



Neuromodulators effects in rehabilitation of neurological patients

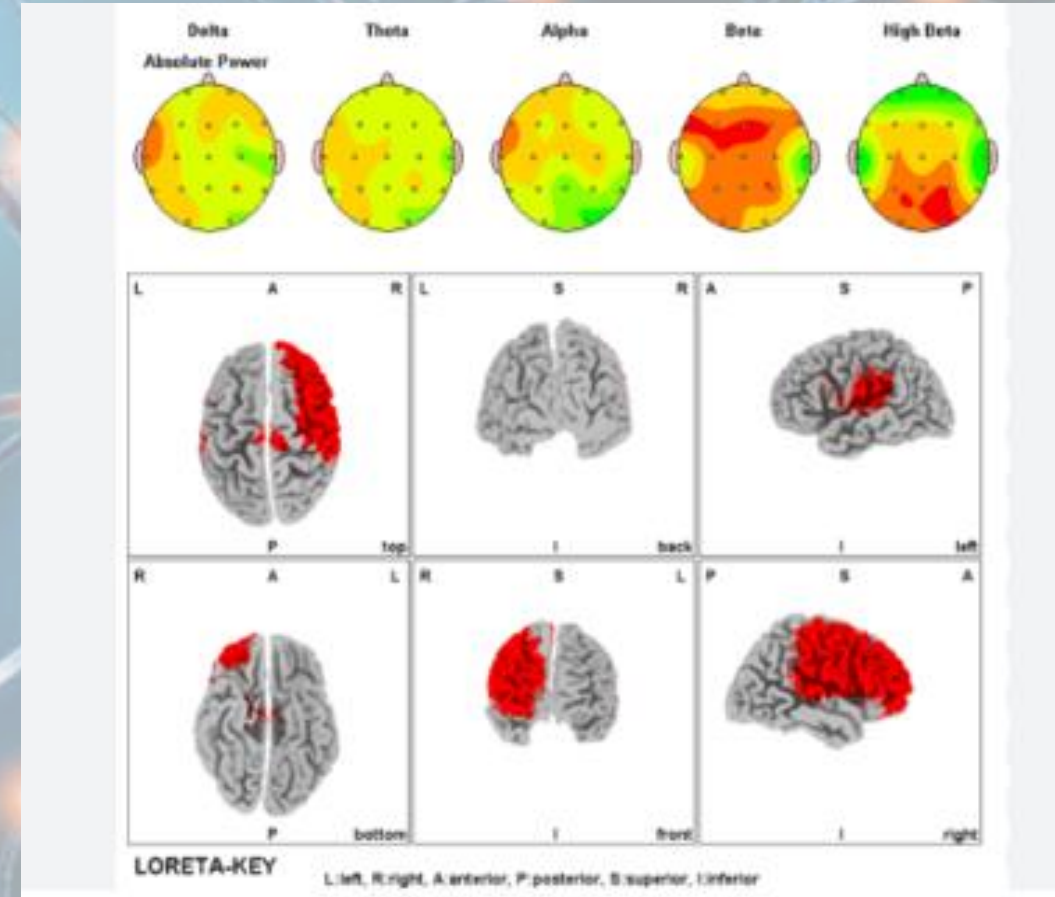
Dr. Fatemeh Ehsani

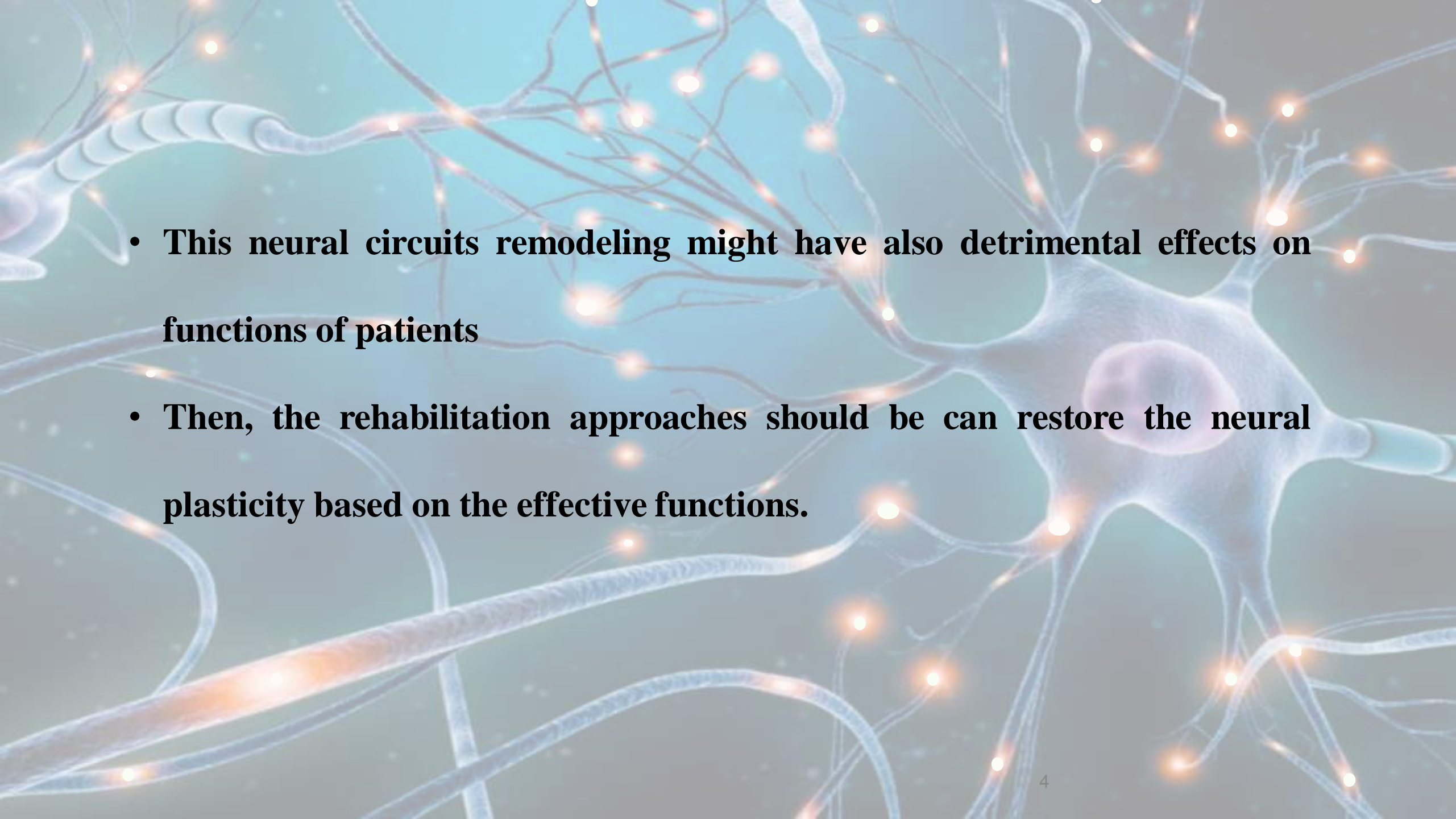
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Introduction

- **The largest increases in the incidence rates of neurological disorders in 1990-2019**
- **Neurological disorders, the most common of which are stroke, neurodegenerative, autoimmune, and spinal cord injuries cause significant damage to cognitive and motor functioning, resulting in one of the highest rates of disability and mortality globally.**

- During brain repair following injury, plastic changes are occurred towards maintaining function (optimize) in spite of the damaged brain.
- Changes in their function and shape that allowed them to take on the functions of the damaged cells.
- Focal brain lesions may functionally impair remote regions, including the hemisphere contralateral to the affected side.



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- **This neural circuits remodeling might have also detrimental effects on functions of patients**
 - **Then, the rehabilitation approaches should be can restore the neural plasticity based on the effective functions.**

Brain Plasticity management

Synaptic plasticity or reorganization of synapses: Activity-dependent

Glutamate: the main excitatory neurotransmitter which plays a crucial role during synaptic plasticity.

