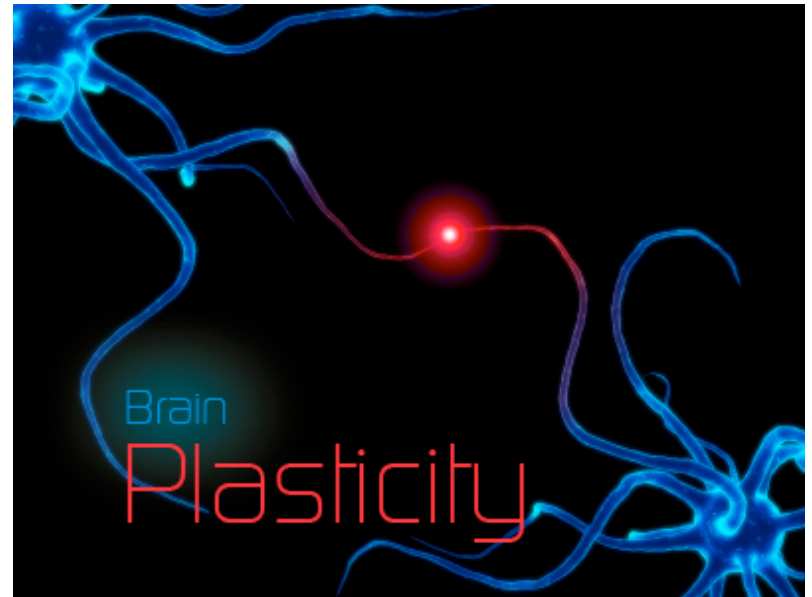


Plasticity

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Overview

- What is Plasticity?
- What are the neuroanatomical changes associated with Plasticity?
- What are the anatomical substrates for Plasticity in the motor cortex (MC)?
- Is Plasticity use-dependent or learning-dependent?
- What changes constitute local & remote plasticity after lesions of MC?
- What are the Clinical implications of Plasticity?

What is Plasticity?

- Capability of the cerebral cortex to alter its functional organization as a result of experience
- Refers to the phenomenon of change
- Correlates of plasticity:

Synaptic → Cellular → Molecular → Network → Systems
Level Level Level Level Level

What is Plasticity?

- Processes included in the process of plasticity-
 - Cortical representational maps are altered
 - Synapses change in morphology
 - Dendrites and spines grow and contract
 - Axons change their trajectory
 - Neurotransmitters are modulated
 - Synapses are potentiated or depressed
 - New neurons differentiate and survive

What factors drive Plasticity?

- Sensory stimulation
- Skill acquisition
- Peripheral injury
- Central injury
- Growth promoting agents
- Neuro-modulating drugs
- Electrical & magnetic stimulation

