

Pairing TMS and DBS in Parkinson's Disease and Dystonia

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Krembil
Relentless.



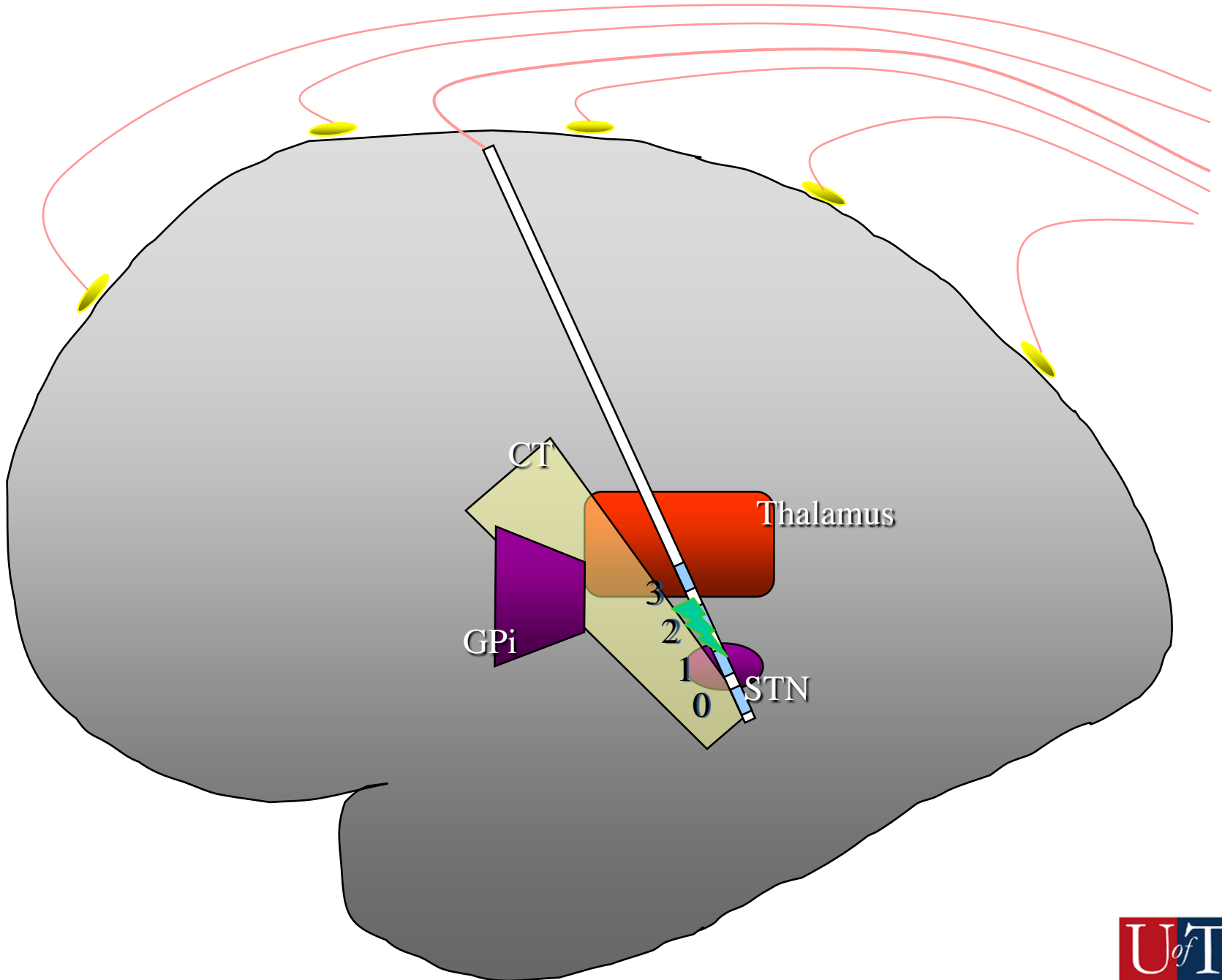
UHN

Toronto General
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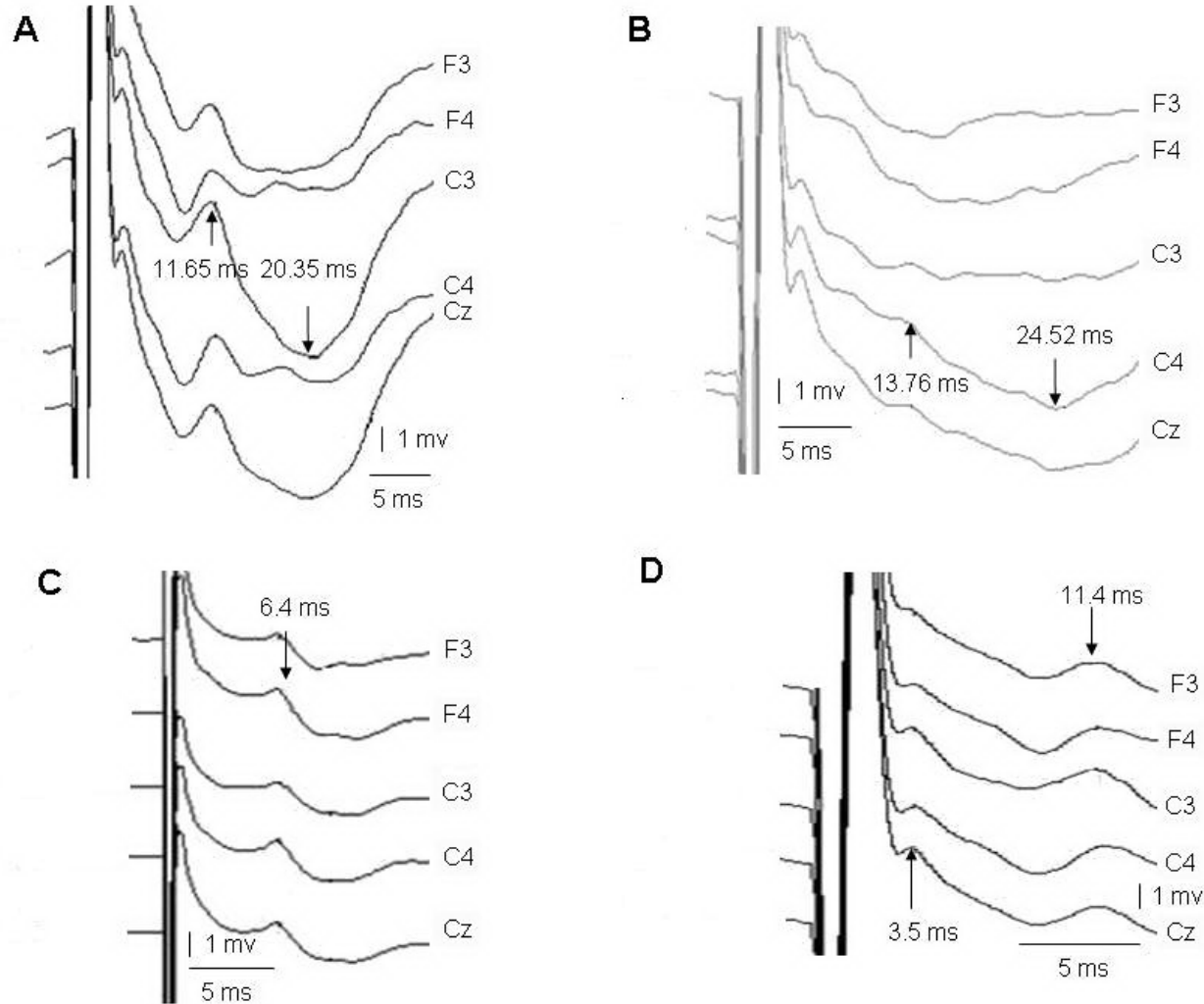


