



Recent advances in paraclinical assessment of patients with disorders of consciousness



11.9.2018

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GIGA Consciousness, Coma Science Group, Liège



Who are we?

Prof. Steven Laureys, MD, PhD

Speech therapists

Physicians

Neuropsychologists

Physiotherapists

Biologists

Nurses

Engineers

Computer
scientists

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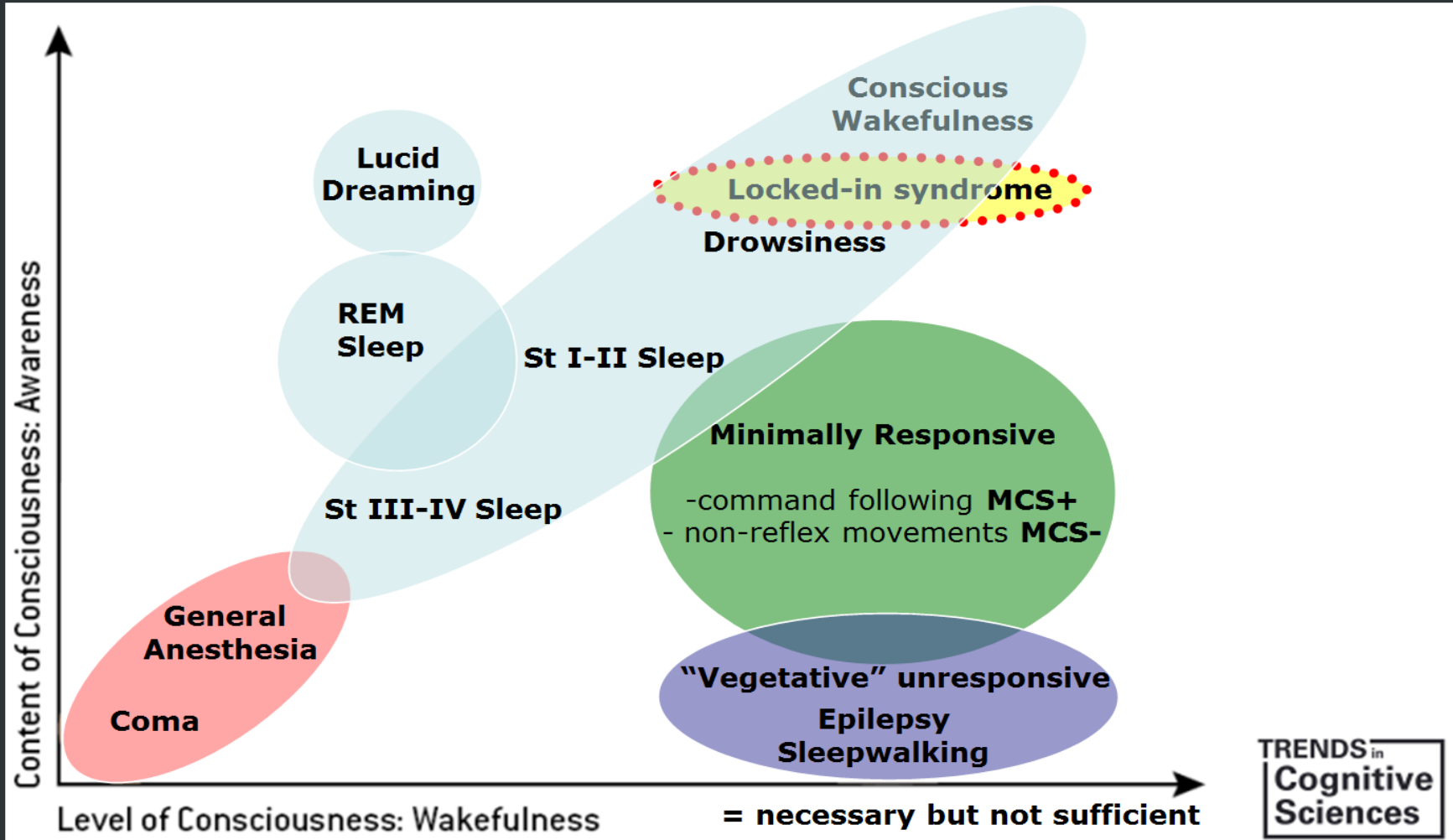
Overview

- Consciousness and Disorders of Consciousness
- Diagnosis
- Paraclinical diagnosis

Reducing consciousness to 2D

CONSCIOUSNESS

4

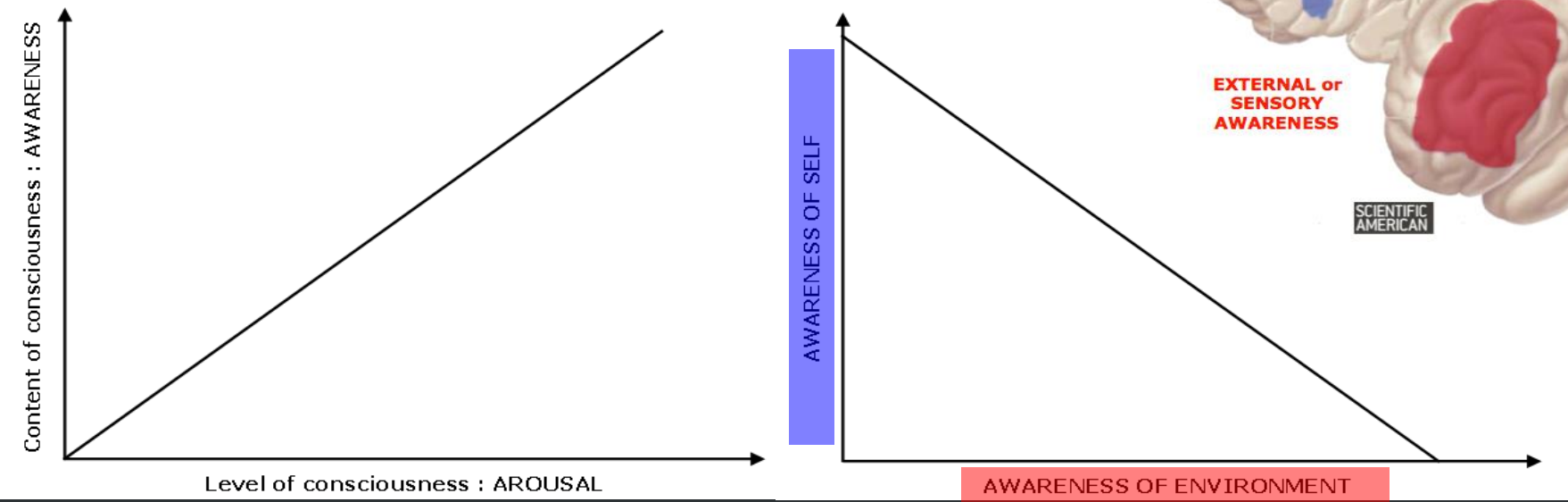
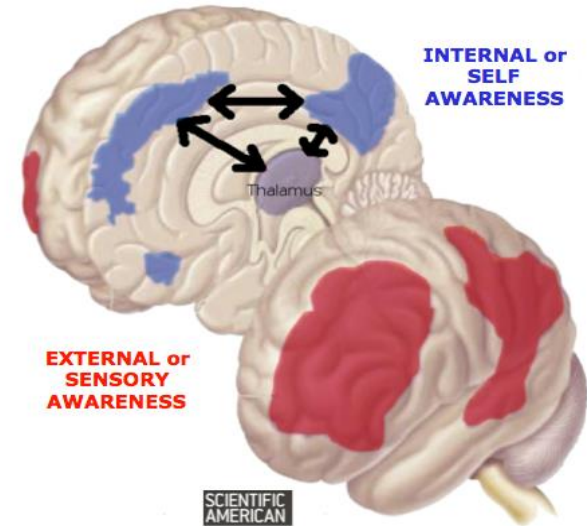




Reducing consciousness to 2D

CONSCIOUSNESS

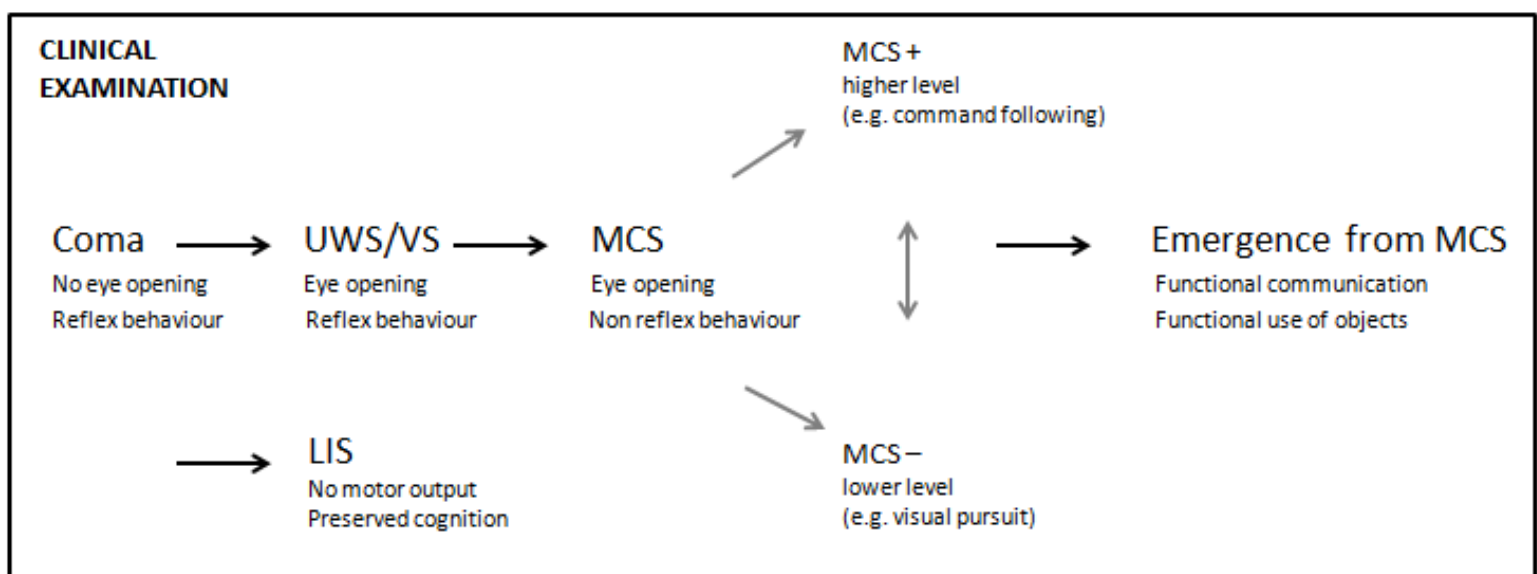
5



Boly et al, Ann NY Acad Sci, 2009
 Vanhaudenhuyse & Demertzi et al, J Cogn Neurosci, 2011



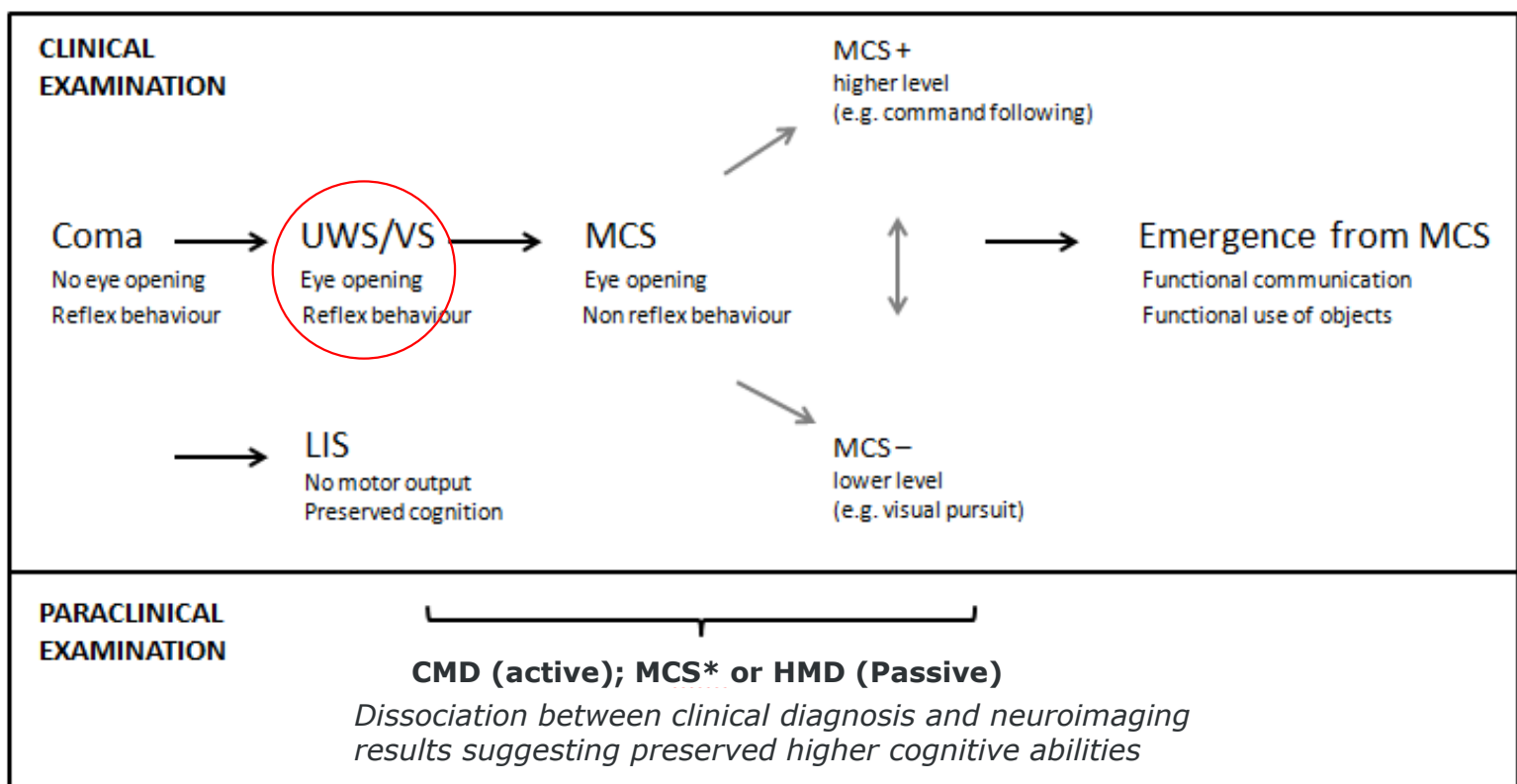
Clinical entities



UWS=unresponsive wakefulness syndrome
 VS=vegetative state
 MCS=minimally conscious state



Clinical entities

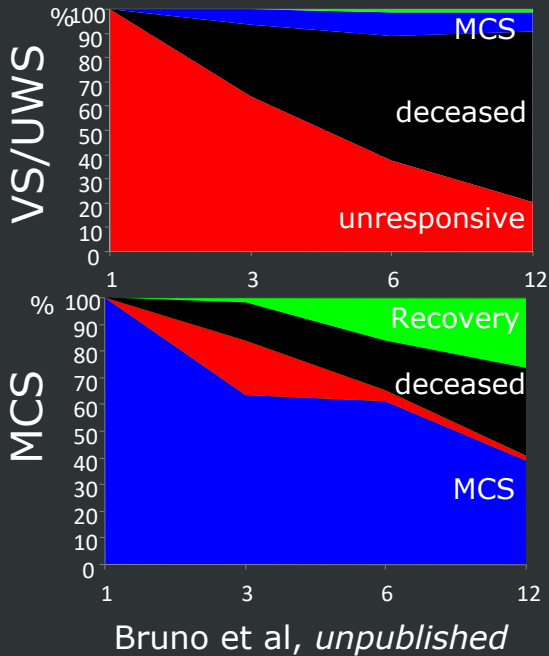




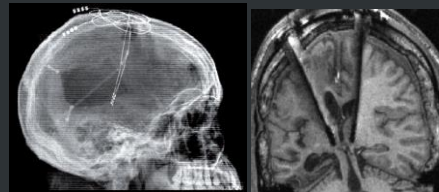
Why is it important to assess consciousness?



