

NEUROPLASTICITY AND EARLY STROKE INTERVENTION

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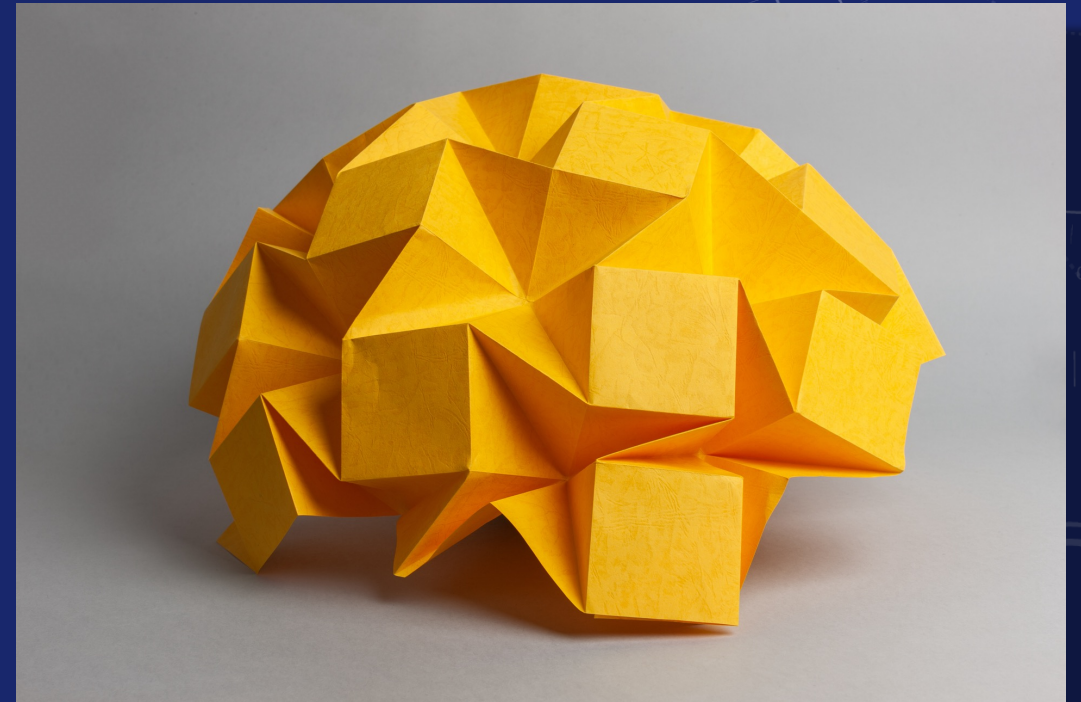
DISCLOSURES

- None

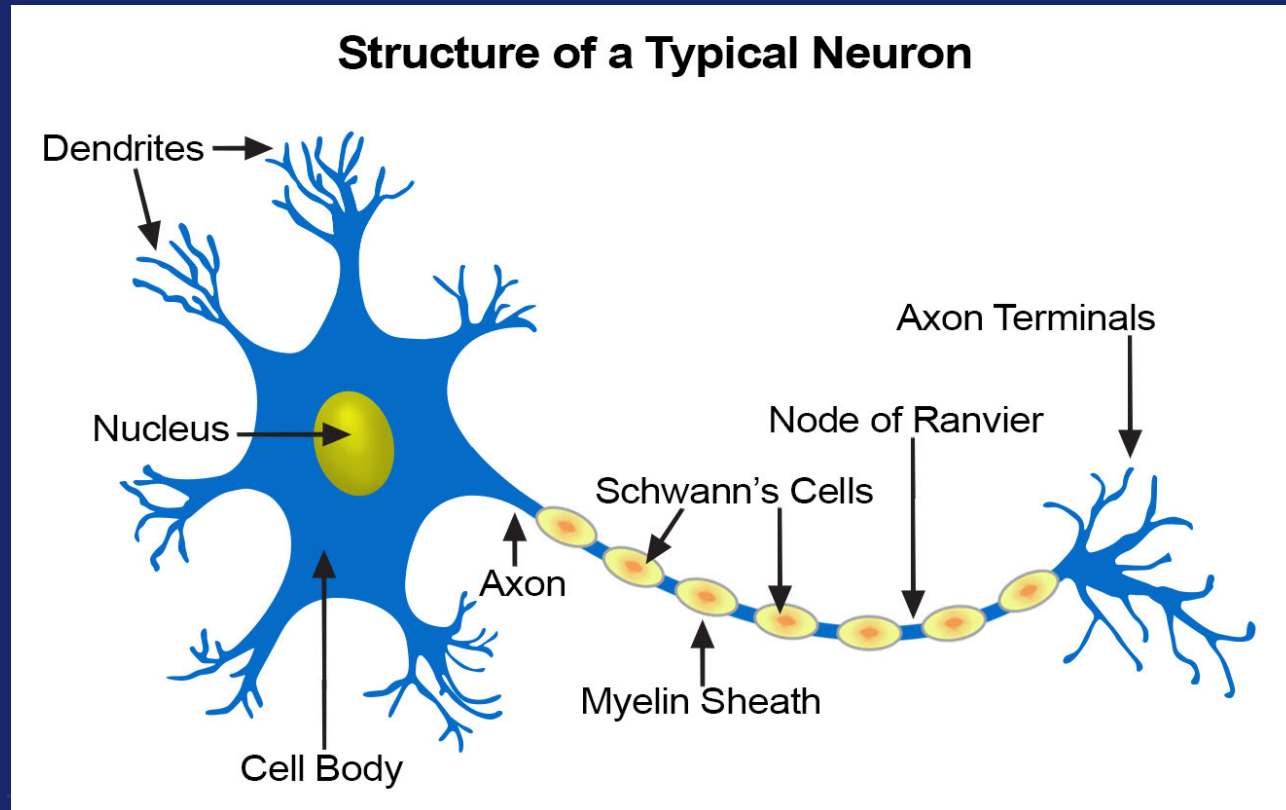
WHAT IS NEUROPLASTICITY

"change in the nervous system...a collective term for all the processes that change the structure and function of the brain."

