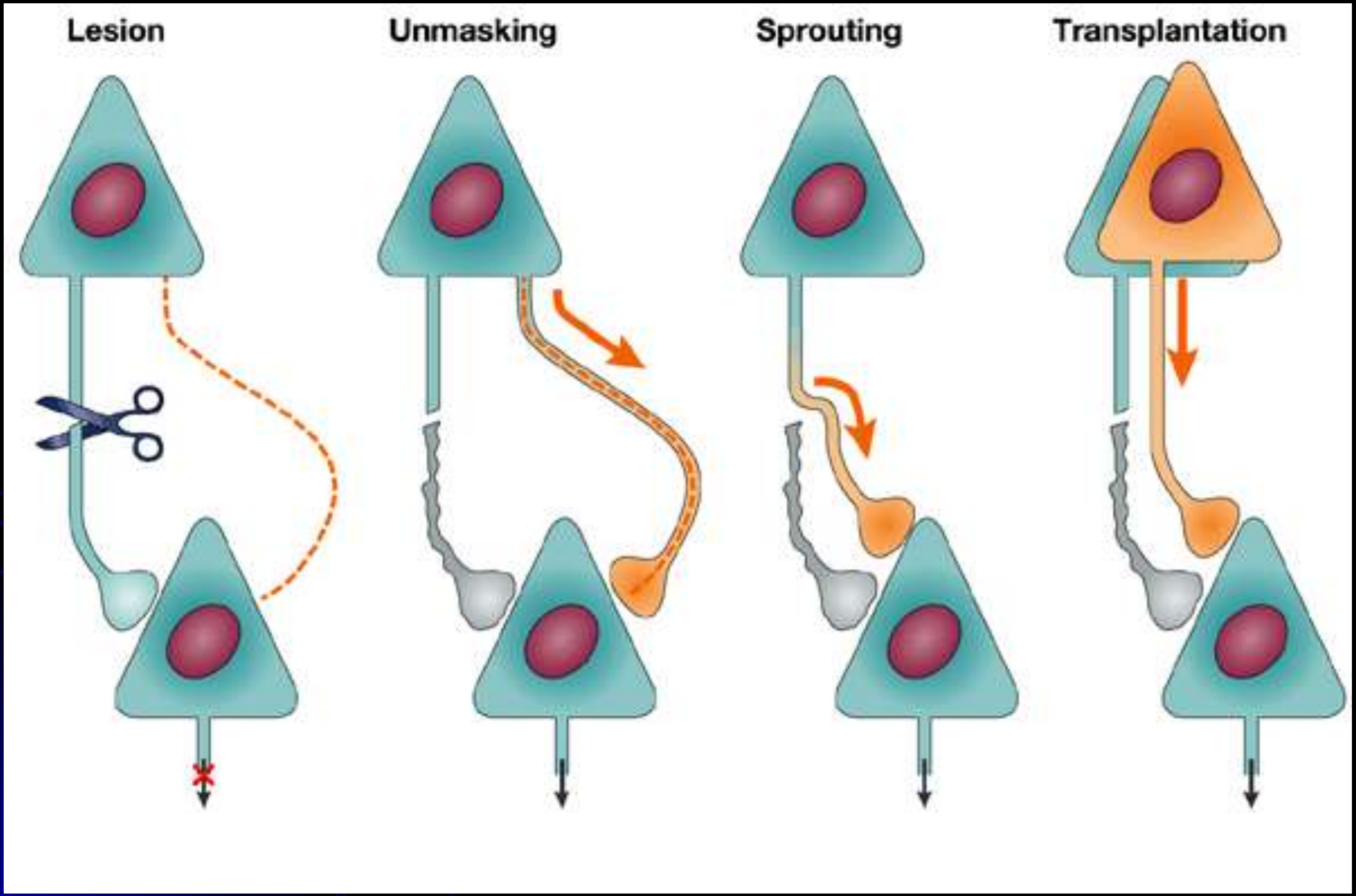
Behavioural consequences of brain lesion



