TMS-EEG to Track Pharmacological and Neuromodulatory Interventions

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Content of the talk

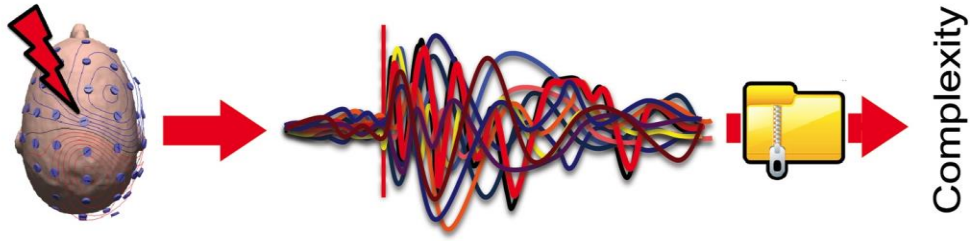
1. TMS-EEG in DoC: diagnosis, prognosis, and treatment testing

2. TMS-EEG in healthy participants: spontaneous transitions & pharmacological treatments

TMS-EEG in DoC: diagnosis, prognosis, and treatment testing

Part 1

Now in the EAN guidelines!



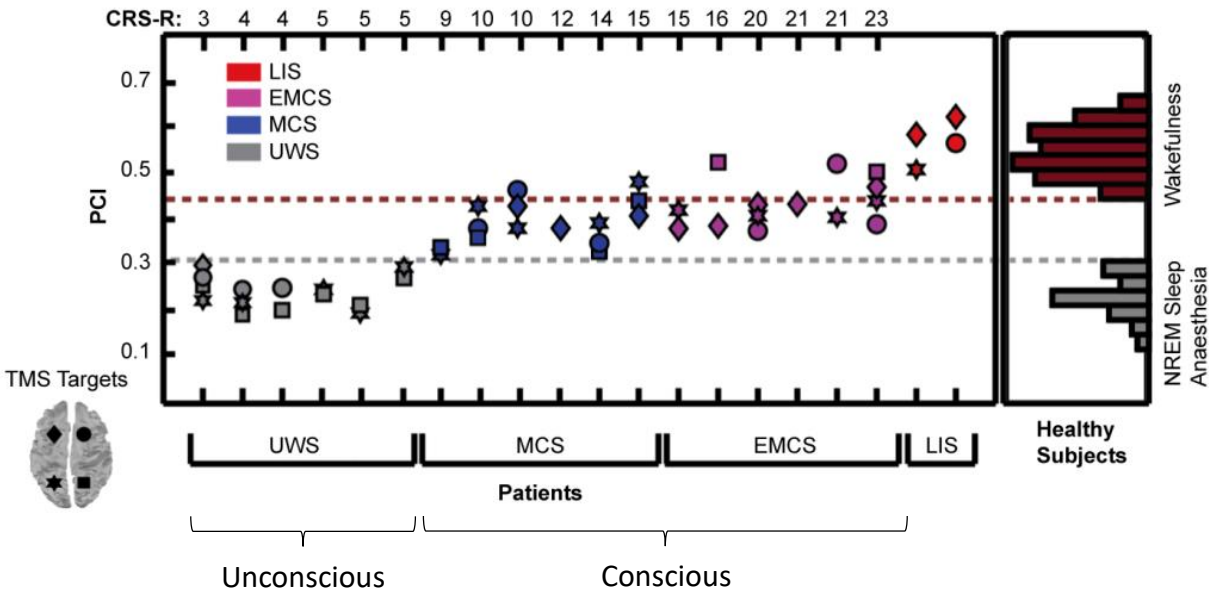
Recommendation: consider **TMS**-EEG to differentiate unresponsive from minimally conscious

Weak evidence, weak recommendation
6 publications

Kondziella et al., *Eur J Neurol*, 2020

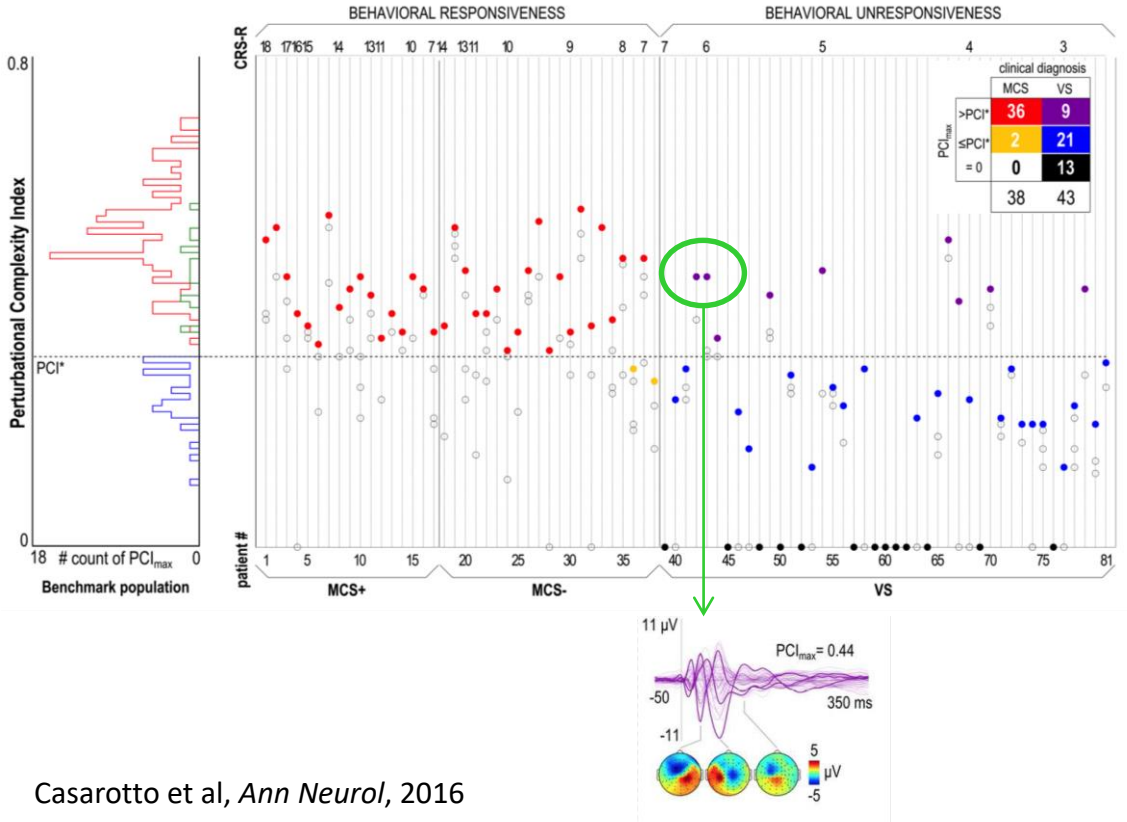
TMS-EEG in DoC

Diagnostic value



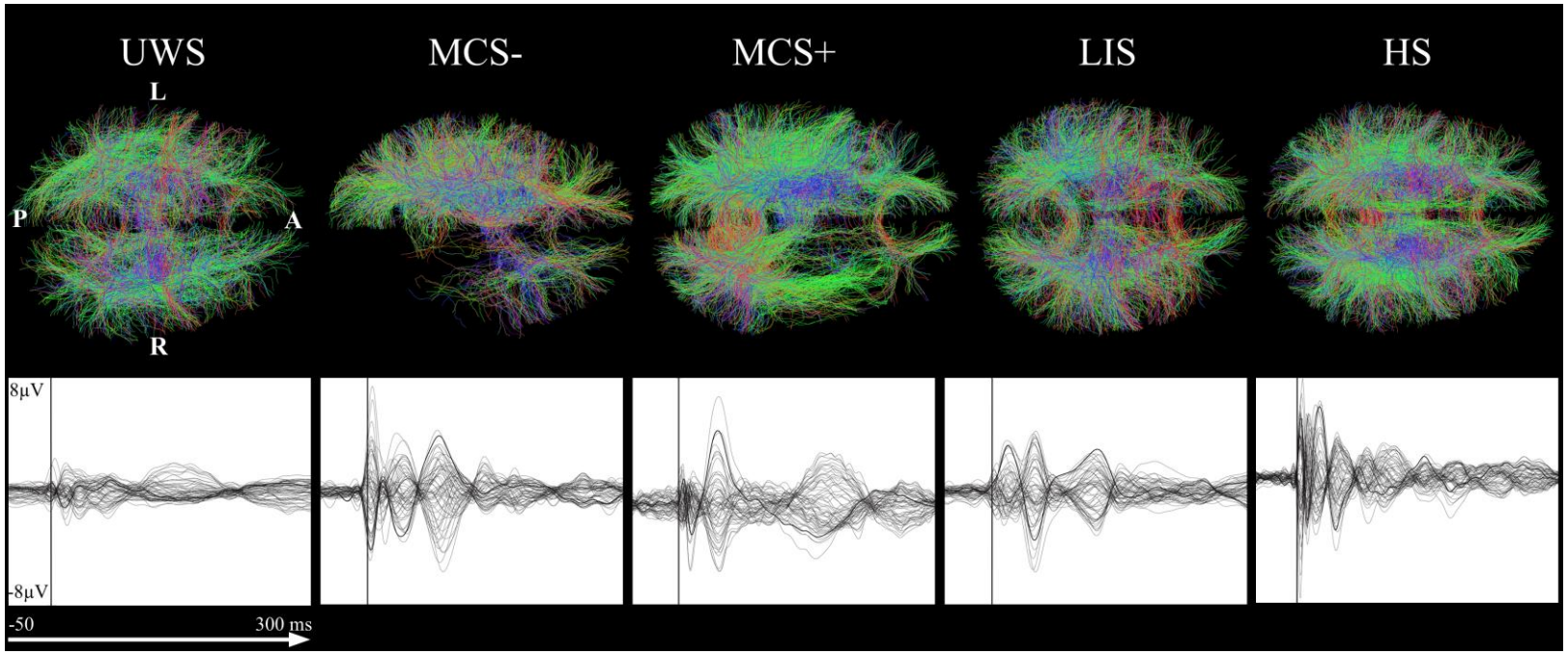
Casali & Gosseries et al, *Sci Trans Med,* 2013