- Moheb Costandi



NEUROANATOMY: NEURON

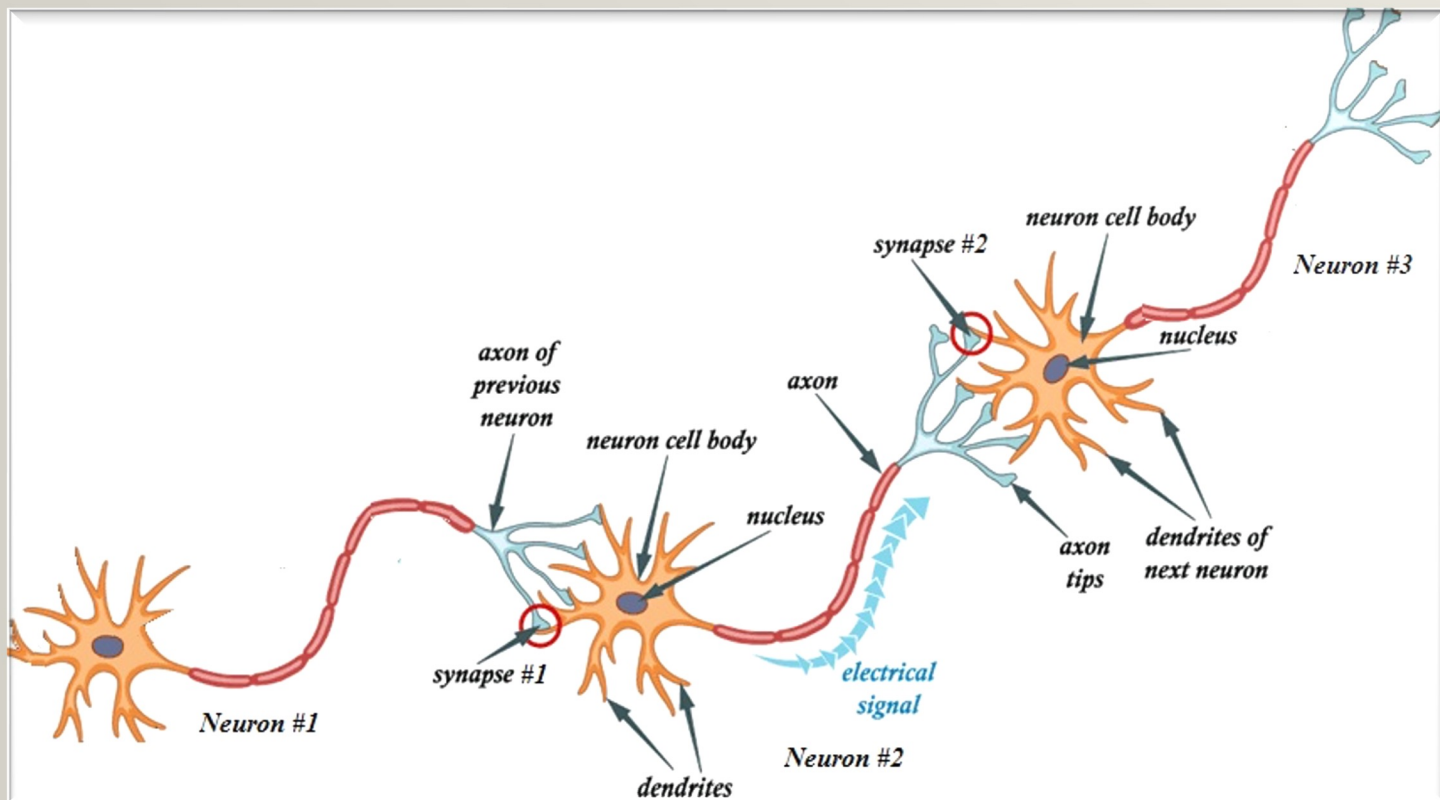


<https://training.seer.cancer.gov/anatomy/nervous/tissue.html>

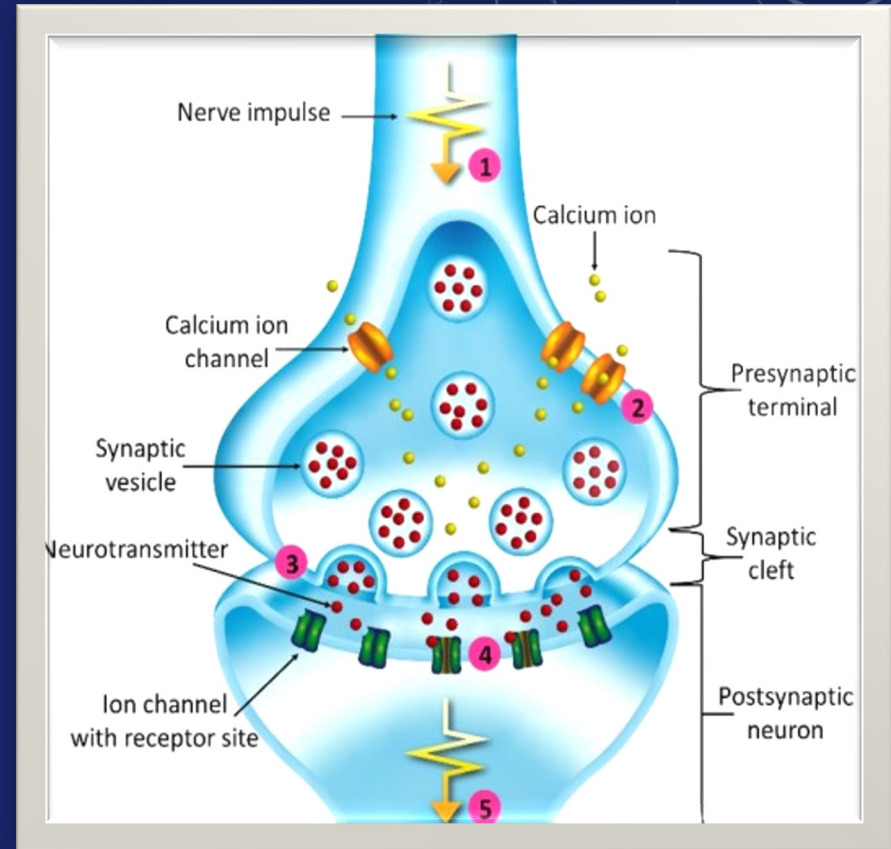


<http://amazon.com>

NEUROANATOMY: SYNAPSE



<https://www.chegg.com/homework-help/questions-and-answers/let-s-put-together-review-steps-action-potential-events-synapses-fill-following-blanks-tra-q41393959>



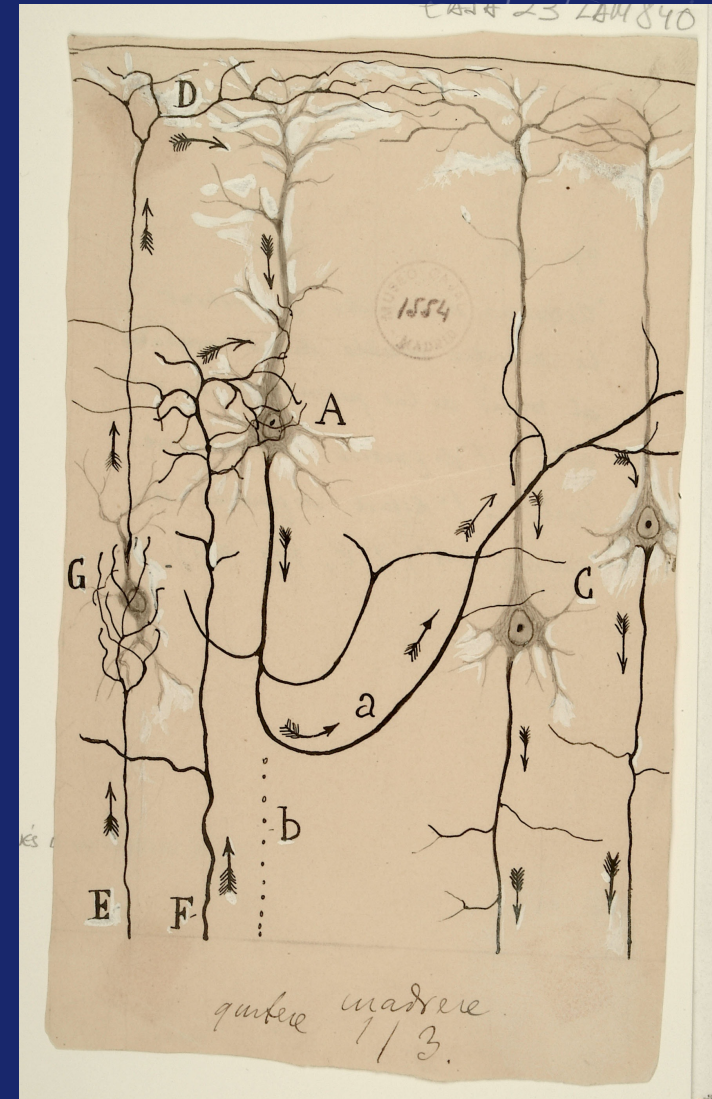
<https://www.oist.jp/image/diagram-synaptic-transmission>

HISTORY OF NEUROPLASTICITY

- 1890 - "Plasticity" was introduced in a textbook, *The Principles of Psychology*, by William James
 - Plasticity = "the possession of a structure weak enough to give yield to an influence, but strong enough not to yield all at once"
 - Described habit formation in relation to formation of new connections
- 1897 - Charles Sherrington named these junctions "synapses"
 - Greek "syn" = together + "haptein" = to clasp
 - Synapses likely where learning takes place

SANTIAGO RAMON Y CAJAL

- Father of Modern Neuroscience
- 1894 - Suggested plasticity occurs at junctions between nerve cells, and mental exercises can result in growth of nerve fiber branches
- 1913 - Created gold stain and used it to study fine structures within the nervous tissues
- Discovered the Nervous System was made of individual cells – Neurons
- Made multiple drawings of nerve cells
- 1913 – He wrote in his textbook "once development was ended, the founts of growth of the axons and dendrites dried up irrevocably"
- Through mid 1900s, consensus: "The brain is not materially affected by learning, experience, or training." (Costandi, 2016)



<https://history.nih.gov/pages/viewpage.action?pageId=1016727>

- Department: BEACH
- Product: BEACH TOWELS
- Subject: NEURONS CAJAL
- All Beach Towels
- View All Subjects
- Medium: ALL
- Shape: ALL
- Colors: ALL

Neurons Cajal

BEACH TOWELS

1 - 46 of 46 neurons cajal beach towels for sale



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Science Source

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Pyramidal Cell In Cerebral Cortex, Cajal Beach Towel
Science Source

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Pyramidal Cell In Cerebral Cortex, Cajal #4 Beach Towel
Science Source

