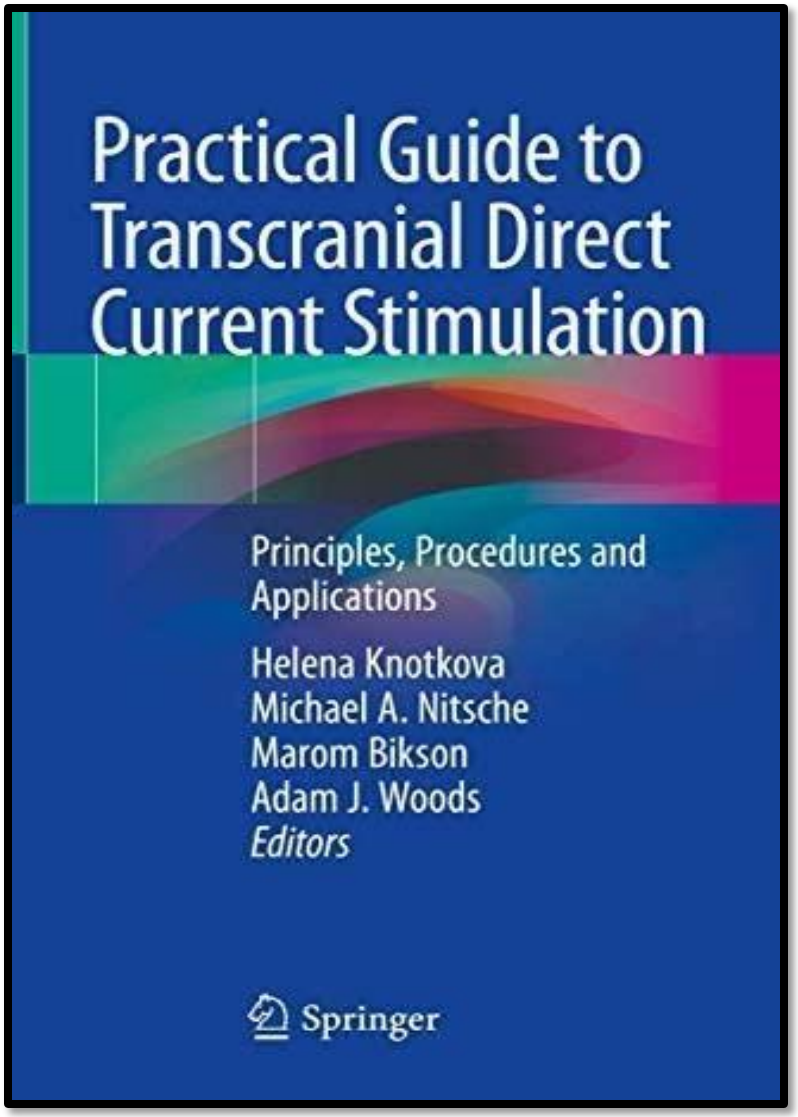
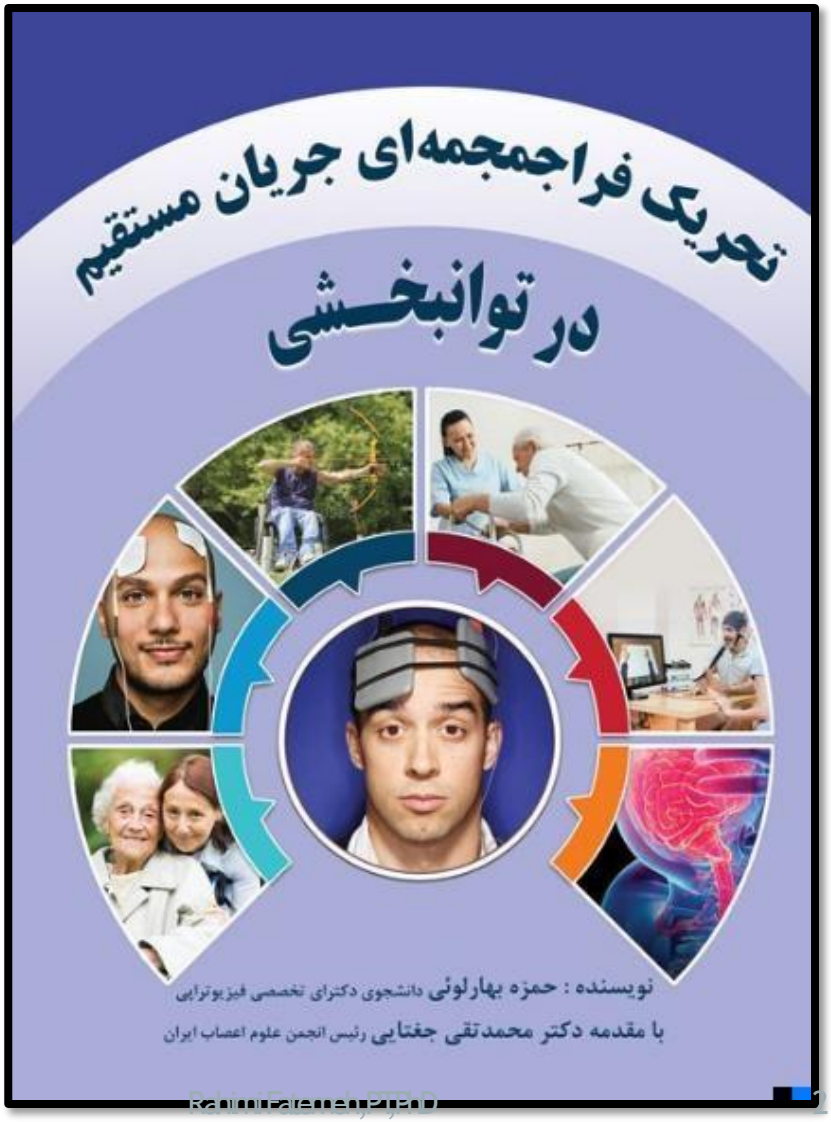
*In the Name of God*

# Transcranial Direct Current Stimulation In Neurologic Conditions

, Pt, Ph.D., Assistant Professor , **Fatemeh Rahimi ,** Shahrekord University of Medical Sciences

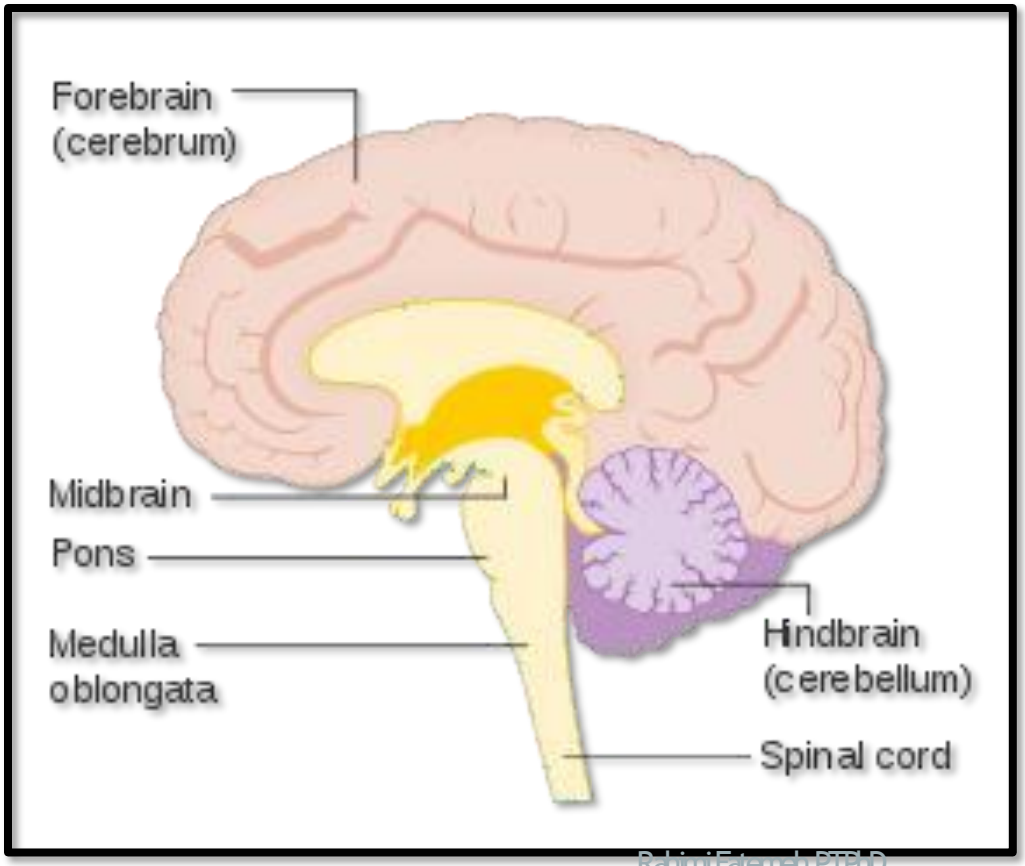
# Reference Books



# Review

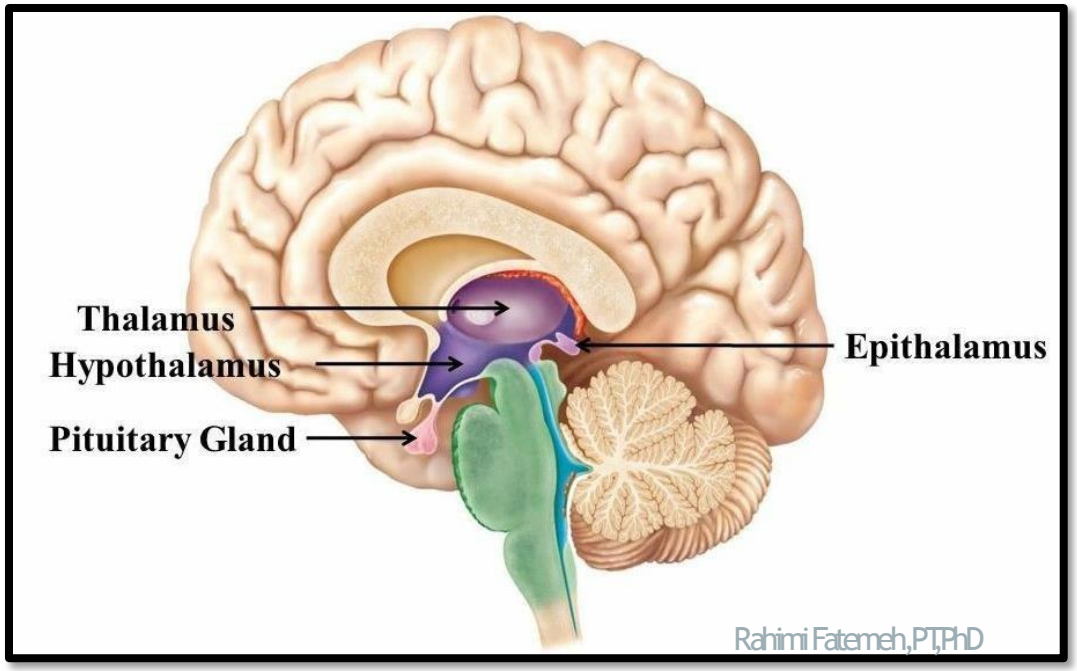
The nervous system includes **central system**( the brain, spinal cord) and **peripheral system**(complex network of nerves: cranial nerves and spinal nerves)



