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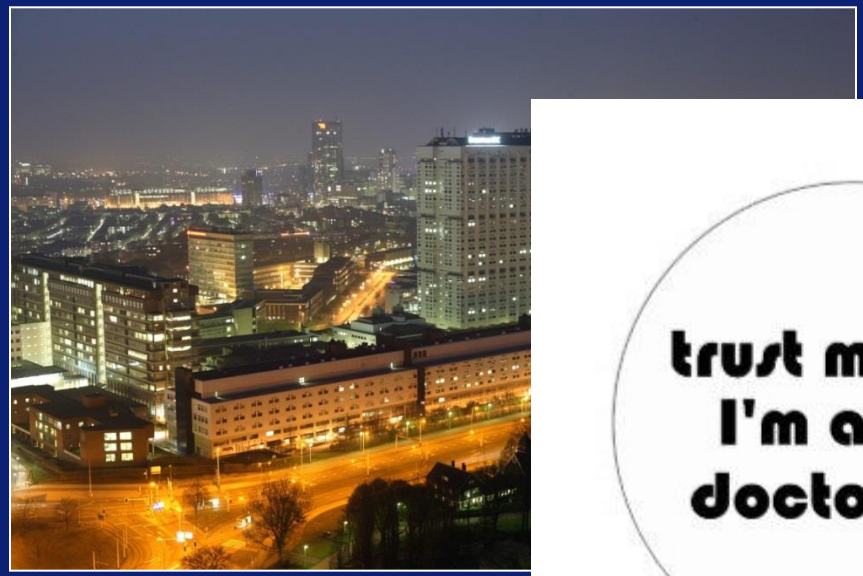
University Medical Center Rotterdam

Rijndam
Rehabilitation Institute

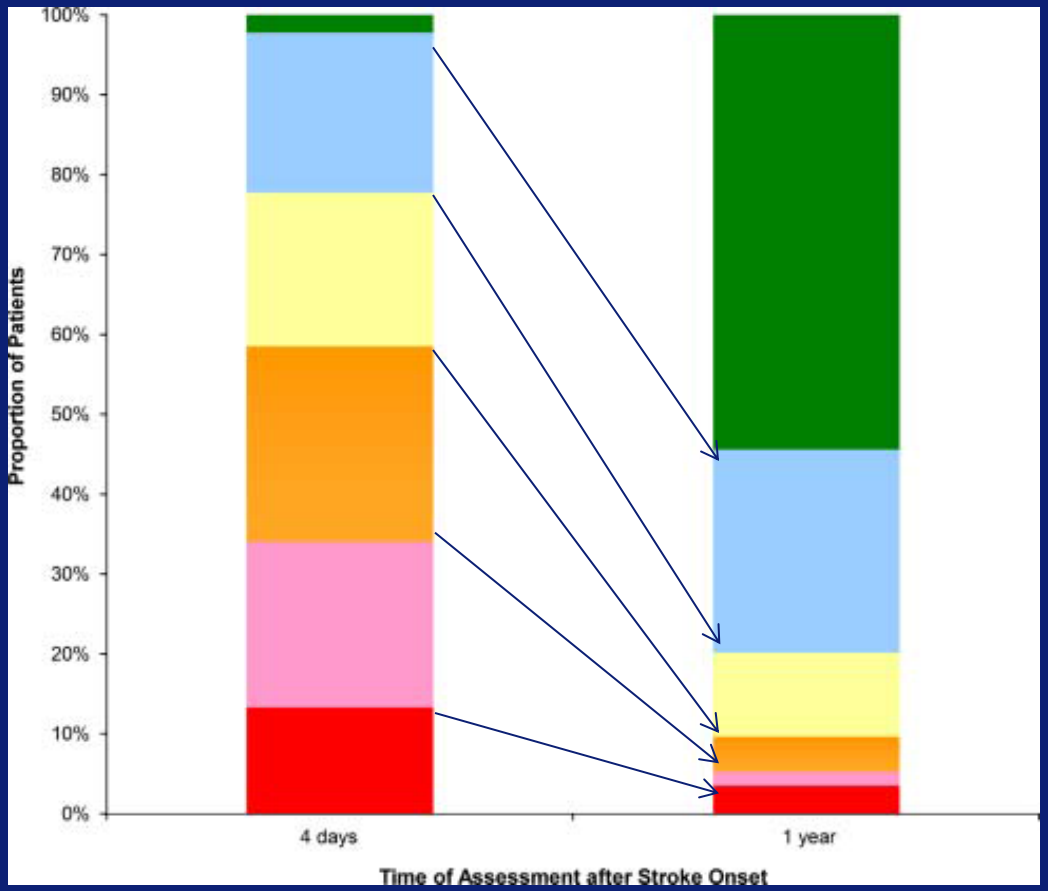
Post stroke aphasia: recovery and reorganization

