

Assessing consciousness using transcranial magnetic stimulation combined with electroencephalography

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Belgium



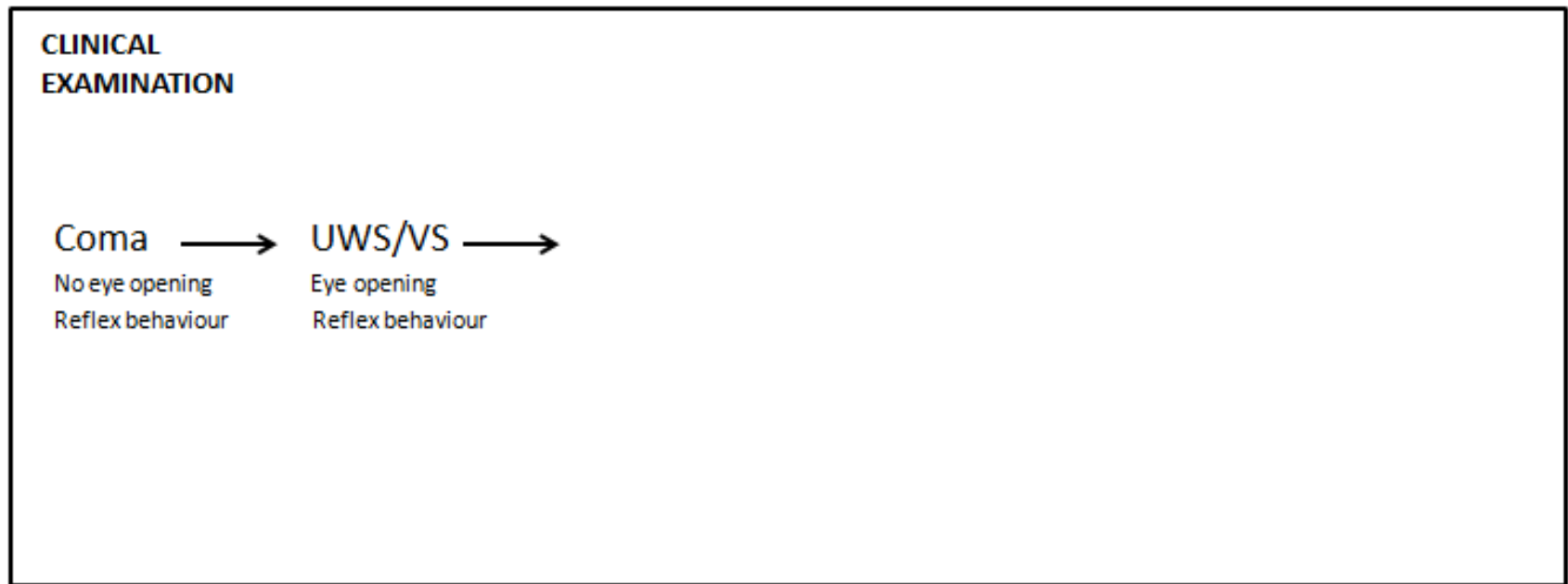


What happens after a coma?

CLINICAL EXAMINATION

Coma →
No eye opening
Reflex behaviour

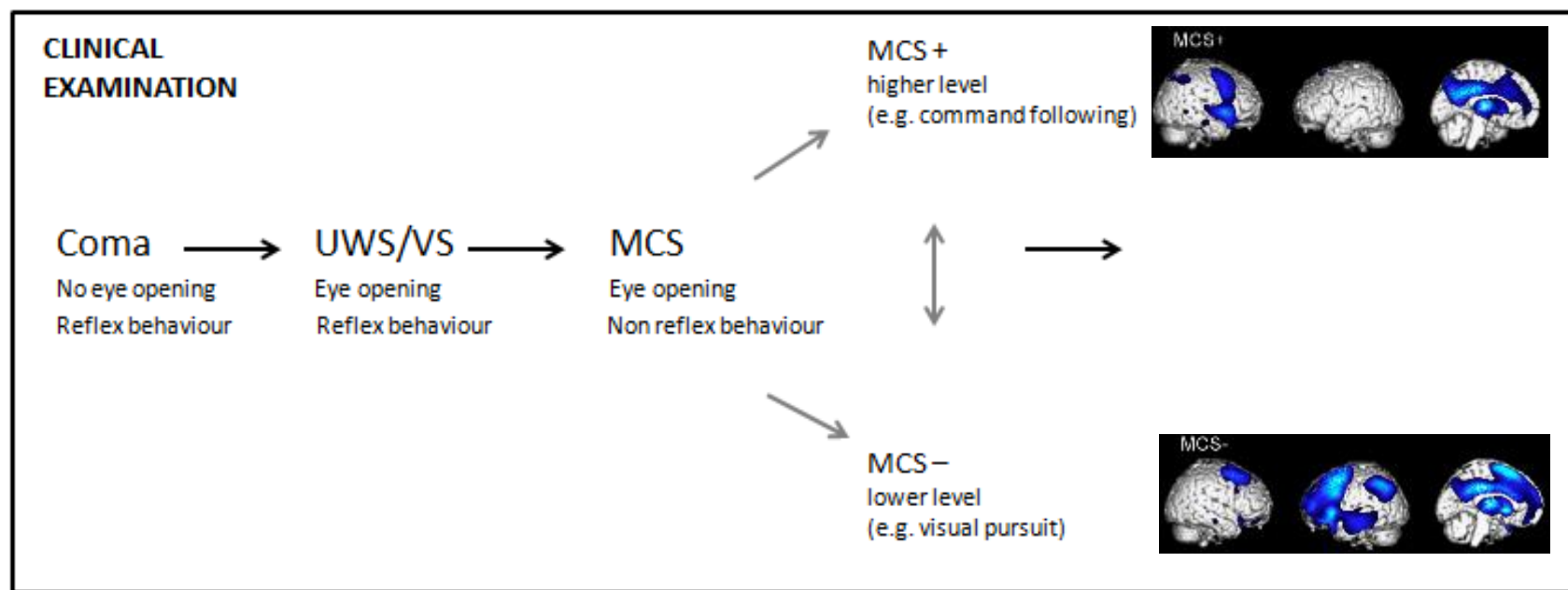
What happens after a coma?



UWS=unresponsive wakefulness syndrome

VS=vegetative state

What happens after a coma?

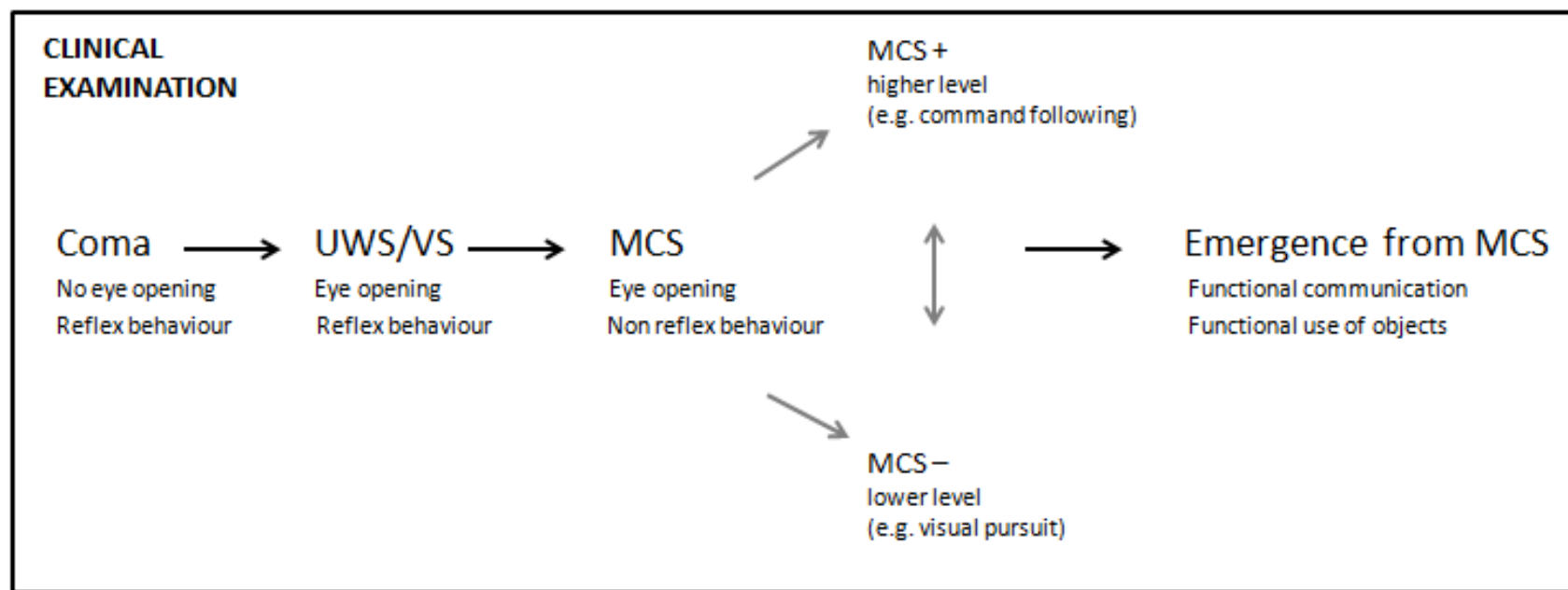


UWS=unresponsive wakefulness syndrome

VS=vegetative state

MCS=minimally conscious state

What happens after a coma?

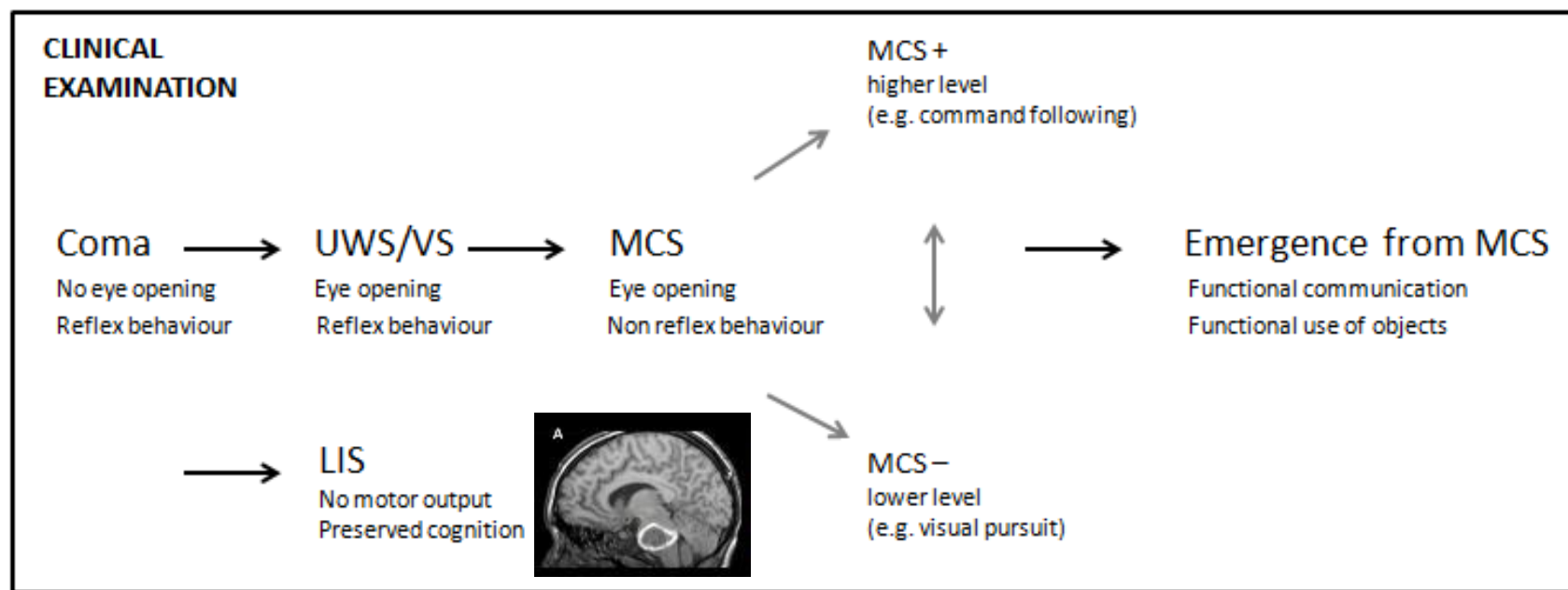


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What happens after a coma?



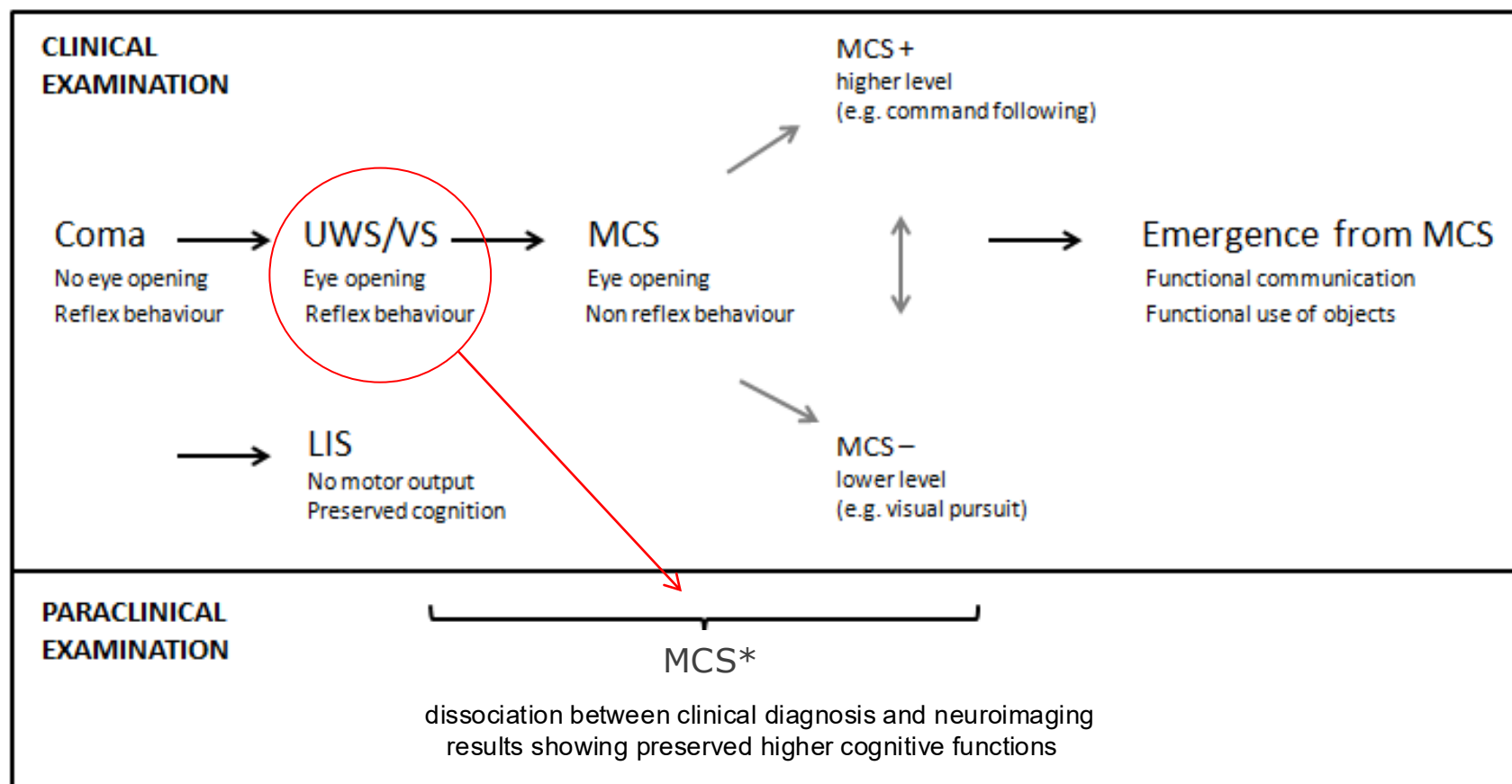
UWS=unresponsive wakefulness syndrome

VS=vegetative state

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LIS=locked-in syndrome

What happens after a coma?

