Neuroimaging in DoC: the role of EEG and (f)MRI as diagnostic and prognostic tools

Recent advances in the assessment and management of people with a Disorder of Consciousness

June 6th 2024

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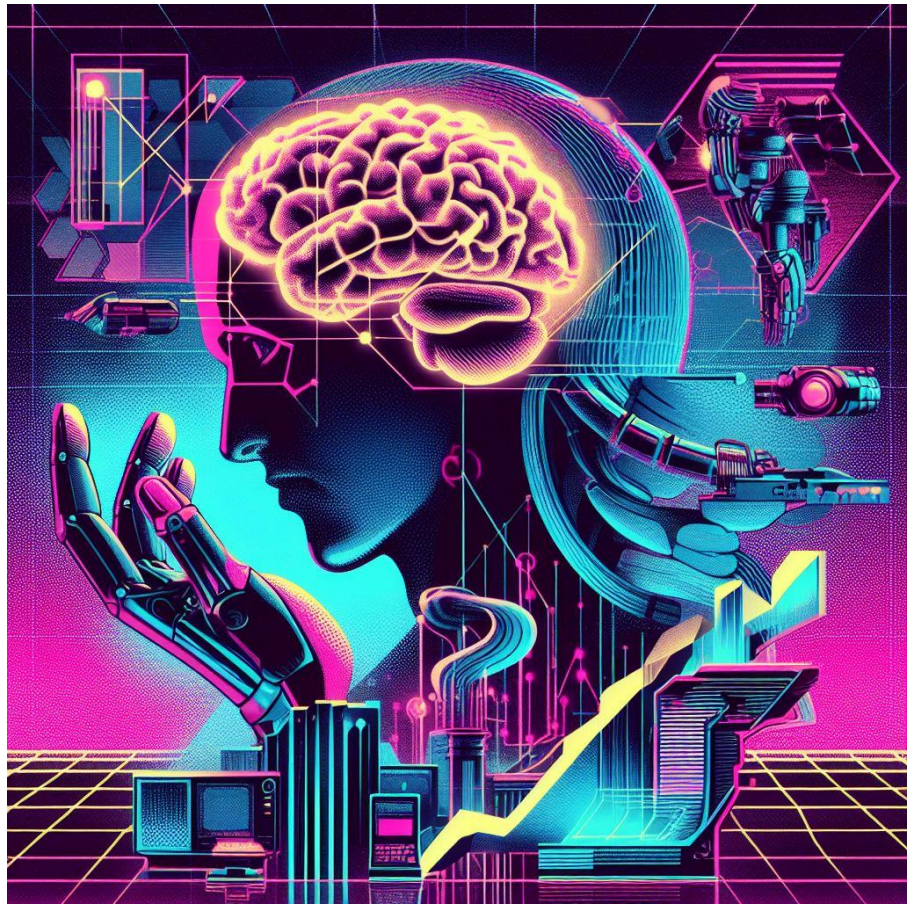
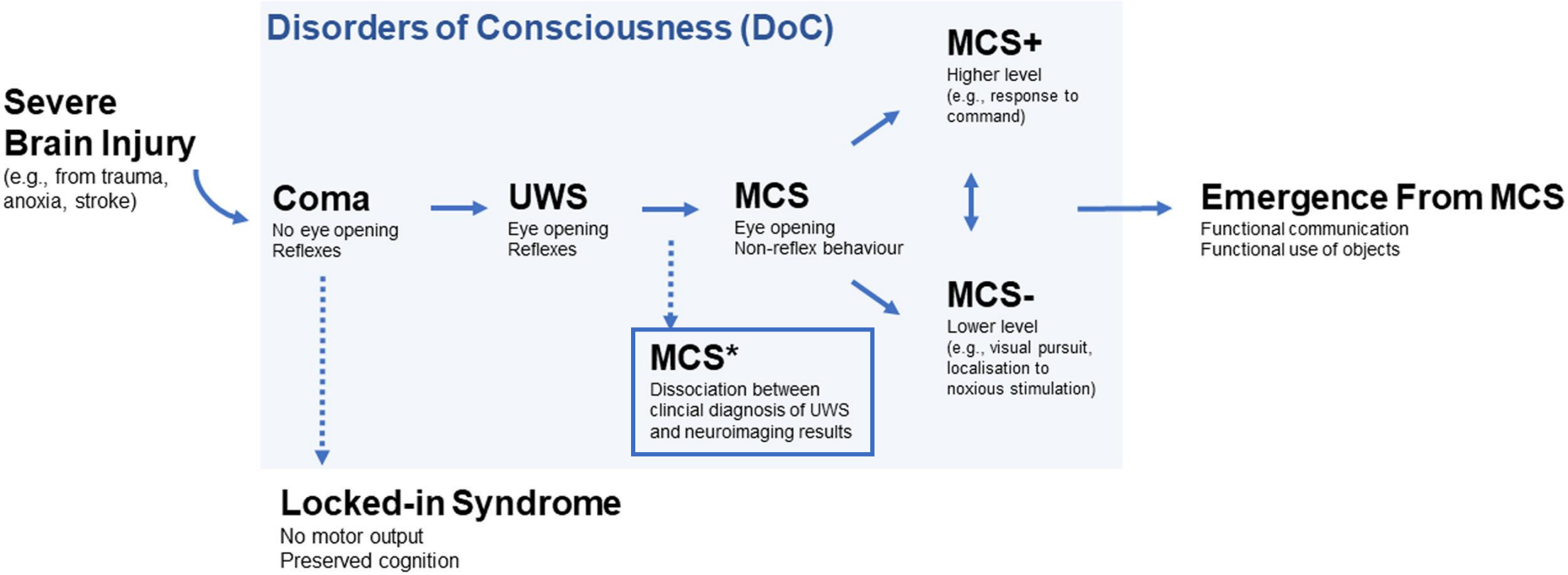
What is consciousness?

- **Very good question!**
- A single accepted definition is yet to be established.
- But what definition can be clinically useful?
  - **Wakefulness** + **awareness.**
- When arousal and awareness are temporarily lost from brain damage:
  - **Coma.**



What happens after a coma?



