Diagnosis and treatment in patients with disorders of consciousness

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Overview

- Disorders of Consciousness
  - Clinical entities
  - Consciousness and the brain
  - Brain processing in DOC
- Diagnosis
  - Consciousness
  - Nociception and pain

Break

Overview

- Paraclinical diagnosis
  - Active paradigms
  - Passive paradigms
  - Case reports
- Treatments
  - Pharmacological
  - Brain stimulation
- Locked-in Syndrome
- Near-death experiences

Disorders of consciousness

Clinical entities

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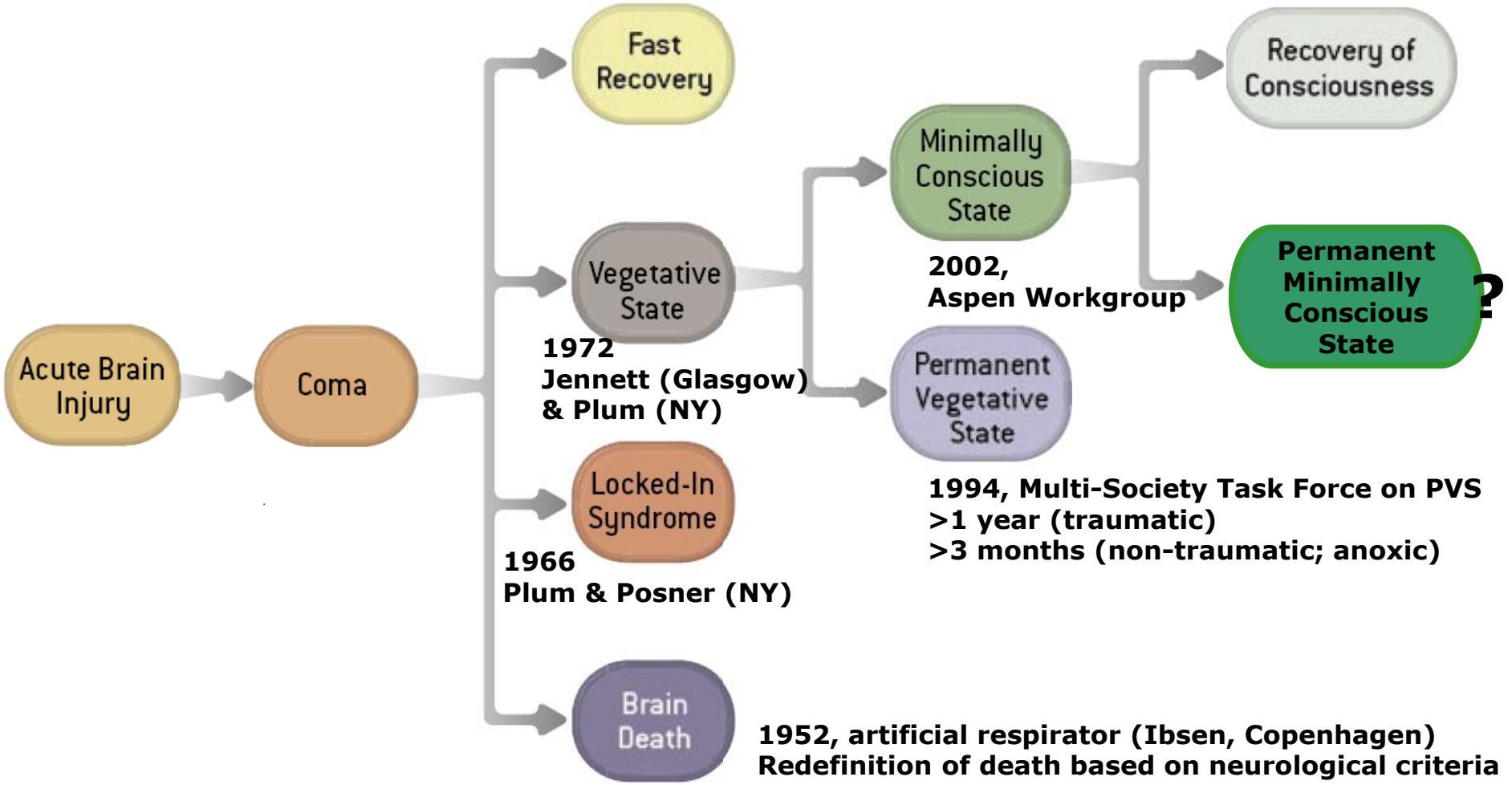
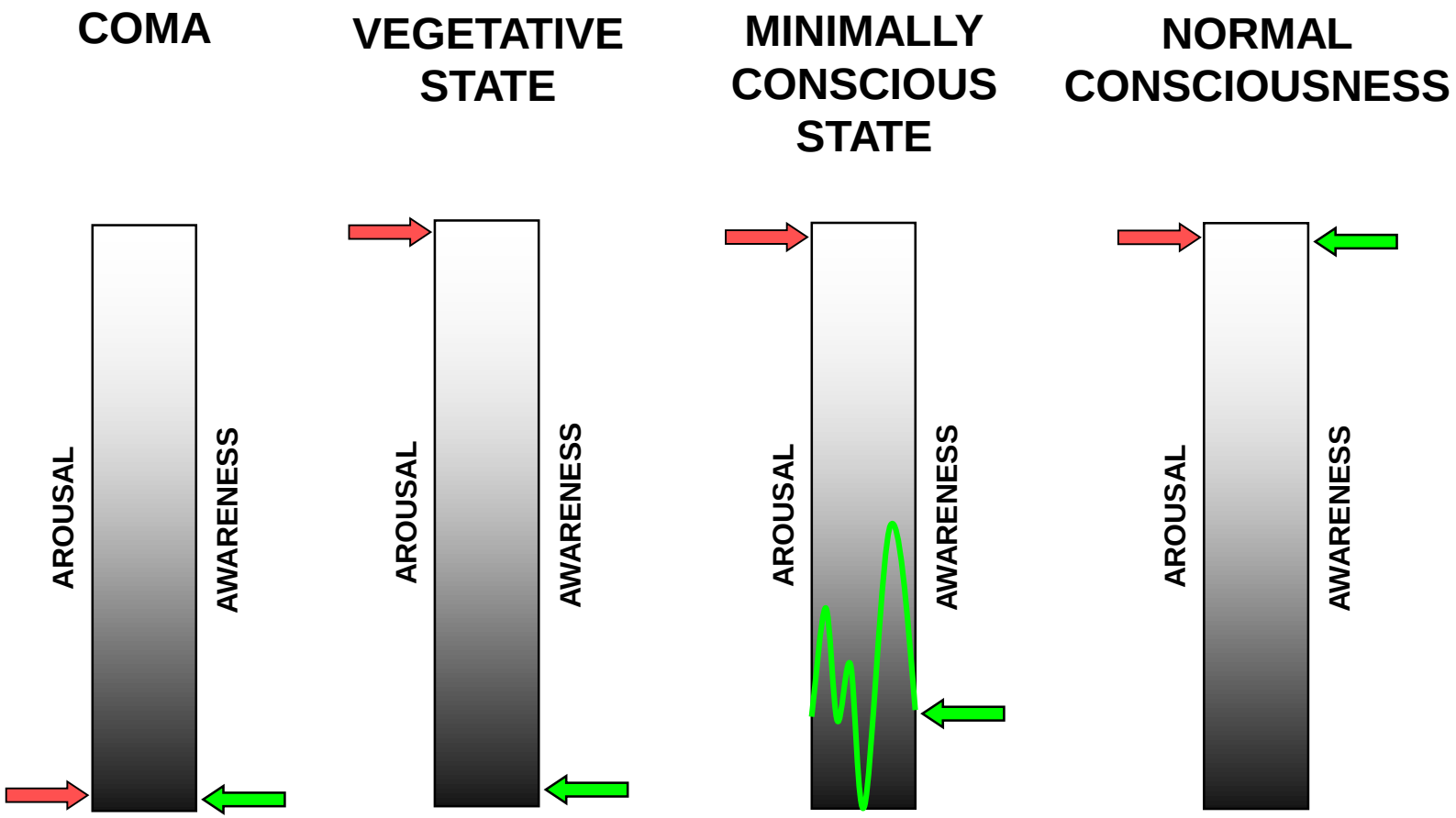
Clinical entities



Laureys, Scientific American, 2007

Clinical entities



Laureys et al, Lancet Neurol, 2004; the European Task Force on Disorders of Consciousness, BMC Med, 2010

Coma

- No eyes opening
- No sign of consciousness
- Lasting min 1 hour

Posner et al, 2007

Vegetative/unresponsive wakefulness syndrome

- No sign of consciousness
- No environment interaction
- No voluntary behavior in response to visual, auditive, tactile and painful stimuli
- No language comprehension – no language expression
- Wake-sleep cycle

Multi-Society Task Force on Persistent Vegetative State guidelines, 1994
Laureys et al., 2010

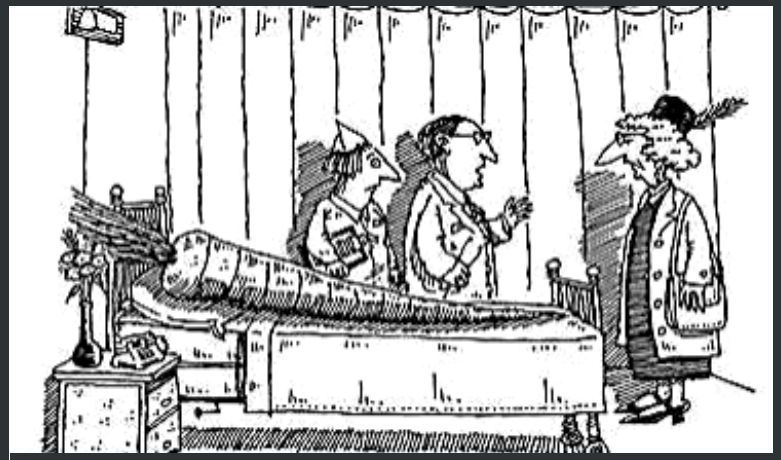
Vegetative/unresponsive wakefulness syndrome

BMC Medicine

Highly accessed | Open Access

Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome

Steven Laureys[1], Gastone G Celesia[2], Francois Cohadon[3], Jan Lavrijsen[4], José León-Carrión[5], Walter G Sannita[6,7], Leon Sazbon[8], Erich Schmutzhard[9], Klaus R von Wild[10,11], Adam Zeman[12] and Giuliano Dolce[13] for the European Task Force on Disorders of Consciousness[1]

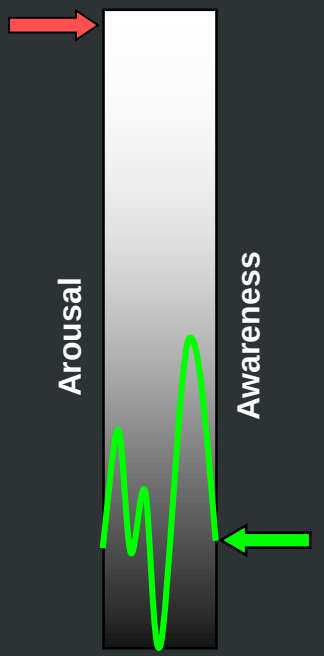


"There's nothing we can do… he'll always be a vegetable."

Laureys et al, *BMC Medicine* 2011

Minimally conscious state

- Limited but clearly discernible evidence of self or environmental awareness - one or more of the following behaviors:
  - Following simple commands
  - Gestural or verbal yes/no responses (regardless of accuracy)
  - Intelligible verbalization
  - Purposeful behavior, including movements or affective behaviors that occur in contingent relation to relevant environmental stimuli:
    - appropriate smiling/vocalizations or gestures
    - reaching for objects
    - touching or holding objects
    - visual pursuit or fixation



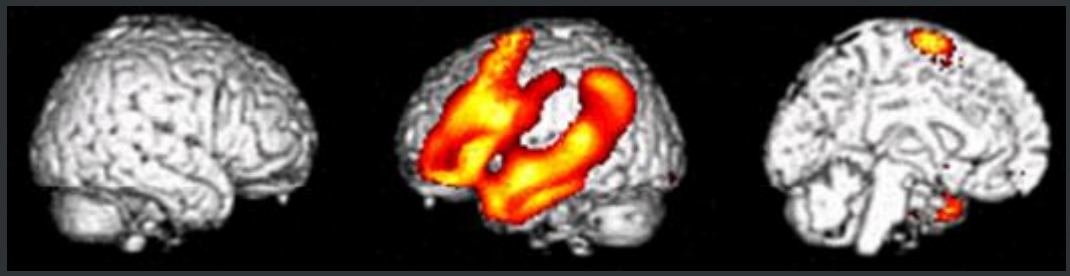
Aspen Workgroup, 2002; Bruno & Vanhaudenhuyse et al., 2011

MCS: new terminology

Minimally Conscious state

MCS +
Following simple command

MCS+ > MCS-

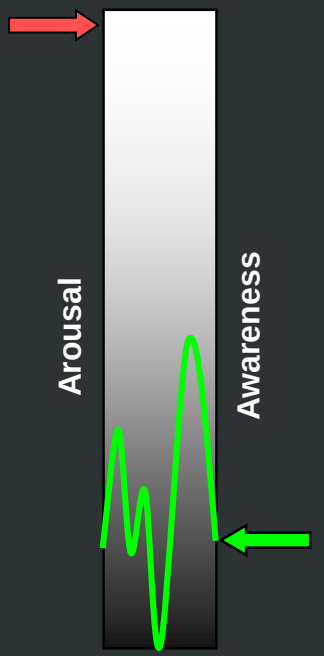


MCS -
Pain localisation
Visual pursuit
Accurate smiling or crying

Bruno & Vanhaudenhuyse et al., 2011; Bruno et al., 2011

Minimally conscious state

- MCS plus
  - reproducible command following
  - intelligible verbalizations
  - intentional communication
- MCS minus
  - Purposeful behavior, including movements or affective behaviors that occur in contingent relation to relevant environmental stimuli:
    - appropriate smiling/vocalizations or gestures
    - reaching for objects
    - touching or holding objects
    - visual pursuit or fixation



Aspen Workgroup, 2002; Bruno & Vanhaudenhuyse et al., 2011

Minimally conscious state

Emergence from MCS:

- Functional interactive communication
- Functional use of two different objects

Aspen Workgroup, 2002; Bruno & Vanhaudenhuyse et al., 2011

Disorders of consciousness

Consciousness and the brain

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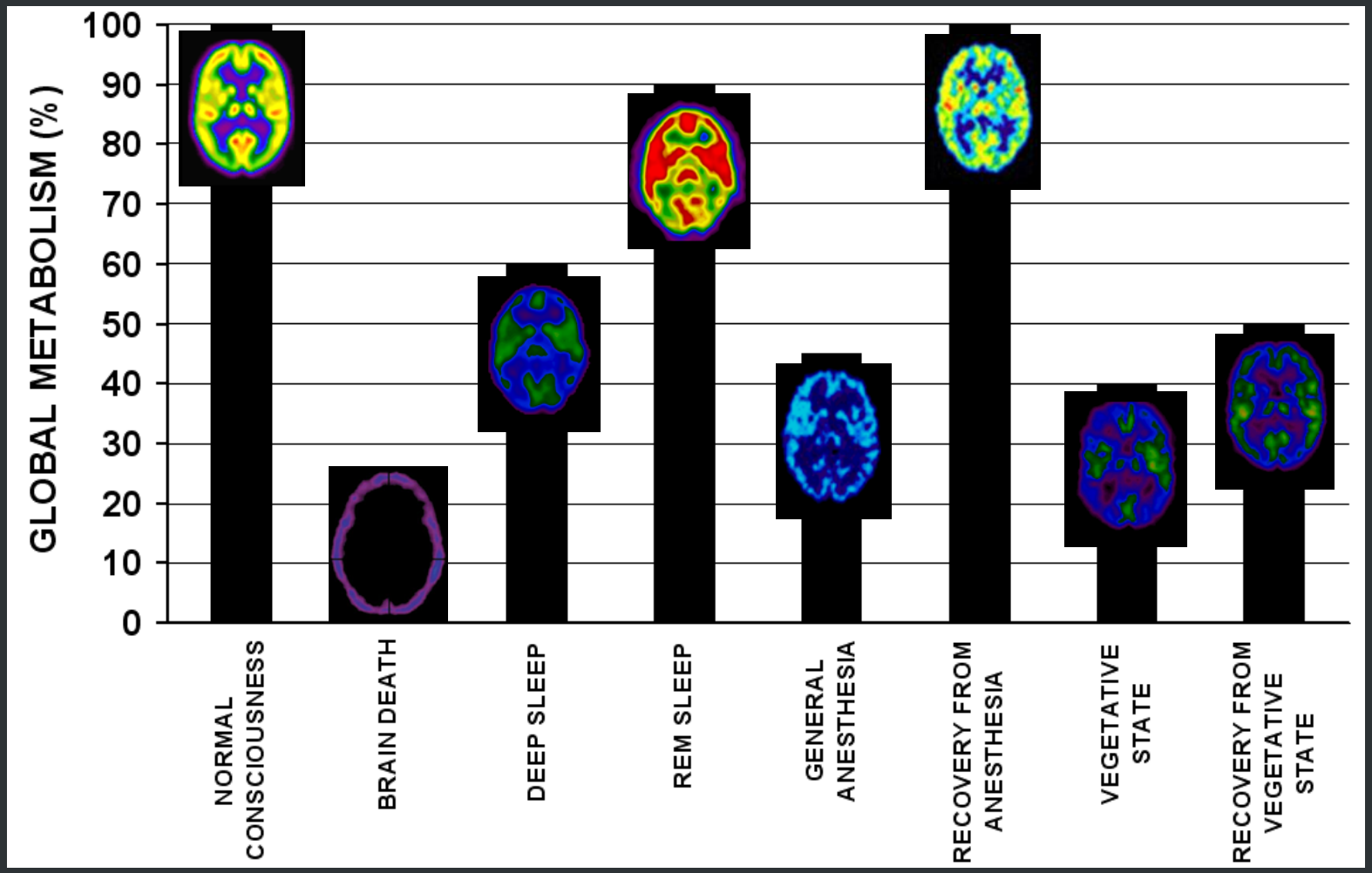
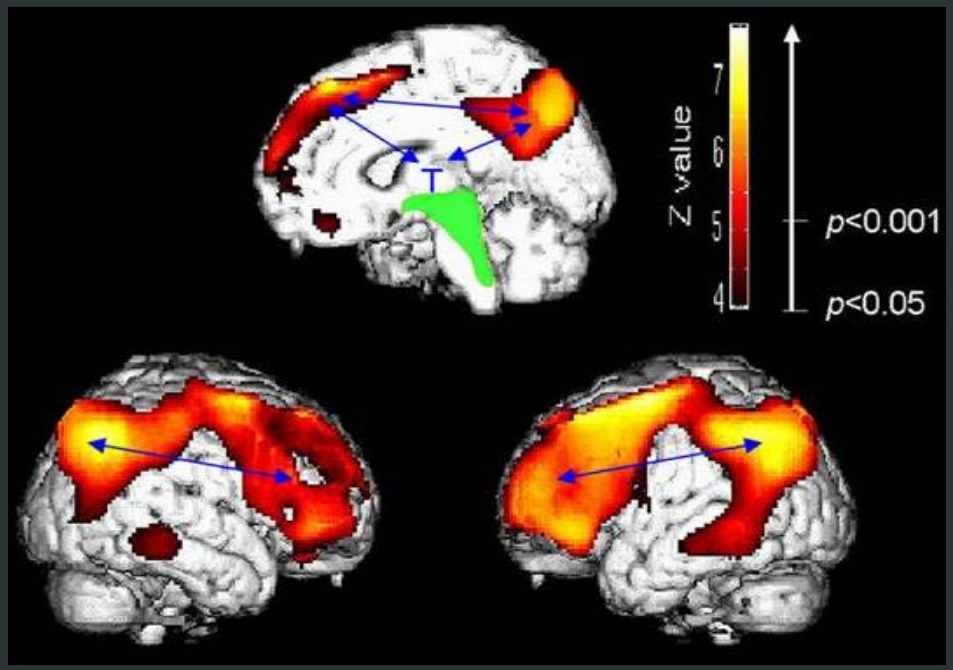
Consciousness # whole brain



Laureys *et al, Lancet Neurology,* 2004

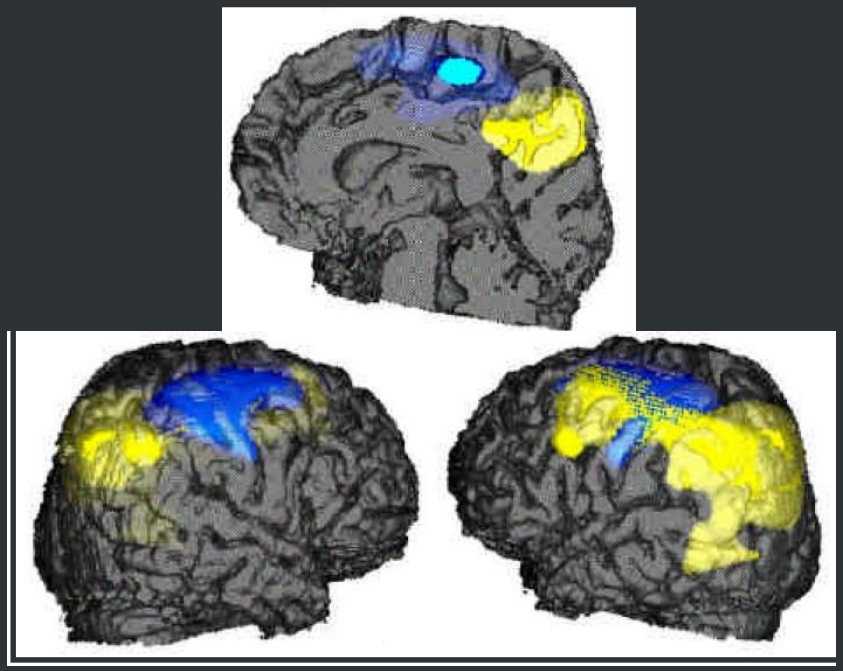
Consciousness ≈ frontoparietal

areas that are systematically dysfunctional in the vegetative state



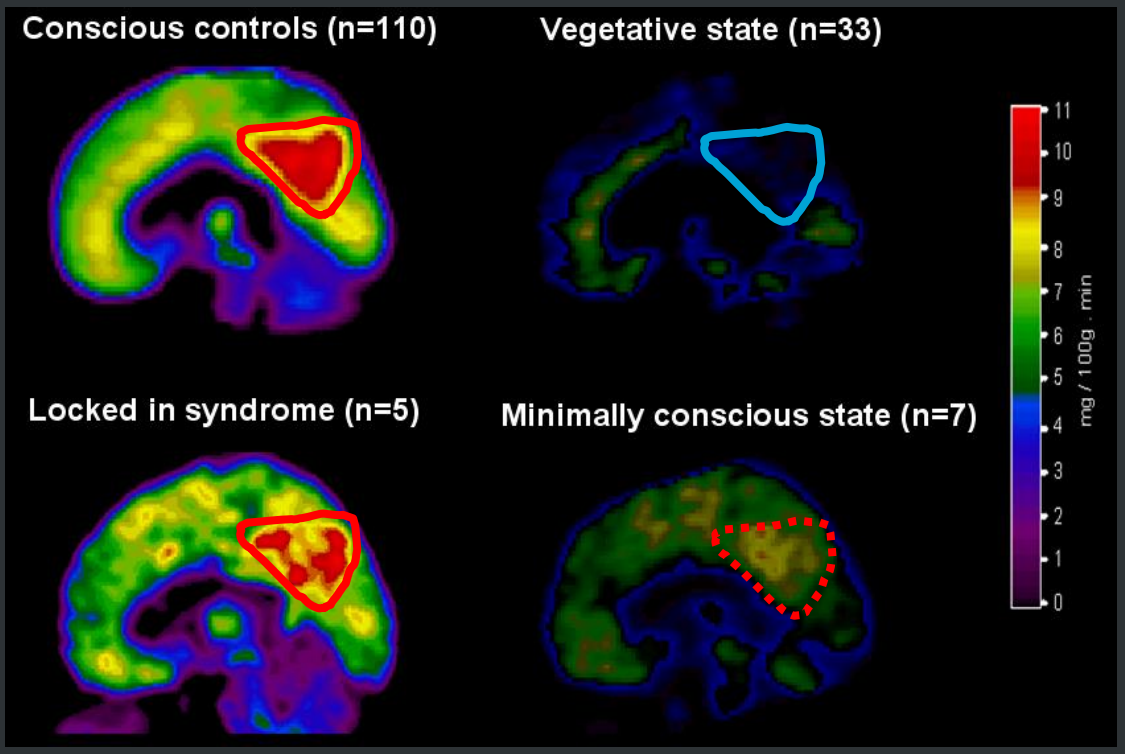
Laureys et al, Neuroimage 1999

areas that recover metabolism after recovery from the vegetative state



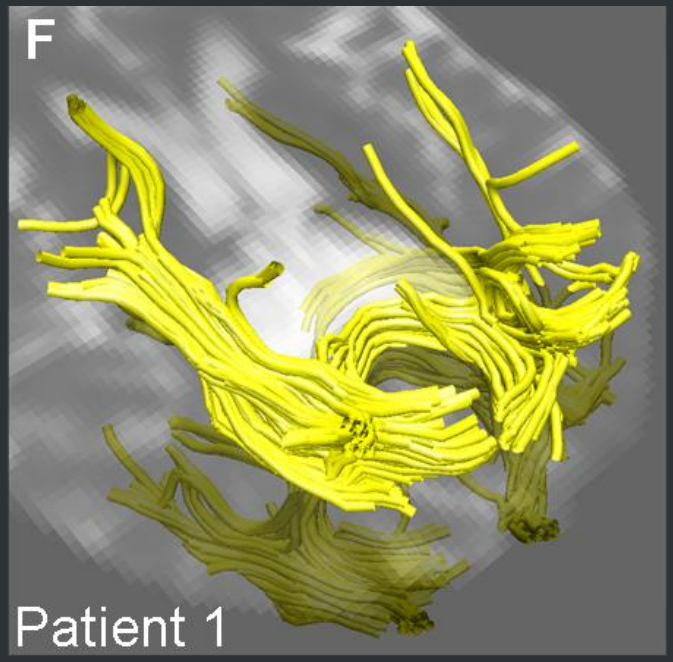
Laureys et al, J Neurol Neurosurg Psychiatry, 1999

