

DEVELOPMENTS IN THE FIELD OF NEUROPLASTICITY

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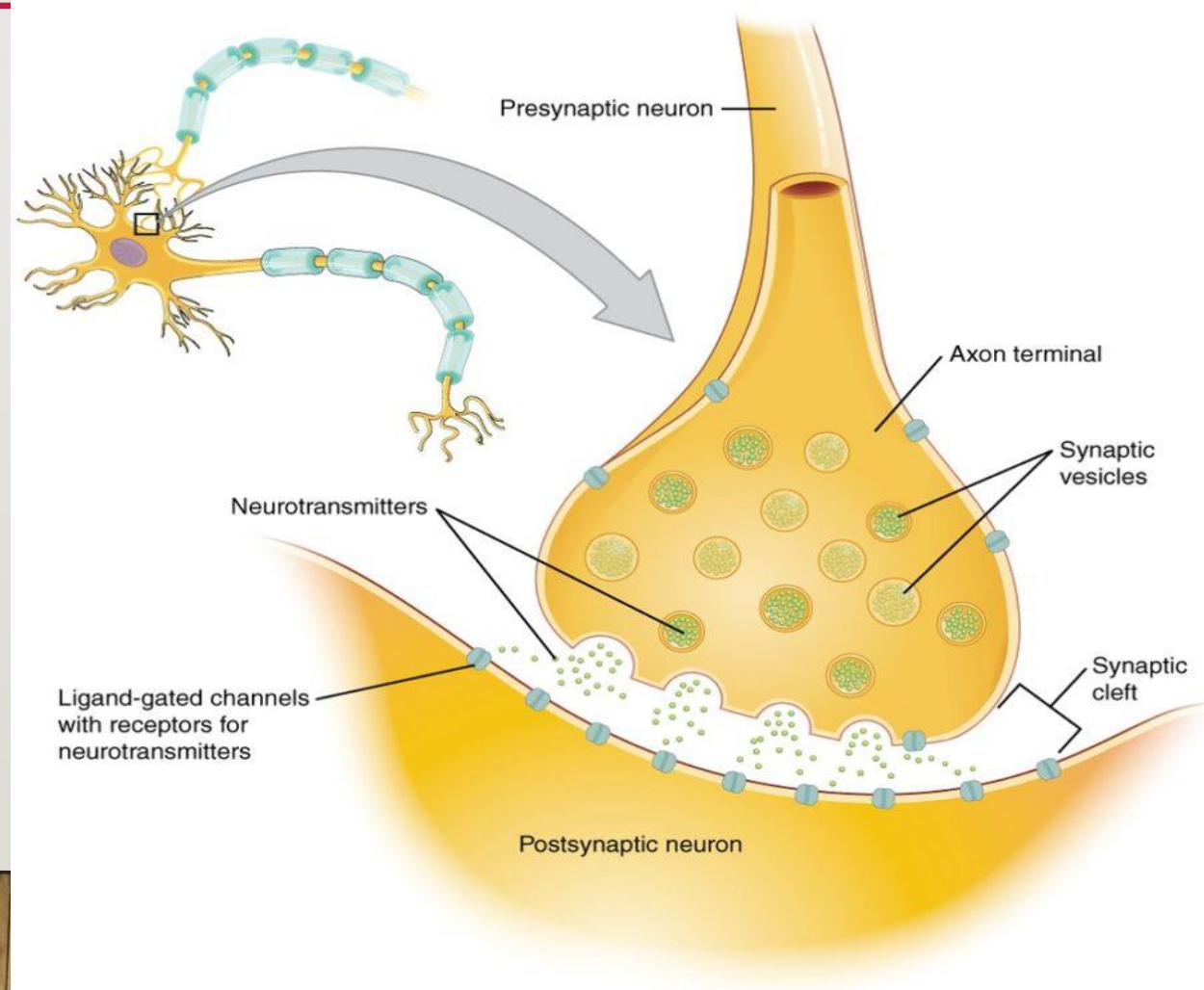


FUNDAMENTALS

- Neuroplasticity occurs on a variety of levels, ranging from cellular changes from learning to large-scale changes involved in cortical remapping after injury. The role of neuroplasticity is widely recognized in healthy development, learning, memory, and recovery from brain damage. During most of the 20th century neuroscientists maintained a scientific consensus that brain structure was relatively immutable after a critical period during early childhood. This belief has been challenged by findings revealing that many aspects of the brain remain plastic even into adulthood.