Alnagger & Cardone et al, *La Presse Médicale,* 2023

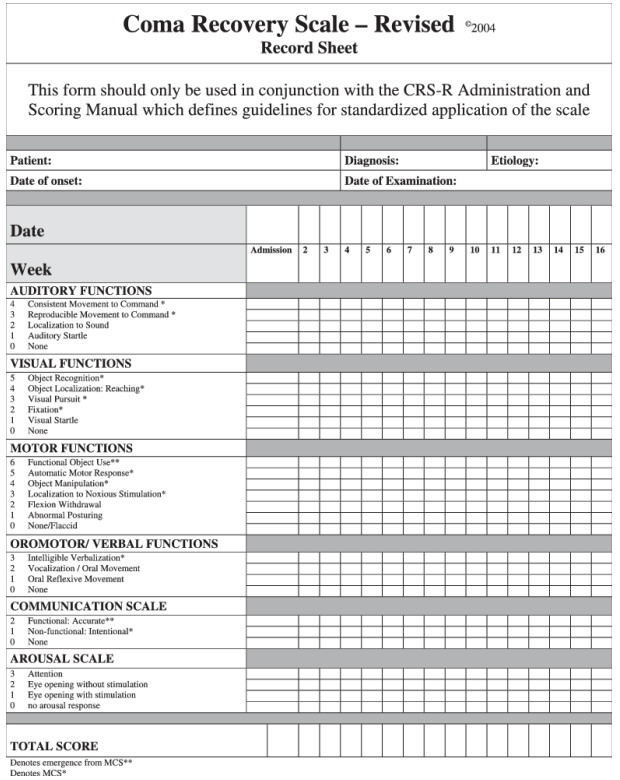
Signs of consciousness

Clinical diagnosis:

- State-of-the-art: Coma Recovery Scale Revised (CRS-R)

- However, it's not perfect!
  - Circadian-driven fluctuations in arousal.
  - Repeated assessments necessary.
  - Time-demanding (20-25 minutes)

- Presence of consciousness in apparently unresponsive patients: MCS*/covert awareness/cognitive motor dissociation
  - **Neuroimaging assessment**



Coma Recovery Scale – Revised ©2004
Record Sheet

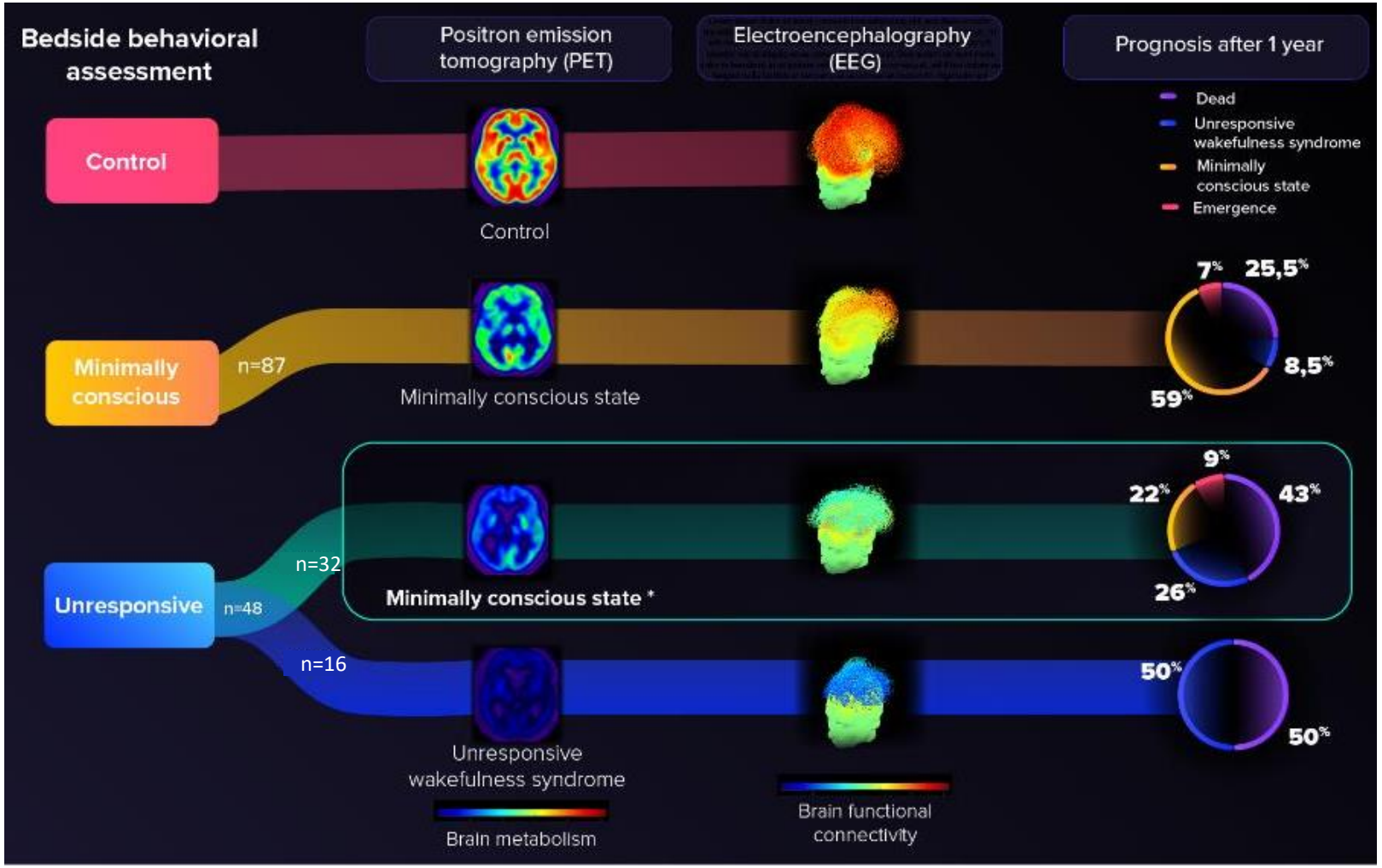
This form should only be used in conjunction with the CRS-R Administration and Scoring Manual which defines guidelines for standardized application of the scale

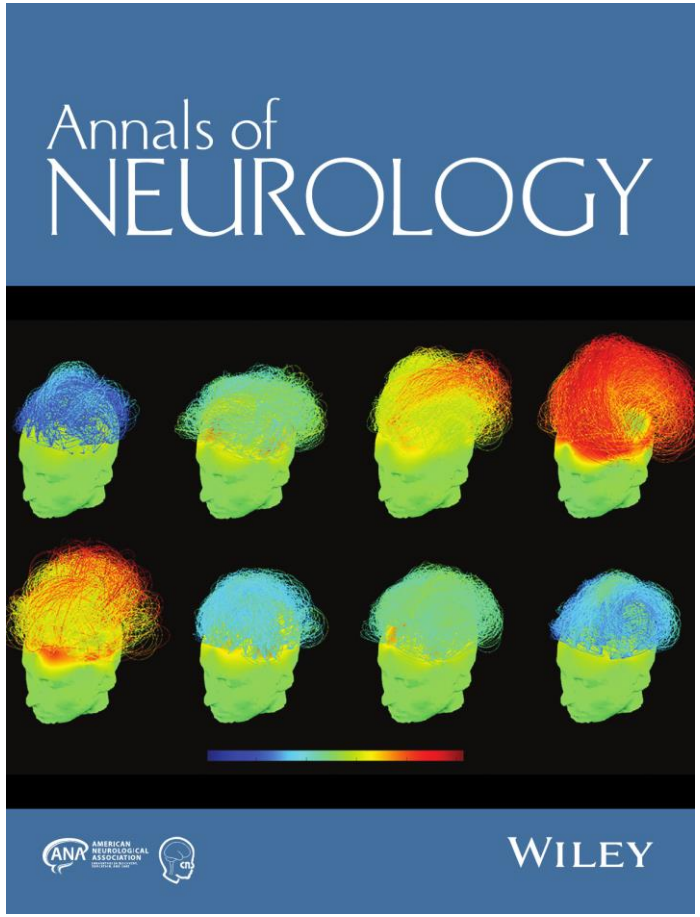
Patient:	**Diagnosis:**	**Etiology:**
Date of onset:	**Date of Examination:**	

