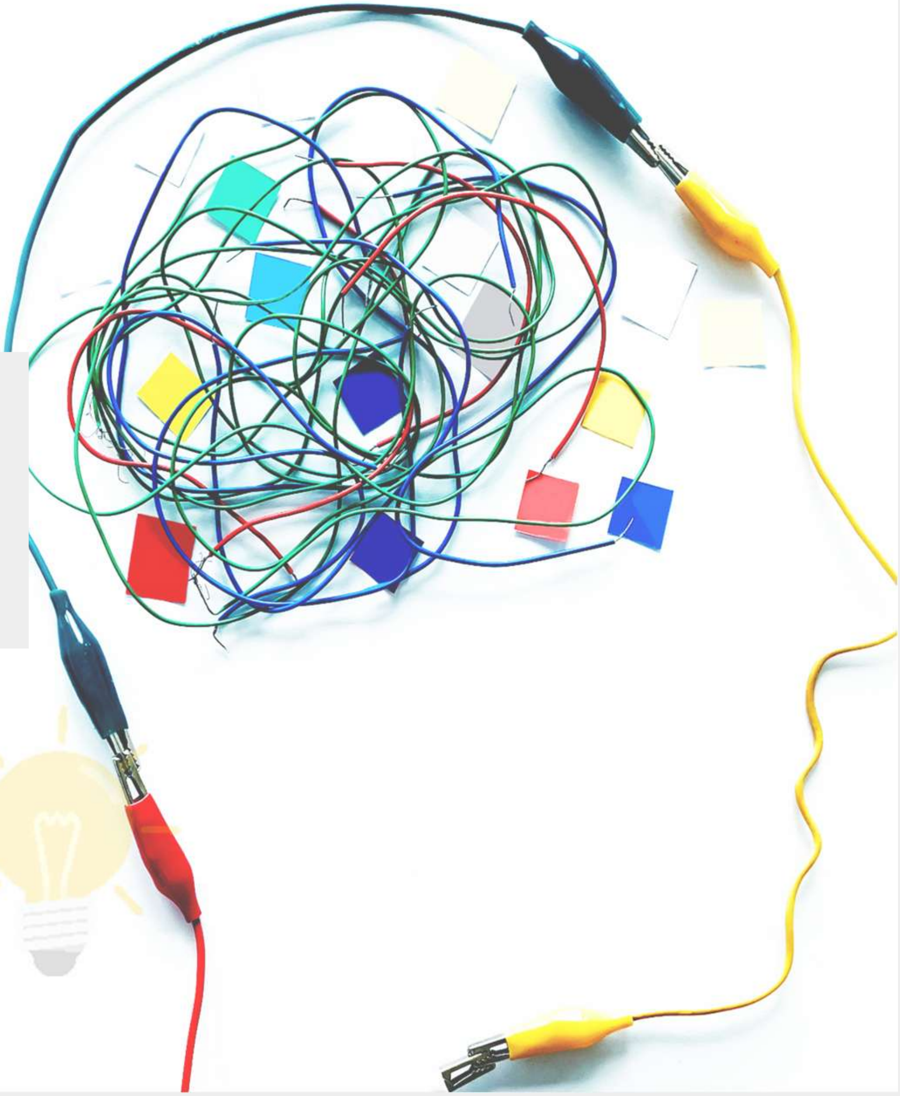
Basics of tDCS

An electrochemical organ

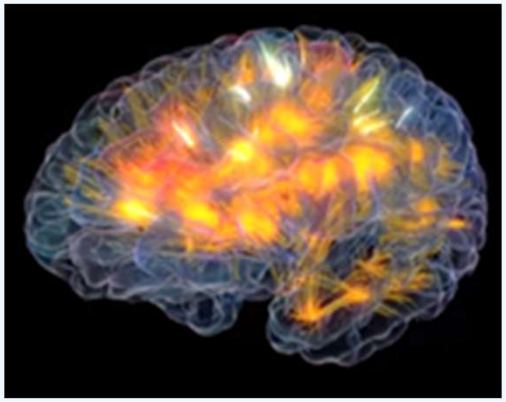
The brain functions as both a chemical and electrical organ, with intricate processes involving neurotransmitters and electrical impulses working together to facilitate various functions such as thinking, feeling, and controlling bodily functions.

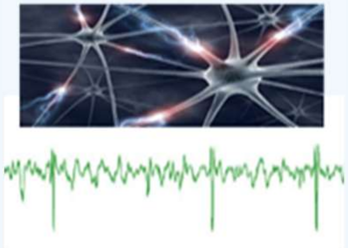


Chemical Function:
In Major Depressive Disorder, there are often imbalances in neurotransmitters like serotonin, dopamine, and norepinephrine, which are crucial for regulating mood. Conventional antidepressant medications work by altering the levels of these neurotransmitters in the brain. However, for some individuals, these medications may not be effective. Brain stimulation techniques, such as transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), and electroconvulsive therapy (ECT), offer alternative approaches to introducing electrical fields to the targeted brain areas, but eventually, through modulating the neuronal excitability, they all alter the brain neurotransmitter levels.