Gerard M Ribbers

Context



Recovery of aphasia: a one year follow up



5 ASRS: minimal handicap

4 ASRS: loss fluency

3 ASRS: conversation +

2 ASRS: conversation +/-

1 ASRS: fragmentary

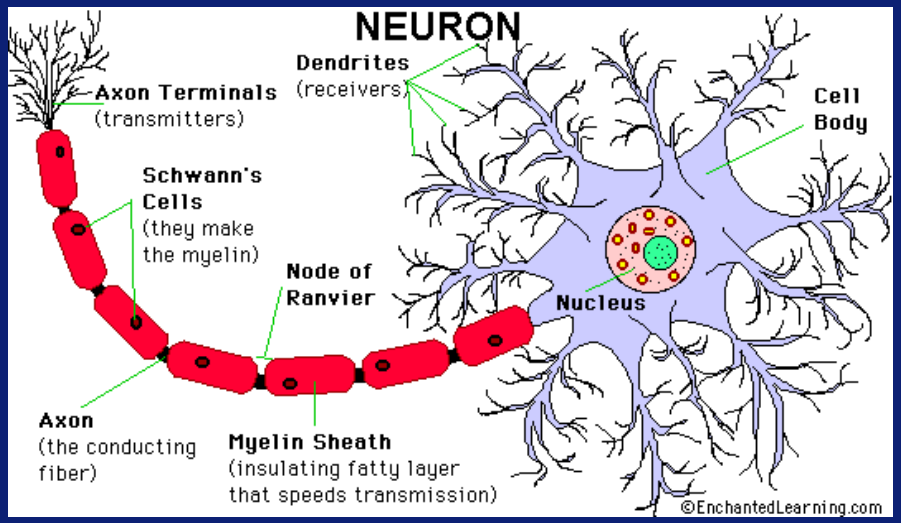
0 ASRS: very severe

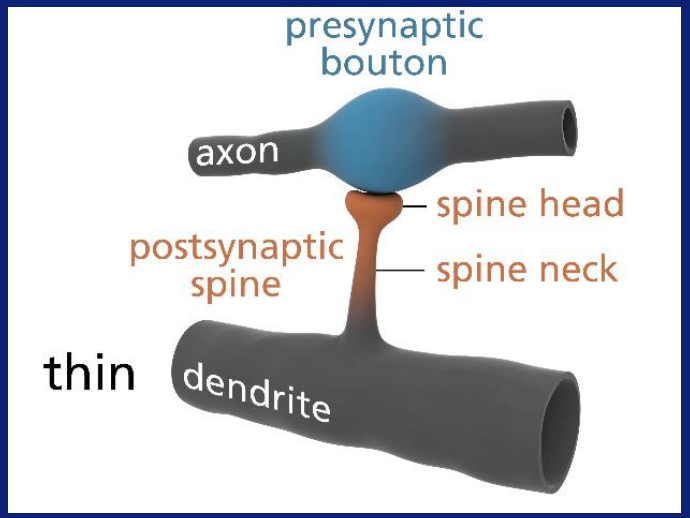
Hachioui,JNNP 2013, N=147

Mechanisms of functional recovery

- Restitution of non-infarcted penumbral areas
  - Tissue repair
  - ‘Vicariation of function’
    - Unmasking
    - Sprouting
    - Synaptogenesis
- Resolution of diaschizis (von Monakow)
- Behavioural compensation (substitution)

About information, bits and synapses





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RESEARCH ARTICLE

Nanoconnectomic upper bound on the variability of synaptic plasticity

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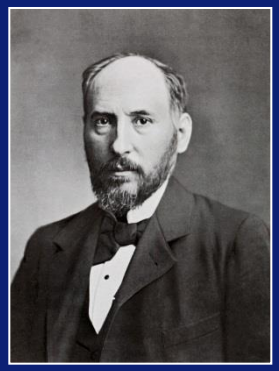
"…the brain could store 1 petabyte (or a quadrillion bytes) of information."
1 PB = 1000000000000000B = 10^{15}bytes = 1000 terabytes

Neuroplasticity: a recap

Neuroplasticity:

reorganization within (residual) neural tissue,

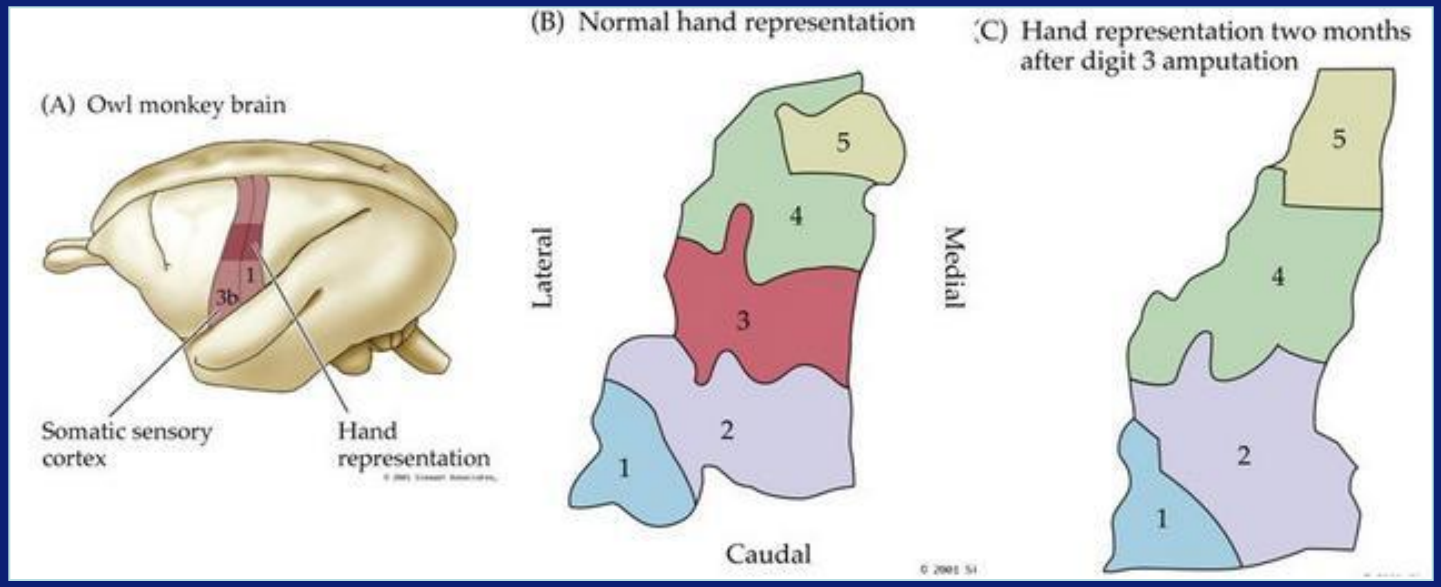
“Neurons That Fire Together Wire Together”