Early studies of Plasticity

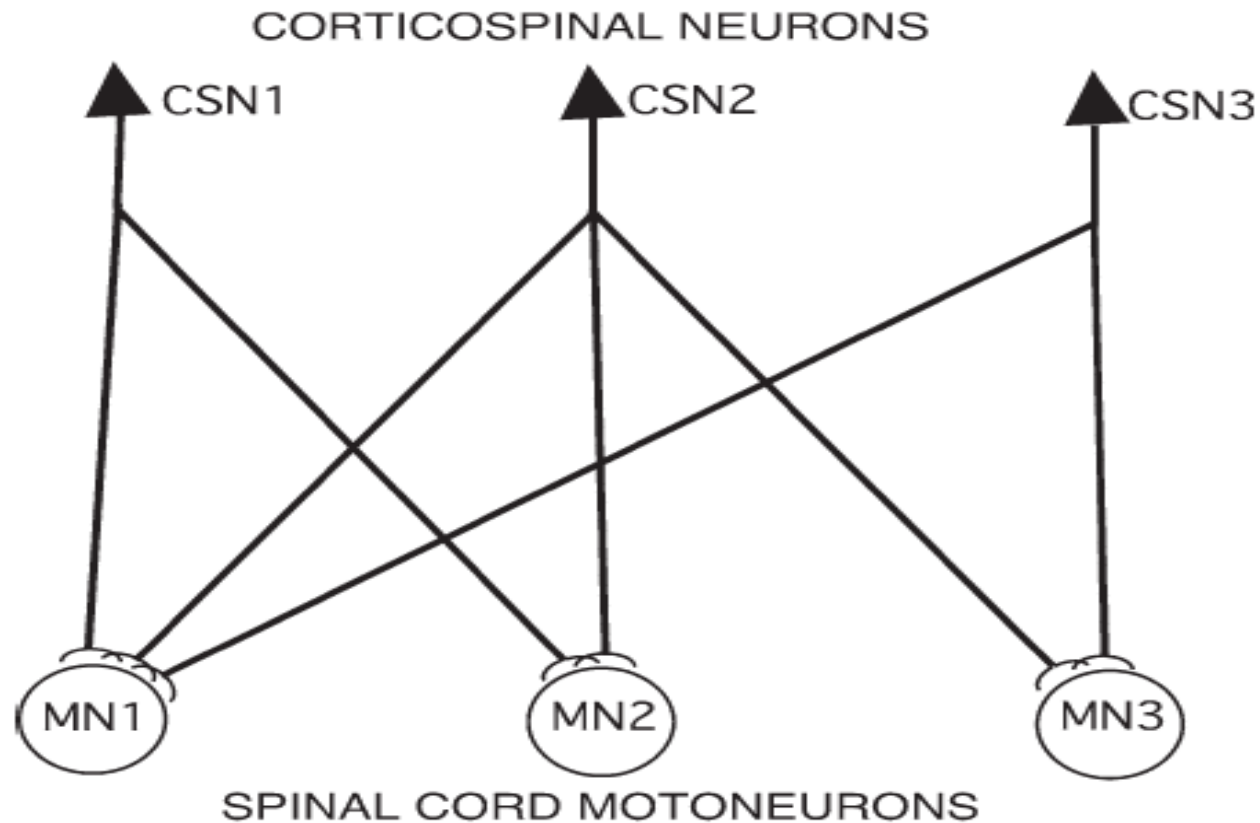
- 1940-1960 – Environmental enrichment studies
 - Larger brains and increased cortical thickness
 - Larger neuronal cell bodies and nuclei
 - Larger synaptic contacts
 - Increased dendritic spine density
 - Increased dendritic branching
 - Higher synapse to neuron ratio
 - Combination of inanimate and social stimulation



Early studies of Plasticity

- 1980- Activity-dependent Plasticity studies
 - Manipulation of sensory experience to observe changes in receptive field of the cortex
 - Receptive field of a sensory neuron is a region of space in which presence of a stimulus will alter the firing of that neuron

Anatomical substrates for Plasticity in the Motor cortex



Convergence and divergence of cortical output pathways to motor neurons.

Anatomical substrates for Plasticity in the Motor cortex (MC)

- Microstimulation techniques in anaesthetized preparations
- Functional representation of a site – Identified by muscles or joint movements activated by the lowest possible current levels

Use-Dependent versus Learning-Dependent Plasticity in MC

- Motor training post injury alters cortical motor maps in a few days
- Skill / Learning dependent and not Use-dependent
- Clinical Implications: Optimal level of task complexity

Local Plasticity after lesions of MC

- Gleees & Cole (1950)- Local lesion to thumb representation area in monkeys – Thumb representation appeared in area surrounding the infarct
- Nudo (1996)- Intracortical microstimulation techniques- Widespread loss of cortical representation of the area of the movements formerly represented in the infarcted zone
- Nudo (1996) – Rehabilitation using principles of Constraint Induced Movement Therapy (CIMT) – Preservation of hand representation