Parkinson's Disease

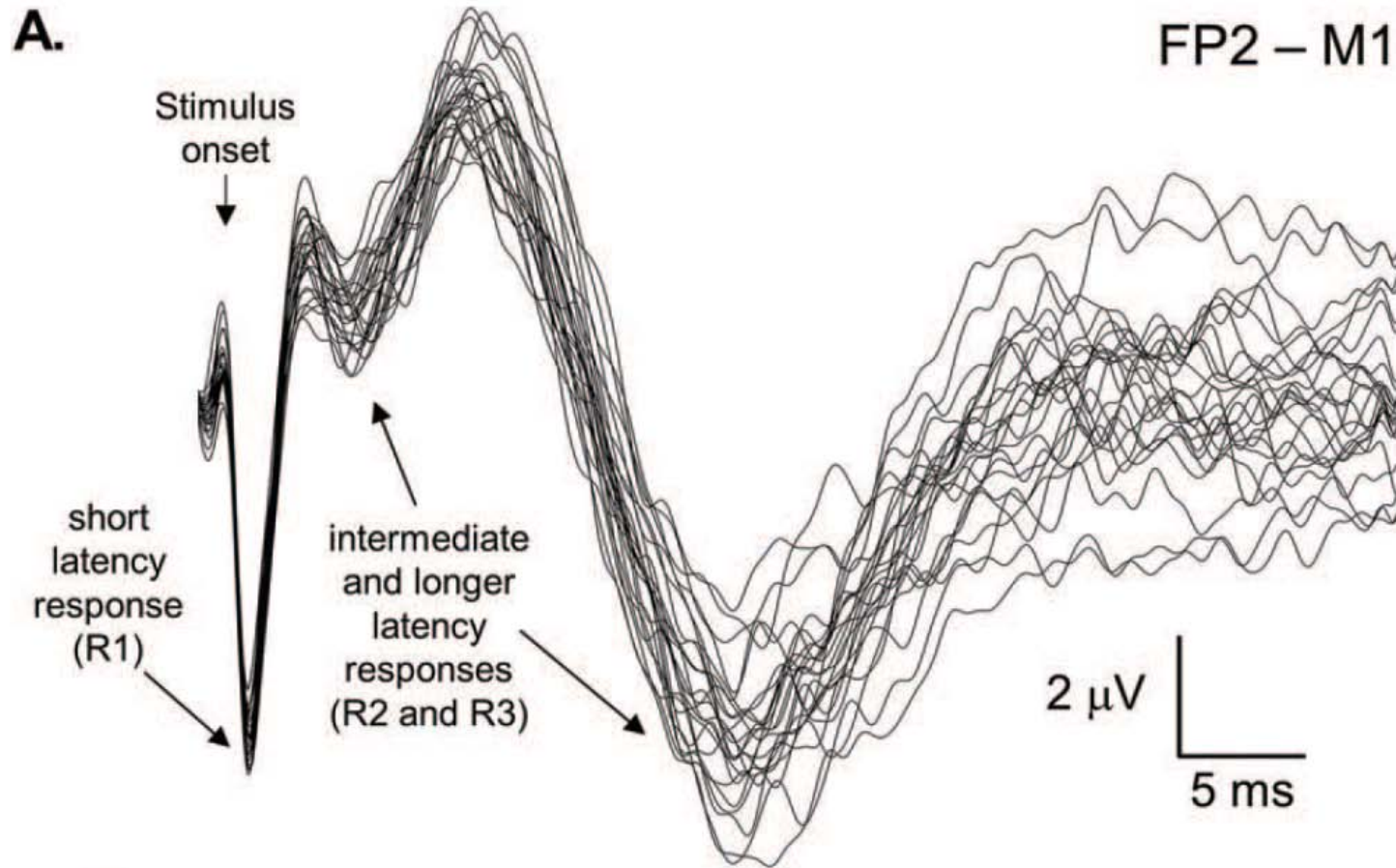
- Cortical evoked potentials and time course of cortical activation following subthalamic nucleus (STN) DBS
- Induction of cortical plasticity by pairing STN DBS and TMS