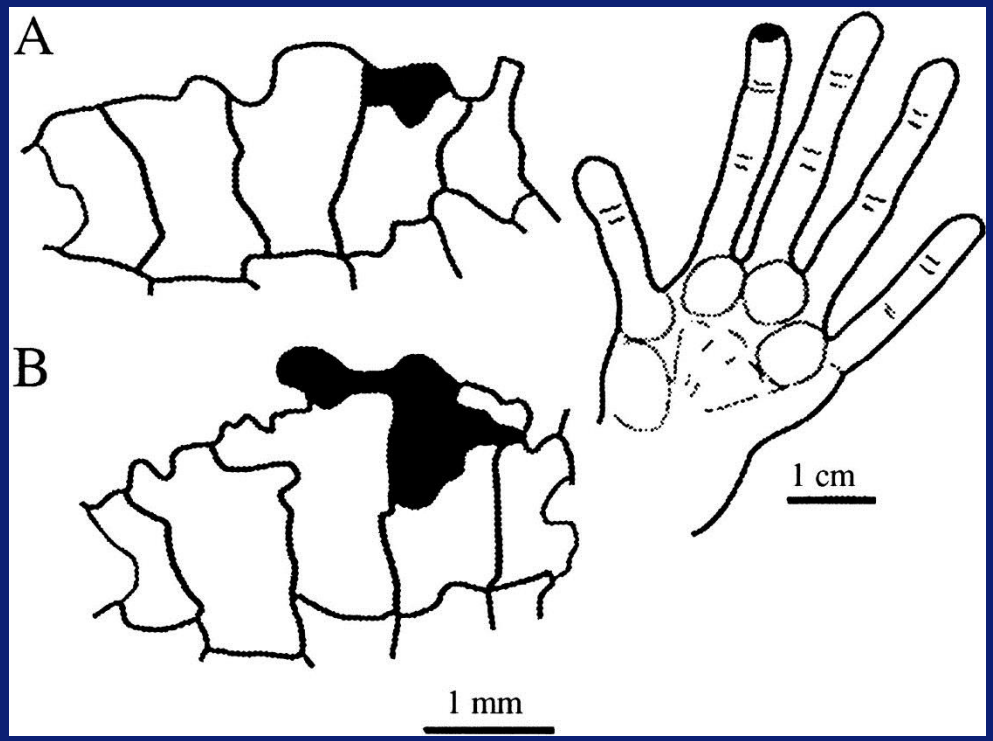
S.R. y Cajal, 1894

DO Hebb, 1949: Hebbian learning

Pruning: eliminating weaker contacts



Sprouting: to strengthen connections



Jenkins and Merzenich (1990):

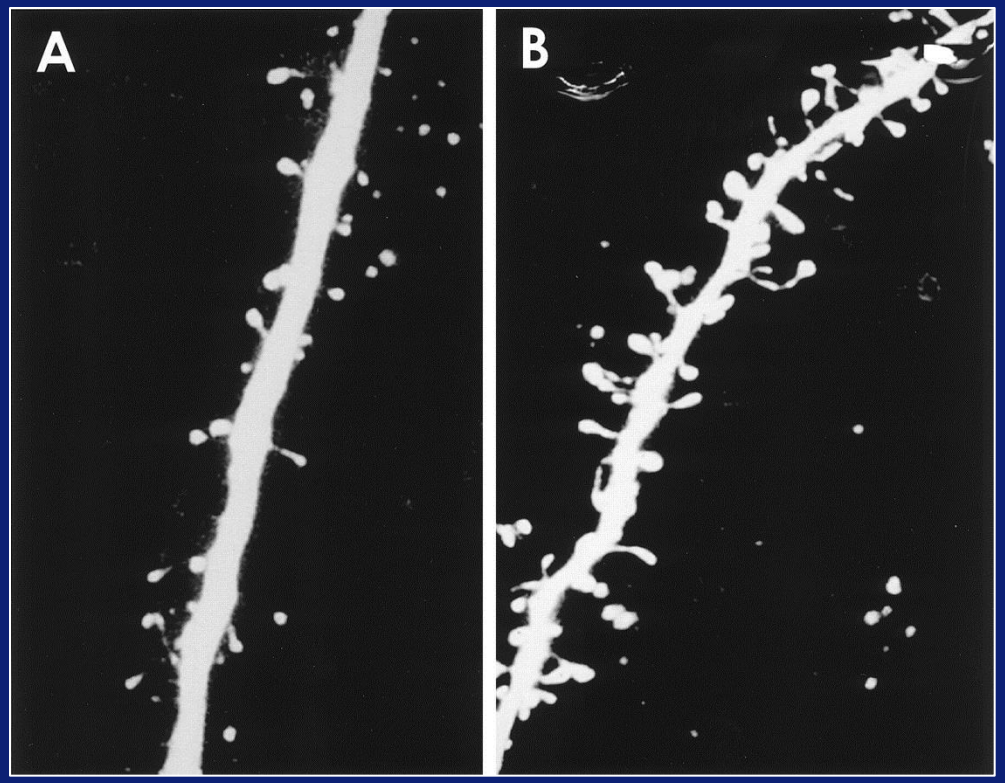
somatosensory cortex before (A) and after (B) tactile stimulation

Synaps structure dendritic spines

1. Protrusions from dendrites
2. Very plastic
3. Spine levels determined by

    - Activity
    - BDNF
    - AMPA receptors
    - NMDA receptors

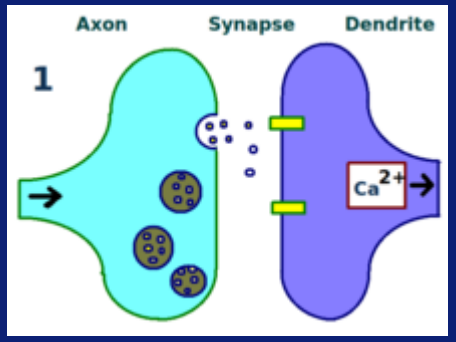
    - Scaling
    - Metaplasticity



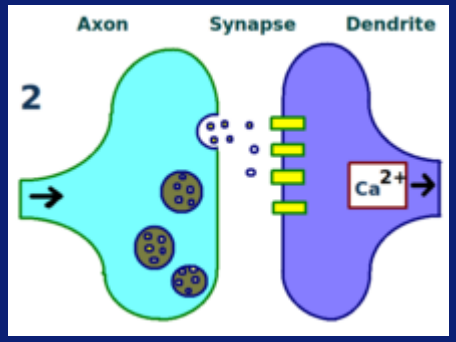
dendritic spines of pyramidal neurons
standard cage (left) vs enriched environment (right)