Electrical Function:
Both tDCS and ECT involve the application of electrical currents to the brain to modulate neural activity. In tDCS, a low-intensity electrical current is delivered through electrodes placed on the scalp. This current penetrates the skull and modulates the resting membrane potential of neurons, thereby influencing their firing rates and activity patterns. While the precise mechanisms of action are still being studied, tDCS is thought to induce changes in synaptic plasticity and neurotransmitter release, leading to therapeutic effects in conditions like MDD.

REDUCING THE BRAIN INTO A CONCEPT OF A 'CHEMICAL BRAIN' LIMITS THE UNDERSTANDING ON THE BRAIN DISORDERS AND TREATMENTS





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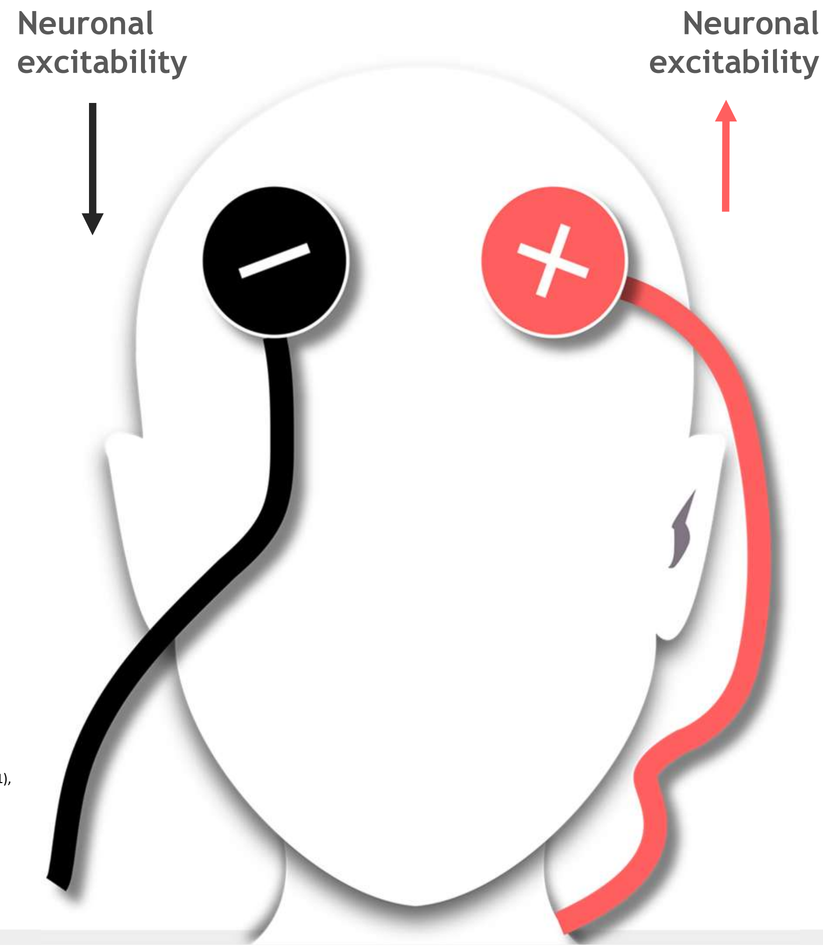
How tDCS works

Depression causes both functional and structural abnormalities in patients with depression.

Functional imaging has shown changes in brain function in the dorsolateral and ventromedial prefrontal cortex[1], as well as in deeper brain structures such as Amygdala[2] and Hippocampus[3]. Imbalance in brain activity between the left and the right prefrontal cortical areas has been linked to depression symptoms[4].

tDCS treatment targets the dorsolateral prefrontal cortex (DLPFC), where the stimulation influences the ongoing neural activity[5] and normalizes the interhemispheric imbalance caused by depression[6].

The stimulation sessions are repeated daily for long-term changes in the brain through induction of neuroplasticity[5].



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Examples of the scientific evidence

Biological Psychiatry
A Journal of Psychiatric Neuroscience and Therapeutics

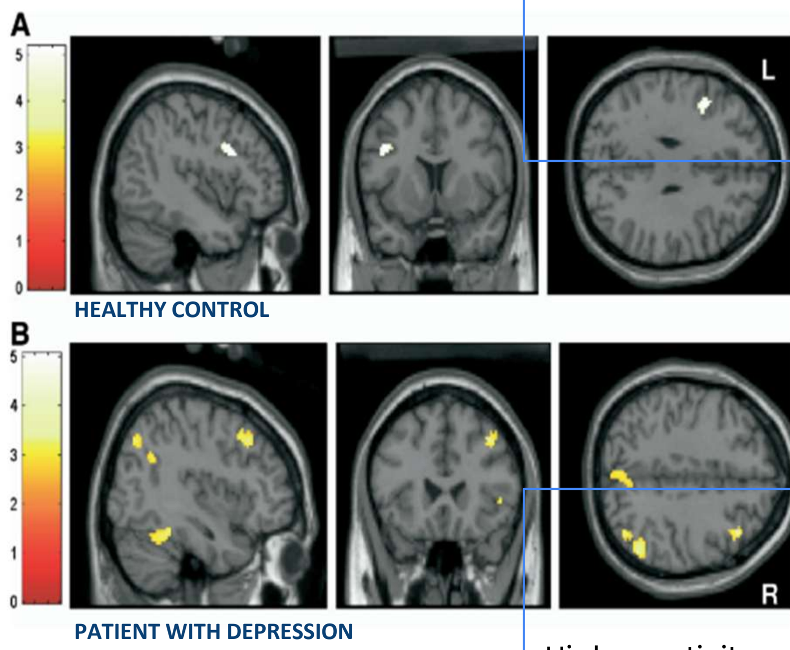
Imbalance between Left and Right Dorsolateral Prefrontal Cortex in Major Depression Is Linked to Negative Emotional Judgment: An fMRI Study in Severe Major Depressive Disorder