Local Plasticity after lesions of MC

Neuroanatomical changes post stroke in peri-infarct area



(3-14 days) GAP-43 – Neurite outgrowth



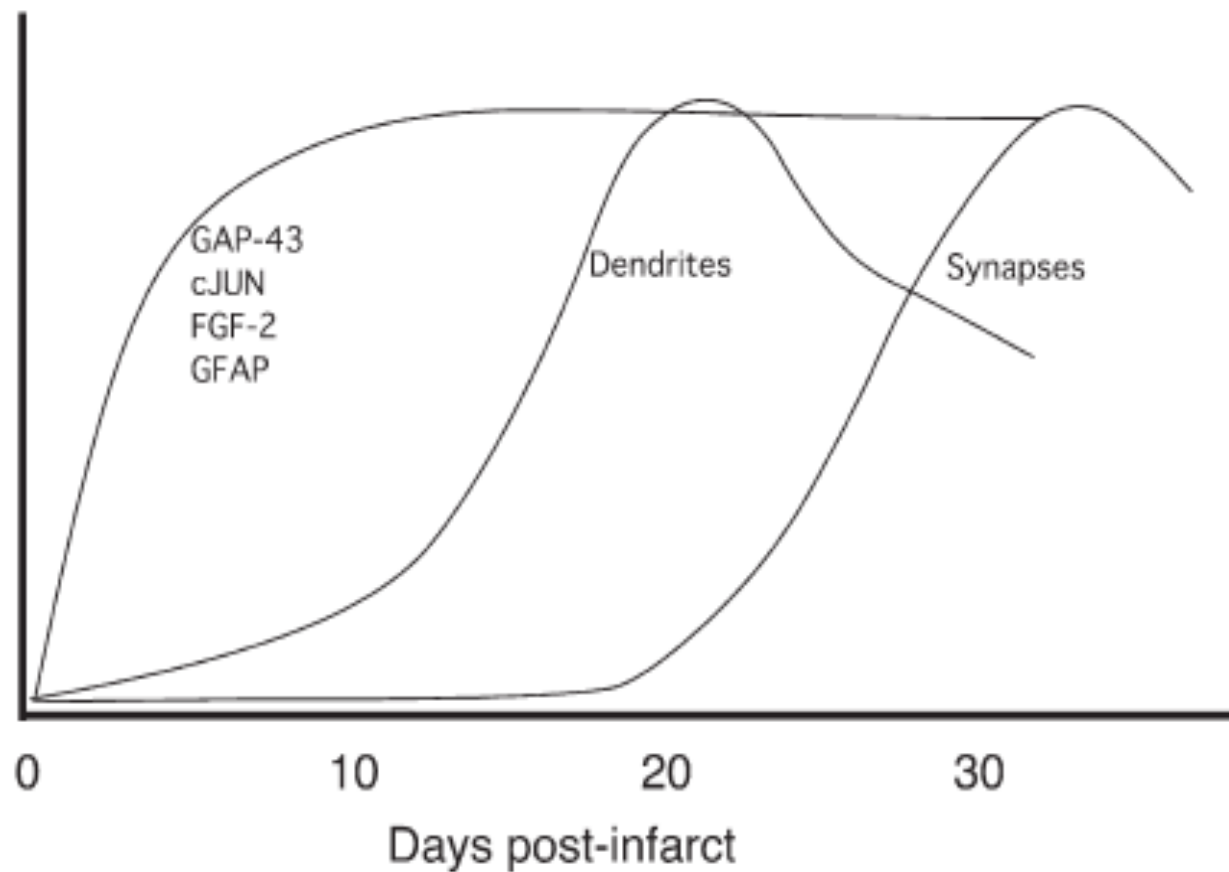
(14-60 days) Synaptophysin- synaptogenesis