Johansson B B Stroke 2000;31:223-230

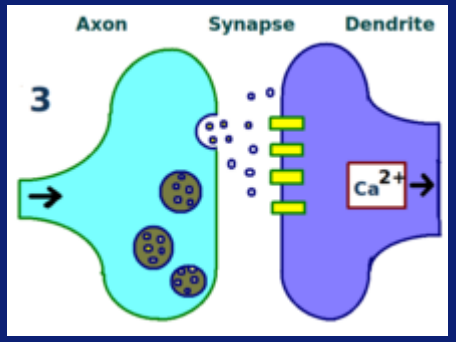
Synaps function:
Long term potentiation / depression



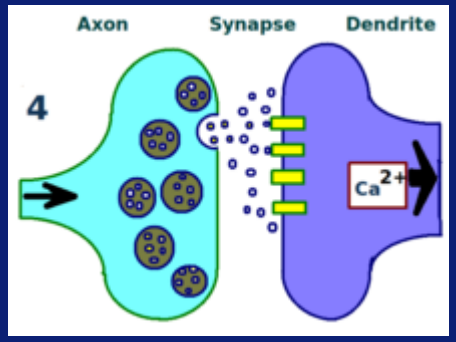
Repeated stimuli



Increased dendritic receptors



Increased neurotransmitters



Increased synaptic strength

Neuroplasticity: overview

	Presynaptic	Postsynaptic	Effect
Synaps function	'release chance'	Number and characteristics of receptors	'Synaptic Strength' (LTP & LTD)
Synaps structure	'axonal boutons'	Number of 'dendritic spines'	Number of synapses
Neural networks	Sprouting / pruning	Growth / retraction dendrites	Rewiring of neural connections
Neuro-genesis	Stam/progenotor cells subventricular of hippocampus		New neurons

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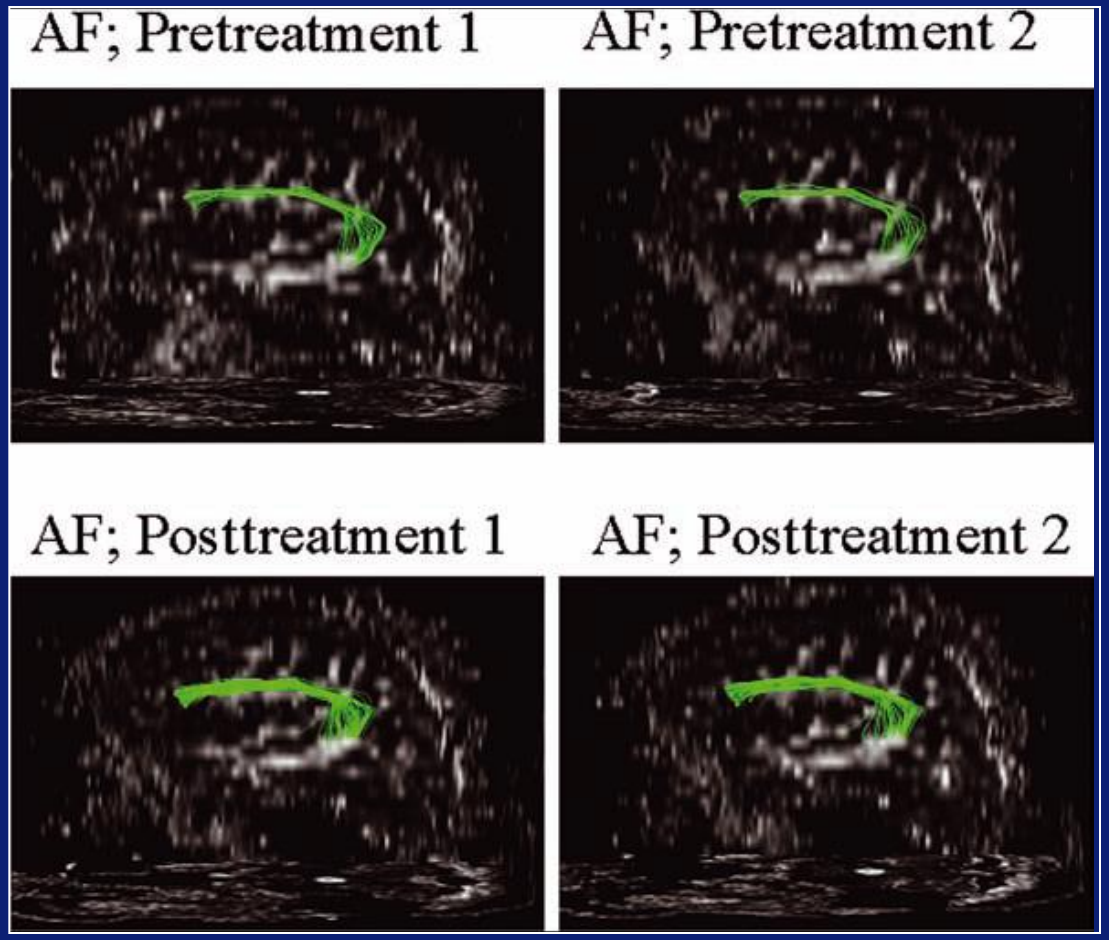
White matter plasticity