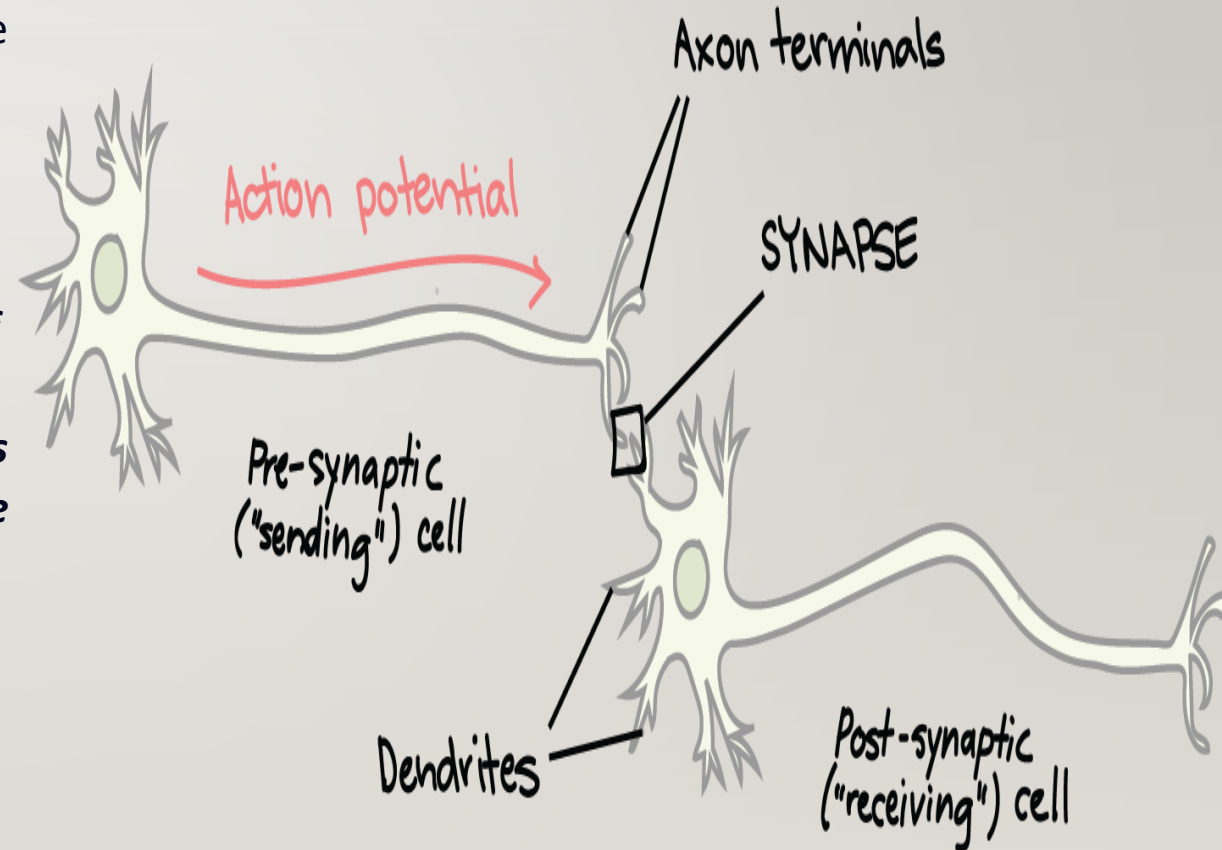
FUNDAMENTALS

- Information in the brain is transmitted from neuron to neuron through specialized connections called synapses. A synapse between two neurons is made up of presynaptic and postsynaptic terminals, which are separated by a synaptic cleft. The presynaptic terminal is filled with small vesicles containing chemical neurotransmitters, and the postsynaptic terminal consists of receptors specific for these neurochemicals. Neurons carry information in the form of an electrical impulse called an action potential that is initiated at the cell body and travels down the axon. At the synapse, an action potential causes the voltage-dependent release of neurotransmitter-filled vesicles, thereby converting an electrical impulse into a chemical signal. Neurotransmitters diffuse across the synaptic cleft, where they bind to receptors and generate an electrical signal in the postsynaptic neuron.



FUNDAMENTALS

- The postsynaptic cell will then, in turn, fire an action potential if the sum of all its synapses reaches an electrical threshold for firing. Since a neuron can receive synapses from many different presynaptic cells, each cell is able to integrate information from varied sources before passing along the information in the form of an electrical code. ***The ability of neurons to modify the strength of existing synapses, as well as form new synaptic connections, is called neuroplasticity. Defined in this way, neuroplasticity includes changes in strength of mature synaptic connections, as well as the formation and elimination of synapses in adult and developing brains. In addition, neuroplasticity includes the regrowth (or sprouting) of new synaptic connections following central nervous system injury.***



NEUROPLASTICITY

HOW DOES IT WORK?