Prognostic value

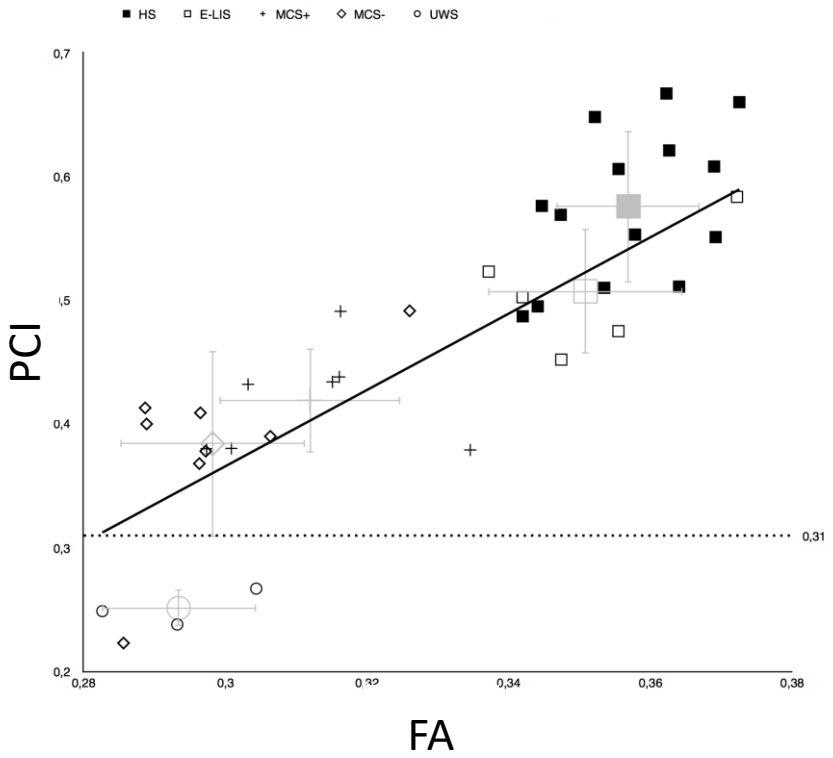


Casarotto et al, *Ann Neurol*, 2016

TMS-EEG and brain architecture

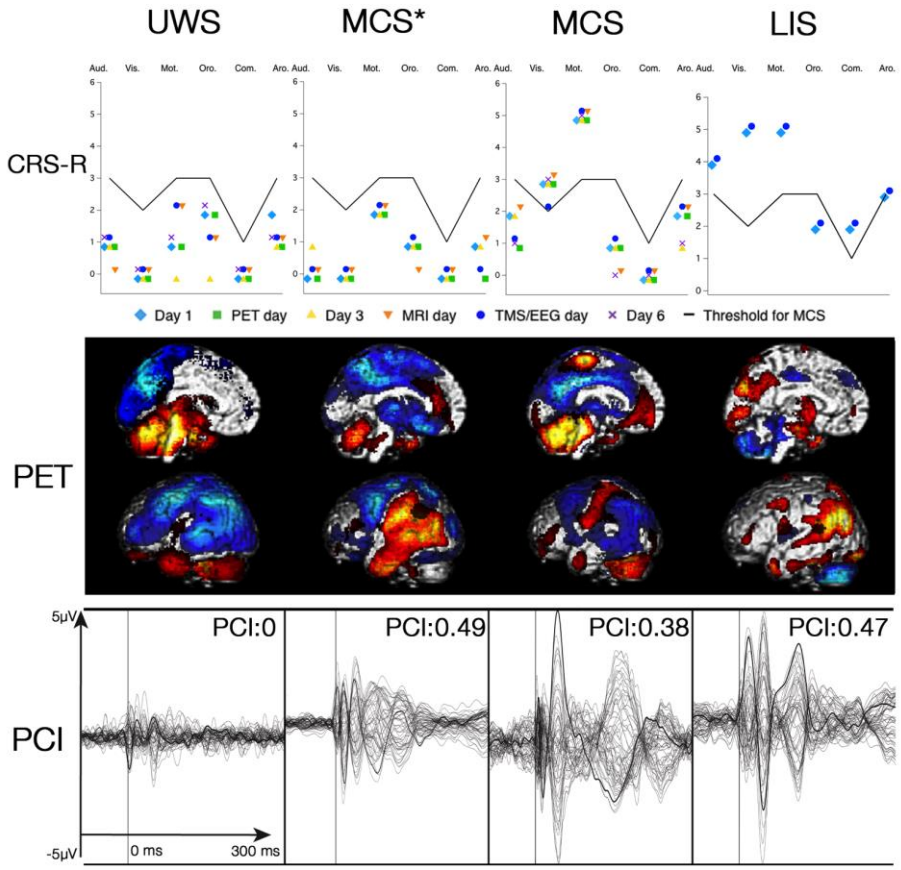


Excellent positive correlation between global FA and PCI

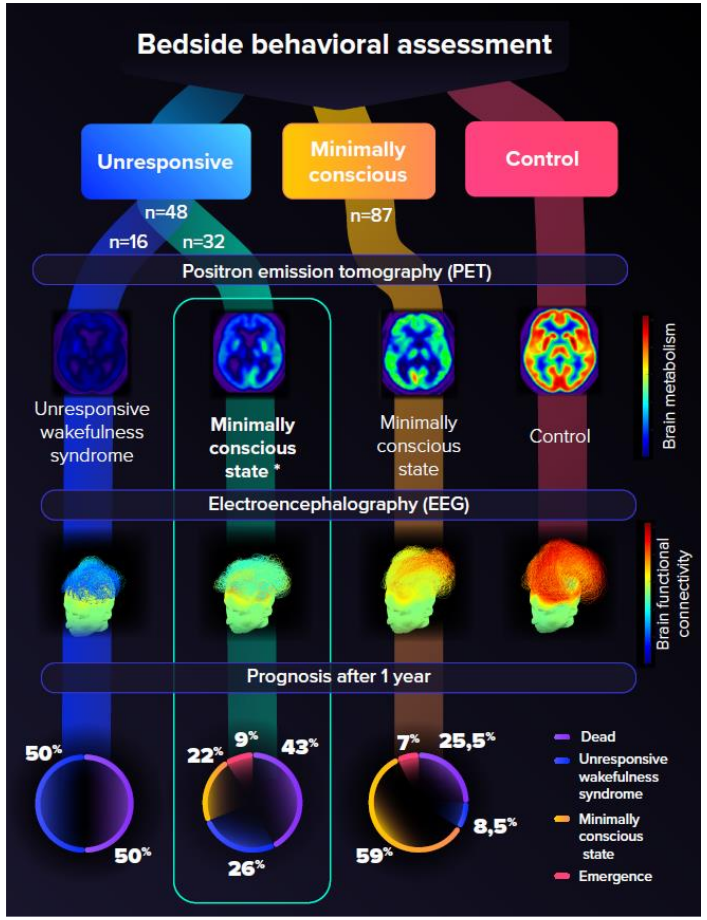


Bodart et al, *Brain Stimul*, 2018

Cases of favourable prognosis of DoC



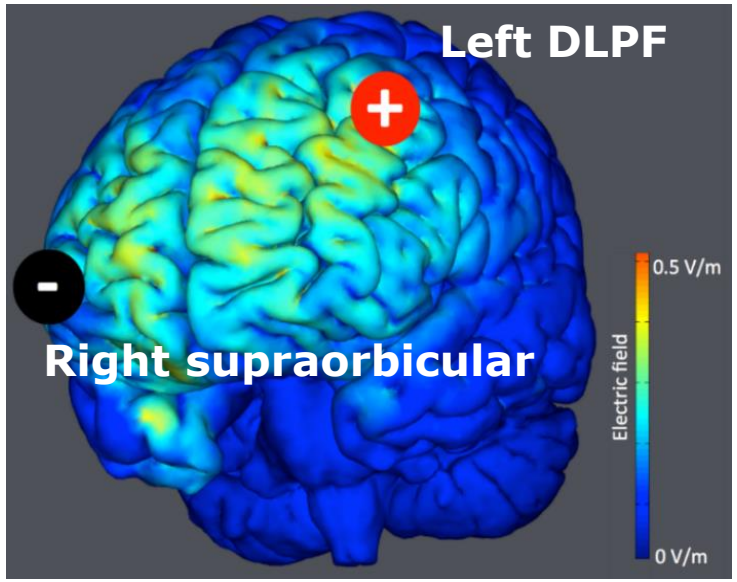
Bodart et al, *Neuroimage Clin,* 2017

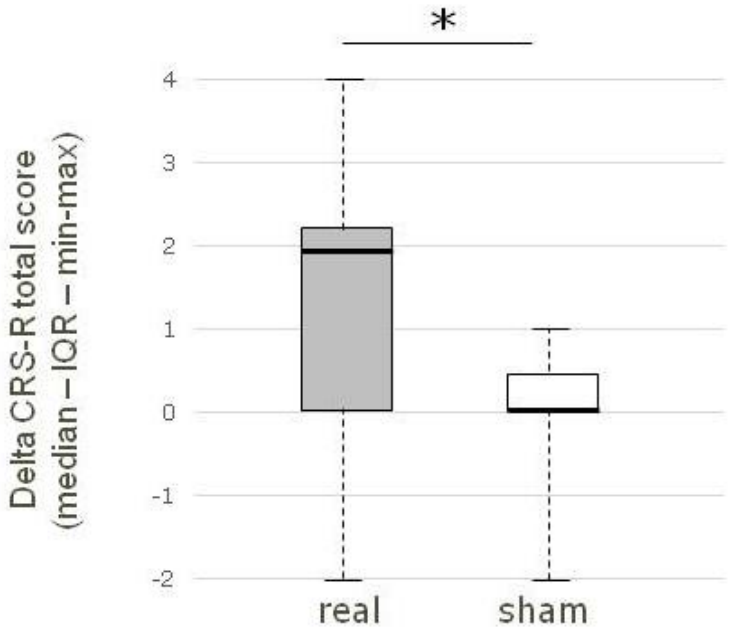


Thibaut et al, *Ann Neurol*, 2021

tDCS in patients with DoC

Crossover RCT (n=55)