Molecular mechanisms for reinforcement of preexistent connections

- Activation and potentiation of functionally silent synaptic connections (LTP dependent on NMDA receptors)
- Deactivation and depression of functionally active synaptic connections (LTD)
- Dendritic arborisation
- Fiber sprouting from surviving neurons
- Synaptogenesis

Type of recovery after CNS lesions



Mechanisms of brain plasticity:timing

- Rapid
  - Uncovering of latent connections
  - Activation of silent synapses
  - Activity-dependent synaptic plasticity
  - Generalized excitability changes in postsynaptic neurons
- Slow
  - Neurogenesis
  - Synaptogenesis
  - Synaptic remodeling

TRAINING STRATEGIES

OPEN ACCESS Freely available online

PLoS one

Motor Learning in Healthy Humans Is Associated to Gray Matter Changes: A Tensor-Based Morphometry Study

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Aims of the study

assessement whether the use of different schemes of motor training

- transitive, object-related and goal-directed motor sequences
- intransitive non purposeful motor actions

are associated to different patterns of GM structural modifications.

Research Paper

MULTIPLE SCLEROSIS JOURNAL | MSJ

Multiple Sclerosis Journal
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Changes of brain resting state functional connectivity predict the persistence of cognitive rehabilitation effects in patients with multiple sclerosis

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Abstract

Objective: We investigated whether the efficacy of 12-week cognitive rehabilitation in MS patients persists six months after treatment termination and, together with resting state (RS) functional connectivity (FC), changes on neuropsychological performance at follow-up.

Methods: Eighteen MS patients with cognitive deficits, assigned randomly either to undergo treatment (n=9) or not (n=9), underwent neuropsychological evaluation at baseline (t0), after 12 weeks of rehabilitation (t1) and at six-month follow-up (t2). RS fMRI was obtained at t0 and t1. Changes in neuropsychological performance and their correlations with RS FC modifications were assessed using longitudinal linear models.

Results: At t2 *vs.* t0, compared with the control group, treated group patients improved in tests of attention, executive function, depression and quality of life (QoL). Neuropsychological scores in these tests at t2 were significantly correlated with RS FC changes in cognitive-related networks and RS FC of the anterior cingulum. RS FC changes in the default mode network predicted cognitive performance and less severe depression, whereas RS FC changes of the executive network predicted better QoL.