synaptic remodeling

Brain Plasticity ...

Impulse (EPSP)

Glutamatergic transmission is important for stabilizing synaptic contacts (**functional synaptic plasticity**).

The formation of new synapses may depend on glutamatergic-related activity (important **first step** in the mechanisms underlying **structural synaptic plasticity**).

NMDA molecules in the postsynaptic membrane are receptors for glutamatergic neurotransmitter.

- Transmission can stimulate NMDA receptor activation and **trigger Ca²⁺ influx** into the cell, which generates a complex signal (**GP43 protein, CaMKII**).
- GP43 protein induce information **encoding and storage** throughout the brain (Hunt DL, Castillo PE, 2012).
- This evidence supports a crucial role of CaMKII in the persistent forms of **structural synaptic plasticity** (the formation of dendritic spines and **new synaptic contacts**).

The aims

Routine PT:

- Each techniques which irritate the sensory imputes to the CNS
- **New approach in PT (Neuro-modulation & neuro-rehabilitation)**
- **EPSP (the number, frequency): a key factor in neural plasticity process**
- **Focus on CNS plasticity management along with the other PT techniques to modulate the neural changes for restoring optimize functions following neural plasticity**

Neuromodulators...

Brain stimulation techniques are used in experimental and clinical fields for their potential effects on brain network dynamics and behavior.