Schlaug et al: 2009

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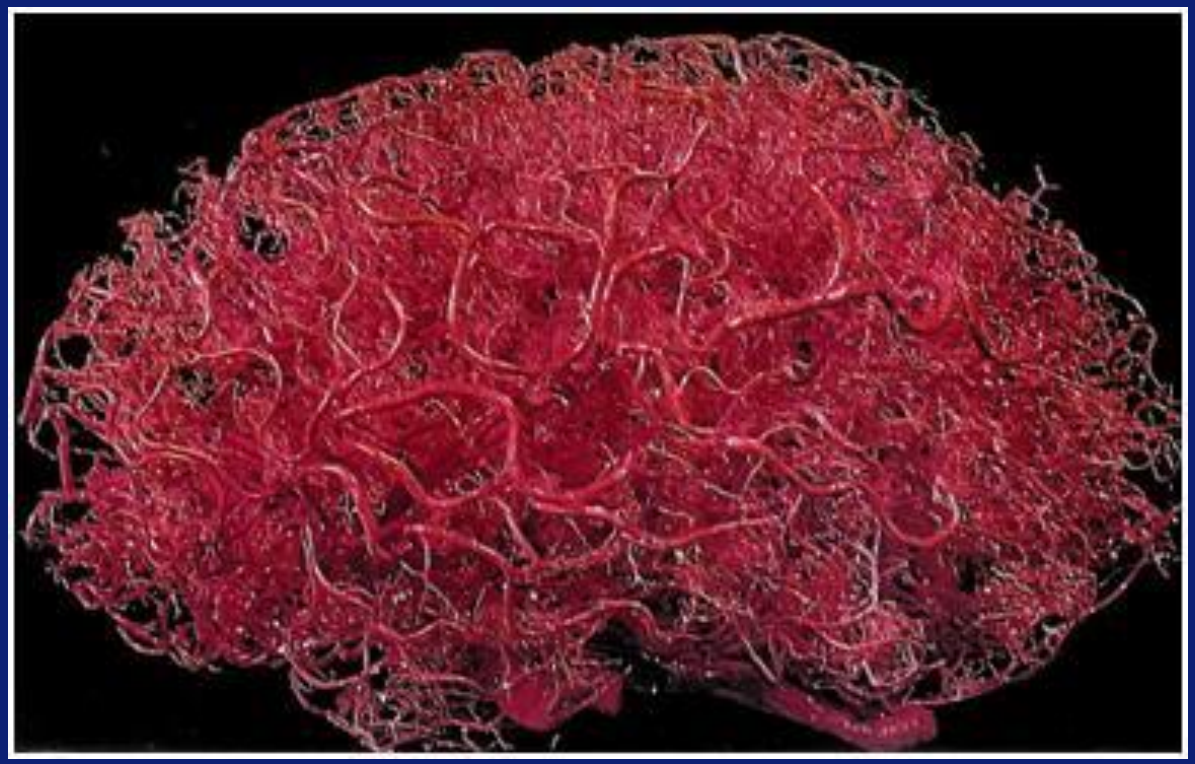
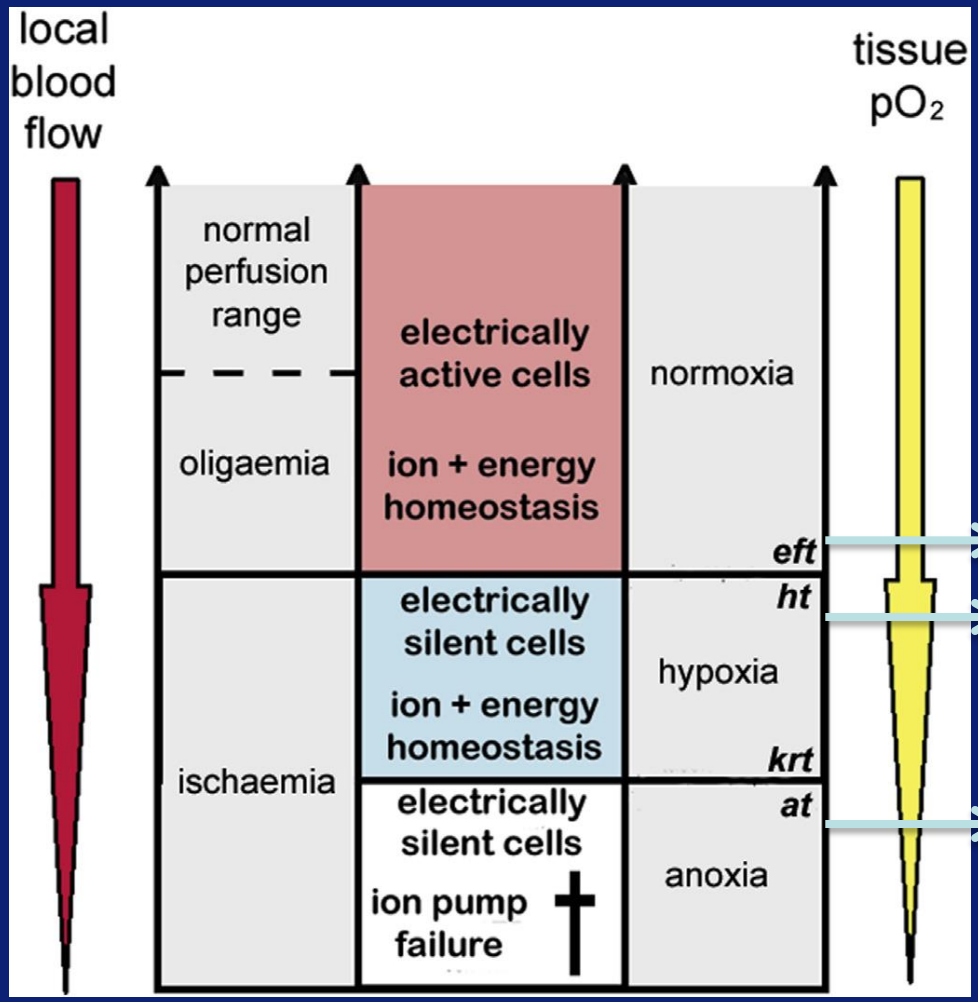
A stroke