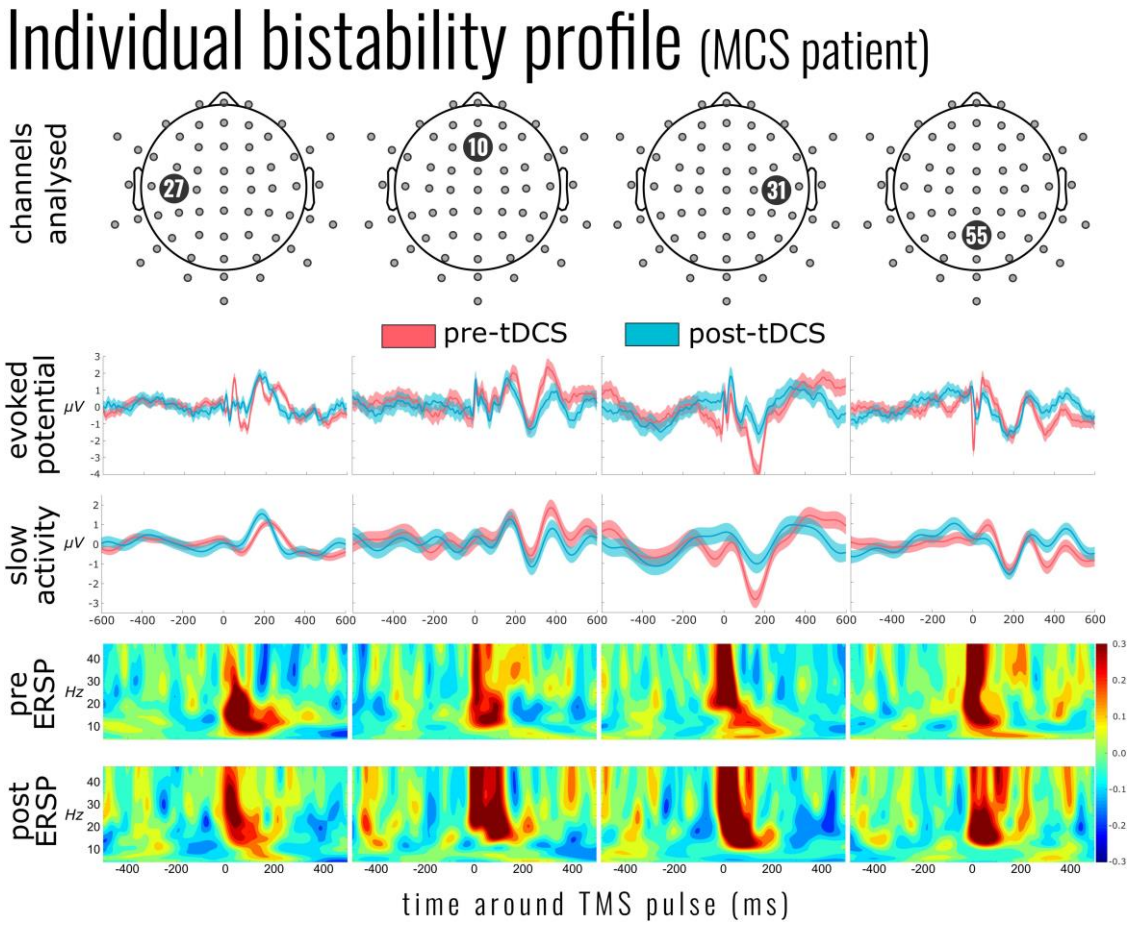


MCS
n=30

➔ No adverse events
➔ Clinical improvement in MCS only
➔ 13/30 responders (5 >1y post-insult)

Thibaut et al., *Neurology*, 2014

Measuring effects of tDCS with TMS-EEG

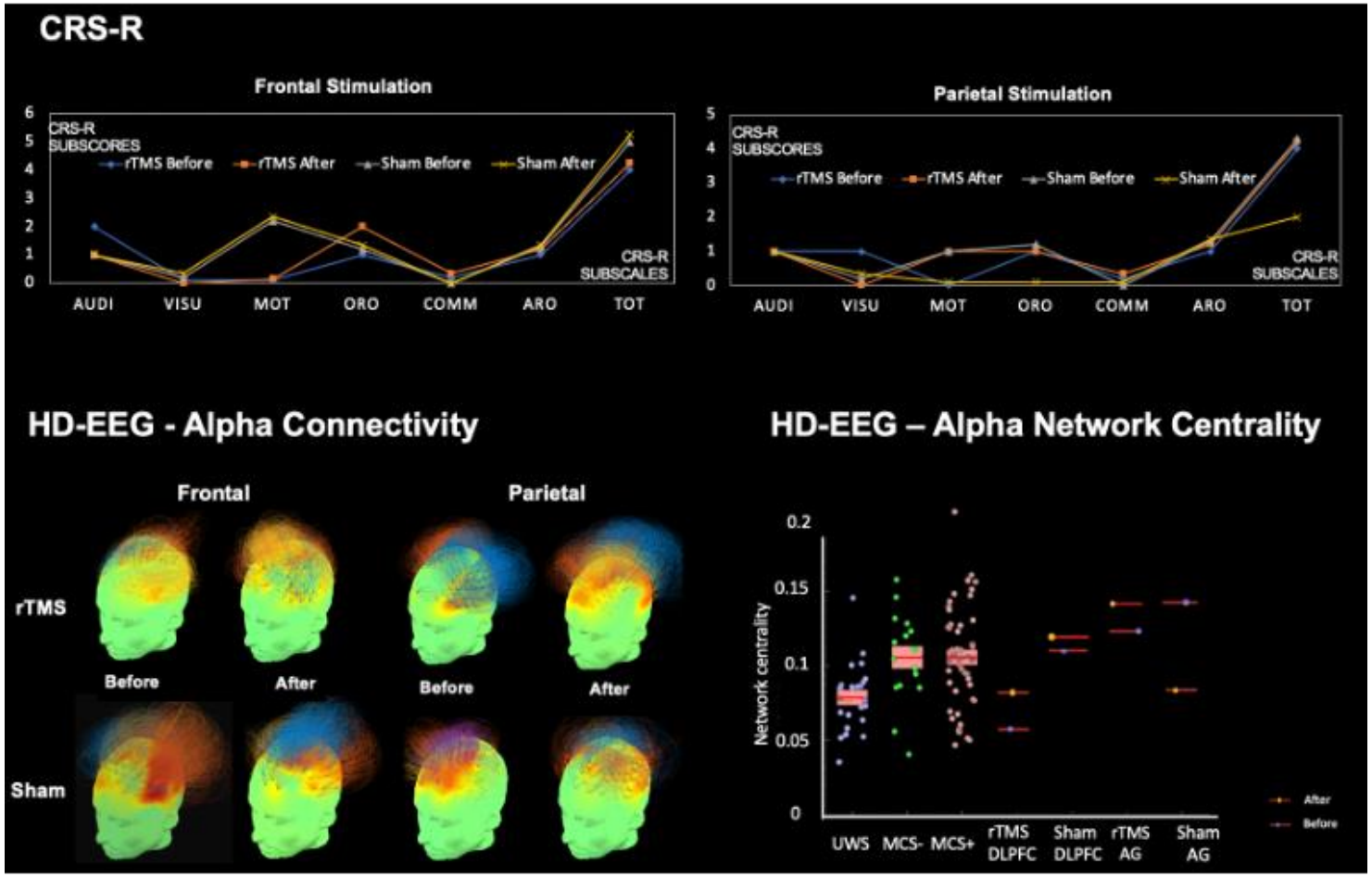


- No tDCS responders → No change in behaviour
- EEG changes:
  - Reduction in slow activity after tDCS but not in high frequency
  - Strong association between slow activity and high frequency suppression