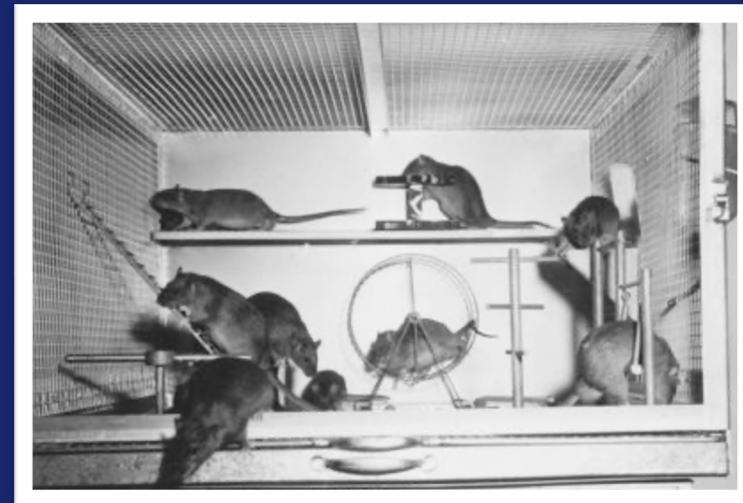
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HISTORY OF NEUROPLASTICITY

- 1964 - Marian Diamond, Ph.D. and her team published “Chemical and anatomical plasticity of brain”
- 1960s - Hubel and Wiesel experiments
- 1973 – Tim Bliss and Terje Lomo discovered Long Term Potentiation
 - Mechanism that strengthens synapses
 - Basis of learning and memory
- Late 1990s – Neural stem cell discovered in adult brain
 - Neuroplasticity = revolutionary new discovery



<https://ib.berkeley.edu/newsletter/spring-2020/marian-diamond-lab>

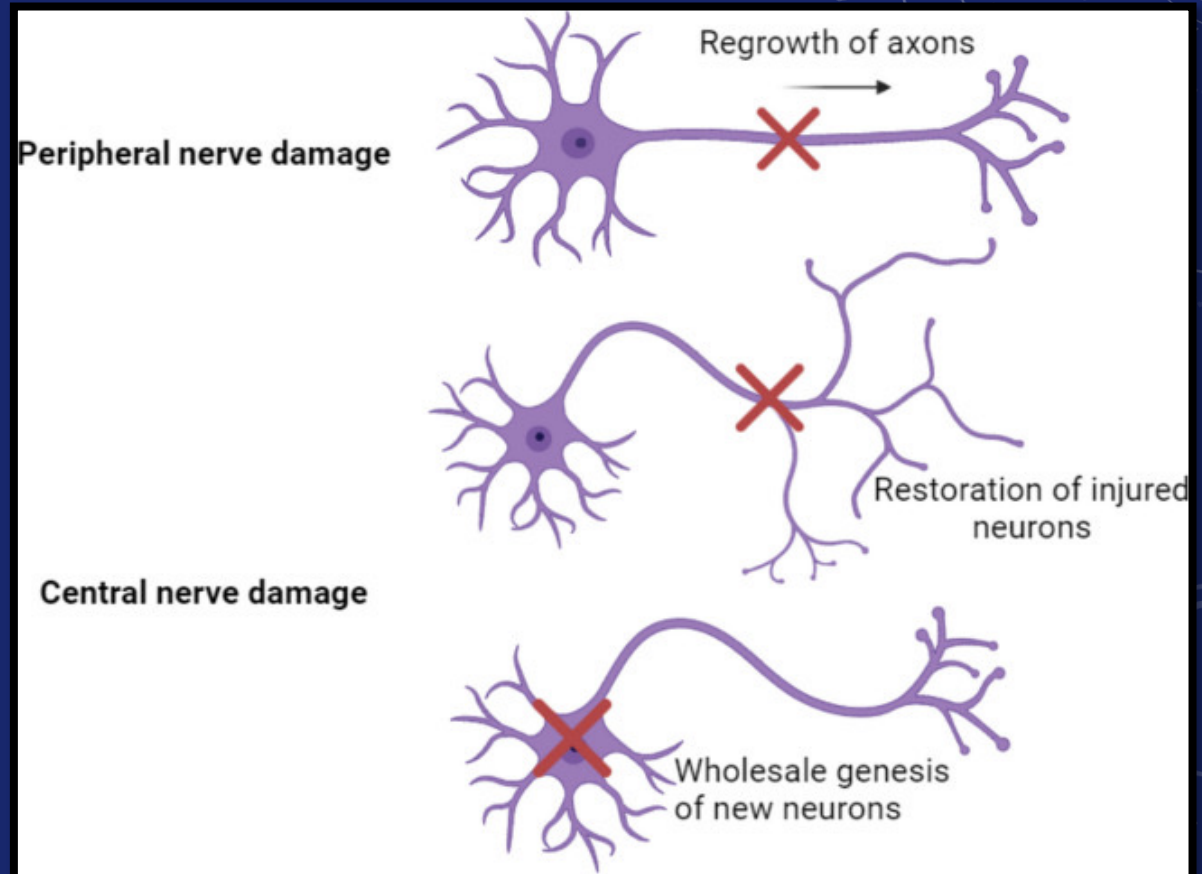


<https://news.berkeley.edu/2017/07/28/marian-diamond-known-for-studies-of-einsteins-brain-dies-at-90/>

MECHANISMS OF NEUROPLASTICITY

- 1) Regrowth of axons after peripheral nerve damage
- 2) Restoration of injured central nerve cells
 - dendritic growth
 - axonal sprouting
 - new synapses
- 3) Generation of new neurons
- 4) Cortical reorganization
- 5) Synaptic pruning