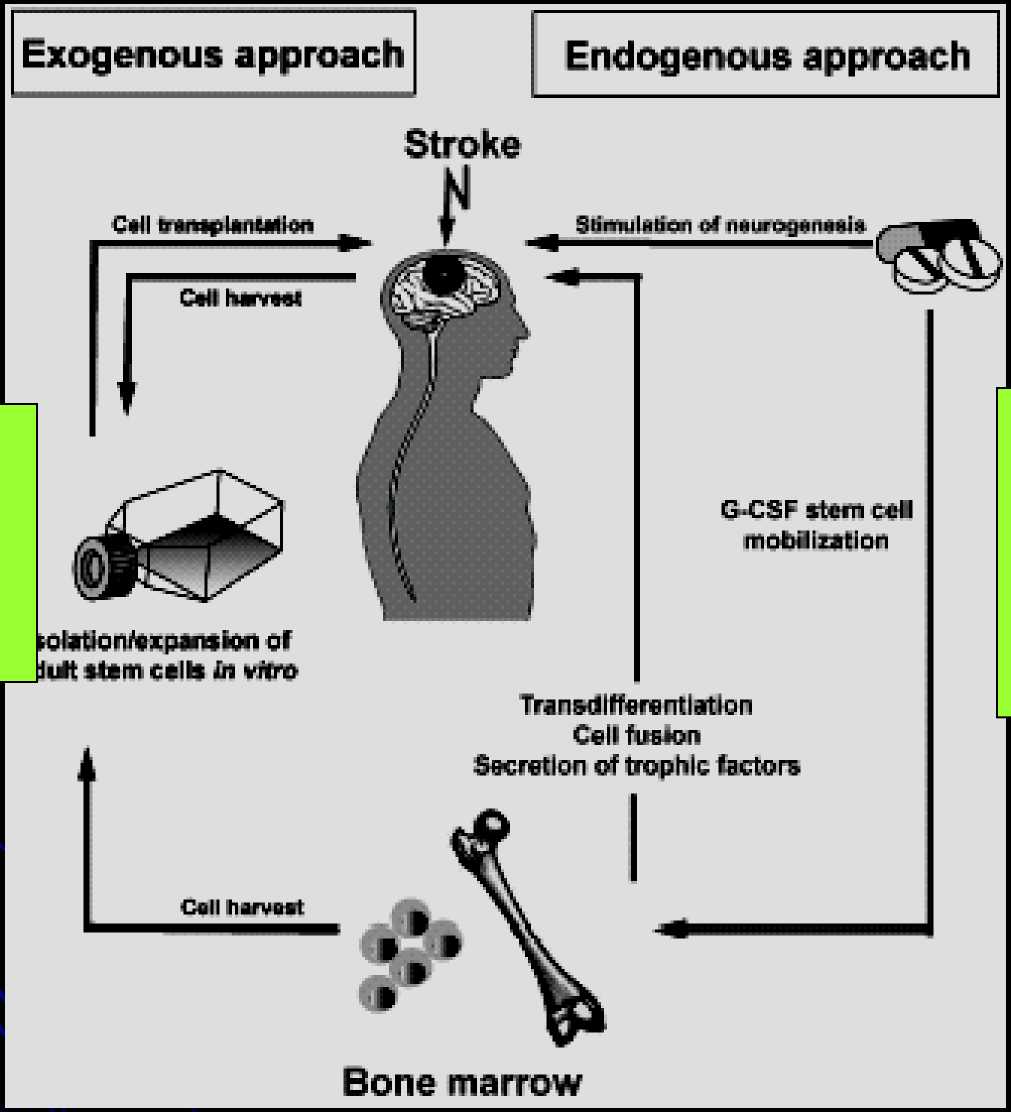
Discussion: Changes in RS FC of cognitive-related networks helps to explain the persistence of the effects of cognitive rehabilitation after several months in relapsing–remitting multiple sclerosis patients and their improvement on depression and QoL scales.

Brain Imaging and Behavior
DOI 10.1007/s11682-012-9160-9

Cognitive rehabilitation correlates with the functional connectivity of the anterior cingulate cortex in patients with multiple sclerosis

Laura Parisi · Maria A. Rocca · Paola Valsasina · Letizia Panicari · Flavia Mattioli · Massimo Filippi

Cellular therapy in CNS lesions



+ different stem cell types
+ large cell numbers
+ possibility of ex-vivo gene transfer

+ different stimulation factors
+ no immunological rejections
+ no surgical interventions

Modified from Haas 2005

Journal of Cerebral Blood Flow & Metabolism
24:441–448
Published by Lippincott Williams & Wilkins, Baltimore

Activated Neural Stem Cells Contribute to Stroke-Induced Neurogenesis and Neuroblast Migration Toward the Infarct Boundary in Adult Rats