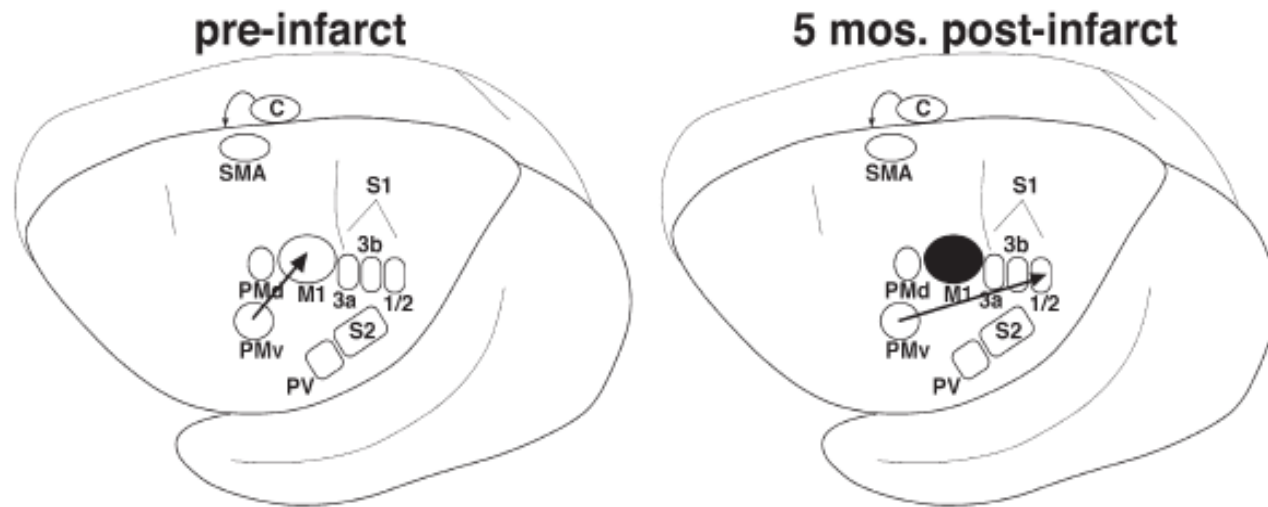
NMDA receptors & GABA receptors

Suppression of growth inhibition for 1 month with subsequent waves of growth promotion

Anatomical changes in intact cortex after focal ischemic infarct



Remote plasticity after lesions of MC



Neuroanatomical changes occur in the contralesional hemisphere as well as in remote areas of the infarcted cortex

Remote plasticity after lesions of MC

- What is the significance of such a new pathway?
 - Repair strategy of the sensorimotor cortex to reconnect motor areas with sensory areas?
 - Adaptive or maladaptive?

Repair strategy

- Normal connections between M1 hand area and parietal lobe
- Anterior portion of M1- proprioceptive input
- Posterior portion of M1 – cutaneous input
- Clinical implications- Lesions in-
 - Anterior region of M1 – Deficits in metrics of reach
 - Posterior region of M1 – Sensory Agnosia

(Thus deficits due to sensorimotor disconnection in addition to disruption of motor output)