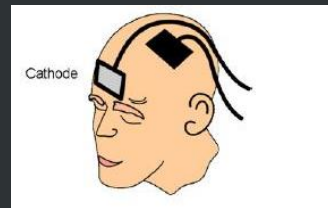
Prognosis (non traumatic)



Treatment

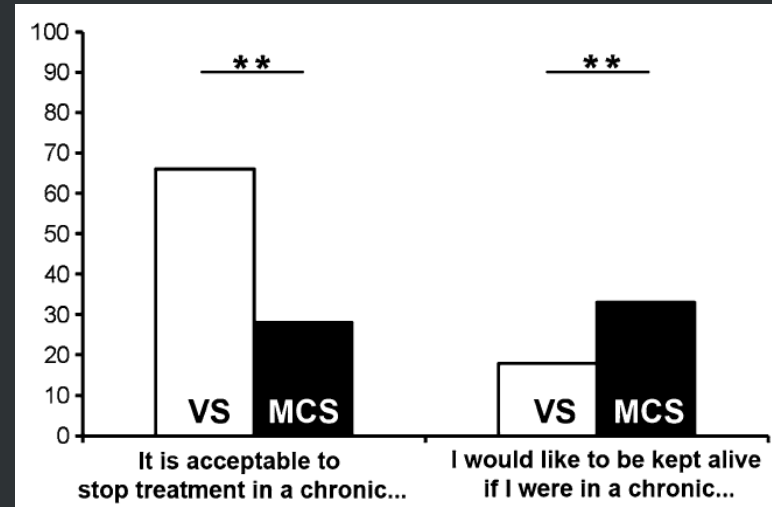


Schiff et al, *Nature*, 2007



Thibaut et al, *J Neurology* 2014

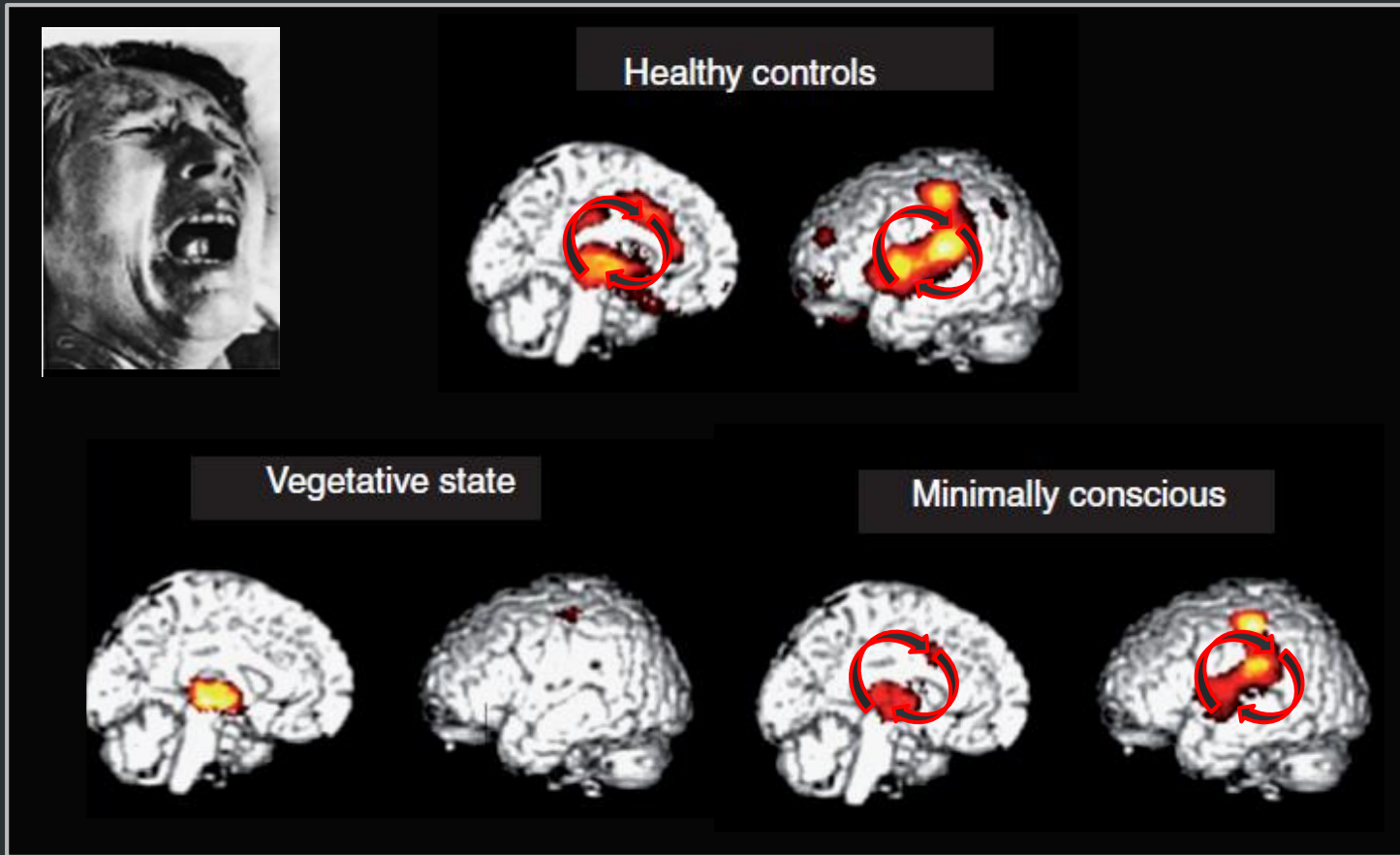
Ethics



Demertzi et al, *J Neurology* 2011

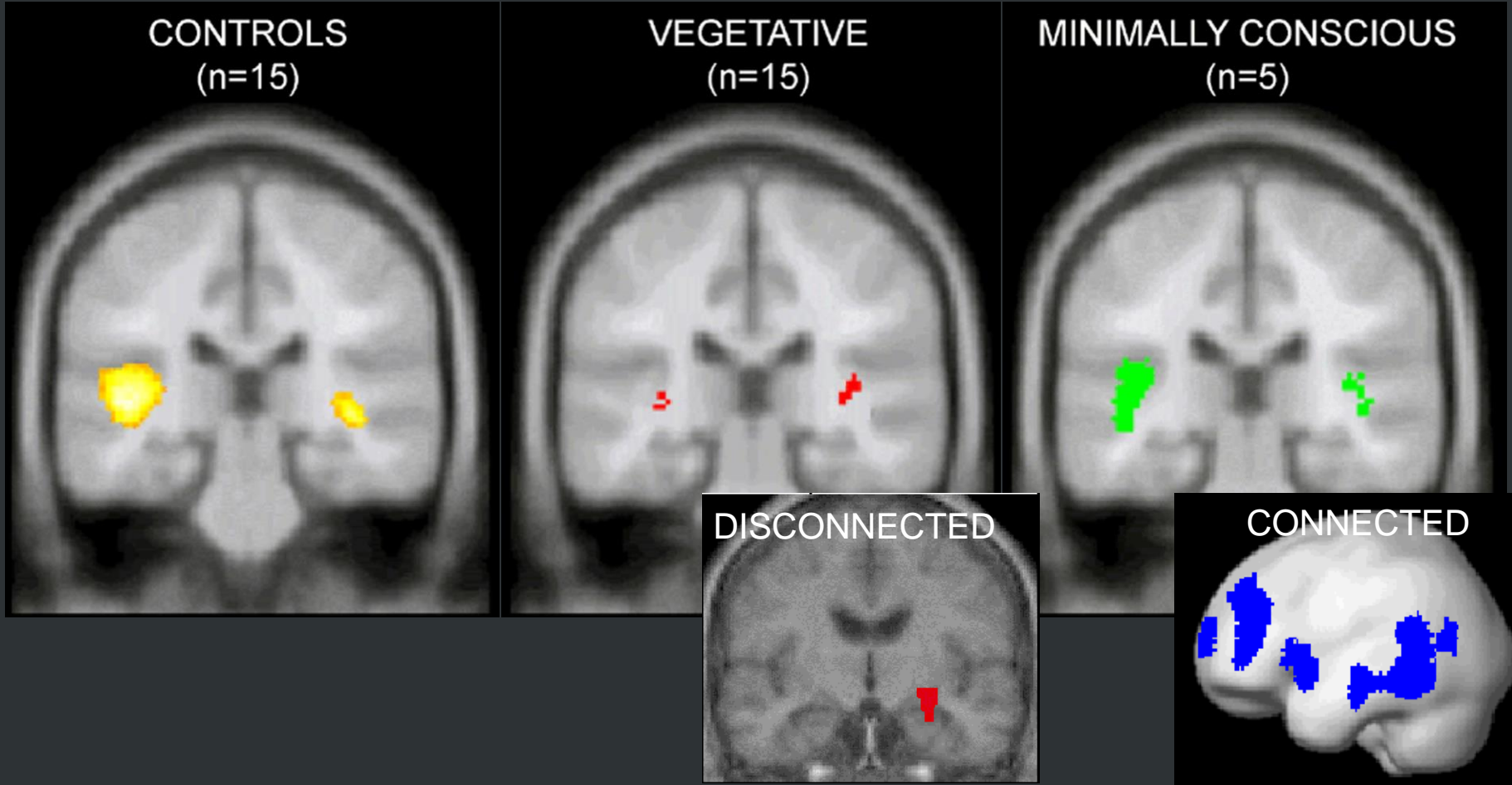


Pain?





Audition?





Summary

- Consciousness \approx 2 components
- DOC: different clinical entities associated with various level of consciousness : coma, VS/UWS, MCS (plus and minus)
- New terminologies with paraclinical diagnosis: CMD, MCS*, HMD
- Impact on care
- Non communicative patients with DOC may be able to perceive external world
 - Audition
 - Pain/emotion



“Reflex” versus “Voluntary”

“VOLUNTARY” / “WILLED”



“REFLEX” / “AUTOMATIC”



Misdiagnosis

n=103 post-comatose patients

- 45 clinical consensus diagnosis 'vegetative state'
- 18 signs of awareness (Coma Recovery Scale-Revised)

 41% potential misdiagnosis

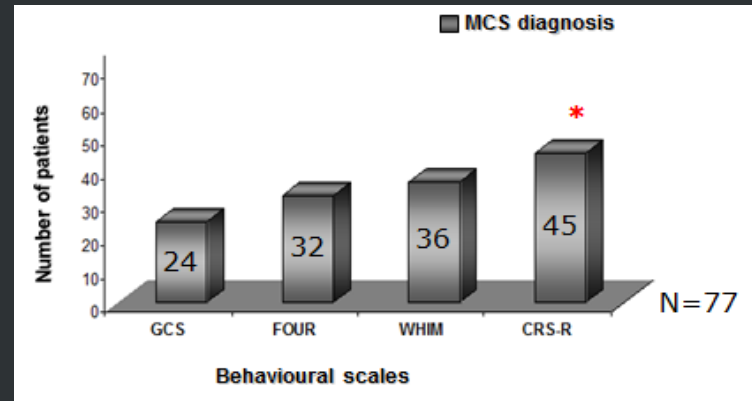


Coma Recovery Scale-Revised



MOTOR FUNCTION SCALE
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 FUNCTION SCALE
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 w/o Stimulation
1 - Eye Opening with Stimulation
0 - Unarousable