Precuneus ≈ hub in the network



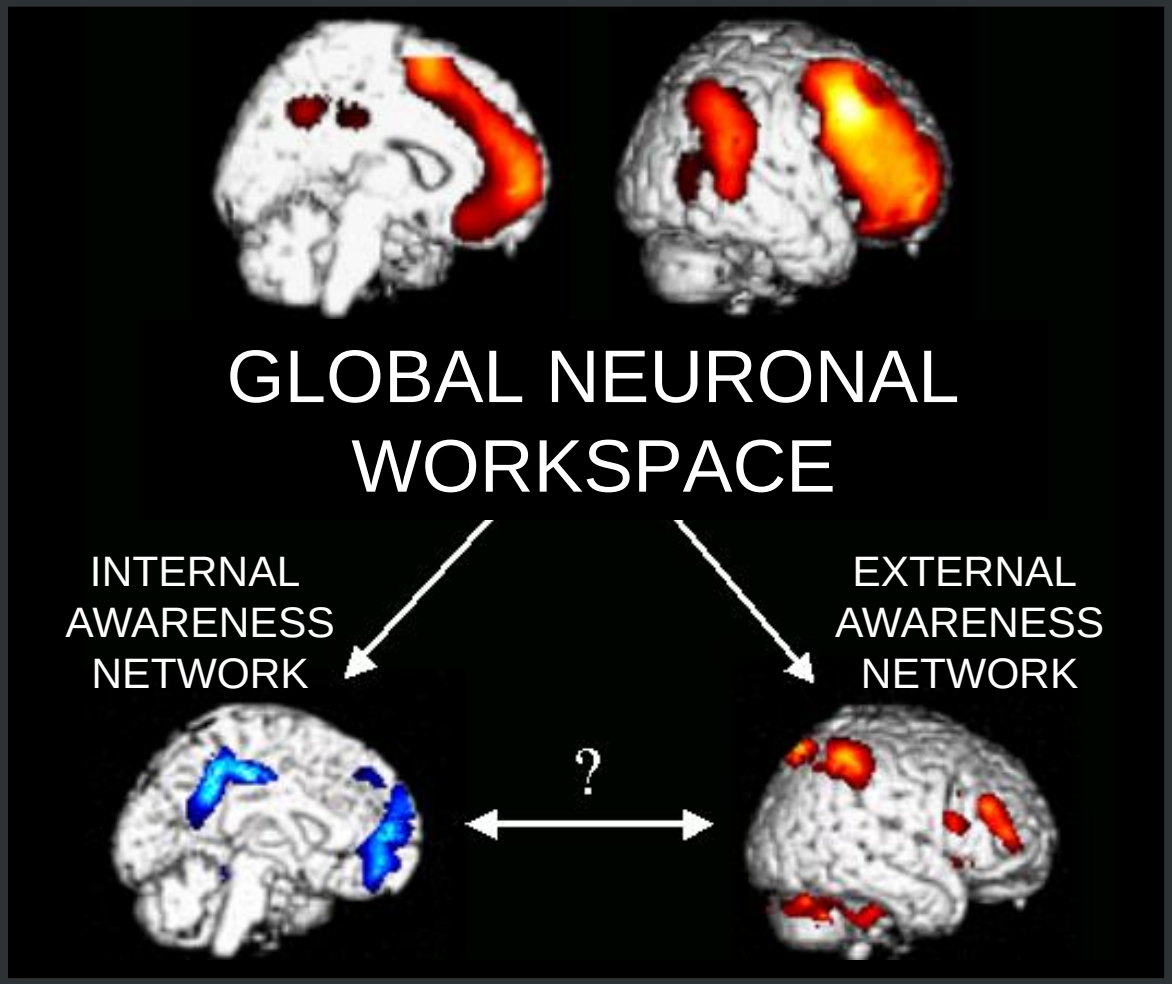
Laureys et al, Lancet Neurology, 2004

Axonal re-growth in Terry Wallis



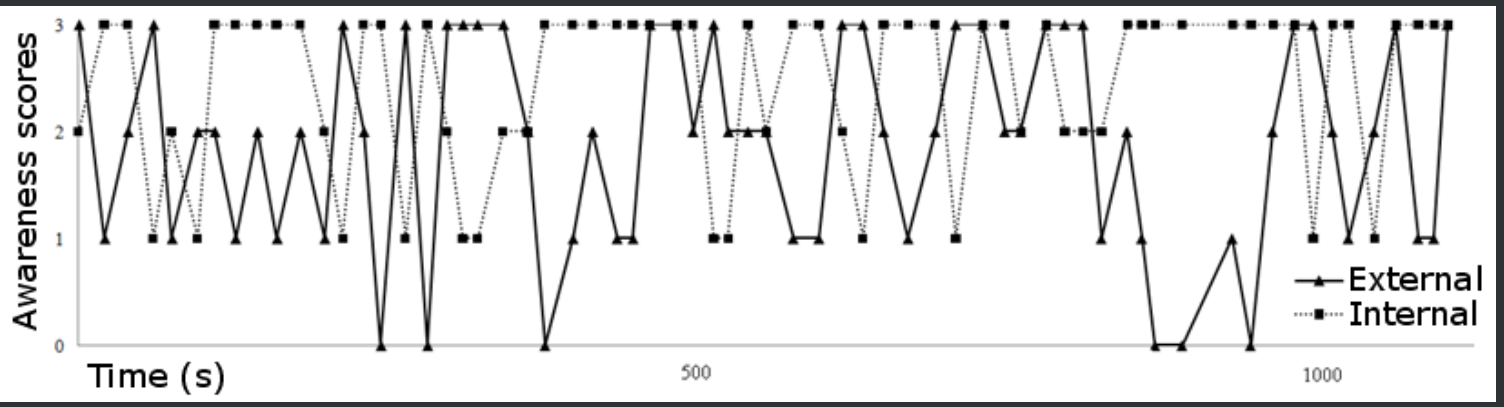
Voss et al, J Clin Invest, 2006

Two awareness networks



Boly… Laureys, *Human Brain Mapping* 2008

External vs internal awareness

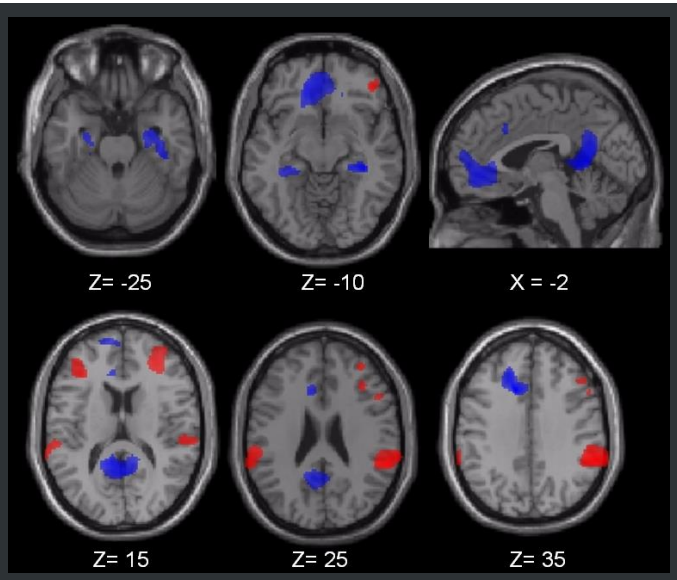


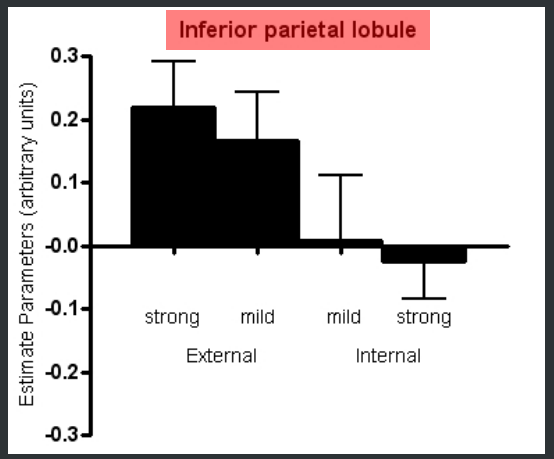
Subjects' ratings

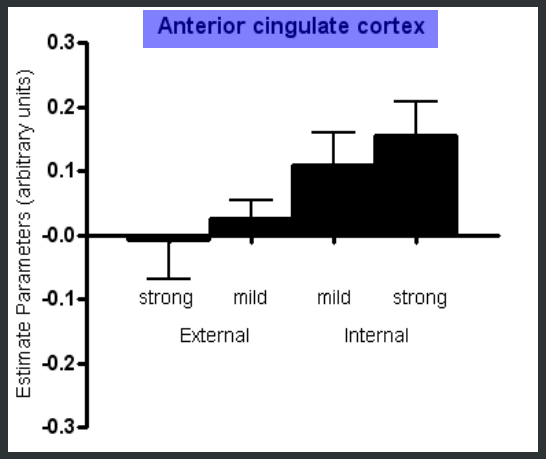
Anti-correlated

Switching 0.05 Hz
(range 0.01-0.1Hz)

/20 s
(range 10-100 s)







Vanhaudenhuyse et al, J Cogn Neurosci, 2010

Disorders of consciousness

Brain processing in DOC

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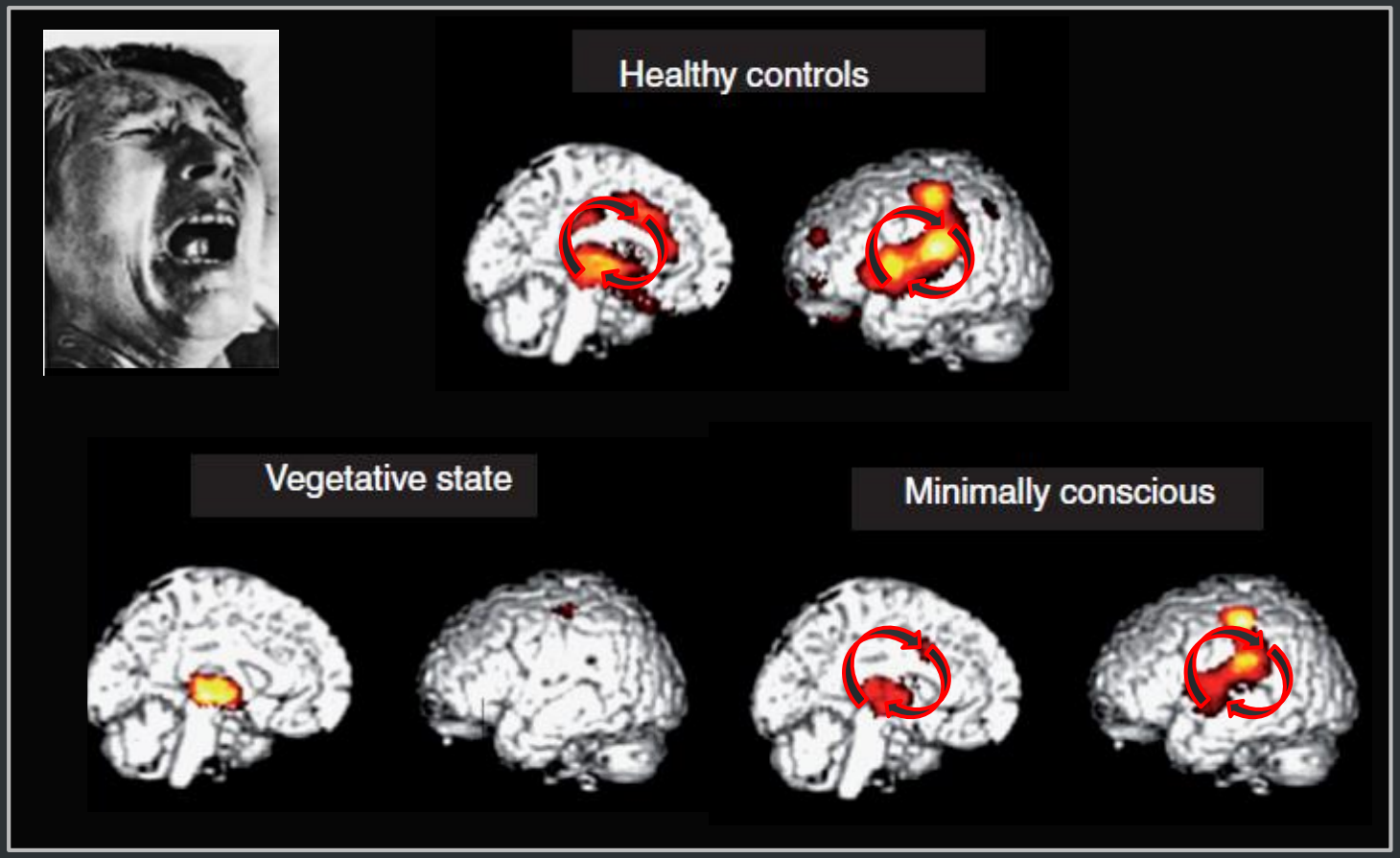
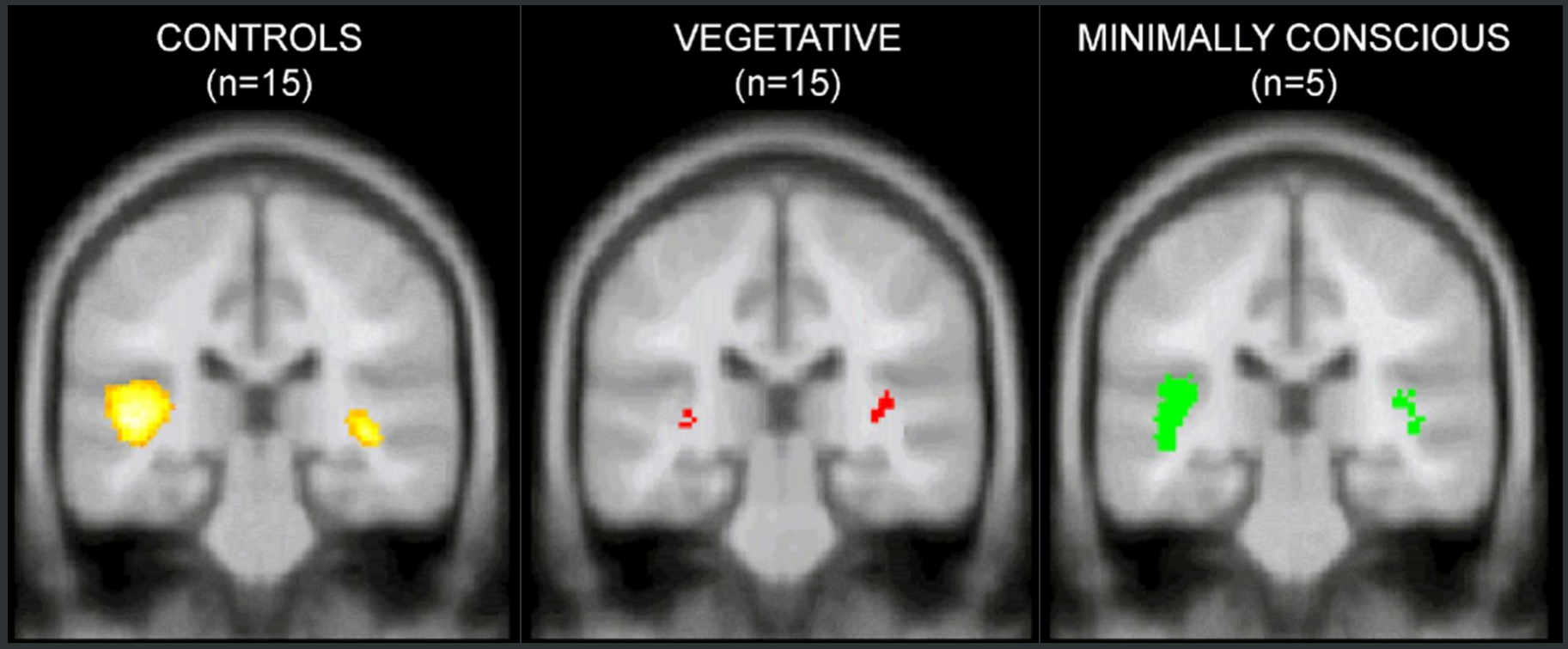
Can they feel pain?



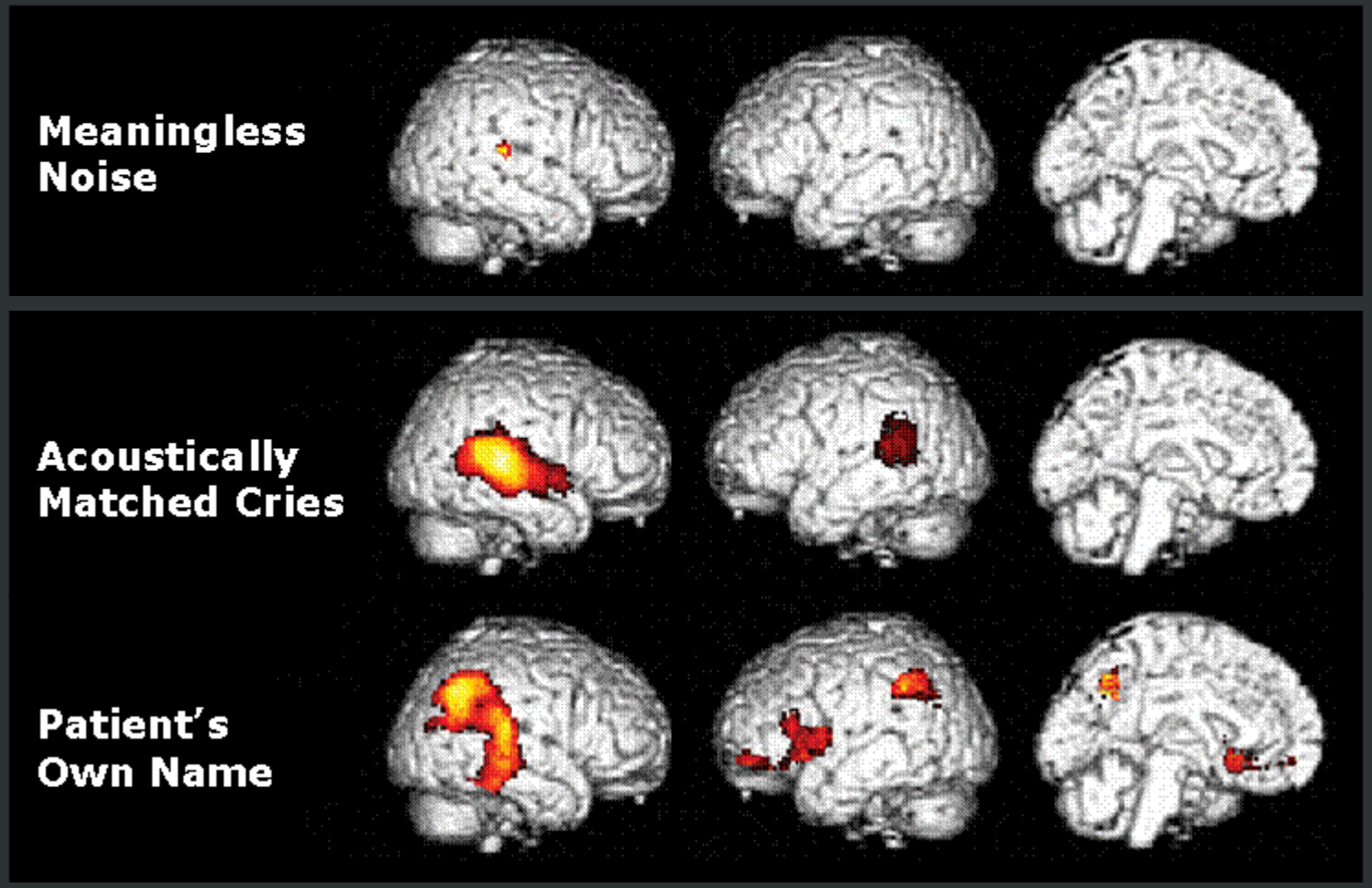
Laureys et al., Neuroimage, 2002 , Boly et al, Lancet Neurology, 2008
Schnakers, Chatelle, Majerus, Gosseries, Deval and Laureys, Experts Rev in Neurother, 2010

Can they hear us?



Laureys et al., Brain, 2000 ; *Boly et al, Archives of Neurology, 2004*

Emotion



Laureys et al., Neurology, 2004

Conclusion

- DOC: different clinical entities associated with various level of consciousness : coma, VS/UWS, MCS (plus and minus)
- Neural correlates of conscious awareness
  - ≈ emergent property of widespread fronto-parietal connectivity
- Non communicative patients with DOC may be able to perceive external world
  - Audition
  - Pain/emotion

Diagnosis

Consciousness

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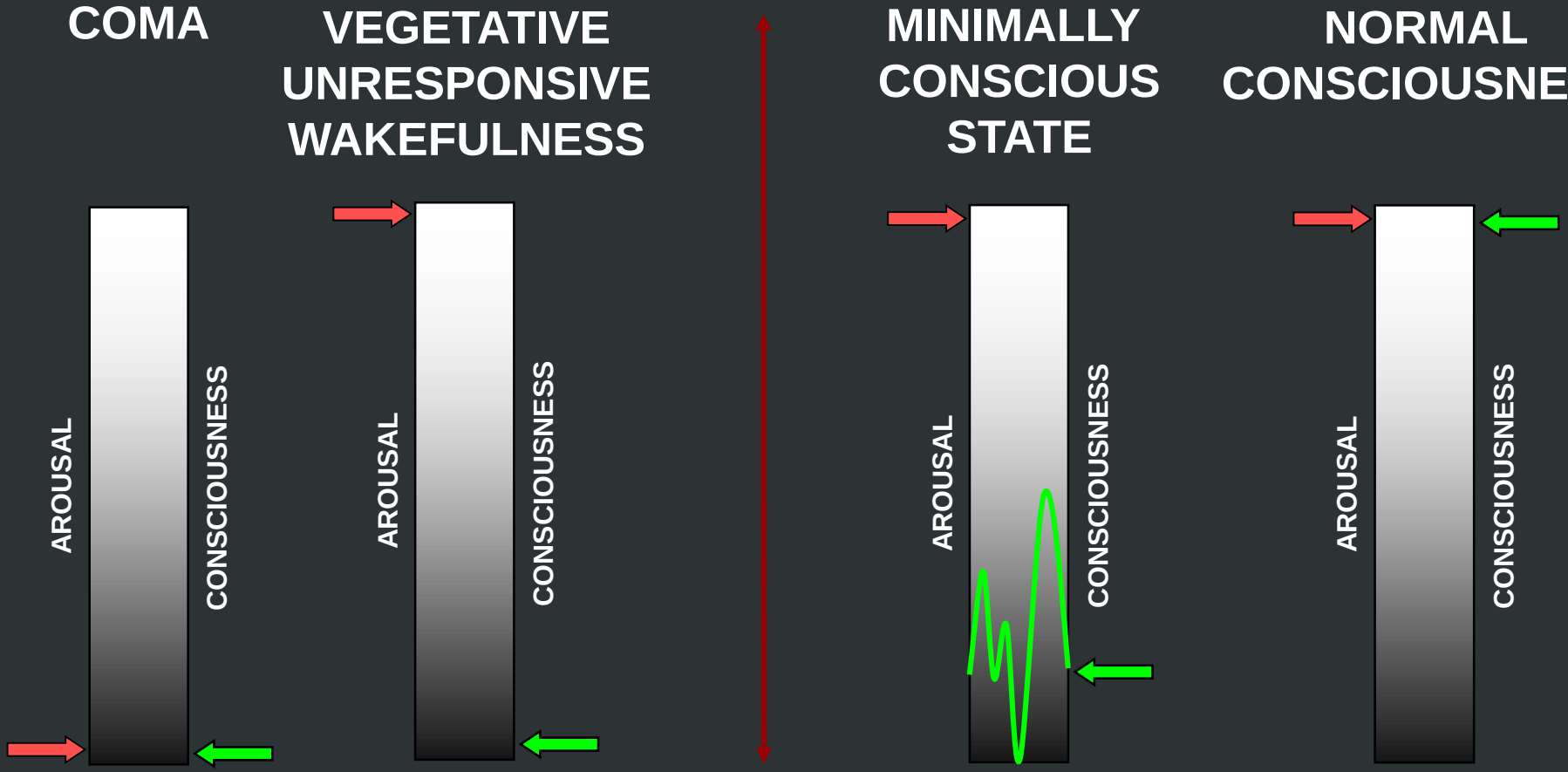
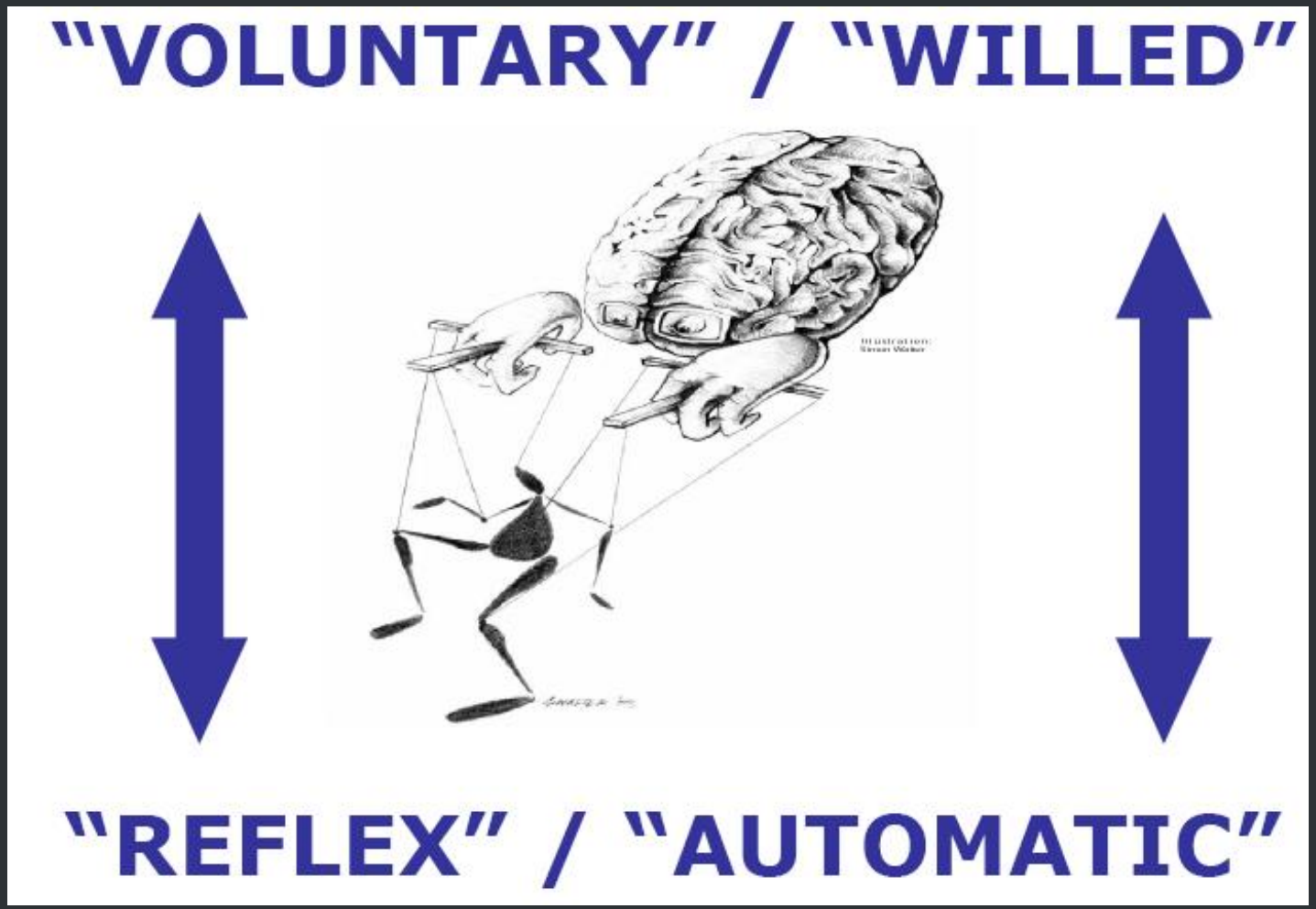
Clinical entities

