

## Millions' lives are shaped by unbearable chronic pain

Today, up to **75% of patients** that seek help are left **without effective relief**.

- Painkillers often provide only weak or shortterm relief and require constant dose increase.
- Opioids are addictive
- Access to invasive therapies is scarce
- Physiotherapy is limited in availability and in efficacy

Chronic pain costs **300B€ annually in the EU**, primarily due to disabilities and lost productivity.



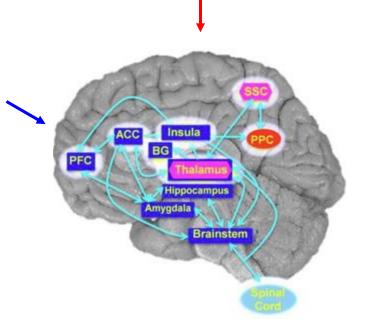


# Treatment options today are mechanistically limited - they are all indirect methods

- Chronic pain is a problem of the brain, for which painkillers, physiotherapy or nerve stimulation have only indirect impact.
- Underlying chronic pain are unwanted function brain mechanisms related to memory and learning (maladaptive neuroplasticity.
  - Pain sensation and preparation for pain signal (catastrophizing) is 'over-learned' -> sensitization of the pain network

#### Sooma Pain Therapy treats chronic pain directly at its source.

- The treatment is targeted to pain networks to normalize natural pain signal processing: Increased control of the pain signal, reduced pain signalling, unlearning the hypersensitivity.
  - Treatment current creates neuroplasticity in the brain and with repeated applications enables functional changes in the pain processing networks.





## Mechanisms of transcranial direct current stimulation (tDCS) for pain in patients with fibromyalgia syndrome (FMS).

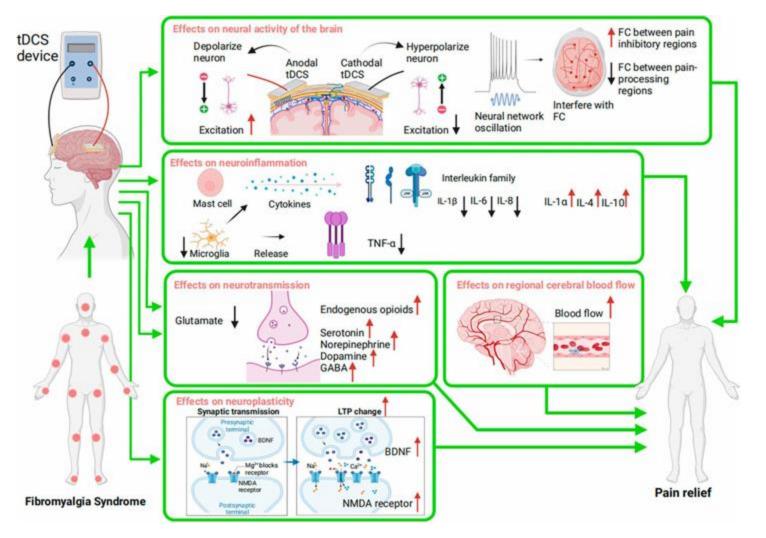
Multiple systems may be involved in how tDCS reduces FMS pain. Possible mechanisms:

- Promotion of cortical excitability
- Effects on neuroinflammation, neurotransmission, regional cerebral blood flow
- Neuroplasticity.

Overall, we found that tDCS may reduce FMS pain by altering neuronal activity, regulating neuroinflammation and neurotransmission, accelerating rCBF, and inducing neuroplasticity.

Wang, S., Du, S.-H., Wang, X.-Q., & Lu, J.-Y. (2024). Mechanisms of transcranial direct current stimulation (tDCS) for pain in patients with fibromyalgia syndrome. Frontiers in Molecular Neuroscience, 17. https://doi.org/10.3389/fnmol.20241269636 doi.org





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### 1. Promotion of cortical excitability

An abnormal mix of enhanced and reduced Functional Connectivity (FC)
patterns across the pain matrix was found in individuals with FMS (Cifre et
al., 2012), indicating the neural networks involved in pain perception and
processing are functioning abnormally.