Date																
Week	Admission	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
AUDITORY FUNCTIONS																
4 Consistent Movement to Command *																
3 Reproducible Movement to Command *																
2 Localization to Sound																
1 Auditory Startle																
0 None																
VISUAL FUNCTIONS																
5 Object Recognition*																
4 Object Localization: Reaching*																
3 Visual Pursuit *																
2 Fixation*																
1 Visual Startle																
0 None																
MOTOR FUNCTIONS																
6 Functional Object Use**																
5 Automatic Motor Response*																
4 Object Manipulation*																
3 Localization to Noxious Stimulation*																
2 Flexion Withdrawal																
1 Abnormal Posturing																
0 None/Flaccid																
OROMOTOR/ VERBAL FUNCTIONS																
3 Intelligible Verbalization*																
2 Vocalization / Oral Movement																
1 Oral Reflexive Movement																
0 None																
COMMUNICATION SCALE																
2 Functional: Accurate**																
1 Non-functional: Intentional*																
0 None																
AROUSAL SCALE																
3 Attention																
2 Eye opening without stimulation																
1 Eye opening with stimulation																
0 no arousal response																
TOTAL SCORE																

Denotes emergence from MCS**
Denotes MCS*

More conscious than expected?





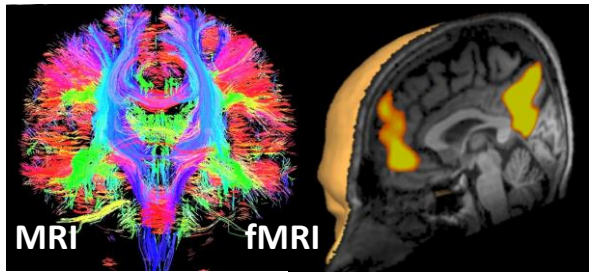
Thibaut & Panda et al, *Annals Neurol.* 2021

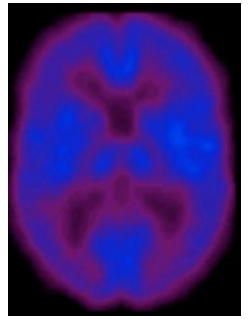
Neuroimaging techniques

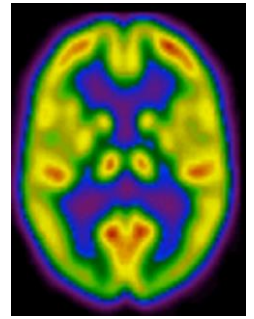
- Quantitative **computational techniques** to study the structure and function of the brain.

- **Diagnosis** + **prognosis** + **insights** into generation of consciousness.

- DoC patients present heterogeneous alterations of structure and function
  - Investigate specific regions + networks







Brain structure

Annen et al., 2016, Human Brain Mapping

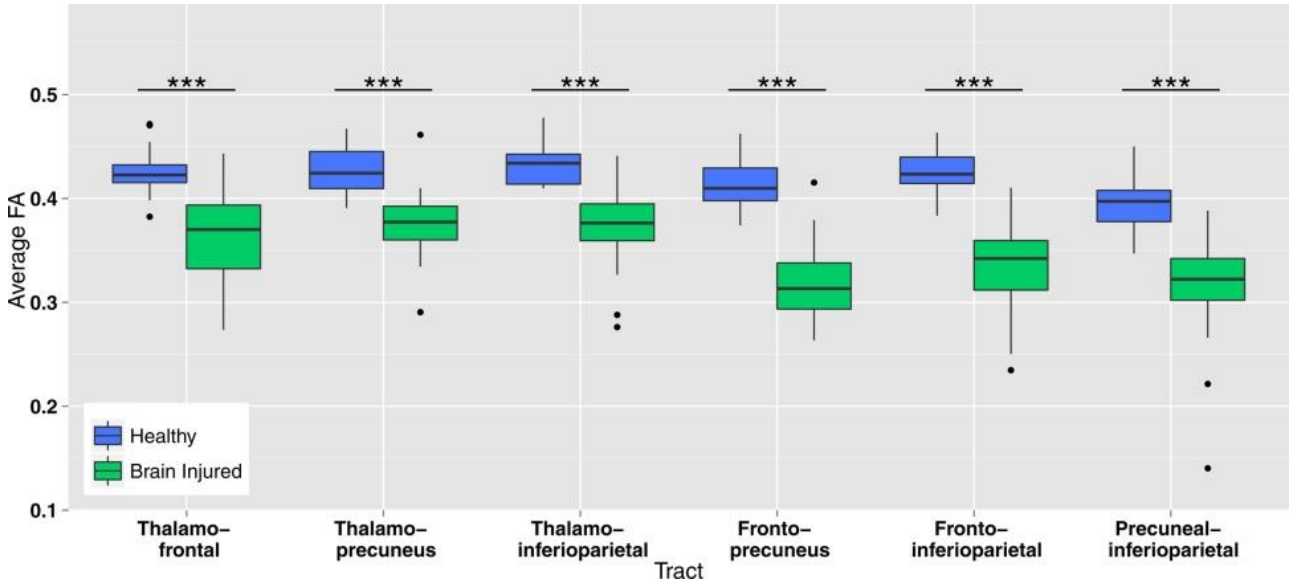
Magnetic resonance imaging (MRI) + Diffusion tensor imaging (DTI)

- **MRI**: measure magnetic properties of water.
  - Different concentration in different tissues.
  - Grey and white matter density.

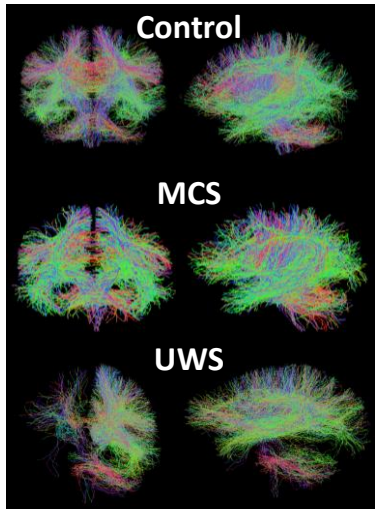
- **DTI:** estimation of white matter connectivity via diffusion of water molecules along white matter tracts.

- Preservation of **thalamocortical** white matter tracts is a key aspect of consciousness.