Evoked potentials from STN DBS



Evoked potentials from STN DBS

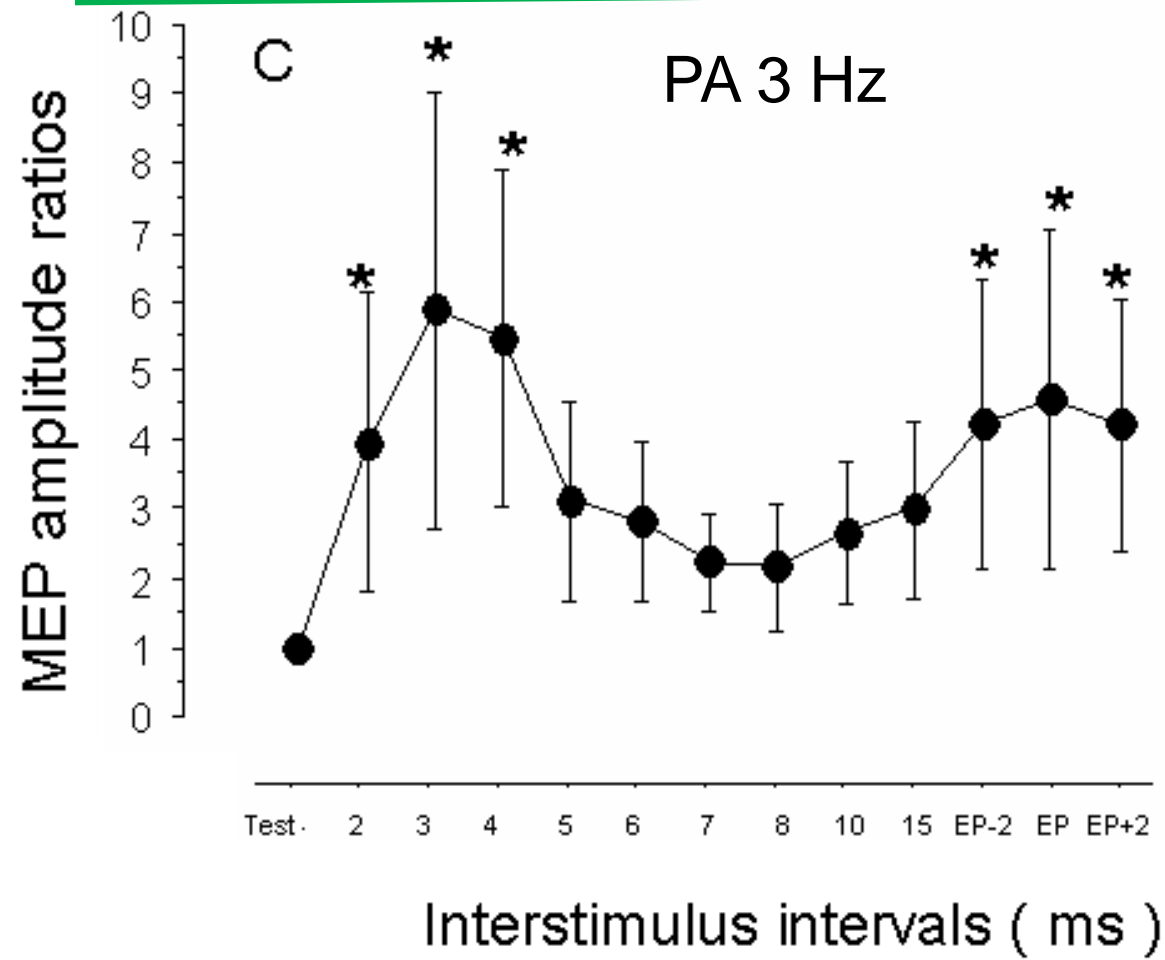


Cortical Evoked Potentials from STN DBS

- **STN DBS**

- Short latency positive potential (~ 1-3 ms)
Antidromic activation of hyperdirect pathway
- Positive potential 5-6 ms – less consistent
- Medium latency positive potential ~ 23 ms:
Indirect pathway?

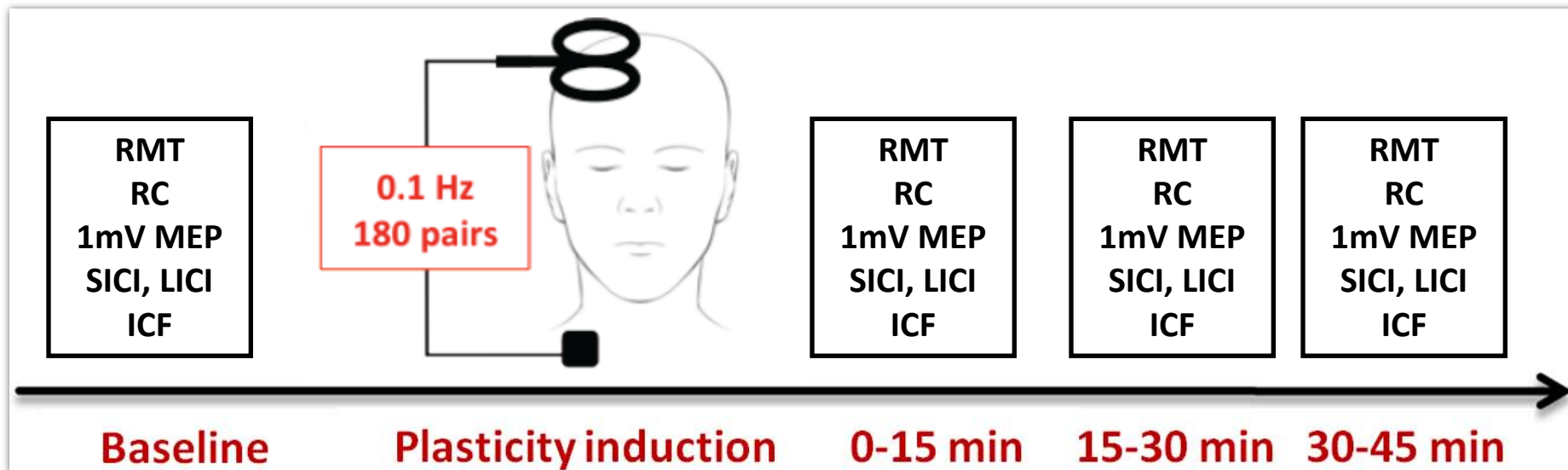
Time course of motor cortex facilitation after STN DBS



- Significant motor cortical facilitation at ~ 3 ms (antidromic hyperdirect) and at medium latency ~ 23 ms (indirect pathway)