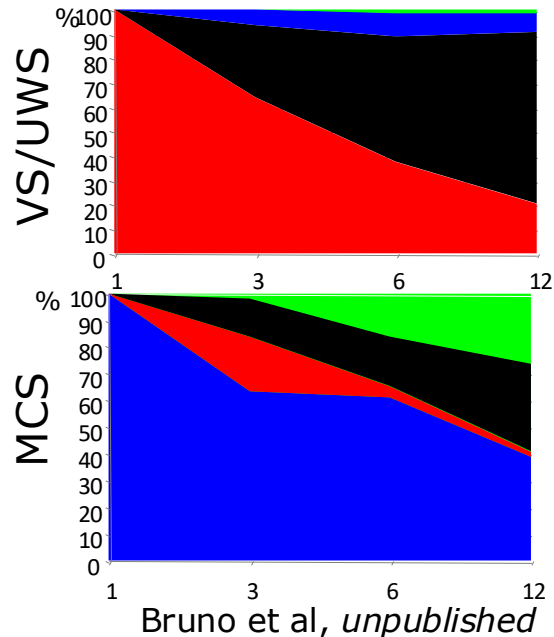


MCS* = non-behavioral minimally conscious state

Accurate diagnosis

Why is it important to properly diagnose patients with disorders of consciousness?

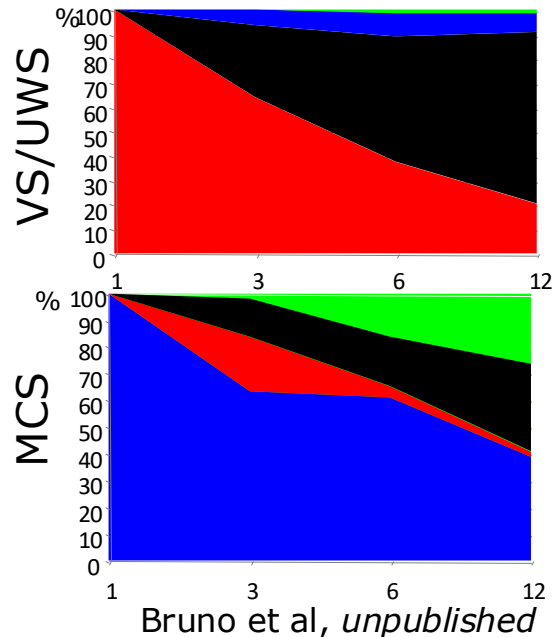
Prognosis (MCS > VS)



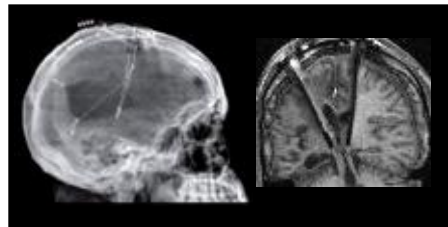
Accurate diagnosis

Why is it important to properly diagnose patients with disorders of consciousness?

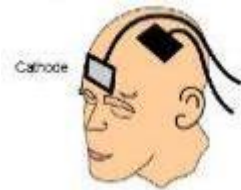
Prognosis



Treatment (MCS > VS)



Schiff et al, *Nature*, 2007

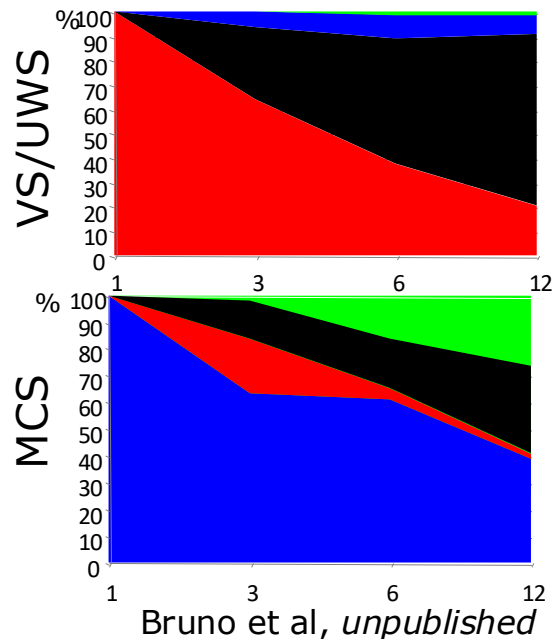


Thibaut et al, *J Neurology* 2014
Angelakis et al, *Arch Phys Med Rehabil* 2016

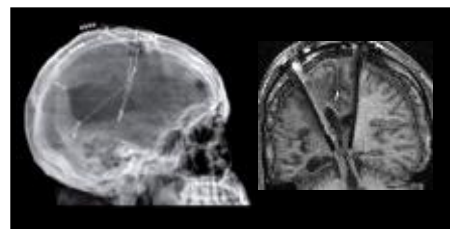
Accurate diagnosis

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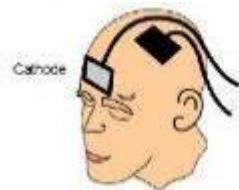
Prognosis



Treatment

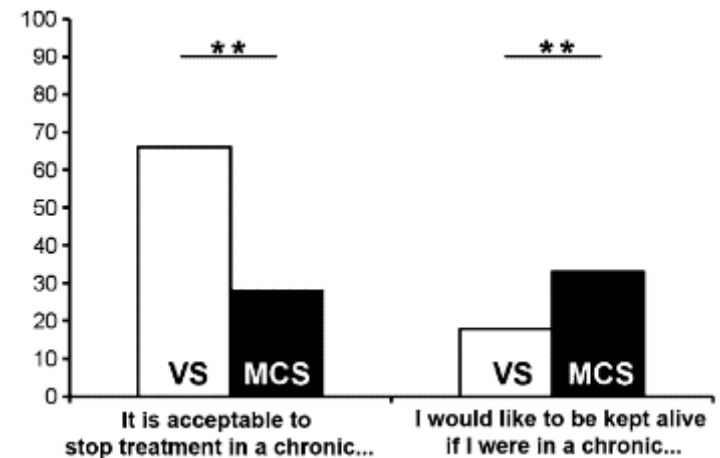


Schiff et al, *Nature*, 2007



Thibaut et al, *J Neurology* 2014
Angelakis et al, *Arch Phys Med Rehabil* 2016

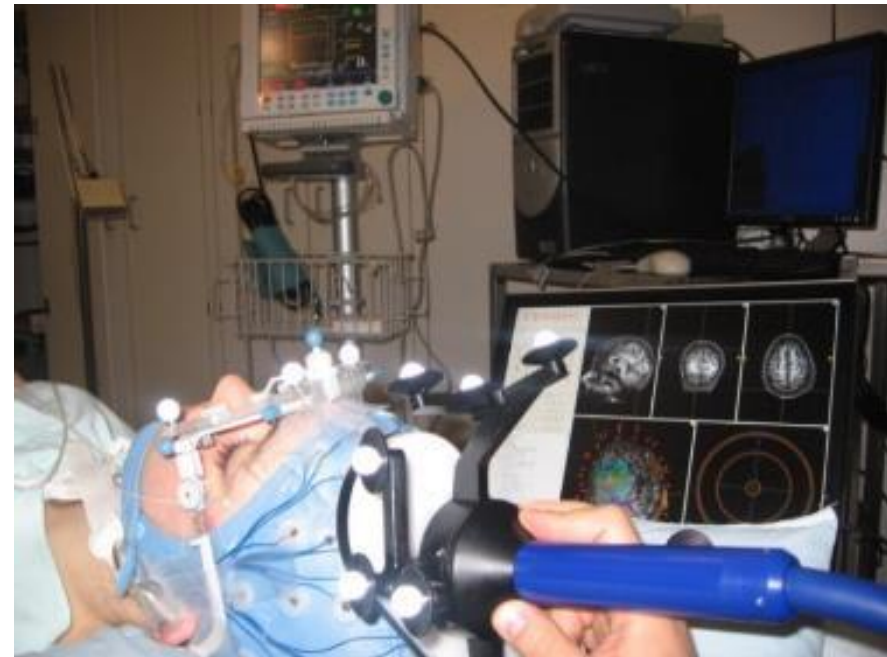
Ethics



Demertzi et al, *J Neurology* 2011

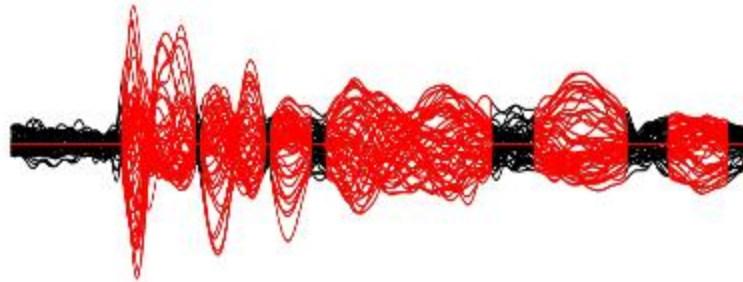
TMS-EEG

Transcranial magnetic stimulation & electroencephalography

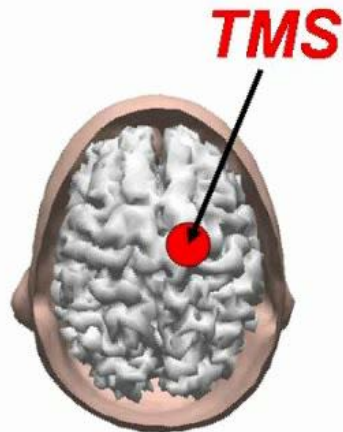


TMS-EEG responses in healthy subjects

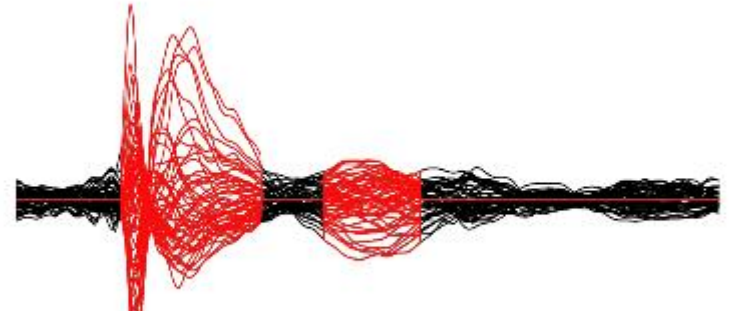
Wakefulness



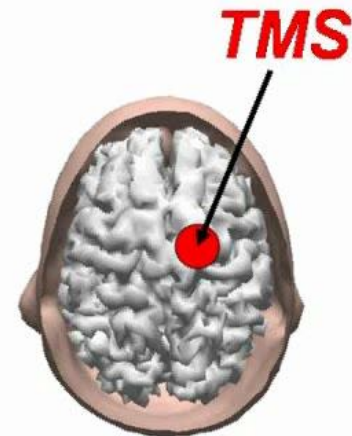
0 ms



Deep sleep



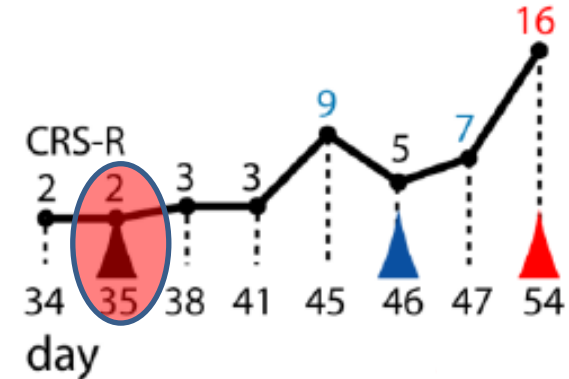
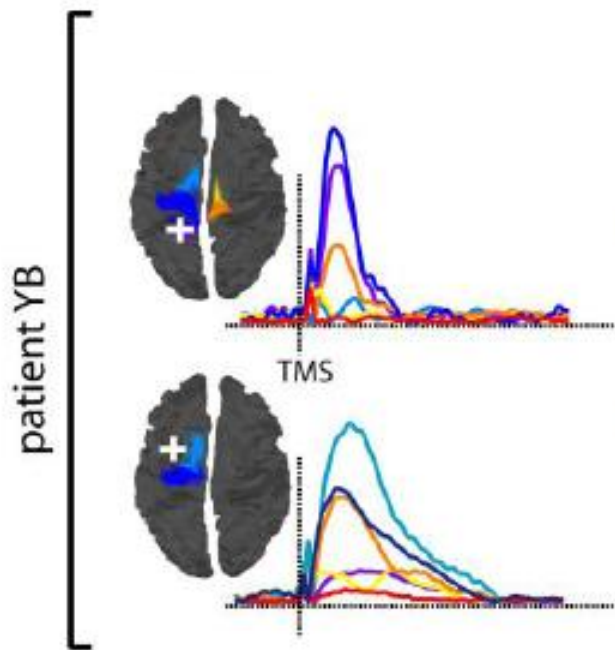
0 ms



