Neural Plasticity

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Why Neural Plasticity?
What is Neural Plasticity

Wide range of possible definitions:

• “If you do something to the nervous system, you will produce a change”, to

• The capability of the damaged brain to “repair itself” to make functional and adaptive recovery, including spontaneous recovery from deficits, or deficits being reduced by pharmacological, physiological, surgical or behavioral treatments.
Levels of Neuromuscular Organization

• Spinal
  – Motor
  – Sensory
• Brain stem movement control
  – Influence of brain stem reflexes
• Cortical/Subcortical movement control
Cortical/subcortical movement control

- Association cortex/prefrontal cortex
- Lateral cerebellum
- Basal ganglia
- Thalamus
- Premotor cortex
- Motor cortex
- Intermediate cerebellum
- Somatosensory cortex
- Distributed control system
- Inhibitory mechanisms
Mechanisms of Plasticity

- Sprouting
- Denervation supersensitivity
- Behavioral compensation
- Unmasking-diaschisis
- Age factors
- Environmental variables
Sprouting

• Must meet sequential criteria
• Collateral sprouting
• May be maladaptive
Denervation Supersensitivity

• Results in permanent increase in a neuron’s responsiveness to diminished output
• Receptor sites may become more sensitive by change in receptor site or receptors may increase in number
• Occurs in the peripheral NS
Behavioral Compensation

• Theory that recovery of a lost function reflected a new behavioral strategy
• Does not describe the actual neural mechanism underlying the recovery of function
Unmasking-Diaschisis

- Diaschisis is a form of unmasking
- Lesion to 1 region of CNS temporarily alters function at a remote area
- Function is lost in both the injured and the non-injured site; brain function is depressed
- Recovery occurs with dissipation of depression in the remote area
Diascheses, part 2

• Injury-induced biochemical and genomic alterations in protein synthesis generating actions multi-synaptically removed from the lesion

• Recovery with dissipation of diaschisis, permanent deficits with permanent diaschisis

• Dynamic diaschisis
Reorganization of Neural Function

• Via microelectrode recording techniques
• Tissue adjacent to the area expands its receptive field
• Dependent on reorganization, recruitment and organizational shifts
Age Factors

• Animal studies
• “uncommitted neurons”
Environmental Variables

- Animal studies
- “overtraining”
Clinical Insights and Applications

• Stroke Model-unilateral animal infarct
• Functional Neuroimaging/brain mapping
  – Initially decreased cortical activity locally
  – Increased cortical activity at distant sites
  – Diaschisis
  – Time window
  – Other factors affecting stroke recovery
Restorative Therapies

• Small Molecules
• Growth Factors
• Cell-based Therapies
• Electromagnetic stimulation
• Device-based Therapies
  – Laser-based
  – Functional electrical stimulation
  – Neuroprosthetic and robotic devices-eg robotic treadmill system
• Task-oriented and Repetitive Training-based interventions
Task-Oriented and Repetitive Training

• Cognitive strategies based on motor imaging
• Motor system interventions
  – Gravity-reduced environment
  – Constraint-induced therapy
Non-invasive Brain Stimulation

- TMS (transcranial magnetic stimulation)
- tDCS (transcranial direct stimulation)
# TMS vs tDCS

<table>
<thead>
<tr>
<th>TMS</th>
<th>tDCS</th>
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<tbody>
<tr>
<td>Equipment higher cost</td>
<td>More easily applied w cog &amp; motor rehab</td>
</tr>
<tr>
<td>Can stimulate more focally</td>
<td>May have tingling at beginning &amp; end of</td>
</tr>
<tr>
<td>Better time resolution-msec accuracy</td>
<td>tx &amp; redness under electrode</td>
</tr>
<tr>
<td>Concern re seizures; seizure pts excluded</td>
<td>No seizures reported</td>
</tr>
<tr>
<td>Occasional transient headaches</td>
<td>Occasional transient headaches</td>
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tDCS

- Primary motor cortex
- Primary somatosensory cortex
- Contralesional motor cortex
- tDCS and virtual reality therapy
Therapeutic Targets for Brain Injury

• Excitotoxicity
• Oxidative injury
• Exogenous growth factors
• Erythropoietin
• Hypothermia
• Protease Inhibitors
Therapeutic Targets, continued

- Inflammation Targets
- Hormones
- Mitochondria
- Catecholamine agents
- Serotonin
- Acetylcholine
- Environmental enrichment
Therapeutic Targets, continued

- Stem cell therapy
- Nutraceuticals
  - Magnesium
  - Magnesium combined with riboflavin
  - CDP choline
  - Creatine
  - Vitamin B3
  - Vitamin E
  - Folic acid
  - Resveratrol
  - Diet-based: ketogenic
Conclusion

• Von Monakow 1914: “instead of thinking of brain modules as hardwired and autonomous, we should think of them as being in a state of dynamic equilibrium with each other and the environment (including the body), with connections constantly formed and re-formed in response to changing environmental needs. Neurological dysfunction, at least in some instances, may be caused not so much by irreversible destruction of a module but by a functional shift in equilibrium.”
Thank You

As he waits to deliver his Andrew Taylor Still Memorial Address, Howard M. Levine, DO (left), sits with the members of the New Jersey delegation, including Margaret Karcnik, DO, and Stephen G. Papish, DO. Dr Levine served for nearly 30 years as an AOA delegate from New Jersey.

known as the man who preaches about “accentuating our distinctiveness.” But rather than define the distinctiveness of osteopathic medicine once again, I am going to describe how osteopathic medicine can cultivate a distinct identity.

Much debate takes place over what A.T. Still would have wanted for the
References

- Bashir S, Mizrahi I, Weaver K, Fregni F, Pascual-Leone A. Assessment and Modulation of Neural Plasticity in Rehabilitation With Transcranial Magnetic Stimulation. PM R 2010; 2:S253-S268

• Pearson-Fuhrhop K M, Cramer S C. Genetic Influences on Neural Plasticity. PM R 2010; 2:S227-S240


• Warraich Z, Kleim J. Neural Plasticity; The Biological Substrate for Rehabilitation. PM R 2010; 2: S208-S219

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