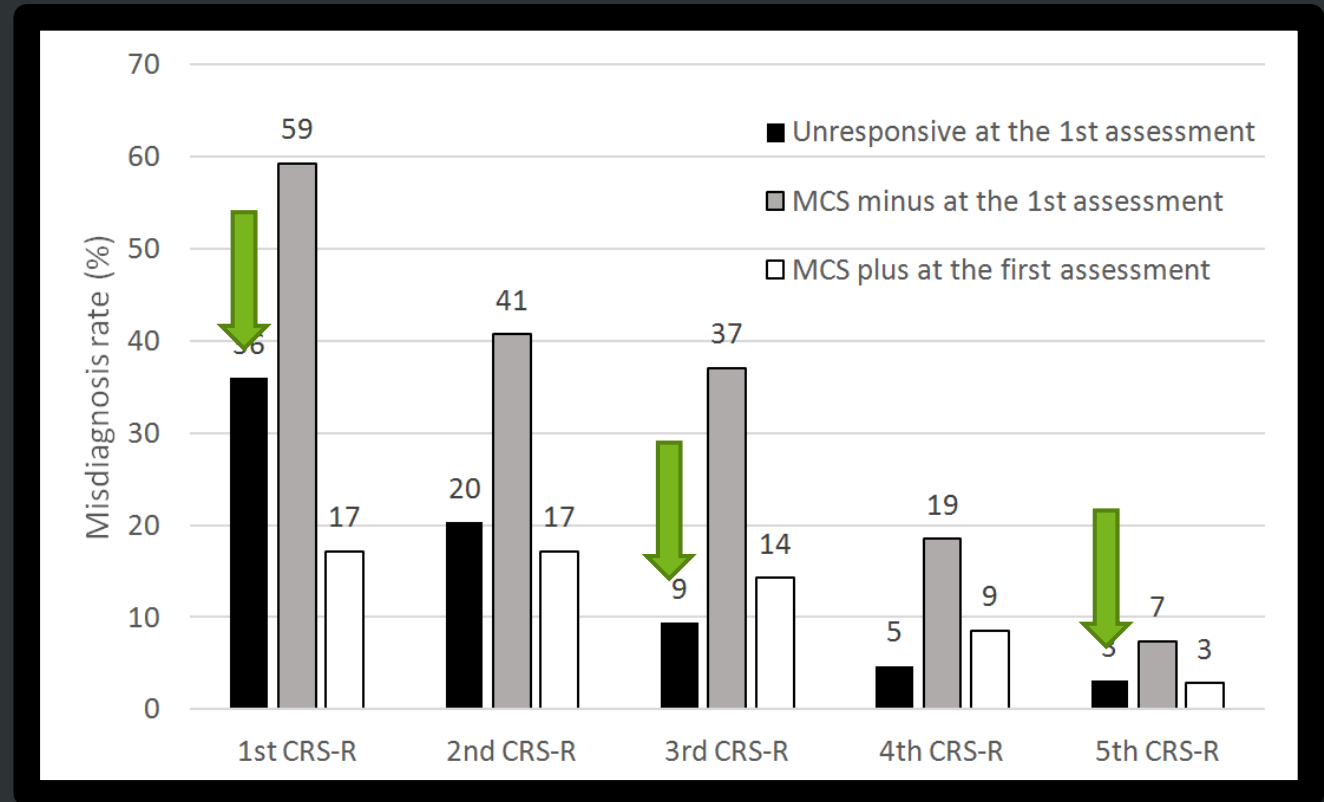
AUDITORY FUNCTION SCALE
4 - Consistent Movement to Command *
3 - Reproducible Movement to Command *
2 - Localization to Sound
1 - Auditory Startle
0 - None
VISUAL FUNCTION SCALE
5 - Object Recognition *
4 - Object Localization: Reaching *
3 - Visual Pursuit *
2 - Fixation *
1 - Visual Startle
0 - None



How many assessments?



- Misdiagnosis
- Chronic
- 6 assessments
- Short time window (3 -10 d)



n=123



Nociception Coma Scale - revised



VERBAL RESPONSE

- 3 – Verbalisation intelligible
- 2 – Vocalisation
- 1 – Groaning
- 0 – None

MOTOR RESPONSE

- 3 – Localization to noxious stimulation
- 2 – Flexion withdrawal
- 1 – Abnormal posturing
- 0 – None/Flaccid

FACIAL EXPRESSION

- 3 – Cry
- 2 – Grimace
- 1 – Oral reflexive movement/Startle response
- 0 – None

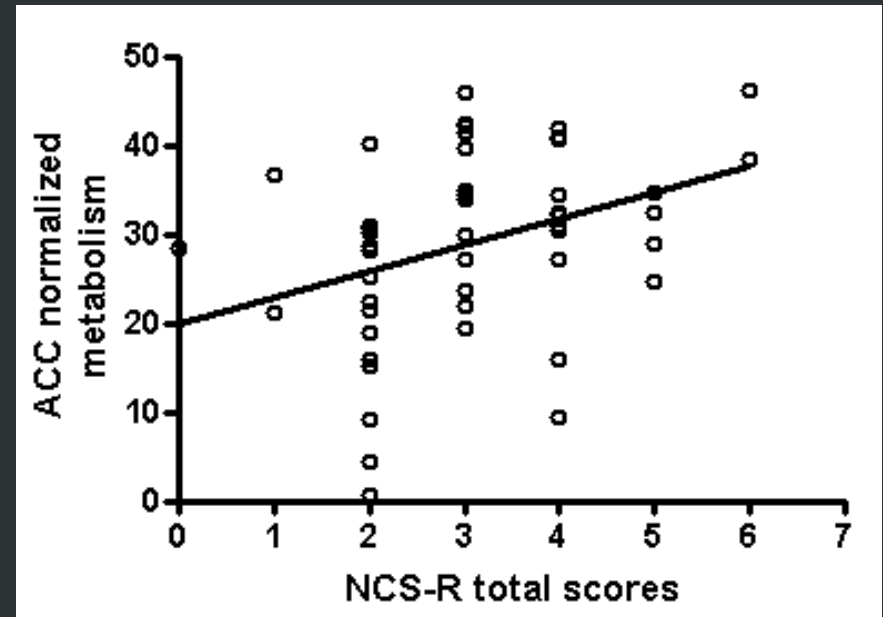
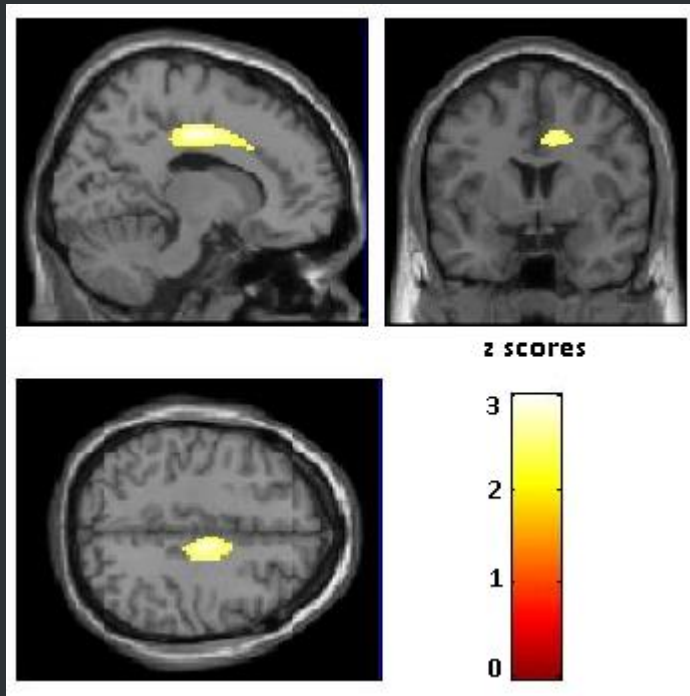
Total score : 9



NCS-R and brain metabolism

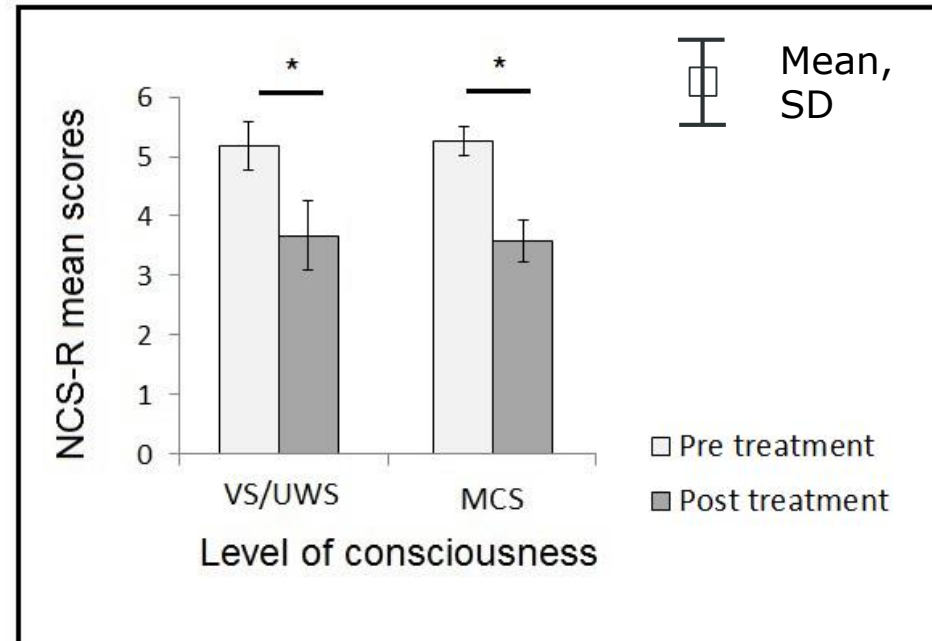
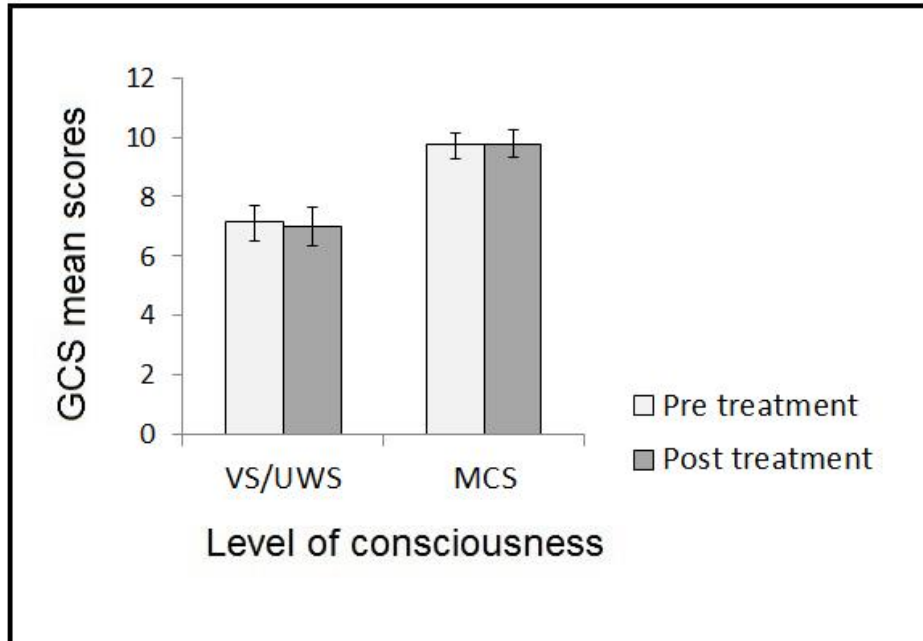
NCS-R total scores correlate with posterior part of the anterior cingulate cortex

→ **cognitive-affective dimension** of pain (Rainville, 1997)





NCS-R in acute setting





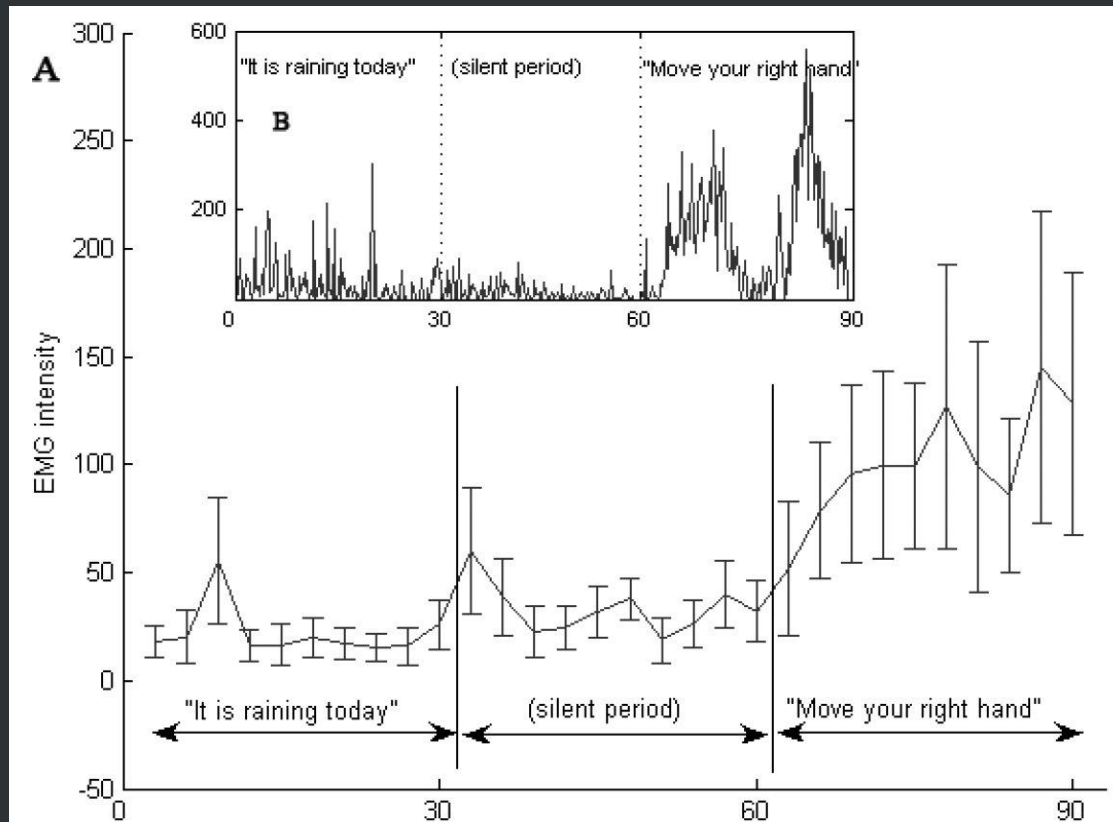
Summary

- High rate of misdiagnosis if non sensitive scales are used (up to 40%)
 - CRS-R
- 76% documented potential pain, 59% not treated with analgesics
 - NCS-R for assessing pain
- Useful for monitoring recovery/medical complications
- Caveats
 - Language dependent
 - Relying strongly on motor abilities



Active paradigm – EMG

« Move your right hand »



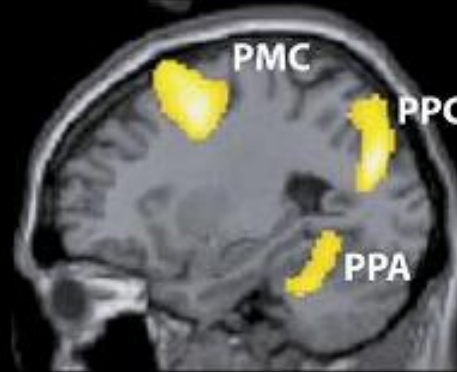


Active paradigm – fMRI

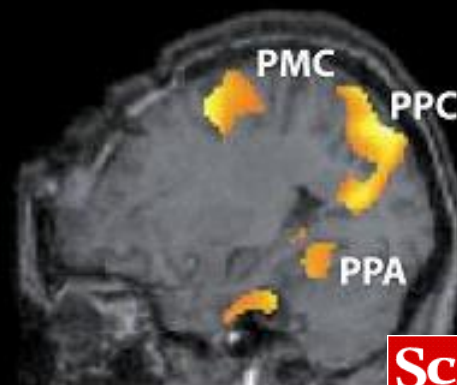
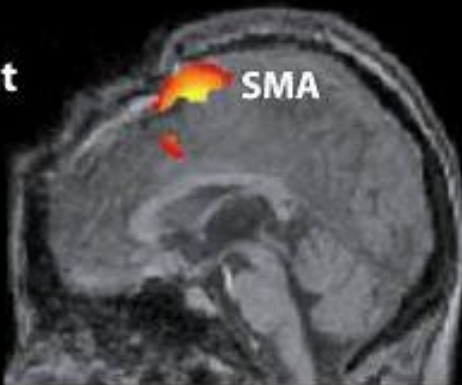
Tennis Imagery

Spatial Navigation Imagery

Controls



Patient



"He's not in coma...
he's playing tennis!"