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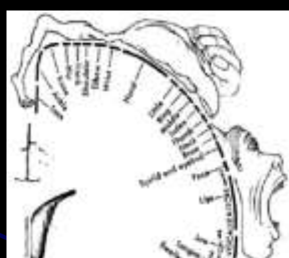
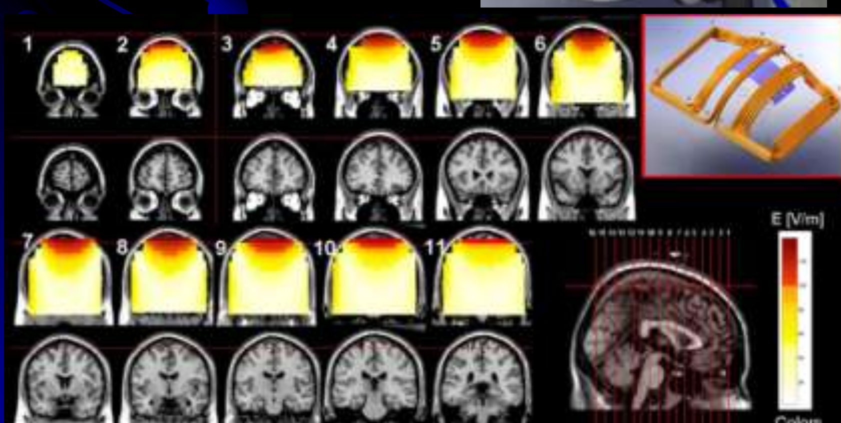
Summary: Stroke increases neurogenesis. The authors investigated whether neural stem cells or progenitor cells in the adult subventricular zone (SVZ) of rats contribute to stroke-induced increase in neurogenesis. After induction of stroke in rats, the numbers of cells immunoreactive to doublecortin, a marker for immature neurons, increased in the ipsilateral SVZ and striatum. Infusion of an antimitotic agent (cytosine-β-D-arabiofuranoside, Ara-C) onto the ipsilateral cortex eliminated more than 98% of actively proliferating cells in the SVZ and doublecortin-positive cells in the ipsilateral striatum. However, the numbers of neurospheres formed *in vitro*, yet the numbers of neurospheres derived from stroke rats significantly ($P < 0.05$) increased. Neurospheres derived from stroke rats self-renewed and differentiated into neurons and glia. In addition, doublecortin-positive cells generated in the SVZ migrated in a chainlike structure toward ischemic striatum. These findings indicate that in the adult stroke brain, increases in recruitment of neural stem cells contribute to stroke-induced neurogenesis, and that newly generated neurons migrate from the SVZ to the ischemic striatum. **Key Words:** Focal cerebral ischemia—

H- Coil effects on walking

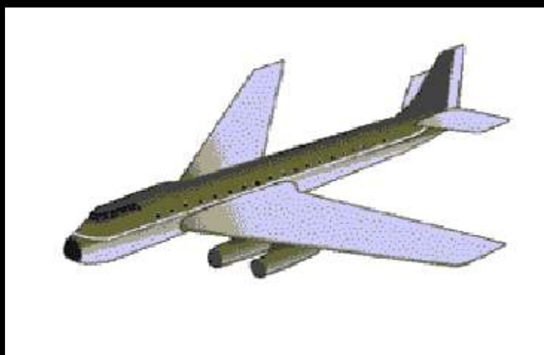
- Deep brain stimulation
- 1.600 stimuli/day/3weeks