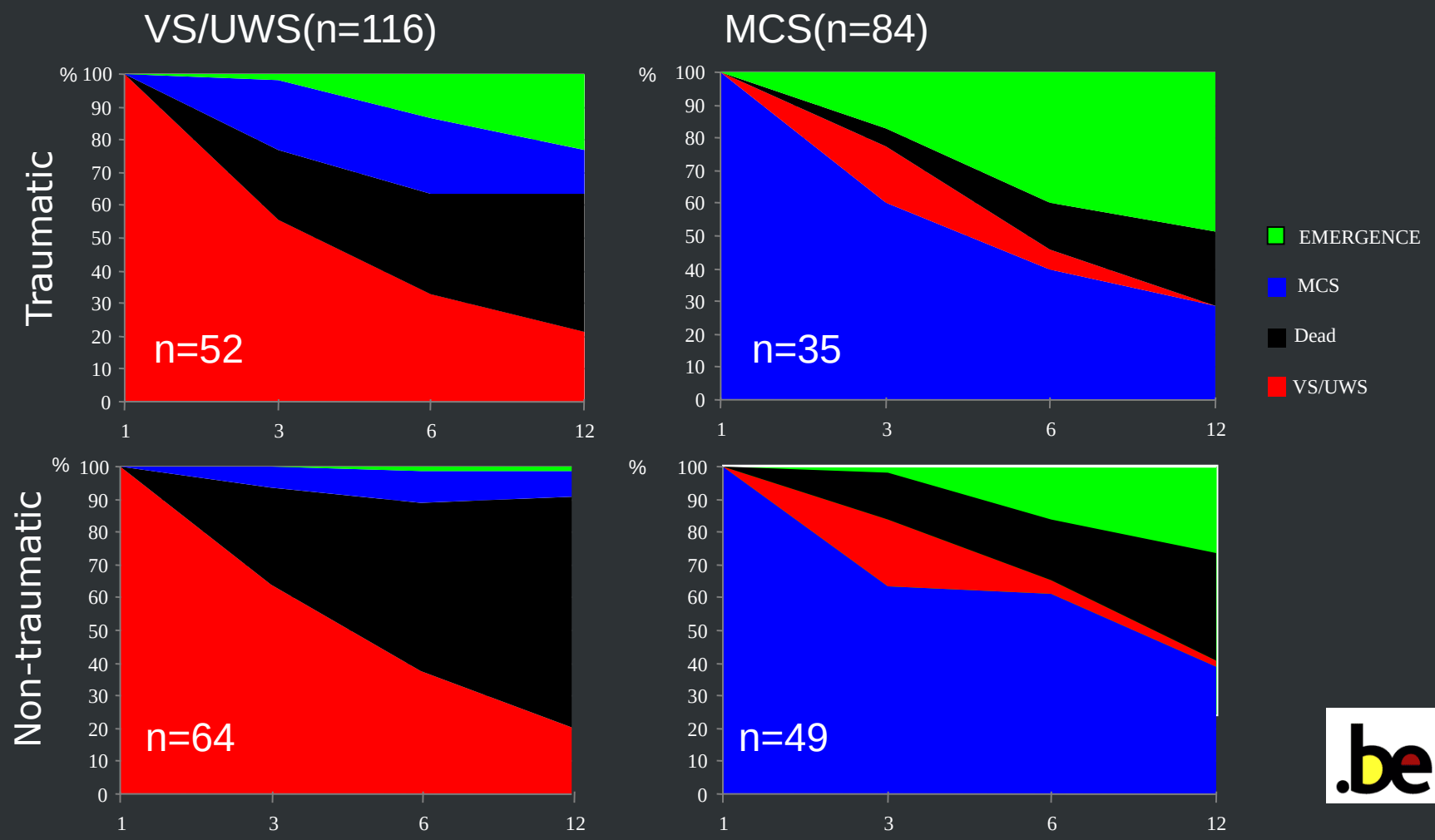


Laureys et al, Lancet Neurol, 2004

“Reflex” versus “Voluntary”

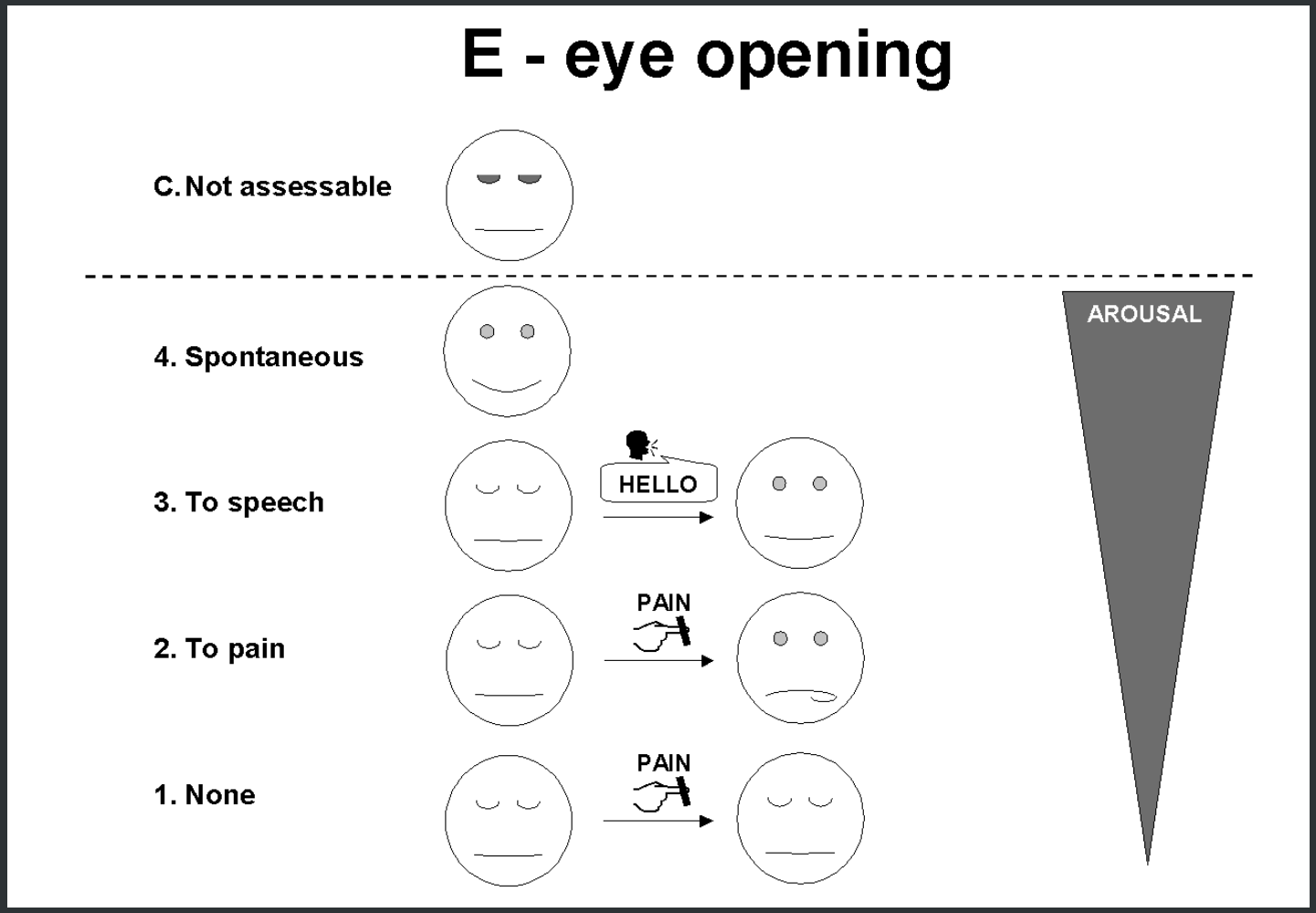


Prognosis



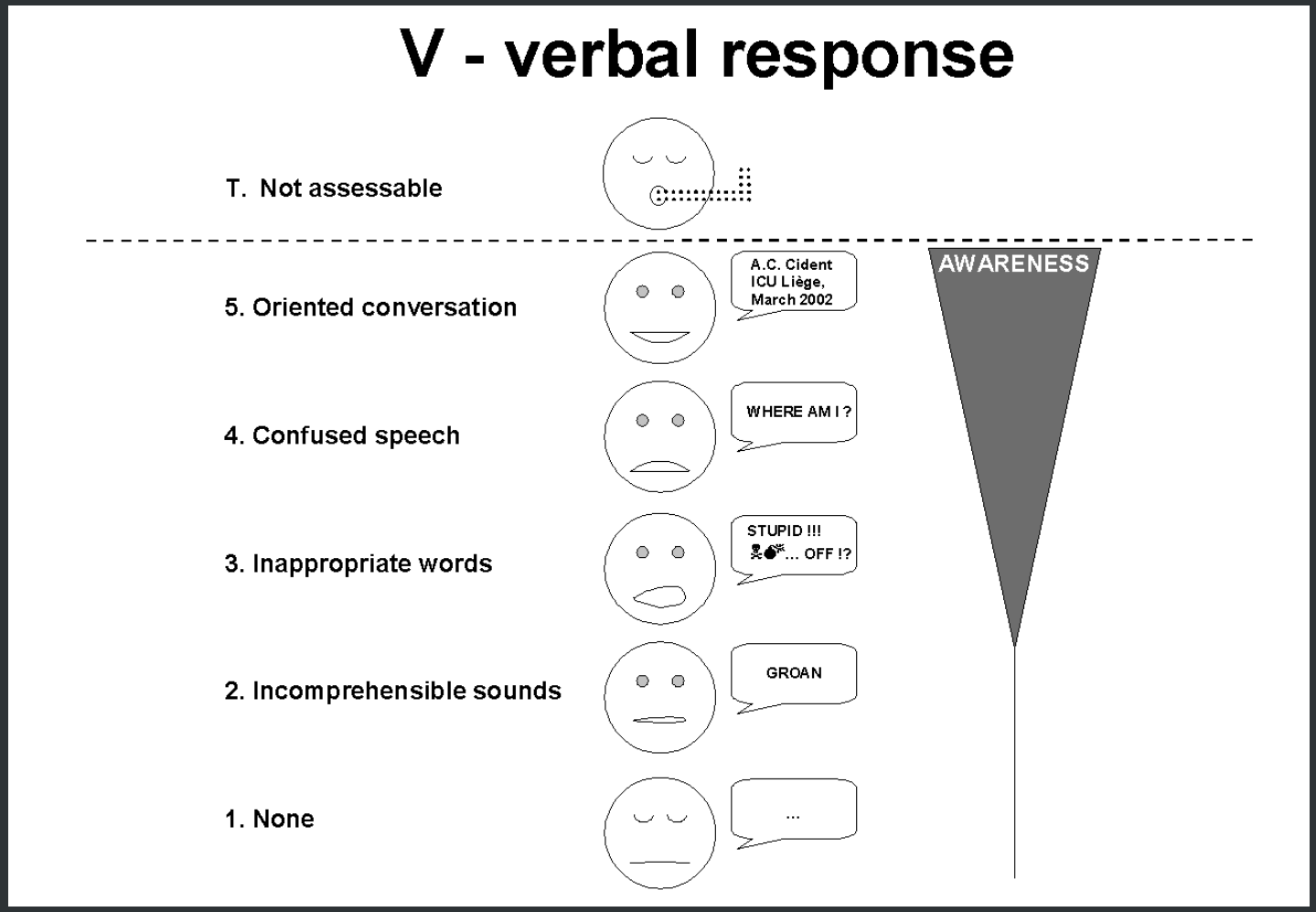
Bruno et al, Coma and disorders of consciousness, Eds Schnakers and Laureys, 2012

Glasgow Coma Scale



Teasdale et al., 1974

Glasgow Coma Scale

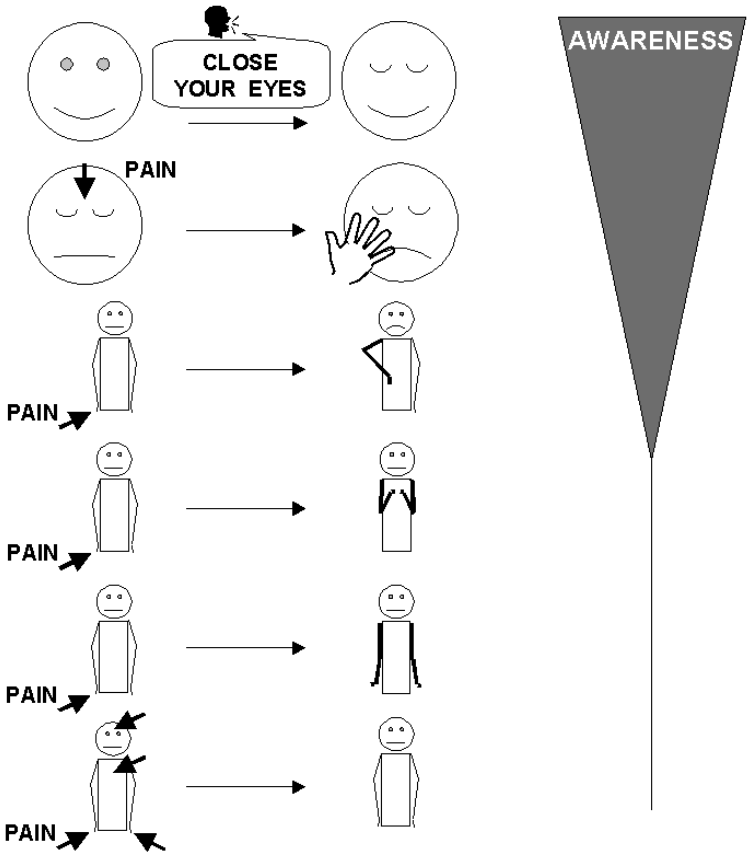


Teasdale et al., 1974

Glasgow Coma Scale

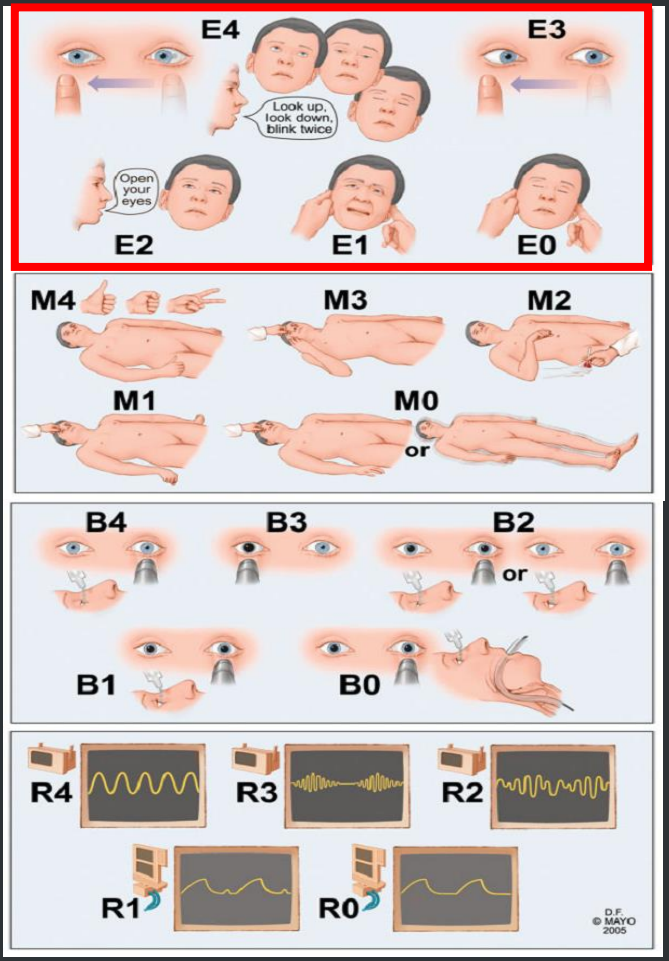
M - motor response

6. Obeys simple commands
5. Localizes pain
4. Withdraws (normal flexion)
3. Stereotyped flexion
2. Stereotyped extension
1. None



Teasdale et al., 1974

Full Outline of Unresponsiveness

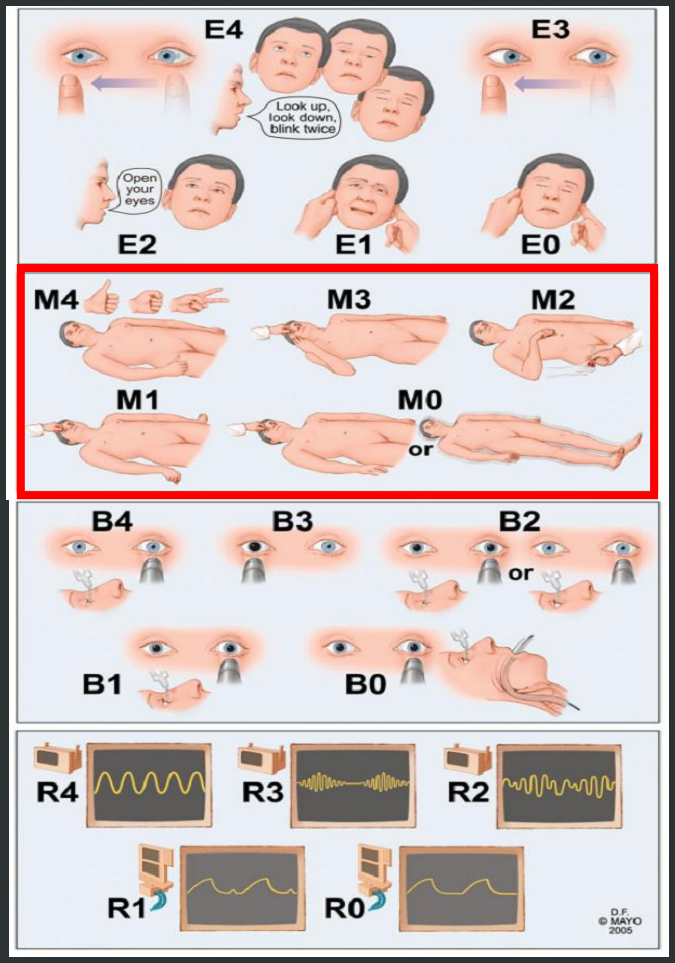


Grade the best possible response after at least 3 trials in an attempt to elicit the best level of alertness. A score of **E4** indicates at least 3 voluntary excursions. If eyes are closed, the examiner should open them and examine tracking of a finger or object. Tracking with the opening of 1 eyelid will suffice in cases of eyelid edema or facial trauma. If tracking is absent horizontally, examine vertical tracking. Alternatively, 2 blinks on command should be documented. This will recognize a locked-in syndrome (patient is fully aware). A score of **E3** indicates the absence of voluntary tracking with open eyes. A score of **E2** indicates eyelids opening to loud voice. A score of **E1** indicates eyelids open to pain stimulus. A score of **E0** indicates no eyelids opening to pain.

- **4** Eyelids open or opened, tracking or blinking to command
- **3** Eyelids open but not tracking
- **2** Eyelids closed but opens to loud voice
- **1** Eyelids closed but opens to pain
- **0** Eyelids remain closed with pain

Wijdicks et al., 2005

Full Outline of Unresponsiveness

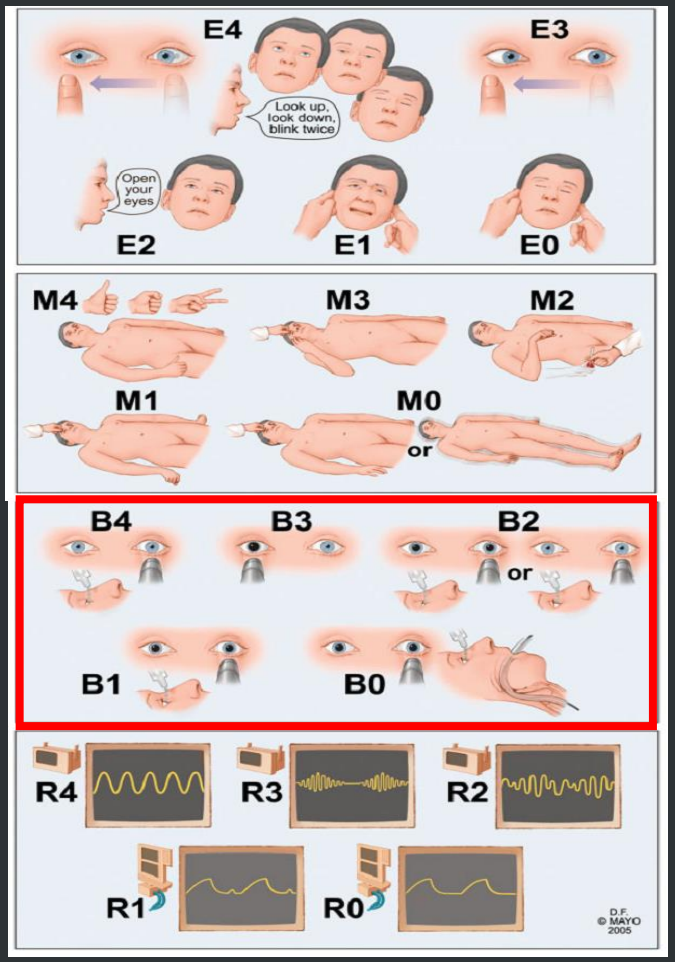


Grade the best possible response of the arms. A score of **M4** indicates that the patient demonstrated at least 1 of 3 hand positions (thumbs-up, fist, or peace sign) with either hand. A score of **M3** indicates that the patient touched the examiner's hand after a painful stimulus compressing the temporomandibular joint or supraorbital nerve (localization). A score of **M2** indicates any flexion movement of the upper limbs. A score of **M1** indicates extensor posturing. A score of **M0** indicates no motor response or myoclonus status epilepticus.

