

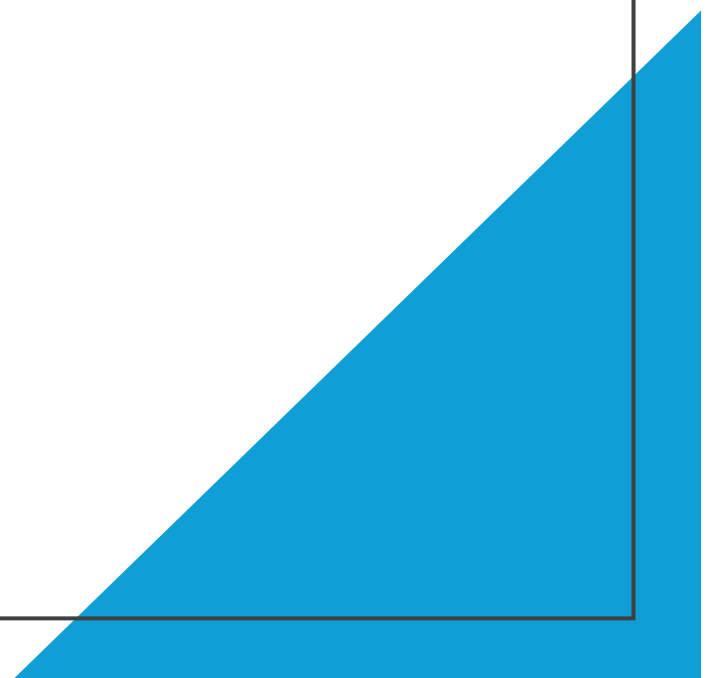
Non-invasive Neuromodulation in Pain Treatment

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Neuromodulation in Pain Medicine

- Electrical therapy in nature
- Modulating pain perception and induction by electrical stimulus
 - Curing headache with electric shocks from torpedo rays in Roman times (c. 1)
- Ranging from surgical to non-invasive technologies
 - Last-resort to option for preventive management

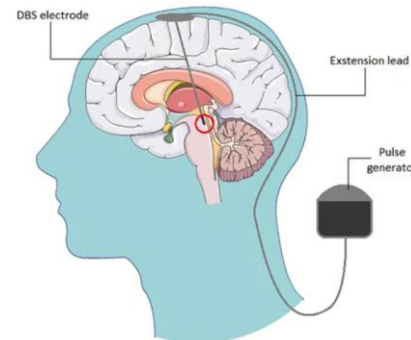
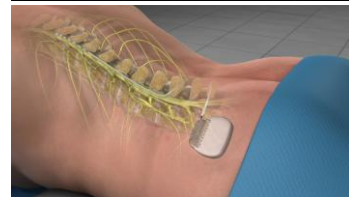




Overview of Methods

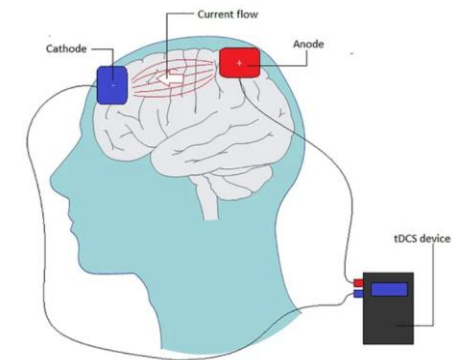
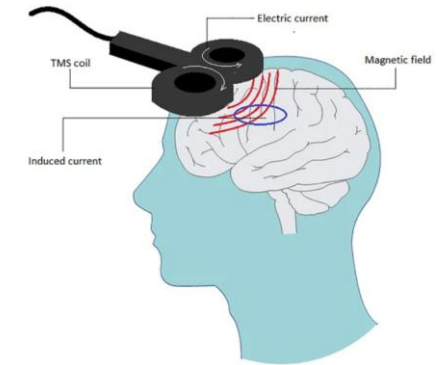
Invasive