Penumbra



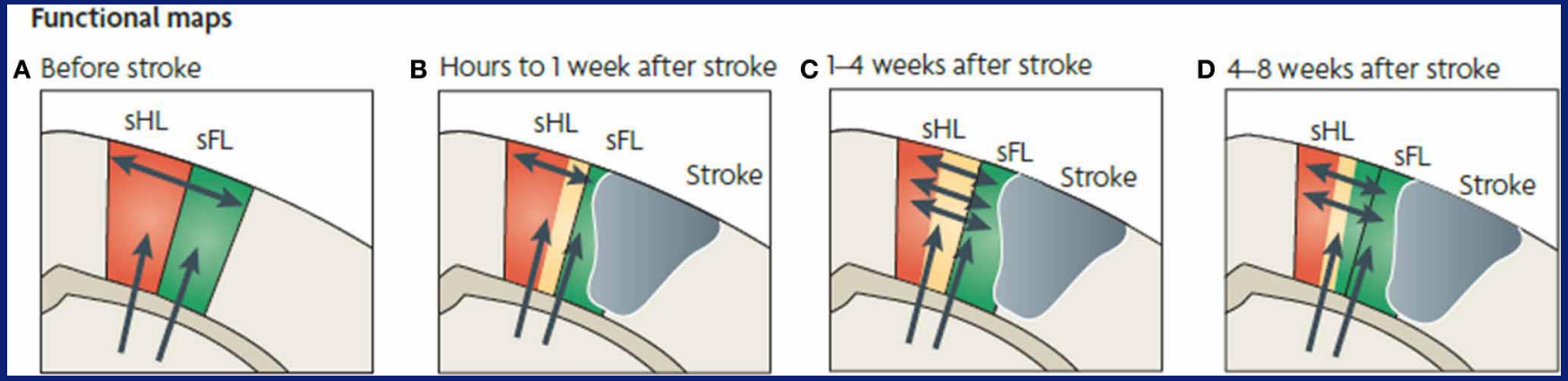
Penumbra

Electrical failure thresshold

Hypoxic hresshold

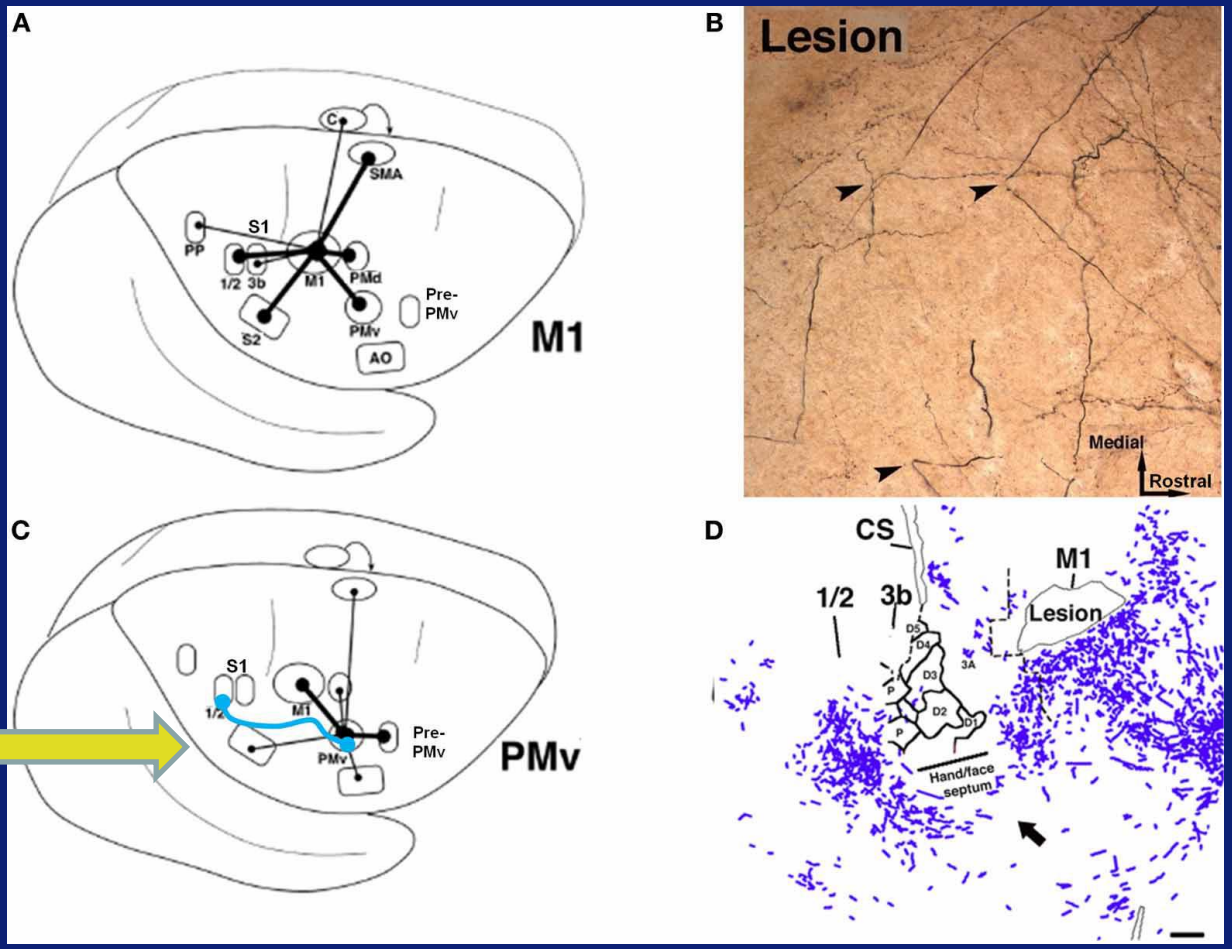
Anoxic thresshold

PLASTICITY IN ADJACENT, INTACT CORTEX AFTER FOCAL INJURY



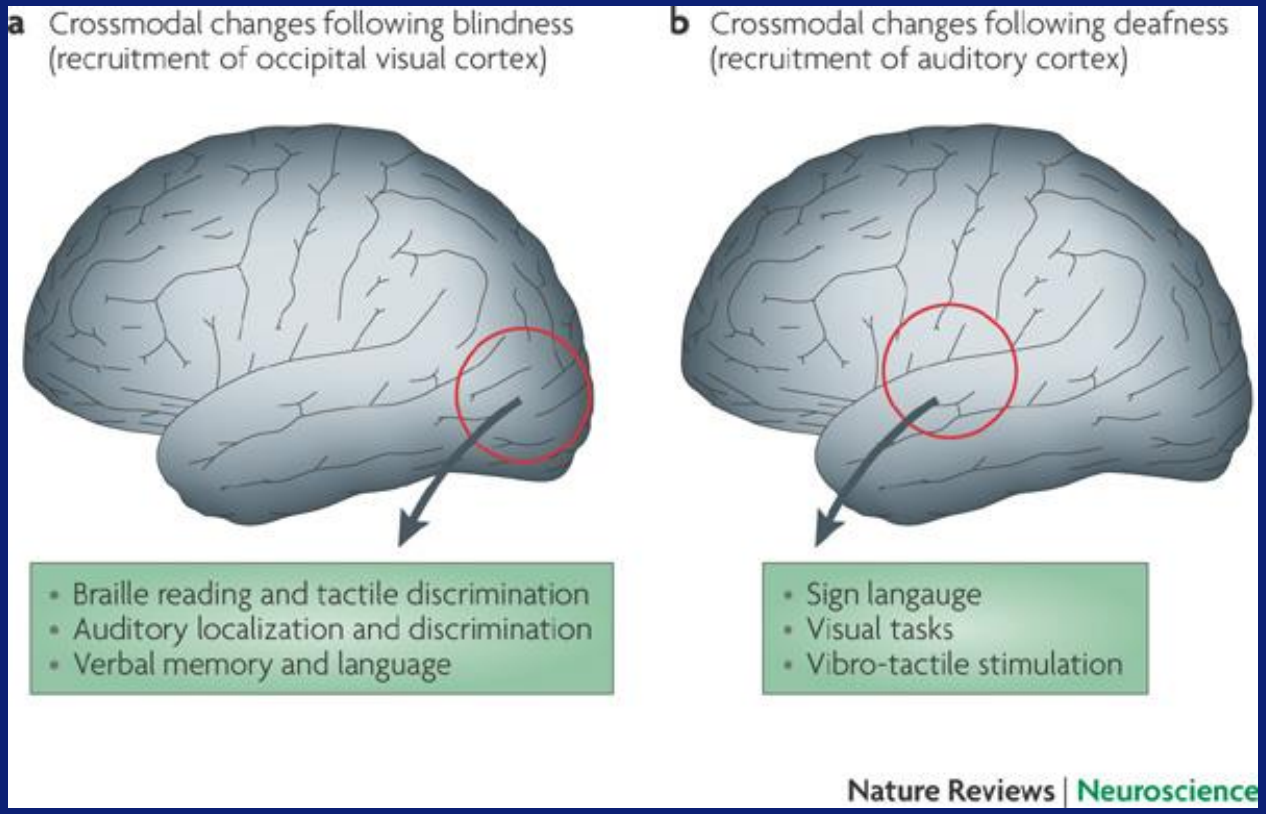
Murphy and Corbett,2009

WHITE MATTER PLASTICITY IN REMOTE REGIONS AFTER FOCAL DAMAGE TO M1



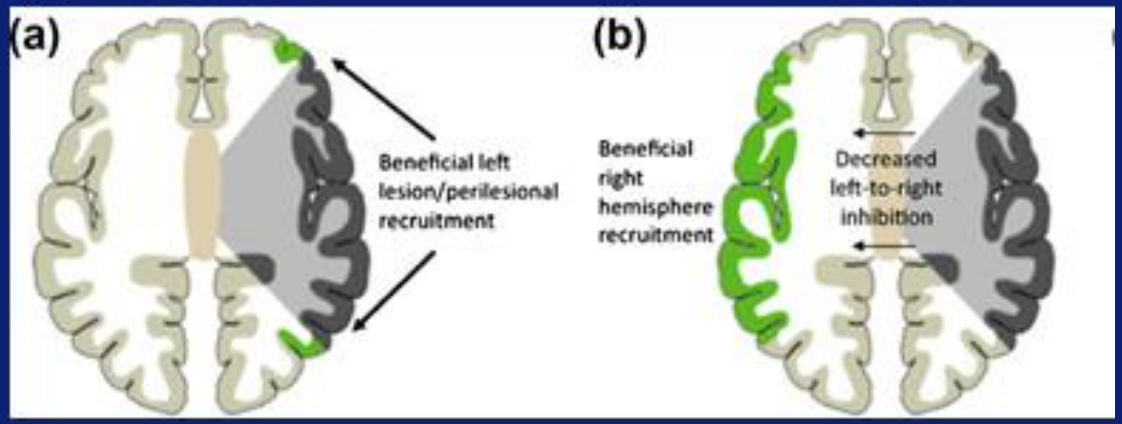
Dancause et al.,2005

Neural networks
Inter- or crossmodal reorganisation



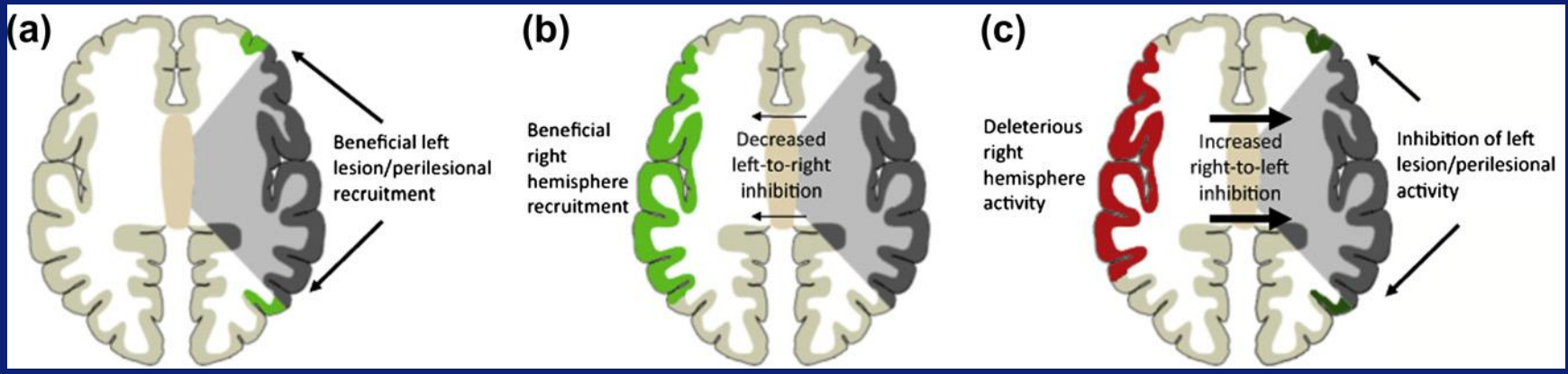
Merabet et al; Nat Rev neurosc: 2010

Neural networks
Intramodal reorganisation



Hamilton et al, Brain & Language 2011

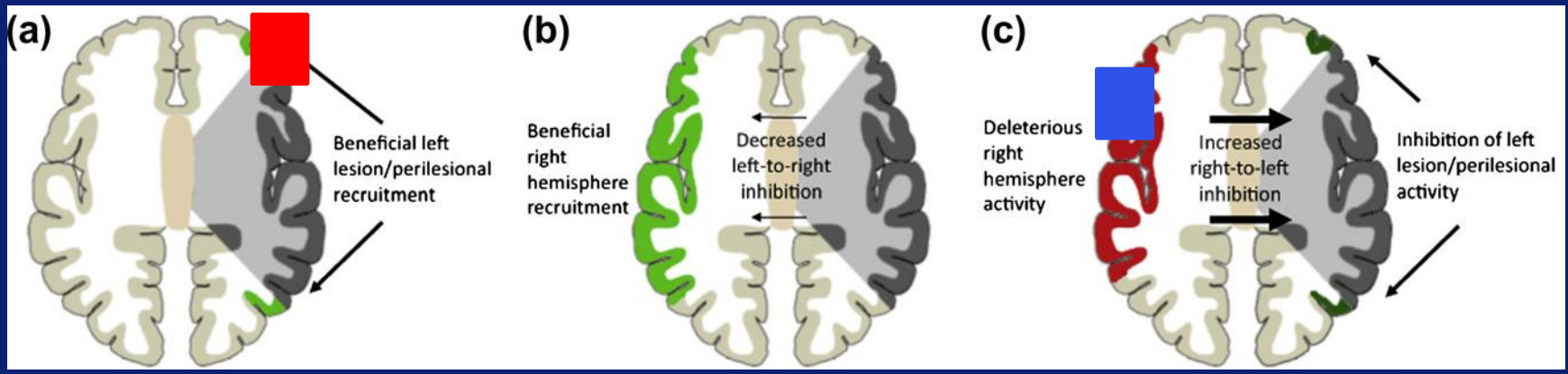
Neural networks
maladaptive intramodal reorganisation



Hamilton et al, Brain & Language 2011

Anodal tDCS
Left Hemisphere

Cathodal tDCS
Left Hemisphere



Hamilton et al, Brain & Language 2011

Post stroke sequence of events
± < 1st week

- **Lesion**
  - Extracellular glutamate ↑ m.a.g. local celldeath and remote neuroplaticity
  - Dysbalanced acivation/inhibition in neural networks
- **Penumbra**
  - Variable in size
  - Eather way: recovery or necrosis
  - Instabile phase with vulnarable braintissue,
- **Perilesional**
- **Remote**

Post stroke sequence of events
± < 1st week

- **Lesion**
- **Penumbra**