- **4** Thumbs up, fist, or peace sign to command
- **3** Localizing to pain
- **2** Flexion response to pain
- **1** Extensor posturing
- **0** No response to pain or generalized myoclonus status epilepticus

Wijdicks et al., 2005

Full Outline of Unresponsiveness

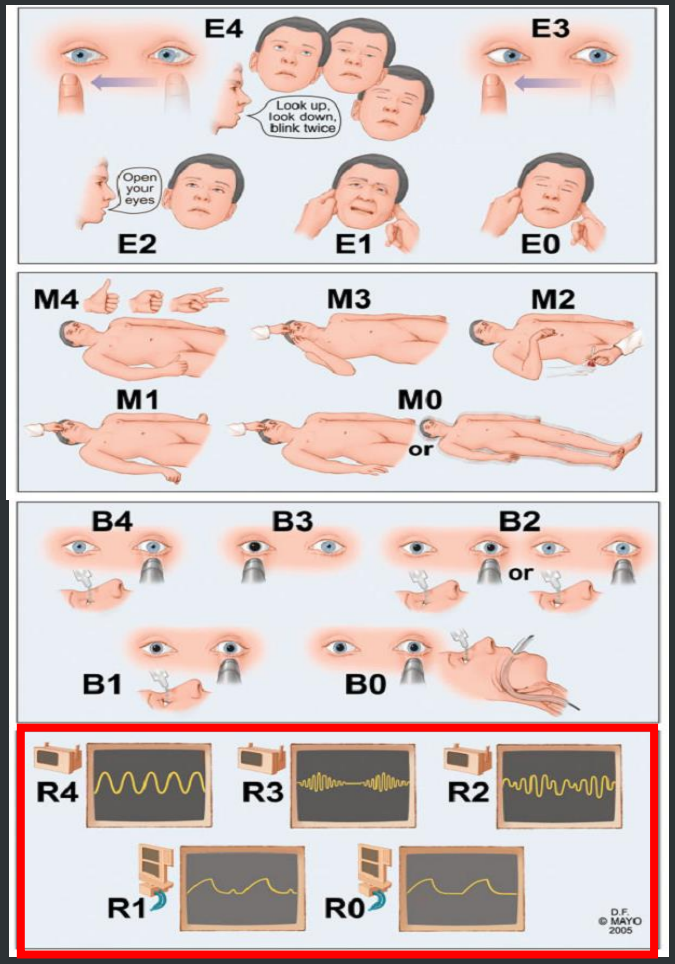


Grade the best possible response. Examine pupillary and corneal reflexes. Preferably, corneal reflexes are tested by instilling 2-3 drops of sterile saline on the cornea from a distance of 4-6 inches (this minimizes corneal trauma from repeated examinations). Cotton swabs can also be used. The cough reflex to tracheal suctioning is tested only when both of these reflexes are absent. A score of **B4** indicates pupil and cornea reflexes are present. A score of **B3** indicates one pupil wide and fixed. A score of **B2** indicates either pupil or cornea reflexes are absent, **B1** indicates both pupil and cornea reflexes are absent and a score of **B0** indicates pupil, cornea and cough reflex (using tracheal suctioning) are absent.

- **4 Pupil and corneal reflexes present**
- **3 One pupil wide and fixed**
- **2 Pupil *or* corneal reflexes absent**
- **1 Pupil *and* corneal reflexes absent**
- **0 Absent pupil, corneal, and cough reflex**

Wijdicks et al., 2005

Full Outline of Unresponsiveness



Determine spontaneous breathing pattern in a nonintubated patient, and grade simply as regular **R4**, irregular **R2**, or Cheyne-Stokes **R3** breathing. In mechanically ventilated patients, assess the pressure waveform of spontaneous respiratory pattern or the patient triggering of the ventilator **R1**. The ventilator monitor displaying respiratory patterns is used to identify the patient generated breaths on the ventilator. No adjustments are made to the ventilator while the patient is graded, but grading is done preferably with PaCO2 within normal limits. A standard apnea (oxygen-diffusion) test may be needed when patient breathes at ventilator rate **R0**.

- **4** Not intubated, regular breathing pattern
- **3** Not intubated, Cheyne-Stokes breathing pattern
- **2** Not intubated, irregular breathing pattern
- **1** Breathes above ventilator rate
- **0** Breathes at ventilator rate or apnea

Wijdicks et al., 2005

GCS or FOUR?

	GCS	FOUR
VS/UWS	71	63
MCS	**75**	**83**

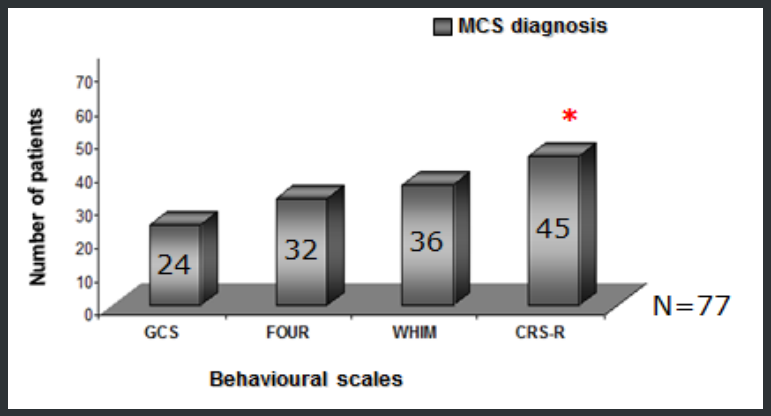
n= 146

Bruno et al., 2011

Coma Recovery Scale-Revised (CRS-R)

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

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



Giacino et al, 2004; Schnakers, et al, Brain Inj, 2008

Misdiagnosis

n=103 post-comatose patients

- 44 clinical consensus diagnosis ‘vegetative state’
  - 18 signs of awareness
  - (Coma Recovery Scale-Revised)

➧41% potential misdiagnosis

- 41 clinical consensus diagnosis ‘minimally conscious state’
  - 4 (10%) had emerged from the MCS

Schnakers, Vanhaudenhuyse, Giacino, Ventura, Boly, Majerus et al., BMC Neurol, 2009

Diagnosis

Nociception and pain

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Pain and nociception

Pain

"Unpleasant sensory and emotional experience associated with real or potential tissue damage"

"The inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment."

International association for the study of pain (IASP) Pain 1994 and 2012

Pain and nociception

Pain

"Unpleasant sensory and emotional experience associated with real or potential tissue damage"

"The inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment."

Nociception

"The neural process of encoding noxious stimuli"

(transduced and encoded by nociceptors).

"Pain sensation is not necessarily implied".

International association for the study of pain (IASP) Pain 1994 and 2012

Pain and nociception

Pain

"Unpleasant sensory and emotional experience associated with real or potential tissue damage"

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Nociception

"The neural process of encoding noxious stimuli"

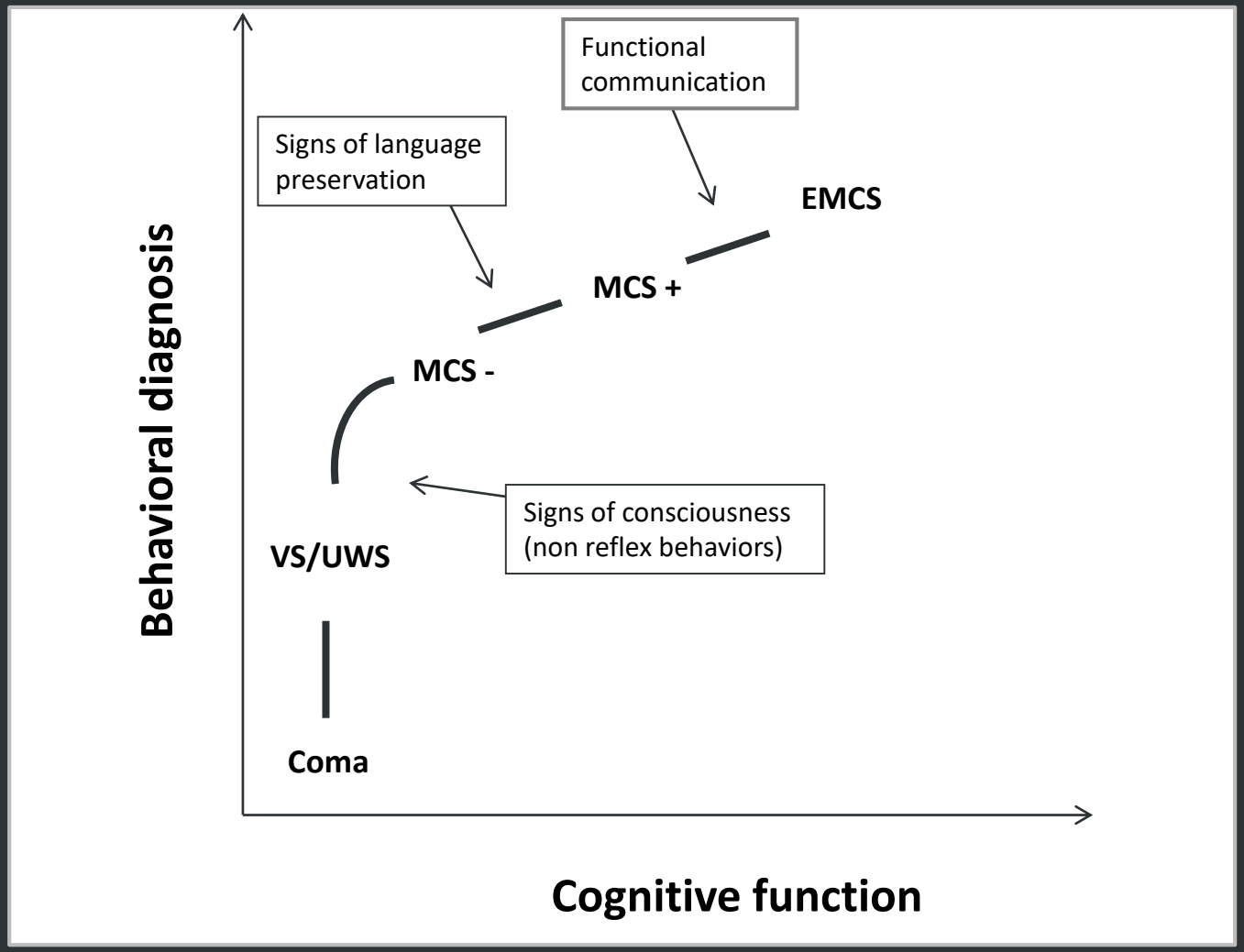
(transduced and encoded by nociceptors).

"Pain sensation is not necessarily implied".

➔ « *Pain is always subjective* »

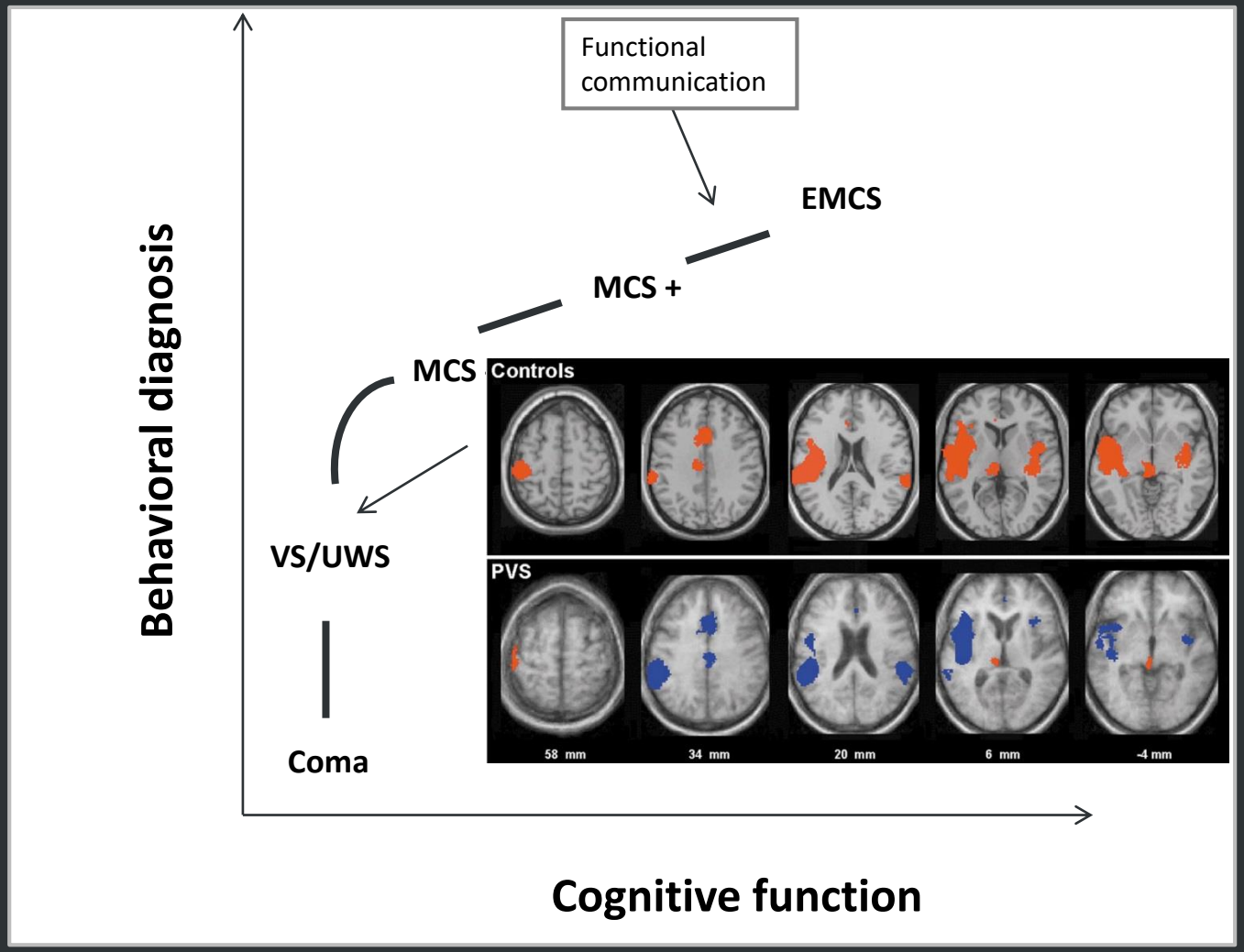
International association for the study of pain (IASP) Pain 1994 and 2012

Pain and nociception



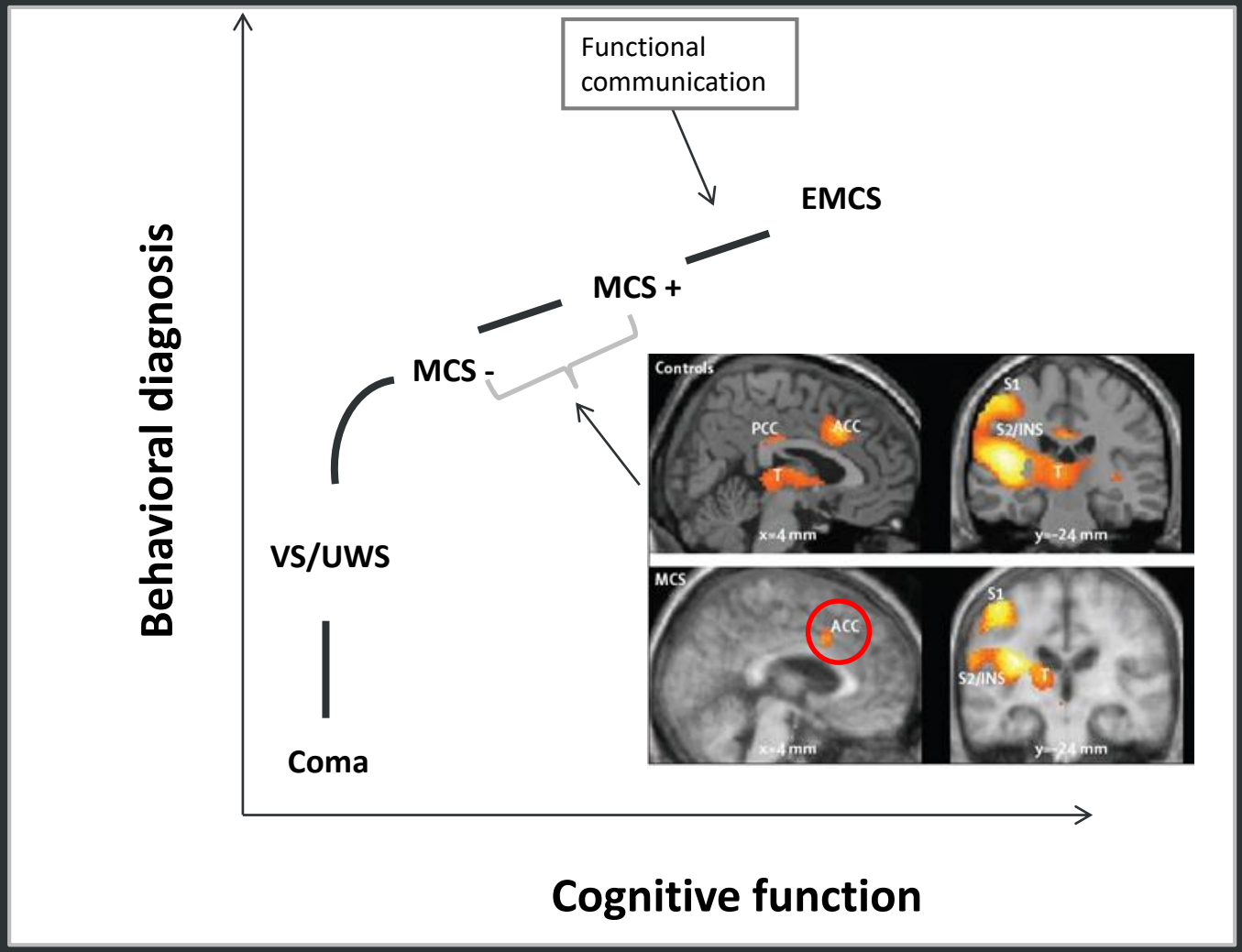
Chatelle & Laureys. Oxford Handbook of Neuroethics 2011

Pain and nociception



Chatelle & Laureys. Oxford Handbook of Neuroethics 2011

Pain and nociception



Chatelle & Laureys. Oxford Handbook of Neuroethics 2011

Behavioral scales

Population	Pain scales	Facial expression	Vocalization/ Verbalization	Body movements	Consolability	Arousal	Physiological parameters	Activity pattern
Demented elderly	DOLOPLUS2 (77)	√	√	√				√
	PACSLAC (Pain Assessment Checklist for Seniors with Limited Ability to Communicate) (78)	√		√				√
	ECPA (L'Echelle Comportementale pour Personne Agées) (79)	√	√	√				√
	PAINAD (Pain Assessment in Advanced Dementia) (80)	√	√	√	√		√	
	NOPPAIN The Non-Communicative Patient's Pain Assessment Instrument) (81)	√	√	√				
	CNPI (Checklist of Nonverbal Pain Indicators) (82)	√	√	√				
	Abbey Pain Scale (83)	√	√	√			√	√
Newborns/preverbal children	PIPP (Premature Infant Pain Profile) (84)	√					√	
	NIPS (Neonatal Infant Pain Scale) (85)	√	√	√		√	√	
	CHEOPS (Children's Hospital of Eastern Ontario Pain Scale) (86)	√	√	√				
	FLACC(Face, Legs, Arms, Cry, Consolability) (87)	√	√	√	√			
	PPPM (Parents' Postoperative Pain Measure) (88)		√	√				√
Sedated/intubated patients	BPS (Behavioral Pain Scale) (89)	√		√				
	COMFORT Scale (90)	√		√		√	√	

Schnakers, Chatelle et al. AAPS 2012

Nociception Coma Scale

VERBAL RESPONSE
3 – Verbalisation intelligible
2 – Vocalisation
1 – Groaning
0 – None

VISUAL RESPONSE
3 – Fixation
2 – Eyes movements
1 – Startle
0 – None

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

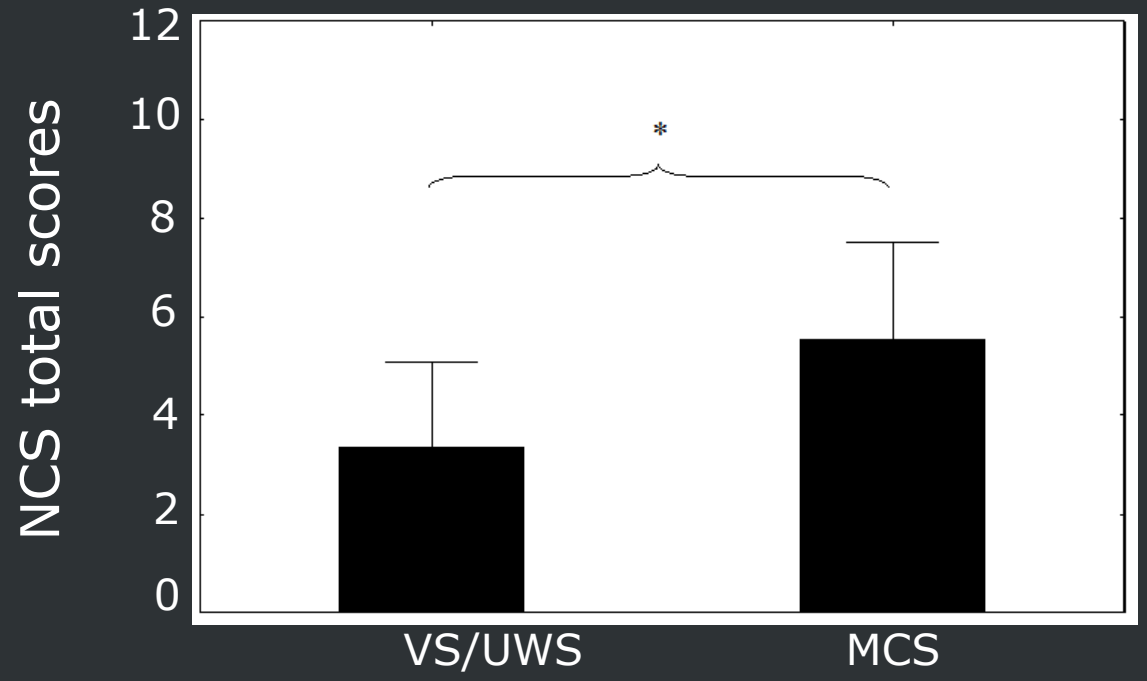
FACIAL EXPRESSION
3 – Cry
2 – Grimace
1 – Oral reflexive movement/Startle response
0 – None

Total score : 12

Schnakers, Chatelle et al. Pain 2010

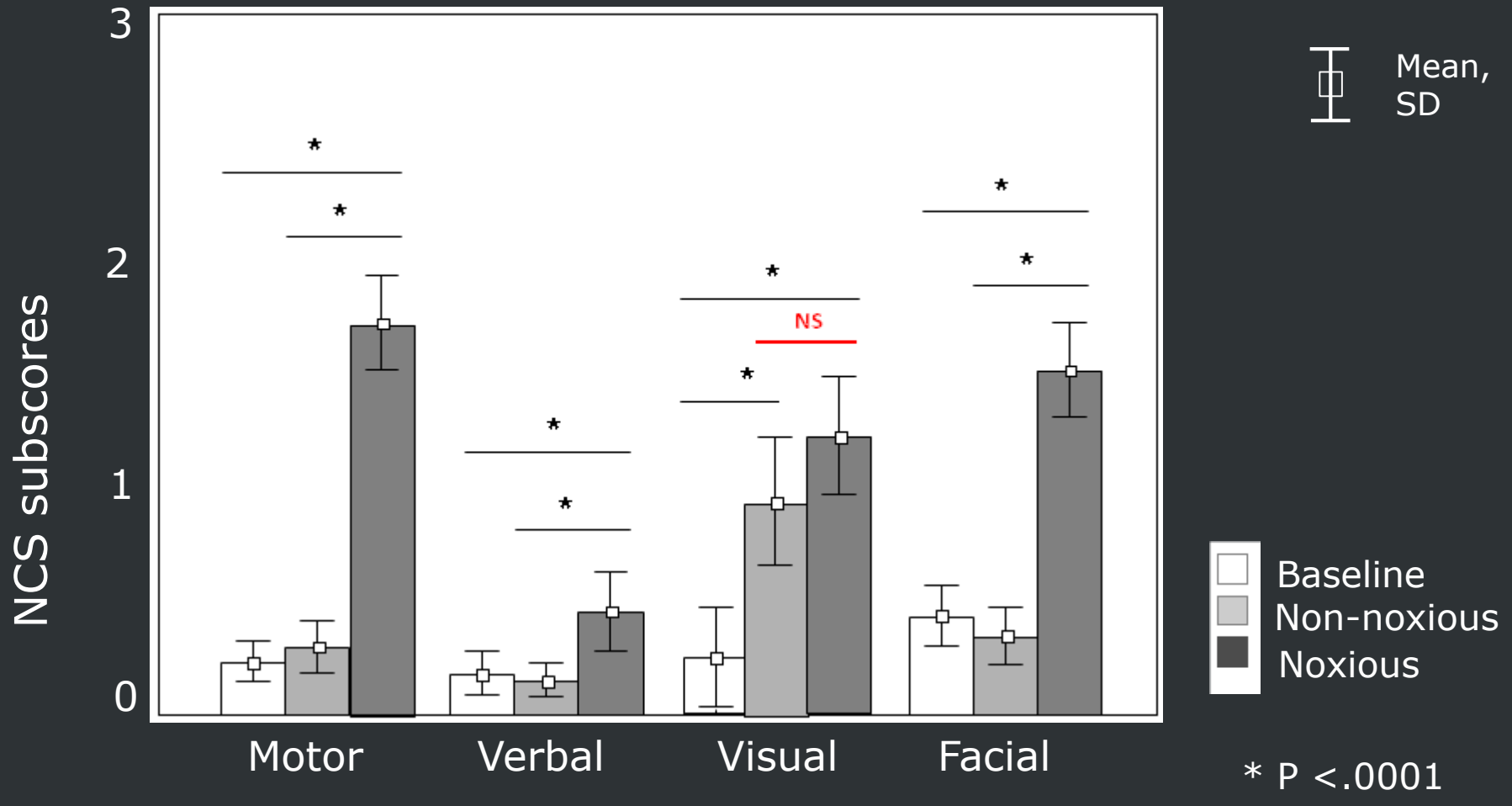
Nociception Coma Scale

- Concurrent validity: good
- Interrater reliability: good to excellent
- Effect of clinical diagnosis: yes