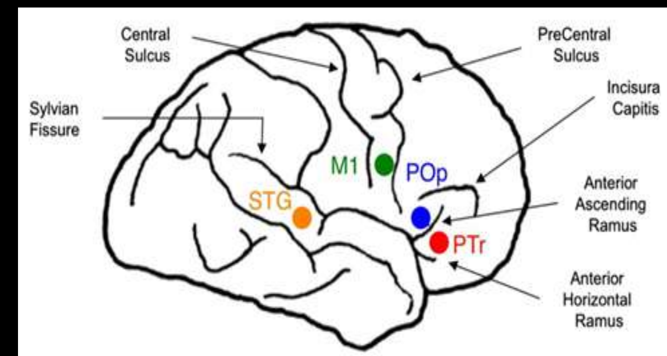


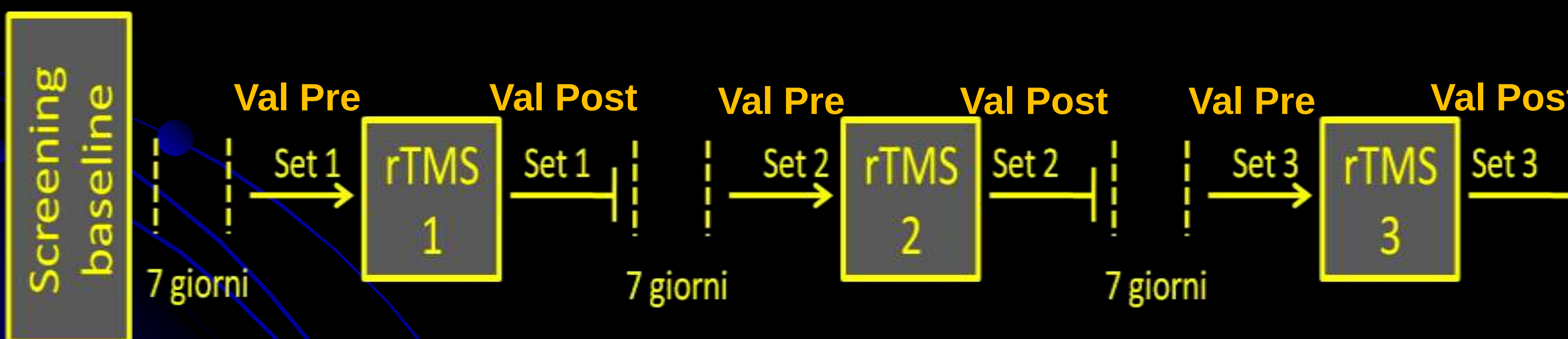
Roth et al. J Clin Neurophysiol 2002

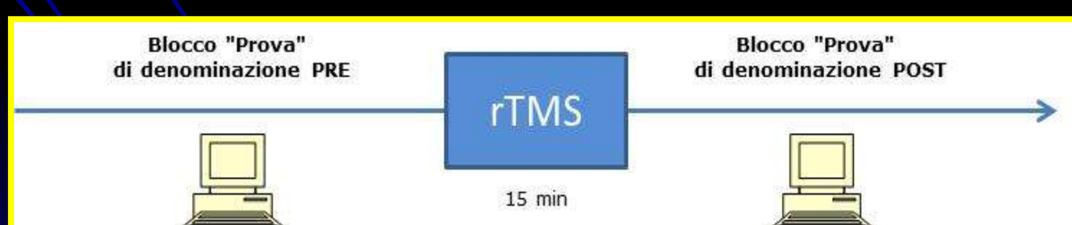
H-coil TMS of right omologous Broca's area in chronic aphasic patients