Induction of plasticity by pairing STN DBS and TMS

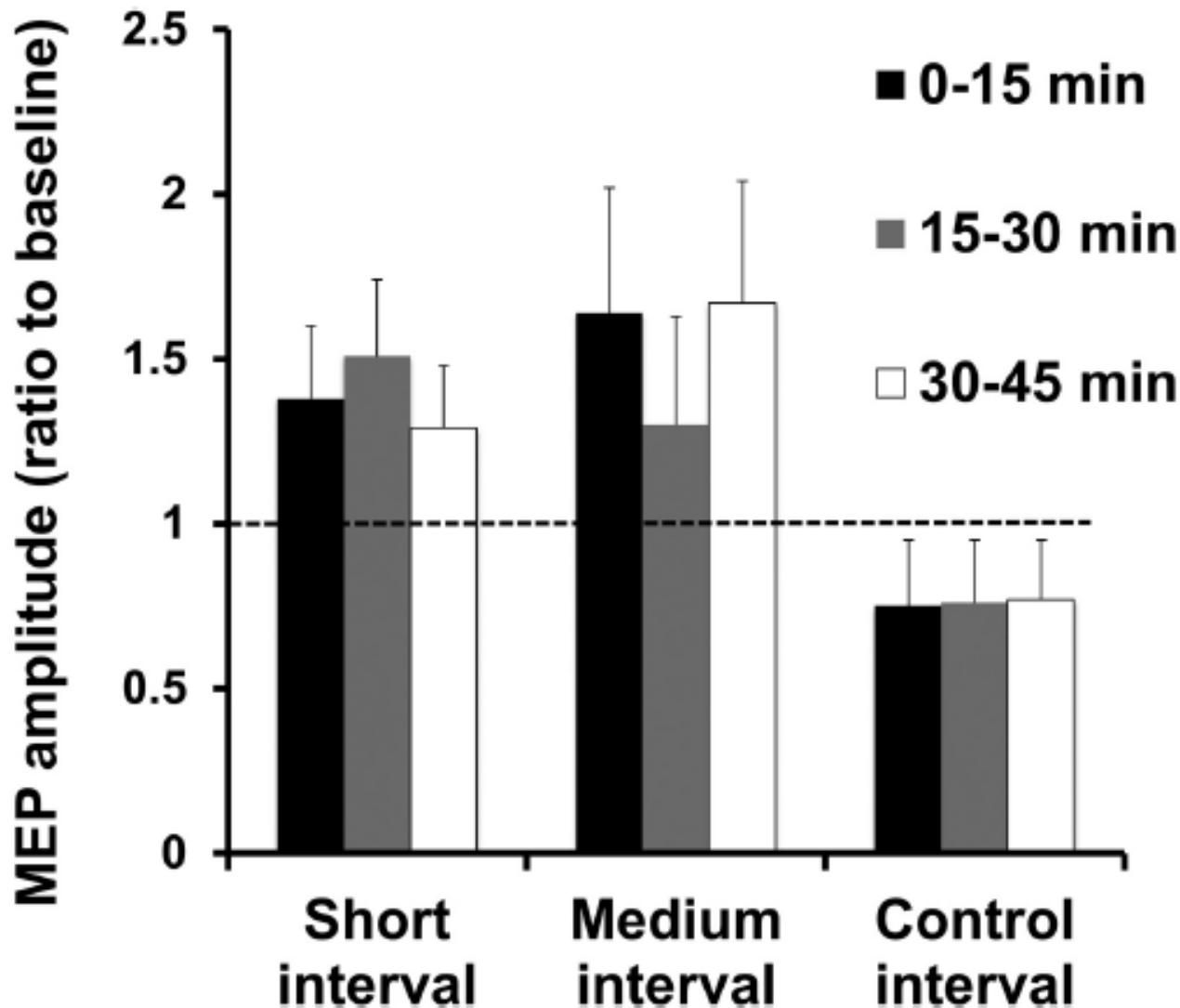
- Hypothesis: Repeated, synchronous activation of M1 by STN-DBS and TMS at short (~3 ms) and medium (~23 ms) ISI will induce LTP-like effects



