# How Therapy Changes the Human Brain

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## Selected Neural Plasticity References


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- Pekna,M., Pekny, M., Nilsson,M.(2012) Modulation of Neural Plasticity as a Basis for Stroke Rehabilitation. *Stroke* 43: 2819-2828 Thorough review for all disciplines
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## References on issues related to when to begin treatment after stroke


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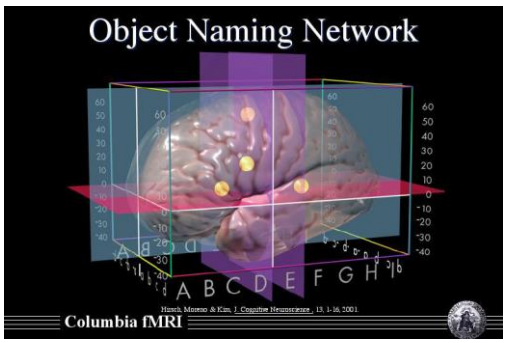
## Experience-Dependent Plasticity of the Cerebral Cortex (Pekna,M., Pekny, M., Nilsson,M.,2012)

- *"The ability to adapt in response to the changing environment is the most fundamental property of the nervous tissue and constitutes the basis for learning*."
- ***Neural plasticity*** - neurobiological basis for ability to adapt & learn in an **experience-dependent manner**
  - At the structural level, neural plasticity could be defined in terms of
    - dendritic and axonal arborization,
    - spine density,
    - synapse number and size,
    - receptor density,
    - and in some brain regions also the number of neurons.

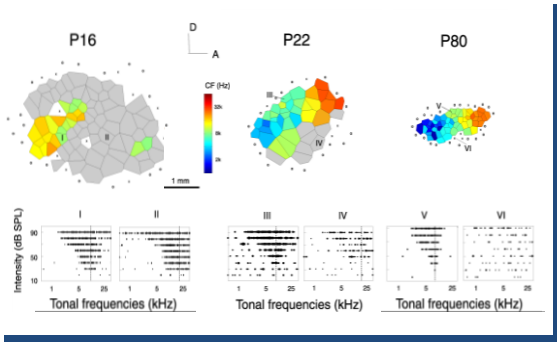
## Experience-Dependent Plasticity of the Cerebral Cortex

- The structural constituents of neural plasticity jointly determine
  - the complexity of ***neuronal networks*** and their **activity** and
  - contribute to habilitation of skills in the developing brain as well as recovery of function after stroke and other CNS injury

Hebbian Axiom - Neurons that fire together wire together in networks



Cortical map development - Normal A1 development




Zhang, Bao & Merzenich, Nature Neuroscience, 2001

## Cortical Map Rearrangements

- Occurs in sensory systems within the cortex including auditory and visual
- The reorganization that occurs after rehabilitation is associated with upregulation chemical neuromodulators in relation to the parameters of the stimulation that occurred

But beyond early infancy, plasticity is modulated as a function of:

1. novelty
2. attention
3. judgment of error
4. punishment
5. Reward
6. et alia

See Kilgard & Merzenich, Science (1998)
Kilgard & Merzenich, Nature Neuroscience (1999)
Bao, Merzenich, et al, Nature (2001)

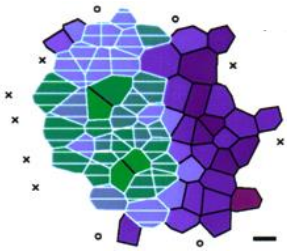
Different dimensions of adult cortical plasticity are enabled by the behaviorally-context-dependent release of:

- acetylcholine (focused attention/reward) (Kilgard, Bao)
- dopamine (reward, novelty) (Bao)
- norepinephrine (novelty) (Bollinger)
- serotonin (Bollinger)
- et alia

In infants, exposure-based plasticity is relatively uniform.
In adults, learning-induced changes are complexly "nuanced" by differences in behavioral context that result in the differential release of 6 or 7 modulatory neurotransmitters.

## In older animals and humans, the brain controls its own plasticity.

acetylcholine-enabled plasticity

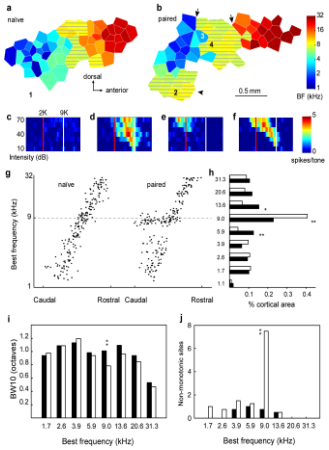


Kilgard & Merzenich Science, 1998

dopamine (VTA) enabled plasticity.