Simone Grimm • Johannes Beck • Daniel Schuepbach • Daniel Hell • Peter Boesiger • Felix Bermpohl • Ludwig Niehaus • Heinz Boeker • Georg Northoff • Show less

ORIGINAL ARTICLE | VOLUME 63, ISSUE 4, P369-376, FEBRUARY 15, 2008

- Functional Magnetic Resonance Imaging measures brain activity by detecting changes in blood oxygenation
  - more neuronal activity consumes more oxygen
  - deoxygenated hemoglobin (dHb) is more magnetic than oxygenated hemoglobin (Hb)

- In patients with major depression, the left dorsolateral prefrontal cortex (DLPFC) was found to have reduced activity, whereas the right DLPFC had elevated activity

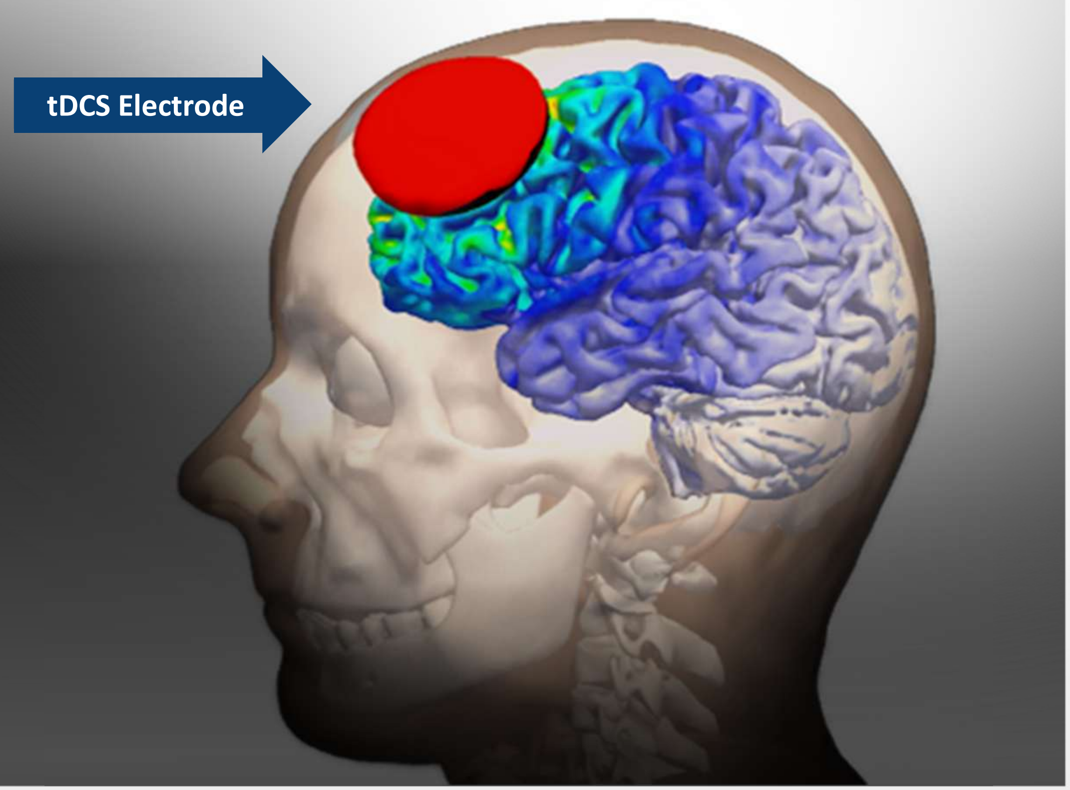


How tDCS works

In this image, the tDCS electrode is shown placed on the scalp, directly above the left DLPFC. The red area indicates the position of the electrode, which is crucial for targeting the desired neural pathways.

Beneath the electrode, the highlighted yellow represents the most intensive effect (near the electrode) and the dark blue/gray being low intensity (further away from the electrode).

The tDCS device sends a gentle, steady current through the electrode, penetrating the skull and affecting the brain's cortical neurons. This targeted stimulation can enhance neural activity to relieve depressive symptoms.