TMS-EEG in comatose patients



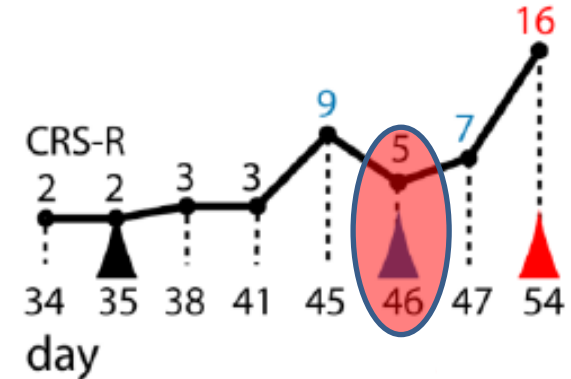
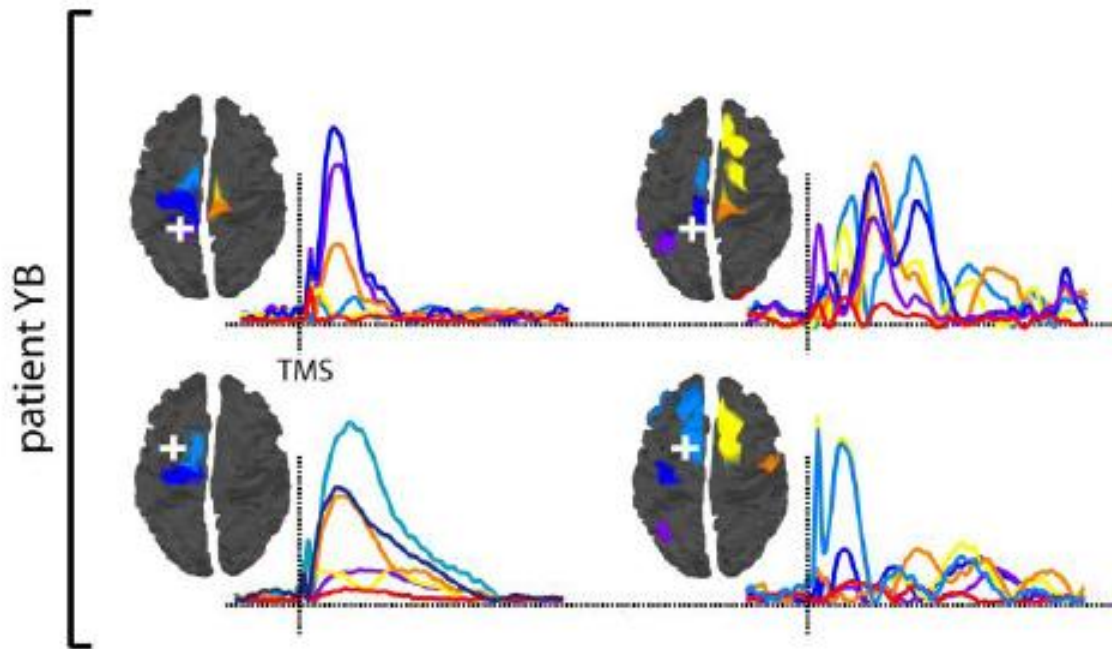
Unresponsive state



TMS-EEG in comatose patients



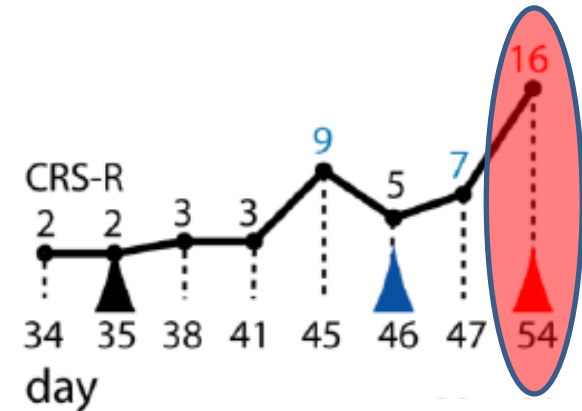
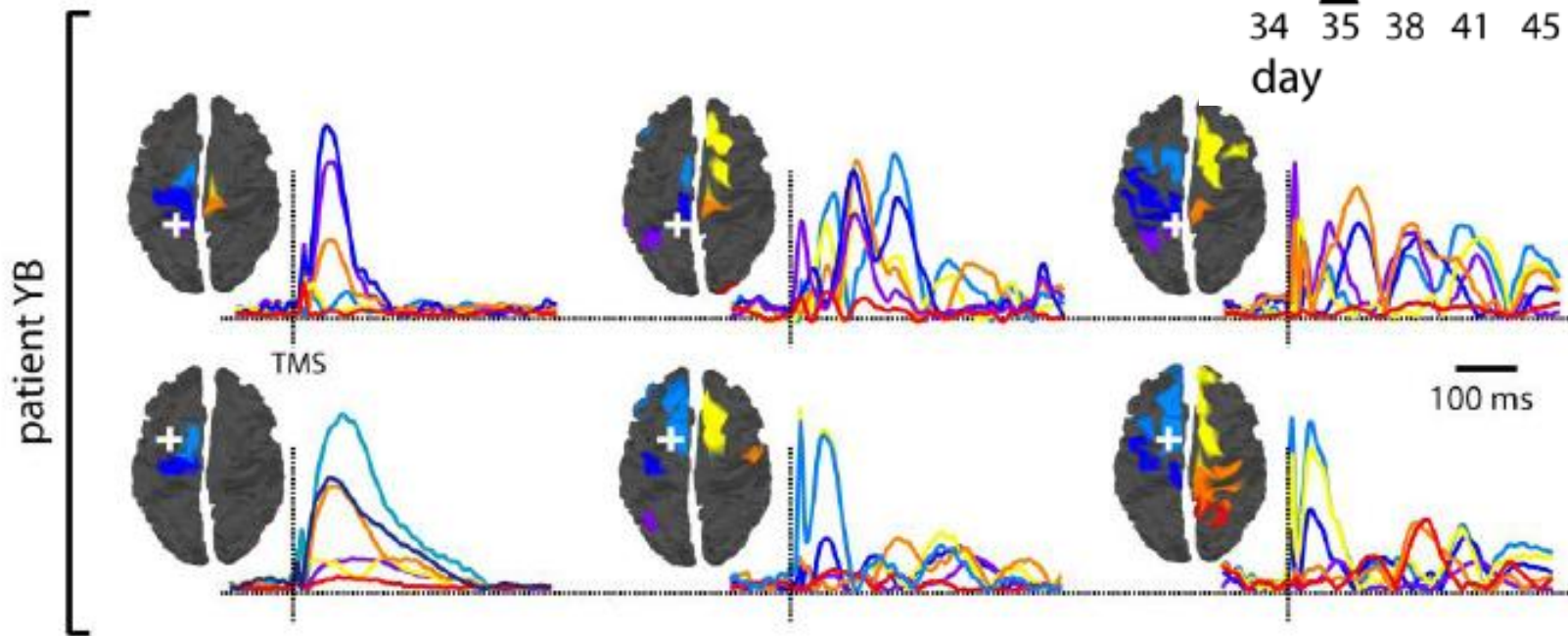
Unresponsive state Minimally conscious state



TMS-EEG in comatose patients



Unresponsive state Minimally conscious state

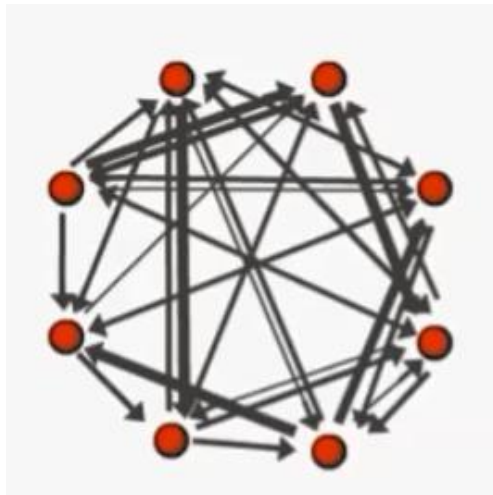


Perturbational complexity index – PCI

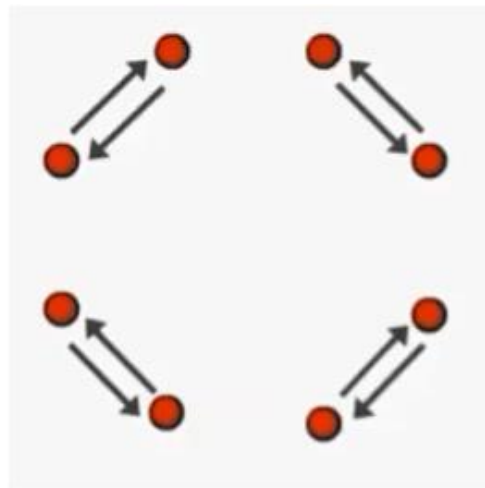


Integrated information theory

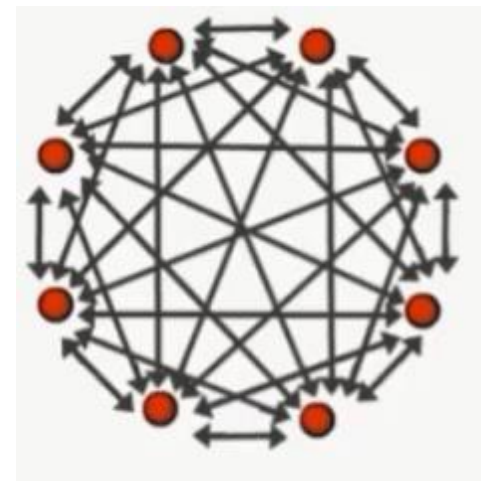
Consciousness = integration and differentiation