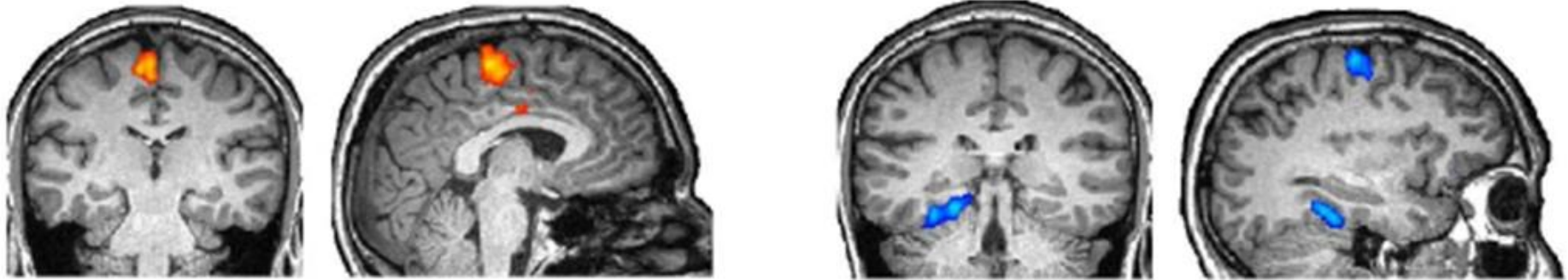
Science



Active paradigm – fMRI

The NEW ENGLAND
JOURNAL of MEDICINE

HEALTHY SUBJECT



Answers « YES »

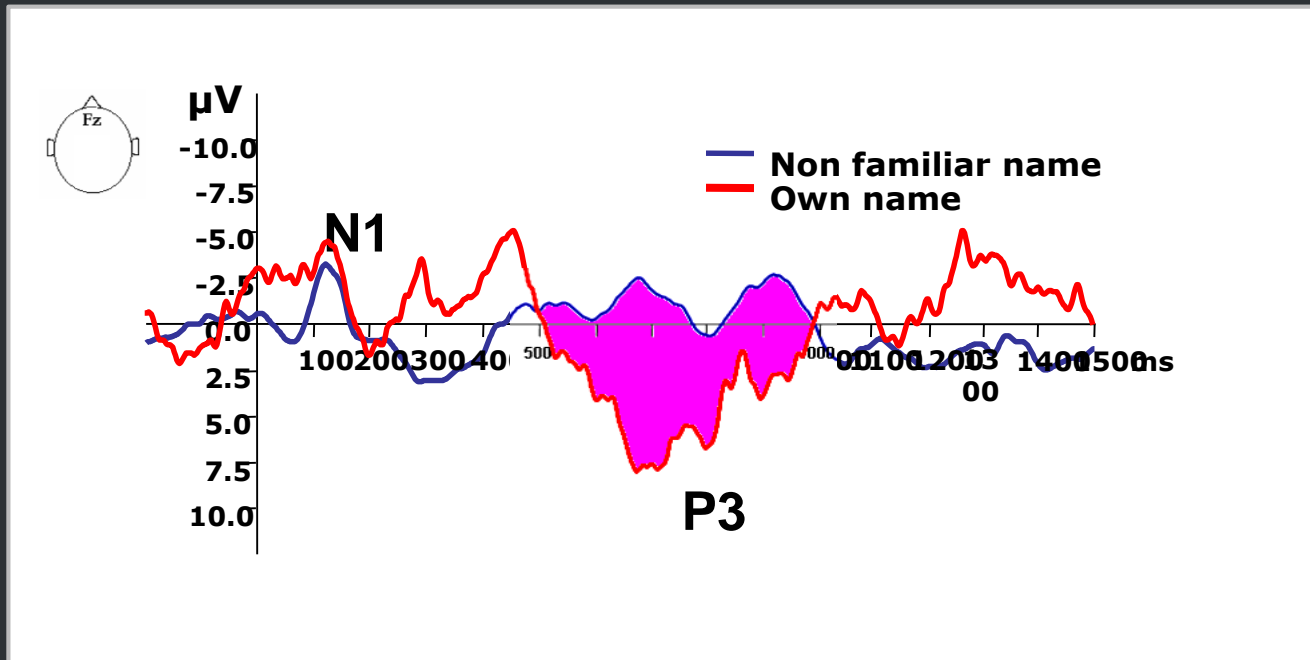
Answers « NO »

« VEGETATIVE STATE »



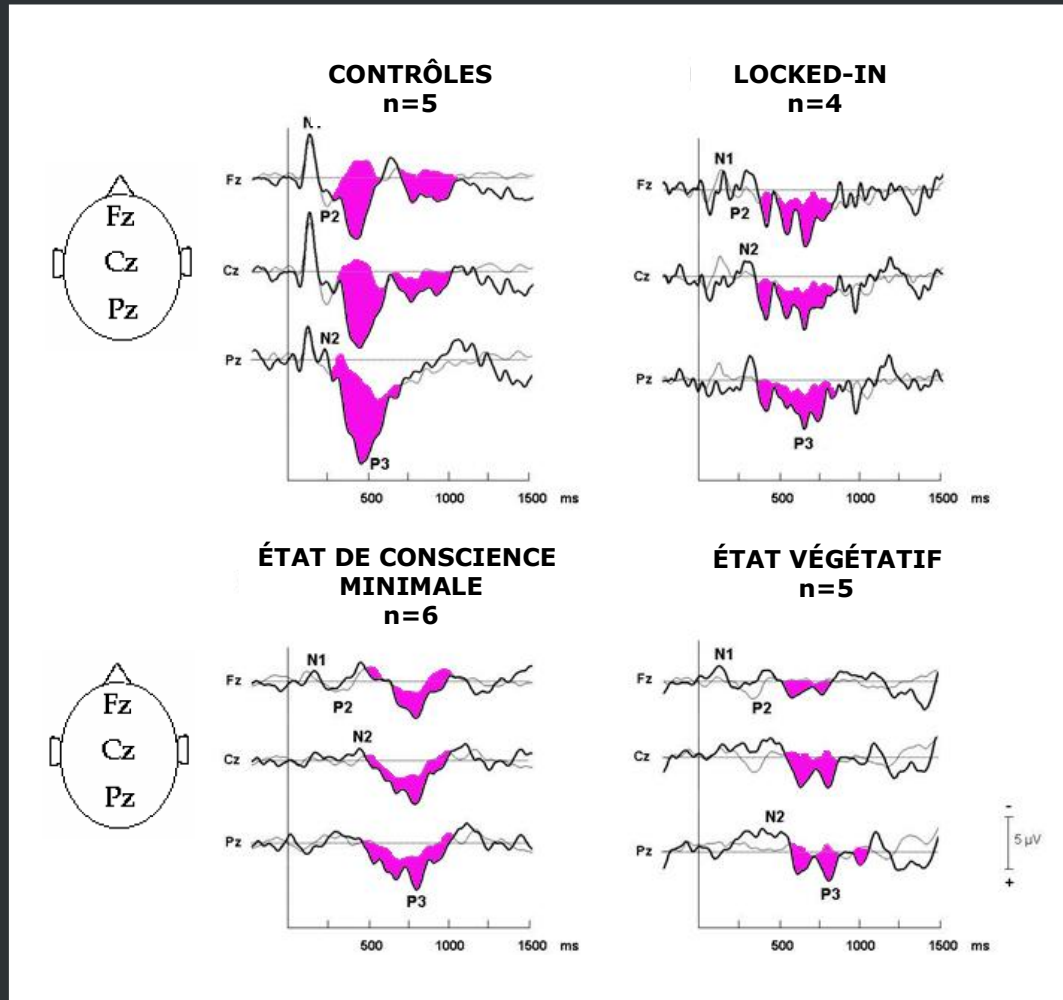


Active paradigm – EEG





Active paradigm – EEG





Active paradigm – EEG



Coma or total locked-in syndrome?

21-y old woman
basilar artery thrombosis - day 49



Other names PASSIVE
 Count TARGET (other name)
 Own name PASSIVE
 Count TARGET (own name)



Active paradigm – EEG

“MOVE YOUR FOOT”

“MOVE YOUR HAND”



HEALTHY
CONTROL
SUBJECT



“VEGETATIVE”
UNRESPONSIVE
PATIENT



www.thelancet.com



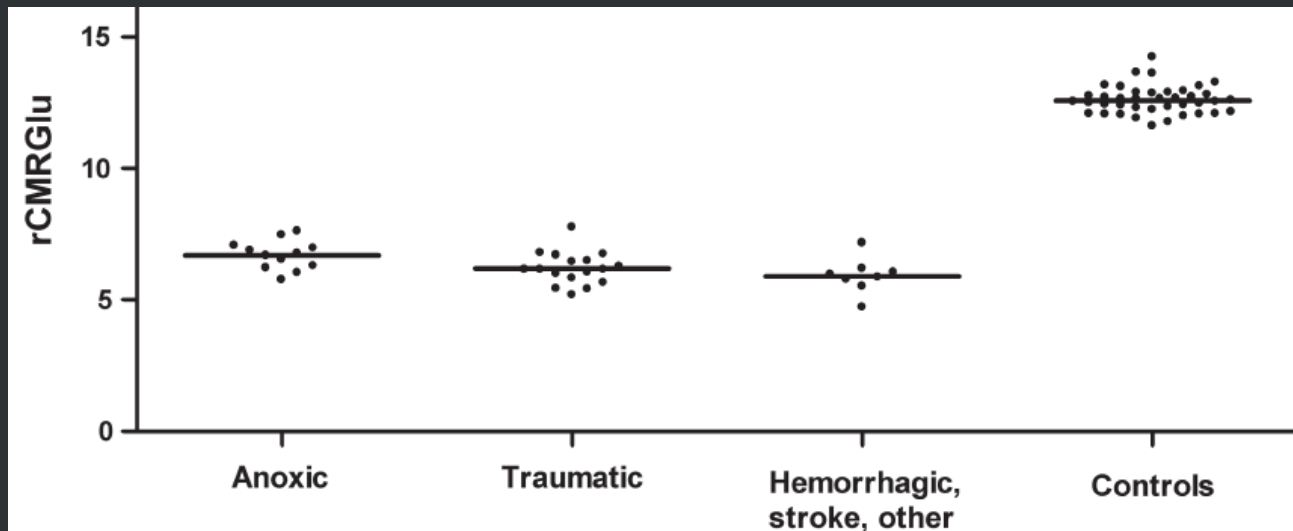
Command-following and aphasia

The problem of aphasia in the assessment of consciousness in brain-damaged patients[☆]

Steve Majerus^{1,3}, Marie-Aurélie Bruno^{2,3}, Caroline Schnakers²,
Joseph T. Giacino⁴ and Steven Laureys^{2,3,*}