Schnakers, Chatelle et al. Pain 2010

Nociception Coma Scale revised

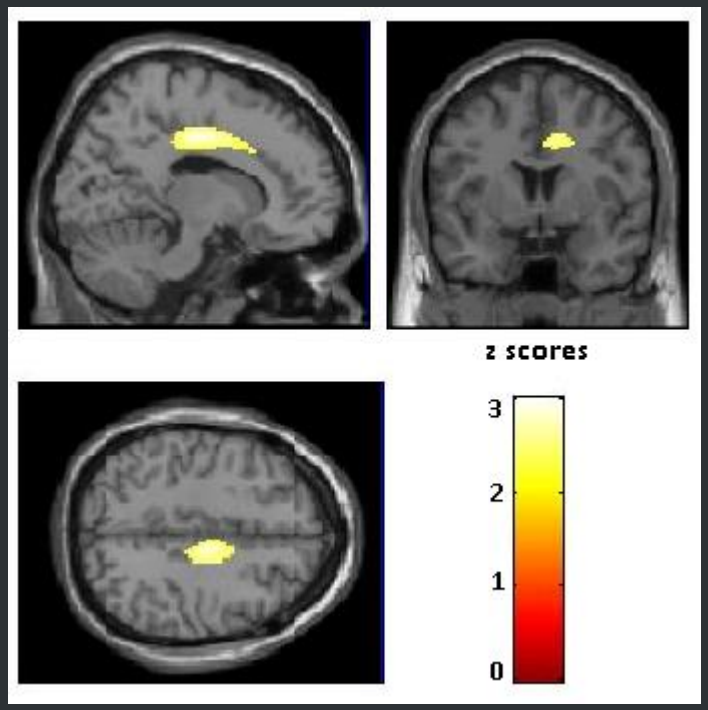


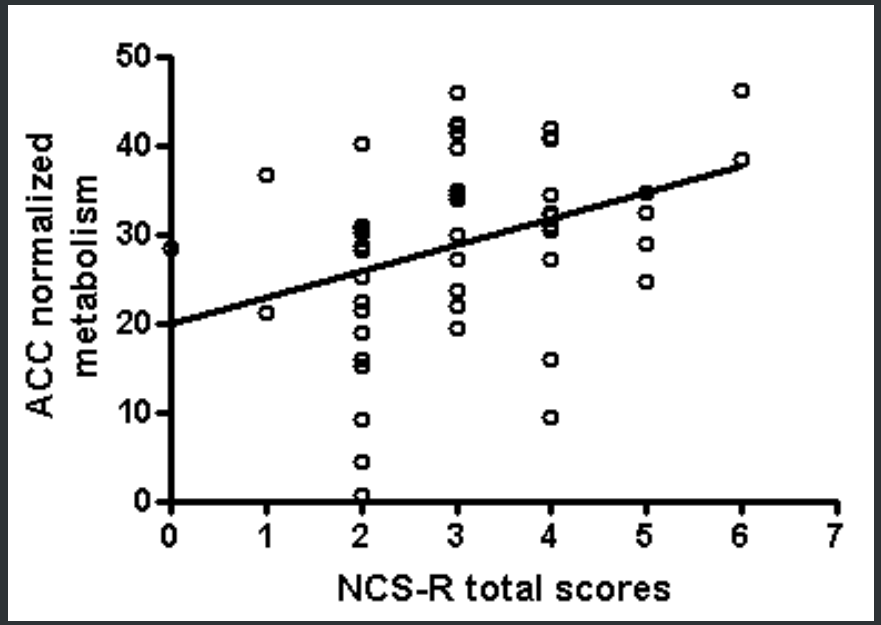
Chatelle, Majerus, Whyte, Laureys and Schnakers. JNNP 2012

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)



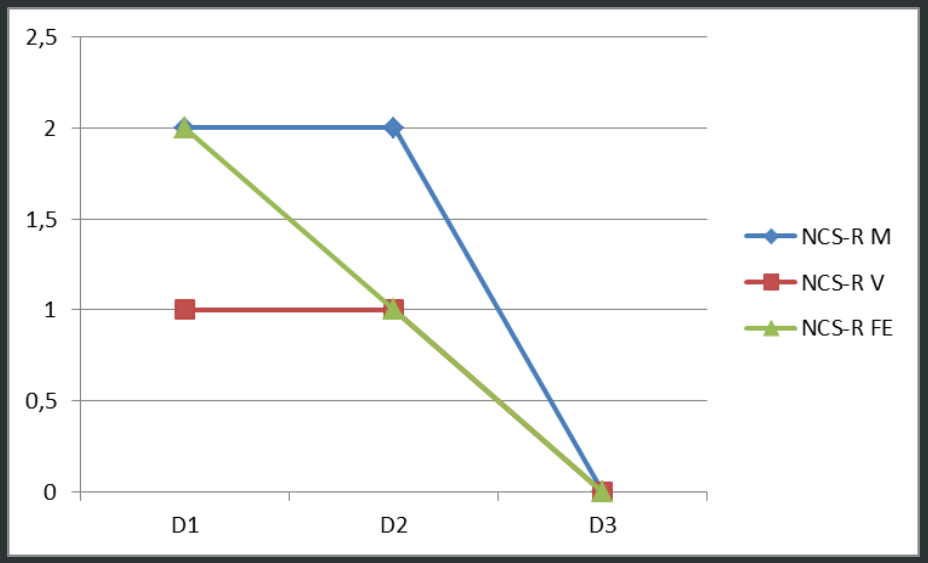


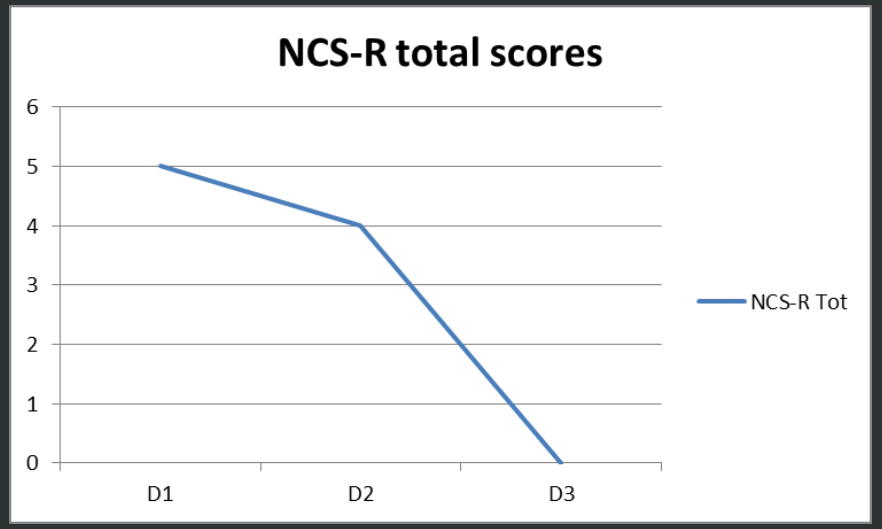
n = 42

Chatelle et al. Neurorehabilitation and Neural Repair 2014

NCS-R and clinic

21 yo, MCS, Polytrauma 8 days post injury
Treatment: 1mg perfuzalgan before cares (mobilisation)
Revised

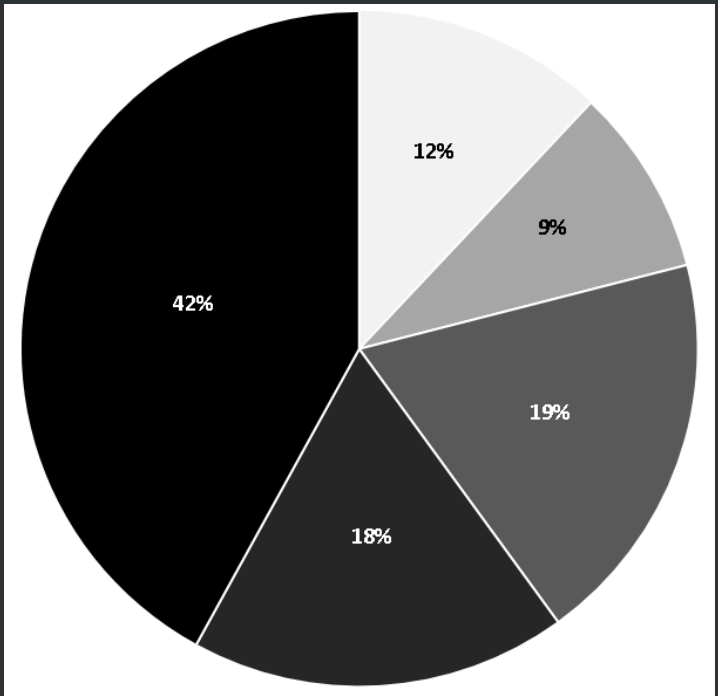




1mg/h morphine (continuous)

Spasticity in chronic DOC

Prevalence: 88% (n=59) suffered from spasticity (MAS≥1) and 60% (n=39) suffered from severe spasticity (MAS≥3)



0 : no increase in muscle tone

1 : slight increase in muscle tone, manifested by a catch or by minimal resistance at the end of the range of motion (ROM) when the affected part(s) is (are) moved in flexion or extension)

1+ : slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM

2 : more marked increase in muscle tone through most of the ROM, but affected part(s) easily moved

Moderate spasticity

3 : considerable increase in muscle tone, passive movement difficult

4: Affected part(s) rigid in flexion or extension

Severe spasticity

n=65

Thibaut, Chatelle, et al., Eur J of Rehab & Phys Med, 2014

Conclusion: guidelines on clinical management

- High rate of misdiagnosis if non sensitive scales are used
  - Acute stage/ICU: FOUR
  - Chronic stage : CRS-R
- Useful for monitoring recovery/medical complications
- Caveats
  - Language dependent
  - Relying strongly on motor abilities

Conclusion: guidelines on clinical management

- Need to improve management of potential pain: 76% documented potential pain, 59% not treated with analgesics
- NCS-R: useful tool for clinical management of nociception/pain:
  - Sudden increase in NCS-R scores can alert clinicians of a potential pain/medical complications, further investigation is needed
- Caveats
  - Motor/verbal dependent

BREAK (~15 min)

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Paraclinical diagnosis

Active paradigms

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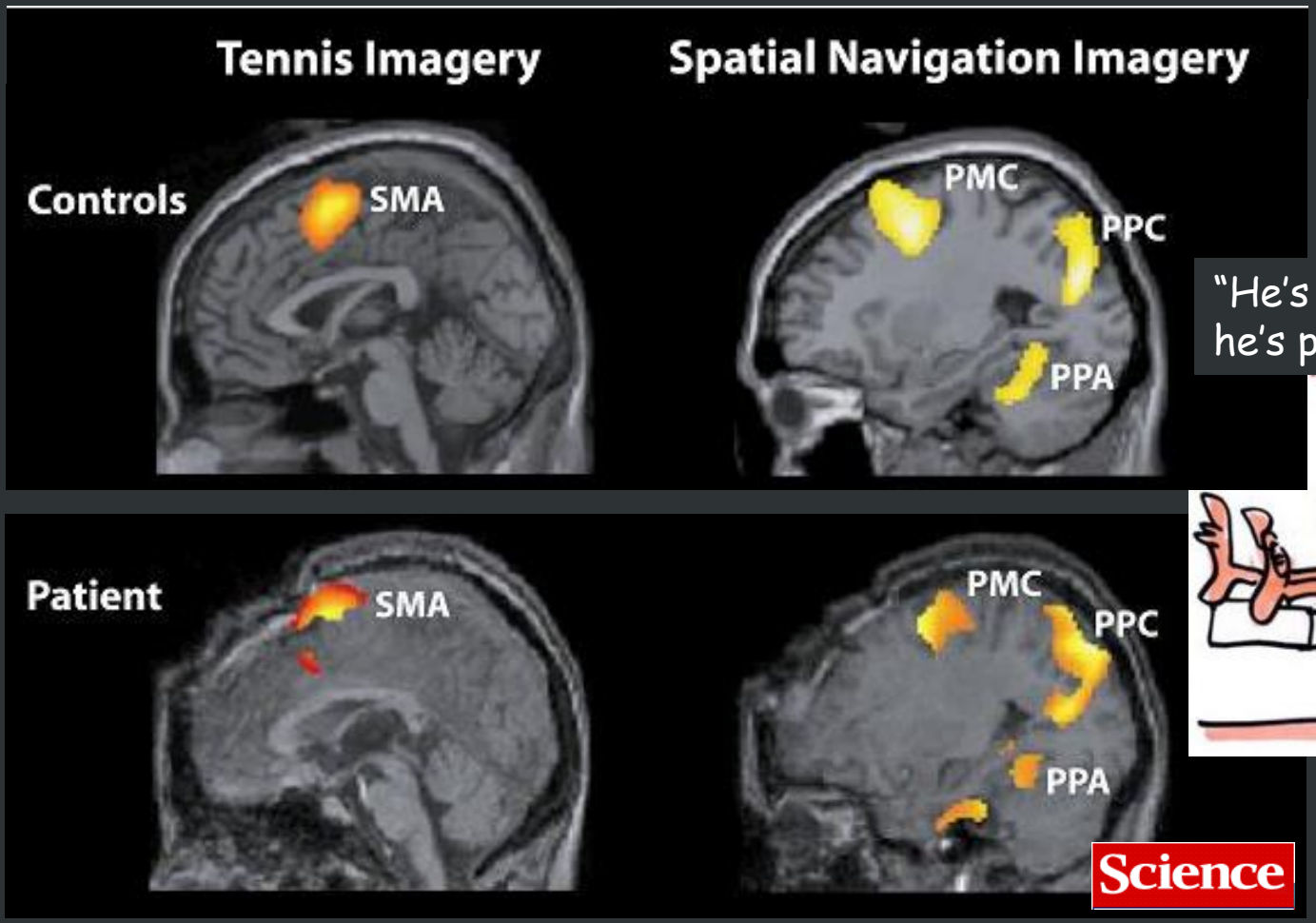
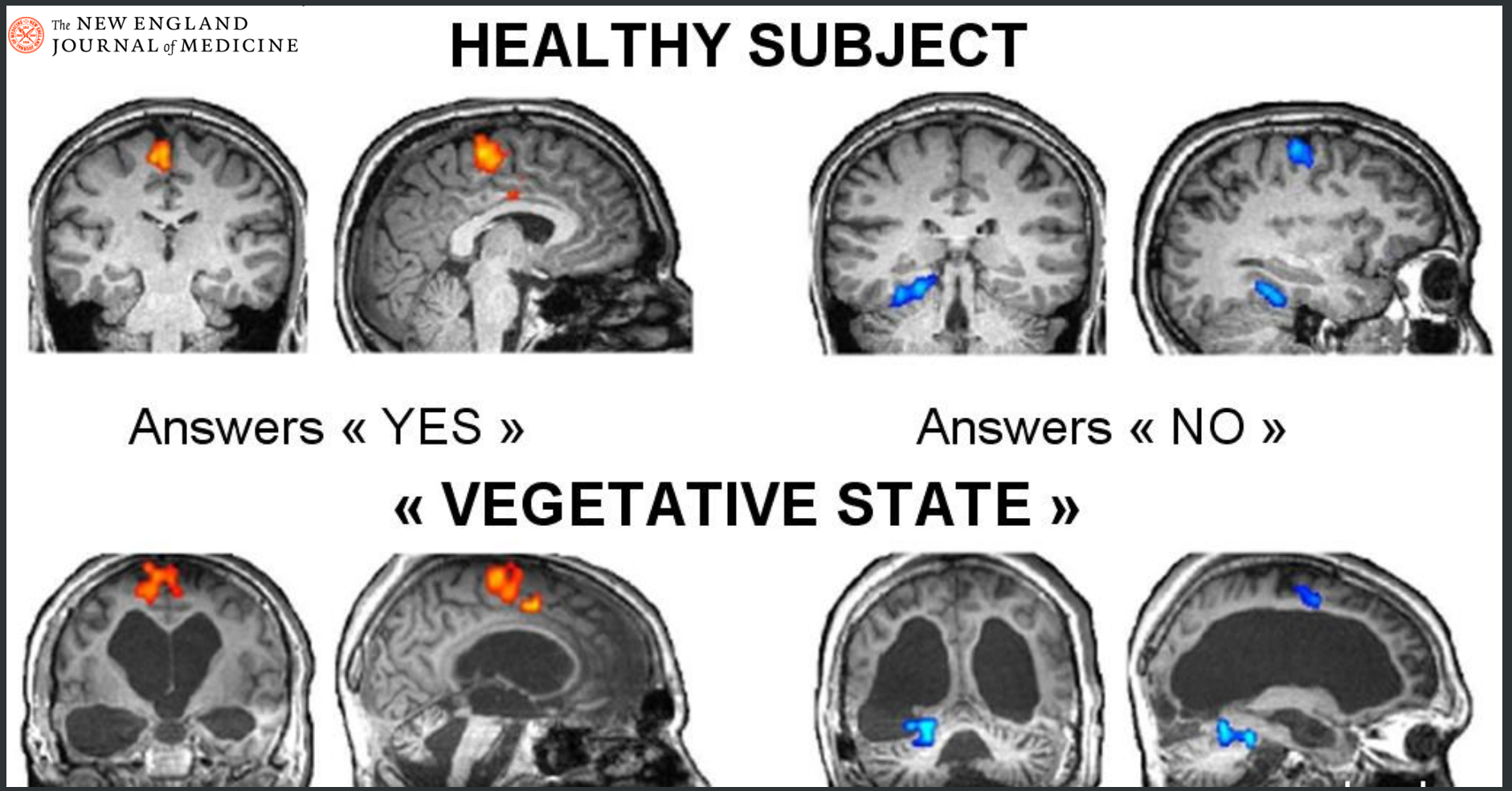
Active paradigm – fMRI



Owen, Coleman, Boly, Davis, Laureys & Pickard, Science, 2006

Active paradigm – fMRI

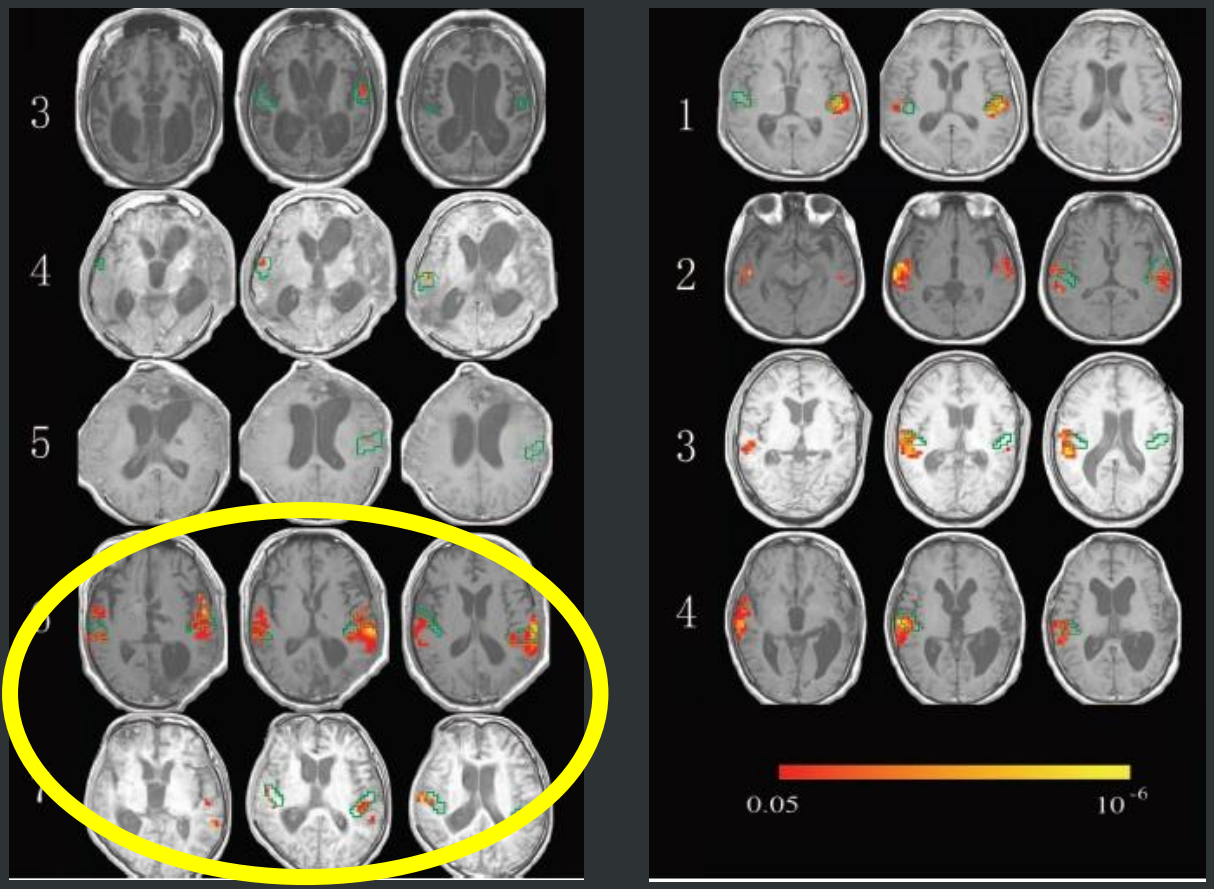


Monti & Vanhaudenhuyse, Coleman, Boly, Pickard, Tshibanda, Owen, Laureys, New England J Med 2010

Active paradigm – fMRI

VS/UWS

MCS



Atypical cortical activity

Di, Yu, Weng, Laureys et al, Neurology, 2007; Di & Laureys, Clin Med, 2008

Activation studies predict outcome

n=48 patients

6 fMRI studies (n=17) and 8 PET (n=32)

32 non-traumatic

38% "high level" activation (n=18)

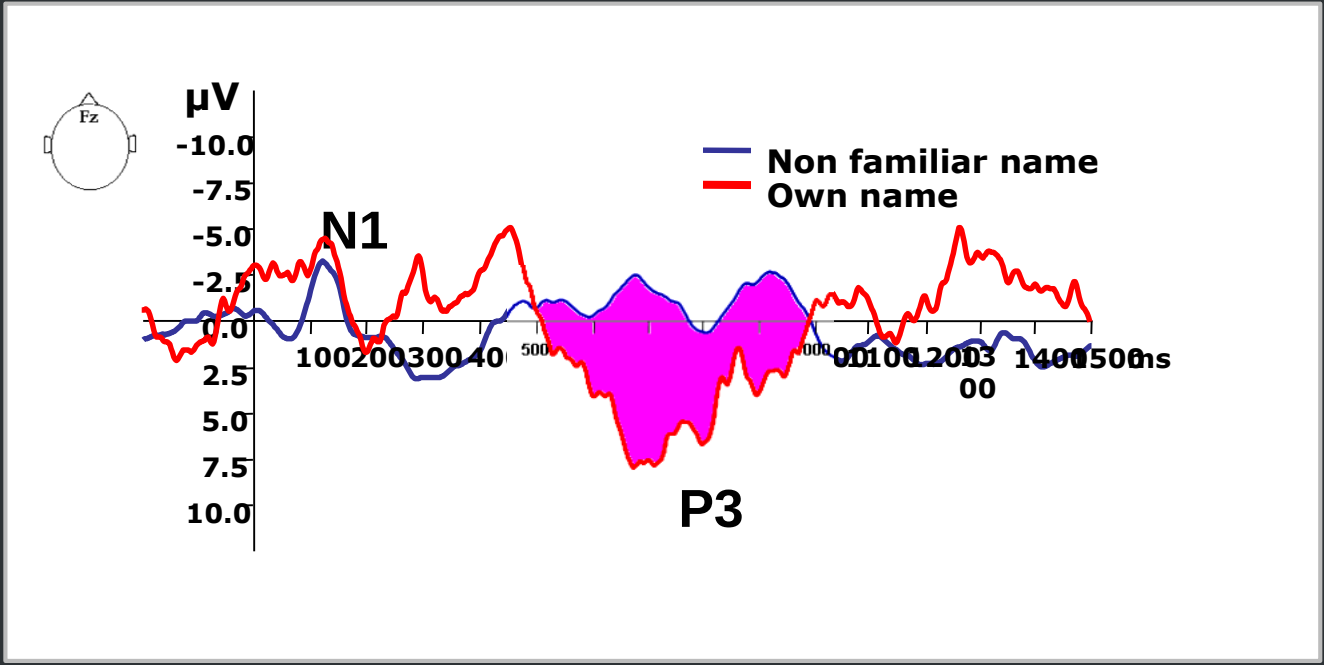
- 7 traumatic
- 82% (9/11) recovered consciousness (6 traumatic)

62% absent or primary "low level" cortical activation (n=30)

- typical activation pattern (n=25; 52%; 8 traumatic)
  - 84% (21/25) failed to recover (7 traumatic)
- no cortical activation (n=5; 10%; 1 traumatic)
  - 100% (4/4) failed to recover (1 traumatic)

Di et al, *Clinical Medicine,* 2008

Active paradigm – EEG



Schnakers, Boly, Majerus and Laureys, Neurol, 2008

Active paradigm – EEG

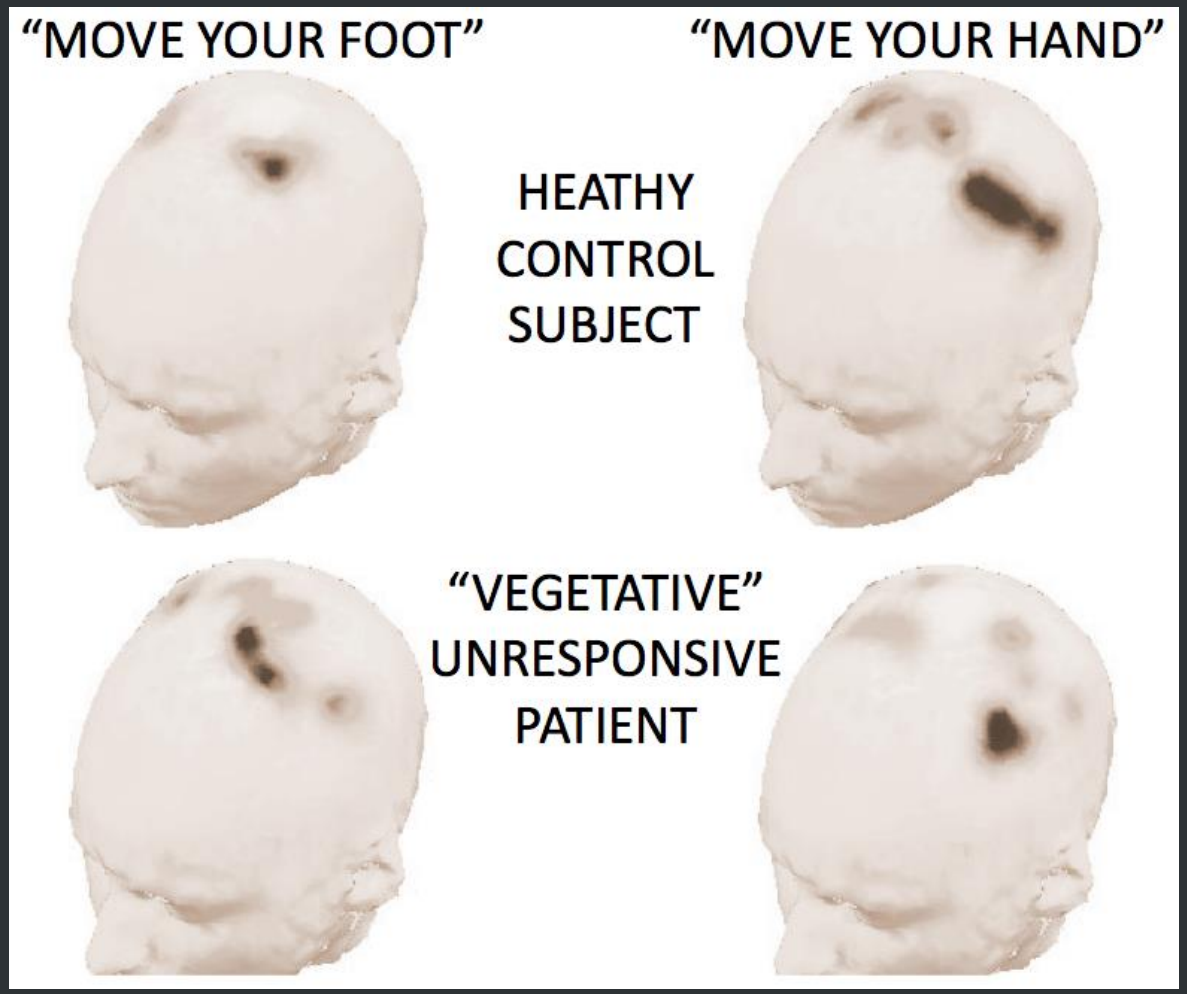
Coma or total locked-in syndrome?