- Motor Cortex Stimulation
- Spinal Cord Stimulation
- Deep Brain Stimulation



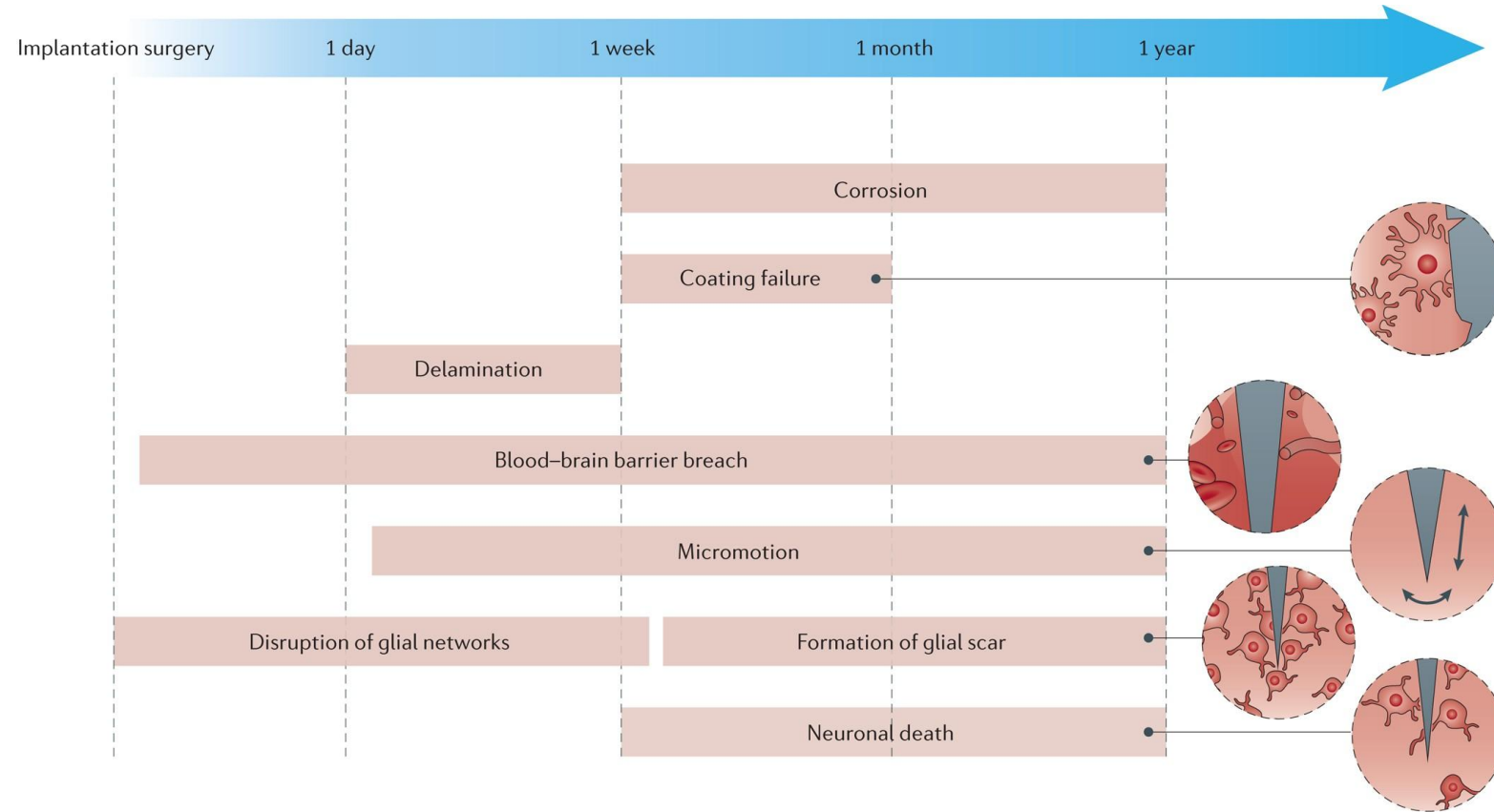
Non-invasive

- Transcranial Magnetic Stimulation (TMS)
- Transcranial Direct Current Stimulation (tDCS)





Underlying Issues with Implants



Transcranial Direct Current Stimulation (tDCS)