# Diencephalon

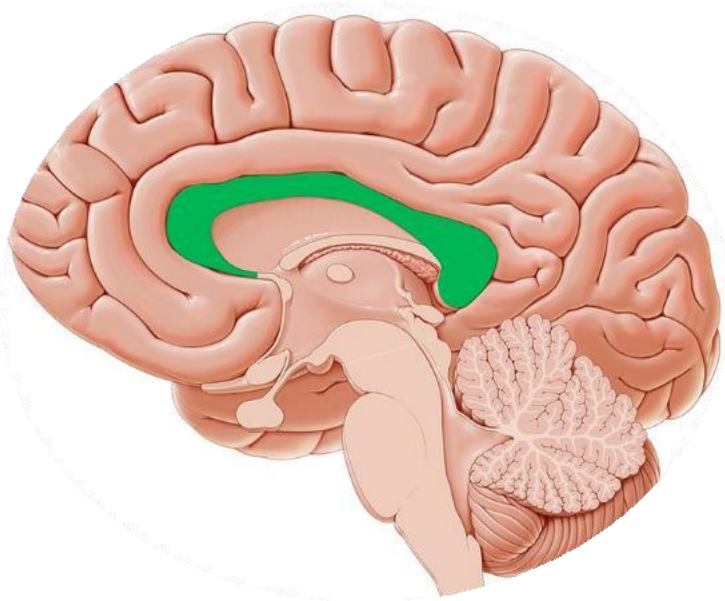
- The central portion of the brain located around the third ventricle, superior to the brainstem, and inferior to the corpus callosum and cerebral cortex.
- It is divided into four main parts including:

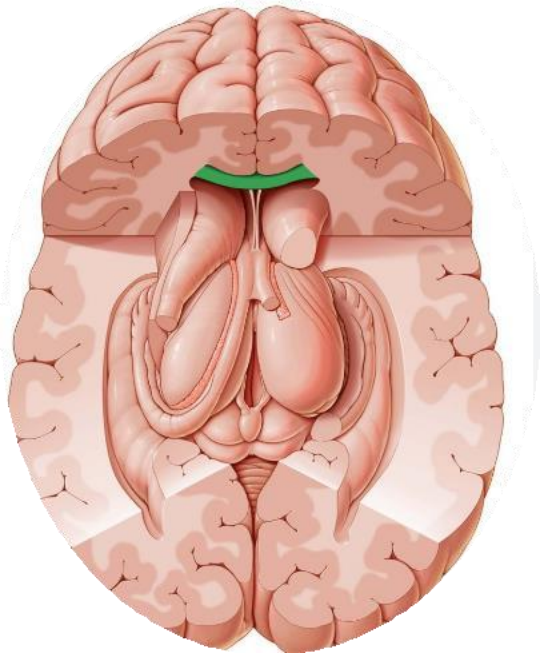
**thalamus, hypothalamus**, **epithalamus**, and **subthalamus**.



# Corpus Callosum

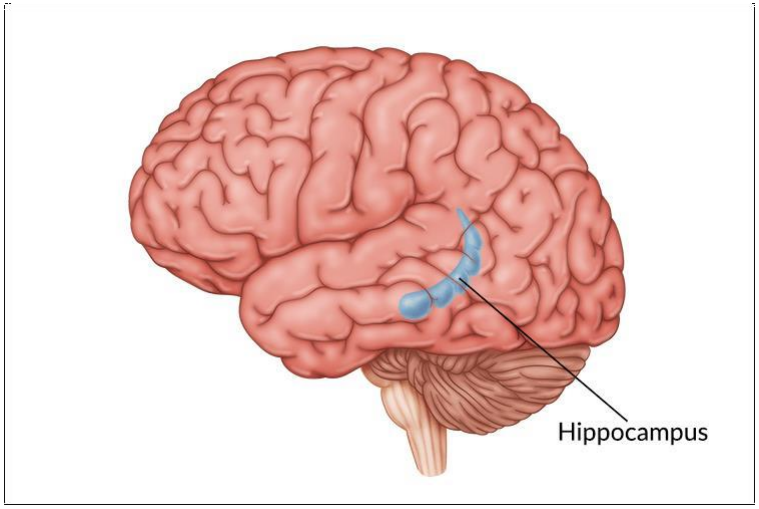
The corpus callosum is a large bundle of more than 200 million myelinated nerve fibers that connect the two brain hemispheres, permitting communication between the right and left sides of the brain





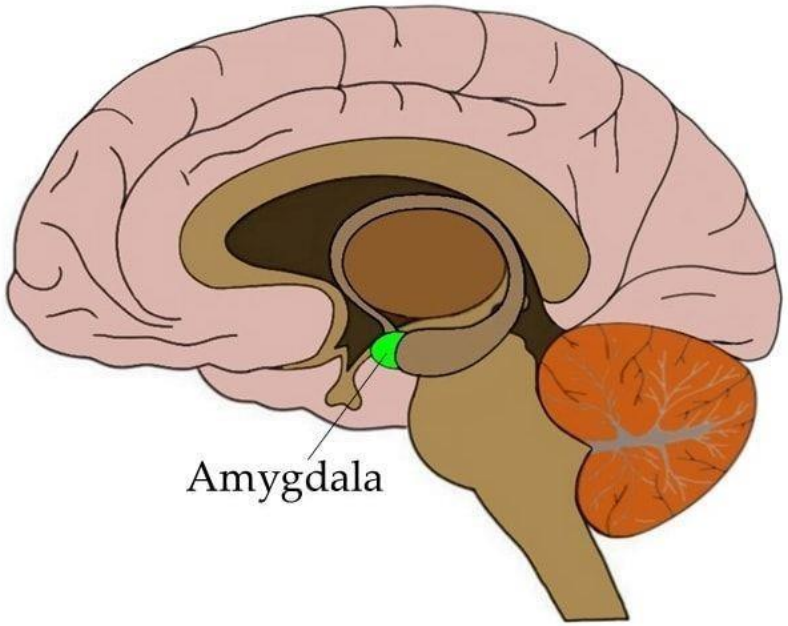
# Hippocampus

Hippocampus is a complex brain structure embedded deep into temporal lobe. It has a major role in learning and memory. It is a plastic and vulnerable structure that gets damaged by a variety of stimuli.



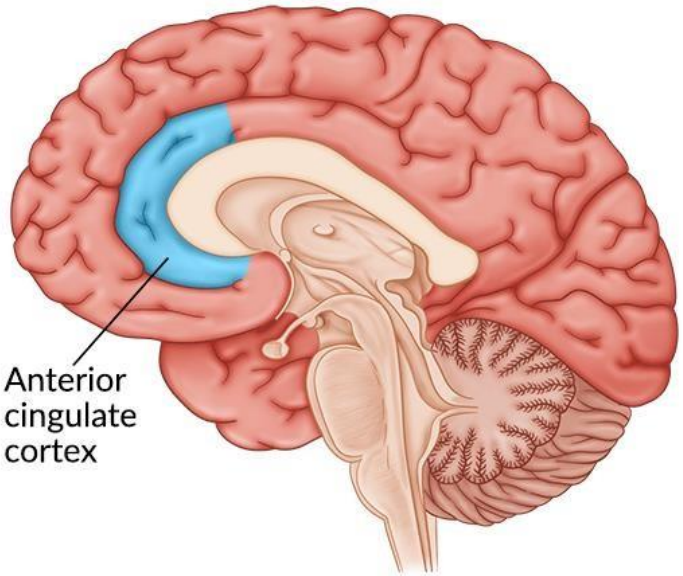

# Amygdala

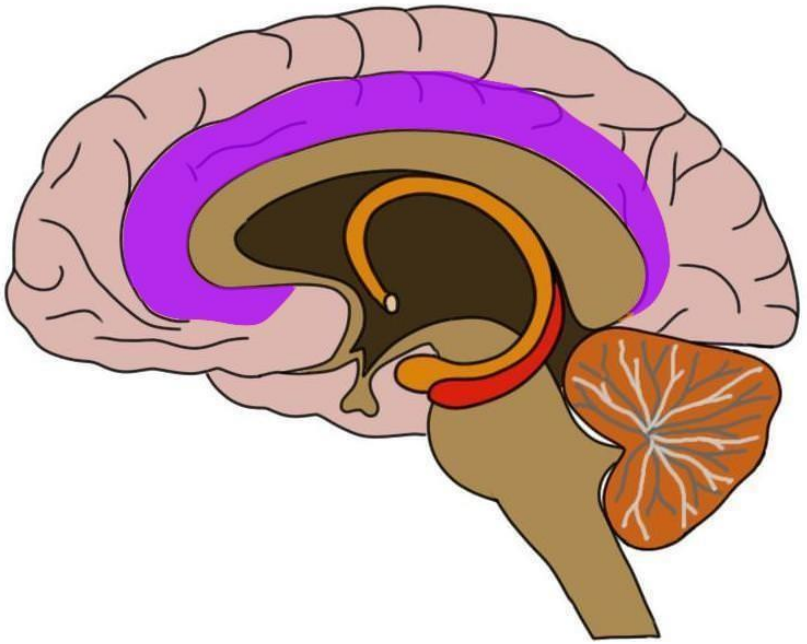
The integrative center for emotions, emotional behavior, and motivation.



# Cingulate Cortex

- The cingulate cortex is a fascinating area of the human brain that has attracted a lot of recent attention. It resides within the medial surface of the cerebral hemisphere and is perhaps most well known as being part of the limbic system.
- The anterior cingulate cortex (ACC) is the frontal part of the cingulate cortex that resembles a "collar" surrounding the frontal part of the corpus callosum



