NEUROPLASTICITY

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WHAT IS NEUROPLASTICITY?

The brain's ability to change, remodel, and reorganize in order to better adapt to new situations[1]

Depending on our experiences, neural networks develop and disappear throughout life since these networks are not fixed[1]

The capacity of brain cells to change in response to both intrinsic and extrinsic factors, and can have positive or negative influences at any age[2]

Synapses within the brain can be strengthened or weakened through synchronous and asynchronous activity between neurons[3]

STRUCTURAL NEUROPLASTICITY

- Synaptic plasticity includes changes in the strength of synapses between neurons
- Synaptogenesis is the formation and addition of new synapses into neural circuits
- Neurogenesis is the creation of new neurons, and mainly occurs during brain development. Recently it was found that neurogenesis occurs in adult brains as well[1]

FUNCTIONAL NEUROPLASTICITY

- Depends on learning and memory, which cause permanent changes in synaptic relationships between neurons[1]

“Every man can, if he so desires, become the sculptor of his own brain.”

-Santiago Ramon y Cajal

HISTORY

- The theory of neuroplasticity first introduced 120 years ago by William James in *Principles of Psychology*, where he suggested the capacity of the brain for continuous functional changes
- First defined in 1948 by Jerzy Konorski. In his theory of conditioned reflexes, he proposed that neurons can be activated by their closeness to an active neural circuit, resulting in the circuit adapting by incorporating the neuron
- Paul Bach-y-Rita the first to demonstrate that neuroplasticity allows healthy brain regions to take over the functions of injured regions
- Academic dogma disapproving of the existence of adult brain neuroplasticity except in development was held up until the "Decade of the brain" (1990-2000)[1]

TYPES OF NEUROPLASTICITY

Homologous Area Adaptation

Cross-Modal Reassignment

Map Expansion

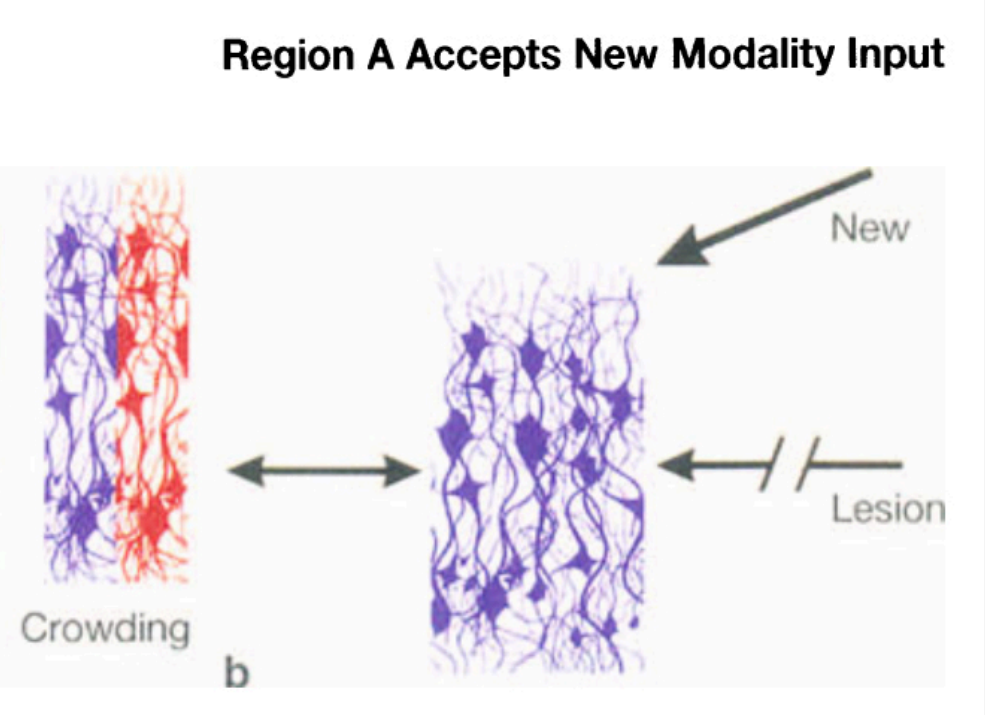
Compensatory Masquerade

HOMOLOGOUS AREA ADAPTATION

- A region of one hemisphere is damaged, and homologous region in the opposite hemisphere takes over the function of the damaged area[5]
- This is able to occur during childhood[4]