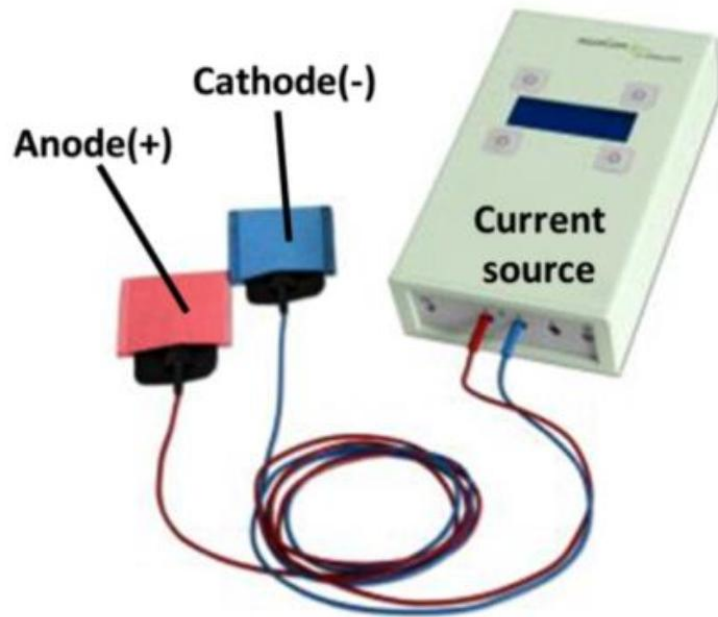


Image source:
www.neuroconn.de

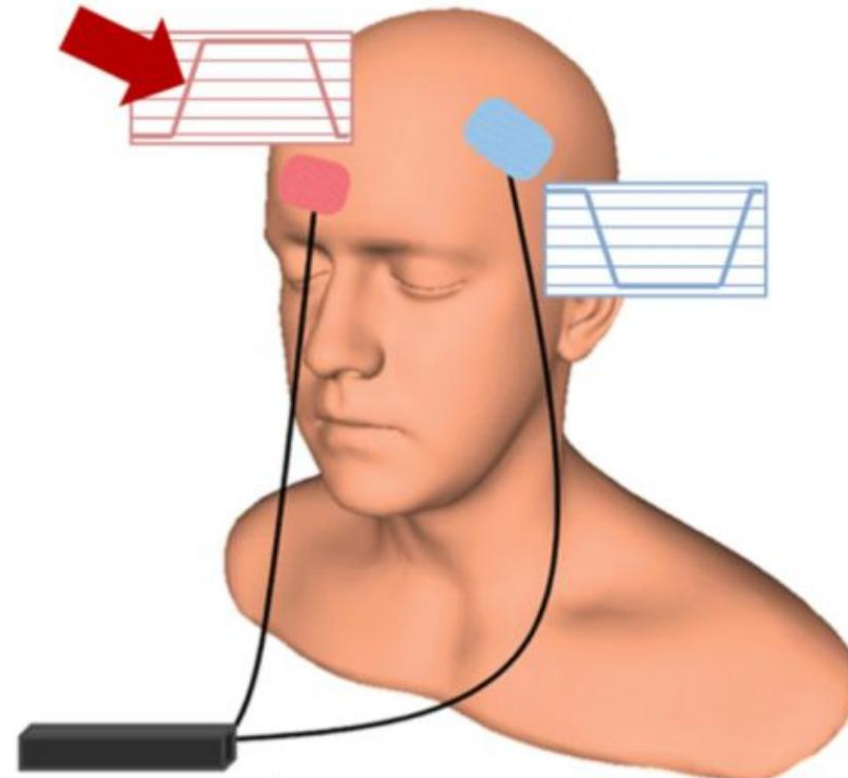
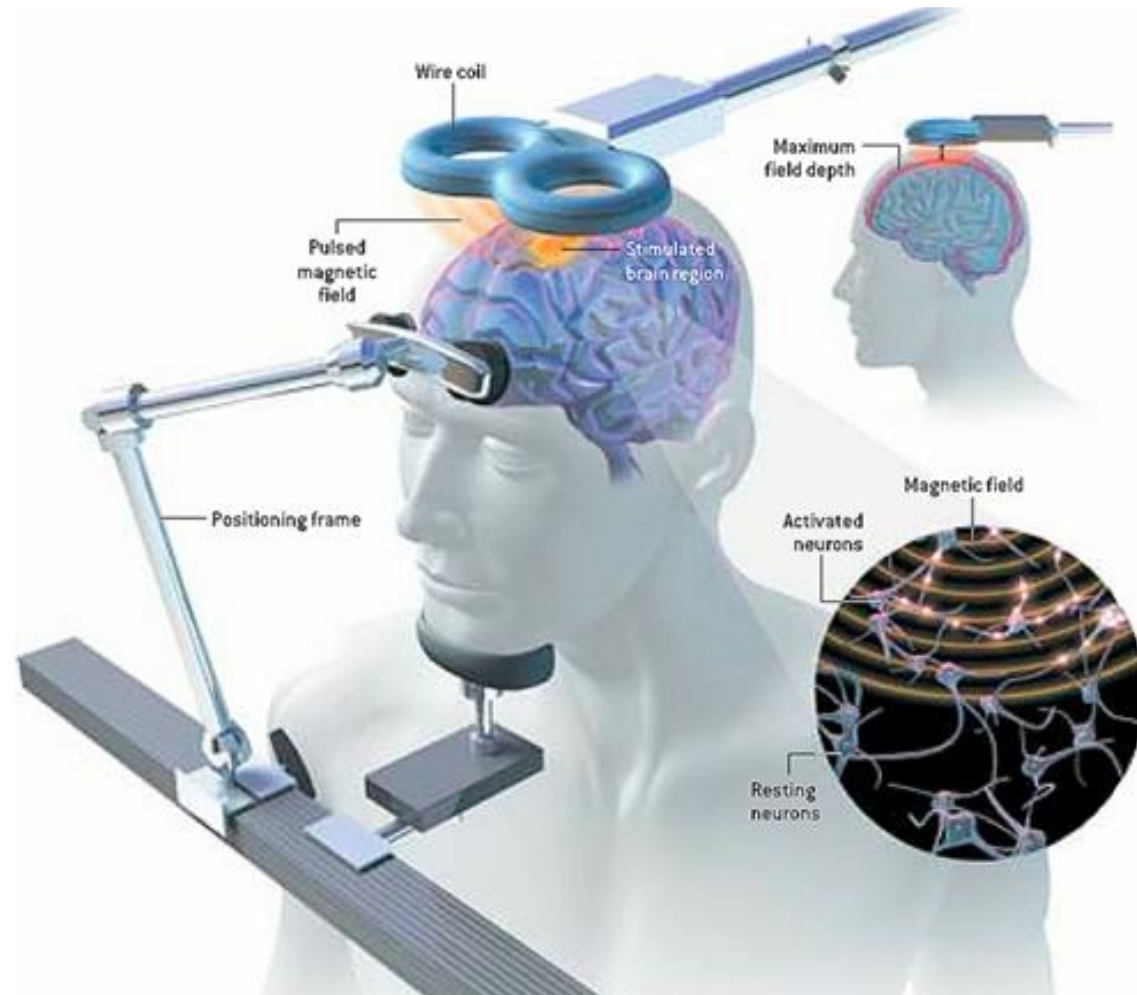