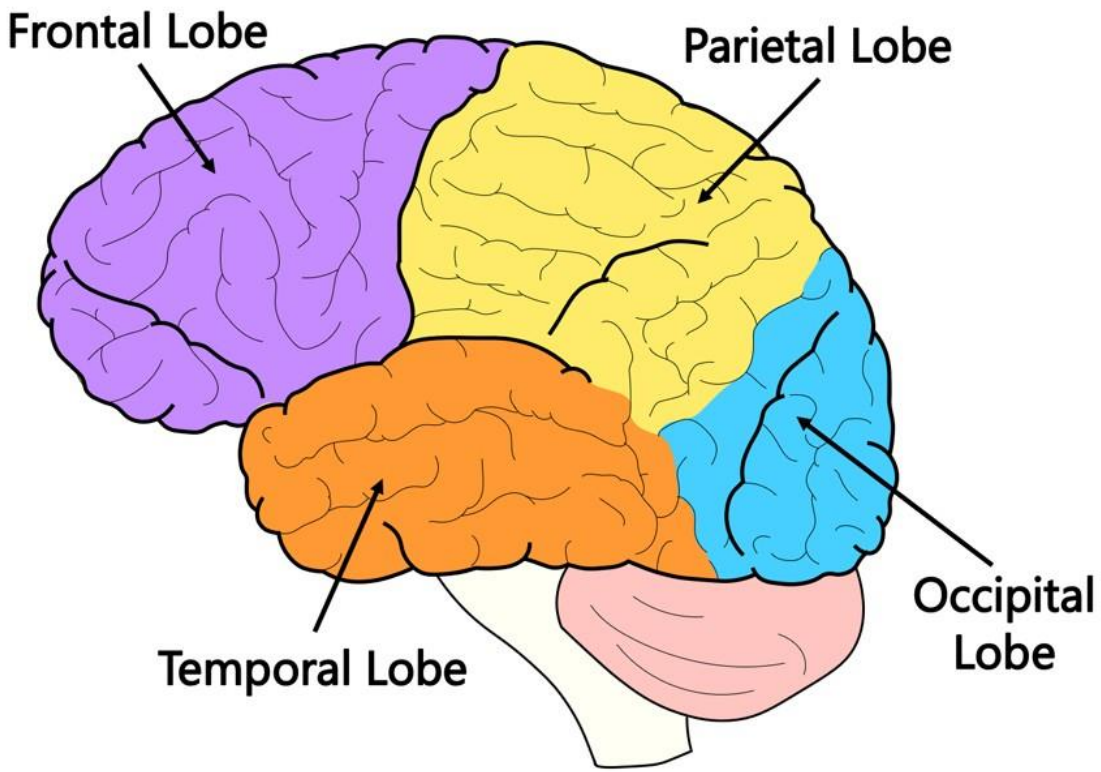



# Cerebral Lobes

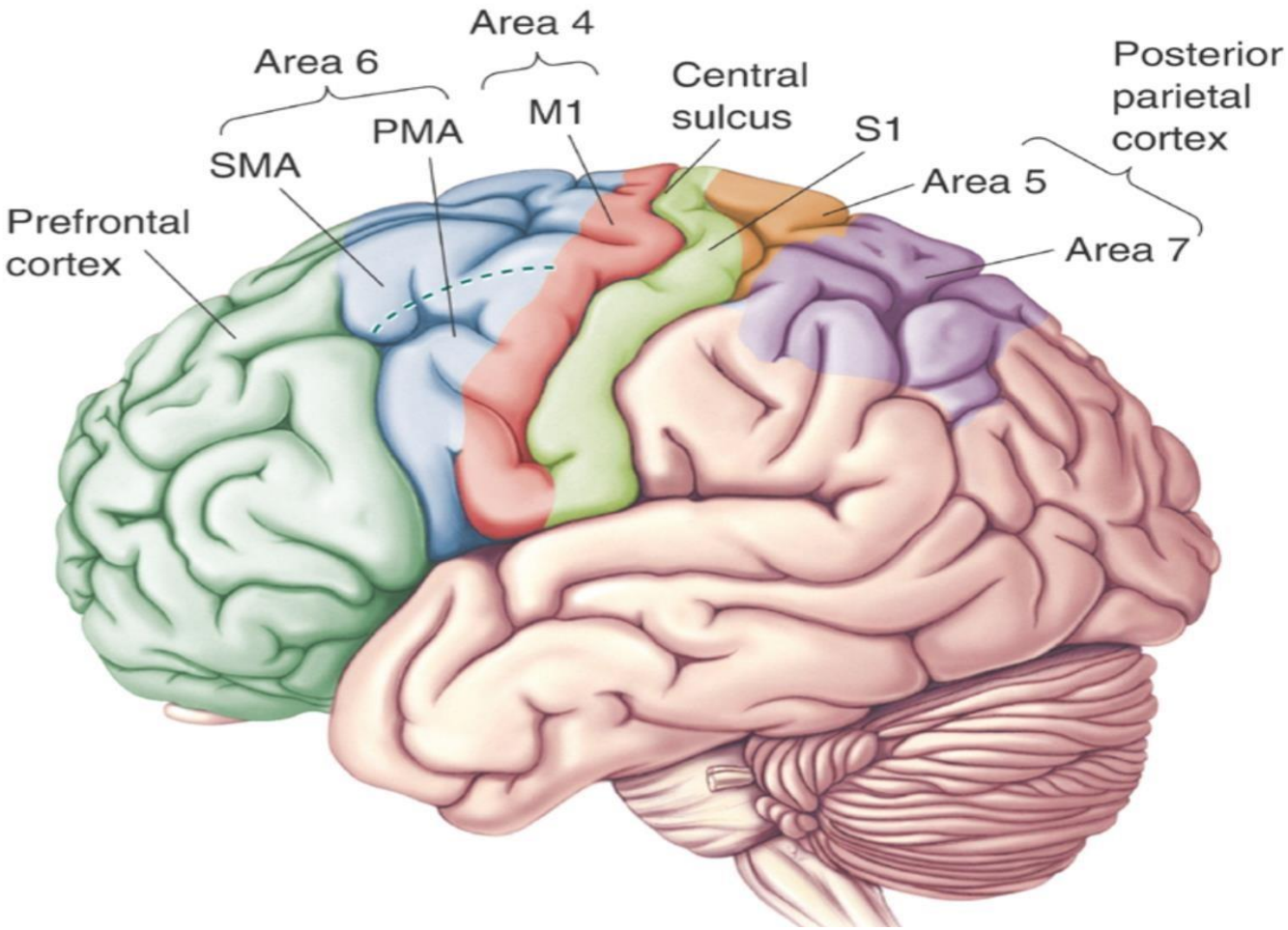
The two hemispheres connected by the corpus callosum. ❖

Each of the hemispheres has been divided into four lobes: ❖

**frontal, parietal, temporal and occipital**



# Cortex Areas



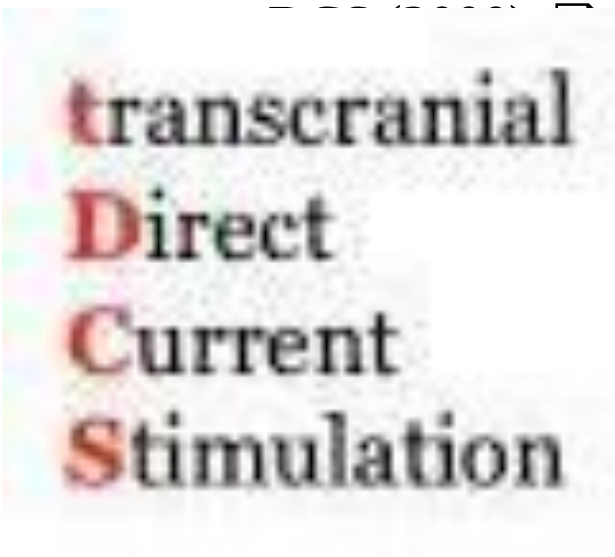
# History

- New old technique
- Torpedo fish to treat pain and headache, Plato and Aristotle
- Avicenna (980–1037)
- Epilepsy, demonic possessions, headaches, and even gout for over 10 centuries

# History

1960s and 1970s, the treatment of some psychiatric disorders was investigated using brain polarization

- Electrosleep therapy (1950s)
- Brain Polarization (1970s)

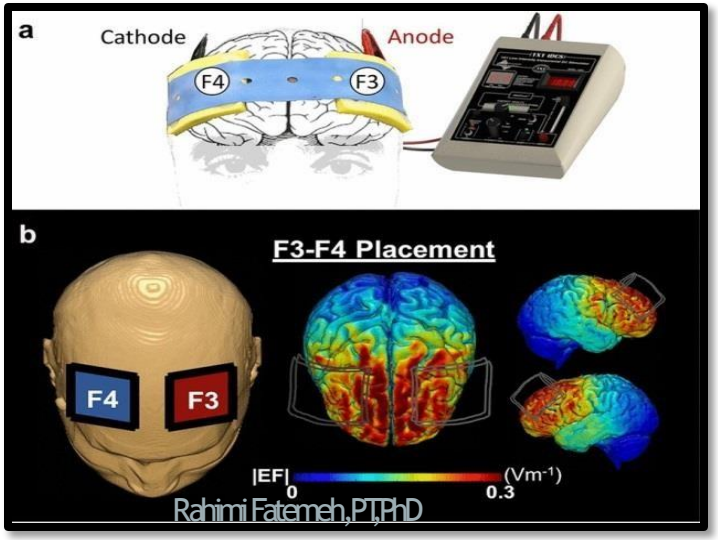


# History

Reappraisal in 1998–2000 ➢

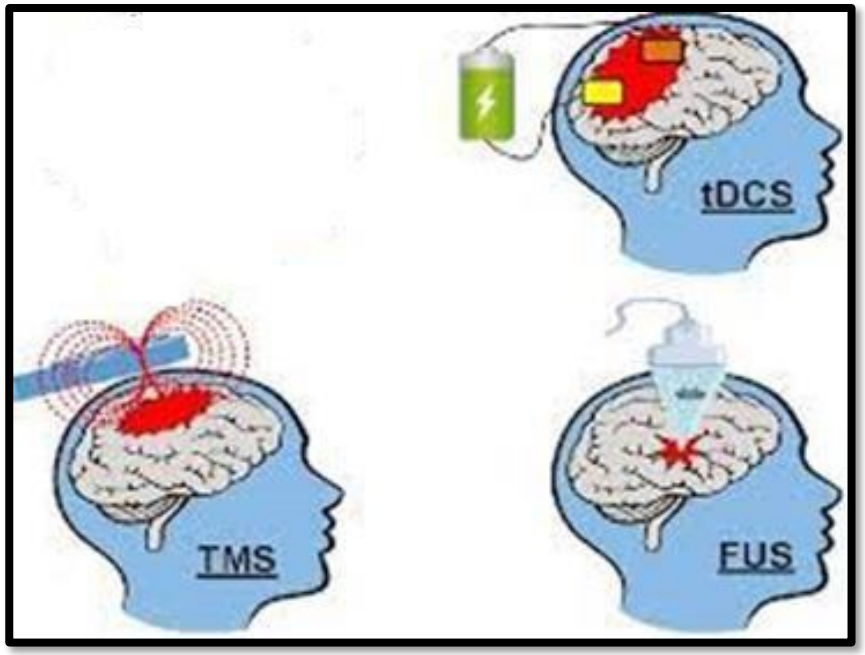
Electric currents applied over the motor cortex ✓ induced changes in human brain excitability

has attracted considerable tDCS has been increasingly investigated and ➢ attention in both basic and clinical research settings

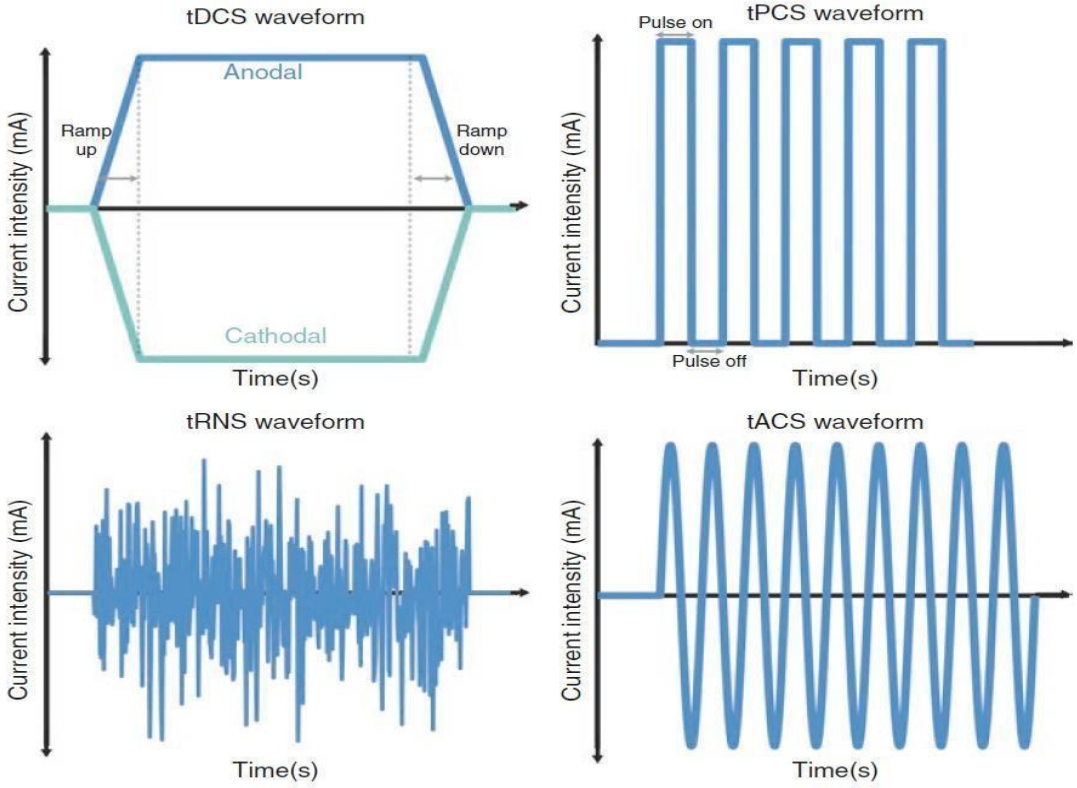


# Noninvasive Brain Stimulation

- Transcranial magnetic stimulation
- Transcranial electrical stimulation
- Transcranial ultrasound stimulation