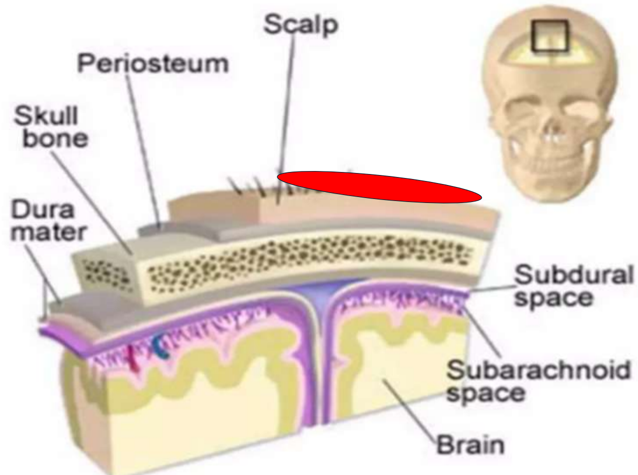


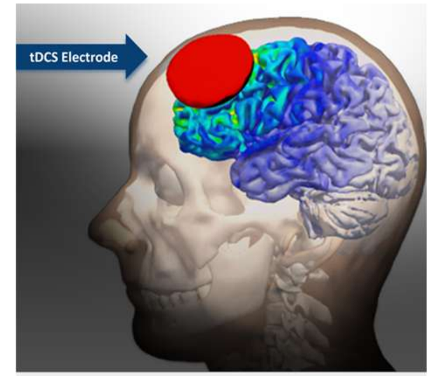
Courtesy of Ilkka Laakso / Aalto University

Examples of the scientific evidence

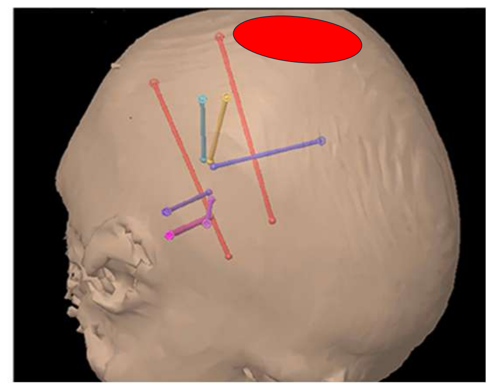
tDCS current reaching the brain affects neuronal activity

- Scalp, skull and brain tissue conduct electricity to allow a significant amount of the current applied via a scalp electrode to reach the brain
  - Appr. 45% of the current reaches the brain, based on mathematical modelling, head models, and recordings in monkeys and humans (Rush and Driscoll, 1968; Guidetti et al 2022)





- Effective electric fields are measured inside live human brain when electric current is applied on scalp (Dymond et al., 1975, Biol Psych; Chhatbar et al 2018,Brain Stim):
  - recording electrodes deep in the brain of patients with temporal lobe epilepsy (diagnostic procedure) or movement disorder patients with DBS electrodes
  - The measured electric fields are linearly related to the applied current (between **6,4 – 24,5 mV/cm** for 0,1 – 2 mA)
  - **10 mV/cm electric fields have been found to modify spontaneous neuronal firing patterns**, whereas 200 mV/cm will fire a silent neuron (Terzuolo and Bullock, 1956)



Guidetti et al. Electric Fields Induced in the Brain by Transcranial Electric Stimulation: A Review of In Vivo Recordings. Biomedicines. 2022 Sep 20;10(10):2333.
Rush S, Driscoll DA. Current distribution in the brain from surface electrodes. Anesth Analg. 1968 Nov-Dec;47(6):717-23. PMID: 4972743.
Dymond et al. Intracerebral current levels in man during electrosleep therapy. Biol Psychiatry. 1975 Feb;10(1):101-4. PMID: 1120172.
Chhatbar et al. Evidence of transcranial direct current stimulation-generated electric fields at subthalamic level in human brain in vivo. Brain Stimul. 2018 Jul-Aug;11(4):727-733
Terzuolo CA, Bullock TH. Measurement Of Imposed Voltage Gradient Adequate To Modulate Neuronal Firing. Proc Natl Acad Sci U S A. 1956 Sep;42(9):687-94.

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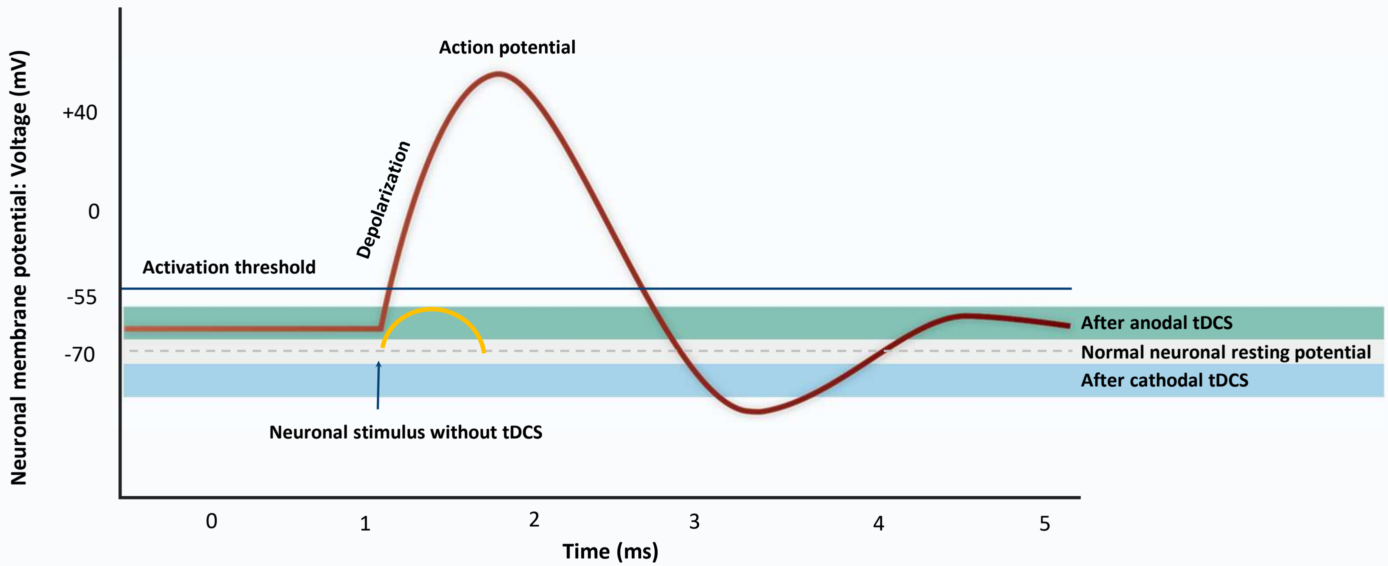
tDCS Mechanism of action: Influencing Neurons