Mensen et al, *Front Syst Neurosci*, 2020

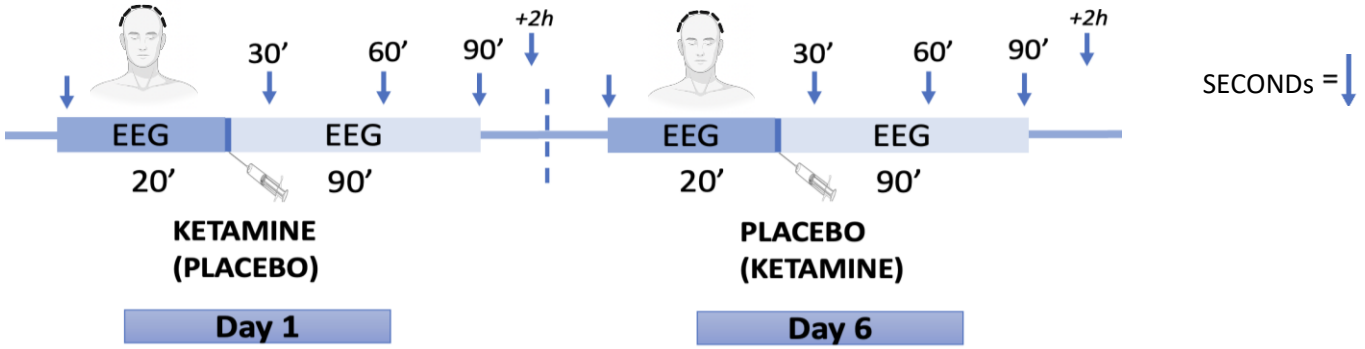
rTMS and DoC

Work by Marie Vitello

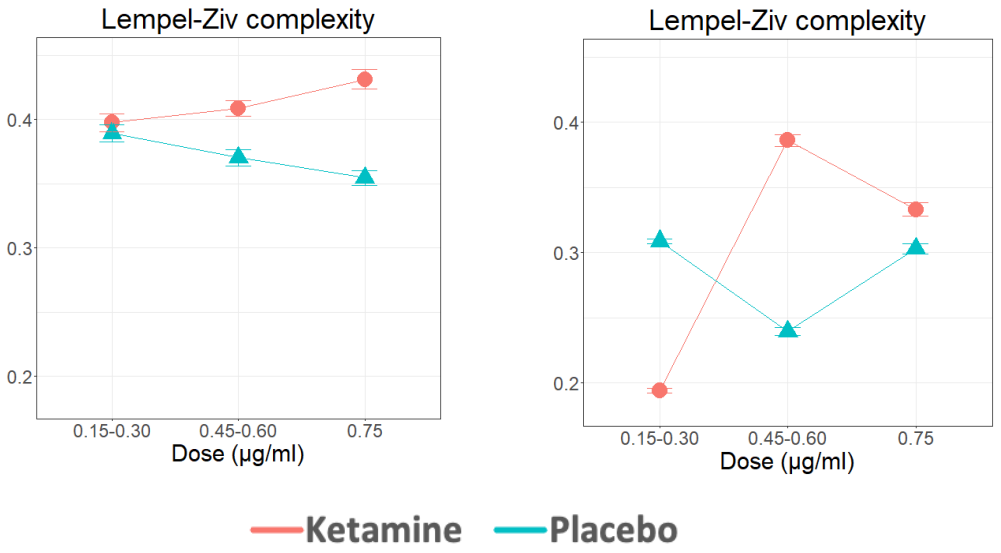


- Protocol of stimulation on two regions (dlPFC; AG) with or without sham
- 53yo UWS male patient 44d after hypoxia
- Change on connectivity in the alpha band after stimulation

Ketamine in DoC patients: preliminary results



SECONDs =



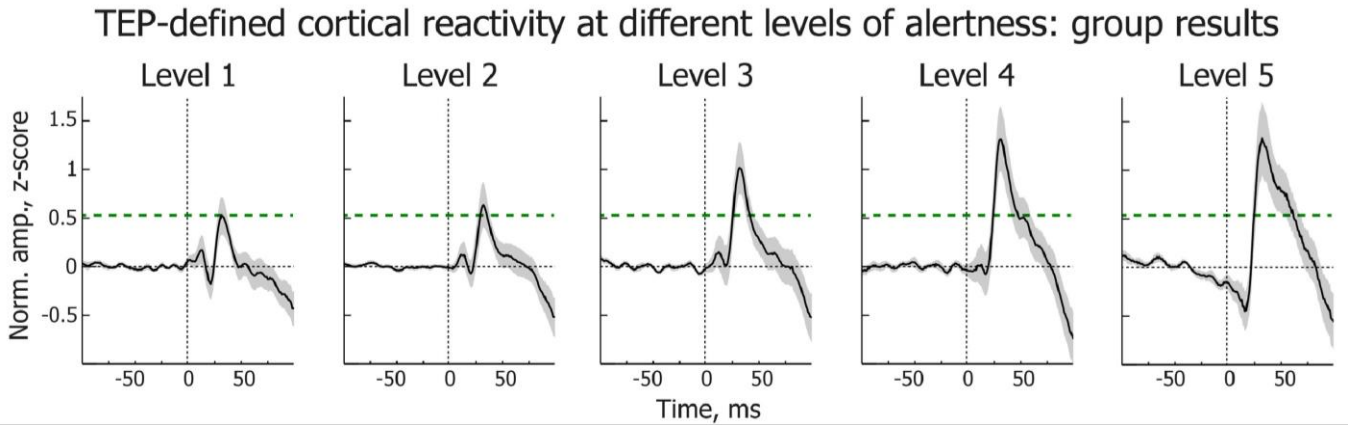
- Ketamine as a treatment for DoC
- Primary outcome: change in behaviour and complexity
- Preliminary results with EEG only. RCT with TMS-EEG

EudraCT

TMS-EEG in healthy participants: spontaneous transitions & pharmacological treatments

Part 2

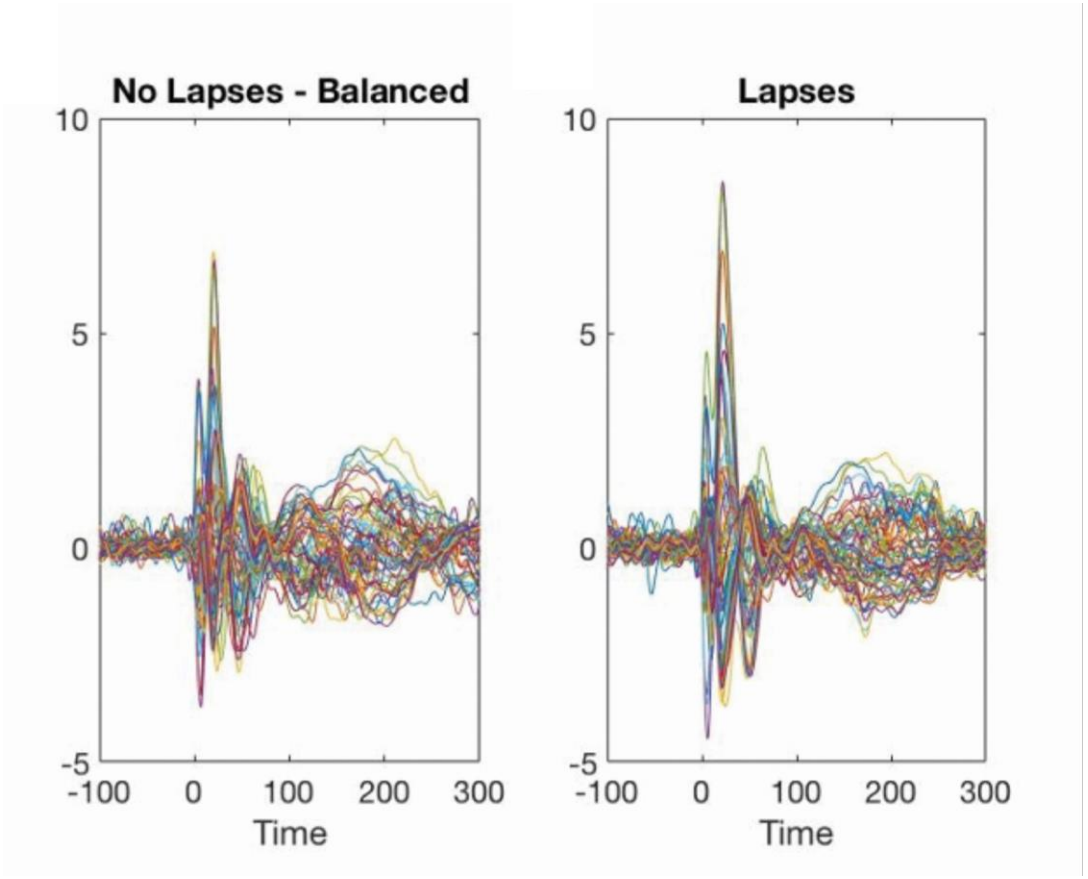
Larger TEP in transition to sleep



- Spontaneous transition towards N1
- TEP amplitude increases with drowsiness
- Similar results in the MEP