# Transcranial Electrical Stimulation



# tDCS Implication

- Neuropsychiatric disorders ✓
- Neurological disorders ✓
- Modulation of autonomic nervous system ✓
- Appetite ✓
- Energy expenditure ✓
- Motor performance ✓
- Motor learning ✓

# tDCS Implications

## Treatment

- Neurological disorders i.e. Stroke
- Psychological disorders i.e. Depression
- Pain relief
- Treatment of drug addicts
- Language disorders i,.e aphasia

## Boosting

- Learning
- Memory
- Cognition
- Mental practice

## Investigatory

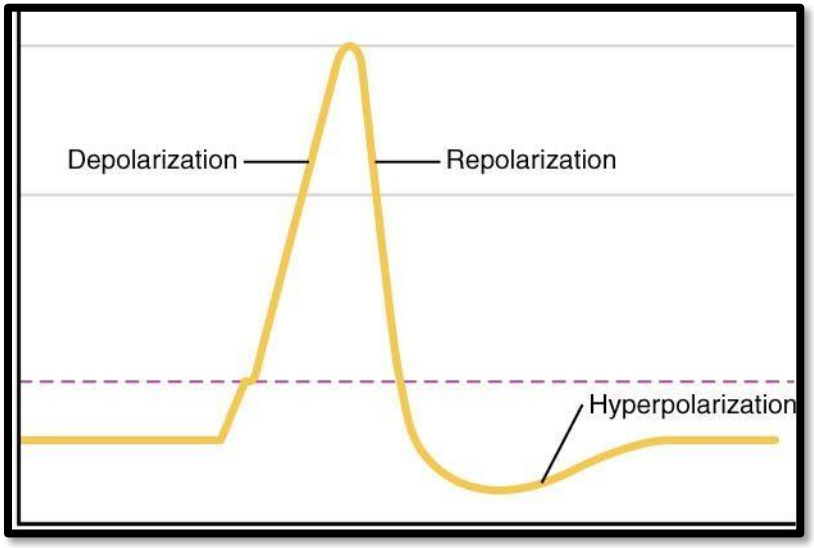
- Optimum stimulation parameters
- Understanding brain function

# Mechanism

Subthreshold shift of resting membrane potentials towards depolarization or hyperpolarization:

Anodal tDCS ↑ ➢

Cathodal tDCS ↓ ➢



# Anodal tDCS vs. Cathodal tDCS

**Anodal tDCS**: ↓ local concentrations of the inhibitory neurotransmitter ❑ gamma-aminobutyric acid (GABA)

- Learning and performance improvements ❑
- Allow for the induction of activity-dependent long- term potentiation ❑
- N-methyl-D-aspartate (NMDA) receptors ❑
- Brain-derived neurotrophic factor (BDNF) ❑

**Cathodal tDCS**: ↓ excitatory glutamate levels ❑

# tDCS Effects

**Immediate effects**: ❖

- modulation of sodium and calcium channels
- intracellular calcium concentrations

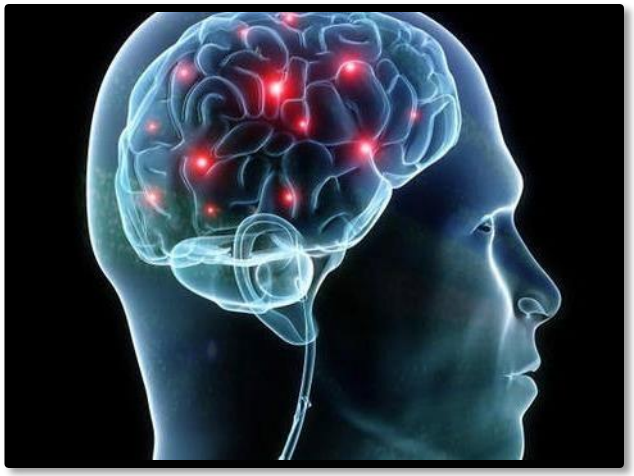
**Long lasting effects**: N-methyl-D-aspartate receptor dependent neuroplasticity ❖

# Hebbian Theory

Neurons that fire together, wire together

If presynaptic and postsynaptic neurons are both active, the result is synaptic strengthening ➢

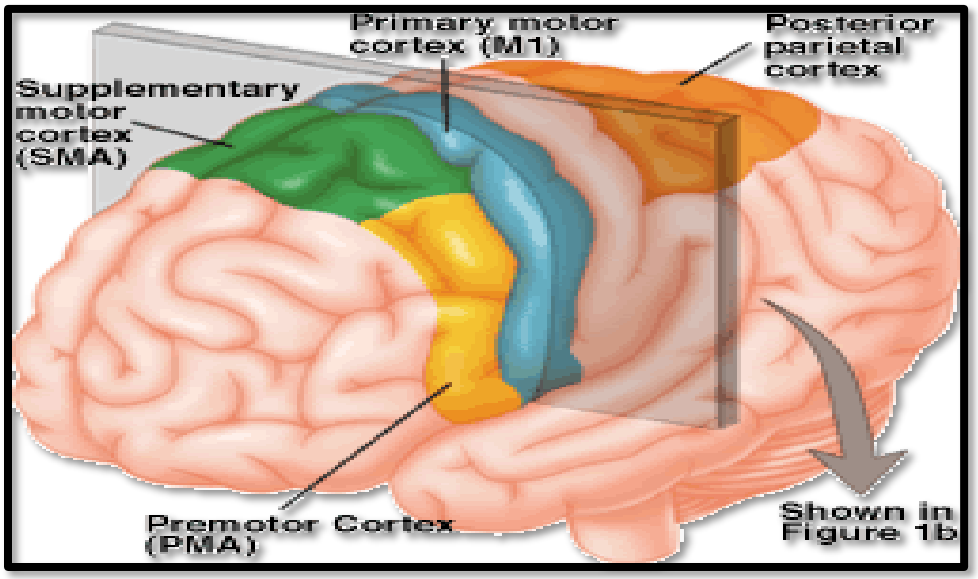
If one or both are inactive synaptic weakening occurs ➢



# Inter-regional Effects of tDCS

- Premotor anodal tDCS enhances intracortical facilitation of M1, most probably due to the activation of premotor-primary motor cortex afferents

- Combined dorsal premotor and supplementary motor area stimulation alters motor and somatosensory evoked potentials



# Effect on Non-neuronal tissues

- In patients with cerebral diseases, besides neuronal damage, other important pathological processes may exist in the axonal microenvironment, such as inflammation
  - Neuroinflammatory Diseases: Multiple Sclerosis
  - Neuropsychiatric Conditions: Alzheimer's Disease
- DC fields can enhance axonal regeneration and neurite outgrowth
- Modulate oxygen supply to cortical and subcortical areas

# Neurophysiological Mechanisms

- Influencing excitability: responsiveness to synaptic input
- Modulating the firing rate of individual neurons
- Change in information processing by cells and networks

# Rationale for Clinical Applications

- Re-adjust or re-balance the system
- Cortical activity/excitability for learning and memory formation
- Hebbian Theory: “neurons that fire together, wire together”

# Alternating Factors of tDCS Effects

- Polarity
- Duration
- Current intensity
- Current density
- Stimulation/return electrode locations
- Underlying pathology/state
- Co-administered drugs/treatments

# tDCS Protocols and Effects

Usually applied via conductive rubber or metal electrodes ✓

Embedded in a sponge soaked with saline or conductive gel or cream ✓

Stimulator delivering constant current ✓

# tDCS Protocols and Effects

- Up to 20-min stimulation duration in most studies
- Slight itching sensation at the beginning, which normally fades with time
- Ramping up and down of current intensity for 8–30 s at both the start and end of stimulation
- Retinal phosphenes due to the tenfold higher sensitivity of the retina compared to the brain to electrical stimulation

# Current Intensity/Density

- 0.5–4 mA
- 0.03–0.06 mA/cm2
- Increasing current density might increase efficacy
  - Larger membrane polarization shift
  - Affect additional neuronal populations

# Current Intensity/Density

- Target tissue
- Skull thickness
- Size of the head
- Changes in brain tissue due to aging, injury or disease
- Interelectrode distance
- Sponge thickness

# Intensity

The influence of tDCS intensity on decision- making training and transfer outcomes:

prefrontal anodal tDCS ✓

0.7, 1.0, or 2.0 mA ✓

only one of the doses (1.0 mA) leading to training transfer ✓

# Electrode Size

35 cm2 ✓

Nonfocal effects of the underlying cortex ✓

Focality can be enhanced by reducing electrode size ✓

Increasing the size of the return electrode ✓

# Electrode Size

The effect of transcranial direct current stimulation (tdcs) electrode size and current intensity on motor cortical excitability: evidence from single and repeated sessions:

(1 ma, 2 ma) / (16 cm2, 35 cm2) ✓

2 ma tdcs does not necessarily produce larger effects than 1 ma ✓

There were greater increases in excitability with the 35 cm(2) electrodes ✓

# Stimulation Duration

Determines the occurrence and length of after effects of DC stimulation 4 s: acute effects without generating after effects ✓

More than 3 min: necessary to induce cortical excitability and activity alterations, which outlast stimulation ✓

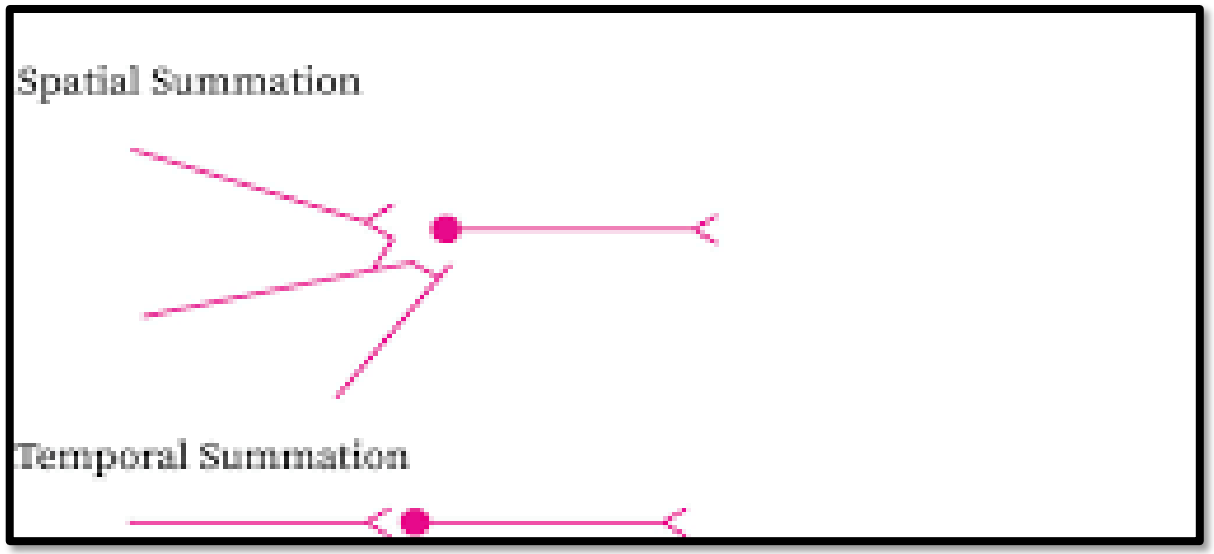
3 to 7 min: polarity-specific excitability alterations for some minutes after the end of stimulation ✓

13 min anodal tDCS, 9 min Cathodal tDCS: after effects lasting for about 1 h ✓

Non-linear relationship between stimulation duration, and duration of after effects anodal tDCS for 26 min results in excitability-diminishing intraneuronal calcium overflow ✓