**Non invasive brain stimulation
(NIBS)**

→ Transcranial direct current stimulation (tDCS)
→ (Transcranial magnetic stimulation (TMS)

Invasive brain stimulation → Deep brain stimulation (DBS)

Cortical Excitability

FACILITATION

rTMS (5-20 Hz)

iTBS

PAS-25

Anodal tDCS

rTMS (1 Hz)

cTBS

PAS-10

Cathodal tDCS

INHIBITION

Indications for therapeutic NIBS

1- Psychiatric diseases

- Depression
- Anxiety
- Obsessive-compulsive disorders
- Post-traumatic stress disorders
- Sleep disorders
- Stopping smoking
- Obesity

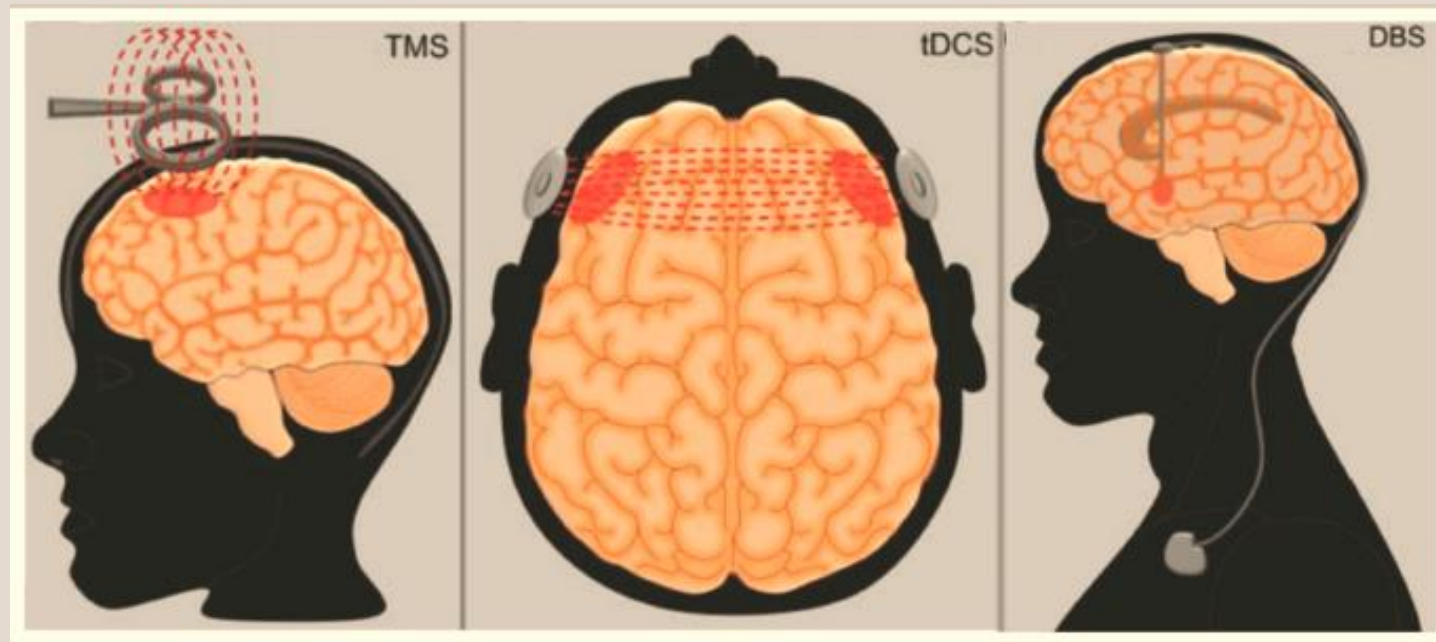
2- Neurological diseases

- Migraine
- Parkinson's disease
- Alzheimer's disease
- Epilepsy
- Stroke
- Traumatic brain injury
- Multiple sclerosis
- Spinal cord injury

3- Pain disorders

- Chronic pain
- Fibromyalgia
- Phantom pain

When a current is applied to brain tissue (as in tDCS, TMS, and DBS), it affects the polarization of cellular membranes, which in turn can alter neuronal excitability.

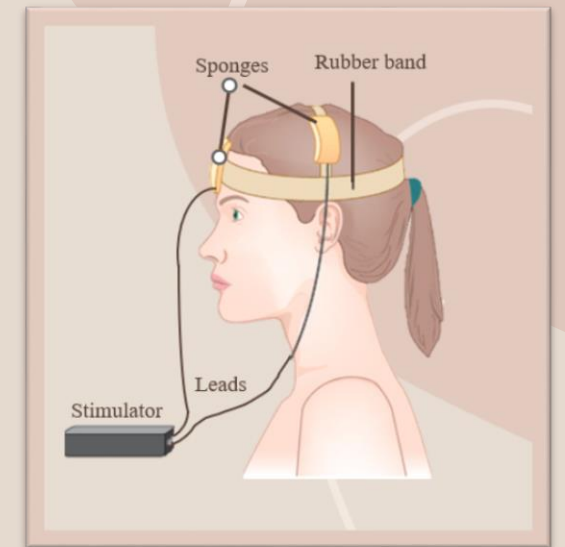


transcranial direct current stimulation (tDCS)

tDCS is an effective, non-invasive, accessible, and painless, cortical stimulation technique.