Average structural integrity



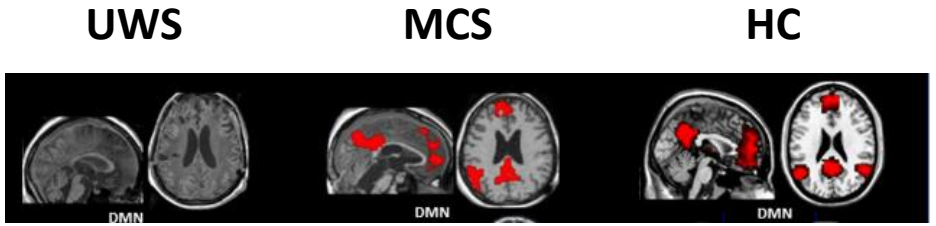
White matter tracts



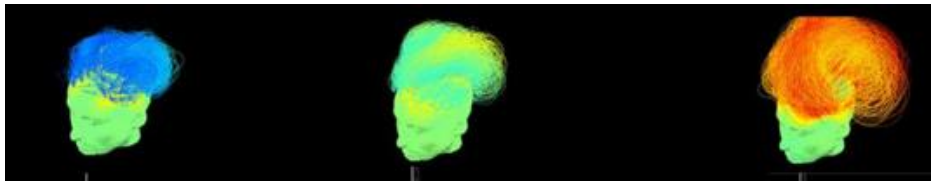
Brain function

Three main techniques:

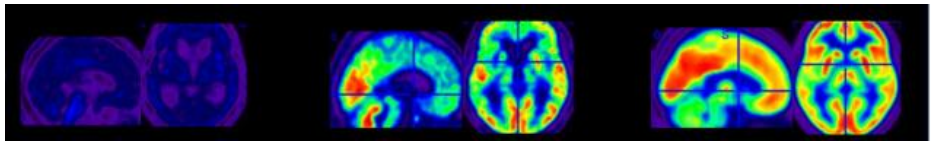
- **Functional MRI (fMRI)**
  - Magnetic properties of blood as a proxy for neural activity via **blood-oxygen-level dependent** (BOLD).



- **Electroencephalography (EEG)**
  - Recordings of **electrical activity** of the pyramidal neurons located in the cerebral cortex.

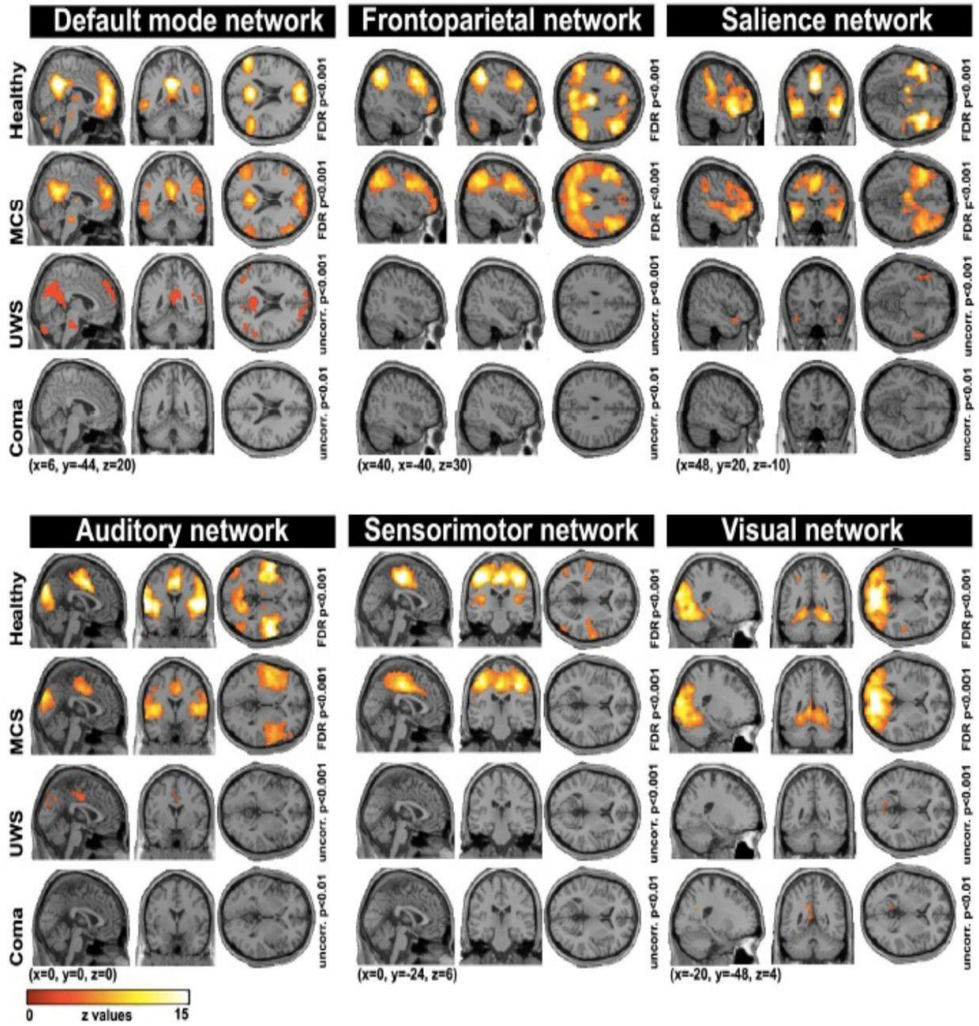


- **Positron emission tomography (PET)**
  - Measure of brain **metabolism** with radioactive tracers to visualize and measure changes in metabolic processes.
  - For brain metabolism: Fluorodeoxyglucose (FDG-PET) and Oxygen-15 as tracers.



- **Different paradigms:** resting state, passive stimulation, active tasks.