AIRPLANE



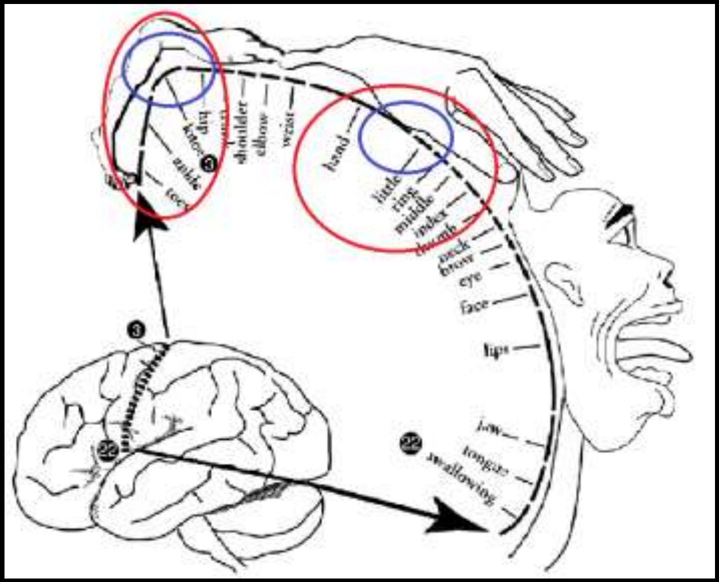




H-COIL stimulation in chronic stroke

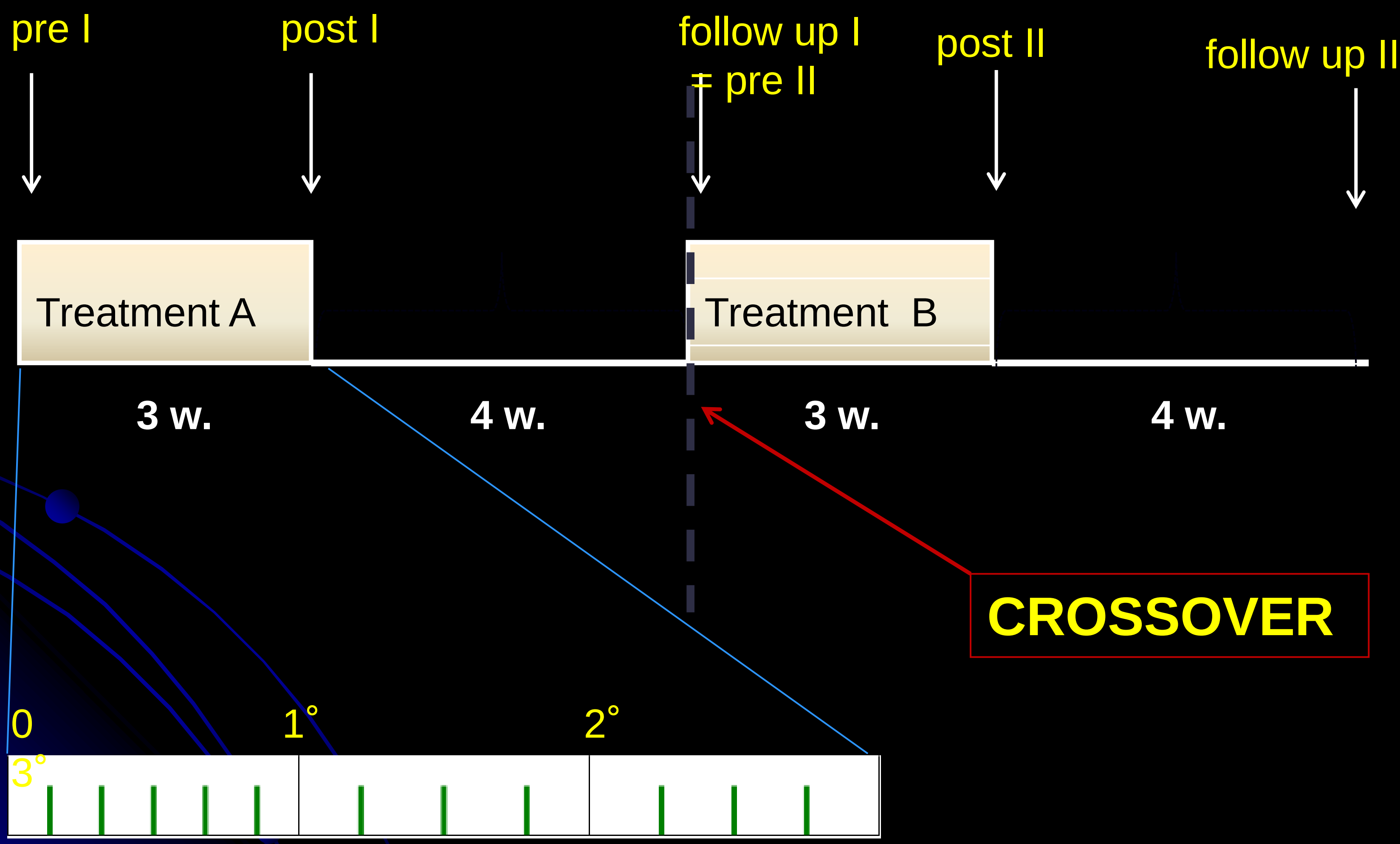
- Affected hemisphere
- 20 Hz
- 90% RMT (healthy emisphere)

- Lower limb
  - 30 trains , duration 2,5 s
  - interval 60 s
  - total: 1500 pulses in ~31 minuts
- Upper limb
  - 40 trains, duration 2 s
  - interval 30 s
  - total: 1600 pulses ~21 minuts