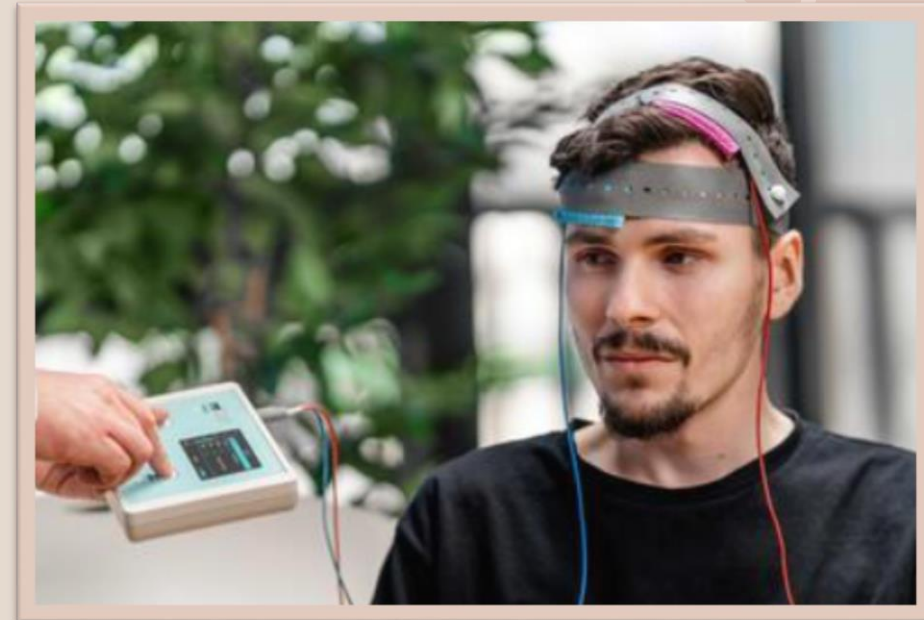
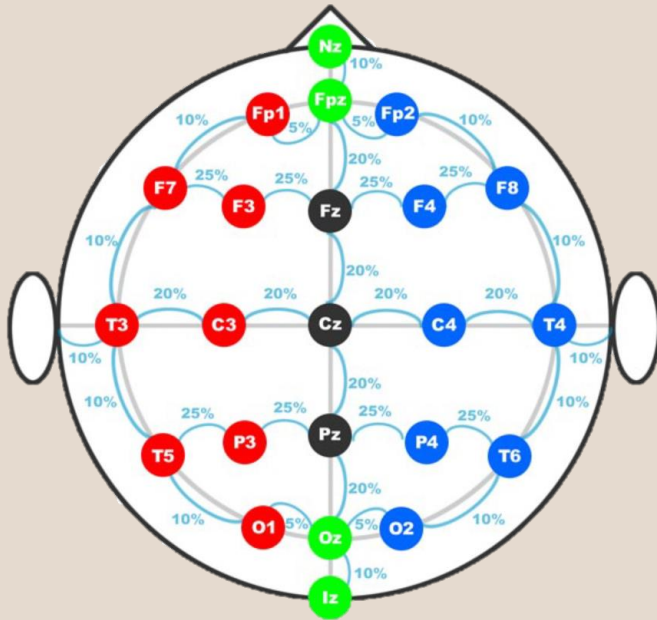
tDCS applies small constant or alternating currents (usually 1–2 mA for several minutes).