Progress in Brain Research, Vol. 177
Copyright © 2009 Elsevier

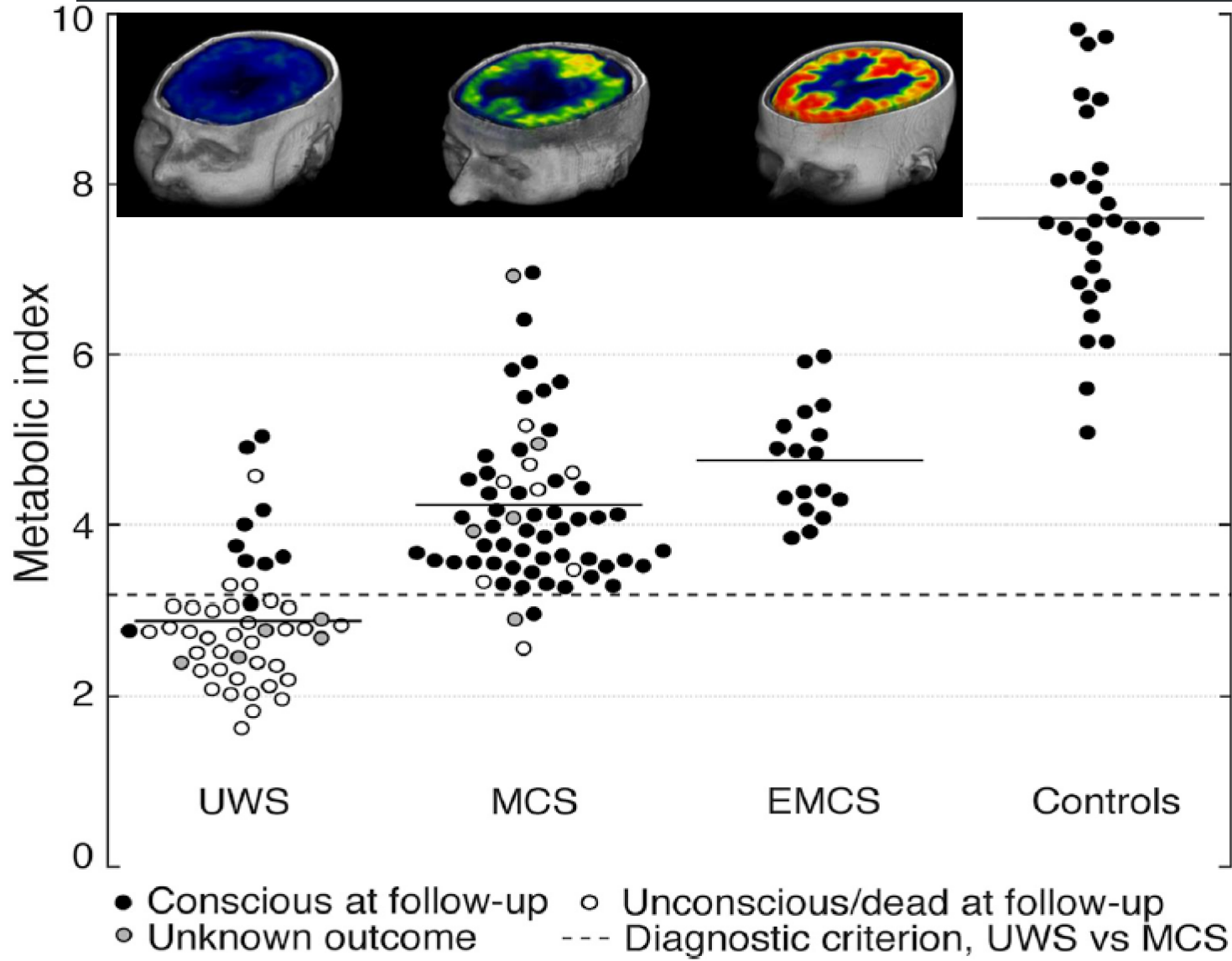
Metabolism in language network





G I
28

Brain metabolism



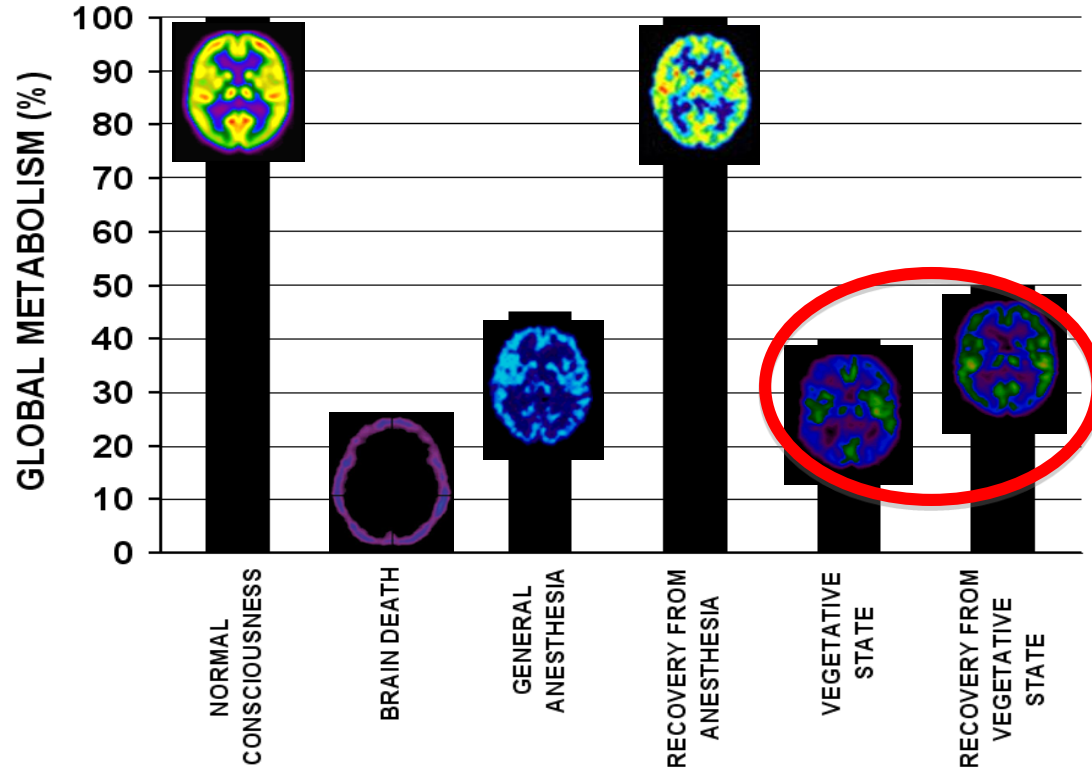
Brain metabolism

CONSCIOUSNESS

29

□ PET

Consciousness
≠ whole brain





CONSCIOUSNESS

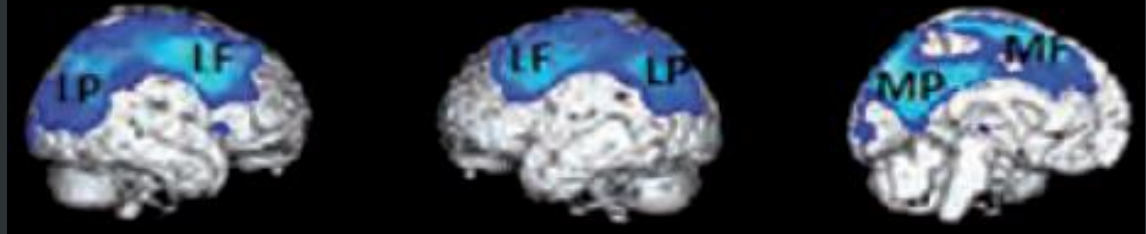
30

Brain metabolism

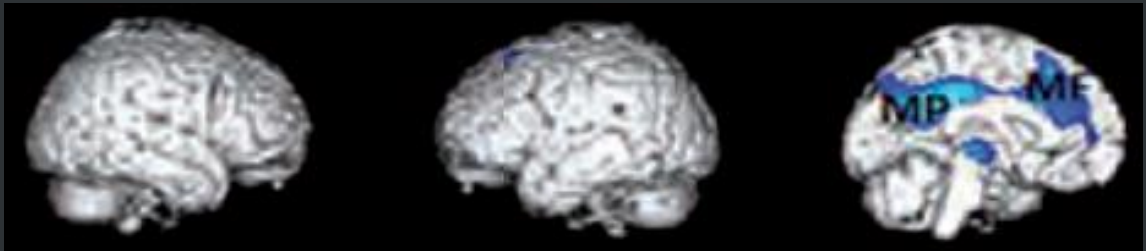
□ PET

Consciousness
≠ whole brain

UNRESPONSIVE WAKEFULNESS / VEGETATIVE STATE



MINIMALLY CONSCIOUS STATE



Consciousness
≈ **fronto-parietal network**

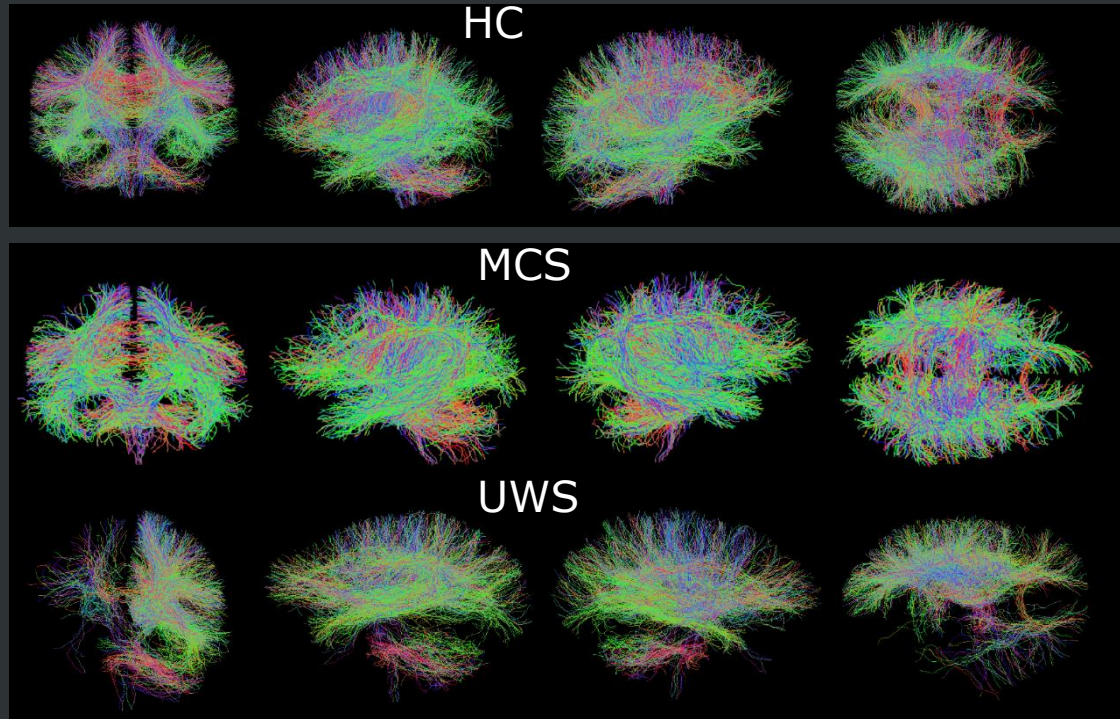
Magnetic resonance imaging

CONSCIOUSNESS

31

□ Structural

White matter





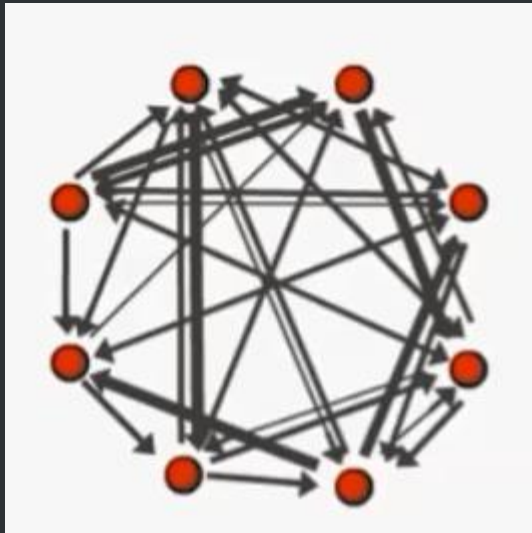
TMS/EEG



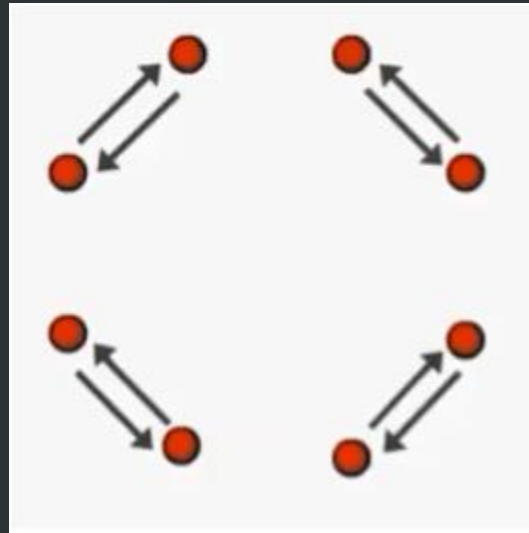


Integrated information theory

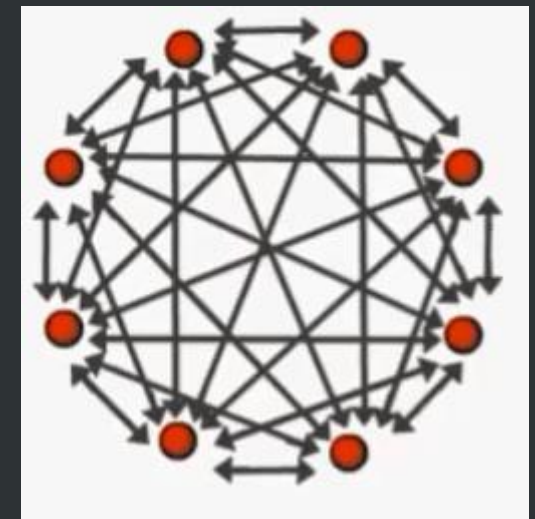
Consciousness = integration and differentiation