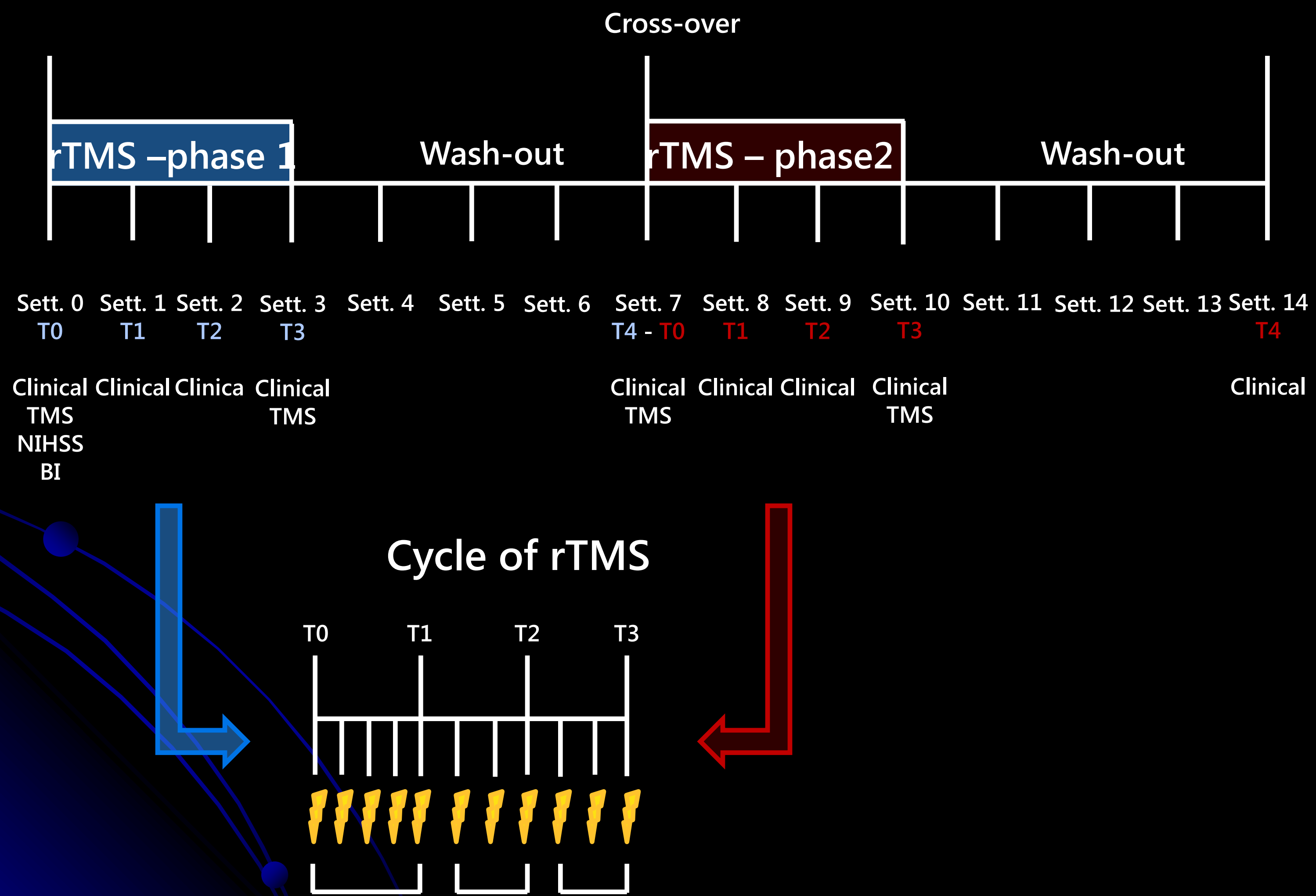
Roth Y. et al., J Clin Neurophysiol (2007)