Image source:
Dayan et al., Nature Neuroscience, 2013



Transcranial Magnetic Stimulation

- Electrical stimulation induced by external coil
 - ~ 1 to 3 Tesla
- Lower clinical risks
- No upfront costs for patients
- Applicable to multiple cortical regions

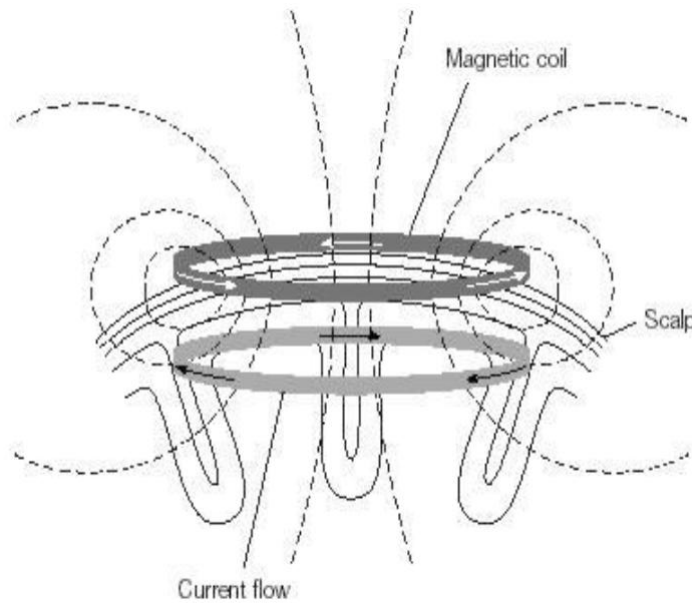




TMS vs. tDCS :