○ Marin-Medina, et al. 2023



<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10761524/figure/Fig1/>

TEN PRINCIPLES OF EXERCISE-DEPENDENT NEUROPLASTICITY

KLEIM & JONES, 2008

1) USE IT OR LOSE IT

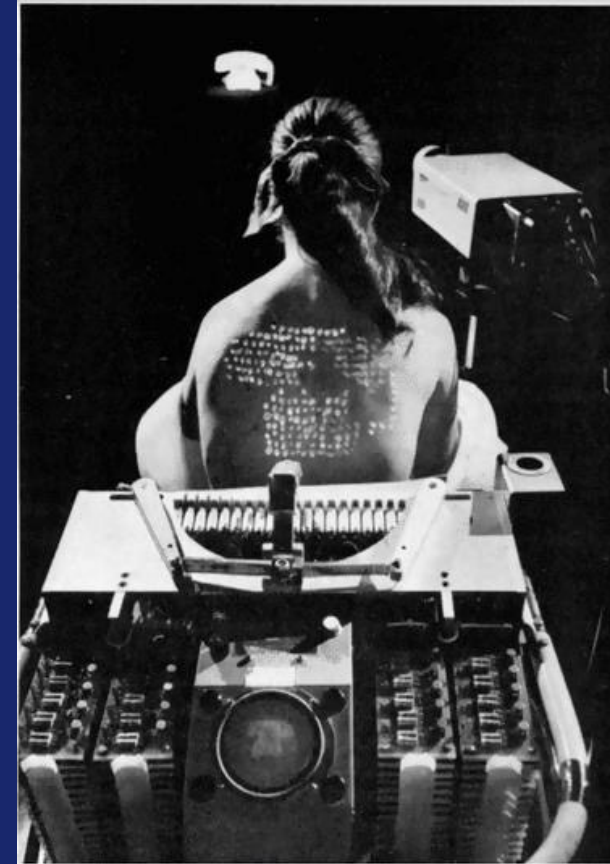
- Lack of use may lead to further loss of function
- Synaptic pruning
- Hubel and Wiesel (1965) performed experiments with light deprivation in kittens
 - Resulted in decreased number of visual cortex neurons that responded to light
 - Reversible to a certain age
- Constraint-induced movement therapy (CIMT) shown to:
 - Promote structural neuroplasticity mostly in contralesional hemisphere as well as bihemispheric functional neuroplasticity
 - Increase expression of growth factor (Aderinto, et al. 2023)



<https://www.bodywithinfit.com/use-it-or-lose-it/>

2) USE IT OR IMPROVE IT

- Extended training induces plasticity in localized brain regions
- Learning a language or musical instrument = brain changes
- Deprivation in one sensory modality may cause its corresponding cortical area to be at least partially taken over by another modality
- Sensory Substitution
 - Paul Bach-y-Rita helped blind people to "see"



https://www.researchgate.net/figure/A-BLIND-PARTICIPANT-USING-THE-TVSS-FROM-BACH-Y-RITA-1971_fig1_308055065

2) USE IT OR IMPROVE IT

- BrainPort

- Created by Paul Bach-y-Rita
- Improved by Wicab
- Revamped in 1990s to use tongue
- Grid of electrodes connected to video camera
- Data from camera becomes an array of electrodes that buzz the tongue



<https://www.asme.org/topics-resources/content/brainport-for-the-blind>

3) SPECIFICITY



- Skill acquisition is necessary for significant changes in patterns of neural connectivity
- fMRI showed activation pattern changes in motor cortex related to skill acquisition (Ungerleider et al., 2002)
- Training in post stroke swallowing may not relate to training in voice production (Huang, et al., 2002)
- Be as functionally specific as we can
 - Make lists vs worksheets
 - Walk in crowded hallways vs hospital room
 - Use toilet vs Purewick

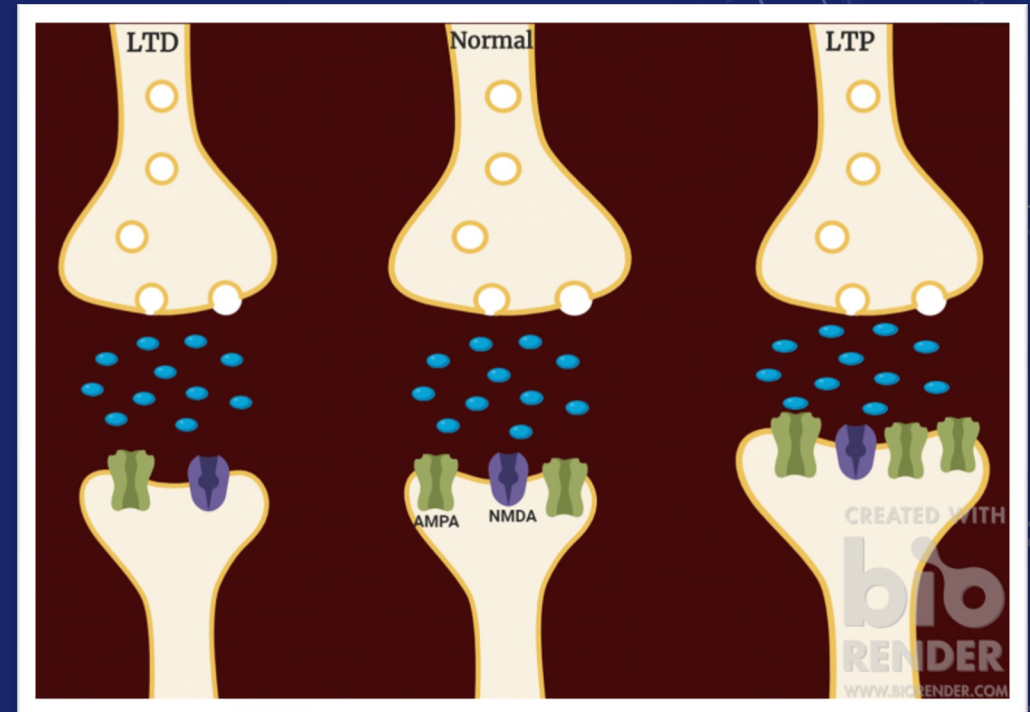
4) REPETITION MATTERS

- Plasticity may require newly learned skill as well as continued use of this skill for lasting effect
- Repetition needed to reach level of brain reorganization for:
 - maintenance of skill
 - continued gains related to skill
- Rats performing a skilled reaching task showed:
 - progressive difficulty of a reaching task caused map reorganization within the motor cortex.
 - repeating task without progression resulted in no effect on cortical mapping. (Kleim et al., 2004)
- We want carryover outside of hospital/therapy setting