Consciousness



Loss of integration

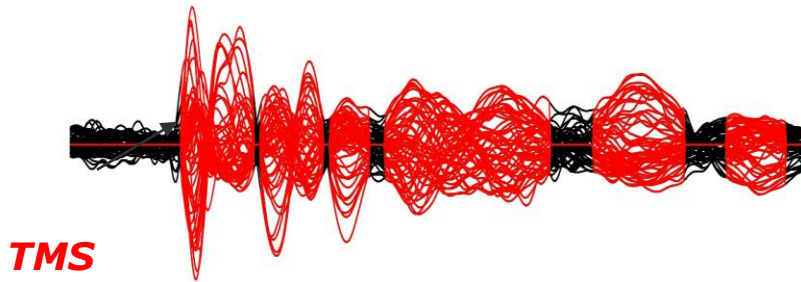


Loss of differentiation



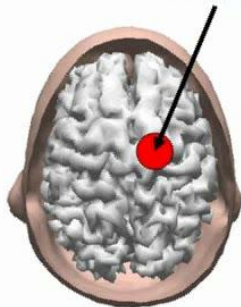
TMS/EEG

Wakefulness

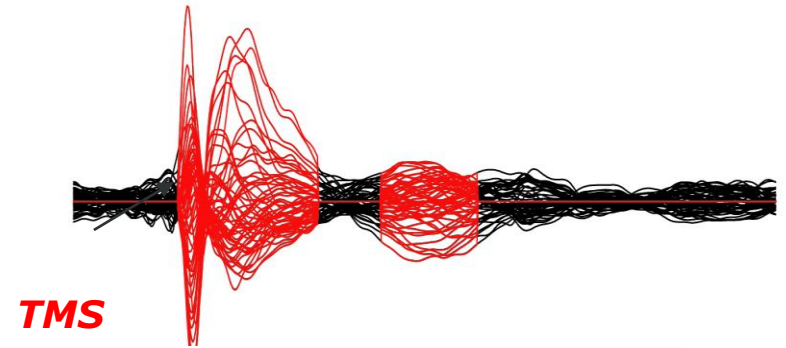


0 ms

TMS

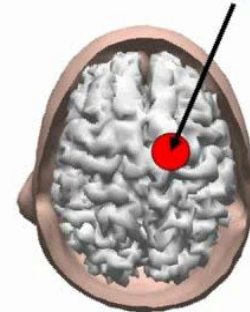


Deep sleep



0 ms

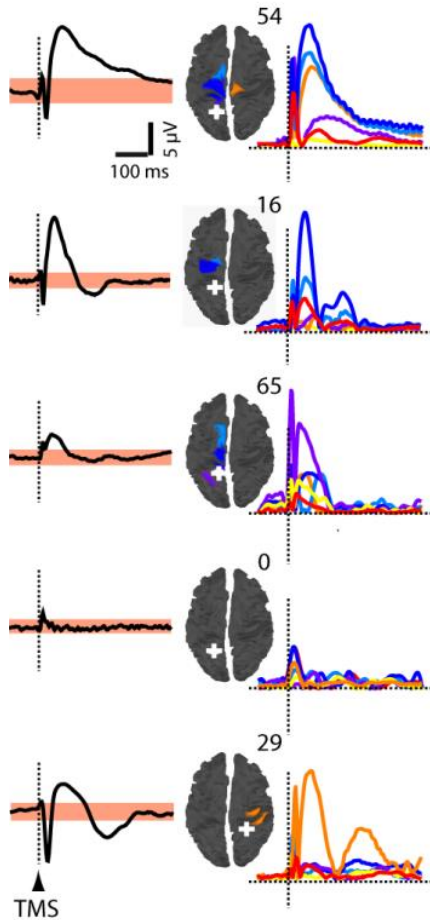
TMS



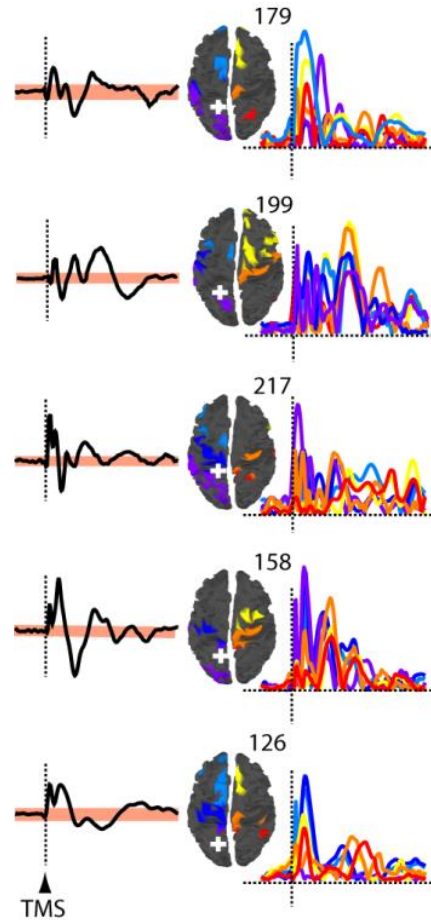


Passive paradigm – TMS/EEG

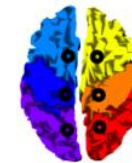
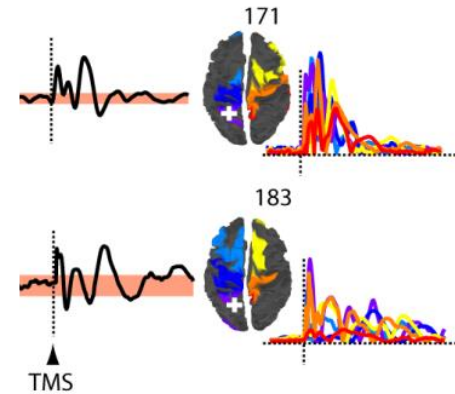
VS



MCS



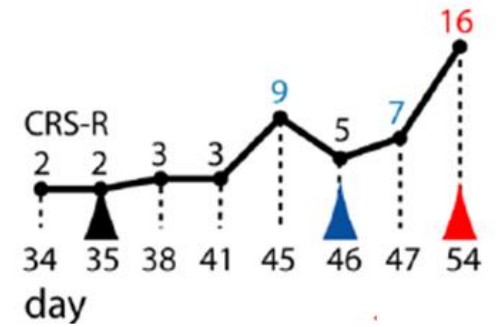
LIS



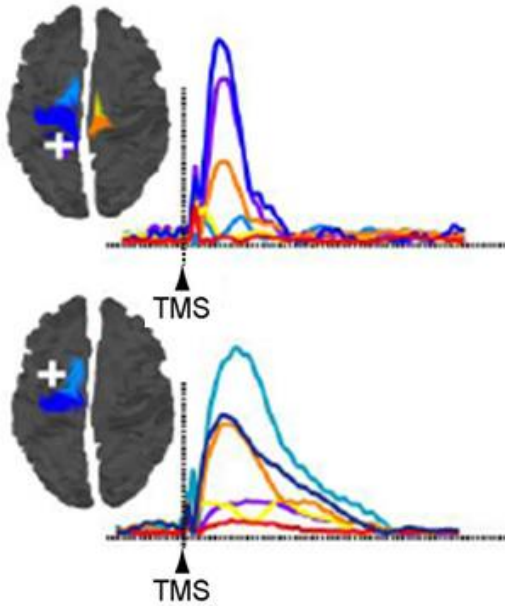
- L frontal
- L sensory-motor
- L parieto-occipital
- R frontal
- R sensory-motor
- R parieto-occipital



Passive paradigm – TMS/EEG

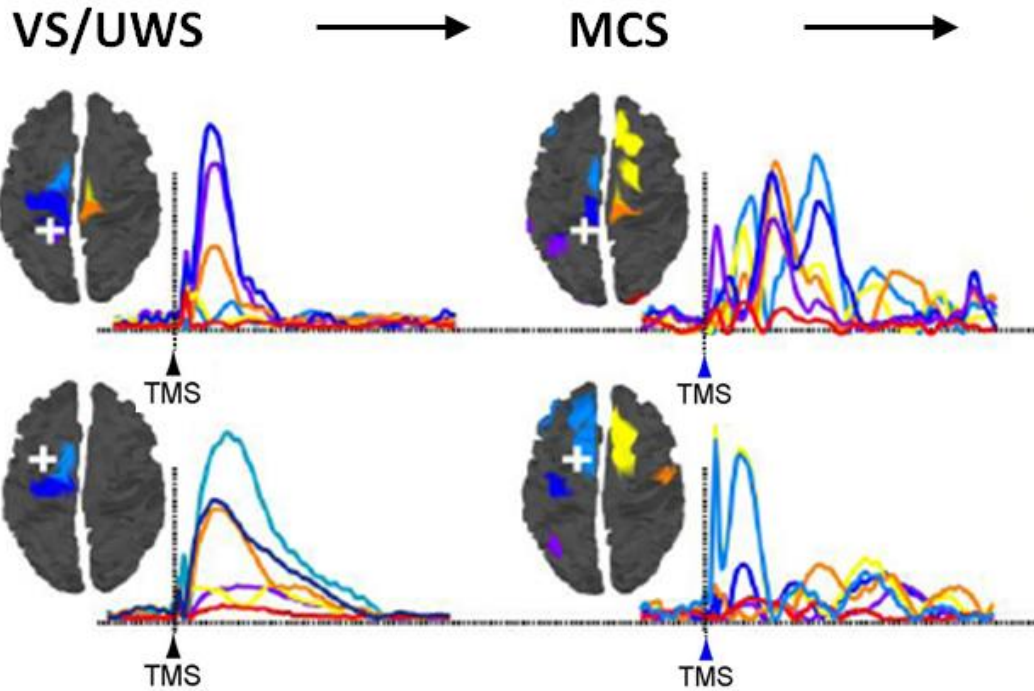
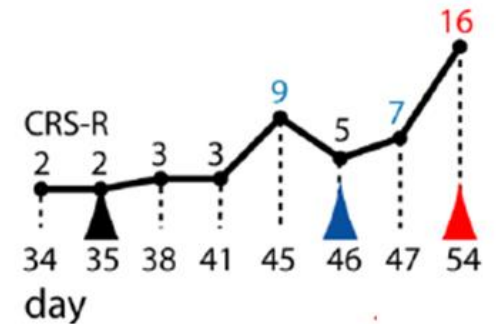