A: short interval ~ 3 ms
B: medium interval ~ 23 ms
C: control ~167ms

Udupa et al. J
Neurosci 2016

Induction of plasticity by pairing STN DBS and TMS



Udupa et al.
J Neurosci 2016

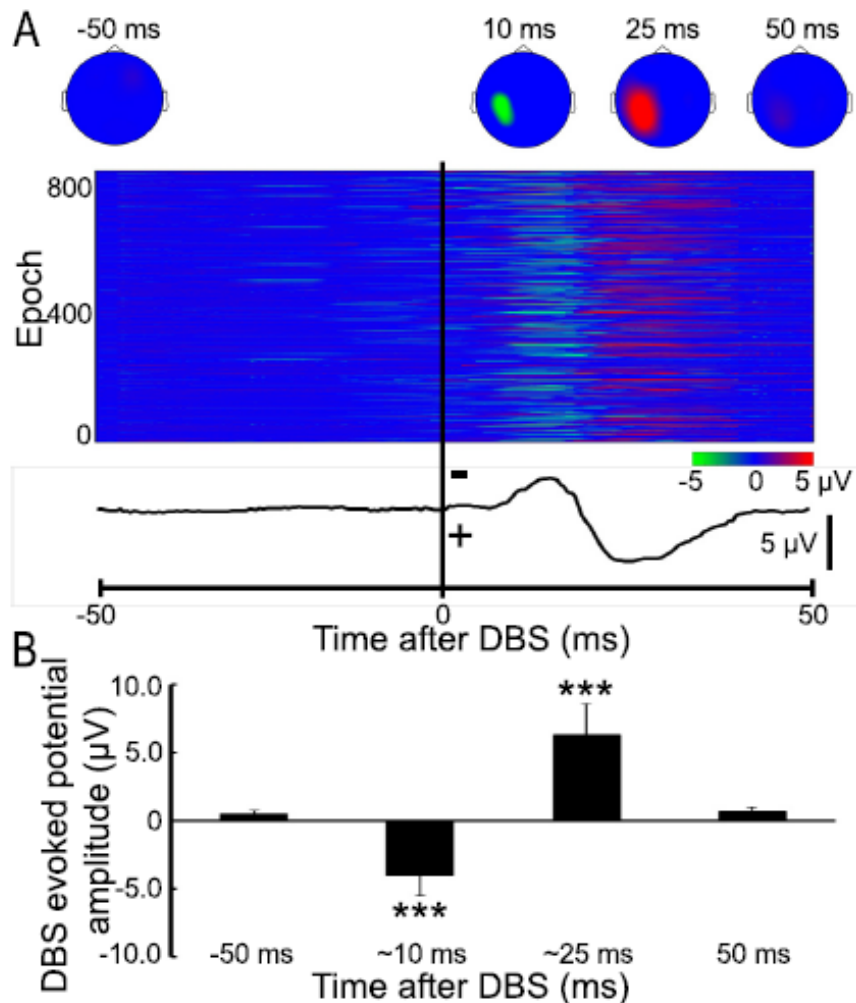
Induction of plasticity by pairing STN DBS and TMS

- Cortical plasticity can be induced by **repeated pairing** of STN DBS and TMS at the **specific intervals** that DBS produces cortical evoked potentials and increases cortical excitability

Dystonia

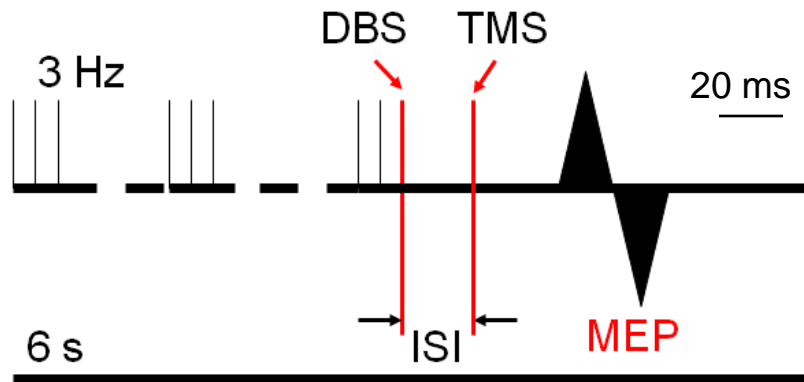
- Dystonia – Movement disorder with excessive muscle contraction leading to twisted postures
- Cortical evoked potentials and time course of cortical activation following internal globus pallidus (GPi) DBS
- Induction of cortical plasticity by pairing DBS and GPi TMS