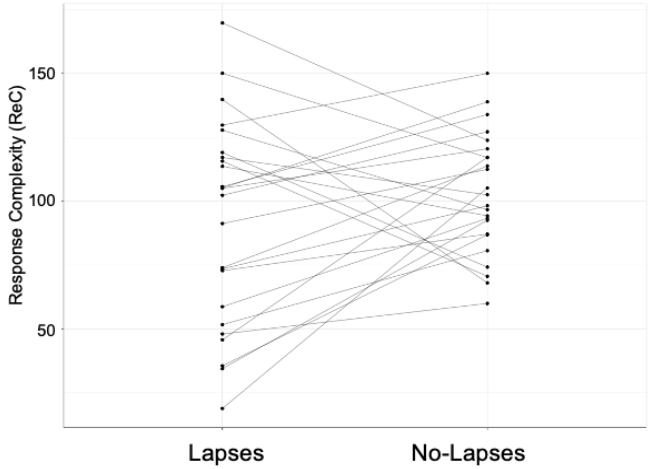
Noreika et al, *Neuroimage*, 2020

Larger TEP in attentional lapses

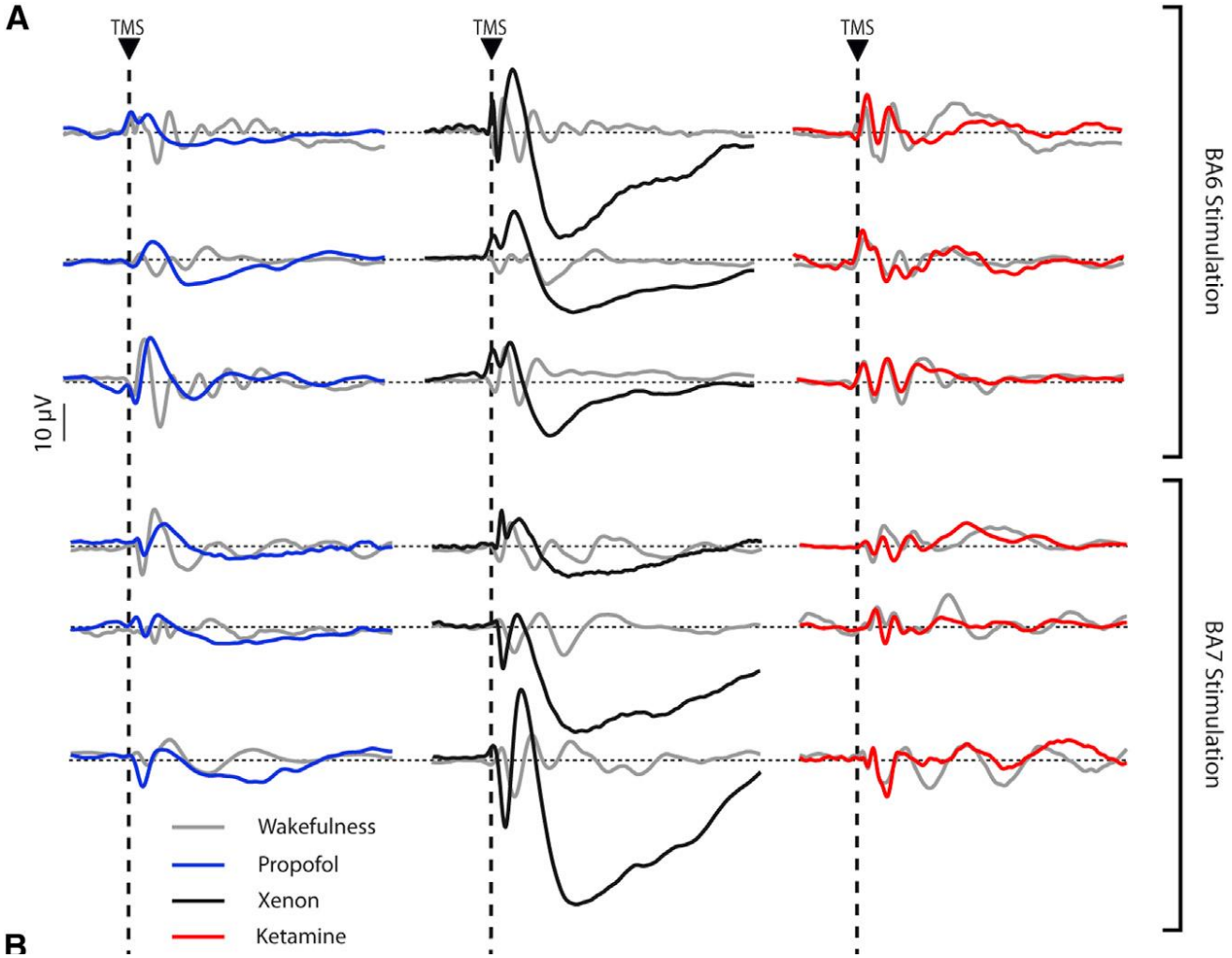


Cardone et al, *Sleep*, 2021

- Increased amplitude and slope of the TEP
- No change in complexity between the trials with lapses and not



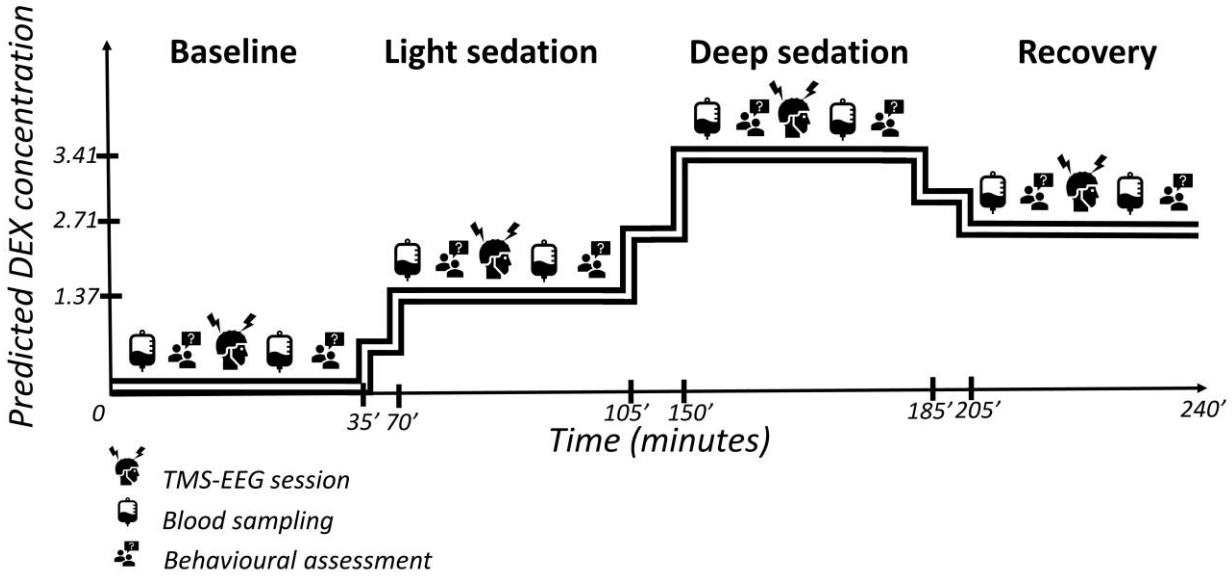
TEP in general anaesthesia

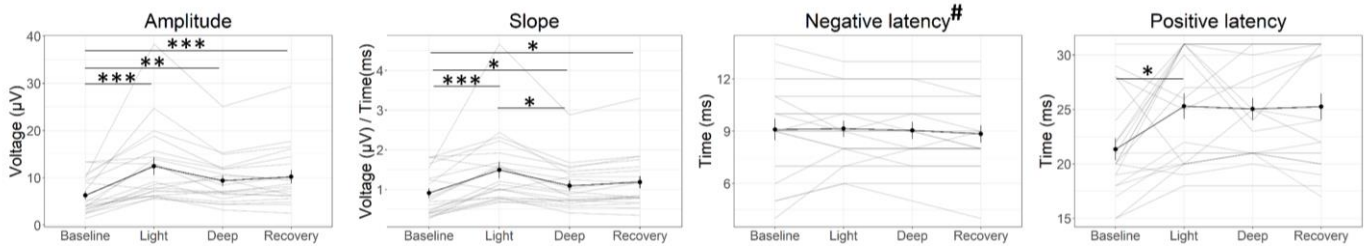


- Anaesthetic drugs leading to unconsciousness are stereotypical
- Ketamine leads to a awake-like response

Sarasso & Boly et al, *Curr Biol*, 2015

Anaesthesia – intermediate states





- Four condition of dexmedetomidine (DEX)
  - Baseline
  - Light sedation (responsive)
  - Deep sedation (unresponsive or max concentration allowed)
  - Recovery (responsive)

- In the frontal cortex, increased amplitude after the drug. No effect in the parietal cortex

Cardone et al, *bioRXiv*, 2021

Take home messages

1. TMS-EEG useful for the prognosis and diagnosis of DoC

2. TMS-EEG offers a unique opportunity to investigate the neurophysiology of pharmacological and NIBS interventions

3. TMS-EEG useful to tracks spontaneous and reversable consciousness transition in healthy participants

Acknowledgments

Pr. Olivia Gosseries

Dr. Charlotte Martial

Patients & families!