21-y old woman
basilar artery thrombosis - day 49

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

Schnakers et al, Neurocase, 2009

Active paradigm – EEG



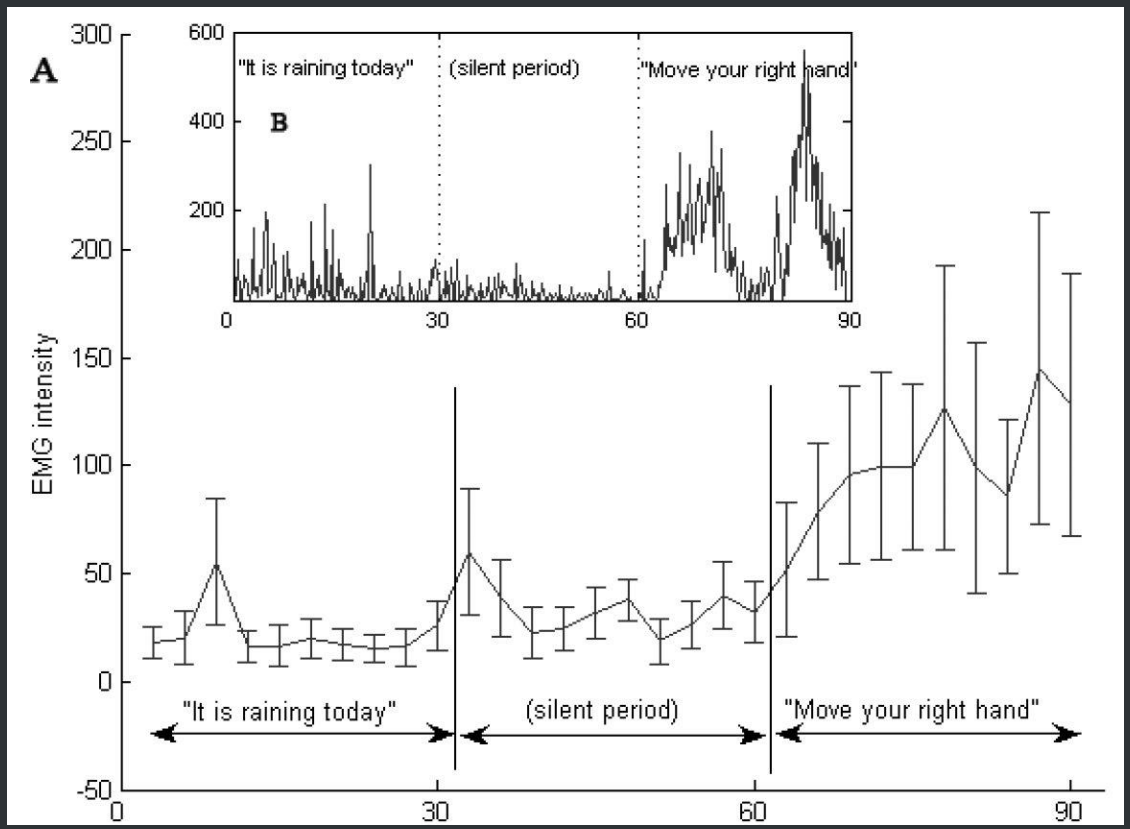
3/16 UWS patients successfully completed task

www.thelancet.com

Cruse, Chennu, Chatelle et al., Lancet 2011; Neurology 2012

Active paradigm – EMG

« Move your right hand » - 1/8 UWS & 2/2 MCS increased EMG



Bekinschtein et al JNNP 2008

Paraclinical diagnosis

Passive paradigms

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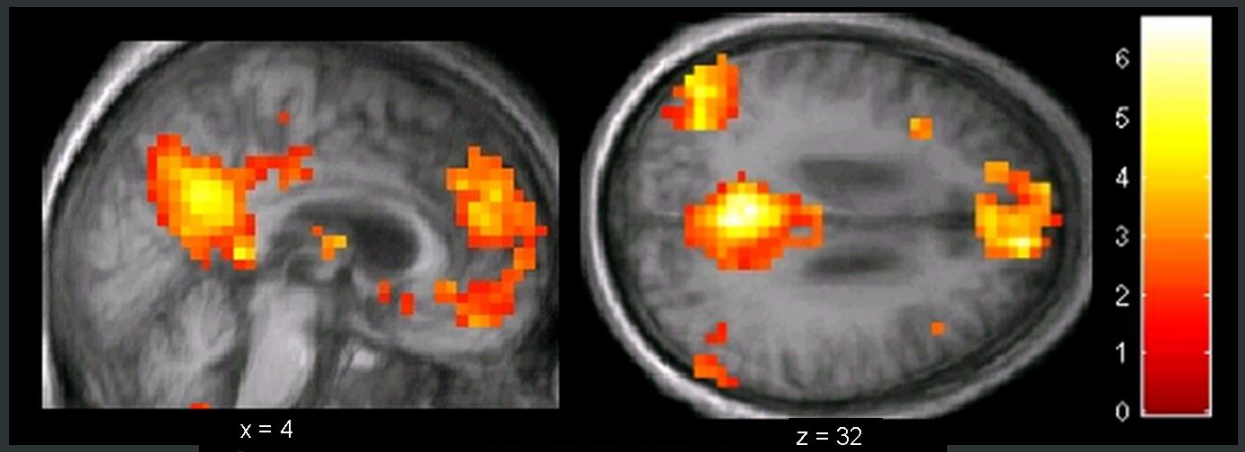
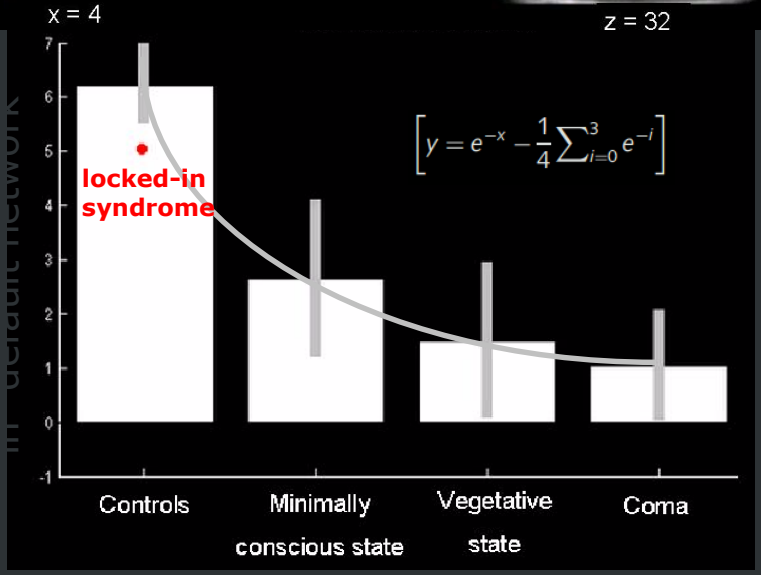
Default mode network





Connectivity in DMN correlated with LOC

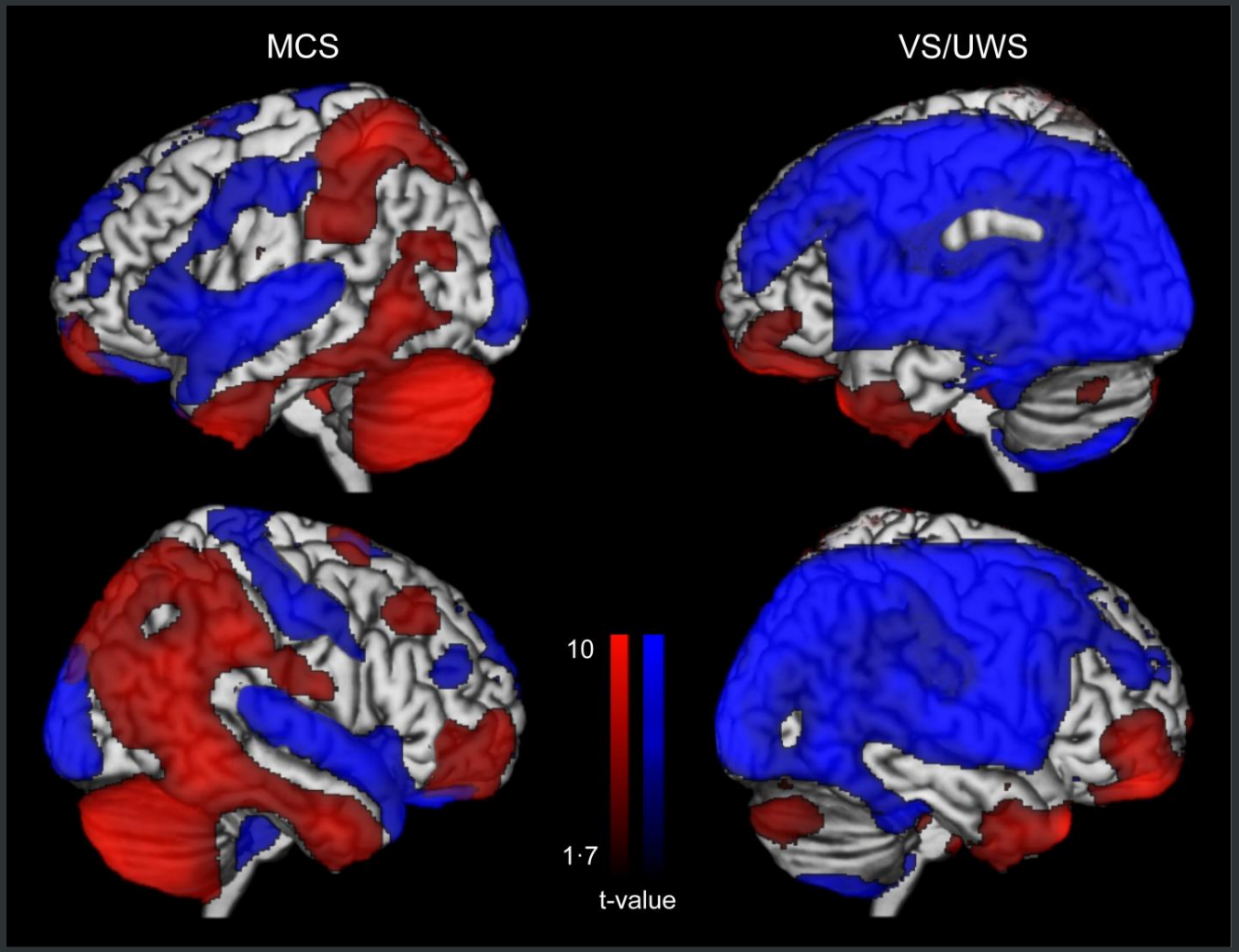
Vanhaudenhuyse et al, Brain, 2010

PET scan

- 126 patients (81 MCS, 41 VS/UWS, 4 locked-in syndrome)
- Traumatic (n=48) and non-traumatic (n=78) etiology
- Chronic (>1 month, n=110) and subacute (n=16) setting
- Coma Recovery Scale – Revised
- Fluorodeoxyglucose positron emission tomography (FDG-PET)
- Functional magnetic resonance imaging during mental activation tasks (fMRI)

Thibaut et al, J Rehabil Med, 2012; Stender and Gosseries et al, The Lancet, 2014

PET scan



Thibaut et al, J Rehabil Med, 2012; Stender and Gosseries et al, The Lancet, 2014

PET scan

	Clinical consensus diagnosis	FDG-PET	Mental imagery fMRI
Completed examinations (out of 122)	122 (100%)	112 (91%)	72 (59%)
Number of interpretable examinations (out of all completed)	89 (73%)	112 (100%)	70 (97%)
Overall congruence with CRS-R (95% CI)	78%	85%	63%
Congruence with CRS-R diagnoses of VS/UWS	95%	67%	89%
Sensitivity to MCS	67%	93%	45%
Overall outcome prediction	-	74%	56%
Positive outcome prediction	-	67%	63%
Negative outcome prediction	-	92%	52%

Stender and Gosseries and al, The Lancet 2014

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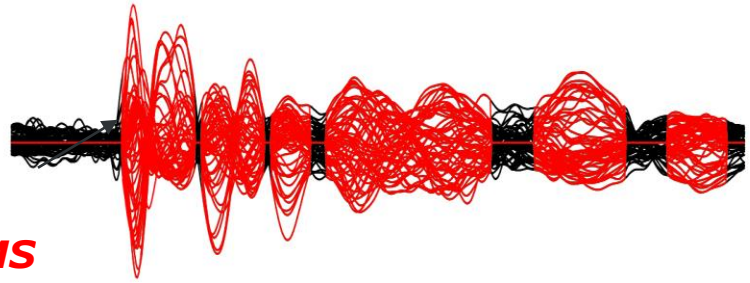
Stender and Gosseries and al, The Lancet 2014

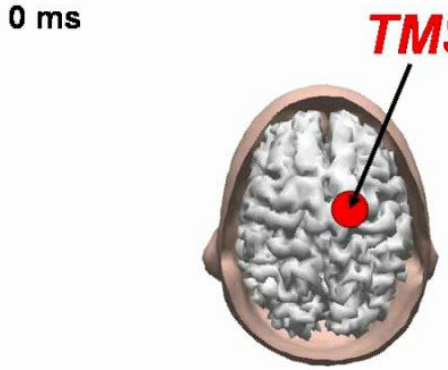
Transcranial Magnetic Stimulation/Electroencephalography (TMS/EEG)