Resting state fMRI – Preserved networks

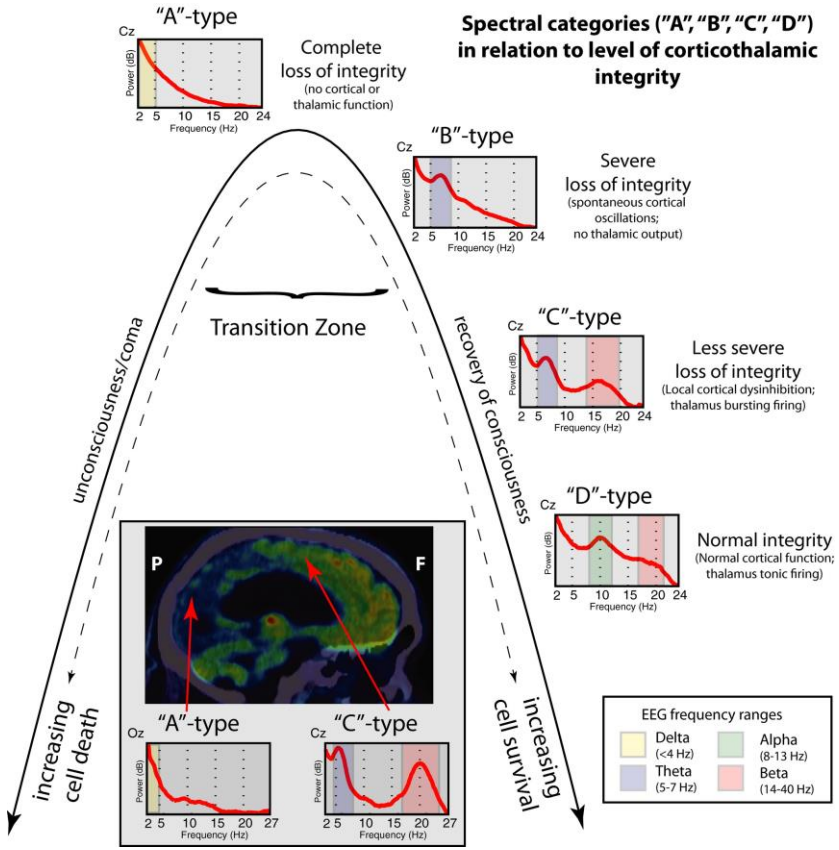


- **Resting state networks:**
  - Regions with related activity through BOLD fluctuations.
- MCS patients present partially preserved **functional network differentiation**.
- Baseline FC within the DMN can index the level of consciousness
- Static difference of functional organization.