Modulating Neuroplasticity after Stroke

DEVELOPMENT OF LEARNED NONUSE

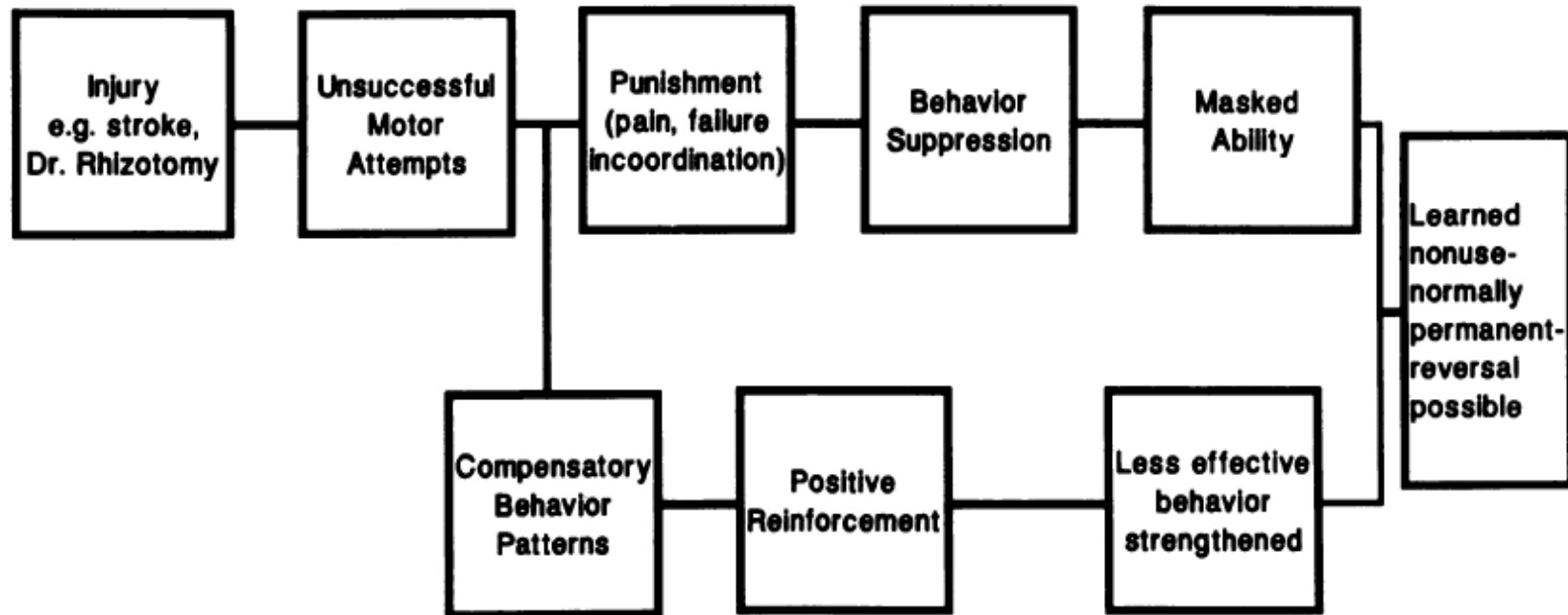


Fig. 1. Schematic model for development of learned nonuse. After Tries (1991).

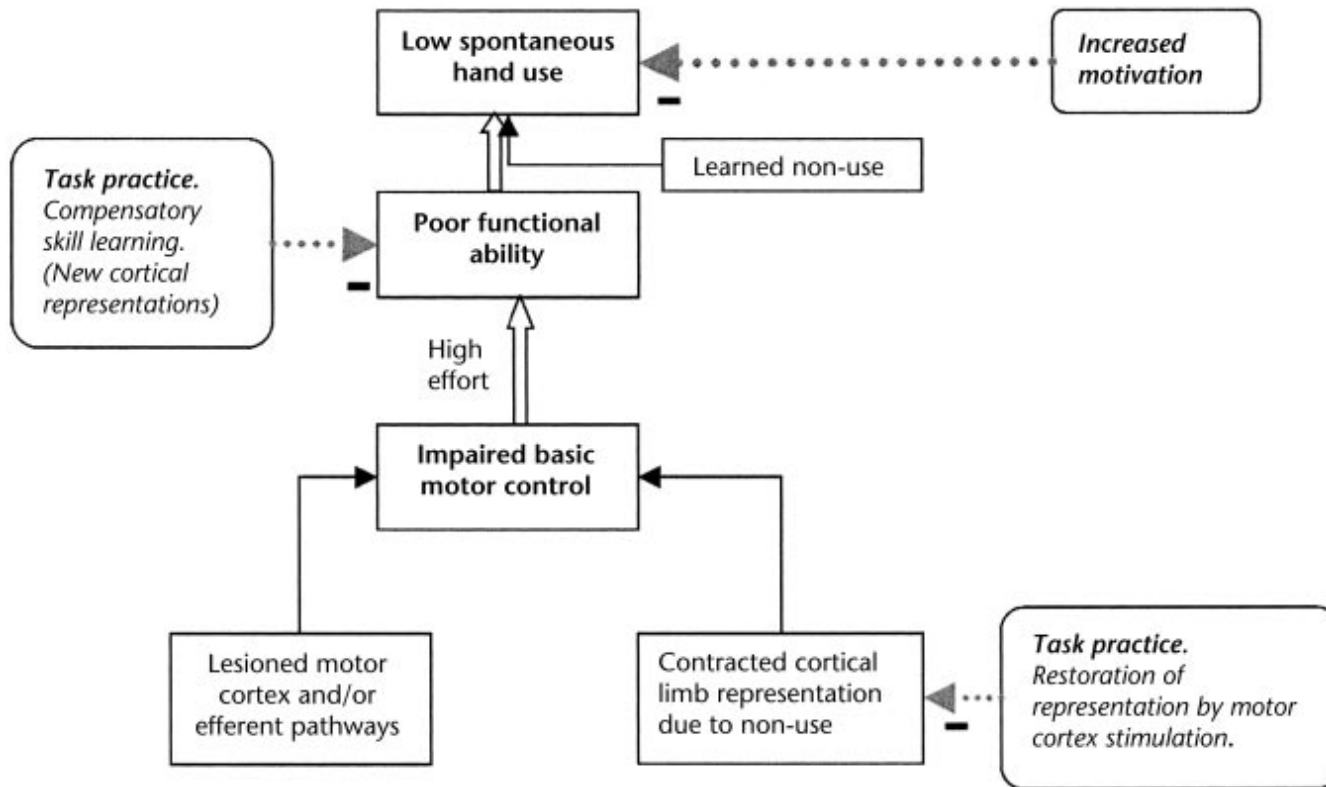
Modulating Neuroplasticity after Stroke - CIMT