SYNAPTIC ACTIVATION

STRONG & FREQUENT ACTIVATION

WEAK ACTIVATION

CHANGES SYNAPTIC STRUCTURE

CONNECTION STRENGTHENS

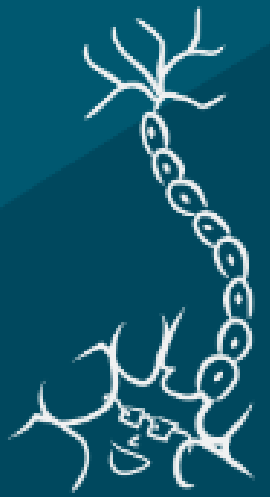
IMPLICATIONS

DOES NOT CHANGE SYNAPSE

SEMINAR-STYLE TRAINING IS NOT ENOUGH

LEARNING NEEDS ONGOING REINFORCEMENT

USE TECHNOLOGY TO KEEP ACTIVATING SYNAPSES



NEUROPLASTICITY

WHY YOU SHOULD CARE ABOUT YOUR **BDNF**



- ▷ BDNF HELPS YOUR BRAIN ADAPT & LEARN
- ▷ IMPROVES ALL FORMS OF PLASTICITY

YOU CONTROL YOUR BDNF LEVELS

EXERCISE

INCREASE BDNF AT ANY AGE