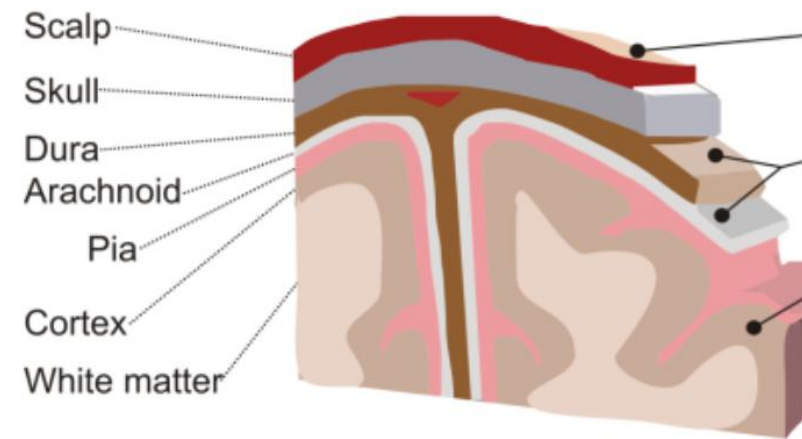
Magnetic fields:

Good penetration with little interference



Electric fields:

Susceptible to individual differences;
Everything 'on route' affects the
stimulation course and intensity



Source: A. Sack (MUMC)

- Cost and treatment environment
- Regulatory approval (FDA indications)



Levels of Evidence of TMS

A: High certainty on net benefit	<ul style="list-style-type: none">• Neuropathic Pain @ M1• Posttraumatic brain injury related headache
B: Moderate – sufficient to determine effects but confidence is constrained by various factors	<ul style="list-style-type: none">• Neuropathic Pain @ F3• Postoperative Pain @ F3• Acute Migraine• Migraine Prevention
C: Insufficient	...



Acute Pain

Acute Migraine

- Administered by *single pulse TMS* (sTMS) devices



- Intensity: ~0.9 Tesla

3 sequential pulses (early) at the onset of migraine
Wait 15 minutes
If needed, treat with additional 3 pulses
Wait 15 minutes
If needed, treat with additional 3 pulses

Prevention of Migraine

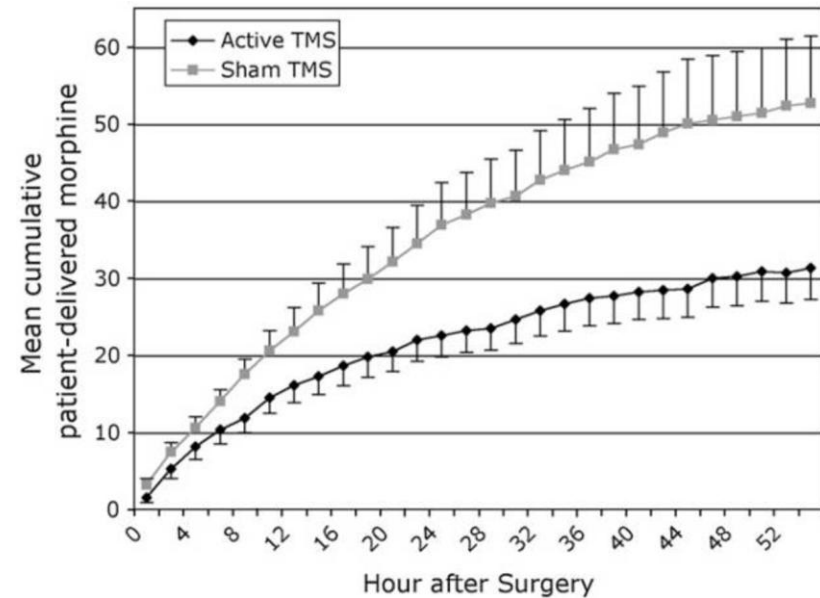
- ESPOUSE Study (2014-16)
 - n=263, open-labelled
- Reduction of 2.75 headache days per month
- 46% responder rate

Treat with 4 pulses each morning and evening
2 consecutive pulses
Wait 15 minutes
Repeat the 2 consecutive pulses