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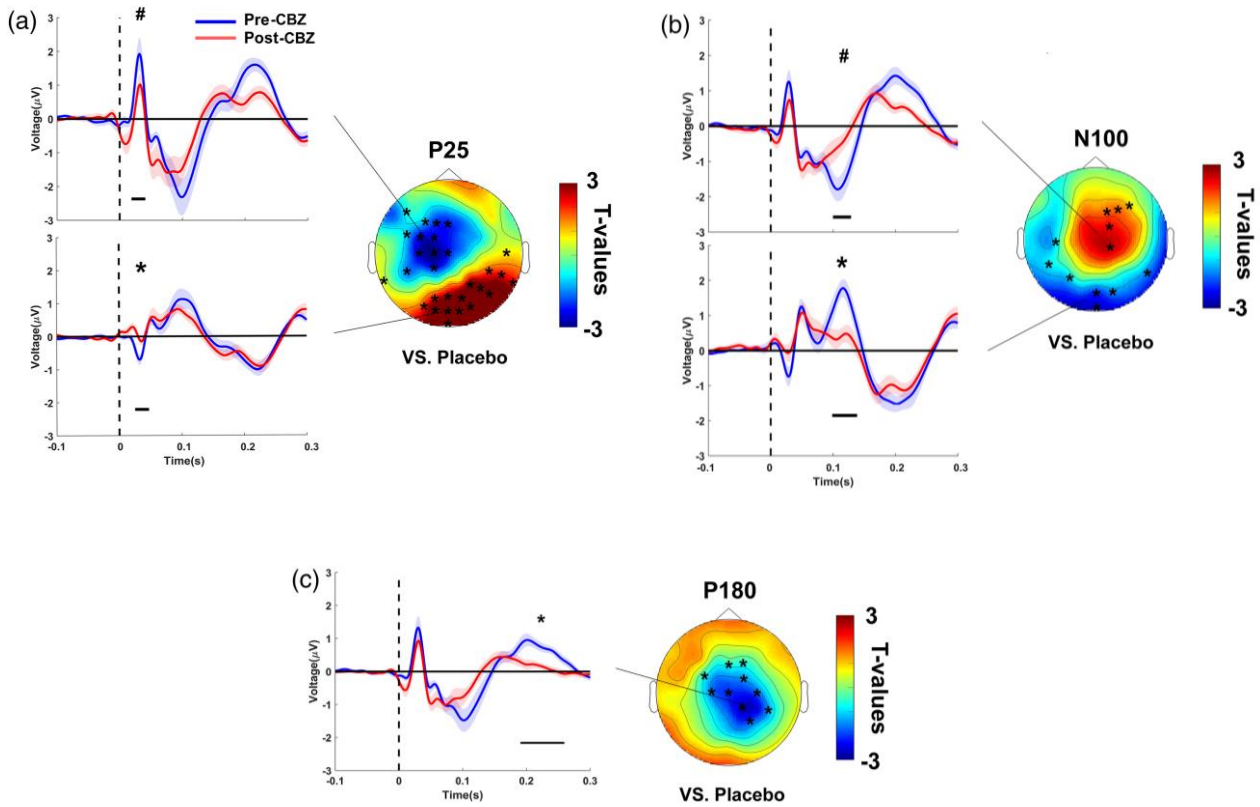
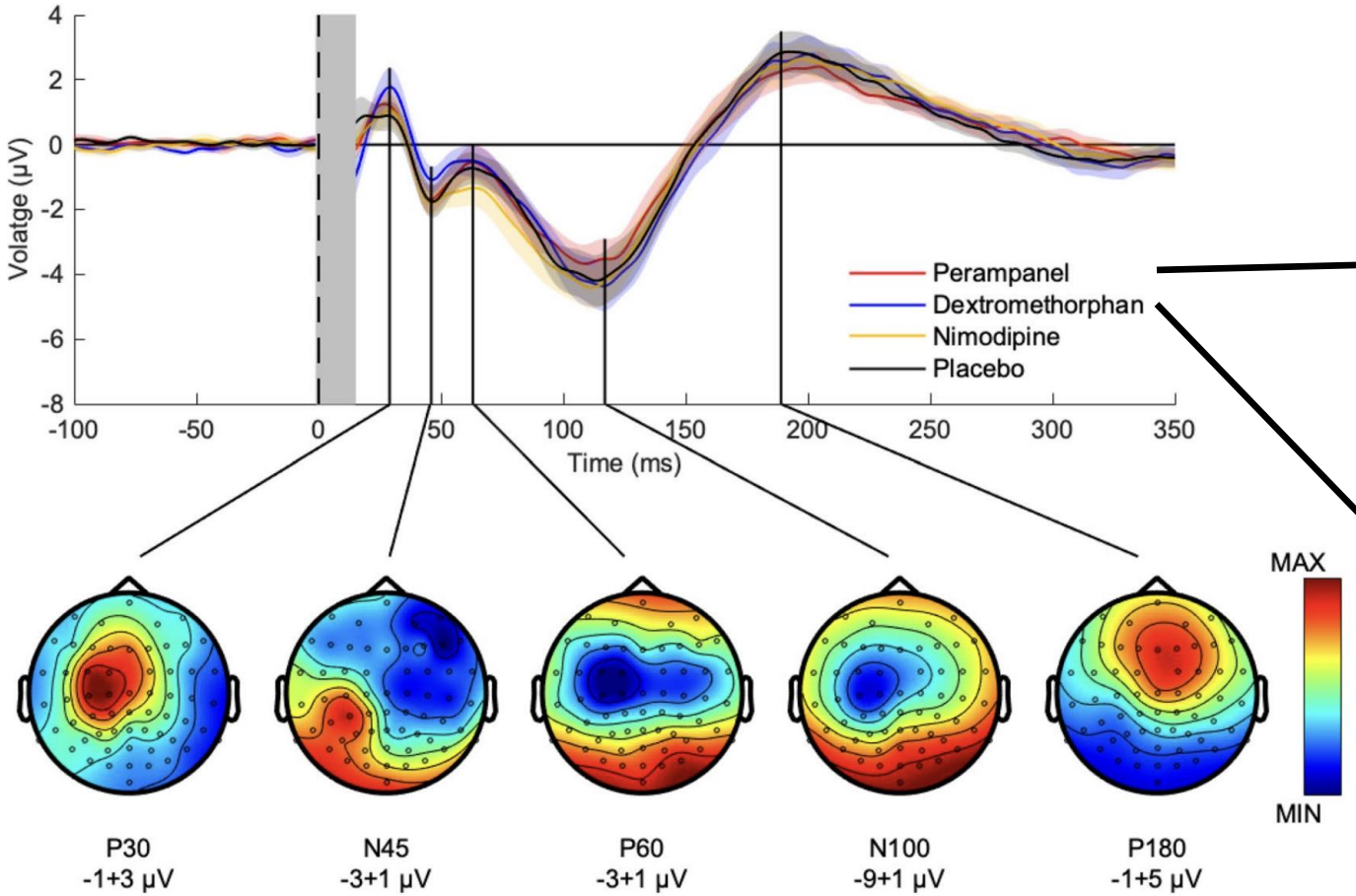
Effects of carbamazepine on TEP