Napolitani and Bodart et al, Brain Inj , 2017

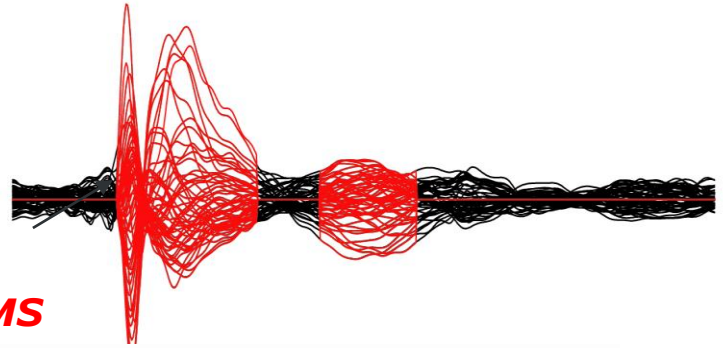
TMS/EEG

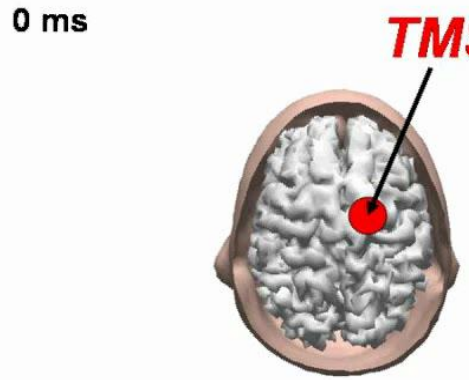
Wakefulness





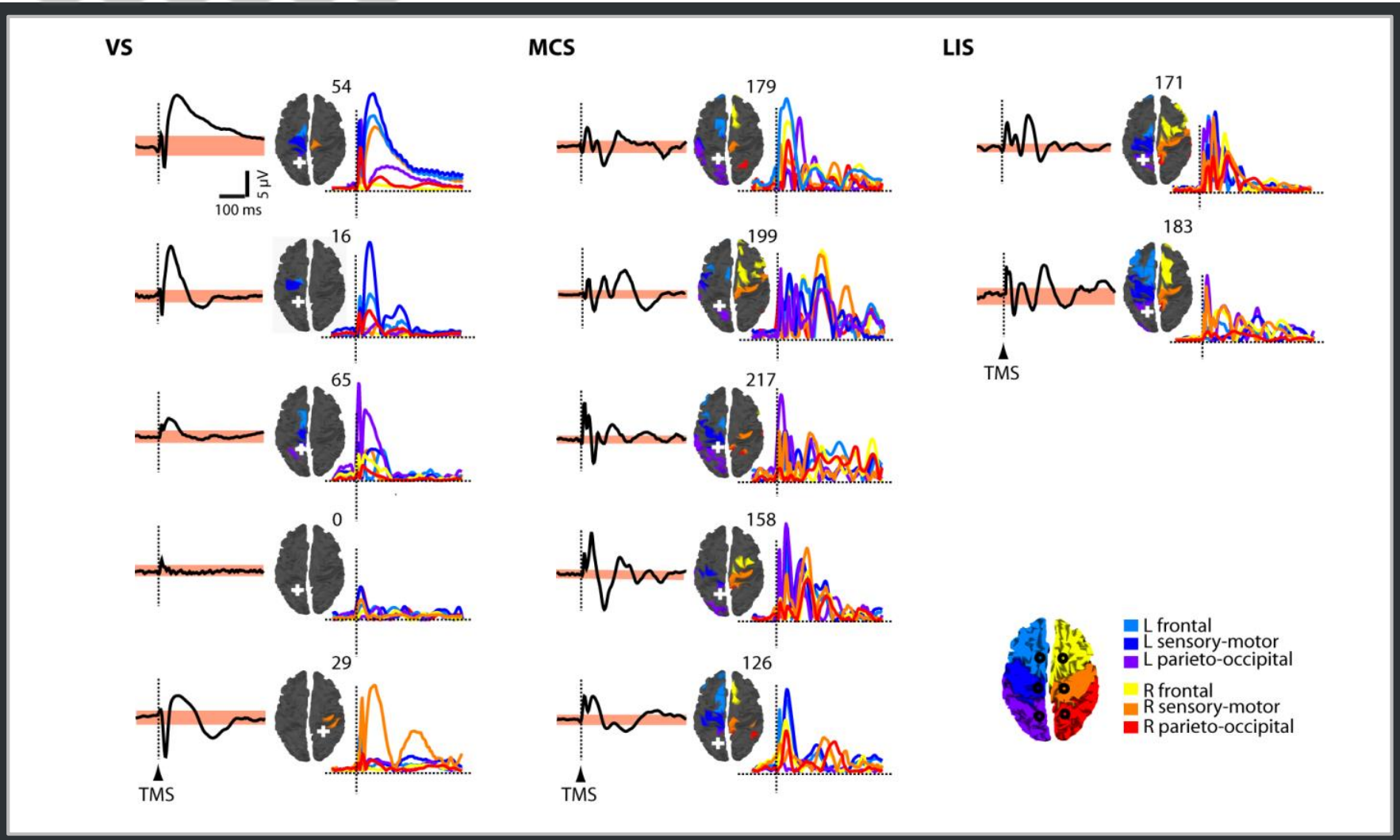
Deep sleep





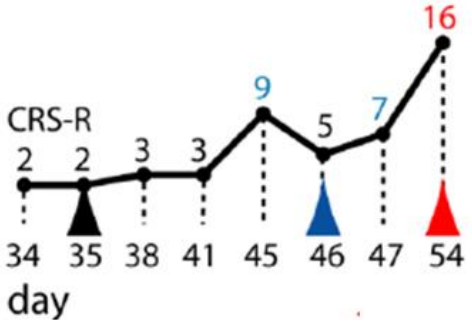
Massimini et al, Science, 2005

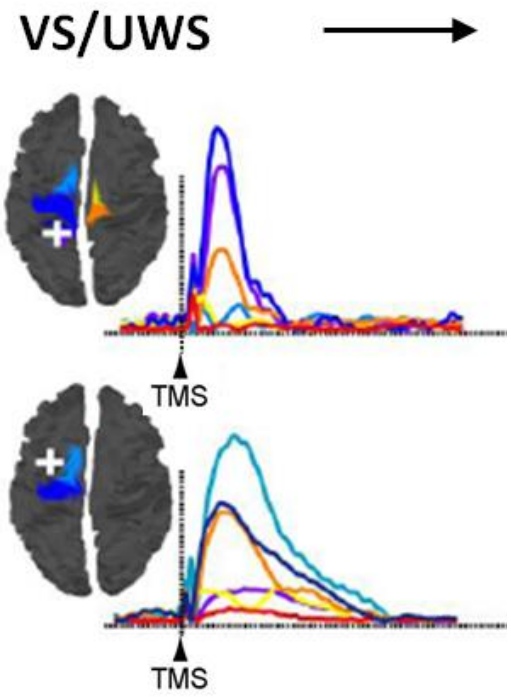
Passive paradigm – TMS/EEG



Rosanova and Gosseries et al, Brain, 2012

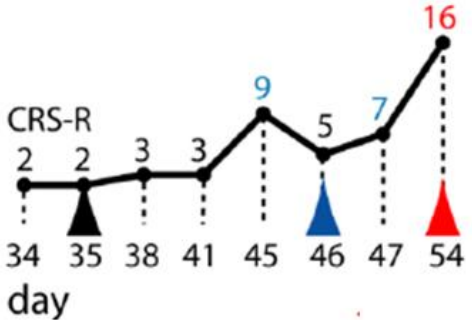
Passive paradigm – TMS/EEG

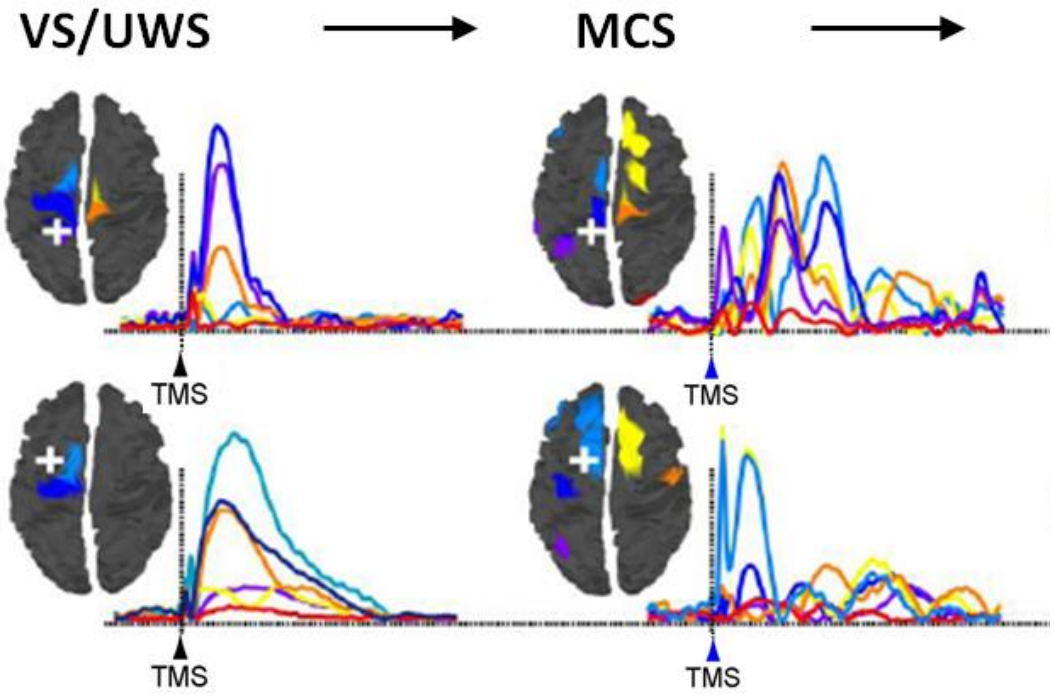




Rosanova and Gosseries et al, Brain, 2012

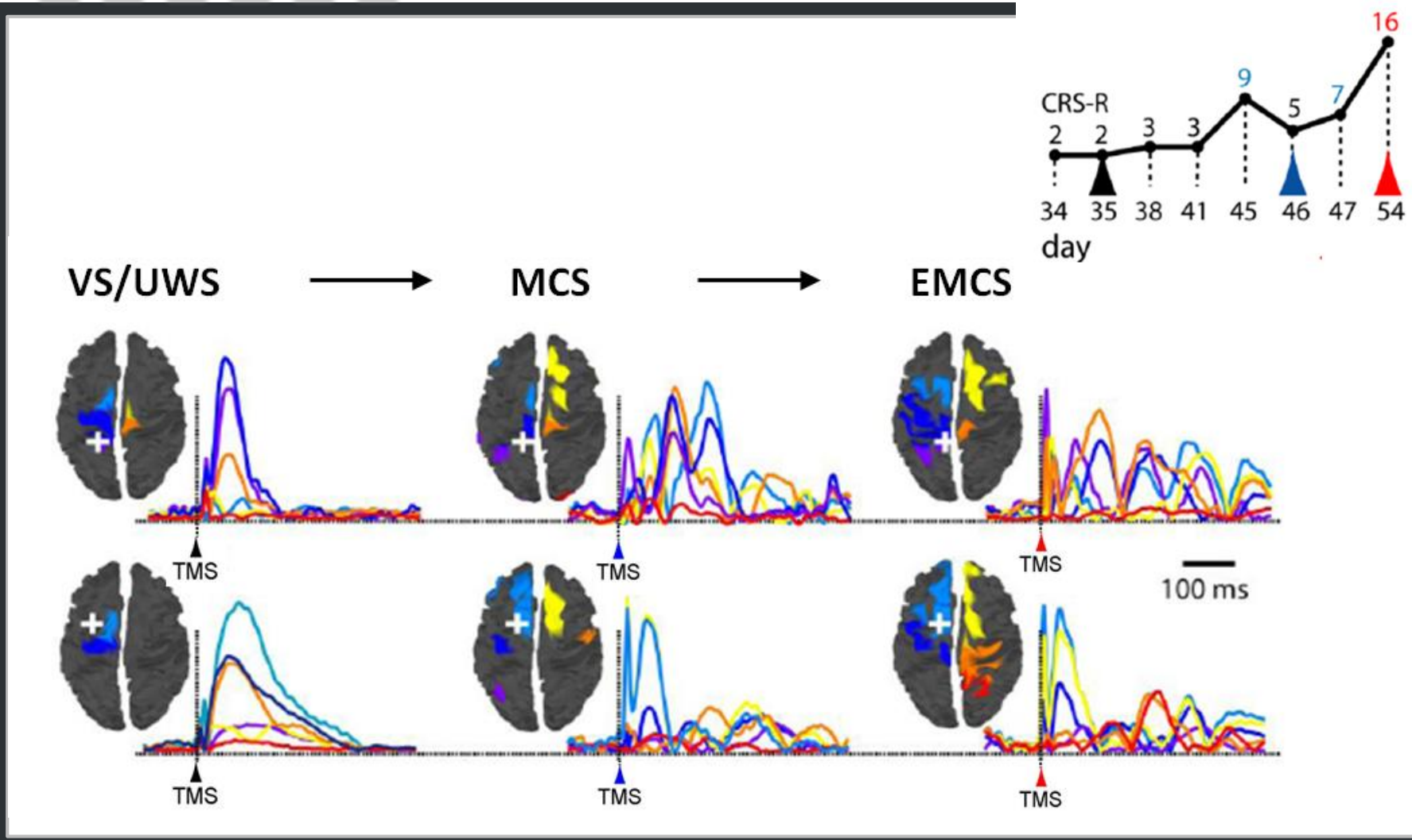
Passive paradigm – TMS/EEG





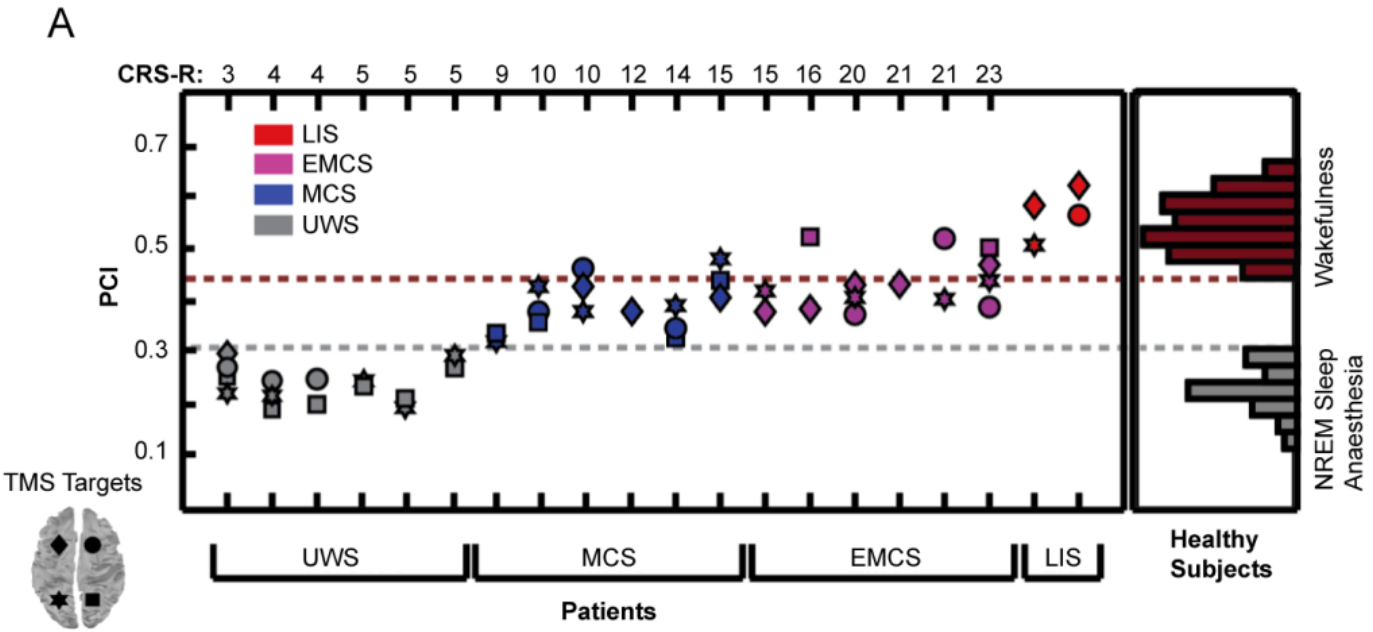
Rosanova and Gosseries et al, Brain, 2012

Passive paradigm – TMS/EEG



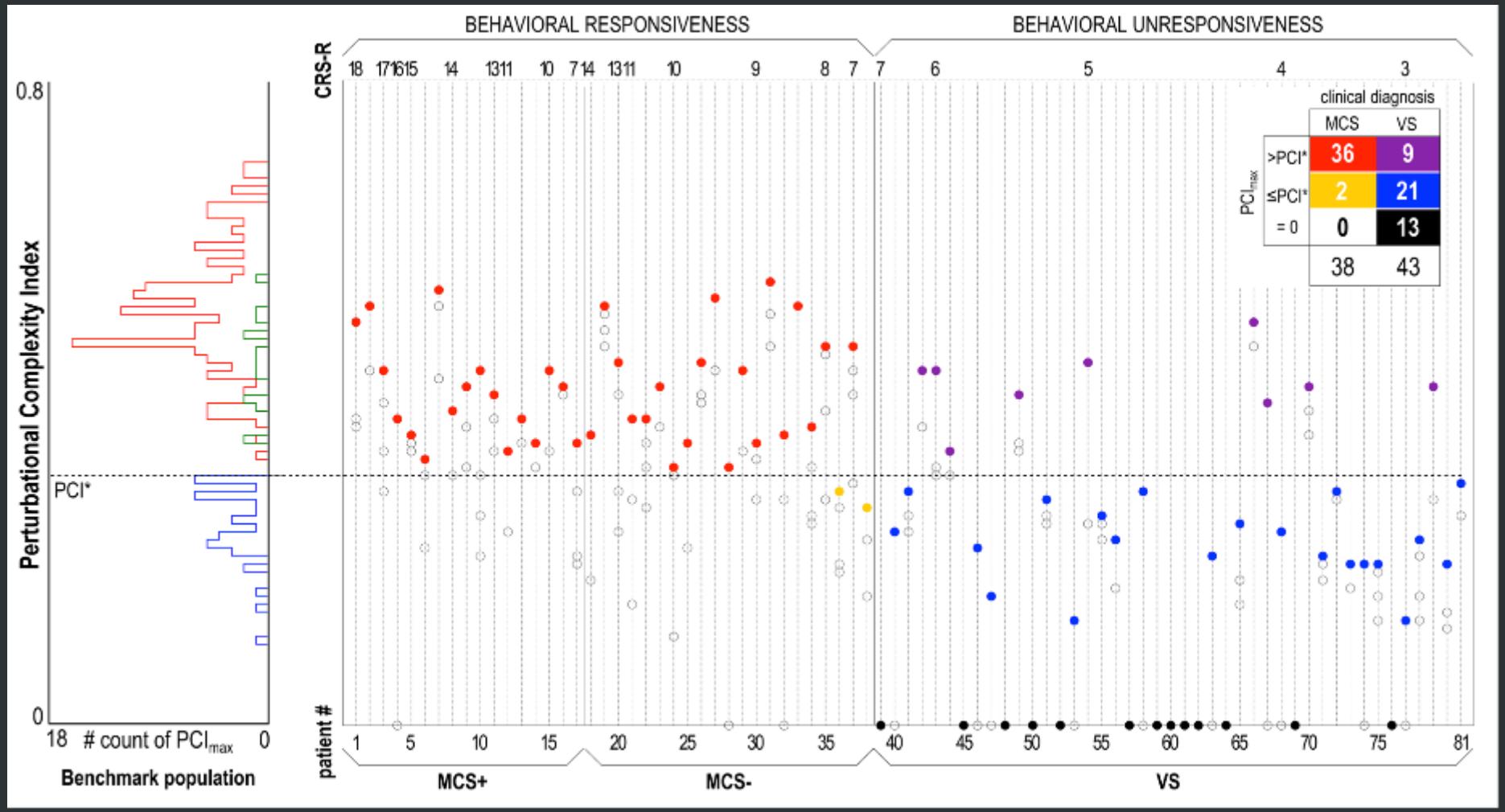
Rosanova and Gosseries et al, Brain, 2012

Perturbational complexity index (PCI)



Casali and Gosseries et al, Sci Trans Med, 2013

Perturbational complexity index in comatose patients



Casarotto et al, *Ann Neurol*, 2016

Paraclinical diagnosis

Case reports

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Case reports

Behavioral assessment

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

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

FONCTION AUDITIVE
4 – Mouvement systématique sur demande*
3 – Mouvement reproductible sur demande*
2 – Localisation de sons
1 – Réflexe de sursaut au bruit
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

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
0 – Néant / Flaccidité
FONCTION OROMOTRICE/VERBALE
3 – Production verbale intelligible*
2 – Production vocale / Mouvements oraux
1 – Réflexes oraux
0 – Néant
COMMUNICATION
2 – Fonctionnelle : exacte*
1 – Non fonctionnelle : intentionnelle*
0 – Néant
EVEIL
3 – Attention
2 – Ouverture des yeux sans stimulation
mulation

NOCICEPTION COMA SCALE – NCS ©2009
Record Form

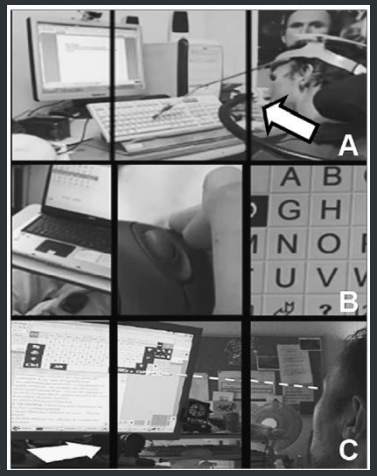
Spontaneous behaviour observation (60sec.) is required before nocioceptive stimulation

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

BCI



PET scan

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

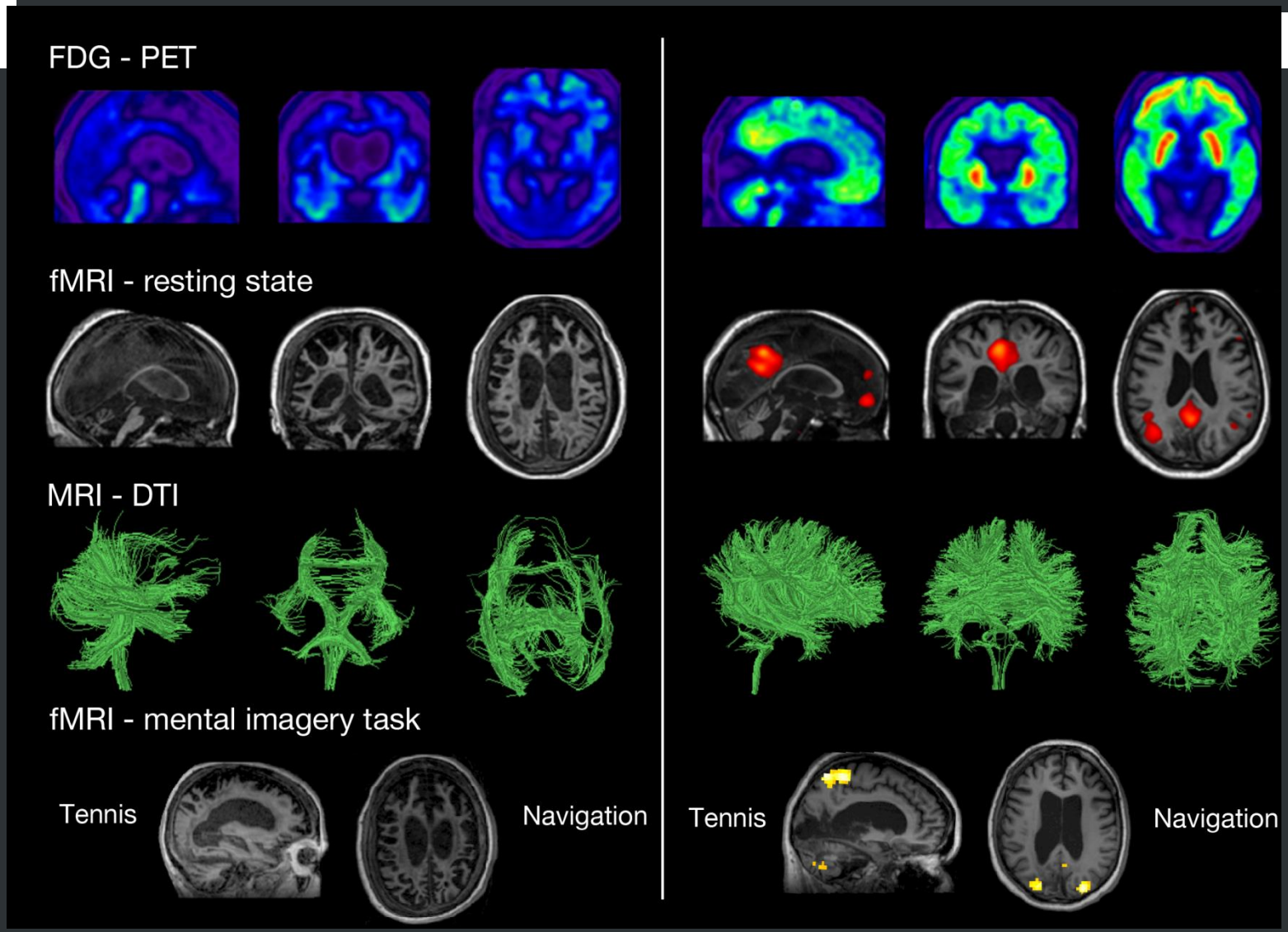
Gosseries, Zasler and Laureys, Brain Inj, 2014

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



Gosseries, Zasler and Laureys, Brain Inj, 2014

Conclusion

- Behavioral assessment ≈ 40% misdiagnosis
- FDG-PET complement beside examinations and can predict long-term recovery of patients in chronic VS/UWS
- 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!

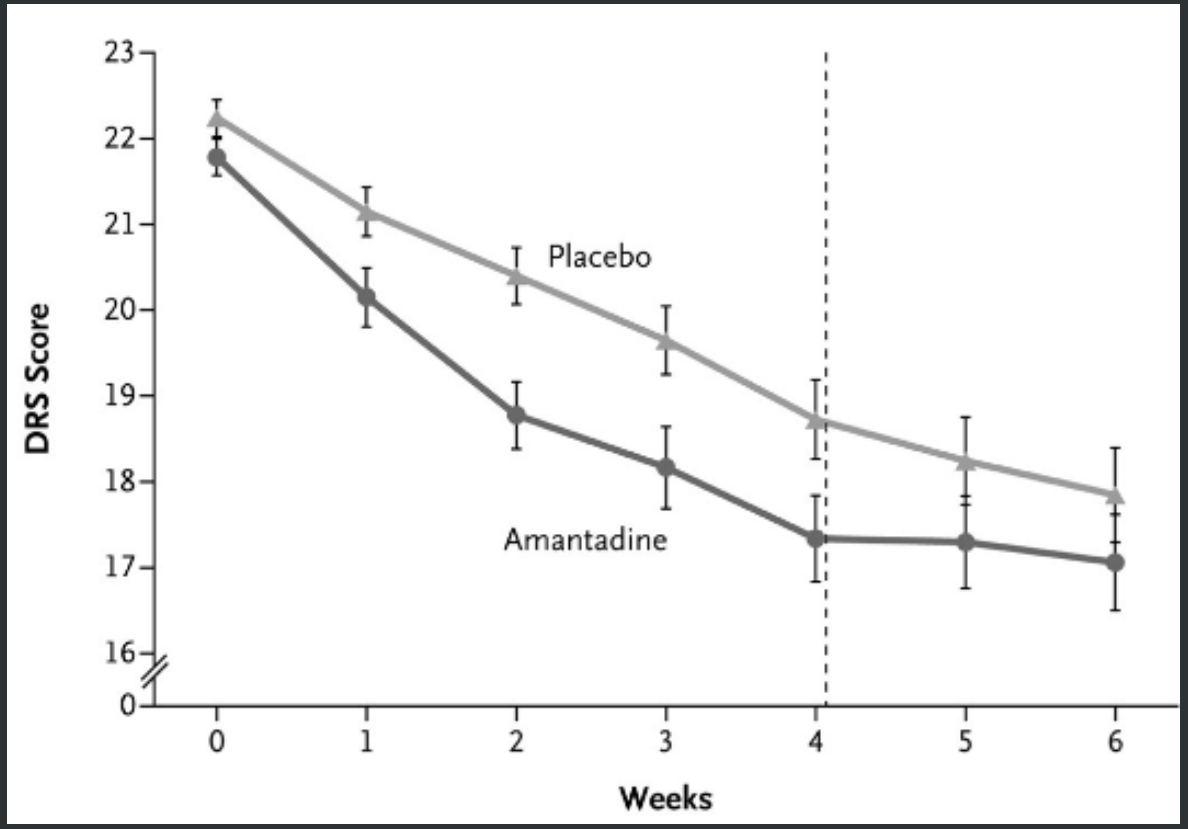
Treatment

Pharmacological

LIÈGE université
GIGA institute

Amantadine

Dopaminergic agent (Parkinson)

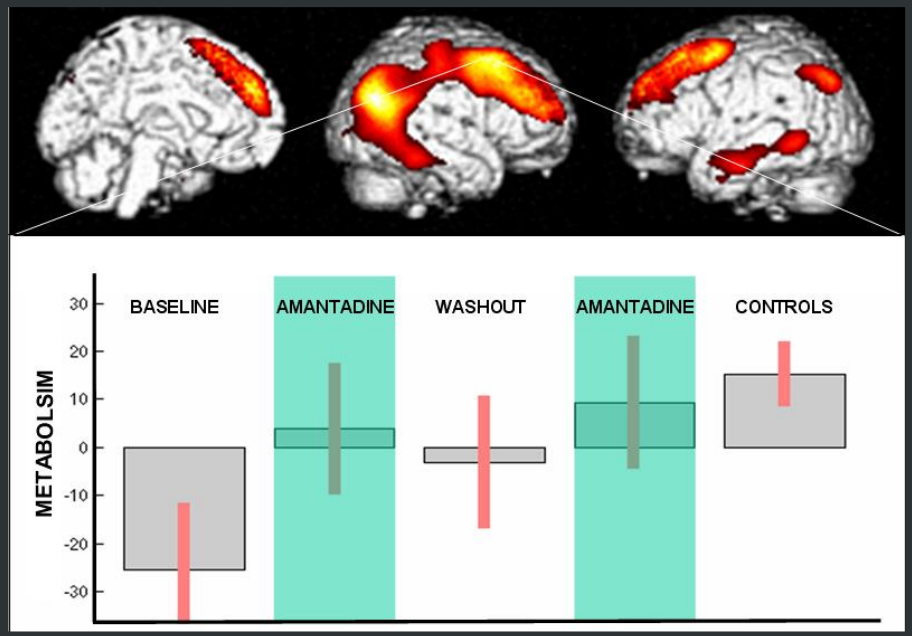


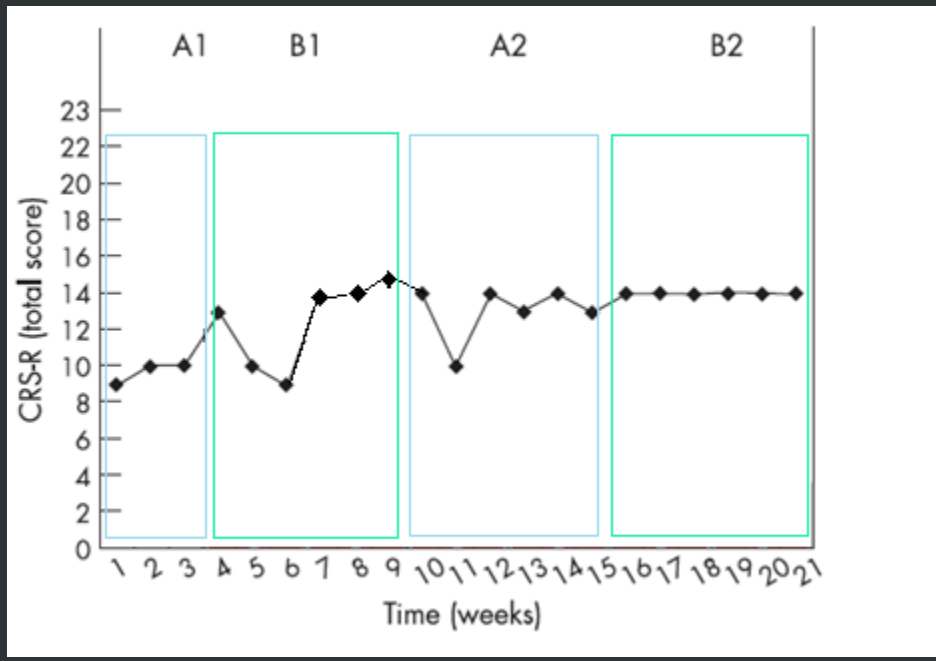
n=184

Giacino et al, N Engl J Med, 2012

Amantadine

Dopaminergic agent (Parkinson)





Schnakers et al, J Neurol Neurosurg Psychiatry 2008

Zolpidem

short-acting nonbenzodiazepine GABA-A agonist hypnotic

1/15 responders = 6.7%

Whyte and Meyers, Am J Phys Med Rehabil, 2009

4/84 responders =5%

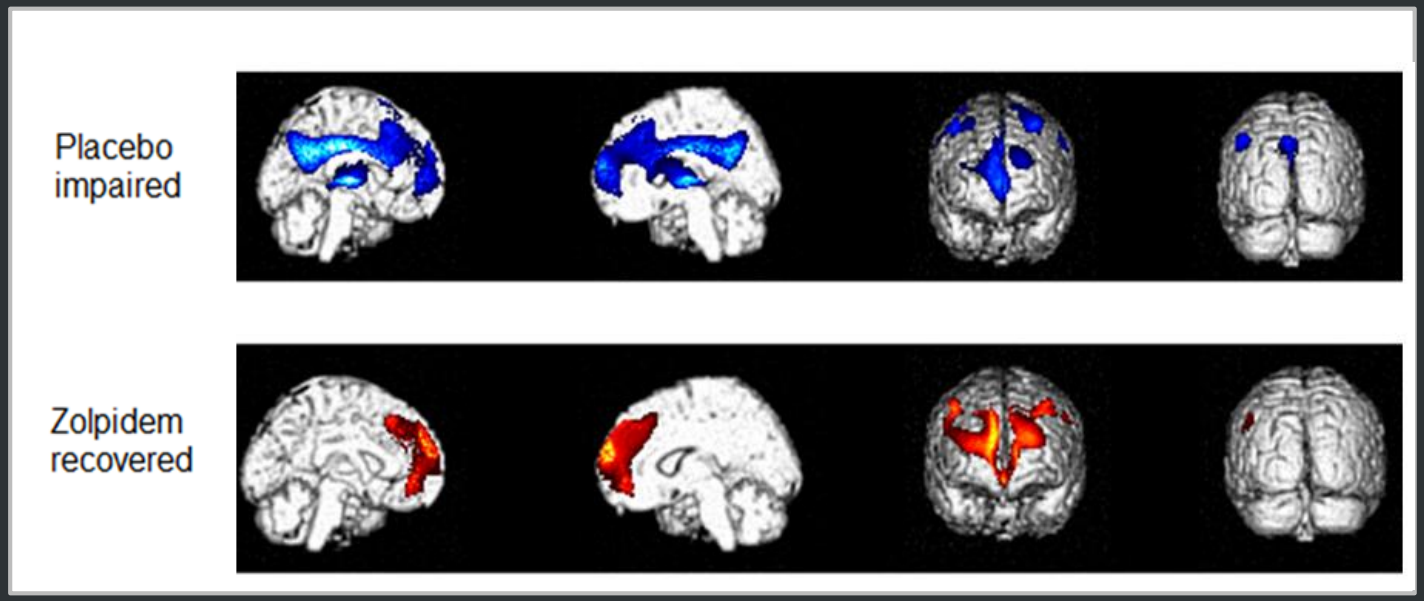
Whyte et al, Am J Phys Med Rehabil, 2014