Consciousness

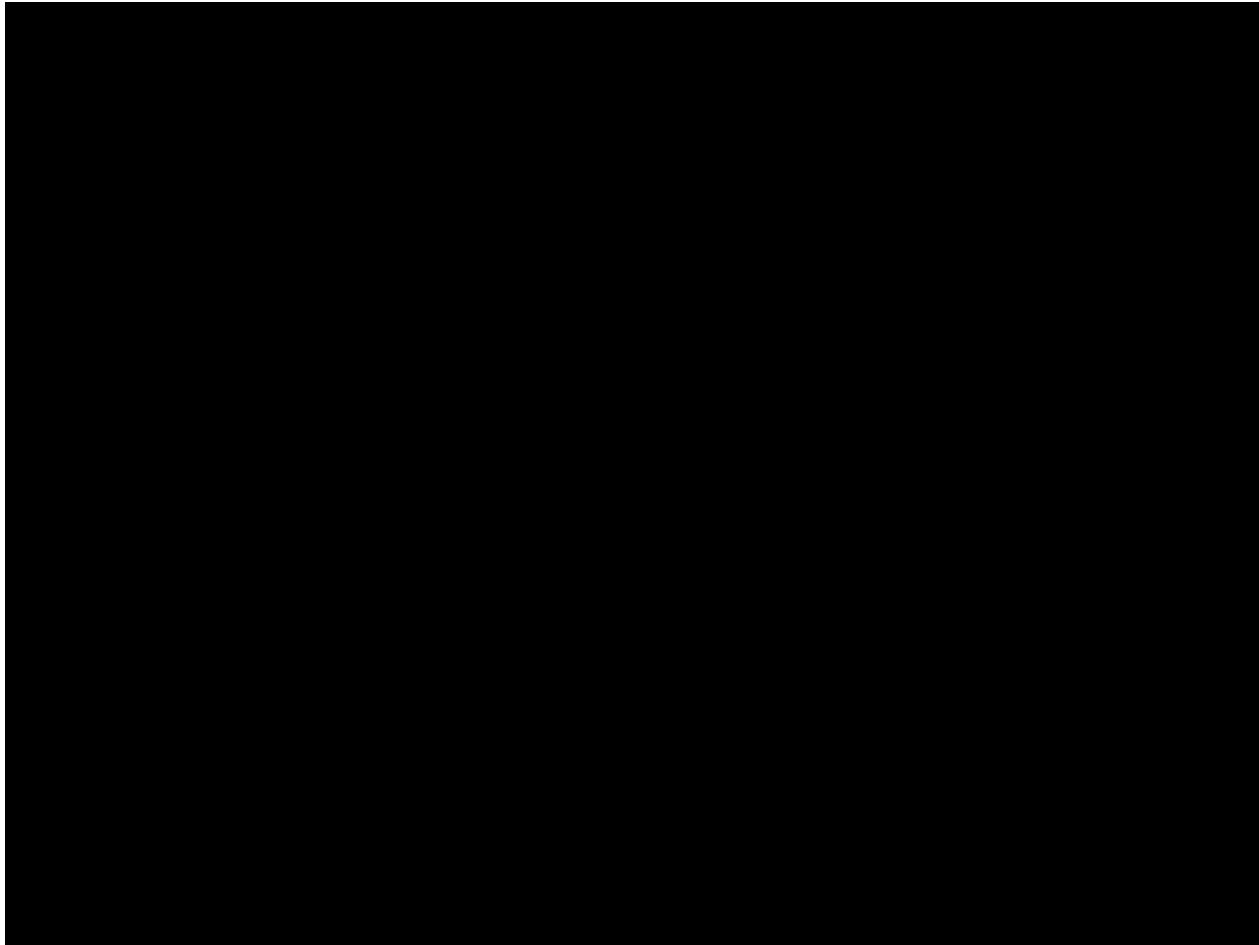


Loss of integration



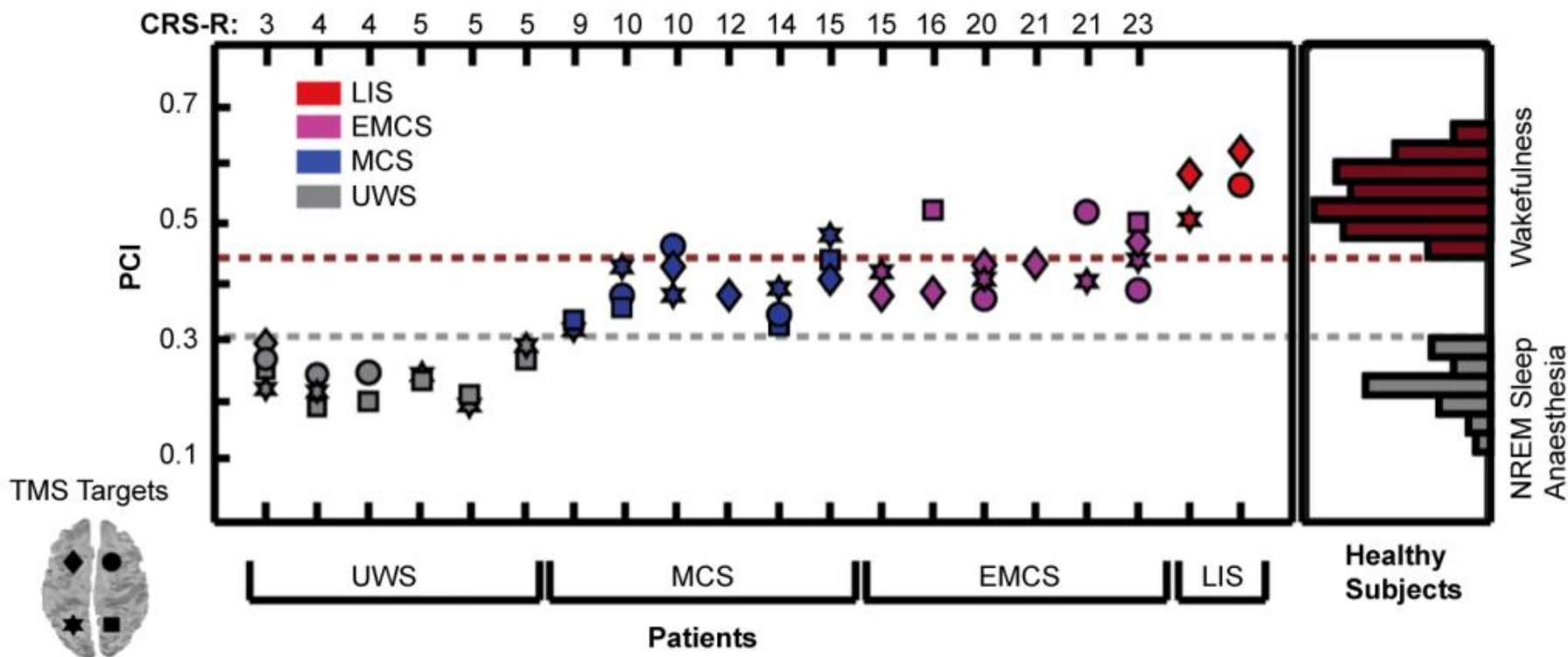
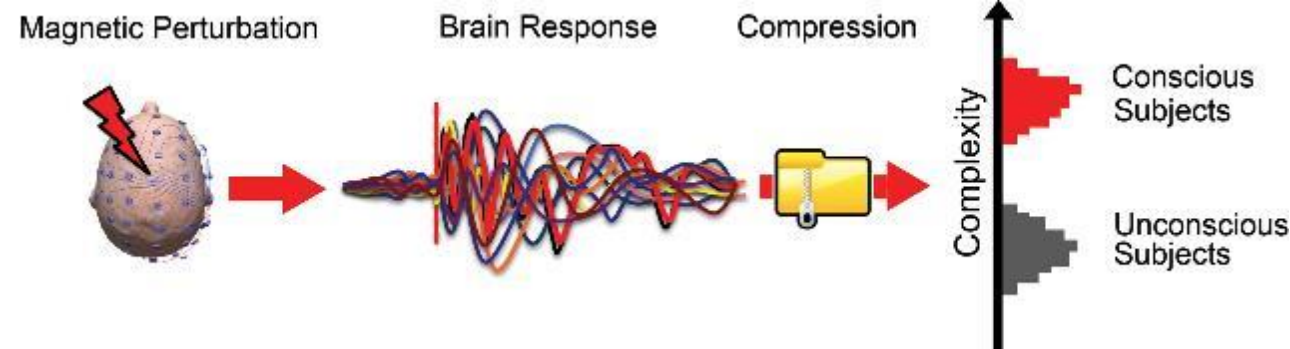
Loss of differentiation

Perturbational complexity index – PCI

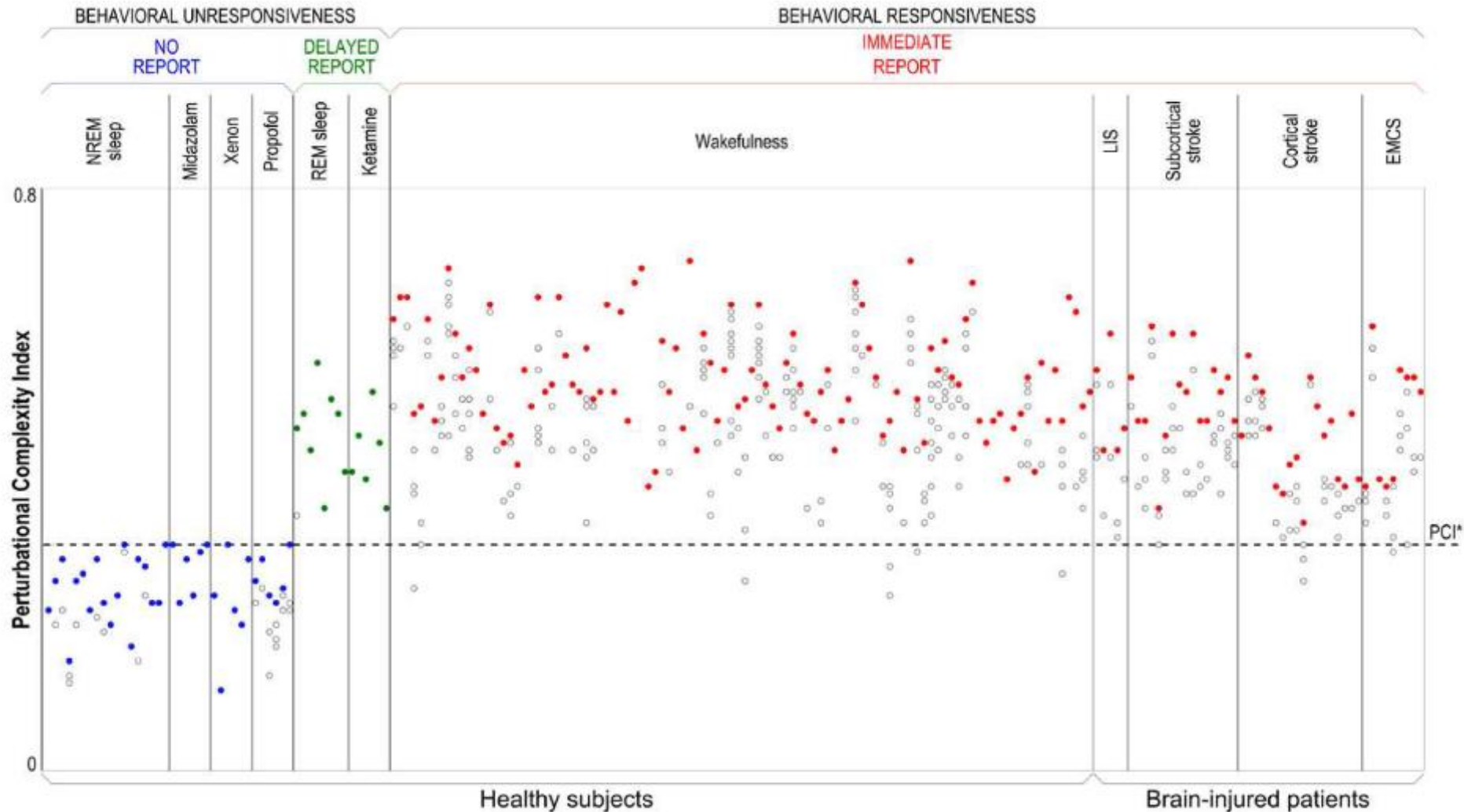


PCI → measures the ability of thalamo-cortical circuits to integrate information (no motor or sensitive processing or subjects' participation)

Perturbational complexity index in comatose patients

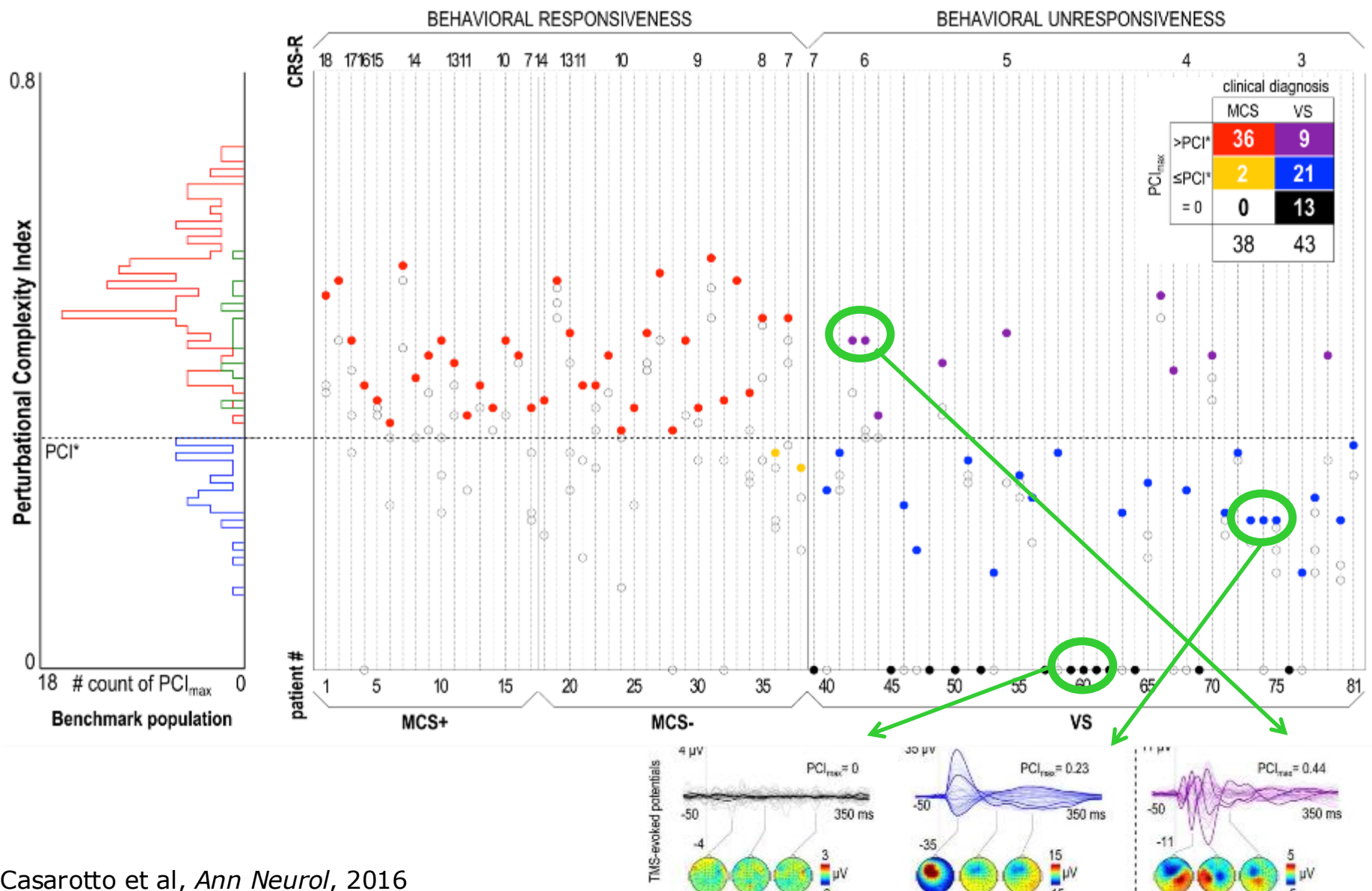


Perturbational complexity index in altered consciousness

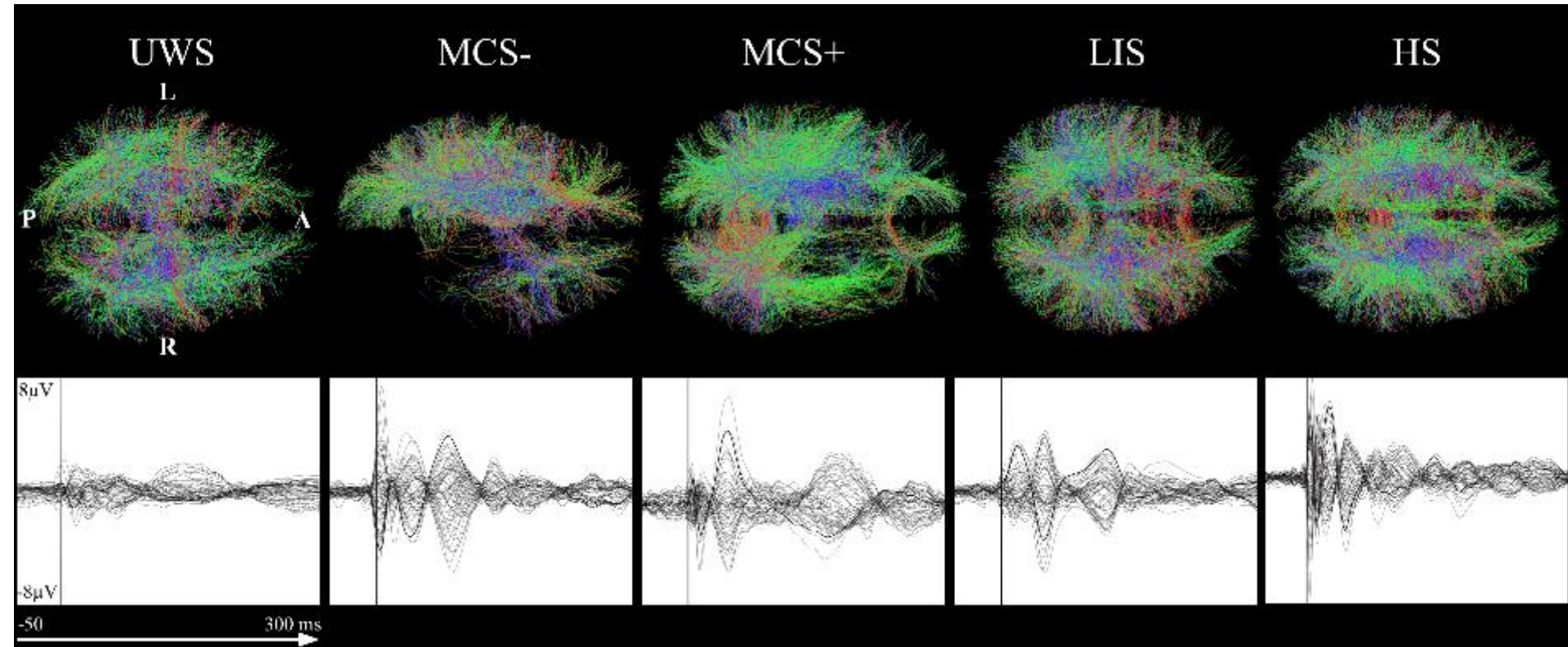


0.31 → cutoff discriminating csc/uncsc with 100% accuracy

Perturbational complexity index in comatose patients



TMS-EEG and DTI



Correlation between complexity of the response and white matter integrity



TMS-EEG and PET-scan

- Excellent congruence between PET and PCI
2/24 mismatches

- 4 UWS: MCS*

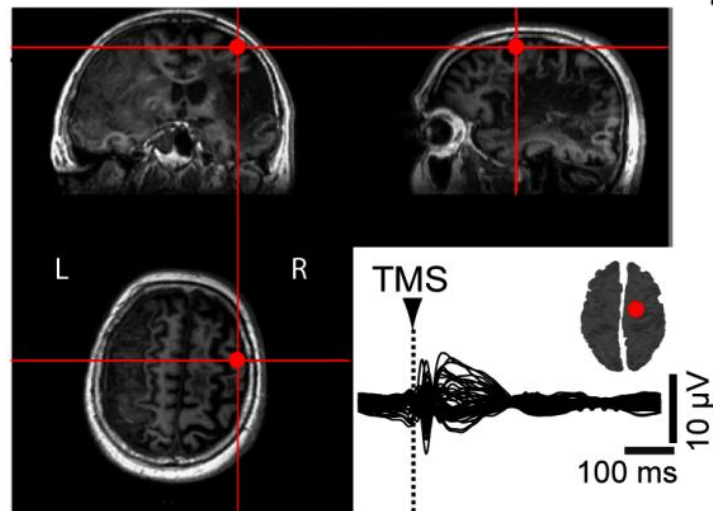
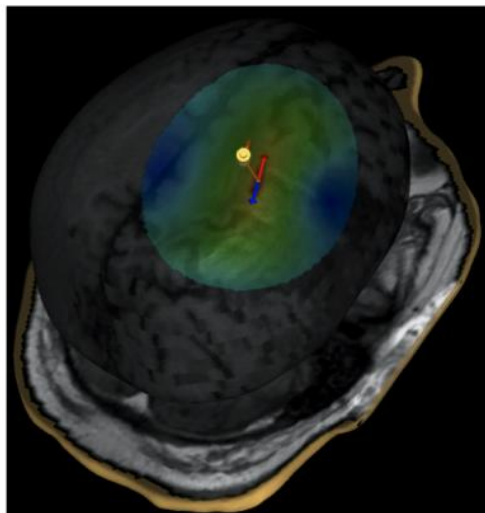