Deeper learning: This slide is offered for those that want to explore the science behind tDCS in greater detail.

Transcranial direct current stimulation (tDCS) exerts its initial effects on the brain primarily by modulating the polarization of the neuronal membrane potential. Specifically, tDCS influences the likelihood of a neuron firing an action potential.



Under the anodal (positive) electrode, the membrane potential depolarizes, moving closer to the threshold for activation. This can be conceptualized as the neuron becoming more excitable and ready to receive and transmit signals.

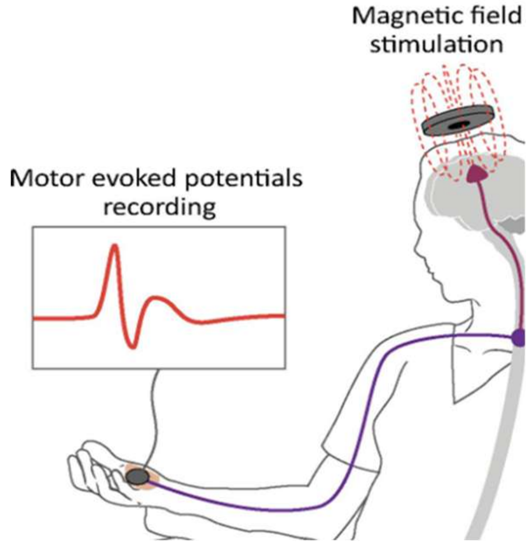
As a result, synaptic inputs that previously would not have triggered neuronal activation may now do so following anodal tDCS.

Conversely, under the cathodal (negative) electrode, hyperpolarization occurs, making neurons less likely to fire.

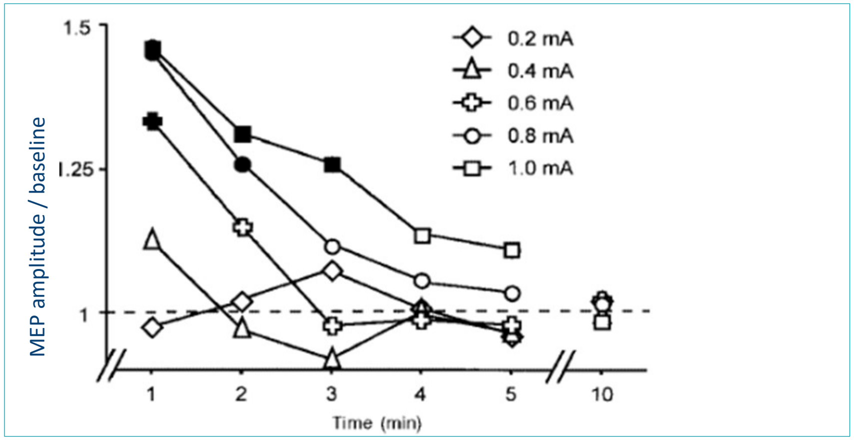
While this is a brief explanation, it provides a foundational understanding of how tDCS modulates neuronal activity and affects brain function.

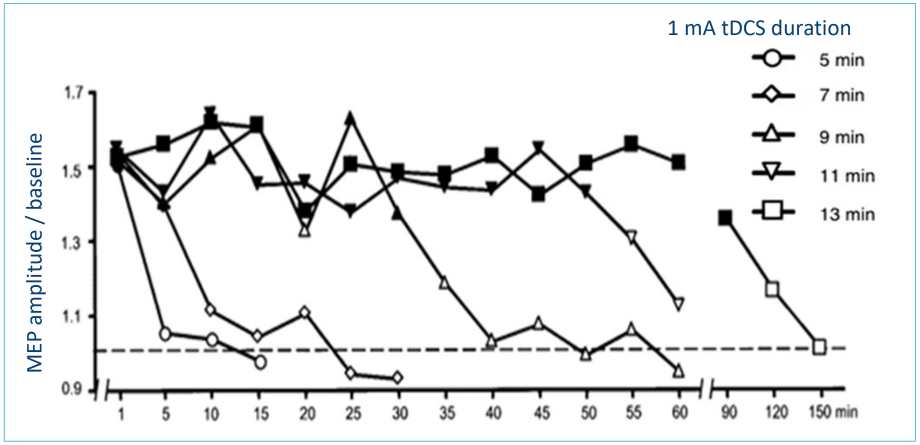
Examples of the scientific evidence

tDCS shifts cortical excitability depending on the dose and direction of polarization