Other pain conditions

Posttraumatic brain injury related headache

- 5 sessions (no MDD)
- > 10 sessions (+MDD)
- 10 - 20 Hz
- 80-90% RMT
- left MC or left DLPFC
- left DLPFC (+MDD)
- Maintenance



Borckardt (2008)

Postoperative Pain

- 10 Hz
- Left DLPFC
- Mean 40% reduction in morphine use during hospitalization for gastric bypass surgery





TMS variables

Physical / “**Hard**” variables

- Coil type



Source: M. León Ruiz (2016)

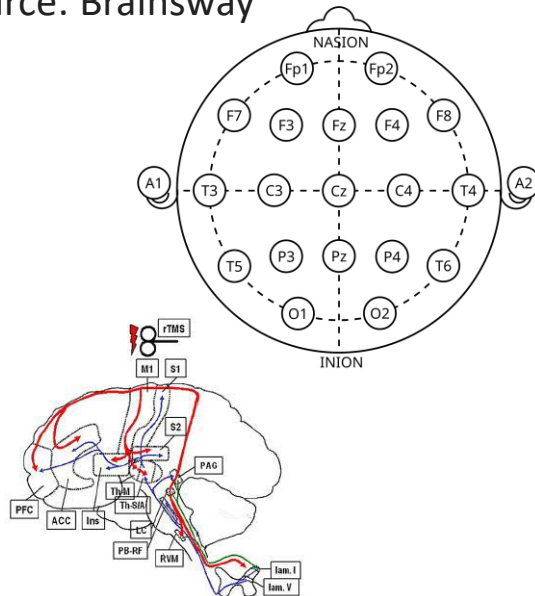


Source: Brainsway

- Target site



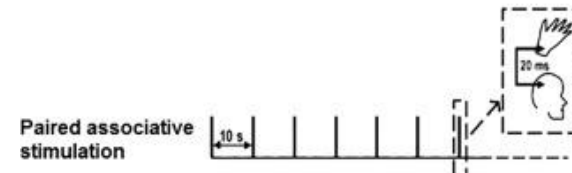
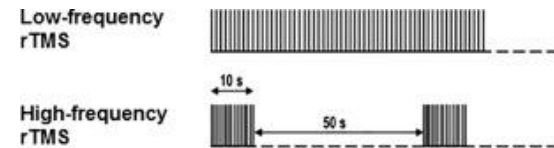
Source: Nexstim