Pat	Best CRS-R	PET	PET CRS-R	PCI
1	23 LIS	LIS	NA	0.62
2	23 LIS	LIS	NA	0.48
3	23 EMCS	EMCS	NA	0.5
4	22 EMCS	EMCS	NA	0.45
5	17 MCS	MCS	17	0.43
6	15 MCS	MCS	12	0.46
7	12 MCS	MCS	NA	0.44
8	11 MCS	MCS	10	0.43
9	11 MCS	MCS	4	0.38
10	11 MCS	MCS	8	0.33
11	11 MCS	MCS	11	0.38
12	13 MCS	MCS	12	0.39
13	8 MCS	MCS	7	0.4
14	7 MCS	MCS	3	0.4
15	10 MCS	MCS	10	0.22
16*	5 UWS	MCS	3	0.49
17*	7 UWS	MCS	5	0.4
18*	5 UWS	MCS	3	0.37
19*	5 UWS	MCS	5	0.38
20*	7 UWS	MCS	7	0.25
21	7 UWS	UWS	7	0.2
22	6 UWS	UWS	5	0.27
23	6 UWS	UWS	5	0
24	5 UWS	UWS	4	0

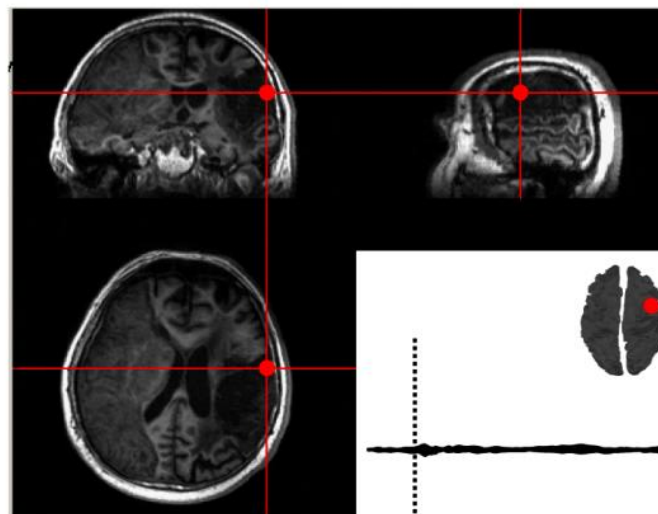
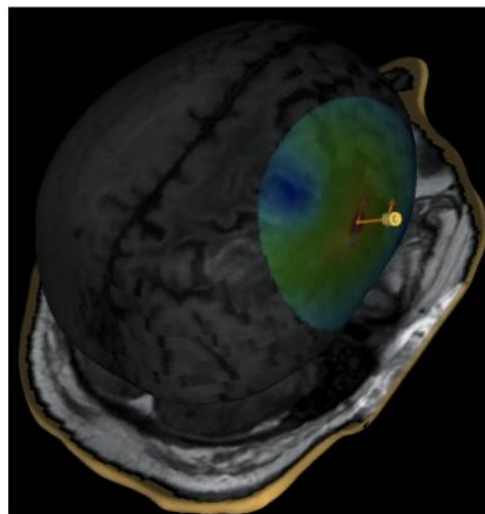


TMS and structural brain lesions

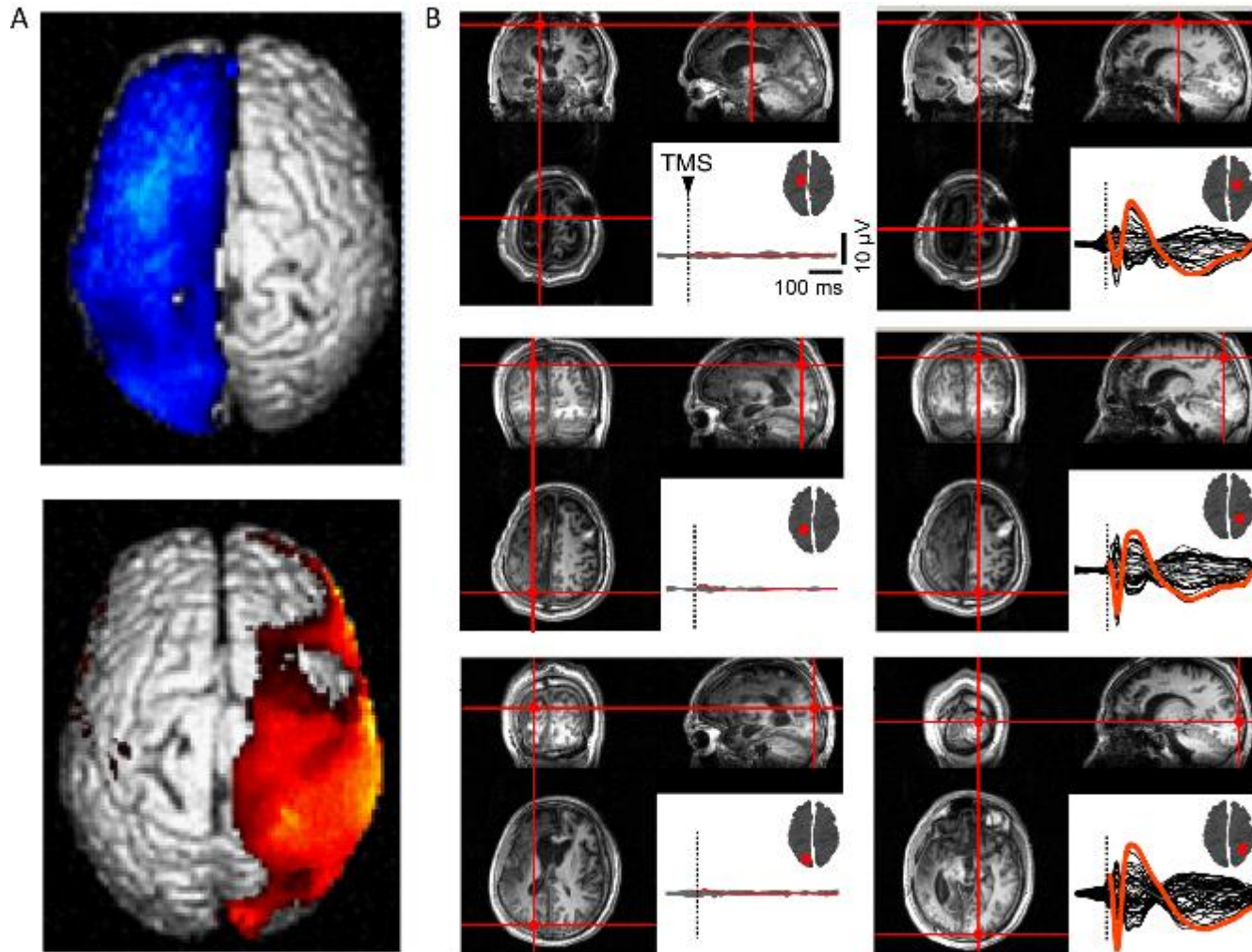
**Healthy
region**



**Brain
lesion**



TMS and metabolic brain lesions





Practically,
how does it work?



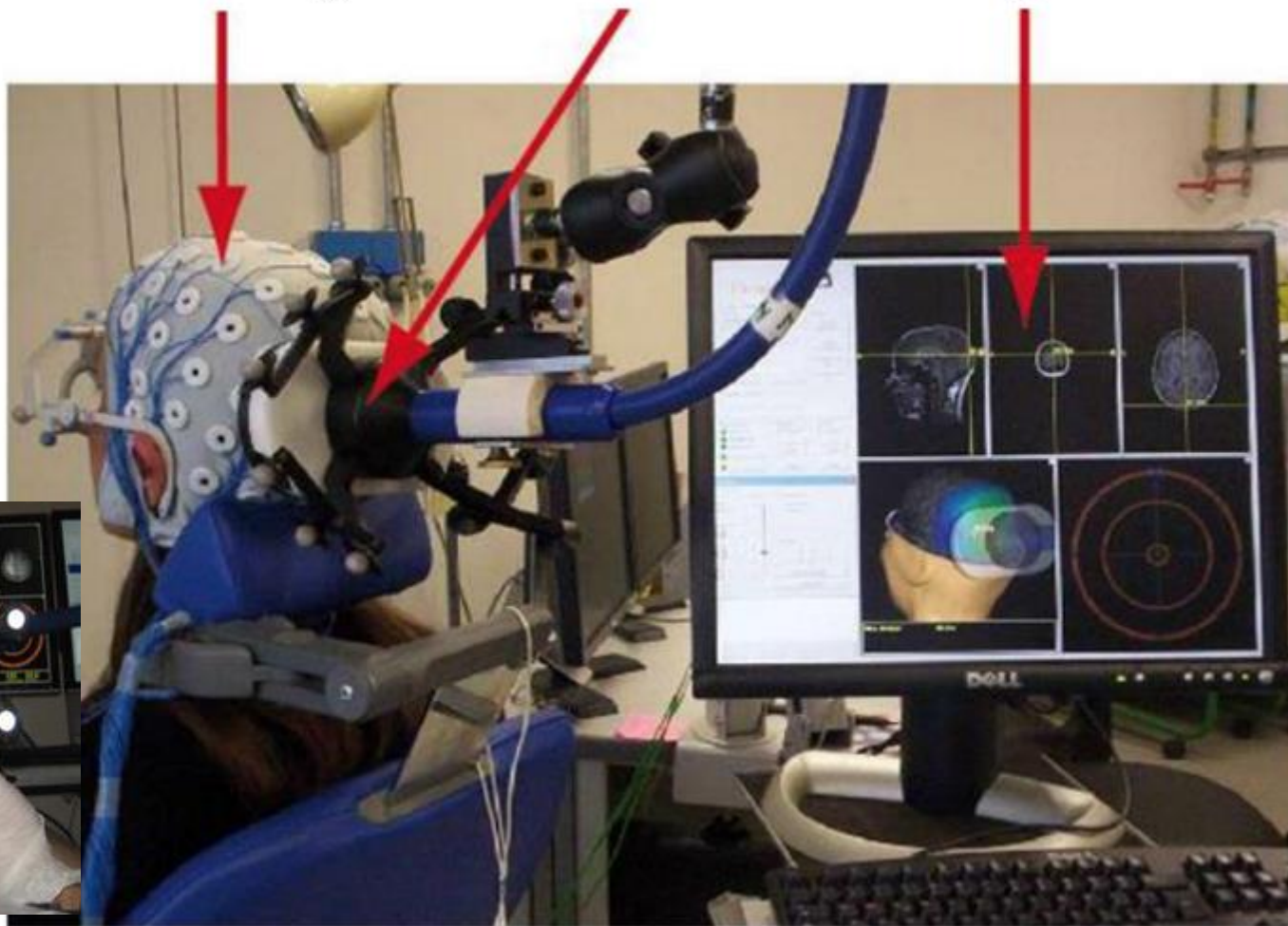
Experimental set-up

Nexstim system
(Helsinki, Finland)

Recording

Stimulation

Navigation



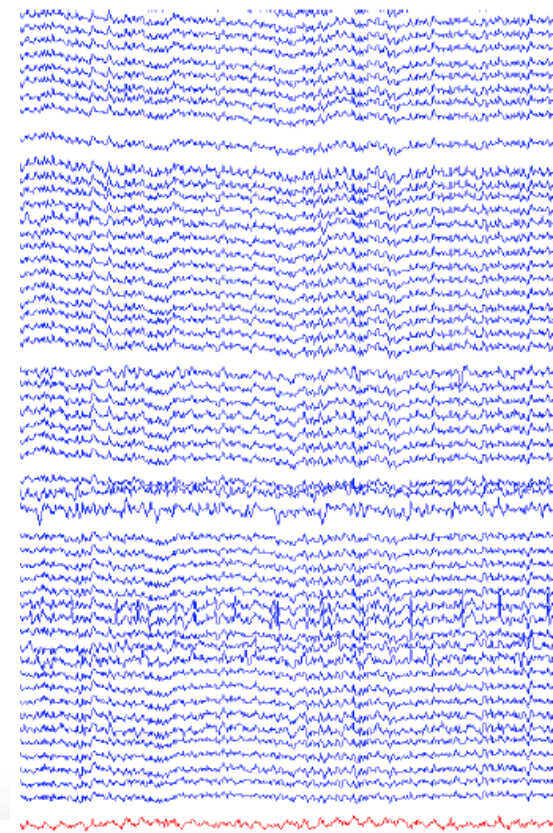


EEG (eXimia)

- Impedances
- Ground & references & EOG electrodes
- Check raw signal
- 5 minutes resting state eyes open

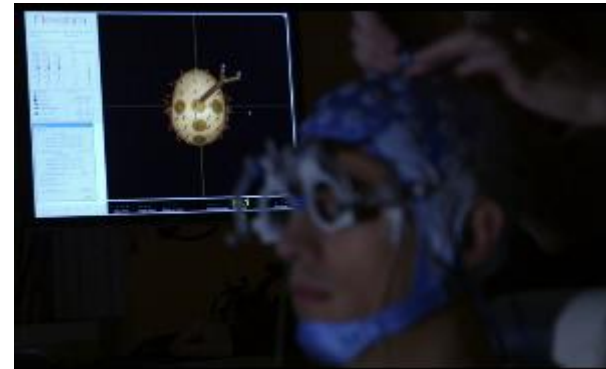
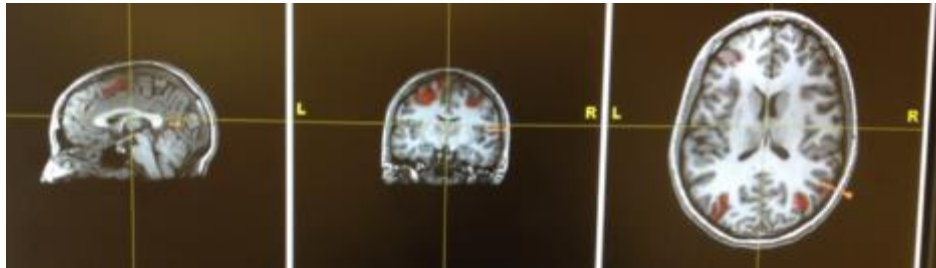
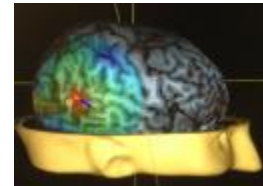


Electroconductive gel: proper viscosity, not too liquid, not too jelly!