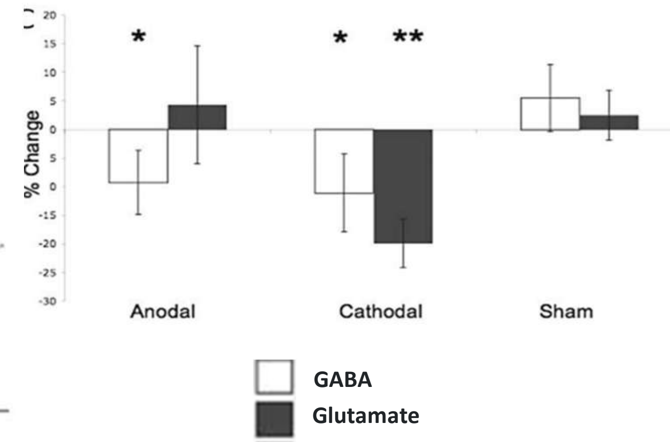
- tDCS over motor cortex changes cortical excitability (studied with MEPs in Nitsche and Paulus, 2000; Nitsche and Paulus, 2001)
  - anodal increases excitability and cathodal decreases it
  - duration of after-effects is dependent on tDCS dose (current level and duration)





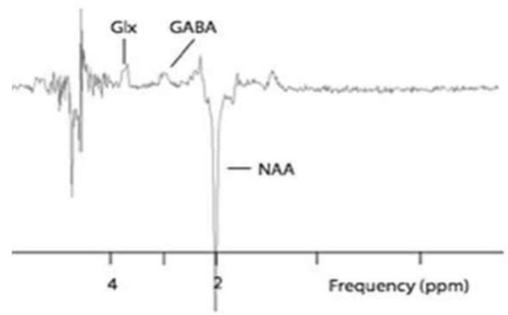
Examples of the scientific evidence

Modulation of neuronal excitability is mirrored in changes in neurotransmitter levels

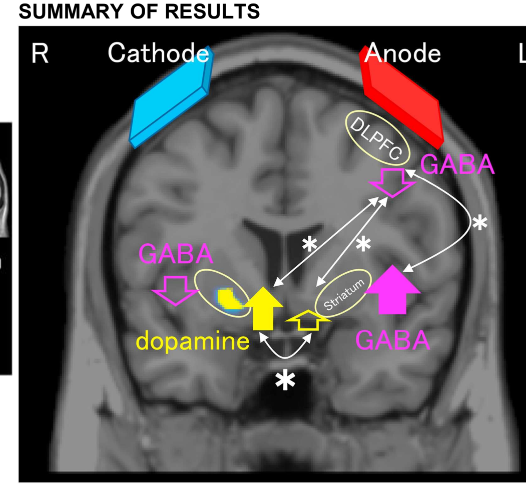


GABA and glutamate

Stagg et al. (2009) and Bunai et al (2021) used magnetic resonance spectroscopy (MRS) and demonstrated polarity-specific changes in GABA and glutamate levels in the stimulated cortical area after tDCS.
(1 mA current, left M1 and right SO)



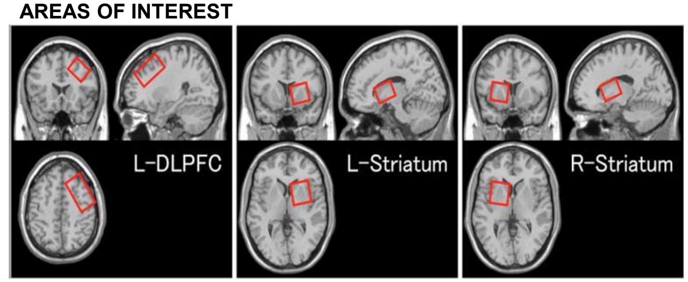
SUMMARY OF RESULTS



Dopamine (and GABA)

Fonteneau et al (2018), Fukai et al (2019), Bunai et al. (2021) used positron emission tomography (PET) imaging and demonstrated that anodal tDCS to the left DLPFC leads to dopamine release in the striatal areas.
(2 mA current, bilateral DLPFC montage)

AREAS OF INTEREST



Stagg et al. 2009. Polarity-sensitive modulation of cortical neurotransmitters by transcranial stimulation. J Neurosci. 2009 Apr 22;29(16):5202-6

Bunai et al. 2021. tDCS-induced modulation of GABA concentration and dopamine release in the human brain: A combination study of magnetic resonance spectroscopy and positron emission tomography. Brain Stimul. 2021 Jan-Feb;14(1):154-160

Fonteneau et al. 2018. Frontal Transcranial Direct Current Stimulation Induces Dopamine Release in the Ventral Striatum in Human, Cerebral Cortex, Vol 28, Issue 7, July 2018, Pages 2636–2646

Fukai et al. 2019. Nature. Translational Psychiatry volume 9, Article number: 115 (2019).