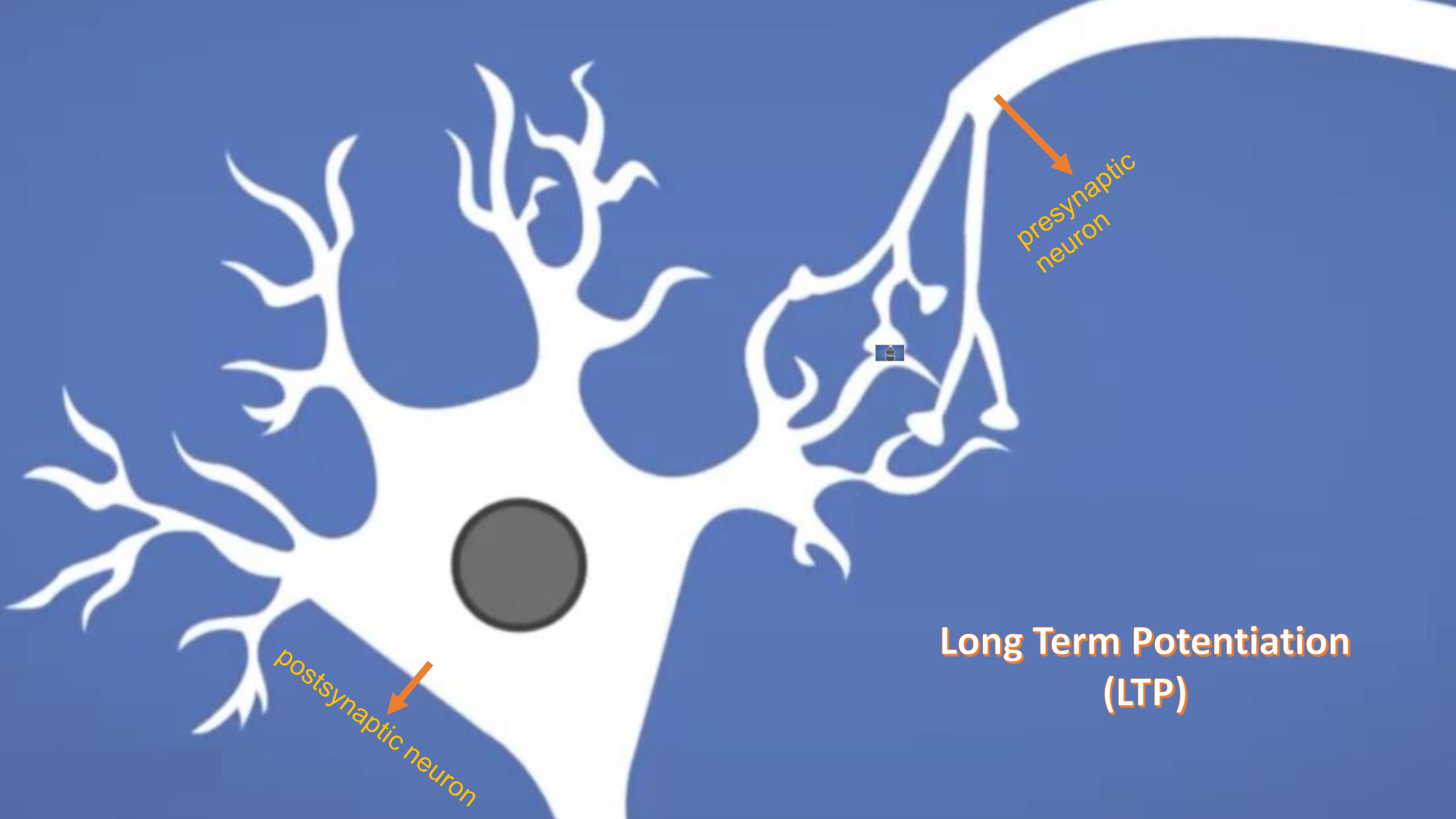
This is thought to change the polarization of the neural membranes by a small amount (<1 mV) and leads to increase or decrease the ongoing discharge rate.



Studies suggest that the mechanisms underlying tDCS are **ion-channel dependent**, selectively affecting neurons, generating inhibitory, excitatory modulations and inducing LTD and LTP effects.

Firing rates are increased by anodal polarization and decreased by cathodal polarization.