SLEEP

MISSED SLEEP = LESS BDNF

NUTRITION

FAT + SUGAR = LESS BDNF

STRESS

CORTISOL ACTS AGAINST BDNF

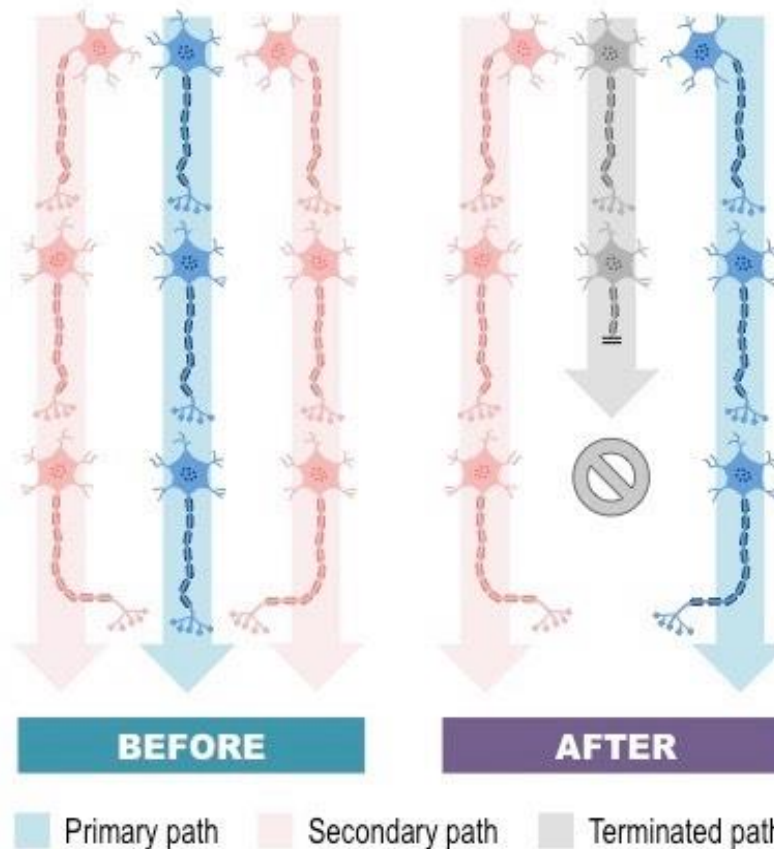
TERMINOLOGY

Strength of Information Transmission (Signal Transmission)

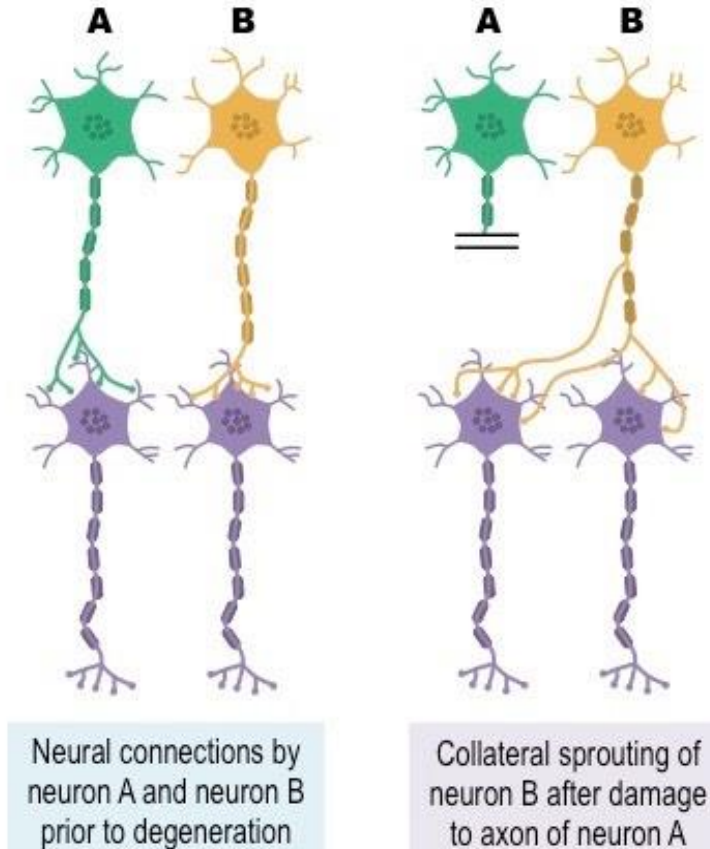
-Potentiation- Action Potential will have a larger target effect

-Depression-Action Potential will have a decreased response and decreased effect

Rerouting: New connections are made between active neurons to create alternate neural pathways