- **Perilesionaal**
  - Electrophysiological overactivity
  - Vicarisation (unmasking, increased in excitability en neuronal transmission)
- **Remote**
  - Increased excitability contralateral hemisphere (dysbalanced inhibition); size matters!

Post stroke sequence of events: subacute phase: 48 hrs – 3 weeks p.o.

- **Perilesional**
  - A state of hyperexcitability
  - Vicarisation
  - Intrinsic ermergent capacity or activity driven?
- **Remote**
  - Hyperactivation of intra- and crossmodal neural networks in ipsi- and contralateral hemispheres (mal-adaptation?)
  - Diaschizis

Post stroke sequence of events: consolidation: ± > 2-3 months

- Increased neuroplasticity
  - In case of good recovery in perilesion tissue
  - In case of poor recovery in contralesional neural networks

"I have to use this call button?! I'm too old to learn new technology. Why can't I just scream when I need you?"

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Patterns of recovery

Phase / Location	(hyper-)acute < 48 hrs	Subacute 48 h – 6 wks	Consolidation > 1.5 mths
Lesion	Cell death		
Penumbra	Instability Reperfusion	Instability Reperfusion	
Perilesional	Diachizis	Hyperexcitability Resolution of diaschizis	Plasticity
Remote	Diachizis	Hyperactivation of homo- and perilogue networks	(mal-)adaptive plasticity

Recovery and time post onset

Phase / Location	(hyper-)acute < 48 hrs	Subacute 48 h – 6 wks	Consolidation > 1.5 mths
Lesion	Cell death		
Penumbra	Instability	Instability	
Perilesional	Diachizis	Hyperexcitability	Plasticity
Remote	Diachizis	Hyperactivation of homo- and perilogue networks	(mal-)adaptive plasticity

challenges

- Repairing the damaged brain by targetting the robust phase of growth, understanding its physiology, enhancing behavioral change.
- To target the right people with a specific treatment paradigm, with the right intensity, at the right time and with the right behavioral paradigm.
- Long term adherence to exercise on what ever domain requires a lifestyle changement.

Personalized Therapy

- Tailoring of medical care to the particular traits (or circumstances or other characteristics) of a patient that influence response to a health care intervention.

- These may include genetic, sociodemographic, clinical, behavioral, environmental, and other personal traits, as well as personal preferences.

- PT does not refer to the creation of interventions that are unique to a patient, but to the ability to classify patients into subpopulations that differ in their responses to particular interventions.

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Rotterdam Neurorehabilitation Research