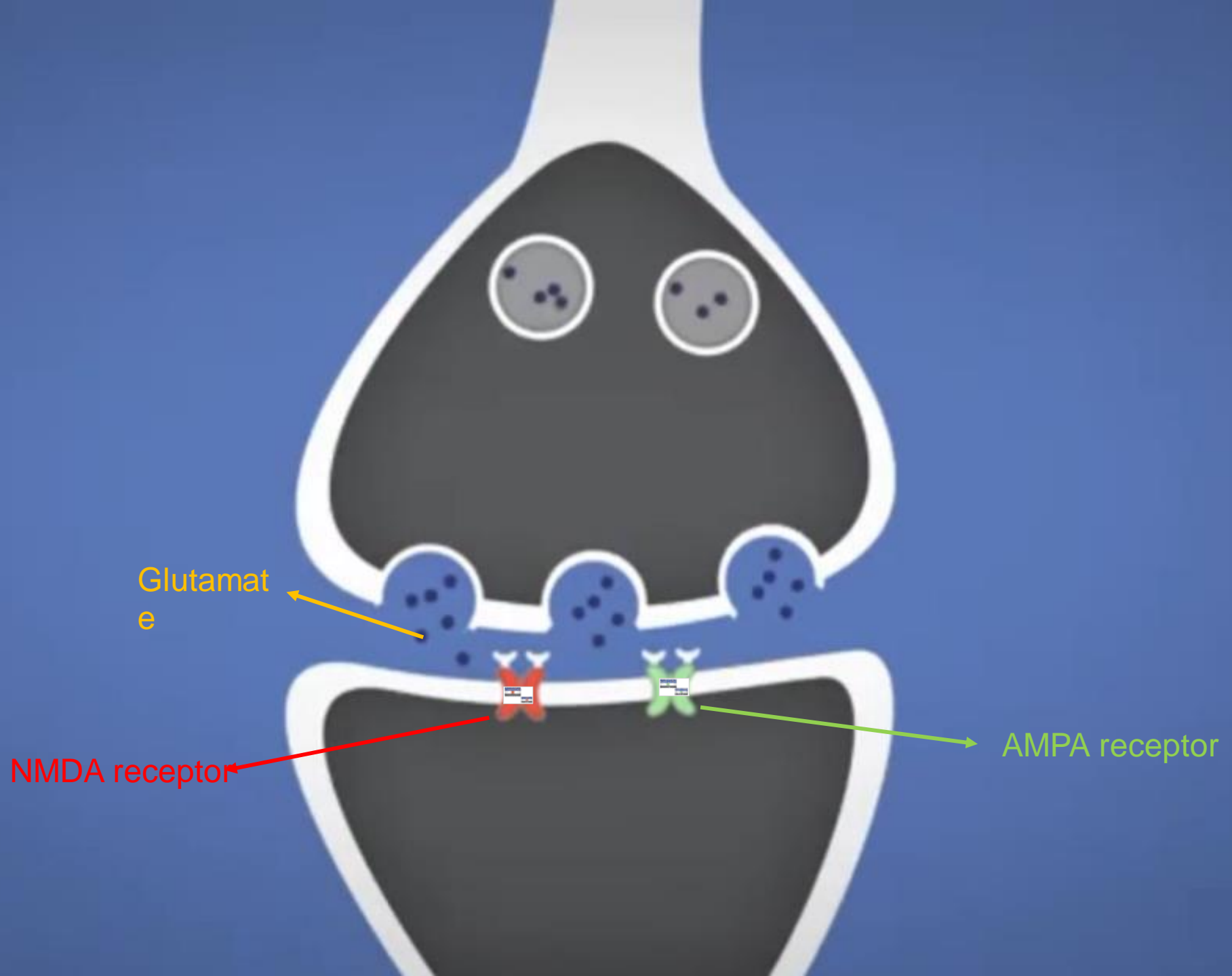


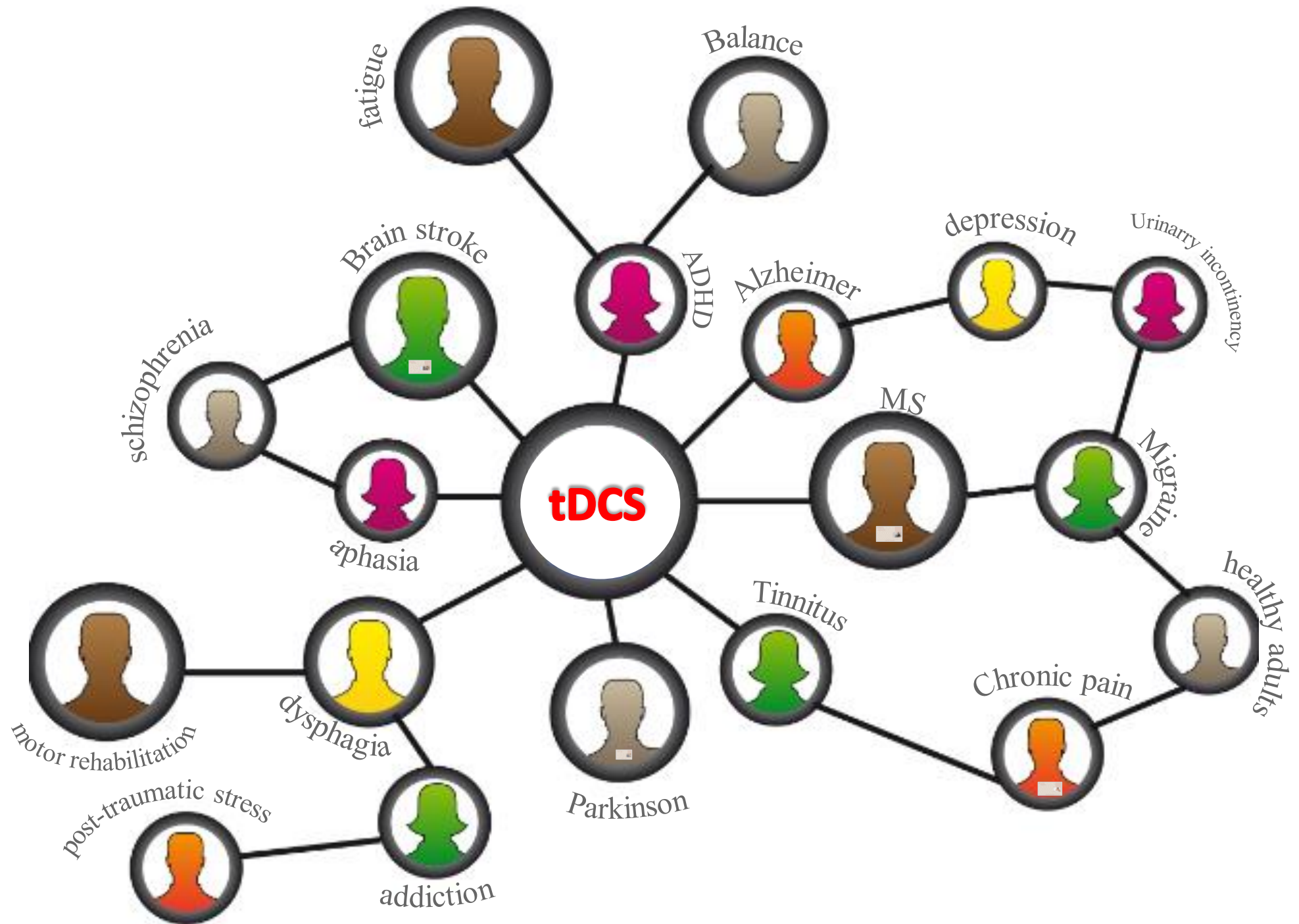


presynaptic neuron

postsynaptic neuron

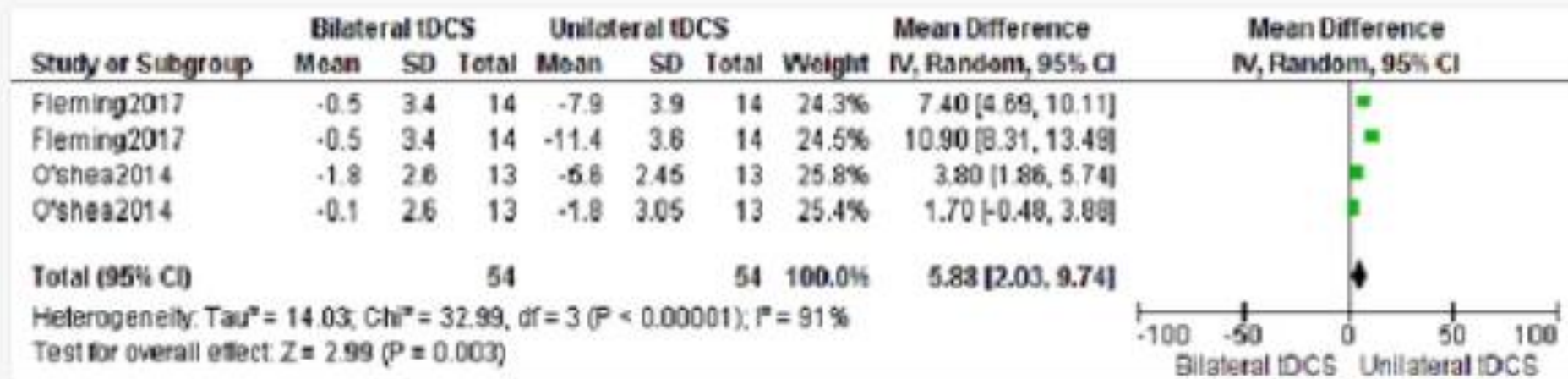
Long Term Potentiation (LTP)





tDCS effects on motor learning

- Evidence has shown more significant effects of anodal or catodal Uni-tDCS compared to Bi-tDCS on motor learning (2023)



- Neurological patients have disturbances in neural activity levels pathologically on both ipsi-lateral and contralateral sides.
- Accordingly, some studies have shown that if the excitability of the contra-lateral M1 region was reduced by using cathodal tDCS or rTMS (<1hz), the motor performance improved on the affected side and balance the additional inhibitory effects from the contra-lesional to affect hemisphere by decreasing the activity of contra-lesional hemisphere.
- On the other hand, anodal tDCS or rTMS (>1hz) can increase the excitability of affected area and enhance the performance of the cortico-spinal pathways