Vanhaudenhuyse et al, *Brain,* 2010, Demertzi et al, *Brain,* 2015

Resting state EEG

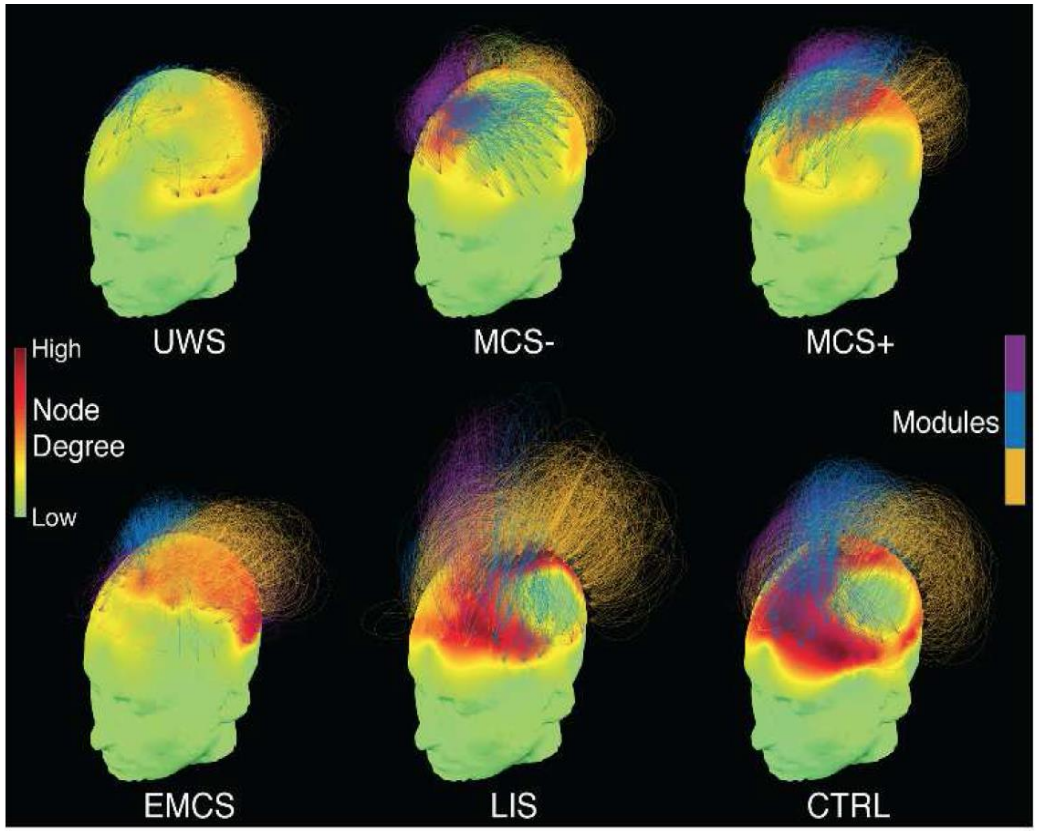
Power spectral density



Forgacs et al, *Annals of clinical and translational neurology*, 2017

Power spectral profile of acute patients related to behavioral diagnosis

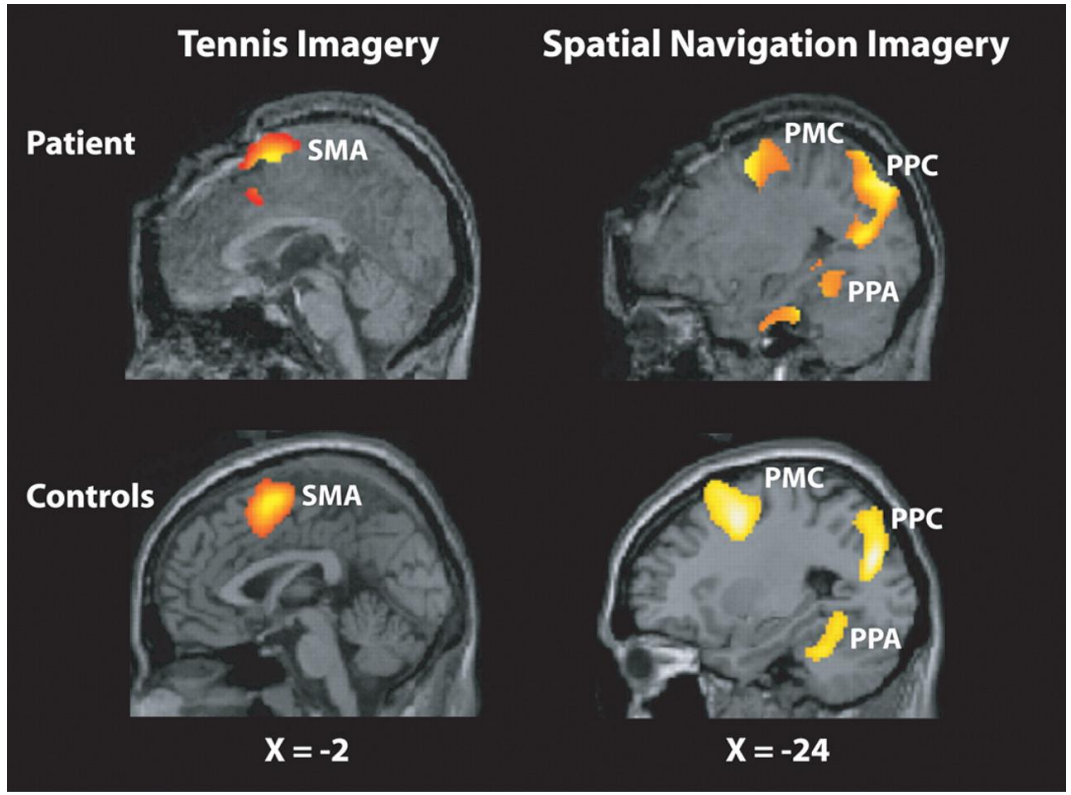
Alpha band connectivity



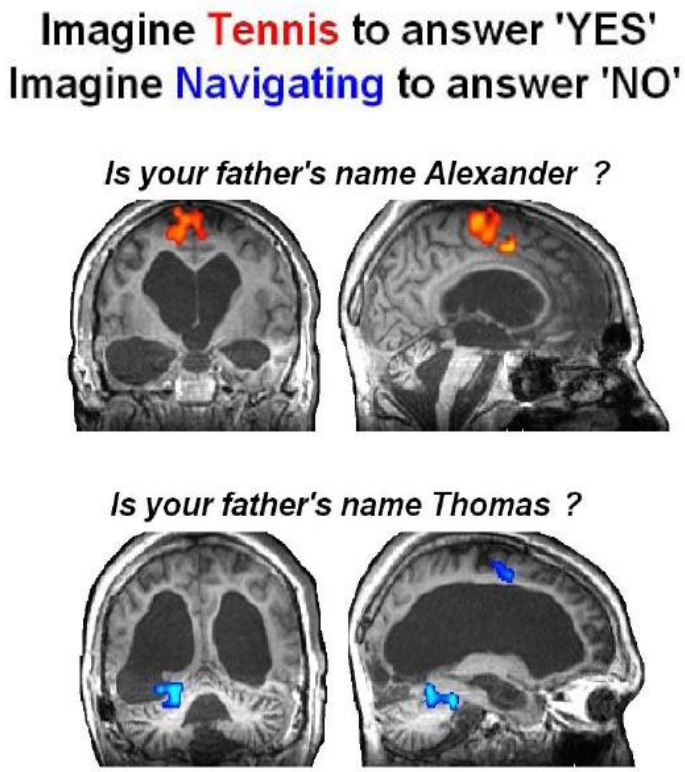
Chennu et al, *Brain*, 2017

Stronger alpha connectivity in MCS patients compared to UWS

Active paradigm – fMRI



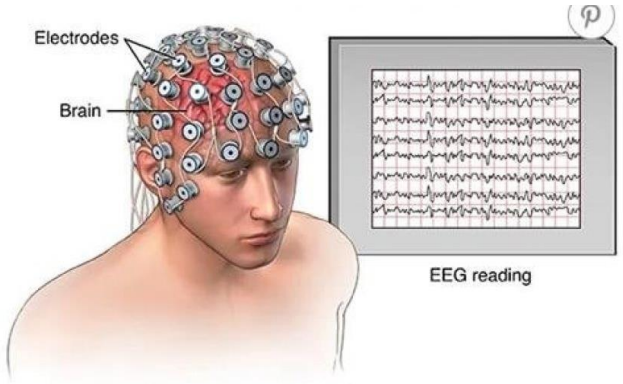
Owen et al., *Science*, 2006



Monti & Vanhaudenhuyse et al, *New England J Med*, 2010
Horki et al, *Front Hum Neurosci*.2014
Edlow et al, *Brain*, 2017;
Bodien et al, *Front Neurol,* 2017
Haugg et al, *Front Neurol*, 2018

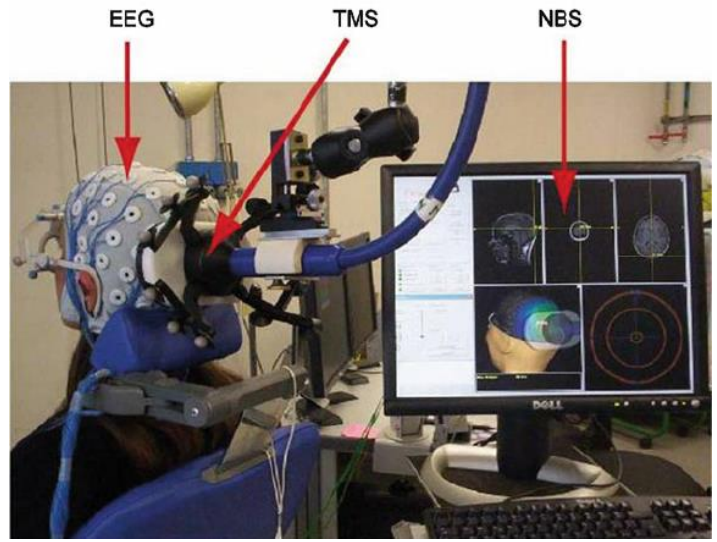
Stimulation: EEG coupled with Transcranial Magnetic Stimulation (TMS-EEG)

Electroencephalography (EEG)