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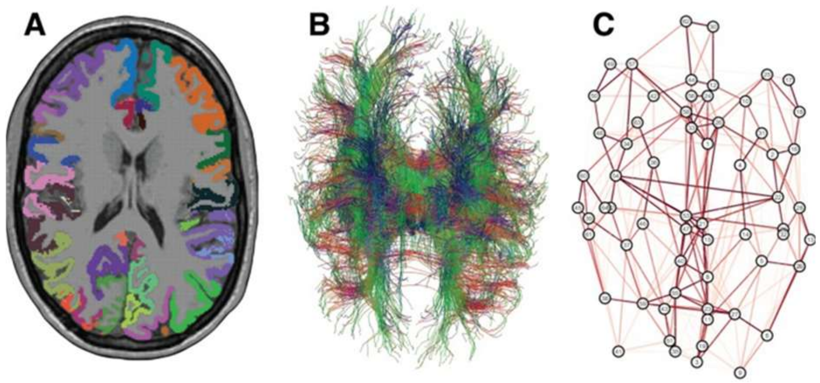
tDCS Mechanism of action: Influencing Neuronal Networks

Deeper learning: This slide is offered for those that want to explore the science behind tDCS in greater detail.

- The brain consists of extensive neuronal network of interconnections that enable information processing[1]
    - This network connectivity is plastic i.e. can change and allows learning and adaptive behavior
- Modern brain imaging used to examine brain connectivity has shown tDCS to lead to changes in[2,3]
    - Structural connectivity (axon bundles which embody connectivity) and
    - Functional connectivity (time courses of neural activity in spatially remote regions and patterns of influence by some neural systems over others)



A) Map of brain areas
B) Tractography (axon bundles)
C) Graph representing the pattern of connections between regions

Clayden 2013

Key takeaway: This, along with the previous slide, demonstrates how tDCS influences both immediate and long-term changes in brain function.

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3. Antonenko, D., Fromm, A. E., Thams, F., Grittner, U., Meinzer, M., & Flöel, A. (2023). Microstructural and functional plasticity following repeated brain stimulation during cognitive training in older adults. Nature Communications, 14(1), 1-13. https://doi.org/10.1038/s41467-023-38910-x

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Effect of tDCS explained in short

tDCS electrical current travels from the electrodes to the brain, creating electric fields in targeted areas. These electric fields are strong enough to modulate the polarization of neuronal membranes, leading to changes in neuronal excitability.

When tDCS is repeated daily for a sufficient period of time, long-term changes in the neurons and networks start to take place. This process is called neuroplasticity, and these similar mechanisms are involved in the learning and memory functions of the brain.

Eventually, tDCS treatment leads to changes in neuronal network connections and activity, relieving depression symptoms.

Treatment response builds over time

How does brain stimulation reduce chronic pain?

Acute pain sensation is very important for our survival

- Get away from the cause! Don't do it again!
  – fear-learning is most effective type of learning (not always most meaningful)

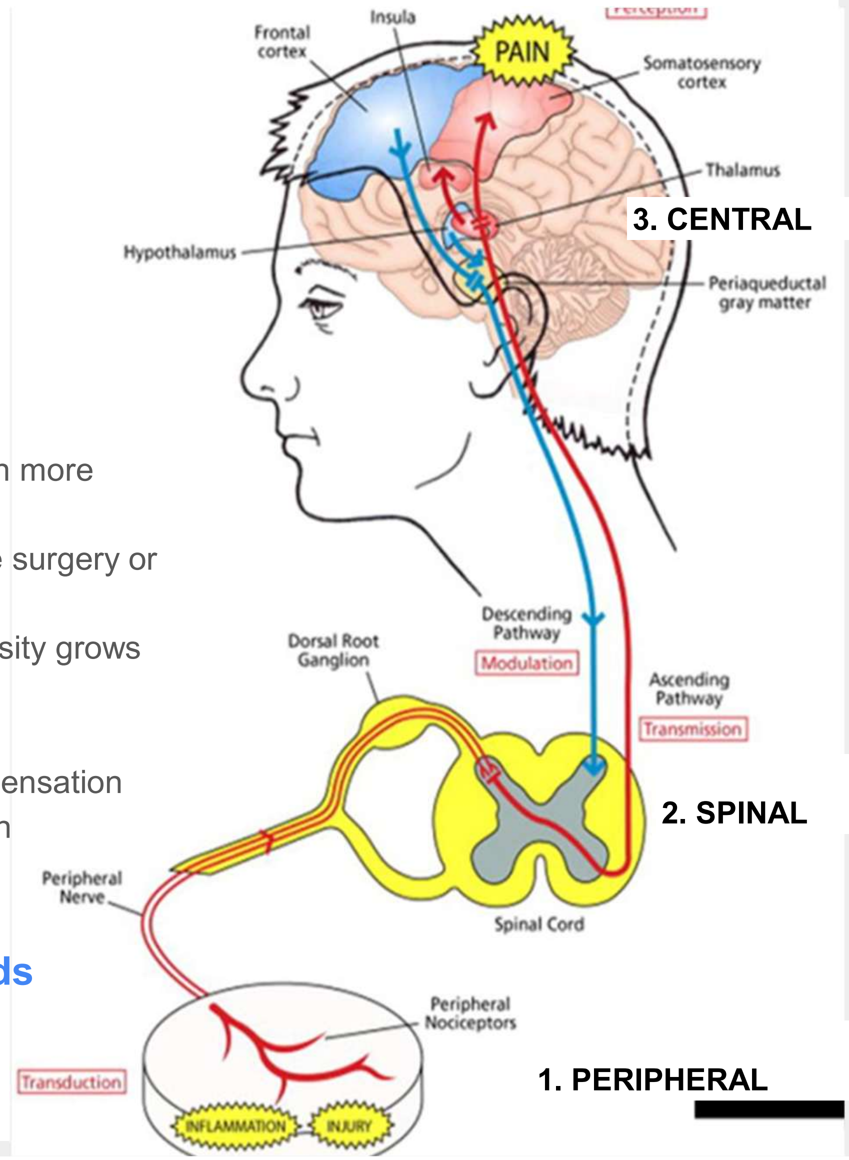
In chronic pain, learning becomes maladaptive