CROSS-MODAL REASSIGNMENT

- Structures previously devoted to processing a particular kind of sensory input accept input from a new sensory modality[4]
- Functions that are ordinarily processed elsewhere in the brain can be diverted to a new region for specific information processing purposes[4]
- Example: one sensory modality (like vision) is damaged, and in response another sensory modality (like touch) provides inputs to the cortical space previously committed to the now-damaged modality[5]



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MAP EXPANSION

- Enlargement of a functional brain region on the basis of performance[4]
- The extend that boundaries between brain regions are committed to different tasks based on one's daily activities[5]

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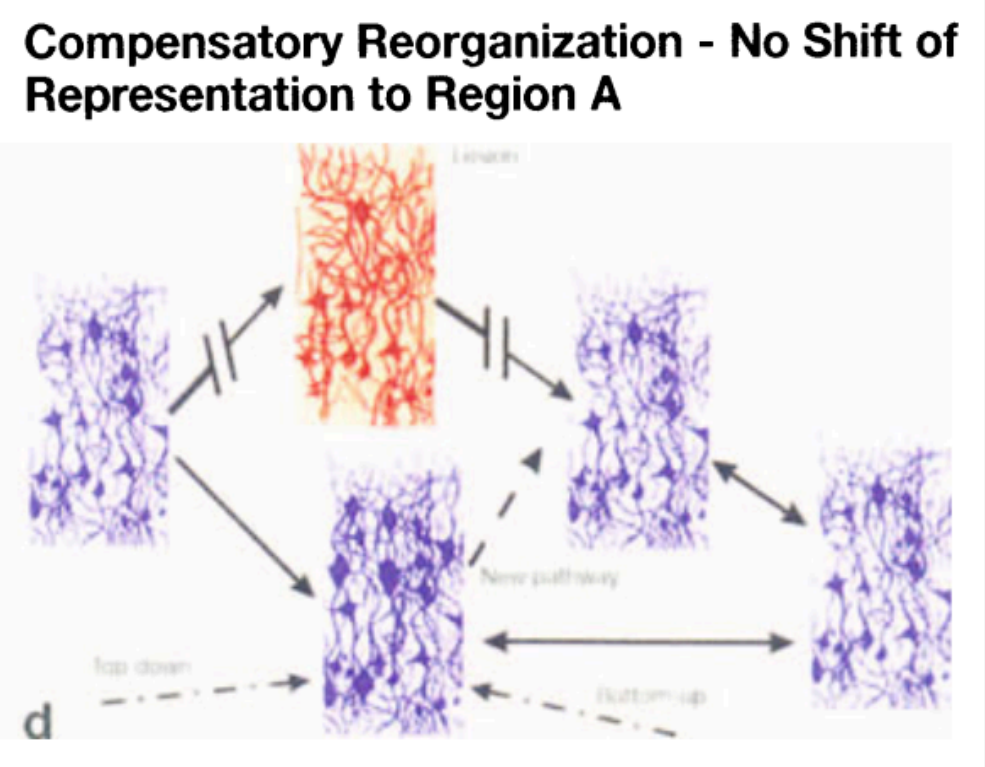
COMPENSATORY MASQUERADE

- Allocation of a particular cognitive process to perform a task[4]
- Brain switches from using one type of strategy to a different type[5]



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MEMORY FORMATION

- Acquiring information from the environment and learning new behaviors requires that experience-induced patterns of neural activity are maintained through the plasticity of specific neural networks
- Depending on how long plastic changes are preserved, the acquired information will persist
  - Structural synaptic plasticity is a persistent form[6]
- Many molecular events occur in order to establish plastic changes