Evoked potentials from GPi DBS

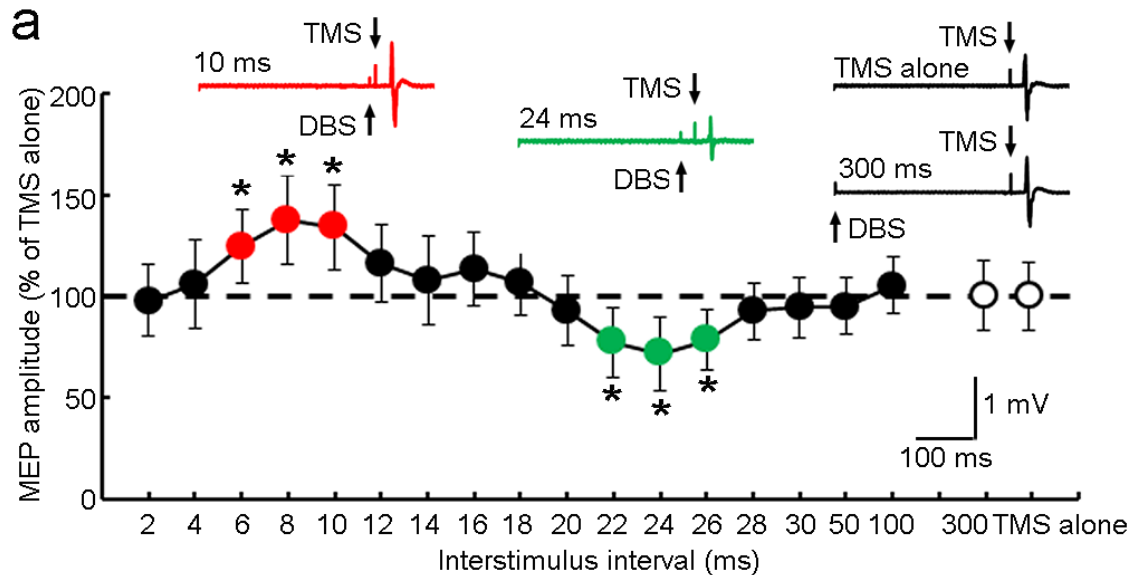


Effects of single pulse GPi DBS – Cortical excitability

◆ TMS to motor cortex at different times after GPi DBS

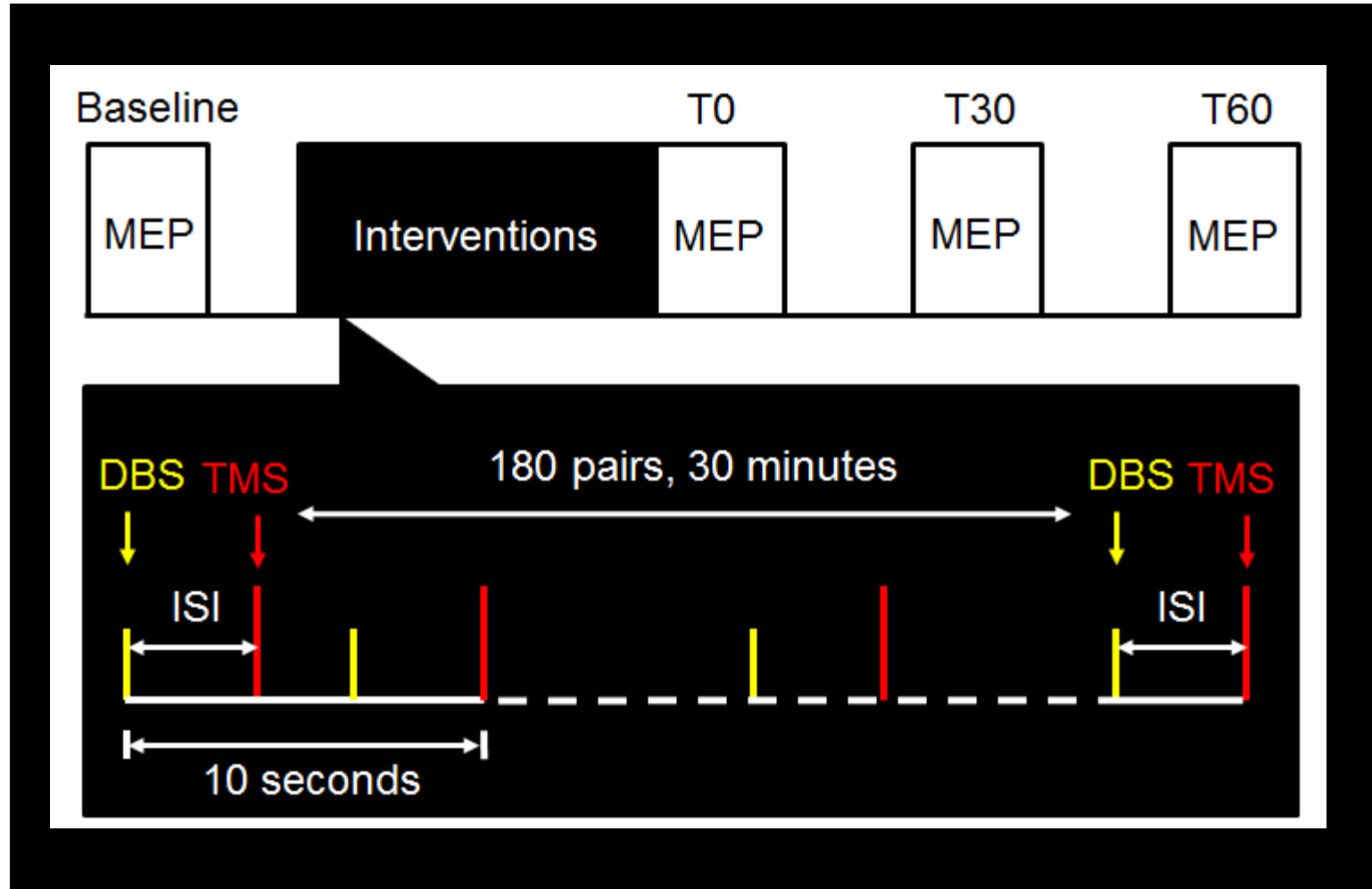


- GPi DBS facilitates the motor cortex at early ISIs of 6-12 ms but inhibits the motor cortex at later at ISIs of 22-26 ms