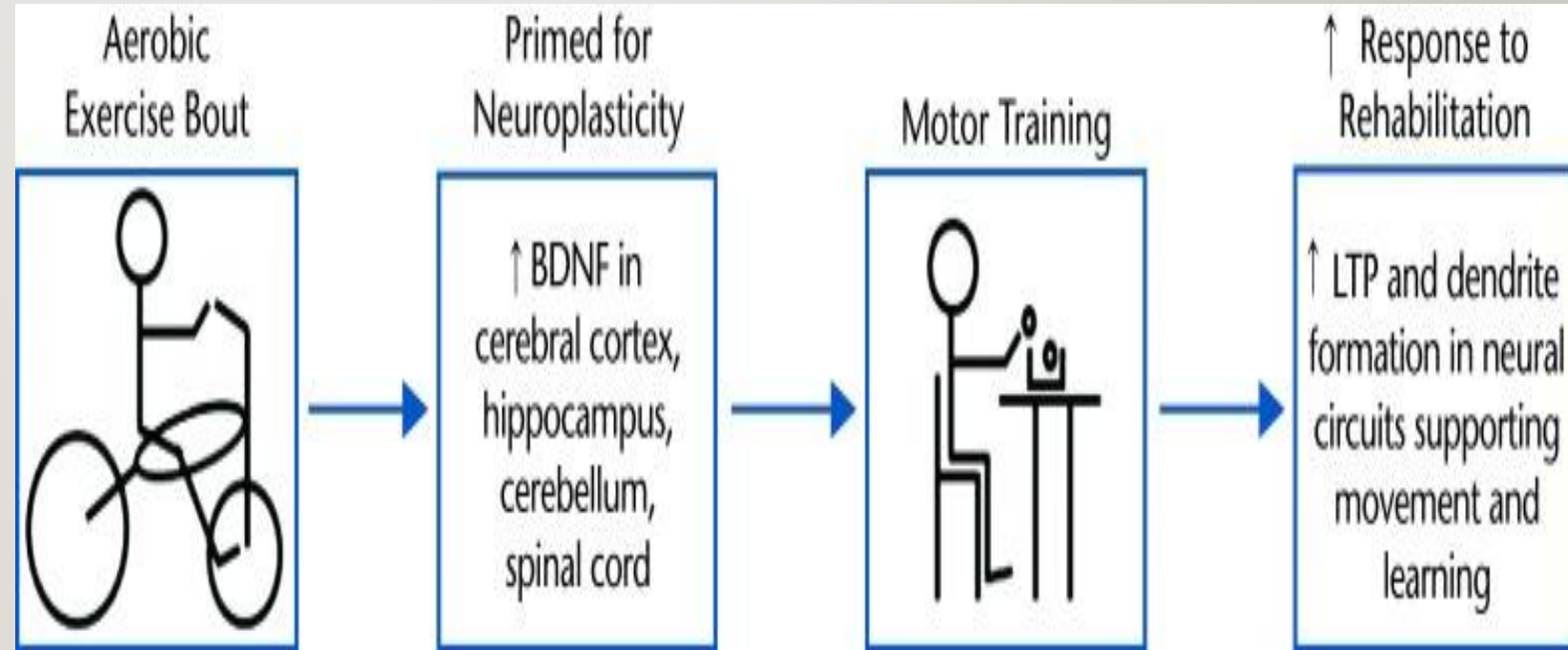


Sprouting: New axon and dendrite extensions allow existing neurons to form new connections