Paradigm / “**Soft**” variables

- Frequency

- Intensity

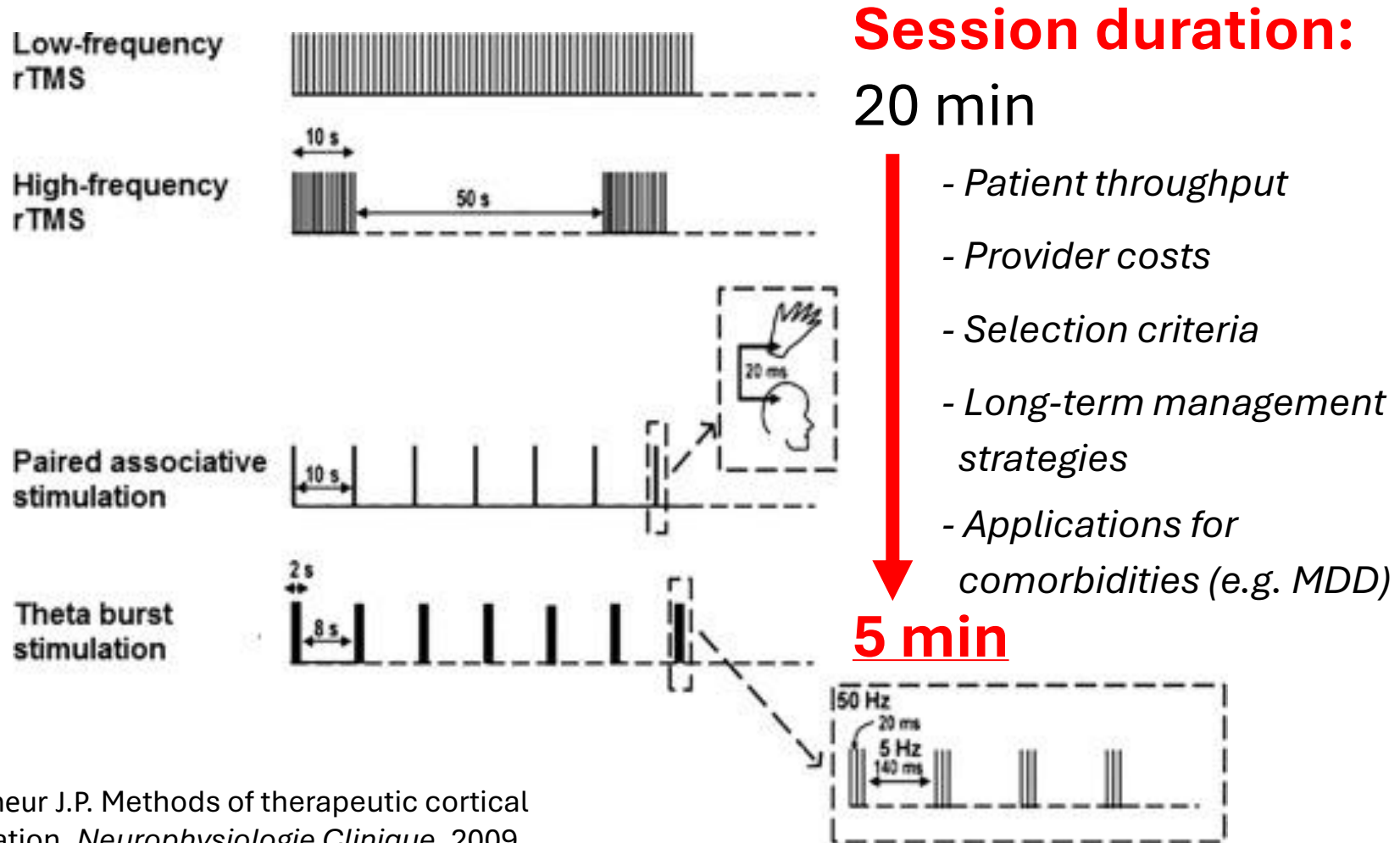


- Pattern





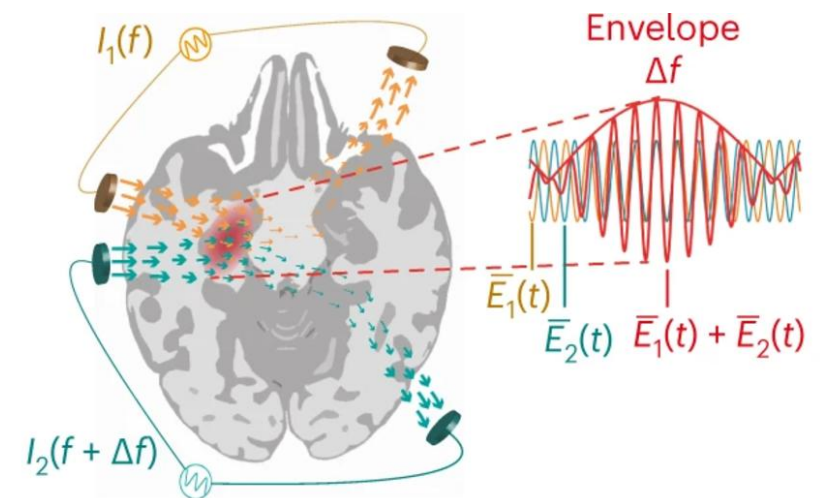
Engineering Advancement driven by Operational Needs





Engineering Advancement Supporting Treatment Discovery

- Limited by pathways to regulatory approval
 - FDA: 510(k) vs. *de novo*
- New tech tweaking **Strength-Duration** – “dosage” in neuromodulation
- Precision across depth
 - Reaching capabilities of invasive counterparts
- Maintenance therapy optimization
 - Avoid / delay relapse and re-admission
 - Shifting to primary care / office-based