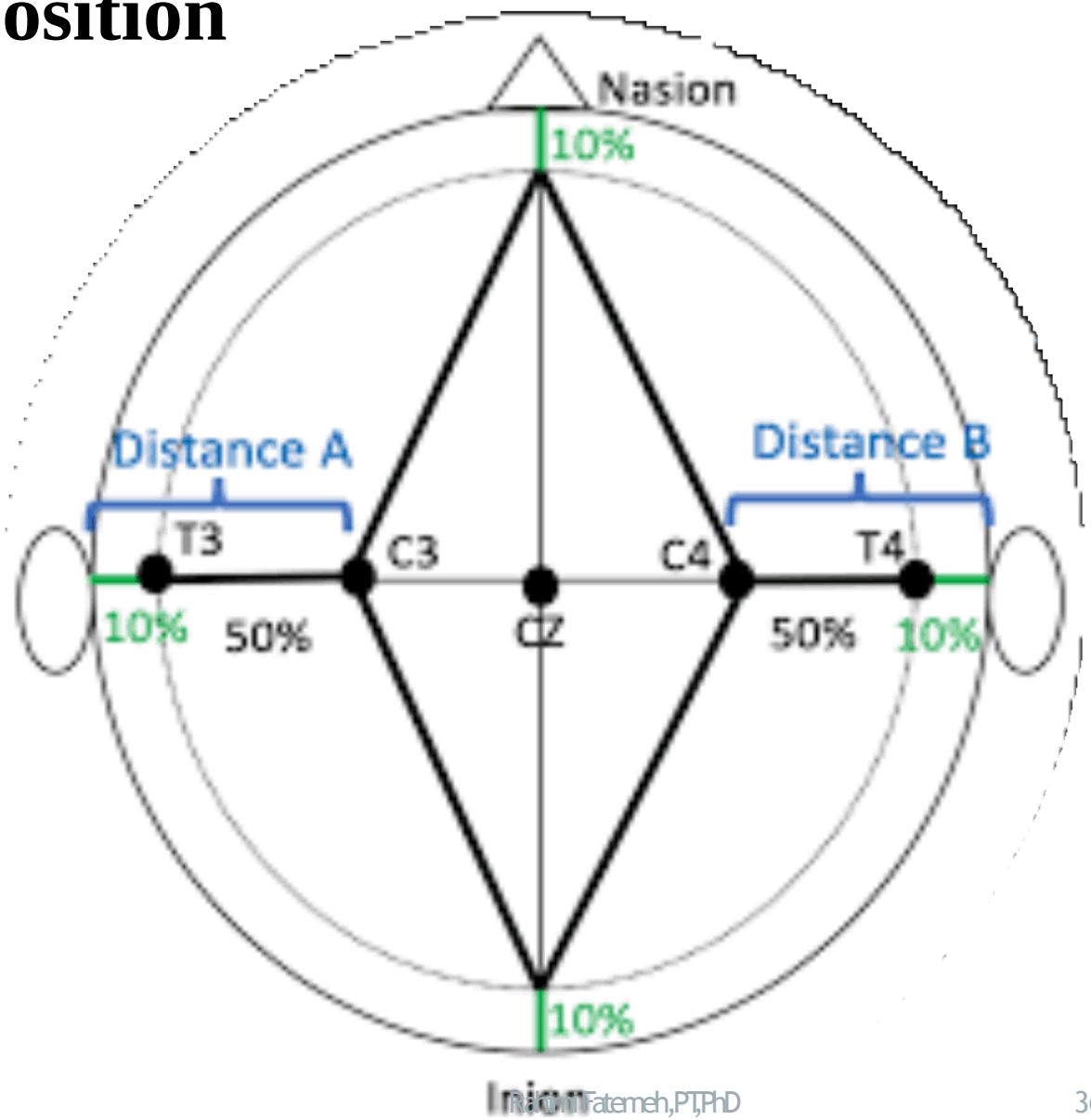
# Consolidation

- Temporal summation ❑
- Spatial summation ❑



# Electrode Position

- F - Frontal lobe
- T - Temporal lobe
- C - Central lobe
- P - Parietal lobe
- O - Occipital lobe
- Z -mid-line



# Electrode Position

**Reference electrode:**

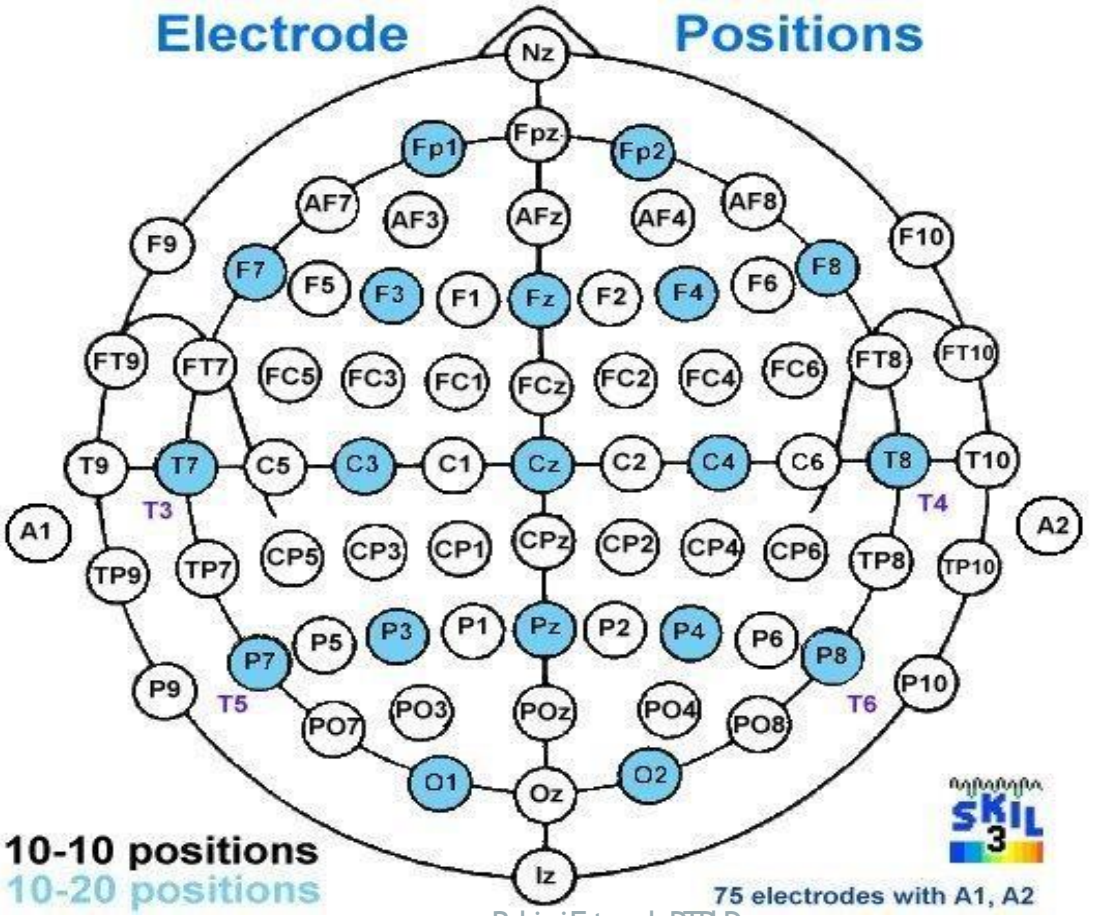
- Shoulder, Contralateral supraorbital, Buccinators muscle
- At least 7 cm

*Too low inter-electrode distance → shunting of current flow between electrodes via the skin*

# Electrode Position

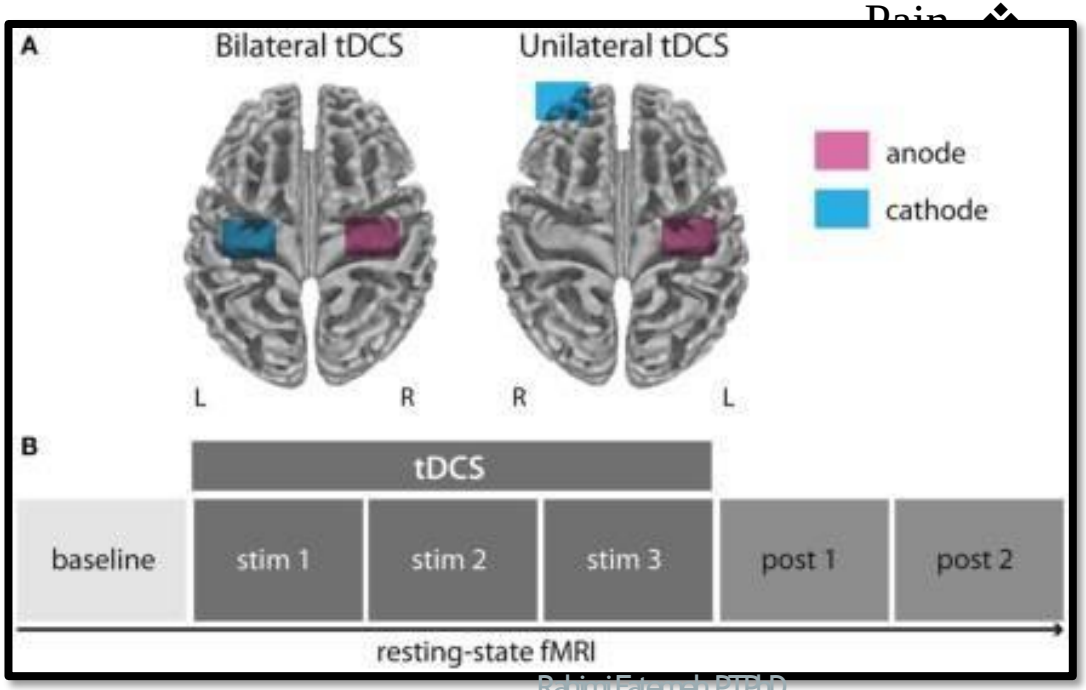
M1: C3- C4✓

S1: CP3-CP4 **(1 cm posterior to C3 or C4)**✓



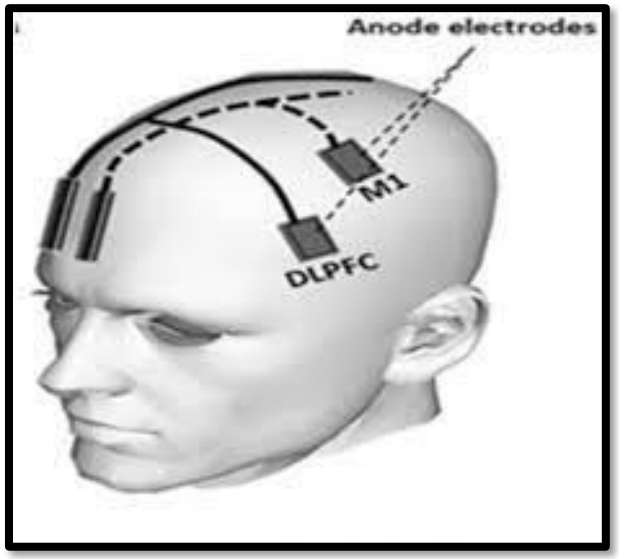
# tDCS on Motor Cortex

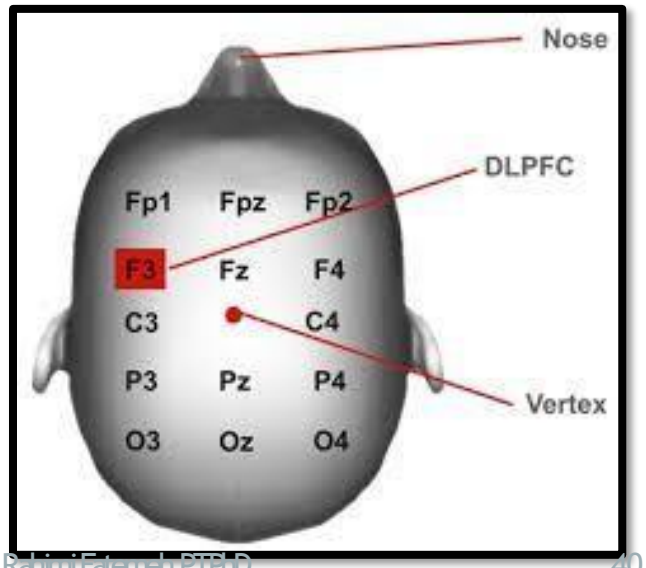
- Motor learning: precision, speed, strength, endurance and execution of daily motor tasks
- Priming
- Pain