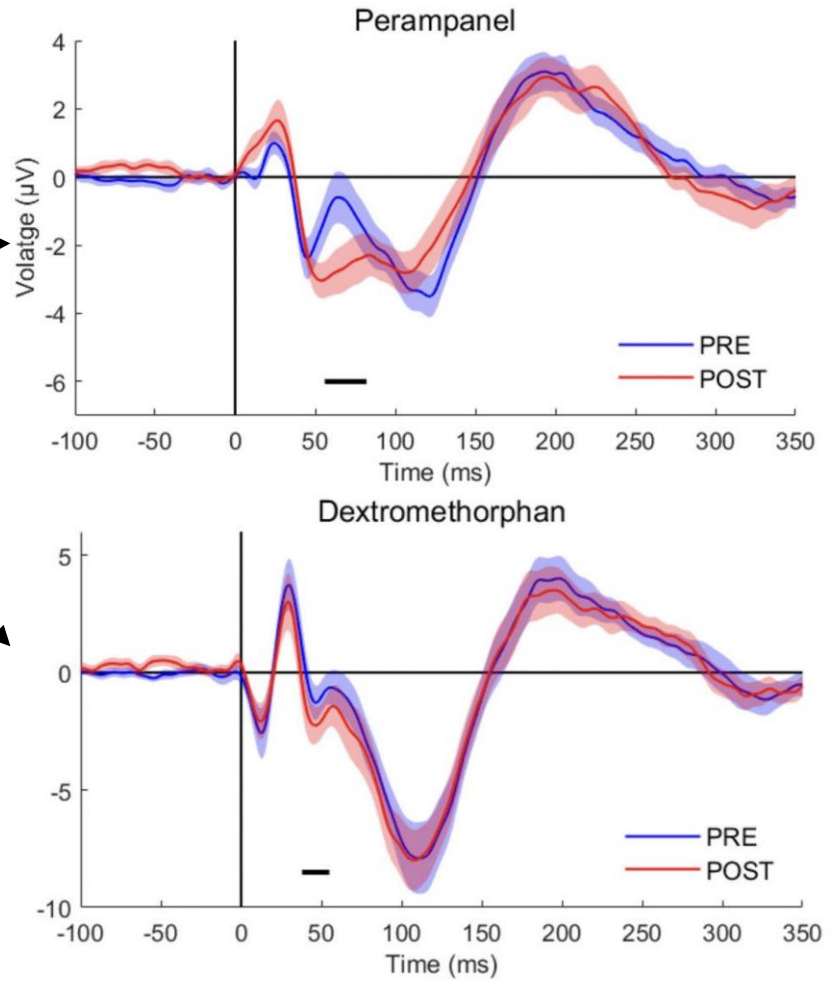


- Changes in TEP after carbamazepine
- Decrease P25, N100, P180 components

Darmani et al, *Hum Brain Mapp*, 2019

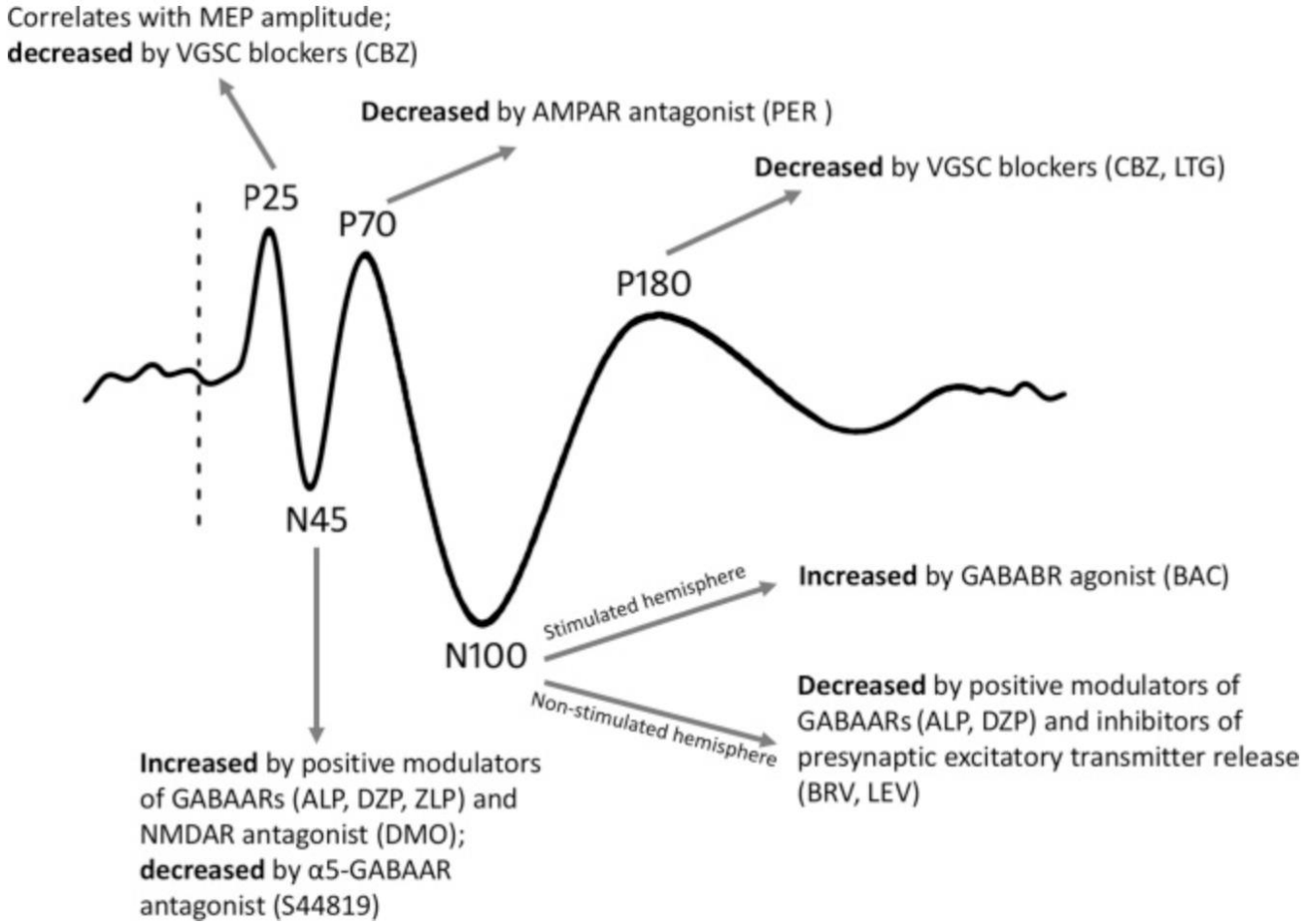
Glutamatergic drugs and TEP





Belardelli et al, *Sci. Rep.*, 2021

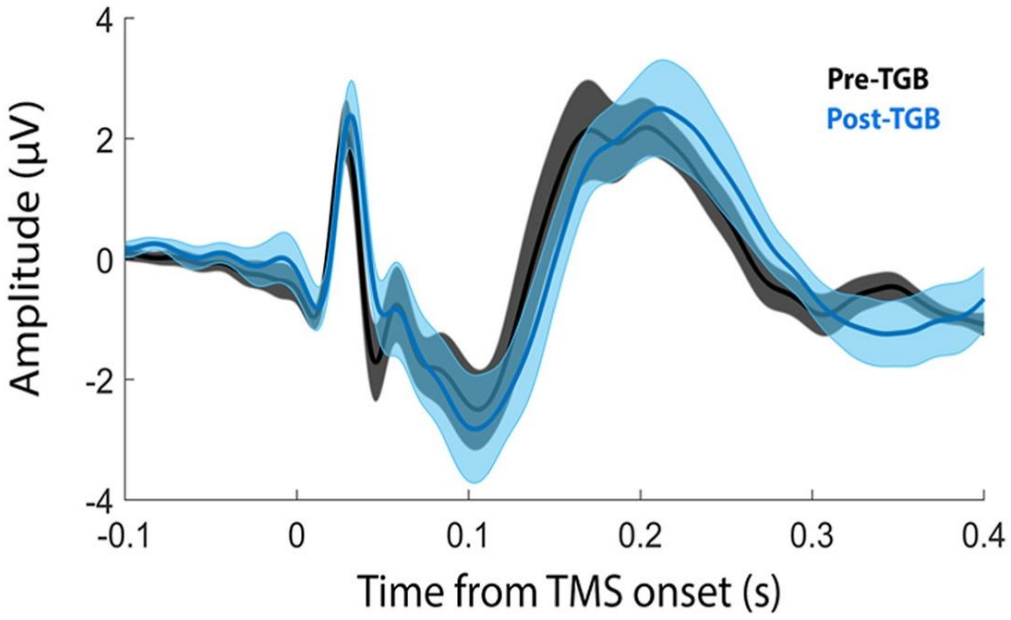
Pharmacophysiology of TEP in M1



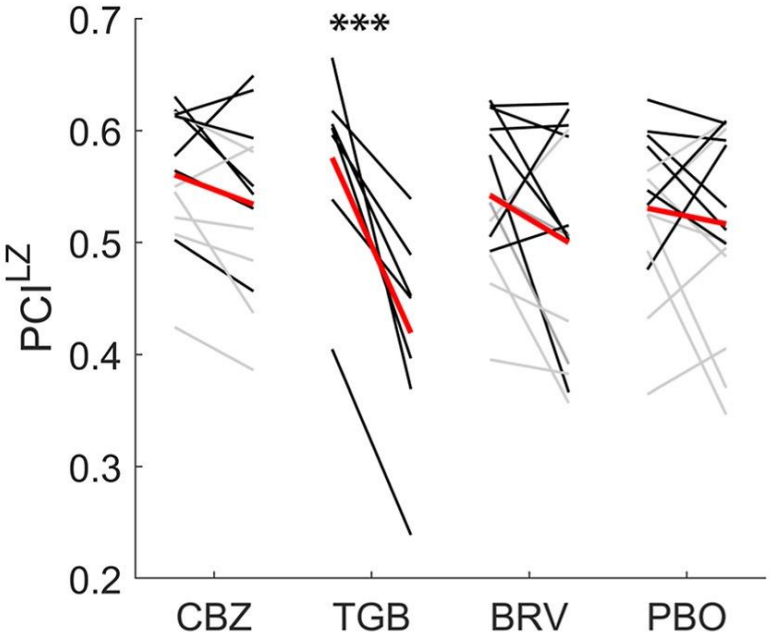
Darmani and Ziemann, *Brain Stim.*, 2019