5) INTENSITY MATTERS

- Low intensity stimulation can weaken synapse responses (long-term depression - LTD)
 - Removes/forms memory traces
- High intensity stimulation causes strengthened synapses (long-term potentiation - LTP)
 - Involved in memory/learning
- Skilled reaching task with animals:
 - 400 reaches/day = increased motor cortex synapses (Kleim et al., 2002)
 - 60 reaches/day = no synaptic change (Luke et al, 2004)



<https://ecampusontario.pressbooks.pub/healthdiseasetopics2019/chapter/ltp-and-memory/>

5) INTENSITY MATTERS

- London taxi drivers and "the Knowledge"
 - Memorize layout of ~26,000 streets, major landmarks, and fastest routes between any 2 points
 - Study 3-4yrs to pass the tests
- 2000 study from University College London
 - Gray matter density in posterior hippocampus (spatial navigation) significantly larger in London taxi drivers vs controls
 - More experienced drivers = larger volume
 - Trainees who failed exam showed similar hippocampi to controls



<https://www.npr.org/sections/parallels/2015/10/21/450235327/london-cabbies-say-the-knowledge-is-better-than-uber-and-a-gps>

7) SALIENCE MATTERS

- Activities must have some level of importance to be encoded
- Animals showed increased auditory cortex representation with salient tones that accompanied rewards vs tones without rewards (Weinberger, 2004)
- Always explain **why**



<https://whathappensonthebackstreet.wordpress.com/2015/05/24/8-phrases-you-cant-say-to-a-backstreet-boys-fan-and-expect-a-normal-response/>