# Dorsolateral Prefrontal Cortex

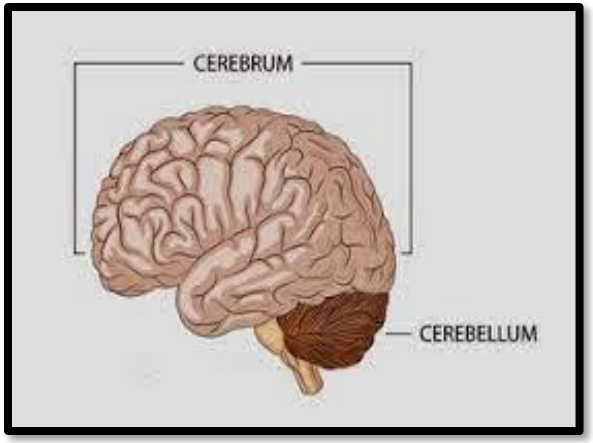
- Thalamus
- Parts of basal ganglia (caudate nucleus)
- Hippocampus



# Cerebellum

- Motor function ❖
- Control of balance ❖
- Intentional voluntary movement ❖
- Emotional processes ❖

# Cerebellum

- Rich inherited plasticity mechanisms
- Dense connections to cortical areas
- Evidence of successful non-invasive modulation of cerebellar function in humans

# HD-tDCS

- High-definition- HD-tDCS
- Smaller electrodes (5 cm2)
- Two or more electrodes
- Higher number of electrodes and/or electrodes in closer proximity
- Increased flexibility in montage design
- Facilitates simultaneous recording of EEG during HD-tDCS
- Increase brain modulat
- 4 × 1 HD-tD

# Safety and Tolerability

- Tolerability: presence of uncomfortable and unintended effects, which do not however induce structural or functional damage tingling, itching
- Safety: damaging effects
- Adverse effect: death, life-threatening condition, hospitalization, disability or permanent damage, congenital anomaly, need of an intervention to prevent permanent impairment or damage

# Tolerability

All side effects were:

- Mild
- Short-lived
- Well-tolerated
- Not different between active and sham stimulation

# Skin Reddening

- The intensity varies in patients
- Most of them experience only mild redness whereas a few others might have more intense skin reddening
- Direct effects of the current on the skin
- Physical pressure of the electrode pad, which must be strapped firmly against the skin

# Skin Reddening

- More prominent over the anode than the cathode, although it was mild in both conditions
- Short-lived, lasting less than 18–24 min
- Less intense in subjects with darker skin color
- Not influenced by gender, age, and smoking habits

# Safety

No serious adverse effects, according to the FDA literature, regarding tDCS have been reported in any tDCS clinical study performed ✓

Safety studies revealed that tDCS: ✓

- Not change heart rate variability at rest
- Not increase the serum levels of neuronspecific enolase, a brain enzyme associated with neuronal death

# Skin Lesions

- Skin damage has been occasionally reported
- It is unclear whether this adverse effect is more common under anode or cathode
- Tap water-soaked sponges
- High impedance

# Skin Lesions

- Screening patients for skin diseases
- Checking the skin site for lesions
- Avoid abrasion of the skin
- Ask patients to report during stimulation whether tDCS induced pain

# Contraindications

- Not be placed directly above areas of impaired skin, areas with chronic skin diseases
- Not be applied directly over areas with implanted metallic plates
- Heating -
- Prefe

# Caution

Neurological or psychiatric conditions ☺

Traumatic brain injury with loss of consciousness ☺

Brain surgery ☺

Seizures ☺

Alcohol or substance abuse ☺

Use of psychopharmacological drugs ☺

Children ☺

Pregnancy ☺

# Safe Dosage

- Not more than twice daily ✓
- Not more than 40 min per session ✓
- In humans burns occur at relatively high current densities of 1.3 mA/cm2 ✓
- Animal experiments demonstrate that brain tissue damage could occur at current densities over 14.29 mA/cm2 ✓

# tDCS stimulation procedure

1. Screen for Skin disease
2. Not in skin damage
3. Skin lightly clean
4. Firm contact
5. Check impedance
6. Report sensation
7. After 2 min checked for pain
8. After tDCS check for redness

# *Clinical Applications of tDCS*

# Pain

An unpleasant sensory and emotional experience associated with actual or potential tissue damage ✓

Maladaptive neuroplasticity ✓

Perpetuating the sensation of chronic pain in the presence of central sensitization ✓

# Pain

Pain is a disabling symptom common to several pathologies and it is considered the primary reason that leads individuals to seek medical care ➢

Pain dimensions ➢

sensory-discriminative ✓

# Pain

Chronic pain → sensitization in the response of the pain system to noxious or innocuous stimuli ✓

Peripheral level: local hormones or inflammatory mediators can heighten the response of nociceptors to lower levels of sensory stimulation ✓

Spinal cord: long-term potentiation (similar to formation of memories in brain) ✓

Brain: Neurons in the nociceptive amygdala and in the anterior cingulate cortex ✓

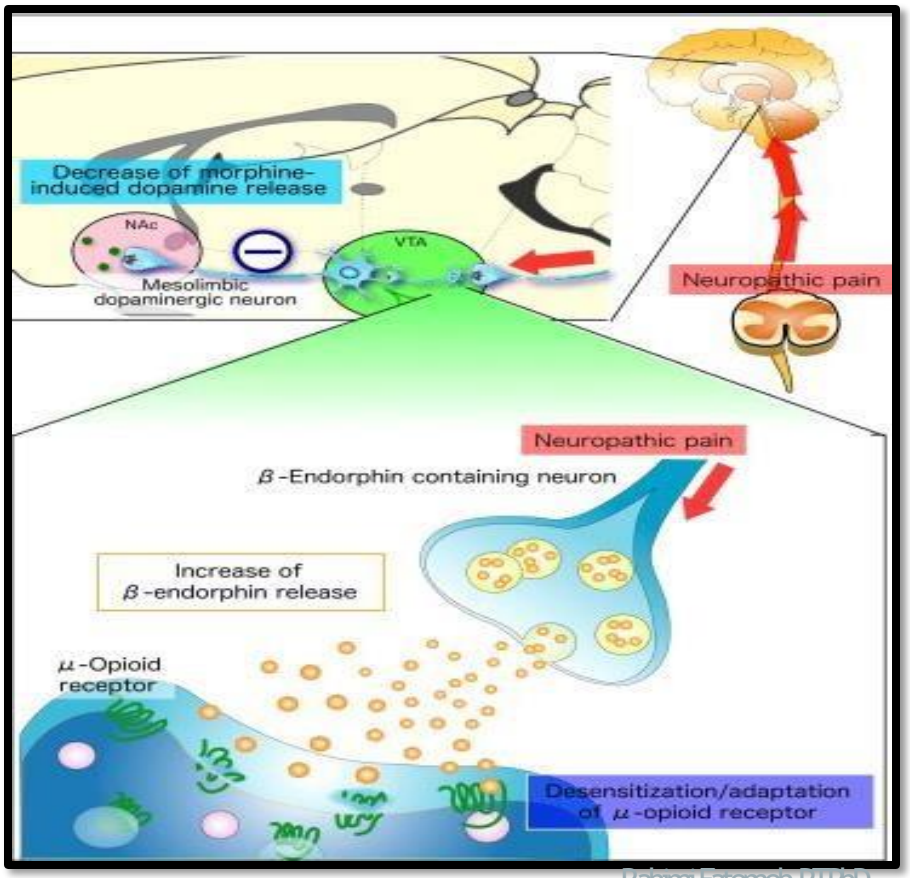
# Peripheral Sensitization

- Increased responsiveness and reduced threshold of nociceptive neurons in the periphery to the stimulation of their receptive fields.

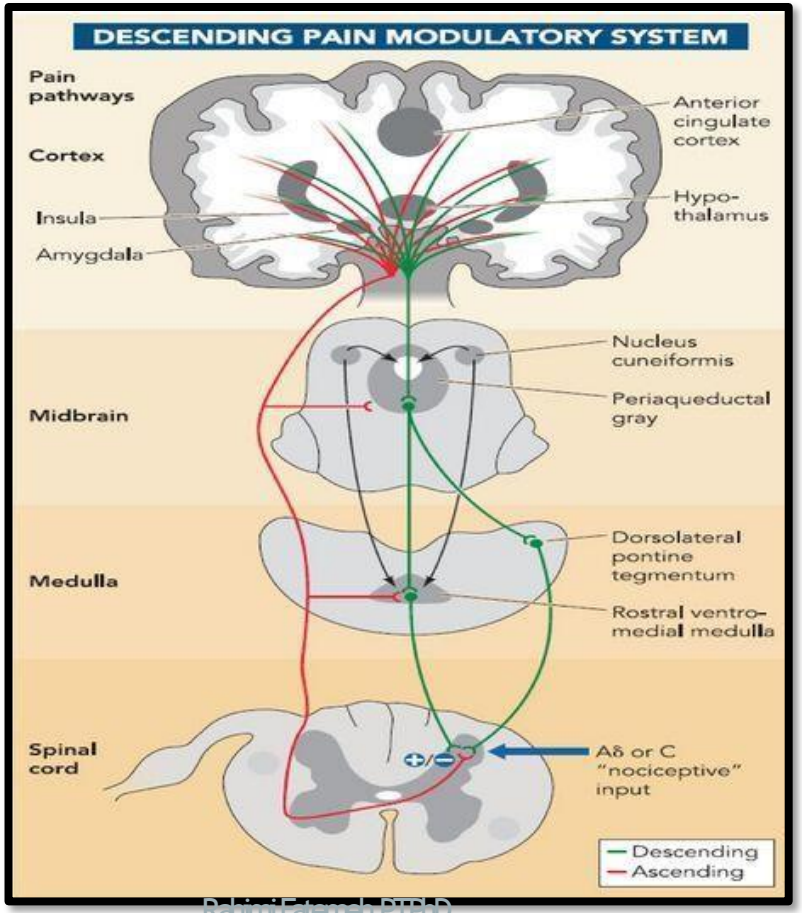
# Central sensitization

- Increased responsiveness of nociceptors in the central nervous system to either normal or sub-threshold afferent input resulting in:
- Hypersensitivity to stimuli.
- Responsiveness to non-noxious stimuli.
- Increased pain response evoked by stimuli outside the area of injury, an expanded receptive field.