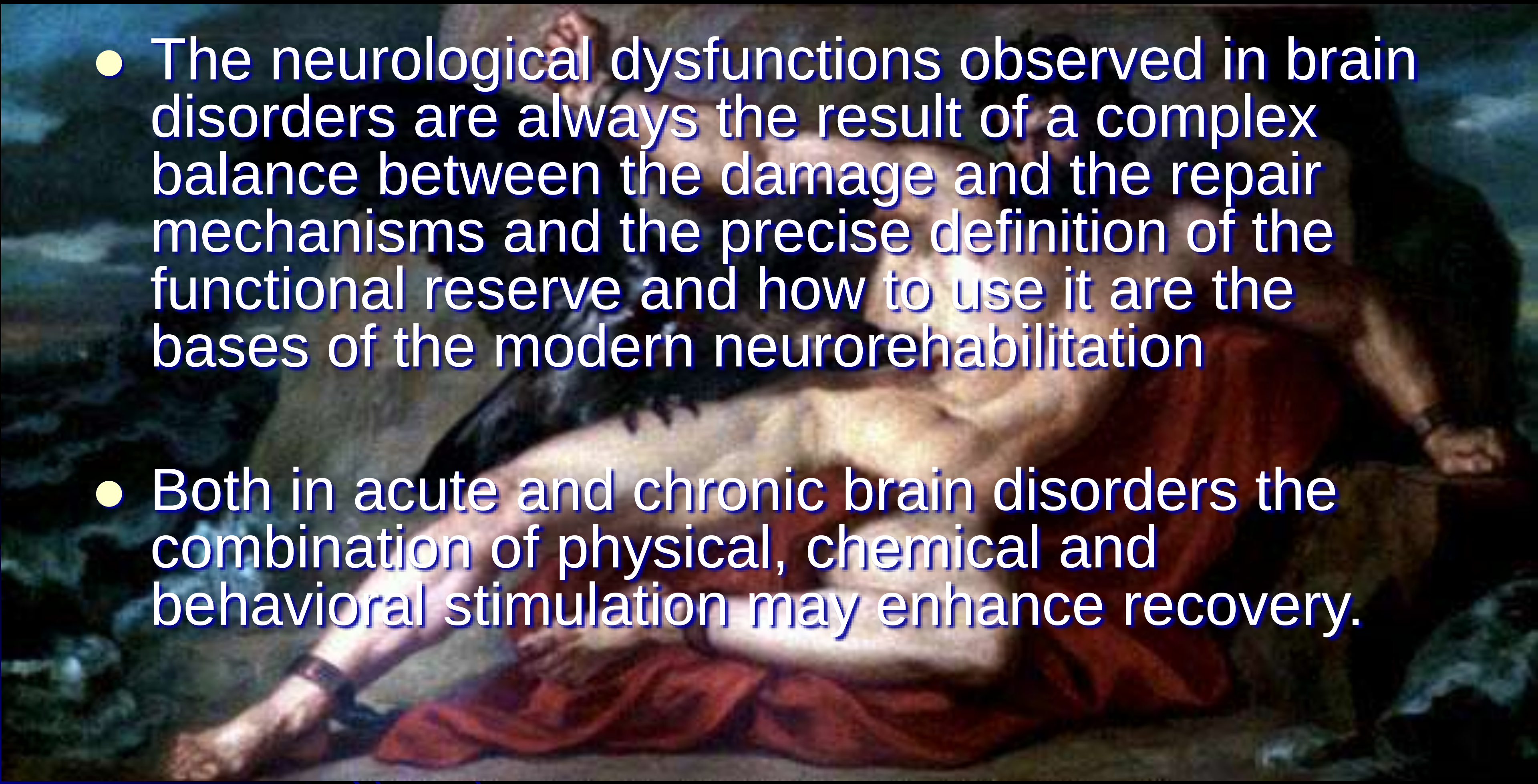
Study design



Cycling combined with rTMS

Study design





- The neurological dysfunctions observed in brain disorders are always the result of a complex balance between the damage and the repair mechanisms and the precise definition of the functional reserve and how to use it are the bases of the modern neurorehabilitation

- Both in acute and chronic brain disorders the combination of physical, chemical and behavioral stimulation may enhance recovery.

Christian Griepenkerl (1839-1916) La punizione di Prometeo