The case of tiagabine

Similar TEP

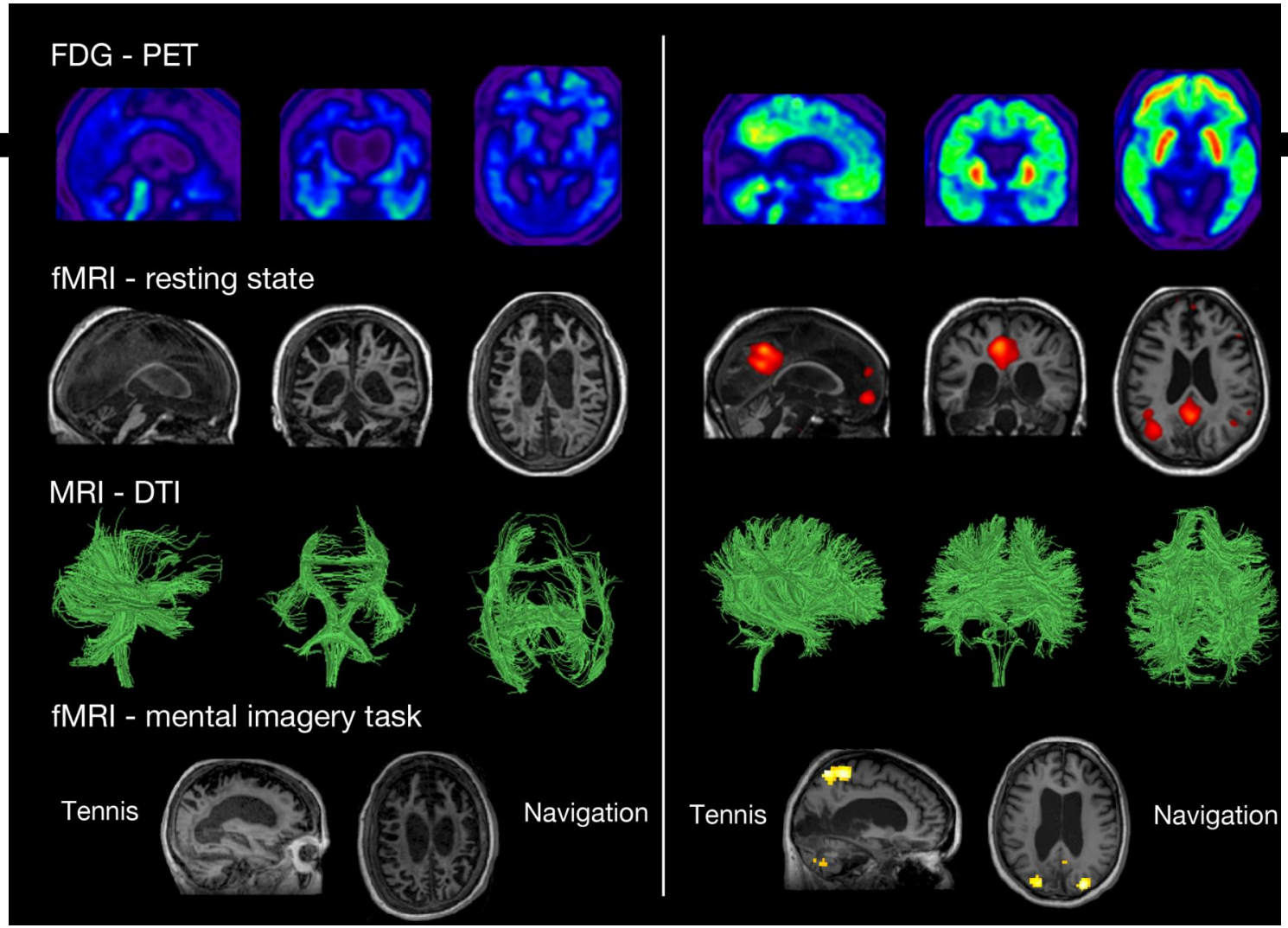


Decreased complexity



Darmani et al, *Brain Stimul*, 2021

Different profiles of non-responsive patients



UWS

End-of-life discussion

MCS*

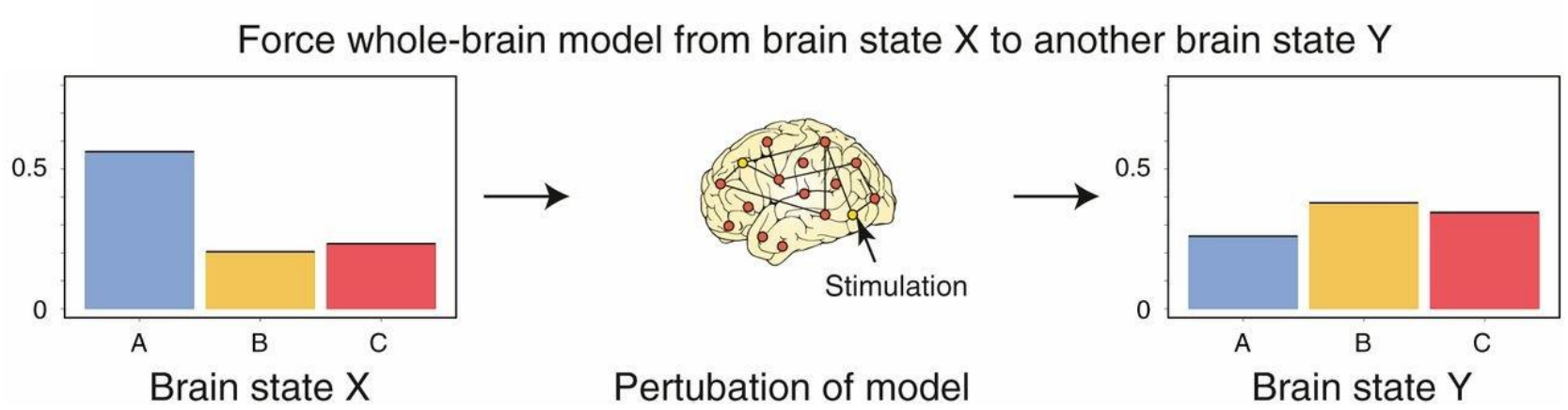
Stimulation

UWS = unresponsive wakefulness syndrome

MCS* = non-behavioral minimally conscious state

Gosseries et al, *Brain Injury*, 2014

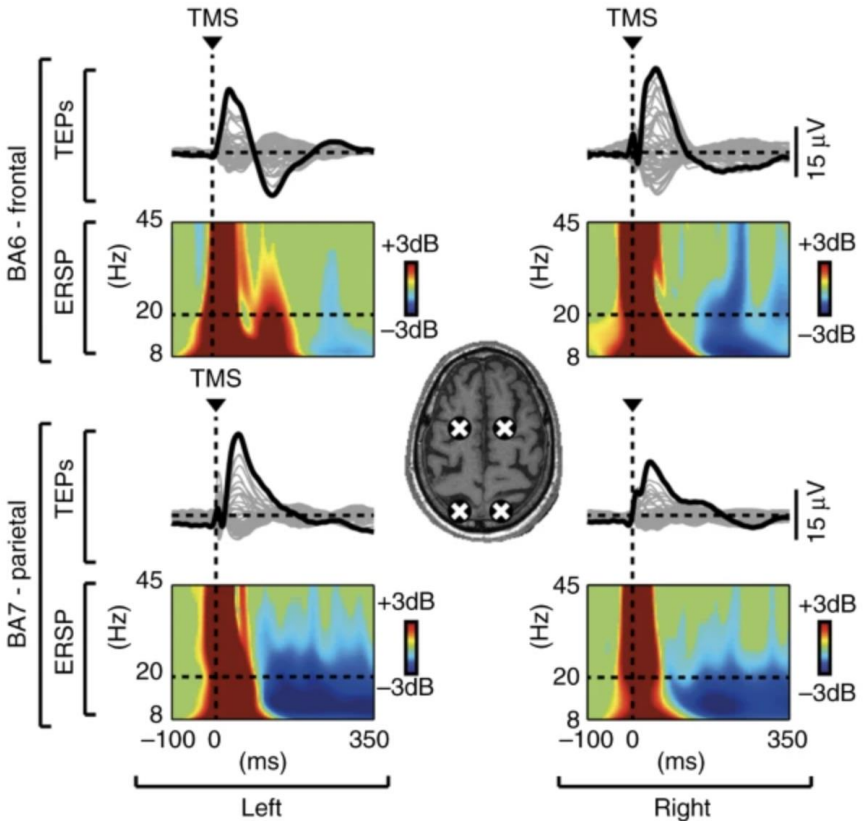
Using TMS to force transitions



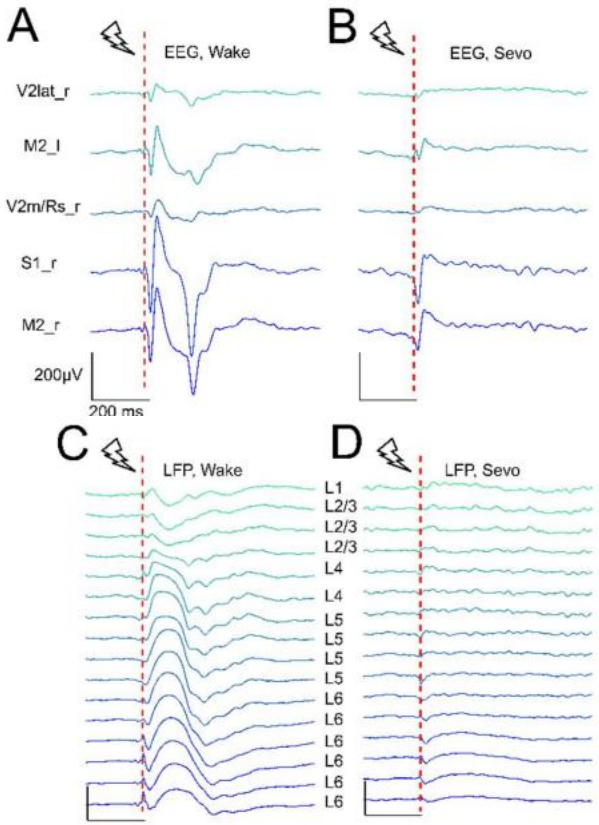
In-silico modeling to promote transition via a perturbation

Deco et al, *PNAS*, 2019

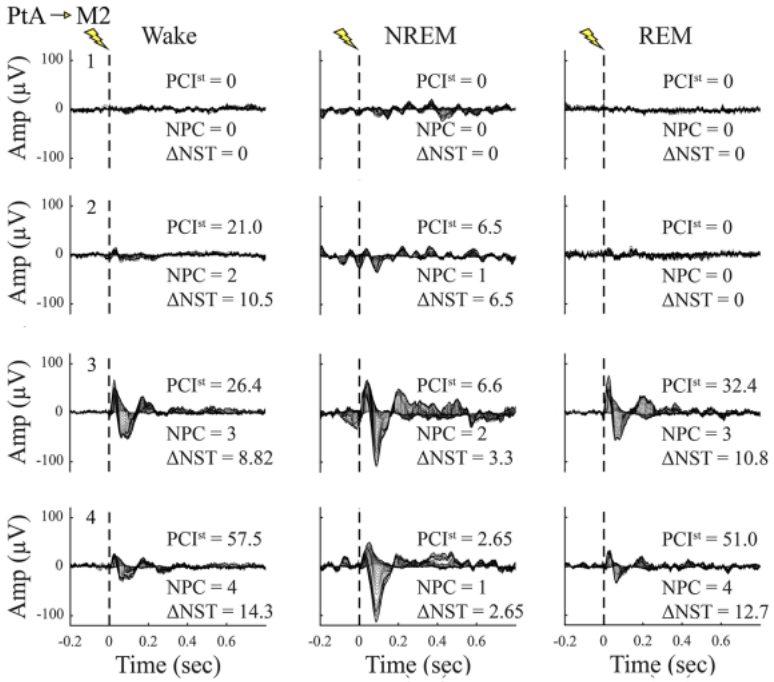
What are the basis of complexity?



Rosanova et al, *Nat. Comm.*, 2019



Hönigsperger et al, *bioRvix*, 2022



Cavelli et al, *bioRvix*, 2022