I. Reward follows stimulus

II. Reward precedes stimulus.



Bao, Merzenich et al (2001) Nature

## Cortical Map Rearrangements (Pekna,M., Pekny, M., Nilsson,M.,2012)

- When normal input to a specific area of the primary somatosensory cortex is altered because of genetics or because of experience
  - **rapid structural and functional reorganization results** in this area being **activated by sensory stimulation of the surrounding intact body regions**

Gerloff, et al. (2006) Multimodal imaging in chronic stroke Brain 129, 791–808 801

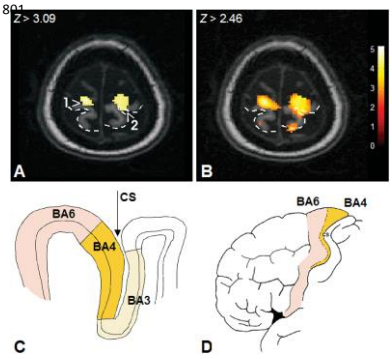
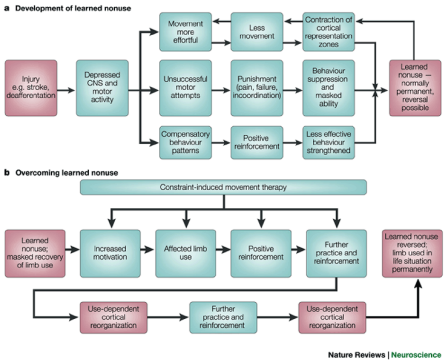



Fig. 7 Detailed illustration of enhanced rCBF during right (recovered) hand movements in stroke patients (n = 9) compared with age-matched controls (n = 9) in the contralesional central region.

## Neuroimaging research on effects of therapy

- Early research on constraint induced therapy after paralysis
- Neuroimaging research on effects of therapy In developing brains
  - Language and reading disorders
  - In adult brains after injury especially visual working memory training
  - Power attained by combining bottom-up and top-down processing activities

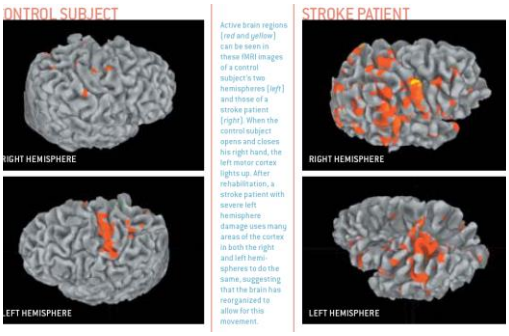
## Taub Model



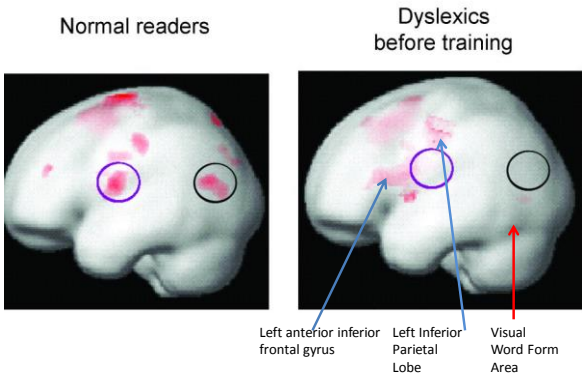

## Importance of Intensive Intervention

Taub – Constraint Induced therapy

E **Taub**, G Uswatte, R Pidikiti - Journal of rehabilitation (1999); J Liepert, H Bauder, WHR Miltner, E **Taub**, C Weiller - Stroke, 2000; E **Taub**, G Uswatte, T Elbert - Nature Reviews Neuroscience, 2002

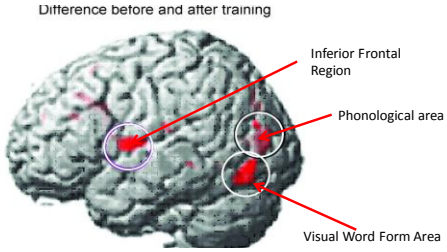


(Temple et al., 2001; Gaab, 2008)




## And the effects of treatment indicate functional connections seen in nonimpaired readers are achieved

(DeHaene, *Reading in the Brain*, pp 260)



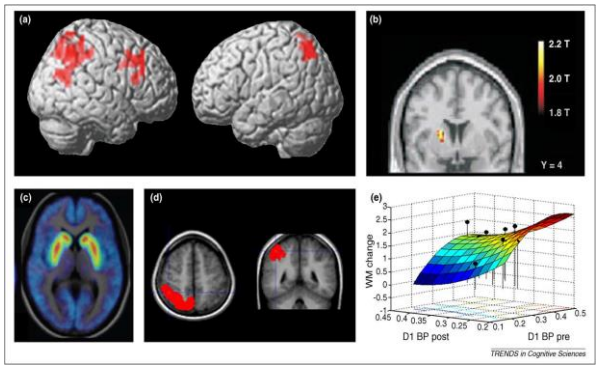




Figure 1. Training-related effects on brain activation and dopamine receptor density from neuroimaging studies. (a) Increases in frontal and parietal activity after training of WM (reproduced with permission from [33]). (b) Increased activity in the caudate nucleus after training of WM tasks requiring updating (reproduced with permission from r

## Specific characteristics of effective language based therapies

The emerging consensus from neuroscience is that combining of cognitive (executive function) top down interventions with bottom-up (perceptual and attention) interventions may be most effective

Q & A