CALCIUM

- Calcium a signal for synaptic plasticity
- Aid in long-term potentiation (LTP), an activity-dependent strengthening of synapses
- At excitatory synapses, Ca^{2+} entry into the postsynaptic cell helps trigger LTP
- CaMKII detects Ca^{2+} elevation and potentiates synaptic transmission by initiating a biochemical cascade[10]
- Ability to interact with actin cytoskeletons making up dendrites, and so regulates structural synaptic plasticity[6]

CAMKII

- Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) an important Ca^{2+} detector in postsynaptic region
- CaMKII's ability to maintain autophosphorylation activity for prolonged periods of time helps sustain signaling and allows for consolidation of long-term synaptic plasticity
- Suggested that CaMKII works as a memory switch, where its activity switches between transitory to stable state depending on interaction between CaMKII and NMDA receptor
- LTP induction in hippocampus also known to rapidly increase synthesis and accumulation of CaMKII, as well as induce its autophosphorylation activity
- CaMKII play crucial role in persistent forms of synaptic plasticity[6]

CAMKII STUDIES

- CaMKII's importance in LTM seen when mutant flies expressing a CaMKII inhibitor peptide exhibited serious learning deficits[7]
- Rats trained in Morris water maze task, a spatial learning task, show induction of activated form of CaMKII in hippocampus, and retention performance of this task positively correlated with CaMKII activity levels[8]
- Another study by Frankland and colleagues found that heterozygous mutations of CaMKII exhibited normal memory for the Morris water maze task 3 days after training, but animals were amnesic 10-50 days after
  - LTM (not STM) depends on CaMKII[9]

NEUROREHABILITATION

Main question for this type of medicine is how to direct neuroplasticity to regain lost functions from neurologic deficits

If we know which neural pathway has been damaged, can determine possible bypasses

MOVEMENT REHABILITATION

- To learn complex movements, the brain first recognizes the basic motor movements and stores them so they can be remembered
- Network of neurons can be activated every time we think, observe, or make the movement. Understanding the purpose of the movement also stimulates other neuronal circuits that aid in the execution of the final goal[1]
- Rehabilitation focus on observation and repetition
  - First learned complex movements using observation during childhood[1]
- Mirror neurons in ventral premotor cx and base of parietal lobe are a neuroanatomical target for rehabilitation exercises
  - Goal is to reach their activation through a connected healthy area of the cortical network
  - Mirror neurons will activate differently in each person, depending on their practice with the movement
  - Reconnection of synapses for different movements depends on experience in those movements prior to stroke[1]

NEURONAL PROCESSING OF DIFFERENT SIGNALS

- Creation of 12-dot code for soldiers to share information on battle field without speech. Usage of this code difficult for soldiers, but easy for blind boy, Louis Braille
- Blind person able to process and translate positions of dots quickly because visual cx does not receive information from a visual pathway, and instead was able to change its function to process touch sensations
- Later proven that occipital lobe is activated when blind subjects read[1]
- This remodeling of brain maps after brain damage is the future of neurorehabilitation. It requires defining neural pathways that can be used to regain lost functions through bypass pathways

COGNITIVE TRAINING

- Virtual reality games successfully aided in improving attention and memory functions in stroke patients[11]
- Stroke patients using vision training computer games (not VR) showed greater improvements in attention, concentration, executive function, memory, visual structure skills, abstract thinking, calculation, and directional force compared to patients using conventional rehabilitation therapies alone[12]

CONCLUSION

- Brain is constantly changing over lifetime
  - Structural changes are dominant during fetal development (neurogenesis, migration of neurons)
  - Functional changes dominant in adult brain, allowing us to adapt to environment and injury[1]
- In order for neurorehabilitation to progress in future, need to discover and define neural pathways that can be used as bypass systems to serve as compensatory neural circuits

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