CLINICAL CORRELATES-STROKE

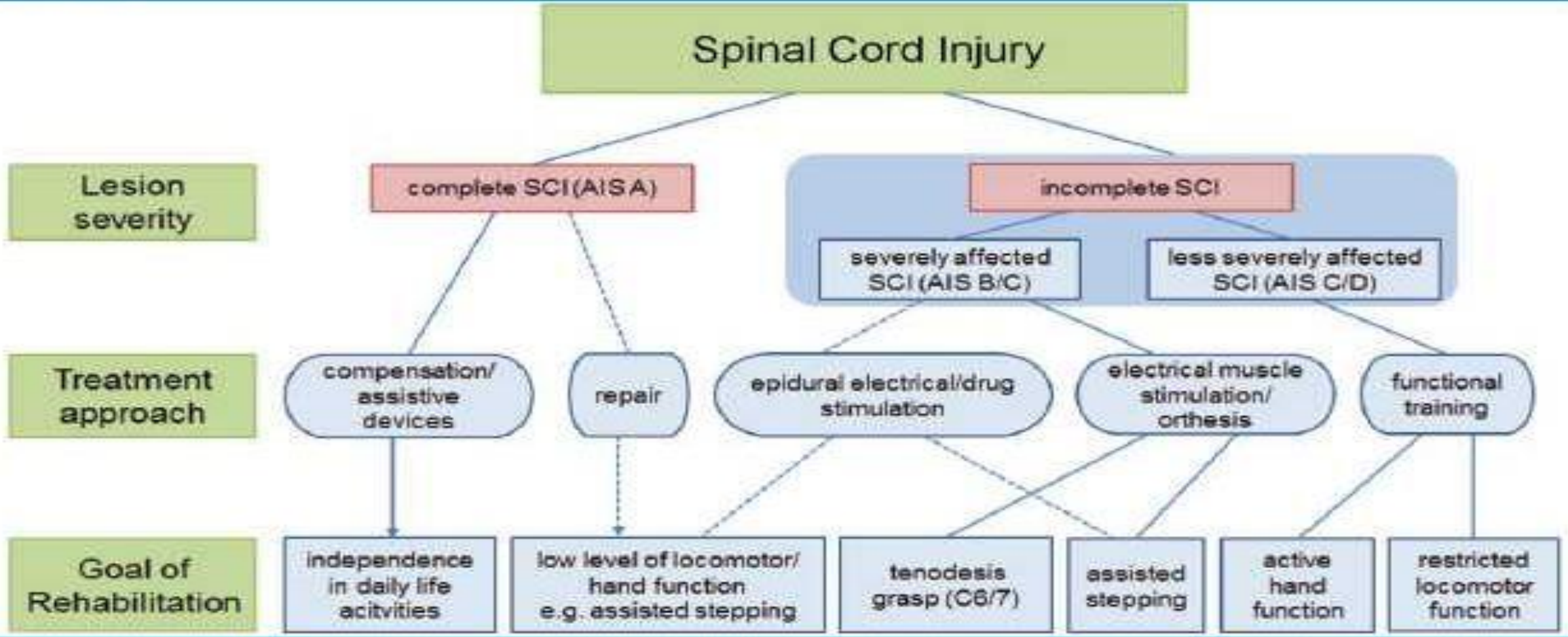
- In the case of stroke, the greatest benefit from rehabilitation is observed soon after injury, at which time in animals rehabilitation efforts can capitalize on the short time window of neuroplasticity that has been demonstrated to occur. Current guidelines recommend that individuals with stroke engage in a minimum of 20 minutes of moderate intensity aerobic exercise 3 days per week. The intensity of the exercise should be greater than 30% of heart rate reserve, the minimal effective training intensity for very unfit individuals, but based on individual exercise stress test results and health status.



CLINICAL CORRELATES-SCI

- The National Acute Spinal Cord Injury Studies (NASCIS) II and III, a *Cochrane Database of Systematic Reviews* article of all randomized clinical trials, and other published reports, have verified significant improvement in motor function and sensation in patients with complete or incomplete spinal cord injuries (SCIs) who were treated with high doses of methylprednisolone within 8 hours of injury.