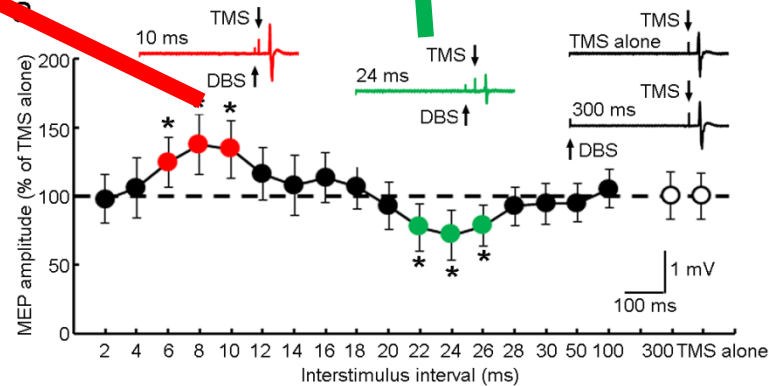
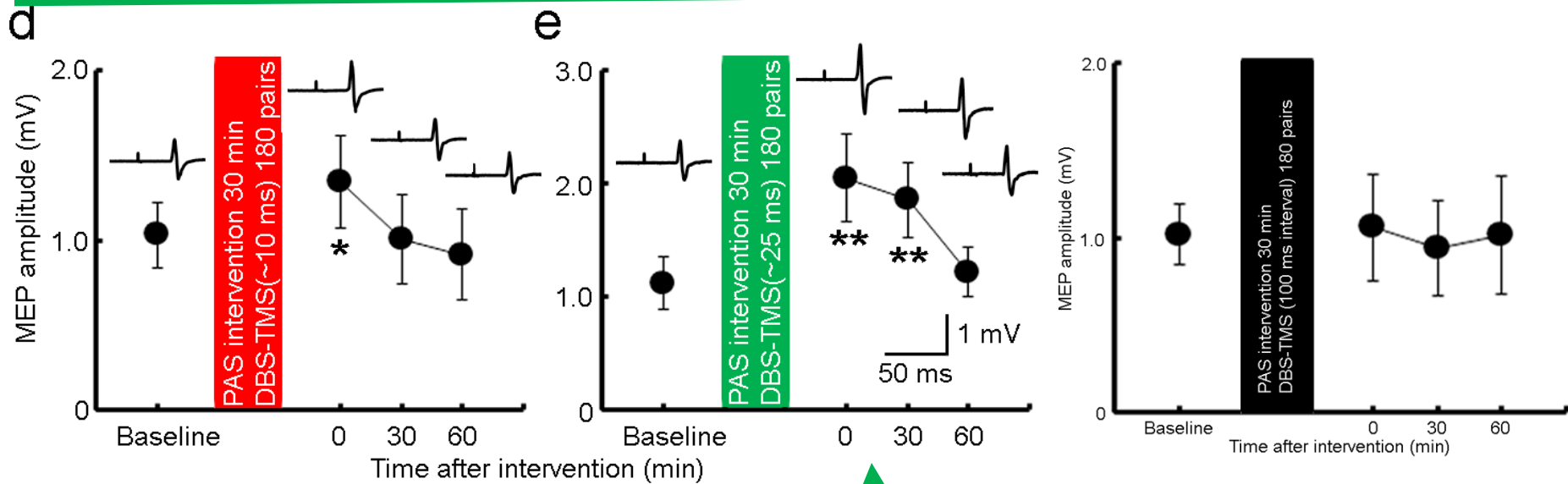
Ni et al., Ann Neurol
2018

GPi Stimulation: Effect of repetitive stimulations



Paired associative stimulation: repetitive DBS-TMS pairing

GPI Stimulation: Long-term potentiation-like Effects



Ni et al., Ann Neurol 2018

Summary: Pairing DBS with TMS in Dystonia

- Internal globus pallidus has both inhibitory and facilitatory connectivity with primary motor cortex.
- Repetitive application of pallidal stimulation paired with motor cortical stimulation at these interval leads to LTP-like effect in the primary motor cortex

Implications

- Cortical plasticity is abnormal in PD and dystonia
- Induction of changes in cortical excitability and plasticity could be a mechanism of action of DBS
- Combining DBS and cortical stimulation at specific intervals could be explored further as a therapeutic option