8) AGE MATTERS

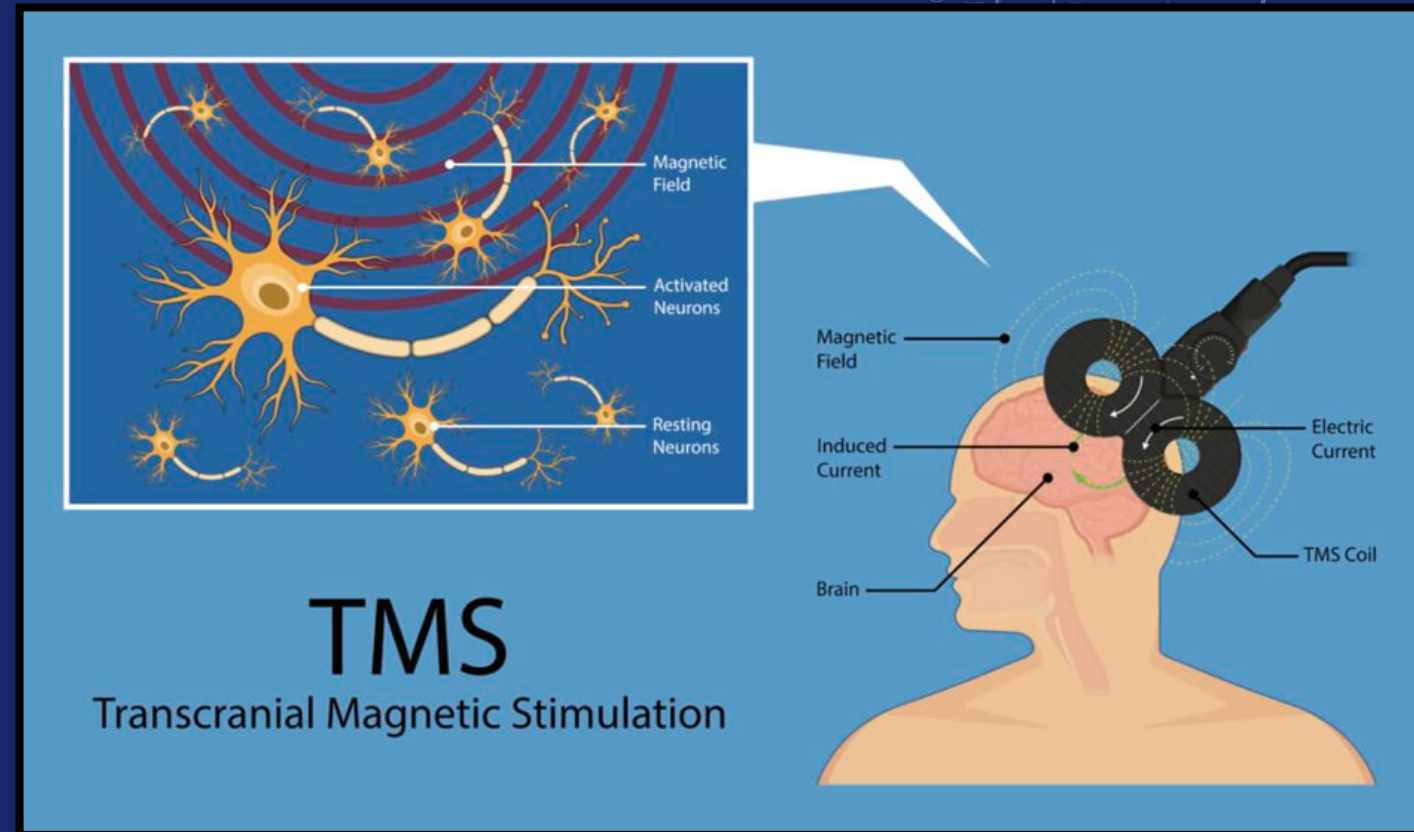


<https://wallpapers.com/funny-rat-pictures>

- Neuroplastic responses are different in older brains
- Aging brains still respond to experience, but may take longer or have reduced response
- Hoff et al studied injured rats and found sprouting onset began about 2-4 days post injury in young adult rats vs 20 days in aged rats
- Good news: learn an instrument or a new language to reduce cognitive decline

9) TRANSFERENCE

- "ability of plasticity within one set of neural circuits to promote concurrent or subsequent plasticity." - (Kleim & Jones, 2008)
- Peripheral stim of pharynx resulted in enlarged cortical representation and improved swallowing post stroke (Fraser et al., 2002)
- Exoskeleton-based therapy promoted neuroplasticity and improved functional outcomes (Aderinto et al., 2023)
- Combining therapies can be more effective than individual therapies at times
 - rTMS combined with rehab training improves motor function (Khedr et al., 2005)



<https://www.rewire.co.za/tms-therapy/>

10) INTERFERENCE

- Plasticity can hinder induction of new, or expression of current, plasticity in the same circuit.
- Allred et al. described "Learned nonuse"
- "Bad Habits"
- Importance of teaching proper, consistent, techniques across all disciplines



6) TIME MATTERS

- Neuroplasticity is a complex cascade of events
- Various types of plasticity precede and may depend on other events
- For motor skill training:
 - 1) gene expression
 - 2) synapse formation
 - 3) motor map reorganization
- Stability of changes may depend on timing of training



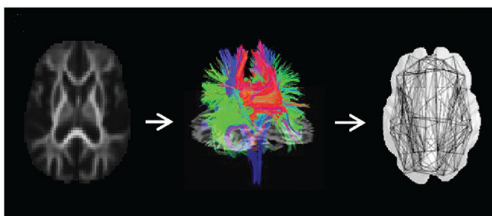
6) TIME MATTERS: CRITICAL WINDOW FOR RECOVERY

- Rodent models
 - 1) Recovery begins within hours post stroke
 - 2) Peaks at 7-14 days
 - 3) Nearly complete by 30 days (Coleman et al, 2018)
 - 4) Zeiler et al, 2016
 - Mice given a 2nd lesion showed near full recovery after previously incomplete motor recovery from primary lesion
 - 2nd lesion reopens neuroplastic window?
- Human critical window is not fully clear yet
- First 24 hours post stroke appears to be a vulnerable period
 - Exercise 6-24 hrs post stroke = increased inflammatory cytokine release (Li et al.)
 - Sundeth et al. showed that VEM resulted in poorer outcomes and higher rates of death with patients mobilized within 48 hrs of stroke
 - AVERT (2017)
 - Initiation of therapy within 24 hrs resulted in increased infarct expansion

6) TIME MATTERS: EARLY REHAB POST STROKE

- Biernaskie et al
 - 5 wks of rehab
 - Starting 30 days post stroke was far less effective for functional improvements and cortical dendrite growth vs starting 5 days post stroke
- Momosaki et al
 - Studied pts who received tPA
 - PT/OT started within 72 hrs of stroke
 - Early rehab was significantly associated with functional independence
 - Reassures safety of early rehab post tPA
- EXCITE phase III trial
 - Showed superior UE motor recovery at 12 mos in an "early" (3 –9 mos post stroke) rehab group receiving CIMT vs conventional rehab controls
- CPASS
 - Subacute intervention (2-3 mos post stroke) resulted in significantly greater UE motor recovery vs controls
 - Acute intervention (<30 d post stroke) showed smaller, but significant recovery vs controls
 - Chronic group (\geq 6 mos post stroke) showed no significant differences vs controls
- **Recovery window in humans lasts at least 3 months but likely ends before 6 months** (Dromerick et al, 2021)

Stroke



White Matter Microstructure and Networks as Seen on DTI

■ Original Contributions

Heritability of White Matter Hyperintensities
Blood Pressure and Risk of Vascular Dementia
Weekend Effect in Children With Stroke
Left Atrial Mechanical Function in Stroke
HRV and Incident Stroke: ARIC
NIHSS Picture Description **CME** **OPEN**
Clinical Prediction of Large-Artery Occlusion
Leukocytosis Reduces Hematoma Expansion
Heart Rate and Outcome in ICH
Atrial Fibrillation and Poststroke Outcome
External Validation of ASTRAL and DRAGON
Stroke After Elective Versus ACS PCI
HDL Subfractions and cIMT
Perfusion MRI in Acute Perinatal Stroke
FA Changes in Acute Stroke and Motor Outcome Predictions
Coronary Atherosclerosis in ICAS
Progressive Cortical Neuronal Damage
Carotid Atherosclerosis, Ischemic Stroke and CHD
FLAIR Hyperintensities in Borderzone Infarcts
Cost-Effectiveness of Oral Anticoagulants
Pharyngeal Electrical Stimulation for Dysphagia **OPEN**
Recanalization Modulates BP in Acute Stroke
Recent Trends of Intravenous Heparin for Ischemic Stroke