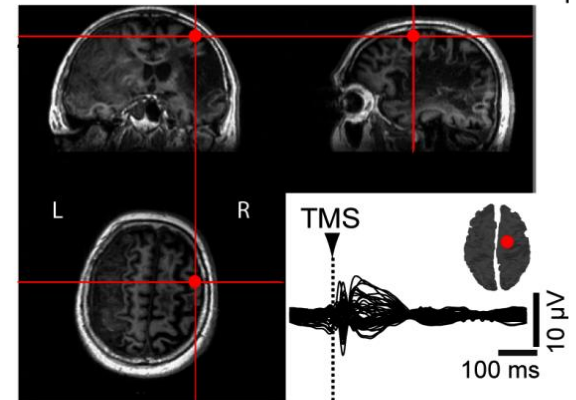
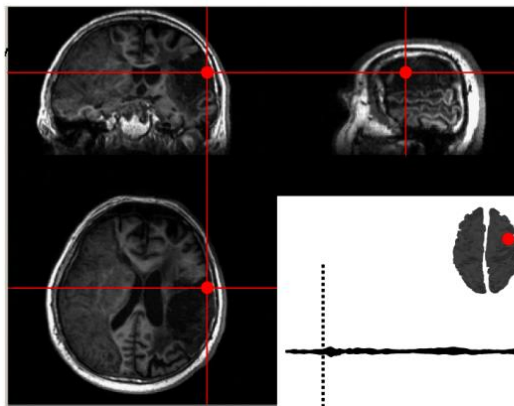
Neuro-navigation (NBS)

- MRI T1
- Set MRI landmarks (nose, L & R tragus)
- Co-registration head/MRI



- Set stimulation points (premotor, precuneus)

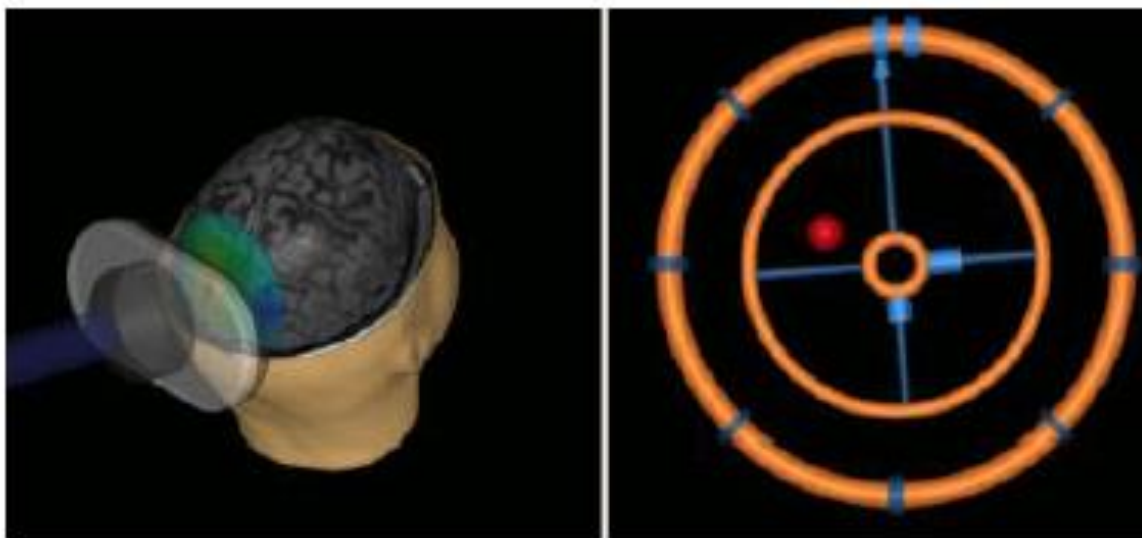
!! Avoid brain lesion !!





TMS

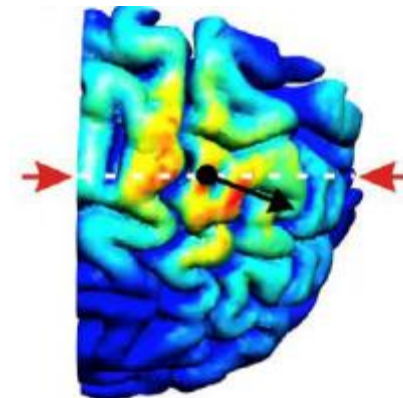
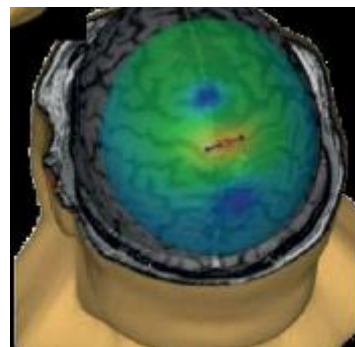
- Double eight coil
- Air cool system
- Single pulses (2-2.3 sec interval)
- Intensity 120 V/m (up to 200 V/m – max output 100%)
- White noise masking + thin layer between coil and scalp
- 250 trials minimum/session





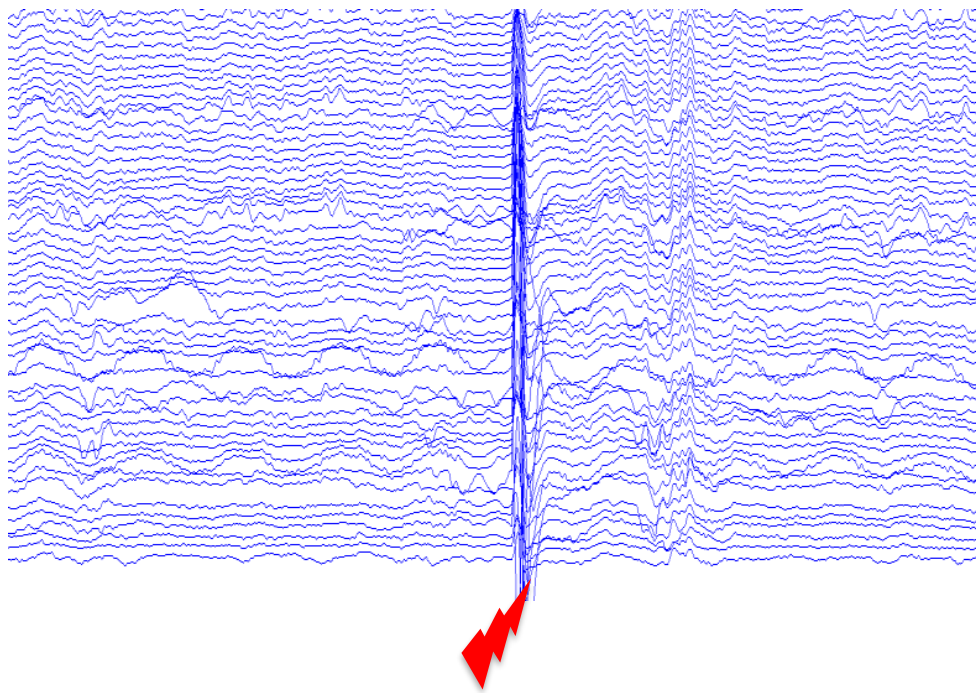
Find a good spot!

- Medial region
- Stimulation on the gyral crowns that lay orthogonally to the induced electric field

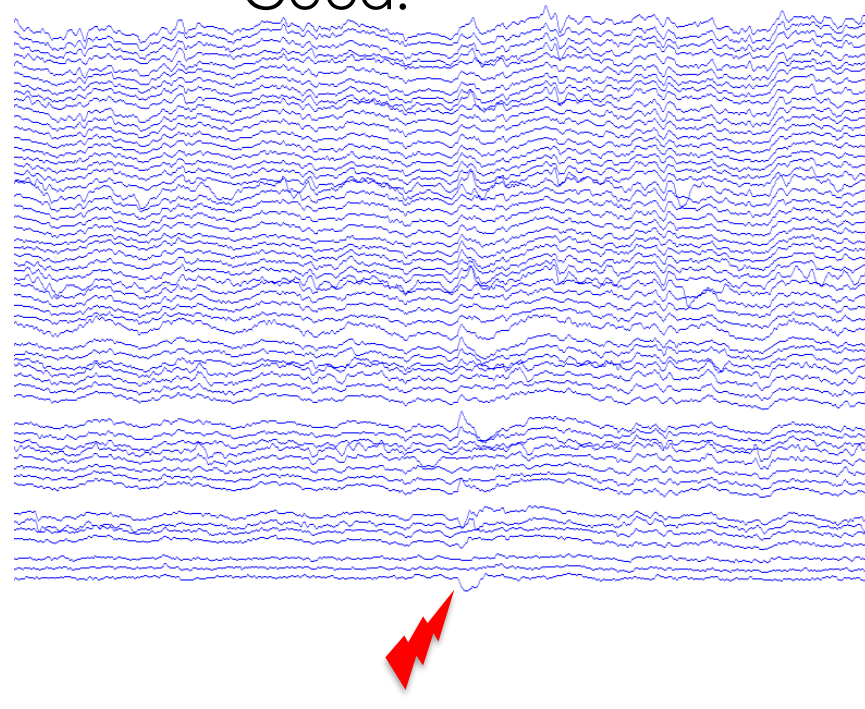


Opitz et al, Neuroimage, 2011

Bad: artifact



Good!



Average TMS-evoked potentials

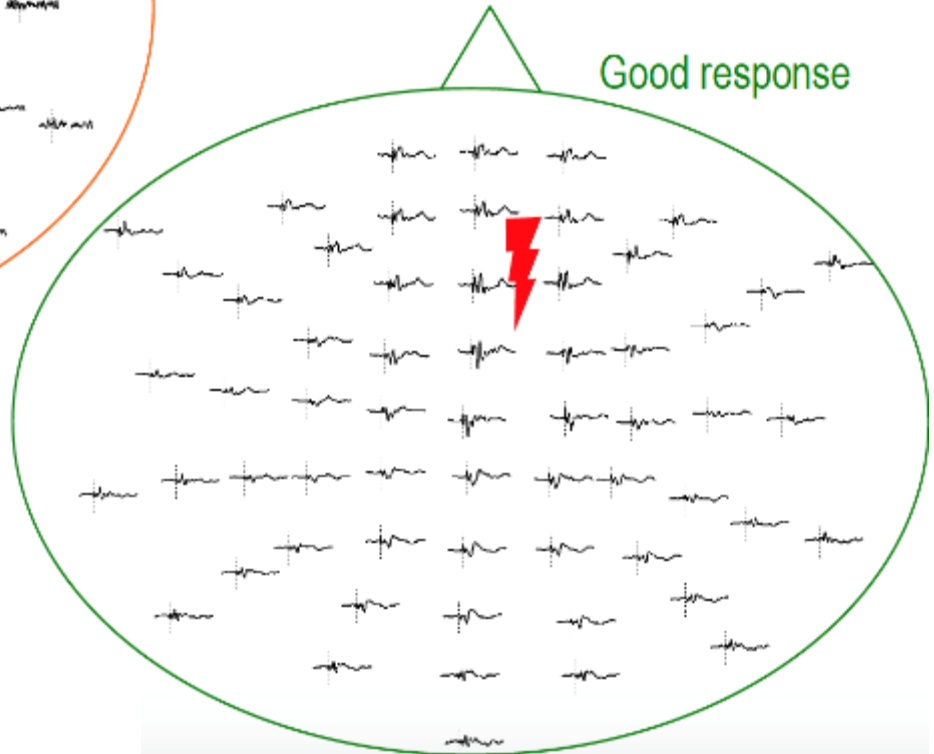
No response



- Peak-to-peak 15-20 μV
- Differentiation L/R
- No muscle
- No auditory response
- Flat EOG

→ continue

Good response

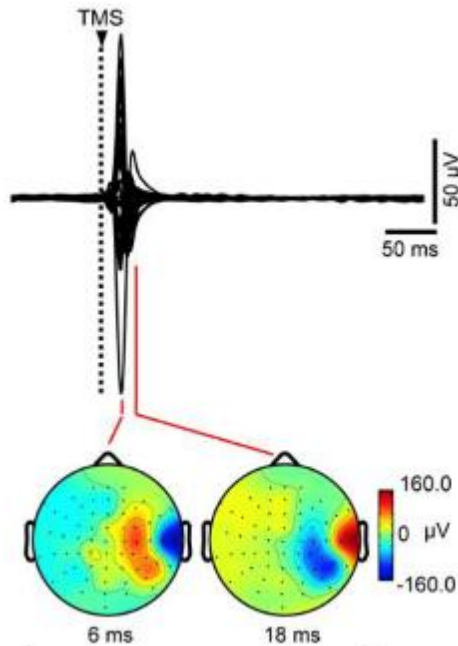


→ Stop

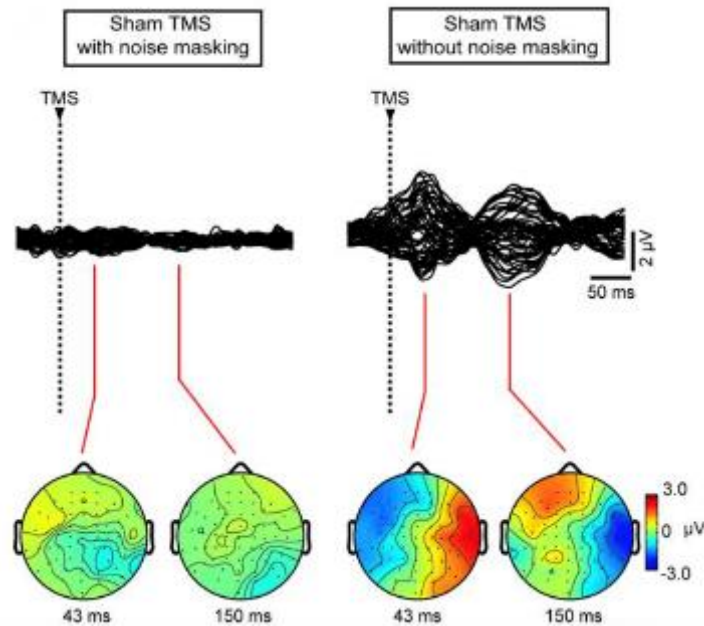
- Change spot
- Rotate coil
- Increase intensity

Check for...