CLINICAL CORRELATES-SCI



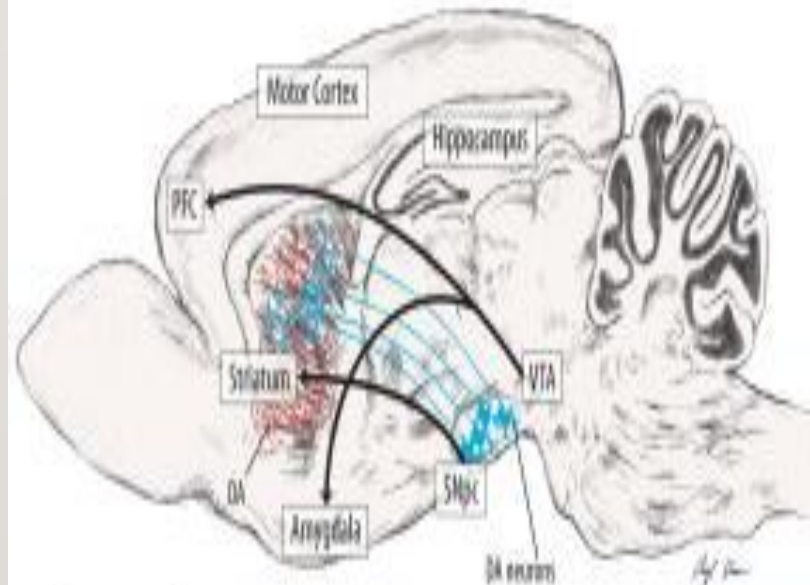
CLINICAL CORRELATES-PARKINSONS

- Based on published studies in both animals and individuals with PD, exercise has been shown to be important in improving motor function in PD and to facilitate neuroplasticity. Future research will continue to add to exercise related mechanisms of neuroplasticity. Thus, exercise should be considered an essential treatment for PD, particularly in individuals with mild to moderate disease
- In Parkinson's disease, serotonin neurons in the raphe switch to producing dopamine with levadopa treatment.

CLINICAL CORRELATES-PARKINSONS

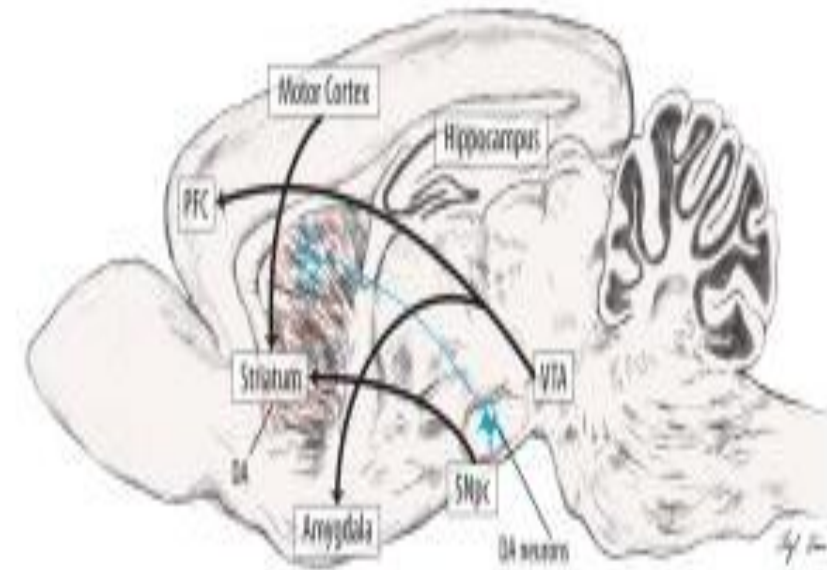
- The figure highlights some reported benefits of the effects of exercise in rodent PD neurotoxin models. The left panel indicates exercise effects when exercise is delivered either before or during the period of toxin-induced (6-OHDA, or MPTP) dopaminergic cell death. Intensive exercise promotes elevation of neurotrophic factors, such as BDNF, and protects from toxin-induced striatal DA depletion and cell loss of SNpc neurons

Exercise and Neuroprotection



↑ BDNF ↑ DA
 ↓ DAT ↑ TH

Exercise and Neurorestoration



↑ DA release
 — DA levels in striatum
 ↑ Glutamate receptor transmission
 ↑ neurogenesis in hippocampus
 ↑ Blood flow (Striatum, PFC, SNpc, Cerebellum)

↑ BDNF
 ↓ DAT ↑ cytokines
 ↑ microglia ↑ leptins
 ↑ IGF-1 ↑ HIF

TREATMENT MODALITIES-EXERCISE

- Aerobic exercise promotes adult neurogenesis by increasing the production of neurotrophic factors (compounds that promote growth or survival of neurons), such as brain-derived neurotrophic factor (BDNF), insulin-like growth factor 1 (IGF-1), and vascular endothelial growth factor (VEGF). Exercise-induced neurogenesis in the hippocampus is associated with measurable improvements in spatial memory. Consistent aerobic exercise over a period of several months induces marked clinically significant improvements in executive function (the "cognitive control" of behavior) and increased gray matter volume in multiple brain regions, particularly those that give rise to cognitive control. The brain structures that show the greatest improvements in gray matter volume in response to aerobic exercise are the prefrontal cortex and hippocampus; Higher physical fitness scores (measured by VO_2 max) are associated with better executive function, faster processing speed, and greater volume of the hippocampus, caudate nucleus, and nucleus accumbens.