 In all, tDCS may relieve FMS pain by modulating cortical excitability, FC, and neural oscillations.



#### 2. Effects on neuroinflammation

- Neuroinflammation refers to inflammatory processes within the central nervous system that are known to exacerbate pain sensations in FMS (Mendieta et al., 2016). An imbalance between pro- and anti-inflammatory cytokines in cerebrospinal fluid (CSF) is common in FMS.
- Transcranial direct current stimulation may reduce FMS pain by modulating neuroinflammation, possibly achieved by stimulating brain immune cells, such as MCs and glial cells, to regulate pro-inflammatory cytokines release.
- These findings suggest tDCS may relieve FMS pain by modulating neuroinflammation through balancing pro- and anti-inflammatory cytokines.



#### 3. Effects on neurotransmission

- Abnormal levels of neurotransmitters were found in the CSF and brain of FMS patients, such as glutamate and substanceP, serotonin (5-HT), noradrenaline, dopamine, and gammaaminobutyric acid (GABA) (Clauw et al., 2011). Changed neurotransmitter levels increased pro-nociceptive transmission and reduced anti-nociceptive transmission. Changed endogenous cerebral opioid activation is another anomaly in FMS (Schrepf et al., 2016).
- Transcranial direct current stimulation shows promise for reducing FMS pain by regulating neurotransmitters implicated in its complex pathophysiology. Increased levels of glutamate (excitatory) and reduced levels of GABA (inhibitory) contribute to FMS hyperalgesia (Harris, 2010; Pomares et al., 2020). Studies (Zhao et al., 2020; Lengu et al., 2021) show that tDCS can modulate cortical levels of GABA and glutamate, impacting neuronal signaling. Bifrontal tDCS (anode over left DLPFC and cathode over right DLPFC with a current of 2 mA) increased dopamine in the ventral striatum in healthy participants (Fonteneau et al., 2018).



## 4. Effects on regional cerebral blood flow (rCBF)

- People with FMS suffer abnormal rCBF and metabolism in pain-related regions, which may contribute to pain severity. Patients with FMS have lower CBF than controls in different brain regions, including the thalamus, caudate nucleus, pontine tegmentum, and basal ganglia (Kwiatek et al., 2000; Schmidt-Wilcke et al., 2007; Shokouhi et al., 2016).
- Jales Junior et al. (2015) found that tDCS significantly increased rCBF in basal ganglia, and this alteration correlates with reduced pain in patients with FMS. These regions are critical to pain processing. Negative rCBF and cortical hypometabolism can affect neuronal function and pain processing. These studies collectively suggest that tDCS modulates rCBF and hypometabolism, which may normalize the dysfunctional neural circuits involved in pain perception, thereby reducing the pain experienced by FMS patients.



### 5. Neuroplasticity

- Transcranial direct current stimulation may reduce FMS pain by altering the brain's pain response by inducing plasticity.
- Neuroplastic changes are associated with brain-derived neurotrophic factor (BDNF), which affects neuronal growth and synaptic connectivity. Research indicates that the BDNF levels in participants with FMS were lower than those in healthy controls (lannuccelli et al., 2022).
- Evidence shows that tDCS can cause cerebral excitability alterations that can persist longer than the stimulation period (Farnad et al., 2021; Santos et al., 2021), offering compelling insights into its potential impact on neuroplasticity.
- Alterations in plasticity-related pathways may be accomplished by inducing long term potentiation (LTP) and upregulating BDNF or NMDARs.