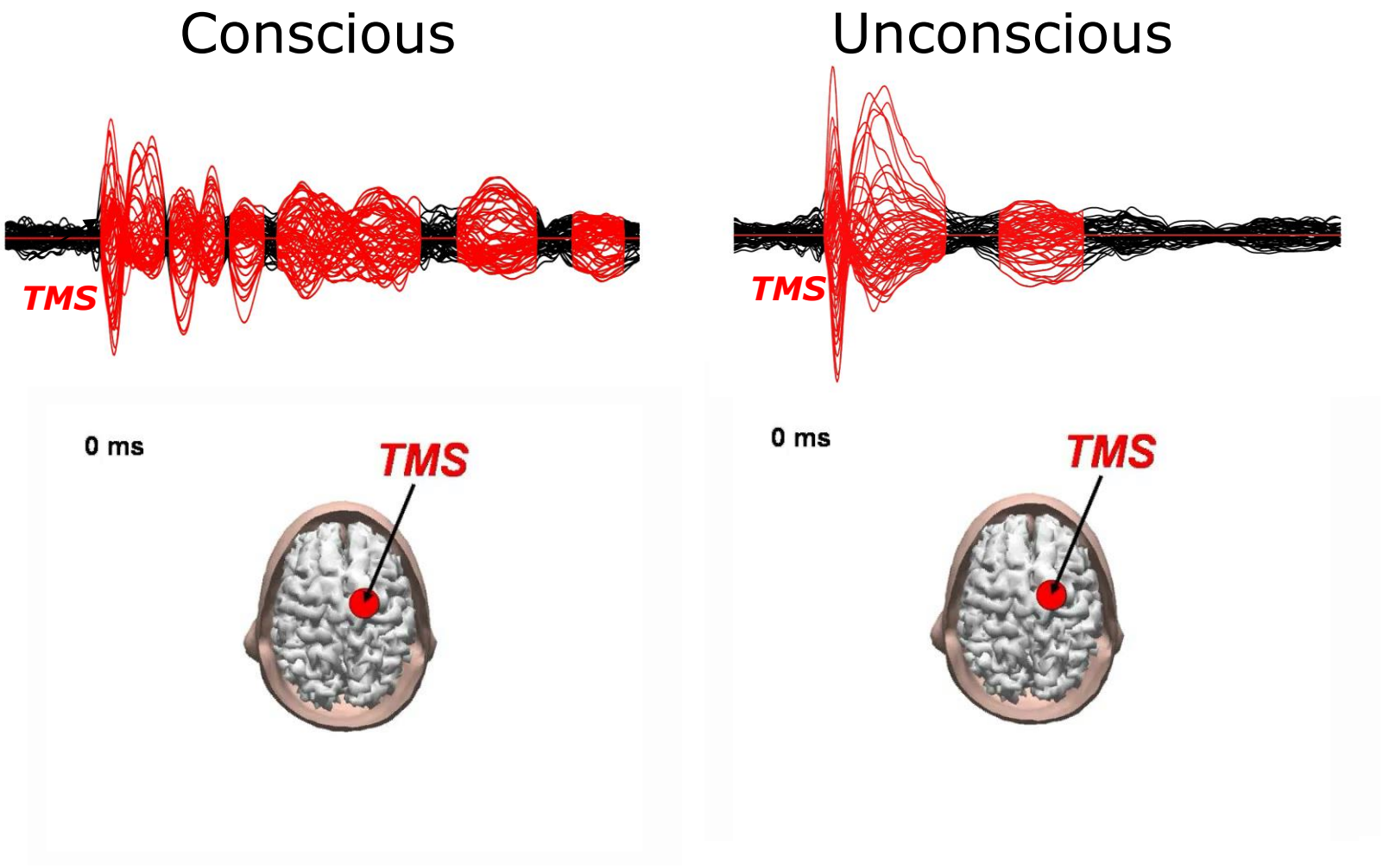


Transcranial Magnetic Stimulation (TMS)

TMS-EEG



TMS-Evoked Potentials & Consciousness

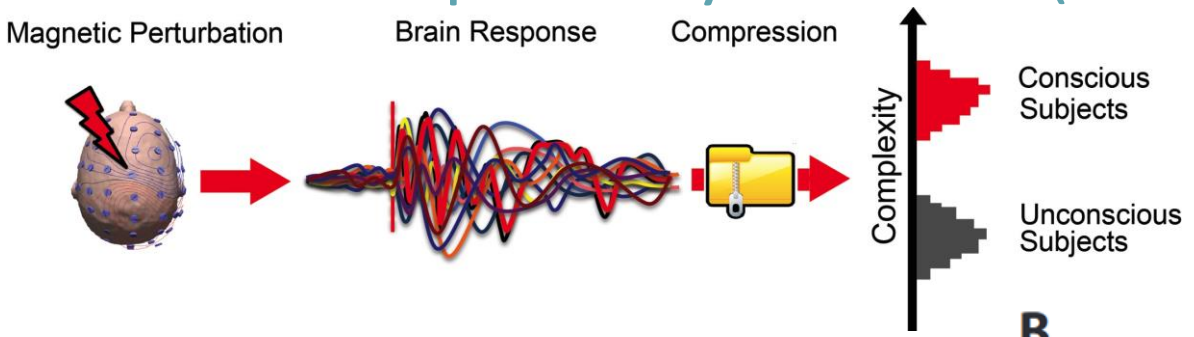


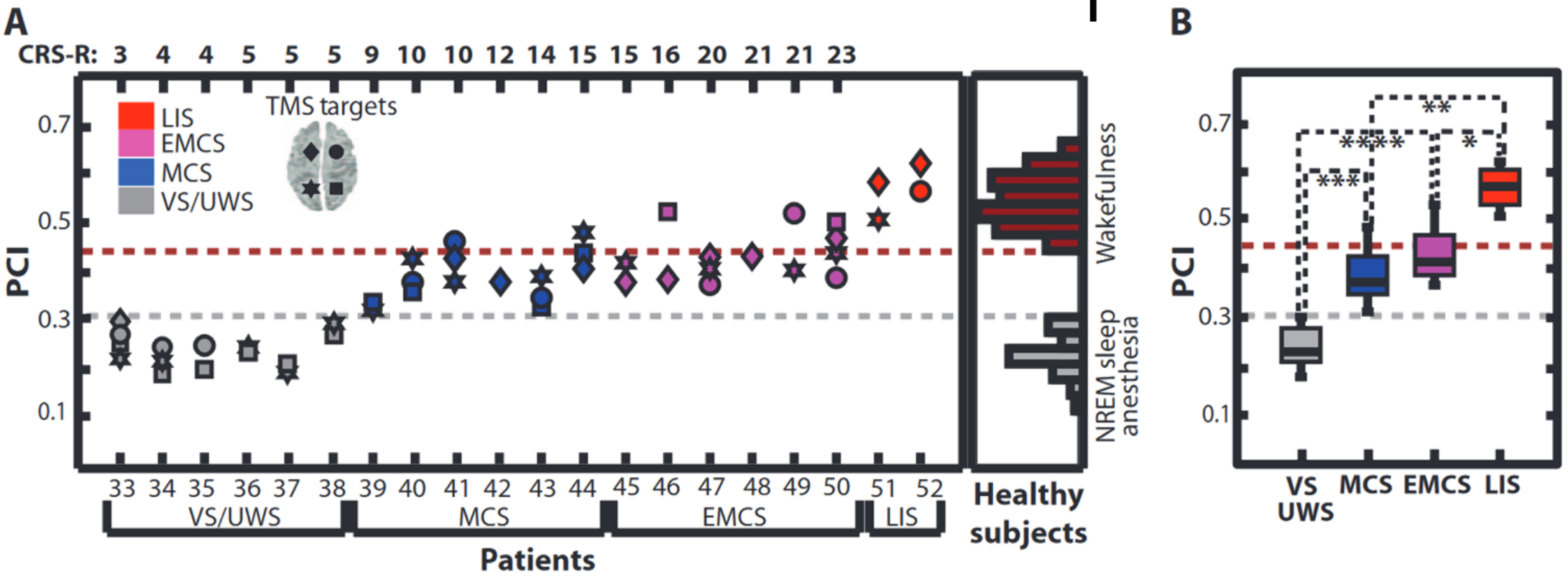
Courtesy of A. Casali

Massimini et al, *Science*, 2005; Rosanova & Gosseries et al, *Brain*, 2012
Casali & Gosseries et al*, Sci Trans Med,* 2013; Gosseries et al, *Brain Stim*, 2015

Perturbational Complexity Index (PCI)

Zap & zip technique

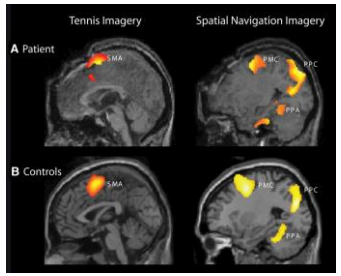




Casali & Gosseries et al, *Sci Trans Med,* 2013

European Academy of Neurology recommendations

Active fMRI



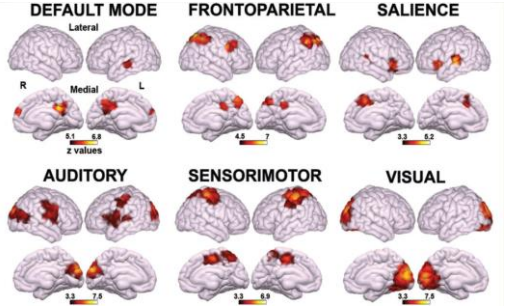
Owen et al, Science 2006

Recommendation: consider active fMRI paradigms as part of multimodal assessment in patients that don't follow commands.