TREATMENT MODALITIES-MEDITATION

- A number of studies have linked meditation practice to differences in cortical thickness or density of gray matter. One of the most well-known studies to demonstrate this was led by Sara Lazar, from Harvard University, in 2000. Richard Davidson, a neuroscientist at the University of Wisconsin, has led experiments in cooperation with the Dalai Lama on effects of meditation on the brain. His results suggest that long-term or short-term practice of meditation results in different levels of activity in brain regions associated with such qualities as attention, anxiety, depression, fear, anger, and the ability of the body to heal itself. These functional changes may be caused by changes in the physical structure of the brain.



DIET AND INFLAMMATION

- Total intake of food and fluid, frequency of intake and content consumed all factor into the molecular events of energy metabolism and neuroplasticity. Calorie restriction with adequate nutrients has been associated with health benefits through increased longevity, Research suggests eating until you are 80% full is an important factor for increased health span, Reducing calories 30% was associated the an average of 20% improvement in verbal memory after 3 months. Some of these cognitive and general health benefits are thought to be related to the reduction of inflammation and oxidative damage. Intermittent fasting in animals showed brain cells that were more capable of resisting toxic injury. Two diets have been recognized as one of the factors in the lives of high functioning centenarians, the Okinawan diet and mediterranean diet.

DIET AND INFLAMMATION

- Both emphasize vegetables, fruits, fish for protein and a low glycemic load. The polyphenol resveratrol has also shown to increase longevity (Dauncey, 2014; Witte et Al., 2014) while preserving memory and hippocampal microstructure. This polyphenol occurs in grapes, blueberries and cranberries. Flavonoids in cocoa provoke angiogenesis, neurogenesis and changes in neuron morphology mainly in regions involved in learning, memory and mood. (Latif, 2013). Curcumin is neuroprotective polyphenol with anti-inflammatory capacity that can increase differentiation of neural stem cells in rats (Chen et Al., 2014). Lastly Omega 3 FA's supplemented patients showed a 47% lower risk for developing dementia in a Framingham heart study (Schaefer et al., 2006)

SLEEP

- Sleep Deprivation and fragmentation resulted in neuroinflammation in the hippocampus and deficits in learning and memory as well as a decrease in neurogenesis that was not quickly reversible (Guzman-Marin and McGinty, 2006). Untreated patients with chronic OSA showed diffuse reduction in white brain matter integrity that was associated with cognitive dysfunction, however after 1 year of compliance with treatment, brain pathology improved significantly (Mueller et Al., 2013). Chronic sleep deprivation results in increased inflammatory molecules, decreased BDNF, impairment of protein translation, and metabolic imbalance. Sleep is essential for removal of waste and distribution of “glucose, lipids, amino acids, growth factors and neuromodulators” (Jessen et al., 2015)

SUMMARY

Diet-Mediterranean/Okinawan, Antioxidants(Berries/Vegetables), Anti-inflammatory (Curcumin), Omega 3 FA

Exercise-Aerobic and Weight Bearing

Support-Financial and Familial

Meditation-Prayer, Yoga

Sleep-Compliance with CPAP, Sleep Hygiene, Pharmaceutical Assistance

Mood- Anti-Depressants, Anxiolytics

We as Clinicians can facilitate the Environment for Neuroplasticity and Neurogenesis to take place. With control of factors such as diet, exercise, sleep, stress reduction and inflammation we can give the central nervous system the tools it needs to regenerate after injury and prevent age related atrophy. Thank you!



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