- Changes in the mu-opioid neurotransmission induced by M1 tDCS have been documented in both healthy subjects and in a case report of chronic pain



- Modulation of the threshold for activation of central structures associated with pain processing
- Activation of descending inhibitory pathways



# Neuropathic Pain

- Fibromyalgia
- Pain due to traumatic spinal cord injury
- Chronic pelvic pain
- Refractory orofacial pain
- Post-herpetic neuralgia
- Painful diabetic polyneuropathy
- Chronic neuropathic pain following burn injury
- Trigeminal neuralgia
- Low back pain
- Chronic temporomandibular disorders

# Pain Montage

- *M1-SO*
  - Anode: primary motor cortex (M1)
  - Cathode: contralateral supra-orbital
- *DLPFC*
  - Both electrodes positioned over the DLPFC (Lt anodal)
- *Cz-Oz*
  - Anode: vertex
  - Cathode: occipital cortex
- S1-SO
  - Anode: primary sensory cortex (S1)
  - Cathode: contralateral supra-orbital

# Neuropathic Pains

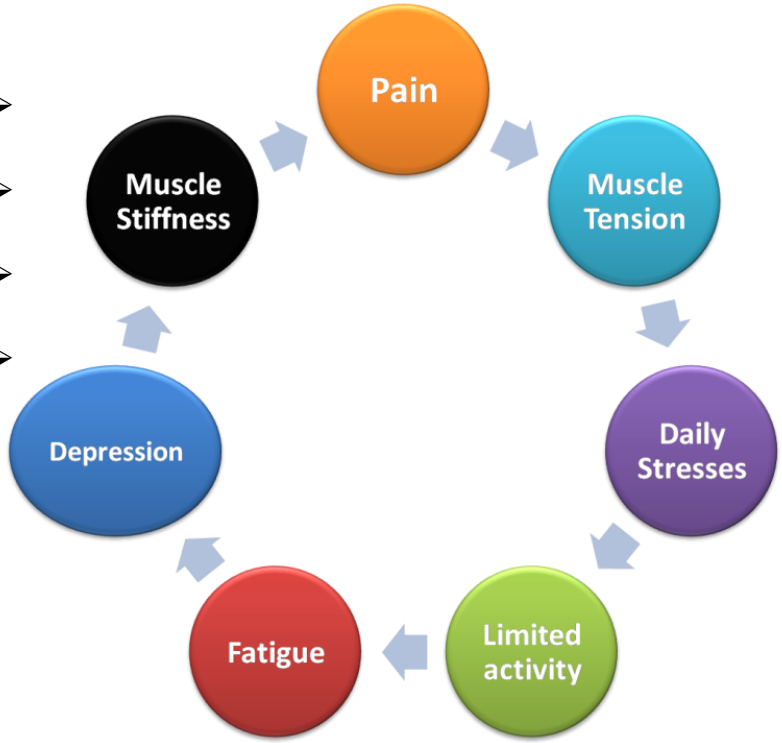
- Pain caused by a lesion or disease of the somatosensory nervous system
- An umbrella term that encompasses distinct disorders
- Trigeminal and post-herpetic neuralgias
- Painful diabetic polyneuropathy

# Fibromyalgia

- 2–8 % of the general population
- Tenderness and chronic spontaneous widespread pain
- Recent diagnostic criteria do not require counting the number of tender points. Instead, it is entirely based on patient's symptoms
- female: male ratio is 2:1

# History

- Regional musculoskeletal pain
- Irritable bowel syndrome
- Headache
- Temporomandibular joint dysfunction



# Fibromyalgia tDCS

1Level B (probable efficacy):a-tDCS of the left M ✓

58%and 14% Mean reduction of pain intensity: ✓

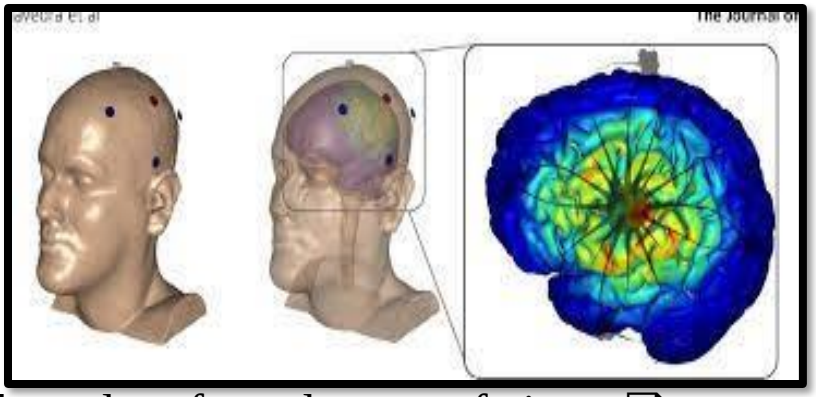
months2 or 1Remained statistically significant up to ✓

Improvement in the quality of life in most tDCS studies ✓

# Fibromyalgia tDCS

Motor cortex: pressure pain threshold, catastrophizing and quality of life ❑

- Anode: Lt M1

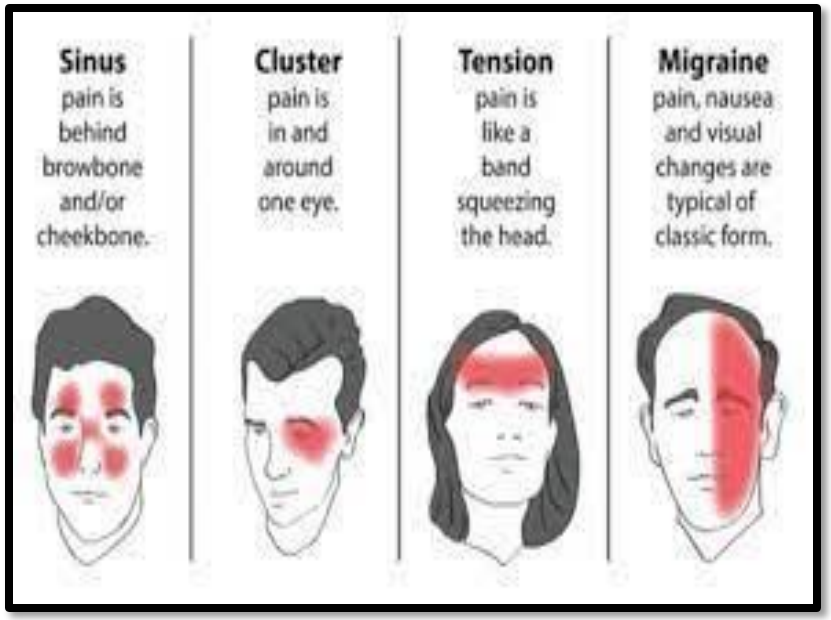


Dorsolateral prefrontal cortex: fatigue ❑

- Anodal stimulation of Lt DLPFC

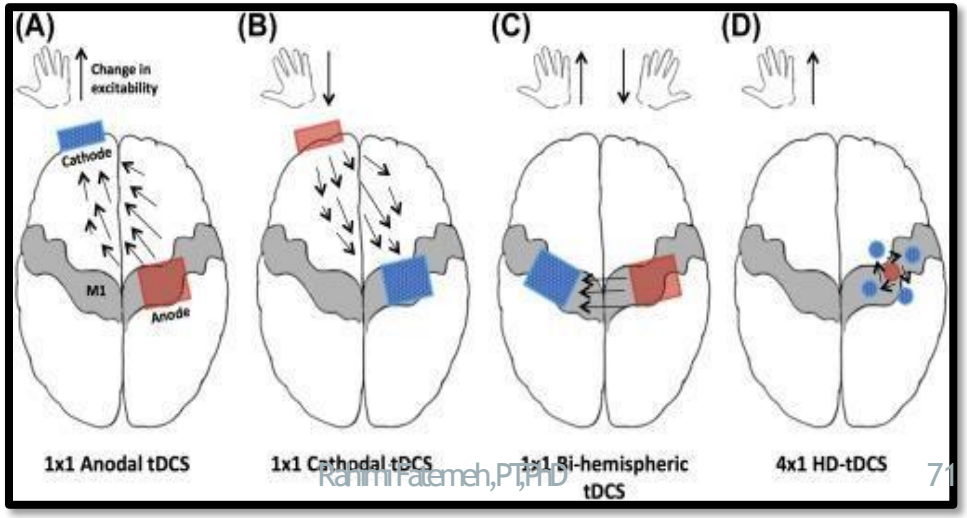
# Migraine

- Global prevalence: 14.7%
- A primary headache disorder with repeated episodic flare up lasting 4–72 hours
- Characteristic:
  - Moderate to severe head pain intensity ✓
  - unilateral location ✓
  - throbbing/pulsating pain quality ✓
- Associated with photophobia, nausea, vomiting



# tDCS & Migraine

- Pain intensity
- Number of migraine attacks per month
- Both anodal and cathodal stimulation
- Daily or near-daily
- 15 to 20 minutes
- Treatment length: 4-6 weeks
- Follow-up duration: 4-16 weeks



# Myofascial pain syndrome(MPS)

- Pain referred from active myofascial trigger points with associated dysfunction ✓
- Pathophysiology: mechanical overload or mechanical trauma increase fiber tension → taut bands, increased muscle tension, restricted ROM ✓
- Perpetuating factors, such as ongoing micro- and macro-trauma from over exertion, poor body mechanics and psychological stress ✓

# MPS & tDCS

:Pain reduction in MPS by anodal tDCS combined with standard treatment

- minutes20 for 1 mA anodal tDCS over M1 consecutive days of 5
- (active stretching exercises (Travell and Simons' procedure

✓ combined with standard treatment appears to reduce 1 Anodal tDCS over M pain intensity and may improve PROM, faster than standard treatment alone

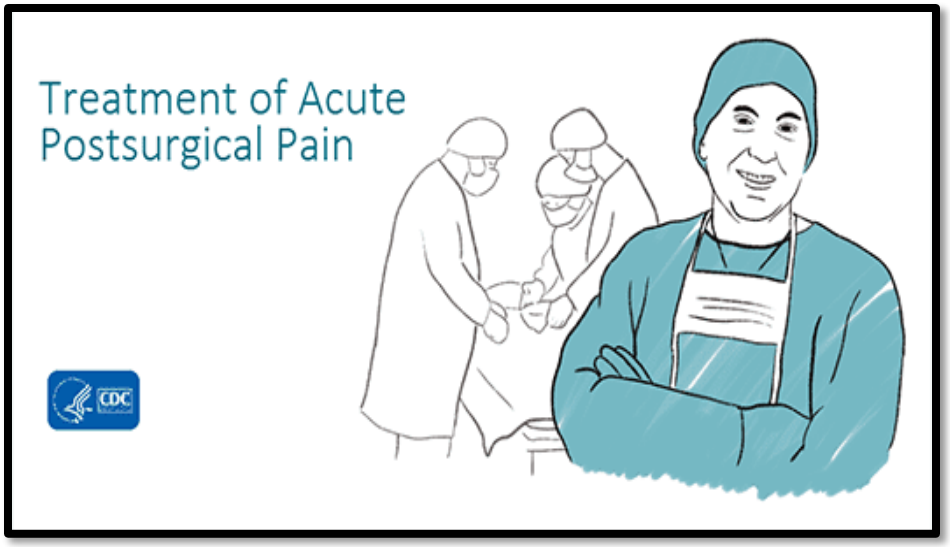
# Postoperative Acute Pain

**Preoperative** transcranial direct current stimulation: exploration of a novel strategy to enhance neuroplasticity before surgery to control postoperative pain:

- Two sessions (morning before the surgery and in the 1 minutes each) of anodal a-tDCS or s-tDCS on the M20
- Lower scores on VAS at rest and during walking
- 73.25%Analgesic doses in
- Disability related to pain

# Postoperative Acute Pain

- M1 anodal tDCS reduced patient-controlled analgesia
- M1 electrode location varied by type of surgery
- tDCS pre- rather than post-operatively → decrease in post-hallux valgus surgery PCA use (72.3%) and pain



# Total Knee Arthroplasty

Role of tDCS on reduction of postsurgical opioid consumption and pain in total knee arthroplasty:

- 2 mA, 20 min, M1 anodal stimulation, postoperative for 4 consecutive days
- 59% reduction in the titrated analgesia

# Low Back Pain

The effects of tDCS combined with group exercise treatment in subjects with chronic low back pain:

- ✓ 5 sessions of brain stimulation followed by 10 sessions of group exercise
- ✓ pain intensity
- 9