Moderate evidence, weak recommendation.

20 publications

Resting state fMRI



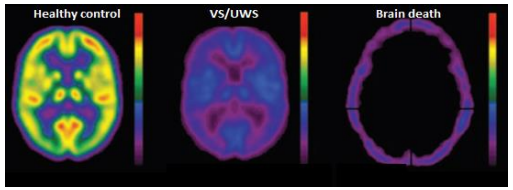
Demertzi et al, Brain 2015

Recommendation: If clinical MRI is indicated, add resting state fMRI as part of multimodal assessment.

Low evidence, weak recommendation.

6 publications

Brain metabolism – PET



Laureys et al, Lancet Neurol, 2004

Recommendation: Resting state FDG PET should be considered as part of multimodal assessment in unresponsive patients.

Low evidence, weak recommendation.

5 publications

Kondziella et al, *Eur J Neurol*, 2020

European Academy of Neurology recommendations

EEG

Recommendation: **visual** analysis of clinical EEG (high specificity, low sensitivity)

Weak evidence, strong recommendation

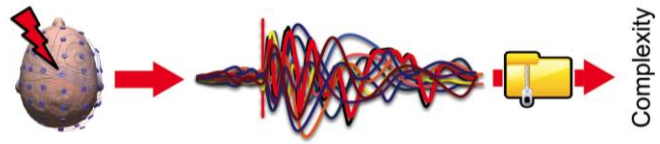
2 publications

Recommendation: use **sleep** EEG

Weak evidence, weak recommendation

6 publications

TMS-EEG



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

Weak evidence, weak recommendation

6 publications

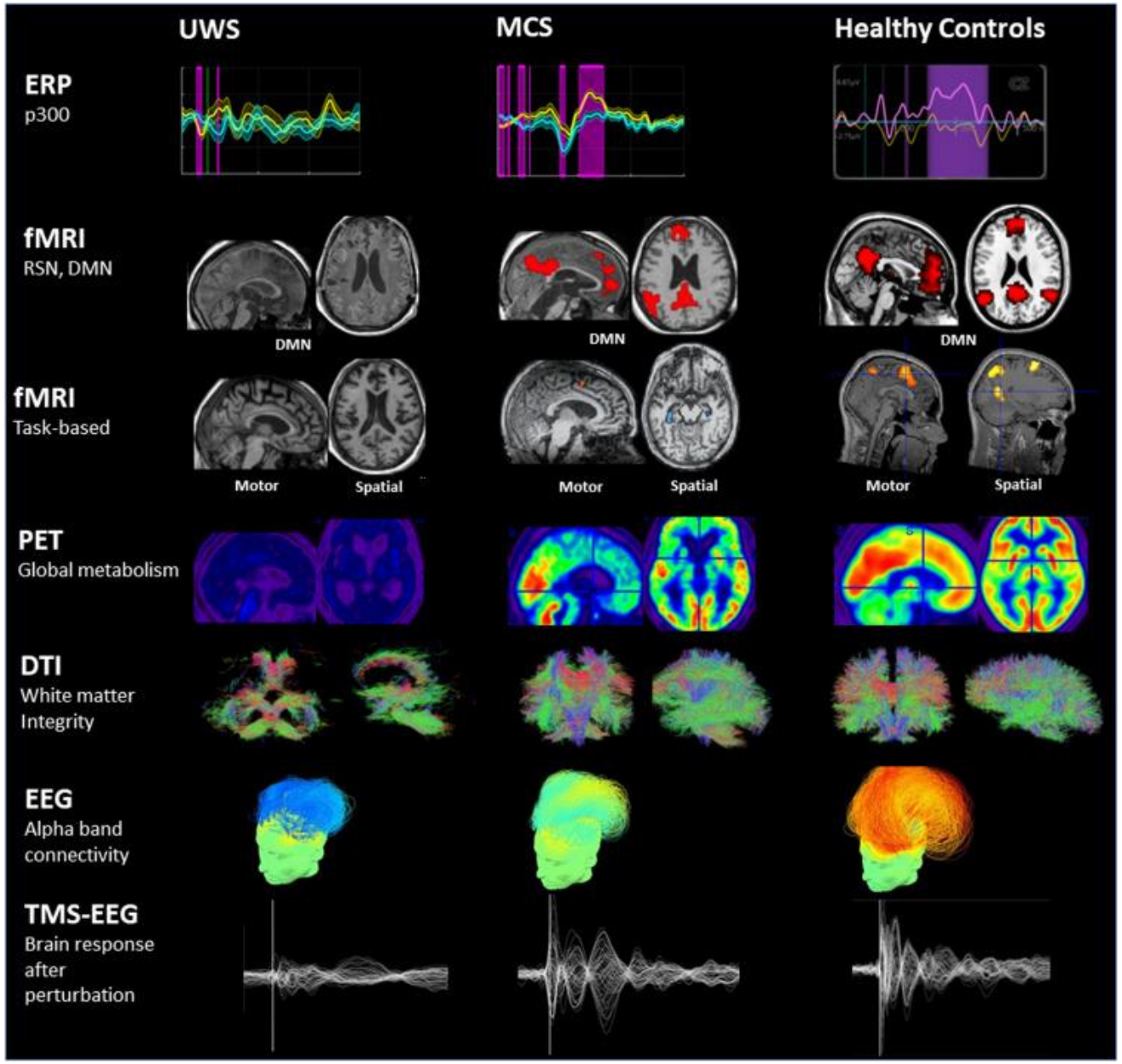
Recommendation: consider **quantitative** analysis of high-density EEG

Moderate evidence, weak recommendation

6 publications

Kondziella et al, *Eur J Neurol*, 2020

Summary


UWS
MCS
Healthy Controls
ERP
p300
fMRI
RSN, DMN
DMN
DMN
DMN
fMRI
Task-based
Motor
Spatial
Motor
Spatial
Motor
Spatial
PET
Global metabolism
DTI
White matter
Integrity
EEG
Alpha band
connectivity
TMS-EEG
Brain response
after
perturbation

Acknowledgments

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Conflict of interest: no conflict of interest to report.