Finally using these techniques: inducing balance of intra-cortical and improve motor function

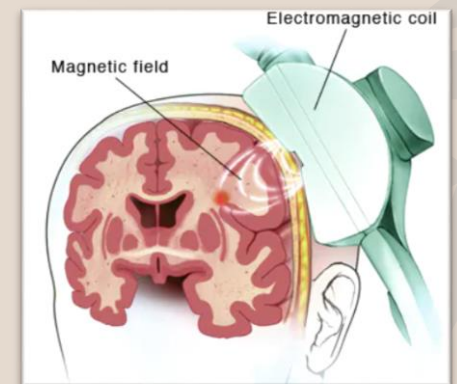
- In the other systematic meta-analysis study (2023):
- neither a-tDCS nor c-tDCS and rTMS had efficacy on backward balance perturbation and gait initiation tasks **during one session** stimulation in patients.
- It seems that **a single session of tDCS or rTMS cannot induce balance and gait performance and then, the application of tDCS should be multi-session along with postural training.**
- The results of this systematic review study have shown **the efficacy of both a-tDCS over affected M1 and c-tDCS over unaffected M1 on the improvement of posture and balance in patients with postural disorders**, however, there were **no differences between a-tDCS over affected M1 and c-tDCS over unaffected M1** in these patients.