VS/UWS



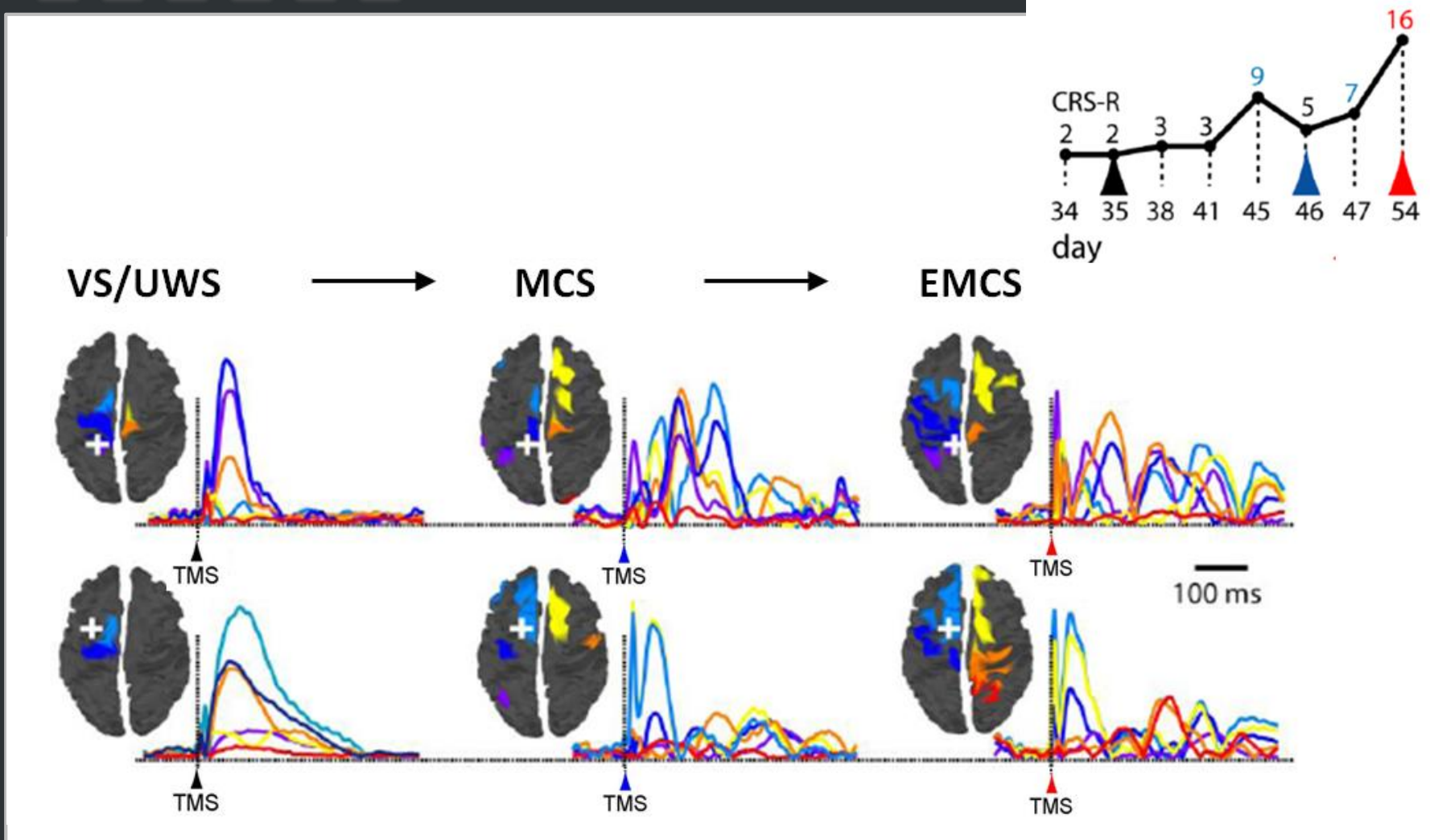


Passive paradigm – TMS/EEG



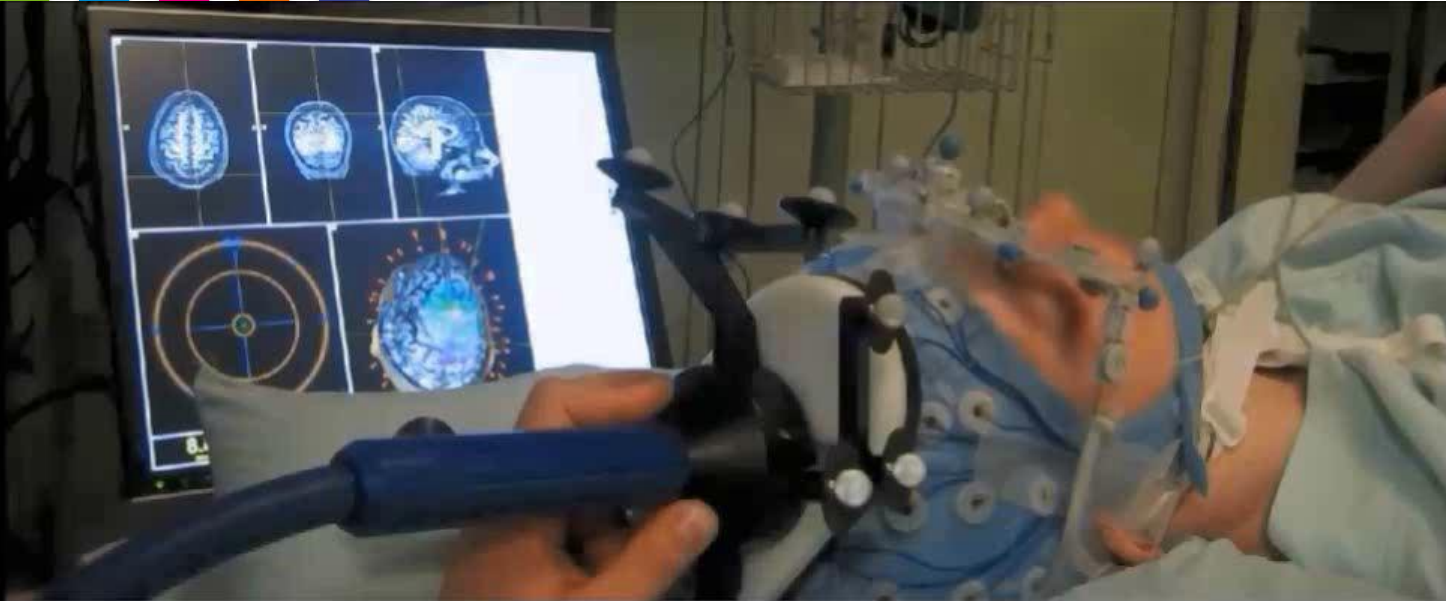


Passive paradigm – TMS/EEG





Perturbational complexity index





Perturbational complexity index

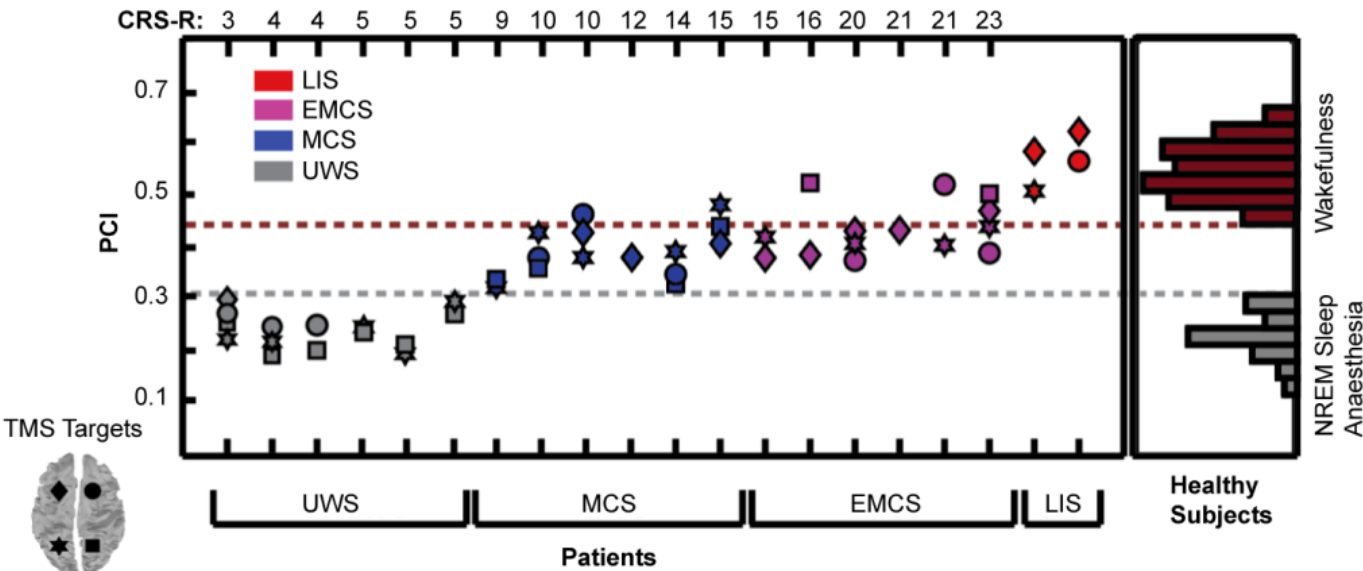
Unconsciousness



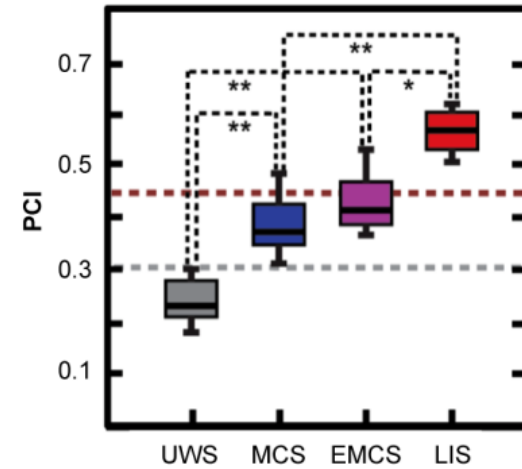
Perturbational complexity index



A



B



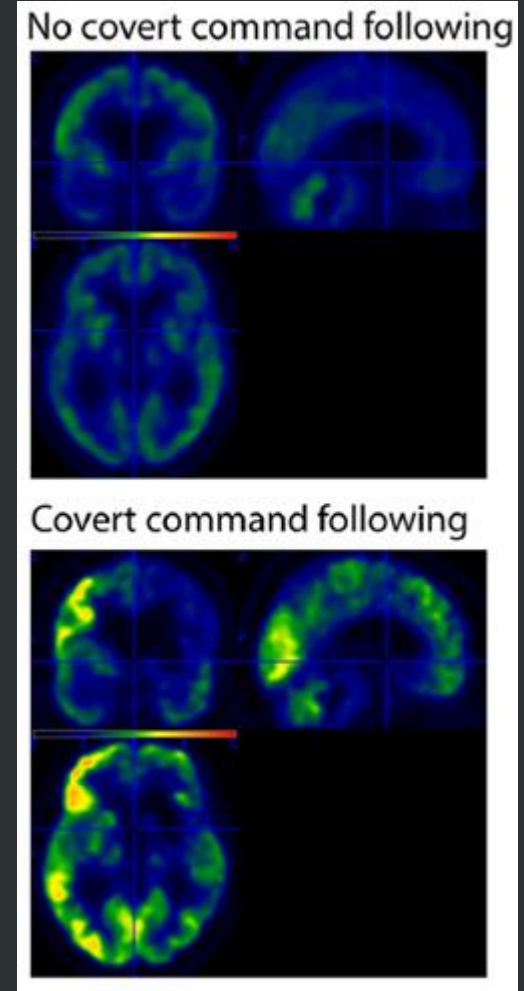
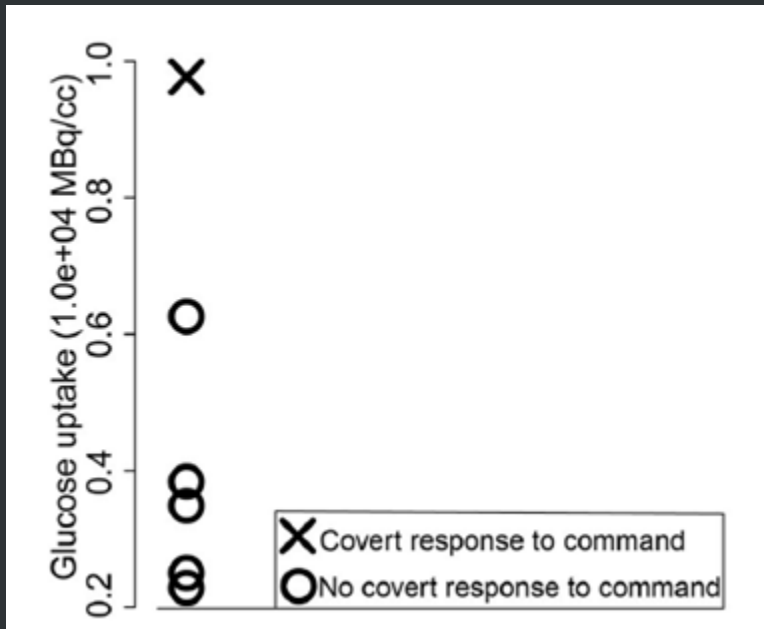


Summary

- Behavioral assessment \approx 40% misdiagnosis
- FDG-PET as a good complement beside examinations
- Active fMRI/EEG/EMG paradigms are less suited for differential diagnosis, but may provide a strong complementary tool
- TMS-EEG may provide for the first time a passive measure of consciousness at the single subject level
- Encourage to use **multimodal assessment** of the level of consciousness!



Multimodality



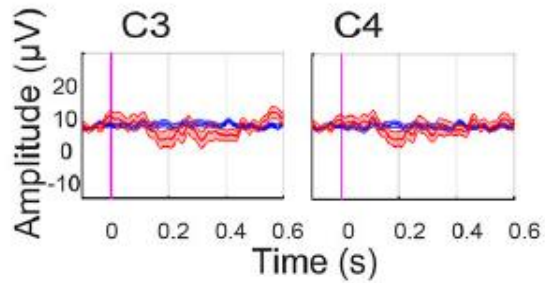


Multimodality

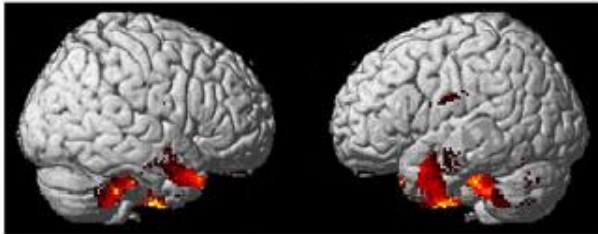


BCI accuracy UWS, PET UWS

Patient UWS 6

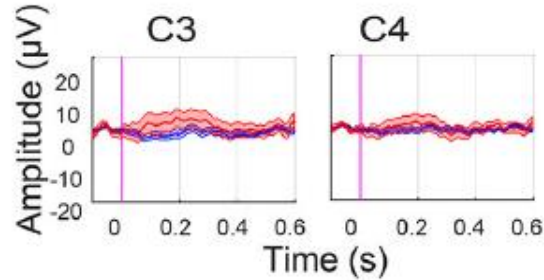


BCI VT2 accuracy: 0%

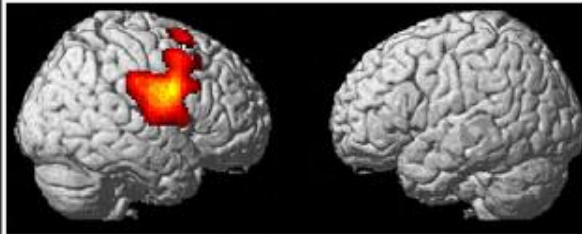


BCI accuracy UWS, PET MCS

Patient MCS- 2

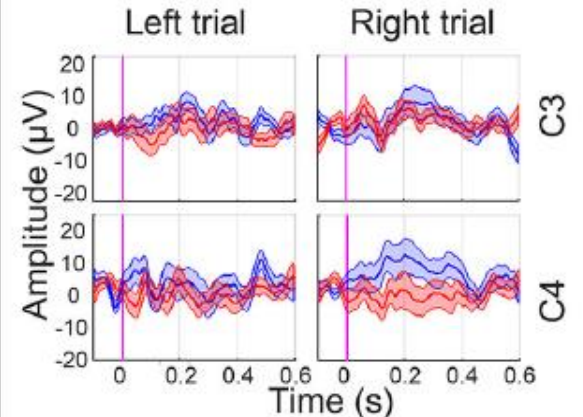


BCI VT2 accuracy: 20%

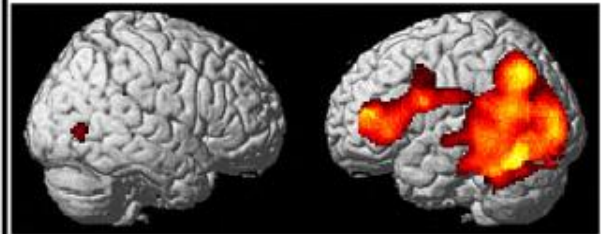


BCI accuracy MCS, PET MCS

Patient MCS- 1



BCI VT3 accuracy: 70%





Case reports

Behavioral assessment

ECHELLE DE RÉCUPÉRATION DU COMA
VERSION REVUE FRANÇAISE ©2004
Formulaire de rapport

Patient :	Date atteinte cérébrale :
Etiologie :	Date admission :
Diagnostic initial :	Date :
Examineur :	

FUNCTION AUDITIVE	FUNCTION MOTRICE
4 – Mouvement systématique sur demande*	0 – Utilisation fonctionnelle des objets*
3 – Mouvement reproductible sur demande*	5 – Réaction motrice automatique*
2 – Localisation de sons	4 – Manipulation d'objets*
1 – Réflexe de sursaut au bruit	3 – Localisation des stimulations nociceptives*
0 – Néant	2 – Flexion en rétro*
	1 – Posture anormale stéréotypée
	0 – Néant/ Flaccidité
FUNCTION VISUELLE	FUNCTION OROMOTRICE/VERBALE
5 – Reconnaissance des objets*	3 – Production verbale intelligible*
4 – Localisation des objets : atteinte*	2 – Production vocale / Mouvements oraux
3 – Poursuite visuelle*	1 – Réflexes oraux
2 – Fixation*	0 – Néant
1 – Réflexe de clignement à la menace	COMMUNICATION
0 – Néant	2 – Fonctionnelle : exacte*
	1 – Non fonctionnelle : intentionnelle*
	0 – Néant
	EVEIL
	3 – Attention
	2 – Ouverture des yeux sans stimulation
	1 – Inattention
	0 – Fermeture des yeux sans stimulation

NOCICEPTION COMA SCALE – NCS ©2005
Record Form

Spontaneous behaviour observation (80sec.) is required before nociceptive stimulation

Patient :	Date :
MOTOR RESPONSE	
3 – Localization to noxious stimulation*	
2 – Flexion withdrawal	
1 – Abnormal posturing	
0 – None/Flaccid	
VERBAL RESPONSE	
3 – Intelligible verbalization*	
2 – Vocalization	
1 – Groaning	
0 – None	
VISUAL RESPONSE	
3 – Fixation*	
2 – Eyes movements	
1 – Startle	
0 – None	
FACIAL EXPRESSION	
3 – Cry*	
2 – Grimace	
1 – Oral reflexive movement/Startle response	
0 – None	
TOTAL SCORE	