## Sooma Pain Therapy Safe future of pain treatment

#### Non-invasive transcranial direct current stimulation (tDCS)

- Targeted treatment with easy-to-use head cap
- Effective therapy for chronic pain of different types and regions

Daily 20-minute pain therage



Stimulation equipment

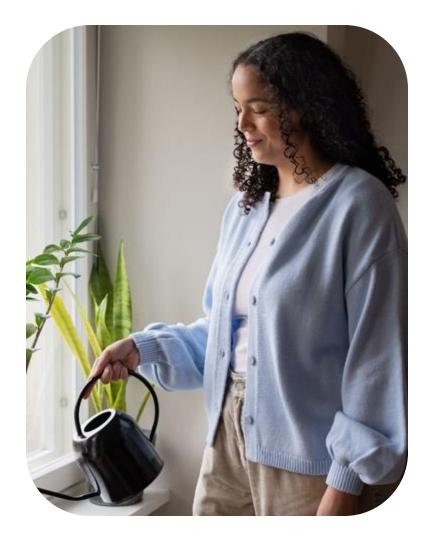


Optional mobile application



Clinician oversight, also remotely





## Starting the therapy

Patient self-administers treatments with included training material.

- 6-week therapy to evaluate benefit using a pain diary.
  - Recommended to track both morning and evening pain
- If treatment is found beneficial, continuation in 6-month periods is recommended.



## Pain types to treat

Treatment is approved and effective for:

- Chronic and neuropathic pain
  - Spinal-cord injury
  - Multiple sclerosis
  - Knee osteoarthritis
  - Phantom limb pain
- Fibromyalgia
- Treatment is also shown effective for depression, which is often a comorbidity with chronic pain.





### **Treatment benefit**

- Half of the patients get significant benefit - depending on the pain type
- The effect size is individual, but some patients find it lifechanging
- Excellent safety profile allows trying out the therapy with a low barrier to evaluate the benefit

"Pain, you wouldn't wish on your work enemy"

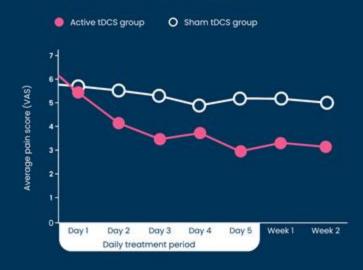


"Askolin has tried 31 different pain killers and many non-pharmaceutical treatments. She finds relief from weight-blanket, hot and cold and most recently, from tDCS."



# Treatment effect is visible quickly on a group-level

Active tDCS reduced MS neuropathic pain after 5 days of treatment and remained lower at Week 2.



Young et al., 2020

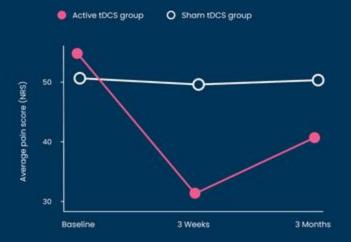


## Treatment effect is maintained for 3 months

#### Home-based active tDCS reduced fibromyalgia pain by 62% after 12 weeks



Active 3-week home-based tDCS treatment significantly reduced pain intensity in older adults with knee osteoarthritis



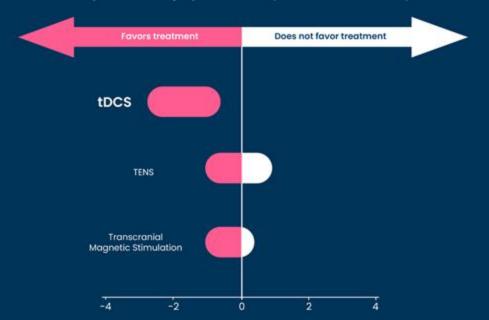
Brietzke, et al., 2020

Martorella et al., 2022



## Meta-analysis shows clear benefit

Efficacy of drug-free approaches on pain relief in patients with spinal cord injury (Meta analysis - 14 studies compared)







## Safety

- tDCS therapy is not associated with severe or long-term side effects
- Most users feel the current as tingling, which may feel slightly uncomfortable especially for patients with hypersensitive pain network
- The treatment effect is limited to head area. Combination to painkillers and other treatment is easy, and potentially beneficial.