Outcome After Thrombectomy and Thrombolysis
Blood Pressure and Restroke Stroke in Young Adults
Reducing Readmissions in Stroke Patients
Aspirin for Primary Stroke Prevention
Infection as an Ischemic Stroke Trigger: ARIC
Pial Collateral Reactivity and Function **OPEN**
Hematoma Changes After Experimental ICH
Bone Marrow Mononuclear Cells in Stroke Models

■ Brief Reports

Stroke and TIA in Argentina
cIMT, Carotid Plaque, and Stroke Risk in AF
Manual Dexterity After Neonatal Stroke
Degree and Timing of BP Lowering on Hematoma Growth
Neutrophil-to-Lymphocyte Ratio and Hemorrhage
Hemodynamic Changes With Diamox Assessed by QMRA
MT for ELVO and IVT Pretreatment
Female Sex and Clinical Outcome in AF Patients on Warfarin
MRI for Cerebral Transmission of Aortic Pulsatility

■ Topical Reviews

Mendelian Randomization and Stroke
WM Microstructural Damage and SVD
Rehabilitation at Home

■ Emerging Therapy Critiques

Review of SPRINT trial

■ Basic Sciences Advances for Clinicians

Intracranial Pressure and Collateral Blood Flow

■ State-of-the-Science Nursing Review ★

Fall and Injury Prevention for Stroke Patients

■ Illustrative Teaching Case ★

Intraventricular Hemorrhage in Thiamine Deficiency

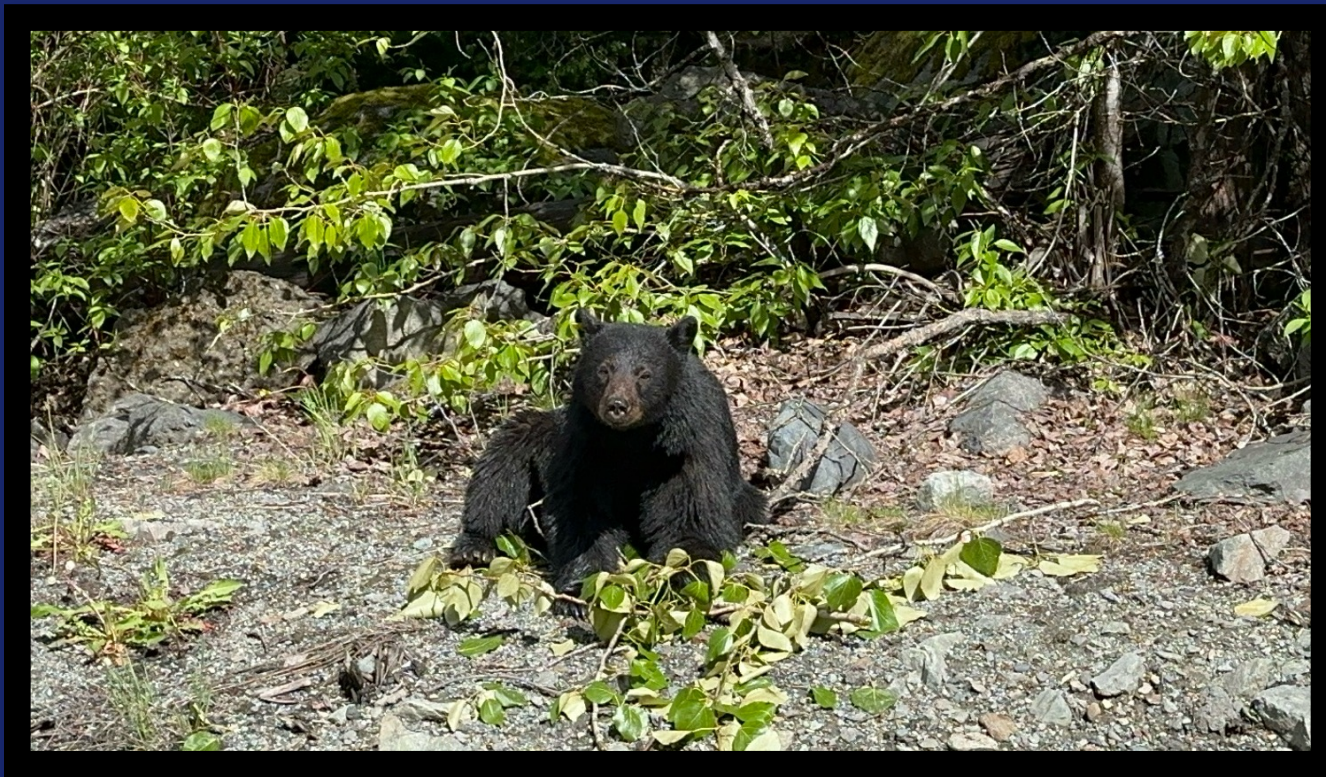
■ AHA/ASA Guideline

Guidelines for Adult Stroke Rehabilitation and Recovery ★

■ Letters to the Editor ★

"The AHA/ASA recommends stroke survivors go to an **inpatient rehabilitation facility** instead of a skilled nursing facility."

6) TIME MATTERS



PRACTICAL NEUROPLASTICITY

- Incorporate affected regions
- Remember the brain can reorganize
- Be functional in your tasks
- Repeat, repeat, repeat
- Do not be afraid (once medically cleared) to:
 - walk farther
 - balance longer
 - increase reps
 - add weights
- Critical Window
 - >24 hrs up to 6 months post stroke
 - Early rehab intervention improves outcomes
 - Avoid very early mobilization <24 hours post stroke
- Give patients the "Why"
- It is never too late
 - Learn a new instrument
 - Learn a new language
- Incorporate traditional therapy with newer ideas:
 - VR
 - Exoskeleton
 - Robotics
 - brain-computer interfaces
 - transcranial brain stimulation
- Avoid bad habits
 - Teach exactly how you want something done
 - Same order, same words across disciplines

QUESTIONS???



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