(Transcranial magnetic stimulation (TMS

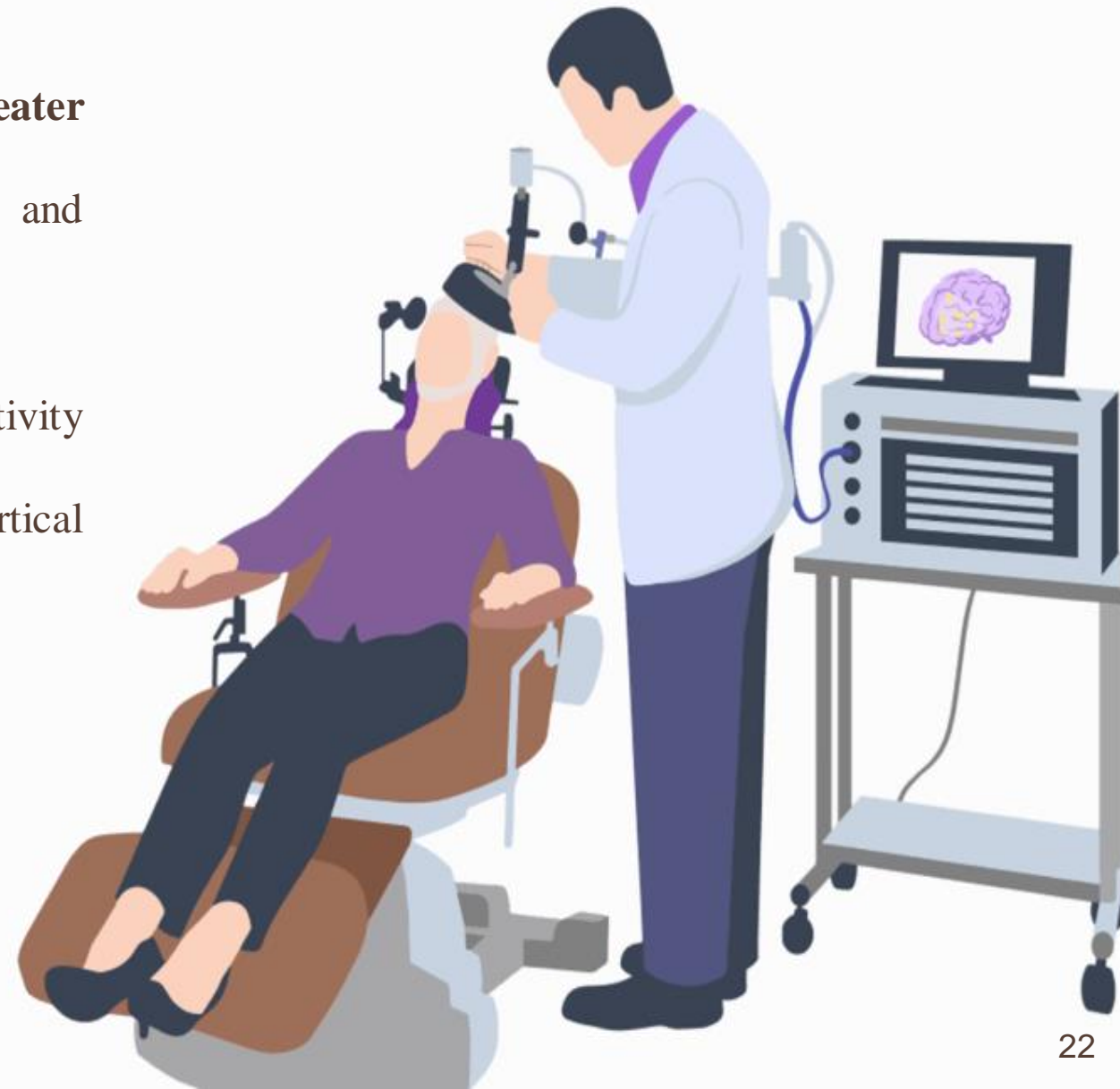
repetitive TMS (rTMS ((upto 2 tesla intensity) with WHO approving is

used to induce **changes in brain activity** that can **last** eht dnoyeb

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- The current **intensity** induced by TMS is **much greater** comparing **tDCS** and is designed to activate axons and **directly initiate action potentials in brain circuits**.
- It produces a highly synchronized bout of neural activity followed by a long period of GABA-mediated intracortical inhibition.



Literature review about TMS on stroke:

- 32 meta-analyses published until July 2019 were focus on the effects on **motor function, manual dexterity, walking and balance, spasticity, dysphagia, aphasia, unilateral neglect, depression, and cognitive function.**
- Overall, both HF-rTMS and LF-rTMS have been shown to be well-tolerated.
- The positive effect of rTMS in the motor and cognitive rehabilitation of all clinical manifestations of patients





Clinical implication

Using neuromodulators during motor and cognitive rehabilitation of the neurological patients for improving the efficacy of intervention

Thank you