Components of CIMT

- Restraining the affected limb
- Intensive practise of using the affected limb
- Reinforcement of successive attempts to use the limb

CIMT



Caution with CIMT

- Detrimental effect of overuse –
 - Intensive forced use during the first week post stroke
 - Contralateral dendritic growth prevented
 - Worsening of function of impaired limb
 - Increased size of lesion due to glutamate excitotoxicity

Glutamate excitotoxicity

- In the 1st week post injury- metabolic & vascular mechanisms that render the tissue susceptible to use dependent glutamate toxicity. By 2nd week recovery from these deficits, preventing further tissue loss
- By the 2nd week – Early exposure to non-toxic levels of glutamate (due to movement of the impaired limb) gives protection against later excessive levels of glutamate (due to constraint of intact limb)

Role of adjuvant therapies in Neurorehabilitation

- Role of d-amphetamine in combination with rehabilitation training to improve recovery post stroke
- Experiment in adult squirrel monkeys- infarct in hand area in M1
 - Spontaneous recovery group (SR)
 - Motor skill training (14 days) + saline (Sal/training)
 - Motor skill training (14 days) + d-AMPH (single dose)
- Outcome measure – Klüver board task

Role of adjuvant therapies in Neurorehabilitation

- Results-
 - Reduction in the number of flexions/retrievals needed to obtain a food pellet due to training
 - Injection of d-AMPH facilitated the ability to retrieve food pellets over and above the saline injected group
 - Follow up – 9 weeks post training d-AMPH group showed greater improvement than the other 2 groups

Mechanism of action of d-AMPH

- Feeney et al – Facilitates recovery by reversing the “remote functional depression” in brain regions remote to the site of injury
- Kasamatsu & Crow et al – Norepinephrine mediated long term neuronal reorganization and synaptic plasticity. Effect mediated in the hemisphere contralateral to the injured hemisphere

Role of adjuvant therapies in Neurorehabilitation

- Direct, low level electrical stimulation of the peri- infarcted cortex leads to –
 - Changes in functional maps
 - Induces dendritic growth

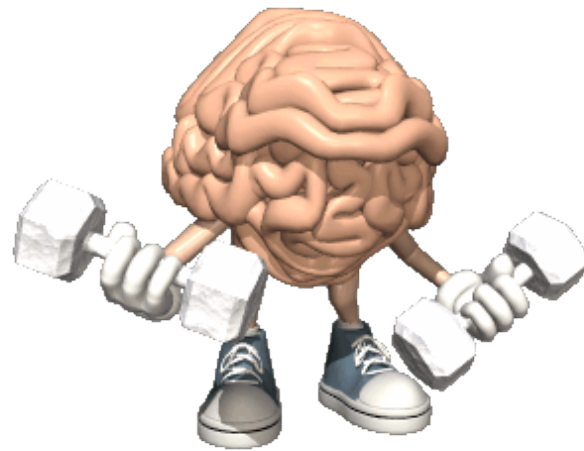
Conclusions

- Plasticity of the MC provides a neuroscientific foundation for the development of several physiotherapeutic interventions
- The brain can undergo structural and functional reorganization throughout life
- Injury to the brain is associated with local and remote adverse effects and plasticity is demonstrated at both sites

Conclusions

- Plasticity can be both adaptive and maladaptive and care must be taken while developing interventions accordingly
- Research in animals suggests that it is possible to create an adaptive environment in spared neuronal tissue for promoting maximal post-injury recovery

Questions?



Thank you!