TMS-EEG



MRI



PET scan



BCI



EEG





Case reports

- 41 years old

- 4 years et 9 months post
anoxia

- Diagnosis :
vegetative/unresponsive
state

- 35 years old

- 6 years and 10 months
post ischemic stroke

- Diagnosis :
vegetative/unresponsive
state



Case reports

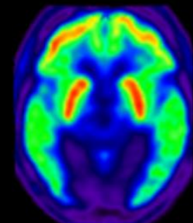
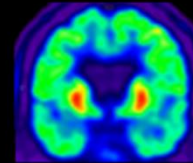
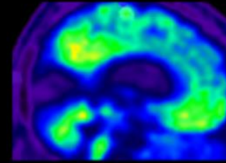
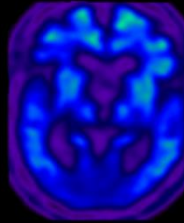
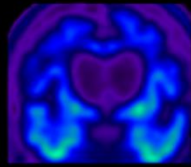
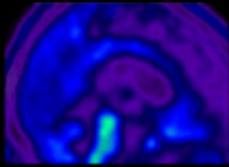
CRS-R						
FONCTION AUDITIVE						
4–Mouvement systématique sur demande*						
3–Mouvement reproductible sur demande*						
2 – Localisation de sons						
1 – Réflexe de sursaut au bruit	X	X	X	X	X	X
0 – Néant						
FONCTION VISUELLE						
5 – Reconnaissance des objets*						
4 – Localisation des objets : atteinte*						
3 – Poursuite visuelle*						
2 – Fixation*						
1 – Réflexe de clignement à la menace						
0 – Néant	X	X	X	X	X	X
FONCTION MOTRICE						
6 – Utilisation fonctionnelle des objets*						
5 – Réaction motrice automatique*						
4 – Manipulation d'objets*						
3–Localisation des stimulations nociceptives*						
2 – Flexion en retrait						
1 – Posture anormale stéréotypée	X	X	X	X	X	X
0 – Néant / Flaccidité						
FONCTION OROMOTRICE/VERBALE						
3 – Production verbale intelligible*						
2 – Production vocale / Mouvements oraux						
1 – Réflexes oraux	X	X	X	X	X	X
0 – Néant						
COMMUNICATION						
2 – Fonctionnelle : exacte*						
1 – Non fonctionnelle : intentionnelle*						
0 – Néant	X	X	X	X	X	X
ÉVEIL						
3 – Attention						
2 – Ouverture des yeux sans stimulation			X	X		
1 – Ouverture des yeux avec stimulation	X	X			X	
0 – Aucun éveil						X
Score total	4	4	5	5	4	3

CRS-R					
FONCTION AUDITIVE					
4–Mouvement systématique sur demande*					
3–Mouvement reproductible sur demande*					
2 – Localisation de sons					
1 – Réflexe de sursaut au bruit					
0 – Néant	X	X	X	X	X
FONCTION VISUELLE					
5 – Reconnaissance des objets*					
4 – Localisation des objets : atteinte*					
3 – Poursuite visuelle*					
2 – Fixation*					
1 – Réflexe de clignement à la menace					
0 – Néant	X	X	X	X	X
FONCTION MOTRICE					
6 – Utilisation fonctionnelle des objets*					
5 – Réaction motrice automatique*					
4 – Manipulation d'objets*					
3–Localisation des stimulations nociceptives*					
2 – Flexion en retrait	X		X	X	X
1 – Posture anormale stéréotypée		X			
0 – Néant / Flaccidité					
FONCTION OROMOTRICE/VERBALE					
3 – Production verbale intelligible*					
2 – Production vocale / Mouvements oraux					
1 – Réflexes oraux	X	X	X	X	X
0 – Néant					
COMMUNICATION					
2 – Fonctionnelle : exacte*					
1 – Non fonctionnelle : intentionnelle*					
0 – Néant	X	X	X	X	X
ÉVEIL					
3 – Attention					
2 – Ouverture des yeux sans stimulation					
1 – Ouverture des yeux avec stimulation	X	X	X	X	X
0 – Aucun éveil					
Score total	4	3	4	4	4



Case reports

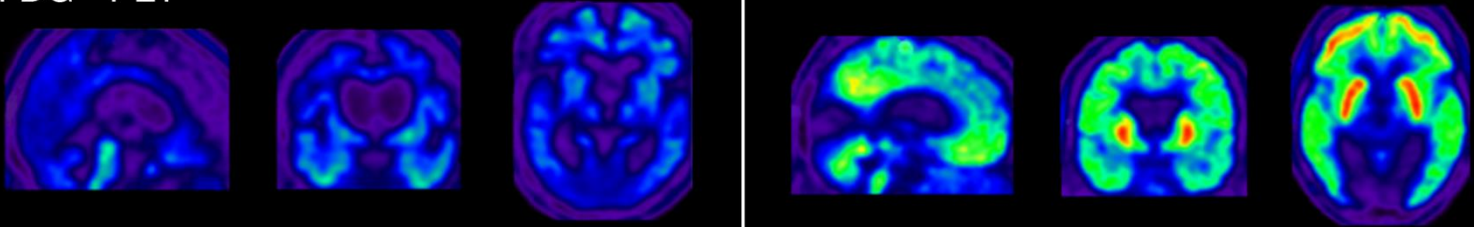
FDG - PET



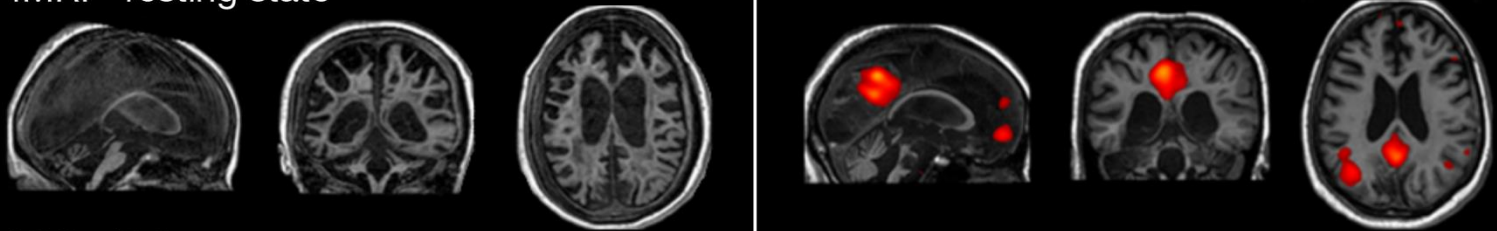


Case reports

FDG - PET



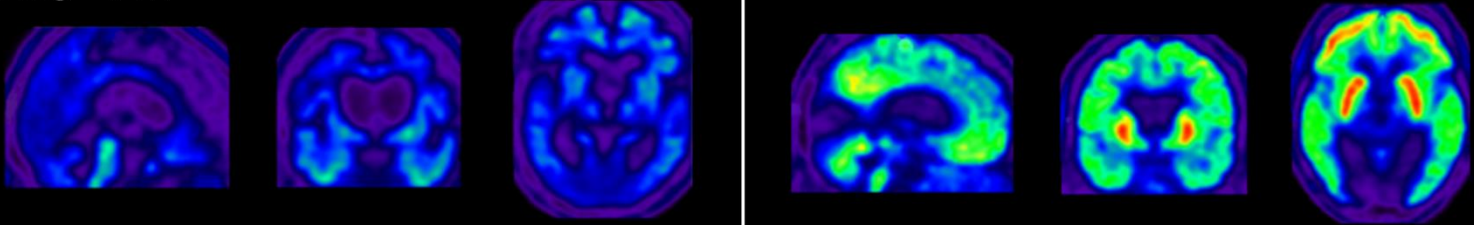
fMRI - resting state



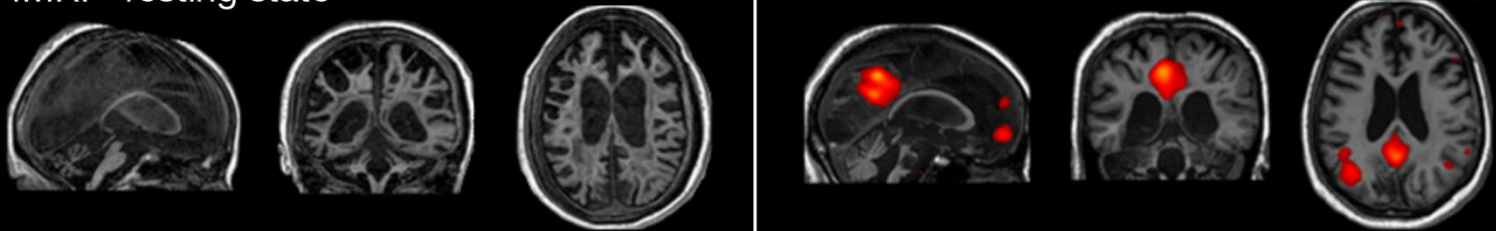


Case reports

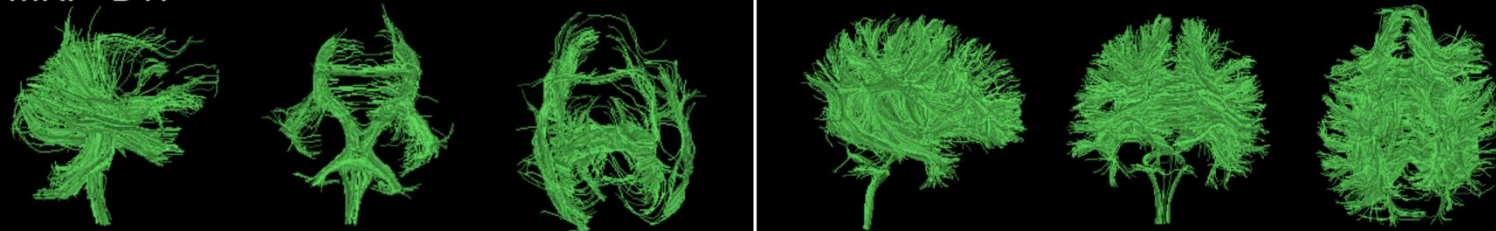
FDG - PET



fMRI - resting state



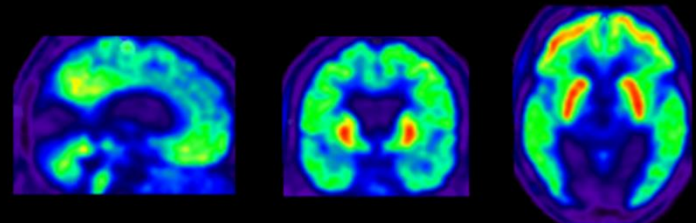
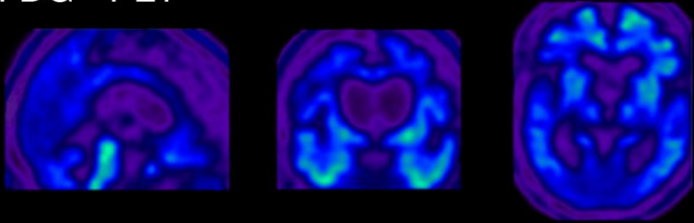
MRI - DTI



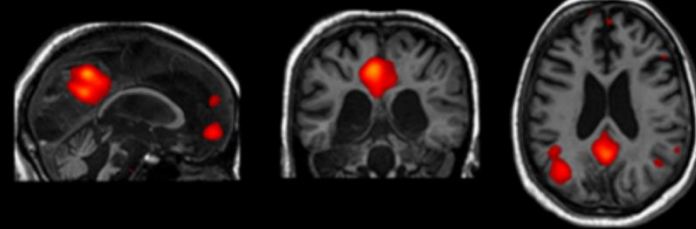
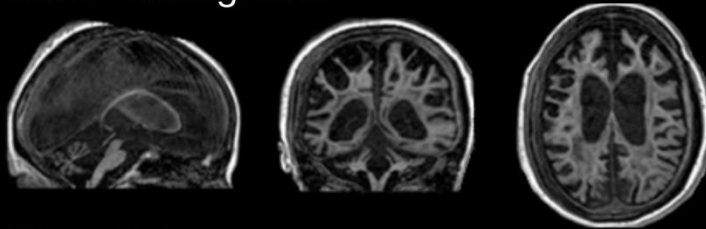


Case reports

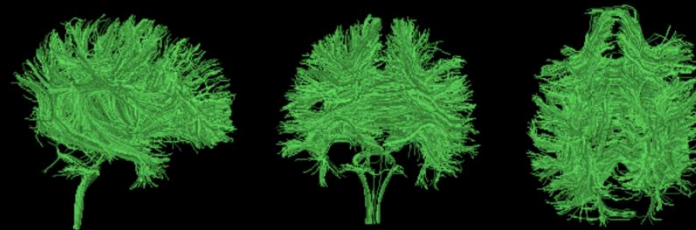
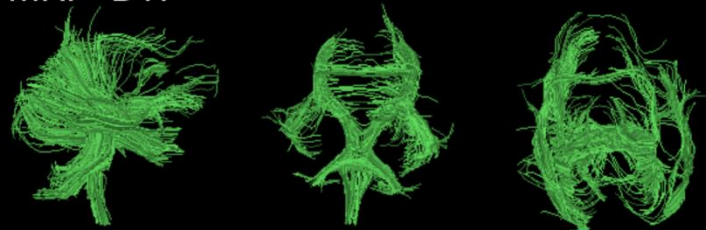
FDG - PET



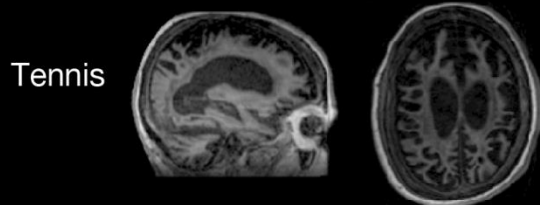
fMRI - resting state



MRI - DTI

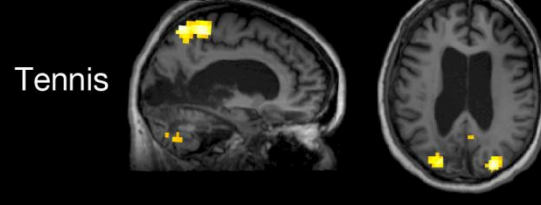


fMRI - mental imagery task



Tennis

Navigation



Tennis

Navigation



Consciousness under the eye of science

52

- 2 components: arousal + awareness of oneself and environment
- 2 awareness networks
- Consciousness \approx frontoparietal / thalamo-cortical network
- Use standardized scales: CRS-R, NCS-R
- Motor and language caveats \Rightarrow misdiagnosis!
- Paraclinical assessments
 - High heterogeneity in sensitivity and specificity!!
 - Multimodality when available
- Ethical challenge: quality of life, care and end of life decisions



THANK YOU!

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