Muscle artifact



Auditory artifact

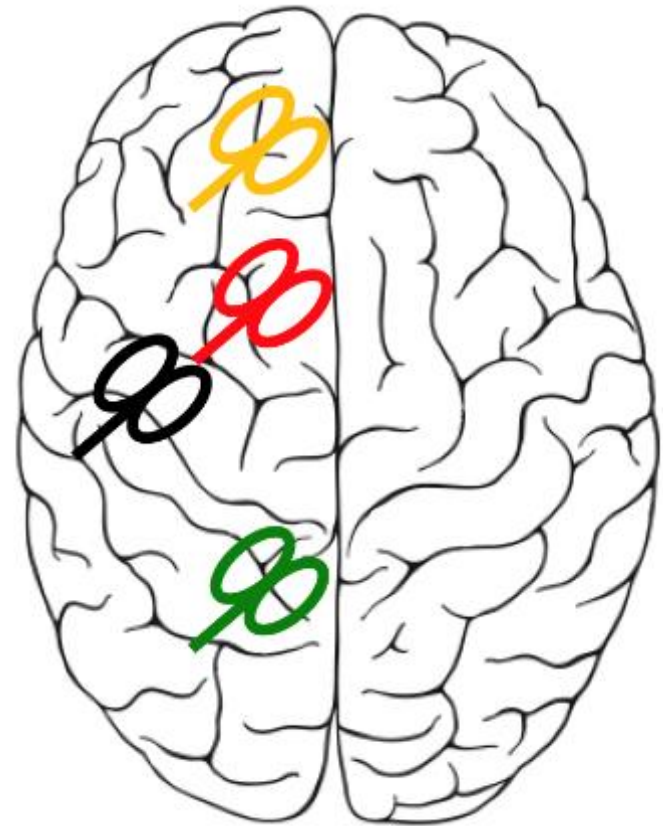
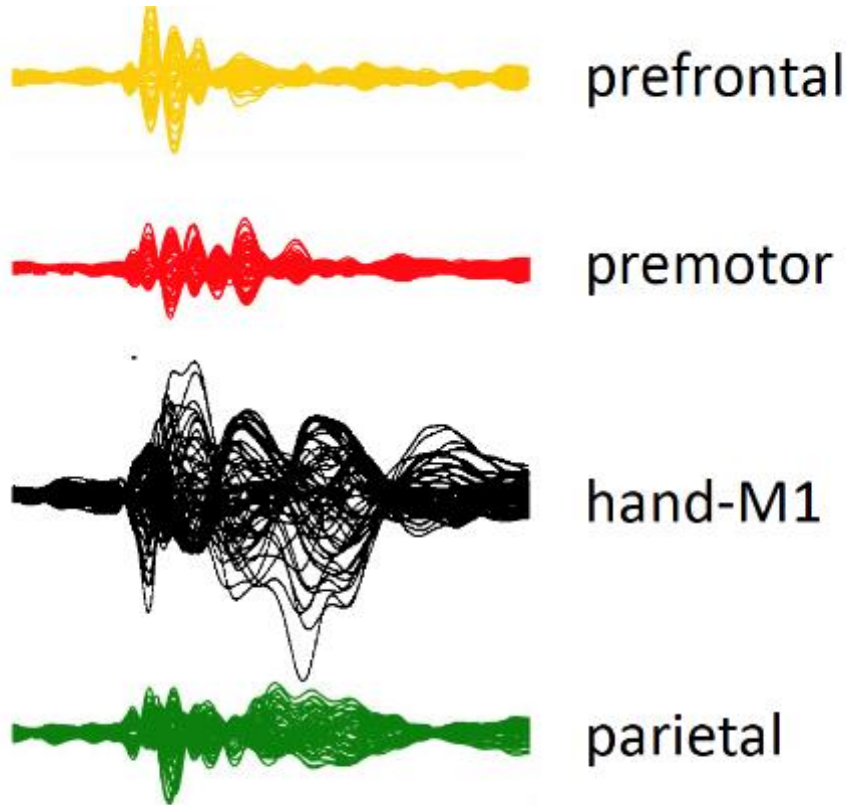


Sleeping?

- Eyes open
- CRS-R arousal protocol
- Breaks

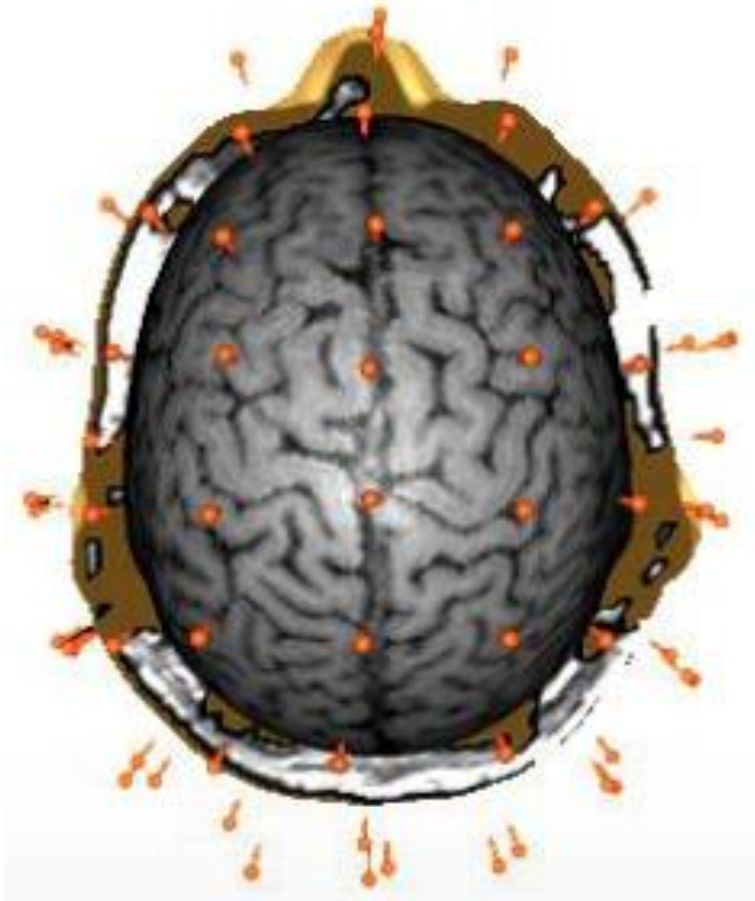
Different responses...

... from different cortical areas





At the end...



Practically...

- **Need 2-3 people minimum**
- **Lots of expertise**
- **Total of 3-4 hours**
- **Heavy set-up**
- **No epilepsy**



Basic analyses steps (ERPs)

1. Create data structure and add all sessions and parameters

2. Filtering

3. Split trials

4. Bad channels rejection

5. Bad trials rejection

6. Epoching

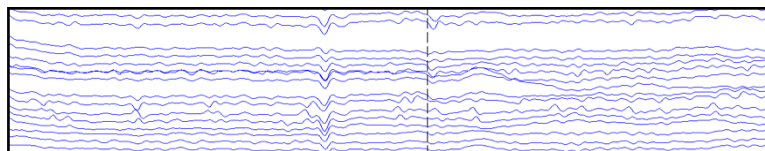
7. Baseline correction

8. Downsampling

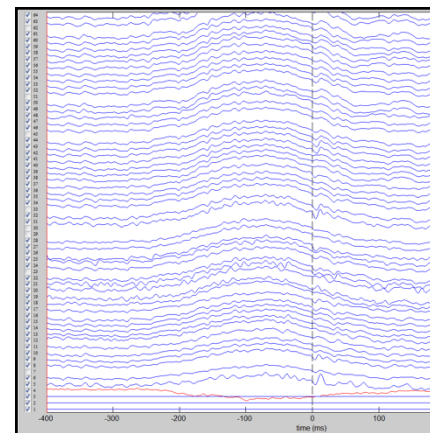
9. Re-referencing to the average reference

10. Data decomposition methods for artefact reduction: ICA

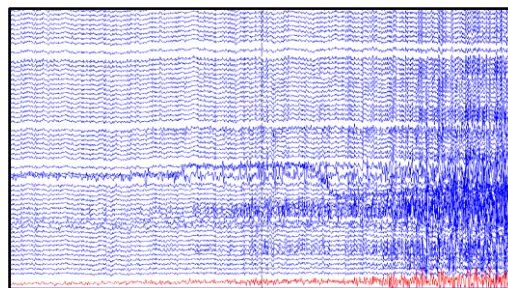
11. Interpolation of bad channels



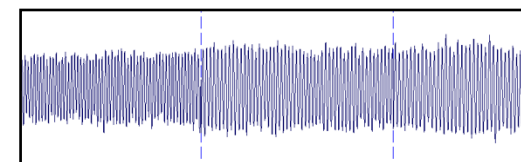
Electrode movement



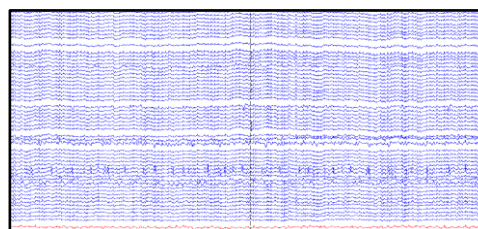
Slow eye movement



Muscle artifact



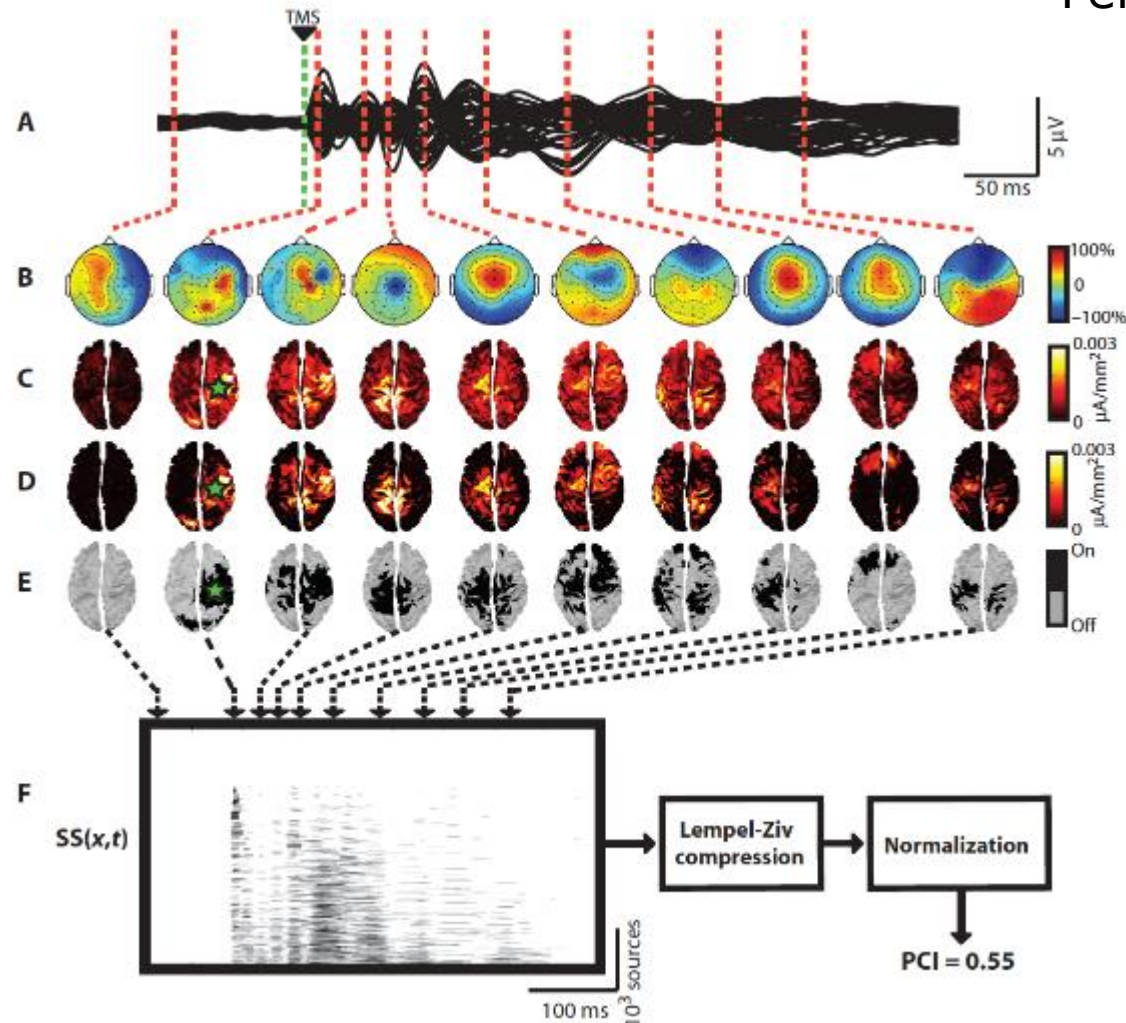
Sector artifact



Good trial

Calculation of PCI

Perturbational complexity index



TMS-evoked response

Instantaneous voltage distributions

Cortical currents

Significant TMS-evoked cortical currents

Binary spatiotemporal distribution of significant sources (SS)

PCI = 0.55

Case-report

- Patient 40yo, Male, 11 months post-trauma (car accident)
- Clinically unresponsive – vegetative
- PET-scan