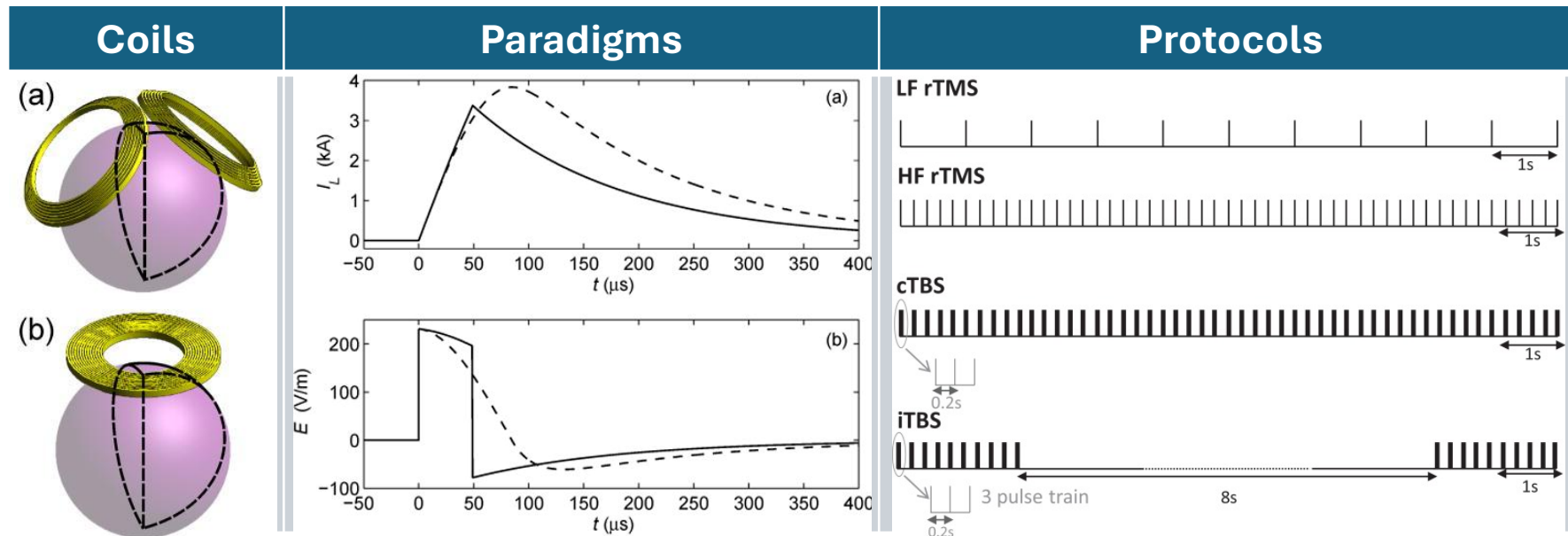


Violante / Grossman (2023)



Aims

- Develop a more advanced TMS prototype which:
 - Enable higher resolution, higher penetration and new protocols for clinical needs
 - Is ready for delivery to AIC for further clinical trials relating TMS parameter & pain relief
- Enhance translational medicine collaboration between local Engineering & Medical research groups with a focus on pain research.
- **Set a cornerstone platform for further translational research and technology transfer → from hardware (e.g. coils) to new clinical treatment protocols.**



Peterchev (2008)



Conclusion

- Non-invasive neuromodulation as a viable treatment option for chronic **neuropathic pain** management and alternative for treating other pain conditions
- Sustainable improvements possible by maintenance treatments
- Technological advancement improves inclusion and long-term efficacy by driving costs down



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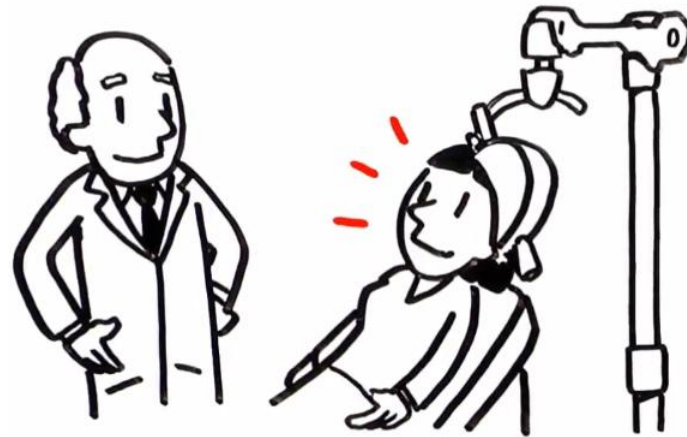
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Q & A



Thank you!



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