- When the brain is repeatedly/ constantly reminded of pain it learns to report pain more easily and strongly
- for ex. degenerative diseases (like arthritis) or during healing from an injury (like surgery or a fracture) where there is prolonged signaling of pain.
- The initial cause doesn't get worse (could even have healed), but the pain intensity grows because the nervous system has reorganized itself

Mood, previous experiences, thoughts, and surrounding situation affect the pain sensation

- just before pain arrives at consciousness, the brain processes pain information simultaneously in various regions

tDCS promotes re-programming of the pain processing towards normal – alleviates the central sensitization of pain



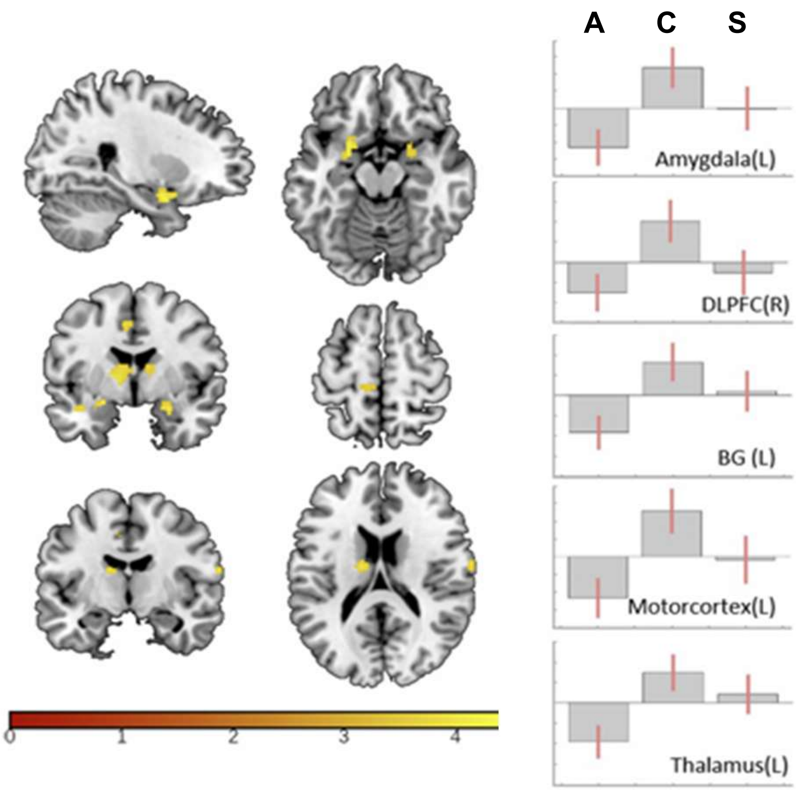
Examples of the scientific evidence

RESEARCH ARTICLE **Open Access**

Polarity-specific modulation of pain processing by transcranial direct current stimulation – a blinded longitudinal fMRI study

Steffen Naegel[1*], Josephine Biermann[1], Nina Theysohn[2], Christoph Kleinschnitz[1], Hans-Christoph Diener[1], Zaza Katsarava[1,3,5,6], Mark Obermann[1,4] and Dagny Holle[1]

- Pain stimulation (healthy subjects) showed a distinct activation pattern within well-established brain regions associated with pain processing (fMRI).
  - Stimulated trigeminal pain (Nociceptive stimuli applied to the right forehead)
- tDCS anode on the left primary motor cortex (M1), cathode over the contralateral supraorbital region, for 20 min with an intensity of 1,5 mA
- Following tDCS activation in the thalamus, basal ganglia, amygdala, cingulate, precentral, postcentral, and dorsolateral prefrontal cortex, were changed (polarity dependently)
- This study demonstrates modulation of cerebral pain processing
  - anodal tDCS activates the central pain-network



Naegel S, et al. Polarity-specific modulation of pain processing by transcranial direct current stimulation - a blinded longitudinal fMRI study. J Headache Pain. 2018 Oct 24;19(1):99.

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Thank you for your attention!

Have a great week ahead!