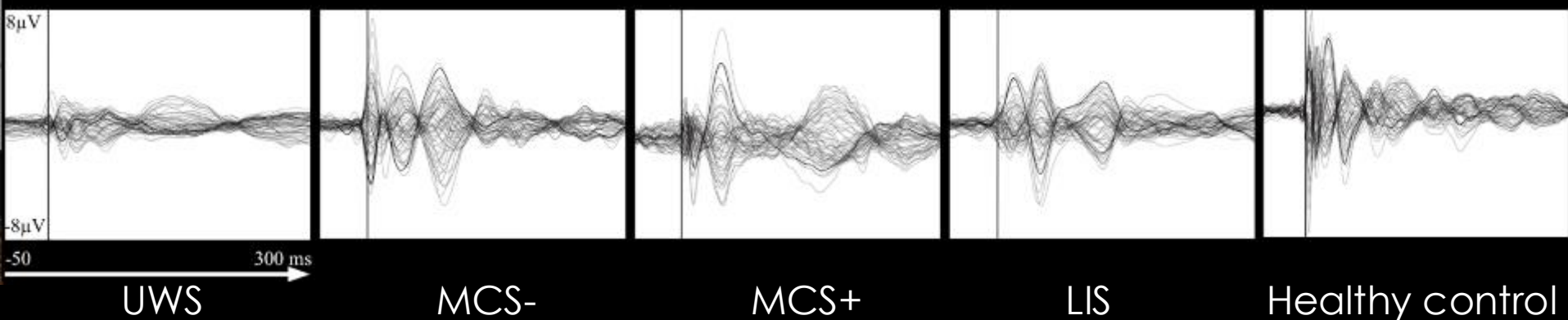
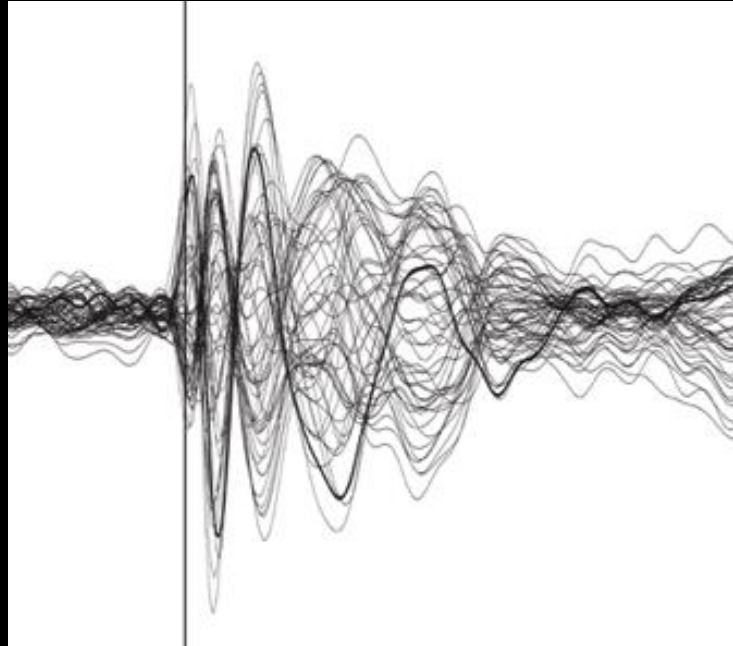


Conscious or not? → prognosis

Patient's best TMS-evoked response

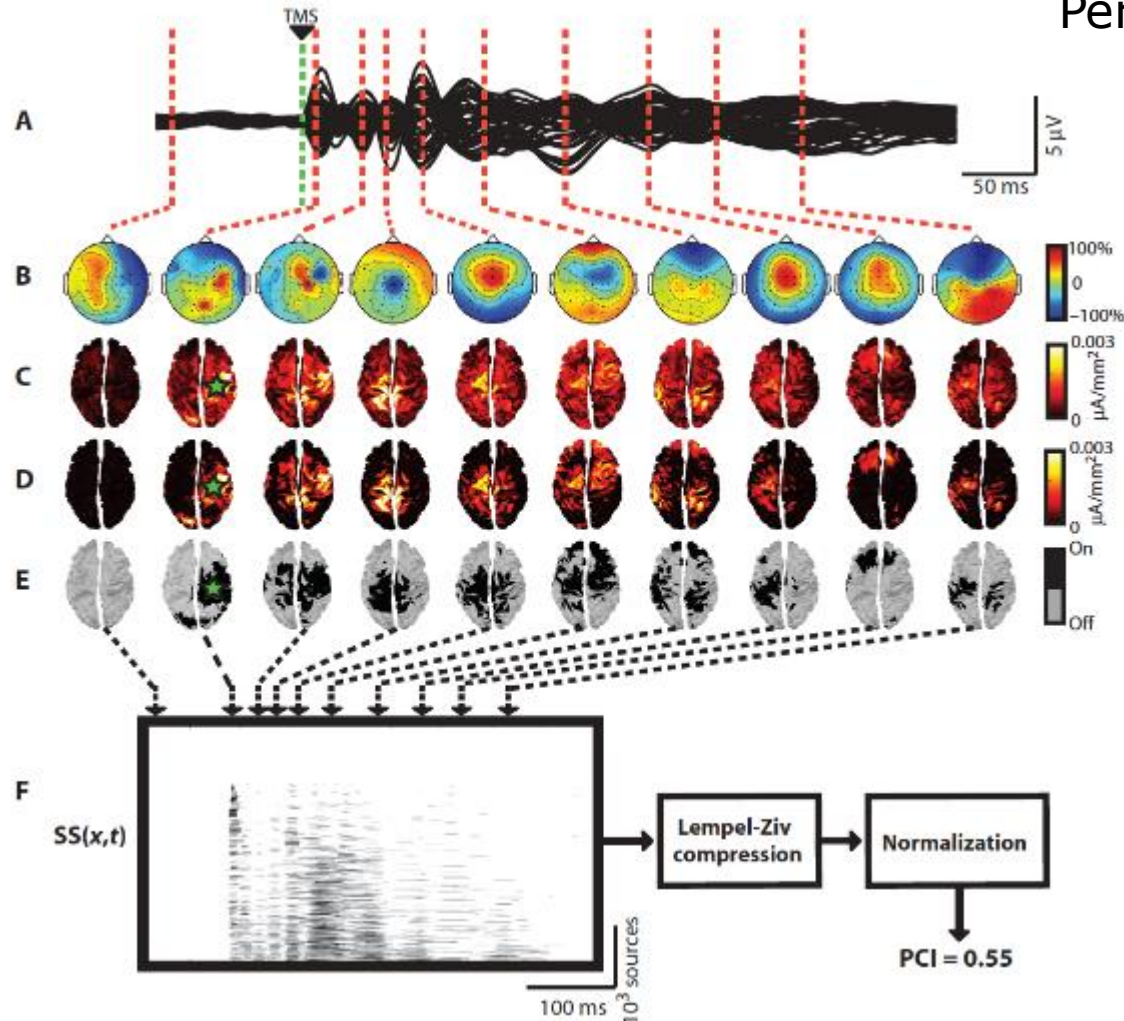


Left premotor
topoplot



Calculation of PCI

Perturbational complexity index



TMS-evoked response

Instantaneous voltage distributions

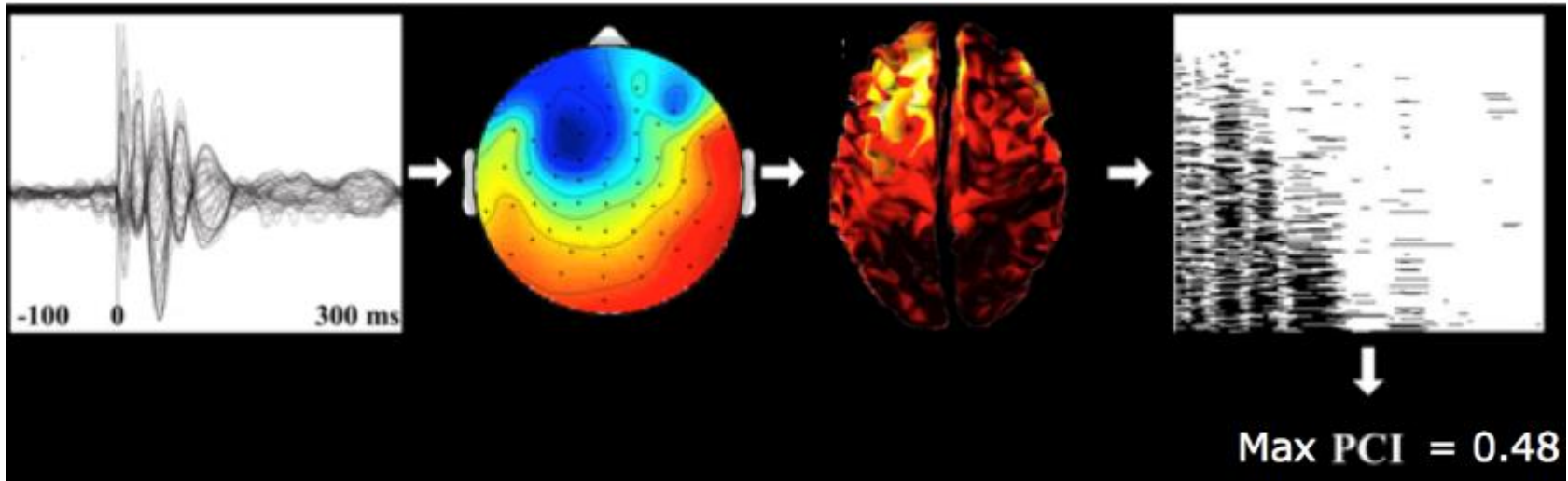
Cortical currents

Significant TMS-evoked cortical currents

Binary spatiotemporal distribution of significant sources (SS)

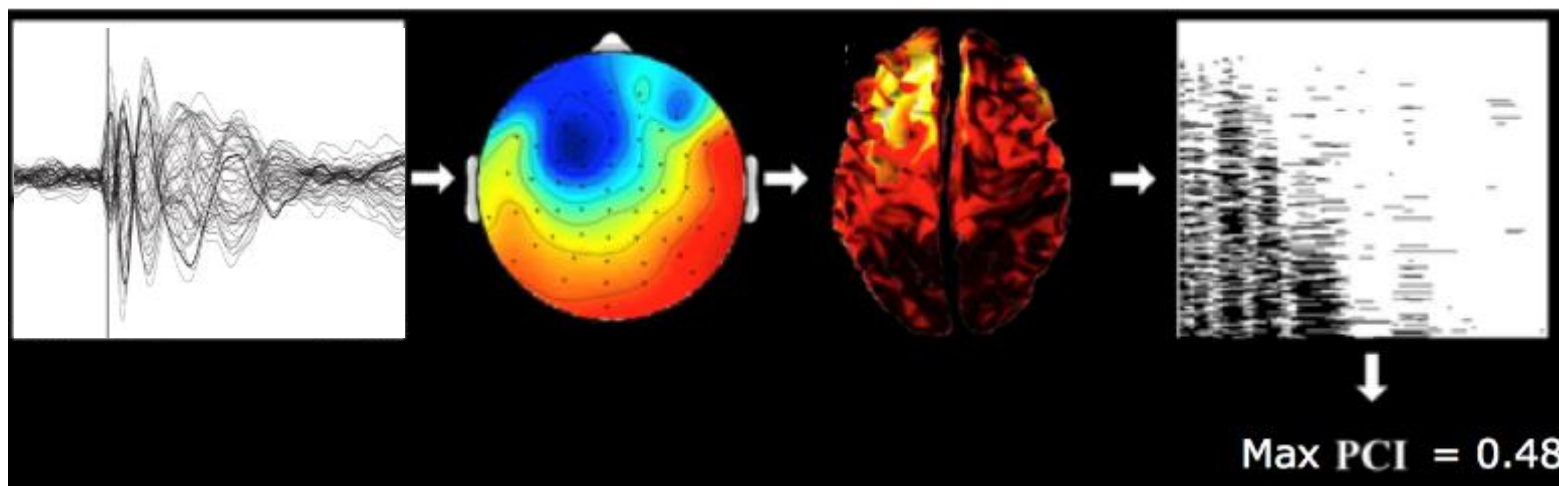
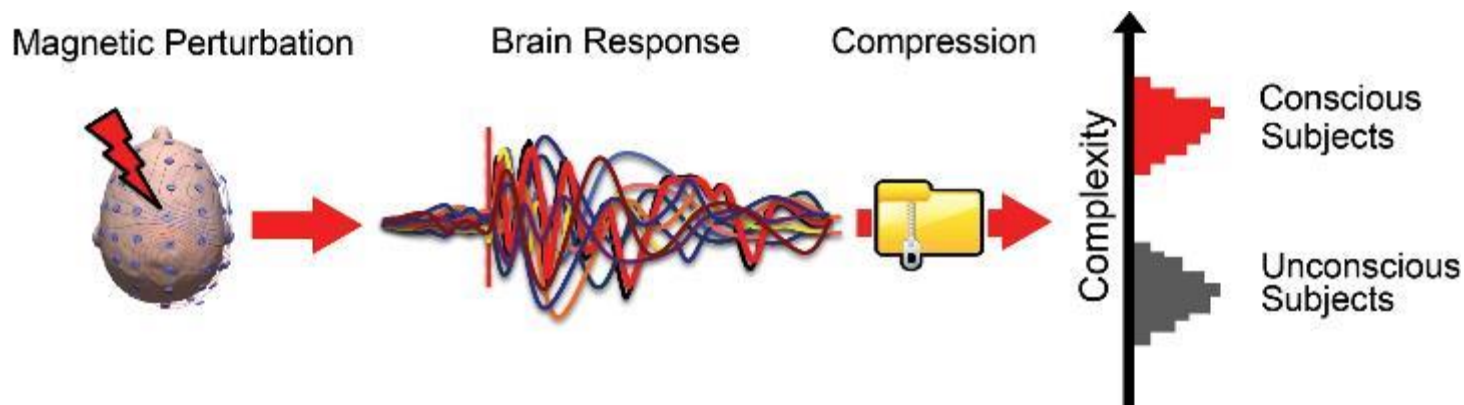
PCI = 0.55

Patient's PCIs



Brain areas	PCI
Left premotor 1 (BA6)	<u>0.484</u>
Left precuneus (BA7)	0.316
Left premotor 2 (BA6)	0.361

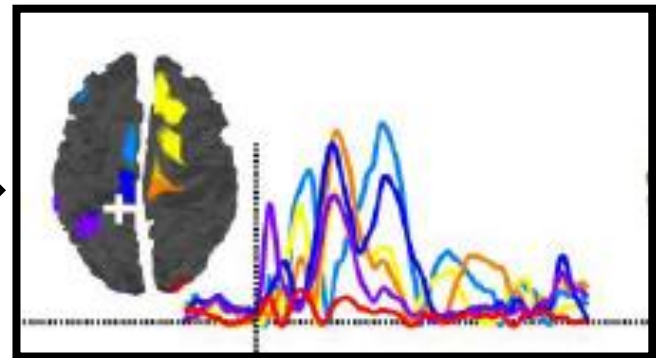
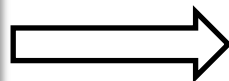
Conclusion for the patient



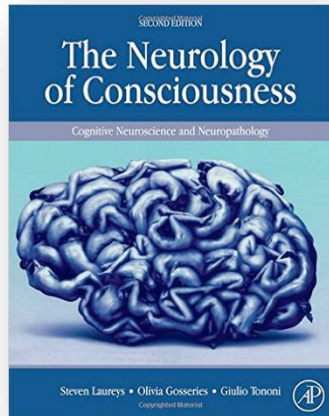
➔ MCS* ➔ better prognosis

Conclusion

- TMS-EEG and PCI are reliable diagnostic tools for *conscious/unconscious* post-coma patients best at the single subject level!
- TMS-EEG and PCI in other neurological disorders to investigate brain connectivity integrity/disturbance or treatment effects (info on temporal and spatial brain reactivity)
- Limitations ++



Thank you!



coma@ulg.ac.be