# Intra-abdominal Pain

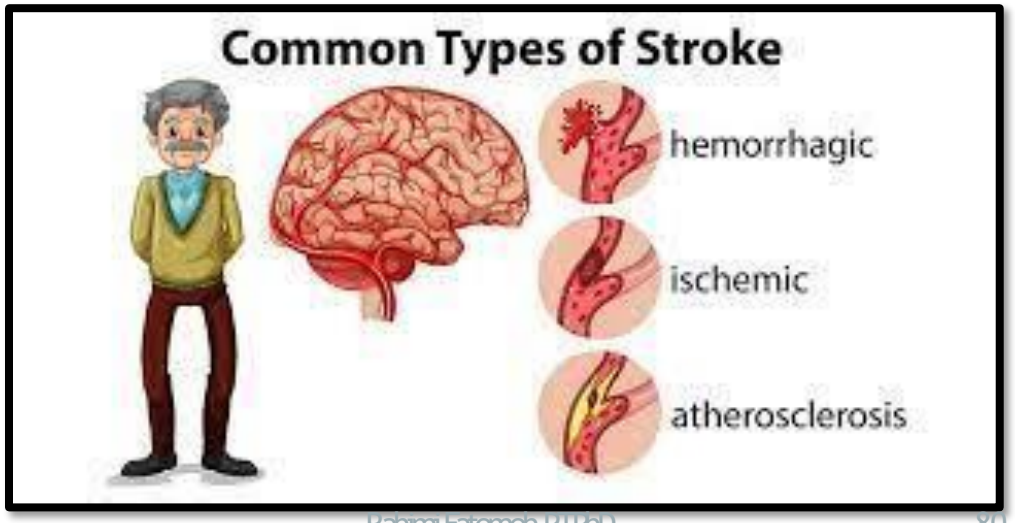
- Reduction of intra-abdominal pain through transcranial direct current stimulation
- pelvic pain, visceral pain,

# Other Applications

- RSDS
- Phantom pain
- Trigeminal neuralgia
- Cervicogenic headache

# Stroke

- Rapidly developing signs of focal or global disturbance of cerebral function
- Lasting more than 24 h
- Leading to death
- With no apparent cause other than that of vascular origin



# Symptoms

1. Motor weakness
2. Coordination and balance problems
3. Apraxia
4. Spasticity
5. Sensory loss
6. Hemi spatial neglect

7. Aphasia
8. Dysarthria
9. Central pain
10. Shoulder pain
11. Depression
12. Cognitive problems
13. Behavioral problems

# Stroke & tDCS

- tDCS could be applied as an adjuvant therapy for rehabilitation in stroke patients as it can potentially facilitate motor, cognitive and language.
  - Chronic
  - Sub- acute

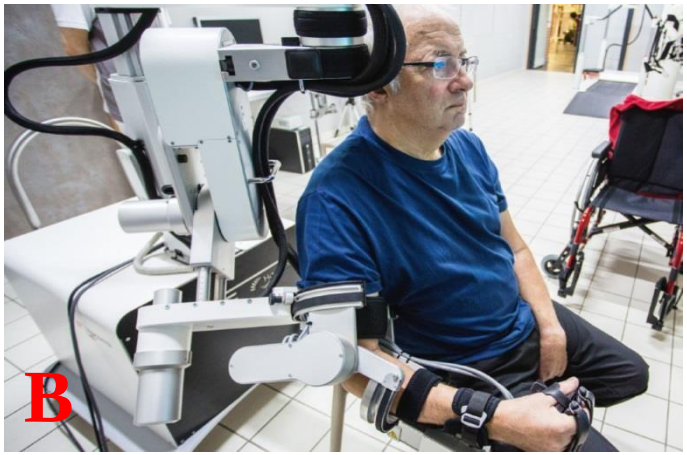
# Motor stroke and tDCS

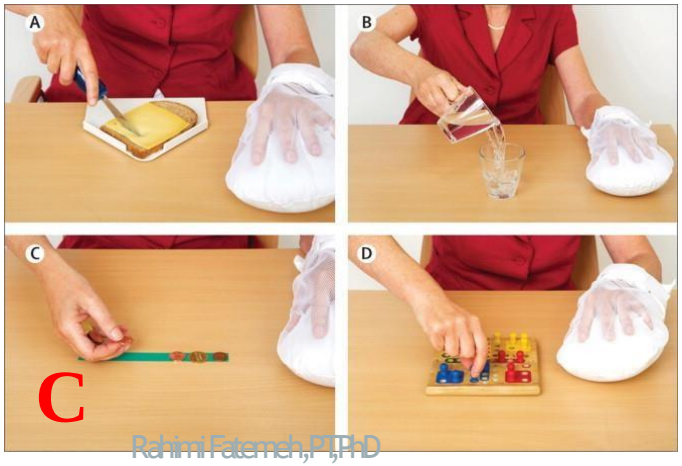
Combination of tDCS with other therapies → synergistic effects

Virtual reality training .A

Robot-assisted training .B

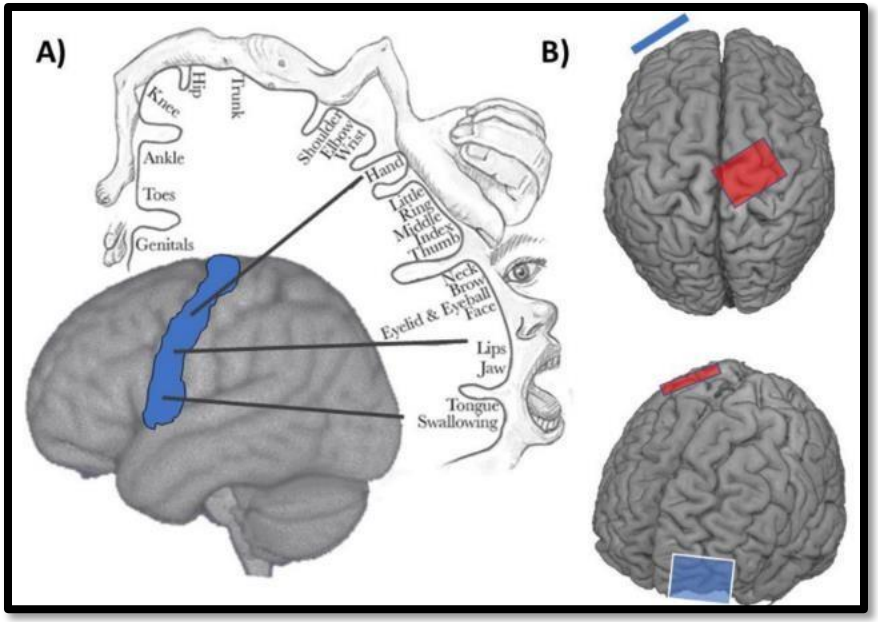
Constraint-induced movement therapy .C

# Pain stroke and tDCS

- Thalamic syndrome
- 8-35%
- Spinothalamic tract, thalamus, thalamocortical tract



# tDCS for Pain in MS

Anodal M1 tDCS : ➢

C3/C4, contralateral to the painful somatic area ✓

5 sessions ✓

Anodal DLPFC tI

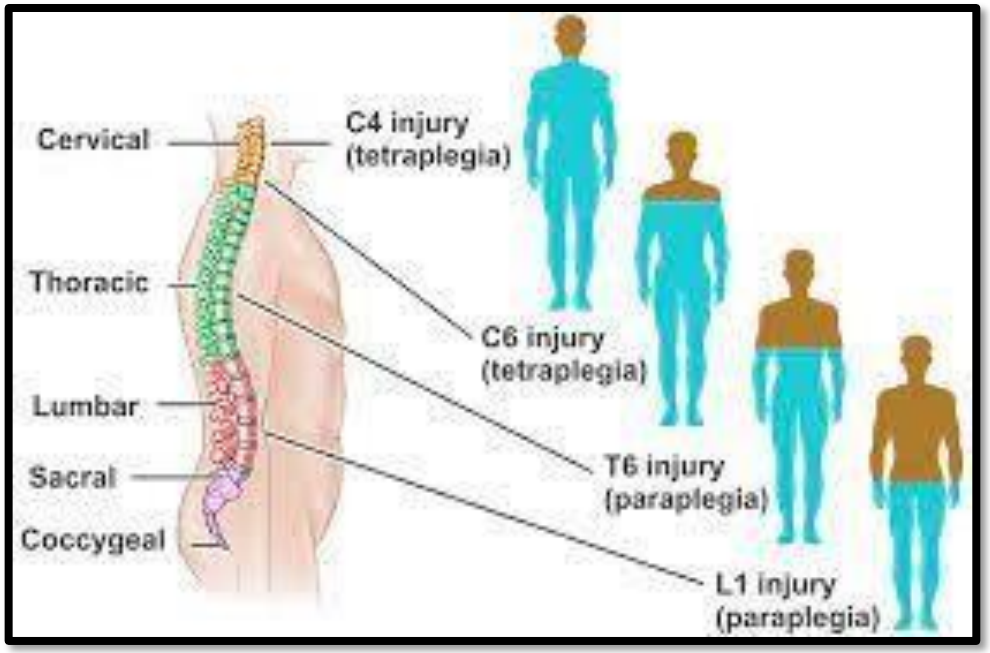
Left DLPFC

3 consecutive daily sessions


a-tDCS$_{LHDS}$ of M1-DLPFC

# Spinal Cord Injury

- Traumatic or non-traumatic event that altered sensory, motor, or autonomic function
- affects a patient's physical, psychological, and social well-being



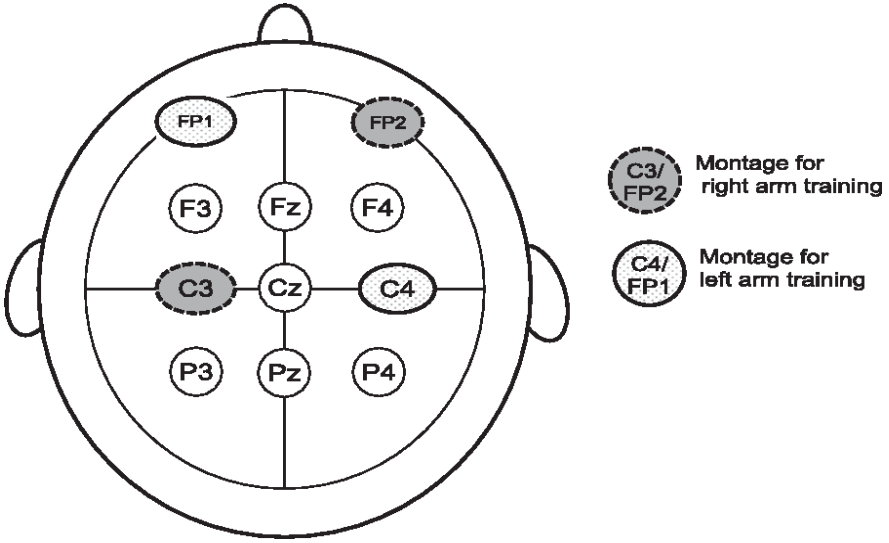
# Spinal Cord Injury (upper extremity)

tDCS protocol:

- Single session
- 2 mA or 1 mA
- Anodal tDCS
- 30 minutes
- M1

Functional tests:

- Nine-hole peg test
- Pinch force
- ensory perception
- Grasp



# Spinal Cord Injury (lower extremity)

:tDCS protocol

- Anodal tDCS
- Vertex
- sessions 36
- During gait training with a robotic gait orthosis

:Functional tests

- lower extremity motor score
- Gait
- Imbalance

# Knee osteoarthritis

- Prevalent and costly health
- M1 anodal tDCS
- 2mA
- 20 minutes
- Twice weekly
- 8 weeks

# Any Question?

*Thank you*