4/60 responders
= 6.7%
Without change of diagnosis

Thonnard and Gosseries et al, Funct Neurol 2014

Zolpidem

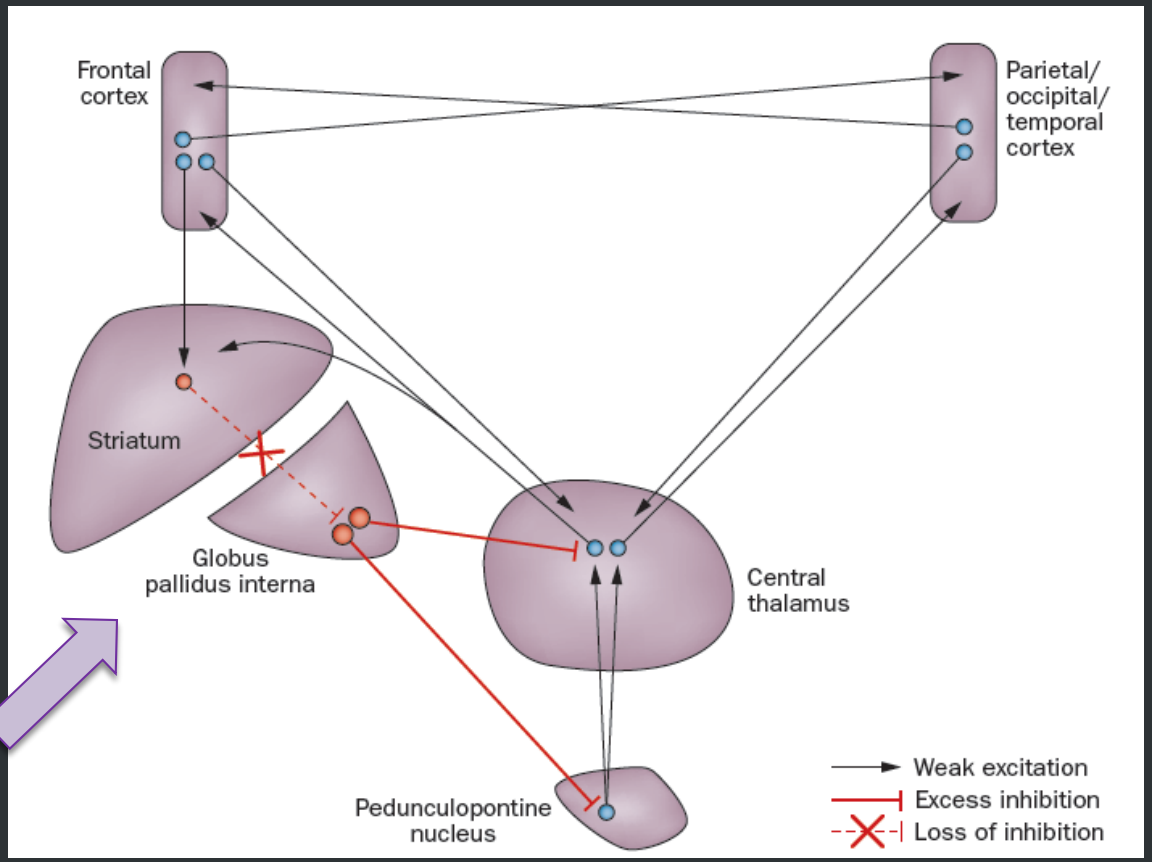
short-acting nonbenzodiazepine GABA-A agonist hypnotic



Chatelle et al, Front. Hum. Neurosci., 2014

n=3 MCS responders

Zolpidem



Zolpidem inhibits GPi

Chatelle et al, *Front Hum Neurosci,* 2014
Williams et al, *Elife*, 2013

Treatment

Brain stimulation

LIÈGE université
GIGA institute

Recent RCTs on NIBS in DOC

NIBS	N	TSO	Procedure	Results	Effect sizes
tDCS Thibaut et al, 2014	55 25 TBI, 30 non-TBI 30 MCS, 25 UWS	1 week to 19 years	Single session (20 minutes) of active and sham stimulation over the left DLPFC with CRS-R before and after tDCS	13/30 patients in MCS and 2/25 patients in UWS clinically improved (recovery of visual pursuit or command following). At the group level, clinical improvement (2 points on the CRS-R) for MCS patients. No side-effects observed.	For MCS (n=30): d=0.38
tDCS Thibaut et al, 2017	16 11 TBI, 5 non-TBI 16 MCS	> 3months	5 sessions of active and sham tDCS (20 minutes a day) over the DLPFC. CRS-R performed before, after 5 days of tDCS and at 1-week follow-up	9/16 responders. Clinical improvement maintained up to one week after the end of the stimulation. No side-effects observed.	After tDCS: d=0.43 ; at 1week follow-up: d=0.57
tDCS Estraneo et al, 2017	13 1 TBI, 12 non-TBI 7 UWS, 6 MCS	> 3months	5 days of active and sham tDCS over the DLPFC (20 min/day). EEG and CRS-R at baseline, after 5 days and 3-month follow-up	Behavioral (CRS-R total score) and EEG changes in 5/13 patients (3 in MCS and 2 in UWS). At the group level, no statistical difference between the two groups.	/
tDCS Zang et al, 2017	26 12 TBI, 14 non-TBI 11 UWS, 15 MCS	1 to 18 months	20 sessions o DLPFC for 20 days		
tDCS Martens et al, 2018	27 12 TBI, 15 non-TBI 27 MCS	10 months to 14 years	20 sessions o minutes per by 8 weeks. tDCS (20 sess up.		
tDCS Huang et al, 2017	33 20 TBI, 13 non-TBI 33 MCS	> 3months	5 sessions of minutes a dc after 5 days up		
tRNS Mancuso et al, 2017	9 1 TBI, 9 non-TBI 9 UWS	30 days to 4 months	5 sessions of for 20 minute at baseline, at 3-day follc		

NIBS	N	Time since injury	Procedure	Results	Effect sizes
rTMS Cincotta et al, 2015	11 2 TBI, 9 non-TBI 11 UWS	9 to 85 months	5 sessions of active or sham 20 Hz rTMS for 10 minutes (1000 pulses in 5 trains) over left M1. EEG and CRS-R before and after rTMS	No behavioral or EEG improvements. No side-effects observed.	/
rTMS Liu et al, 2016	10 4 TBI, 6 non-TBI 5 UWS, 5 MCS	1 to 28 months	One session of active or sham 20-Hz rTMS over M1 for 10 minutes (1000 pulses in 20 trains). CRS-R and CBF velocity of the MCA before and after rTMS	No behavioral (CRS-R) changes Temporary increase in peak systolic velocity and mean flow velocity of the left MCA for MCS. No effects in UWS or in sham group. No side-effects observed.	/
rTMS He et al, 2018	6 4 TBI, 2 non-TBI 3 UWS, 2 MCS, 1 EMCS	1 to 28 months	5 sessions of active or sham 20-Hz rTMS over M1 (1000 pulses in 20 trains). CRS-R and EEG before, after rTMS and 1-week follow-up	No treatment effect on the CRS-R nor on the EEG. Clinical improvement in 1 patient (up to 1-week follow-up - UWS became MCS- paralleled by EEG power spectra improvement. No information on side-effects.	/

Past 5 years:

tDCS ➔ 6 RCTs (170 pts) – 5 DLPFC & 1 M1 - 1 to 20 sessions – ES: 0.38 – 2.22

tRNS ➔ 1 RCT (9 pts) – DLPFC – no clincial/neurophysiological effects

rTMS ➔ 3 RCTs (27 pts) – M1 – 20 Hz – no clinical/neurophysiological effects

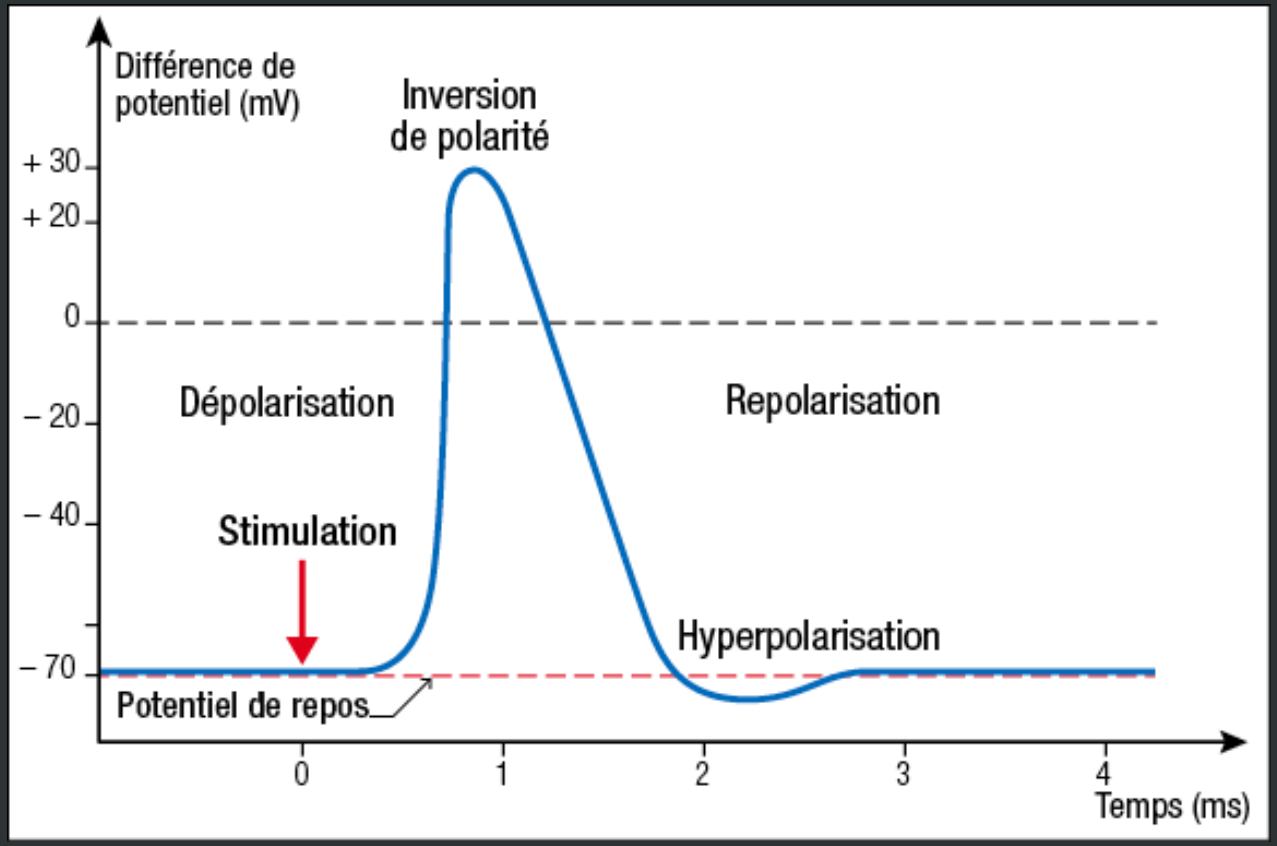
Thibaut et al, *Lancet Neurol*

Transcranial direct current stimulation

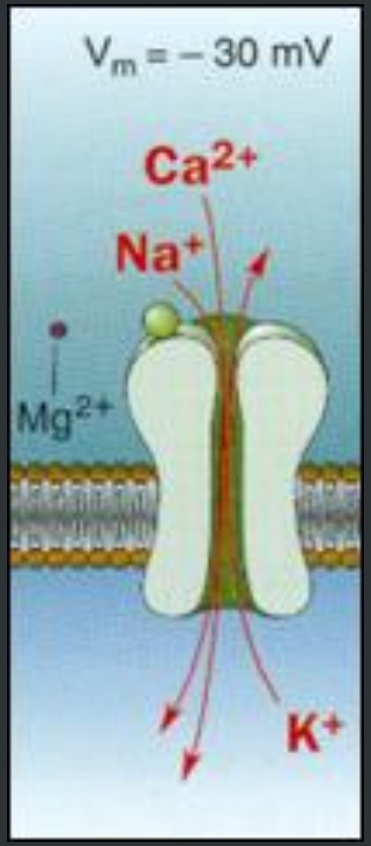
- Transcranial direct current stimulation = tDCS
- Constant, weak direct current through electrodes
- The current induces intracerebral current flow that either increases or decreases the neuronal excitability in the specific area being stimulated

tDCS mechanisms

Short term effects



Long term



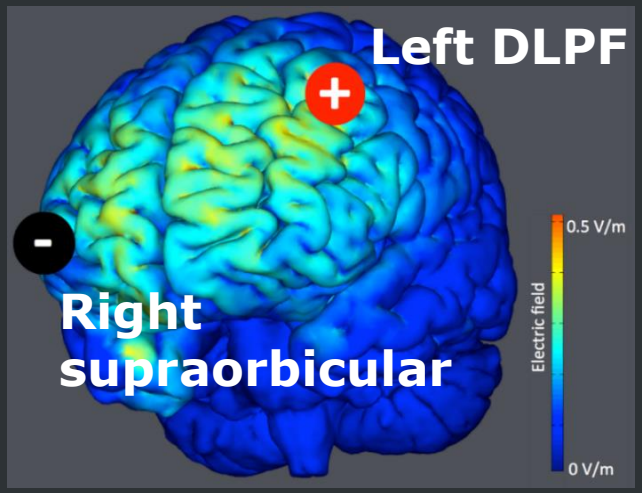
Transcranial direct current stimulation

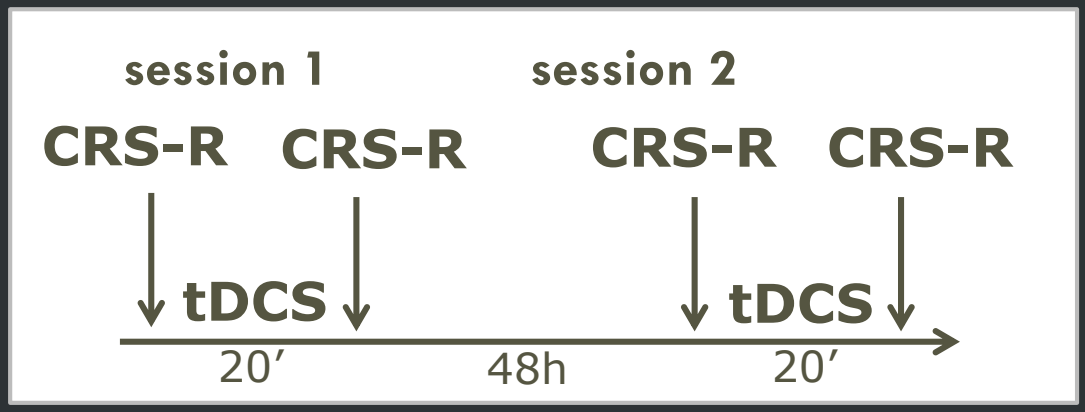
Stimulation	Population	Effects	Authors
Motor cortex	Healthy subjects	Dexterity	Boggio et al. Neurosci Lett, 2006
	Hemiplegic patients	Dexterity and strength	Hummel et al. Lancet, 2006
	Spastic patients	Spasticity & ADL (activity of daily life)	Wu et al., Arch Phys Med Rehabil 2012
Prefrontal cortex	Healthy subjects	Memory	Marshall et al. J Neurosci, 2004
	Alzheimer's patients	Memory	Ferrucci et al. Neurology, 2008
	Stroke patients	Attention	Jo et al. Am J Phys Med Rehabil, 2009
	Aphasic patients	Language	Baker et al. Stroke, 2010

Thibaut et al, Rev Neurol, 2013

tDCS – single session

- Randomized, double blind, sham controlled, cross-over study
- Direct current: 2 mA; 20 min
- 55 patients included
  VS/UWS; 30 MCS;
  TBI; 43±18y)

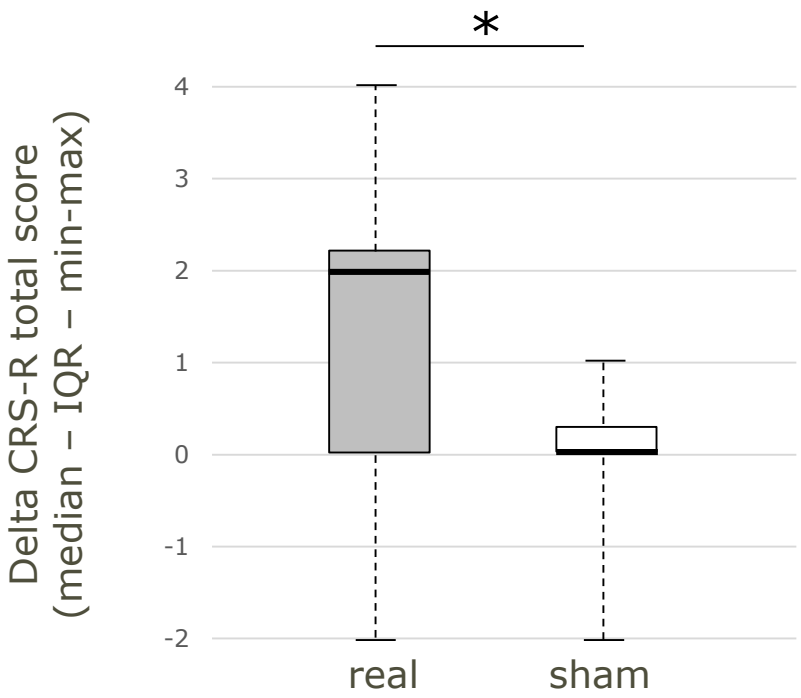




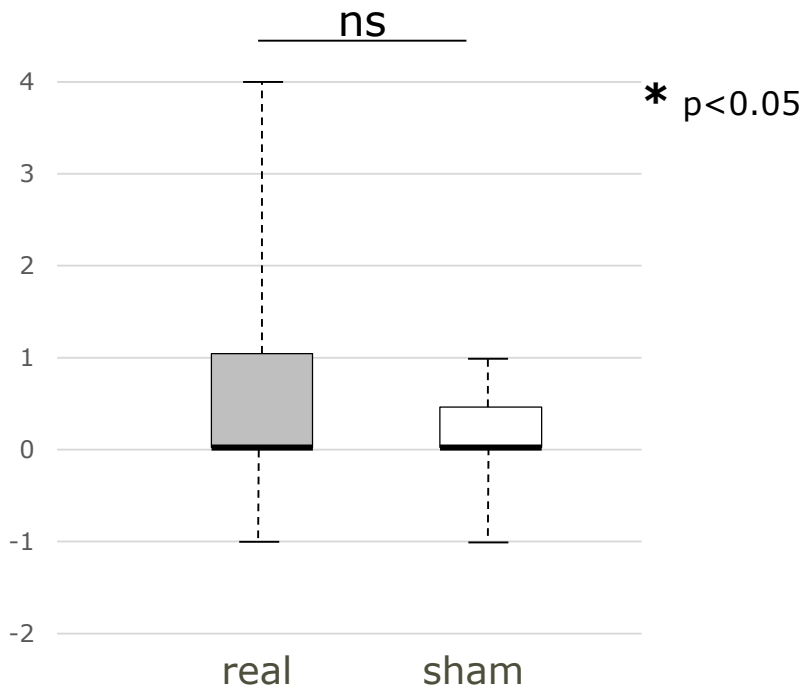
Thibaut *et al.*, Neurology, 2014

Transcranial direct current stimulation

Treatment effect: delta CRS-R total scores



MCS (n=30)



VS/UWS (n=25)

Thibaut *et al.*, Neurology, 2014

tDCS – single session

15/55 responders

Patient who showed new signs of consciousness after tDCS and not before tDCS or before and after sham

- 2 VS/UWS; subacute (<3m)
- 13 MCS (6 >1y post insult)

Diagnostic change

- 2 VS/UWS➔ MCS
- 2 MCS ➔ EXIT (subacute)

Thibaut *et al.*, Neurology, 2014

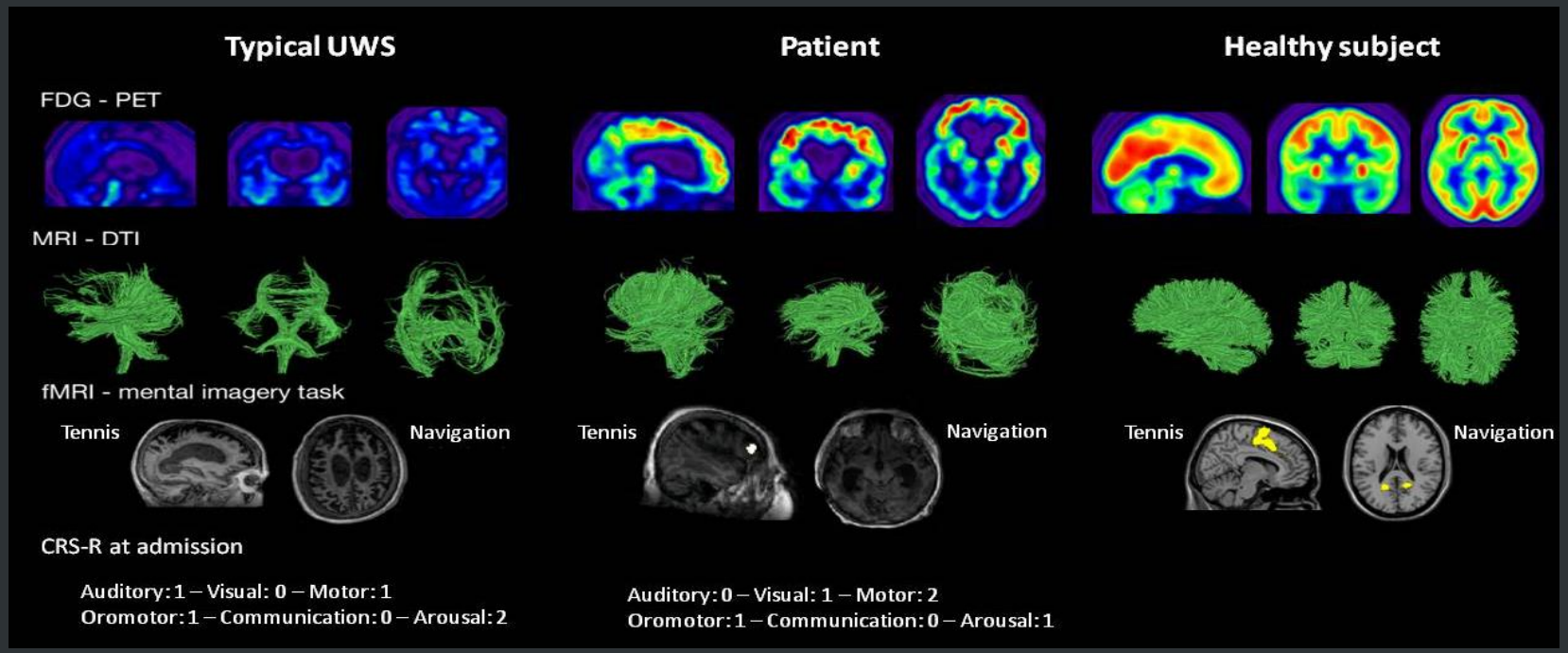
tDCS – single session

SUBSCALES	RECOVERY	NUMBER OF PATIENTS
AUDITORY	Consistent command following	1
	Reproducible command following	4
	Localization to sounds	1
VISUAL	Object recognition	2
	Object localization	1
	Visual pursuit	5
MOTOR	Functional use of object	1
	Automatic motor reaction	2
	Object manipulation	3
OROMOTOR	Vocalisation	3
COMMUNICATION	Functional communication	2
AROUSAL	Without stimulation	2

Thibaut *et al.*, Neurology, 2014

tDCS to unveil covert consciousness

- 67yo woman in UWS for 4y after subarachnoid hemorrhage
- Out of 7 CRS-R, 1 localization to pain
- Consistent response to command only after tDCS
- Neuroimaging consistent with MCS*



➔ tDCS may facilitate motor execution of command when cognitive functions are preserved

tDCS – repeated sessions

Single stimulation: effects ± 60 min[1]

➔ short-lasting improvements, back to initial state

1. Increase the duration of the effects
2. Increase the number of responders

Randomized sham controlled double blind cross-over

S1: real or sham

S2: sham or real

CRS-R

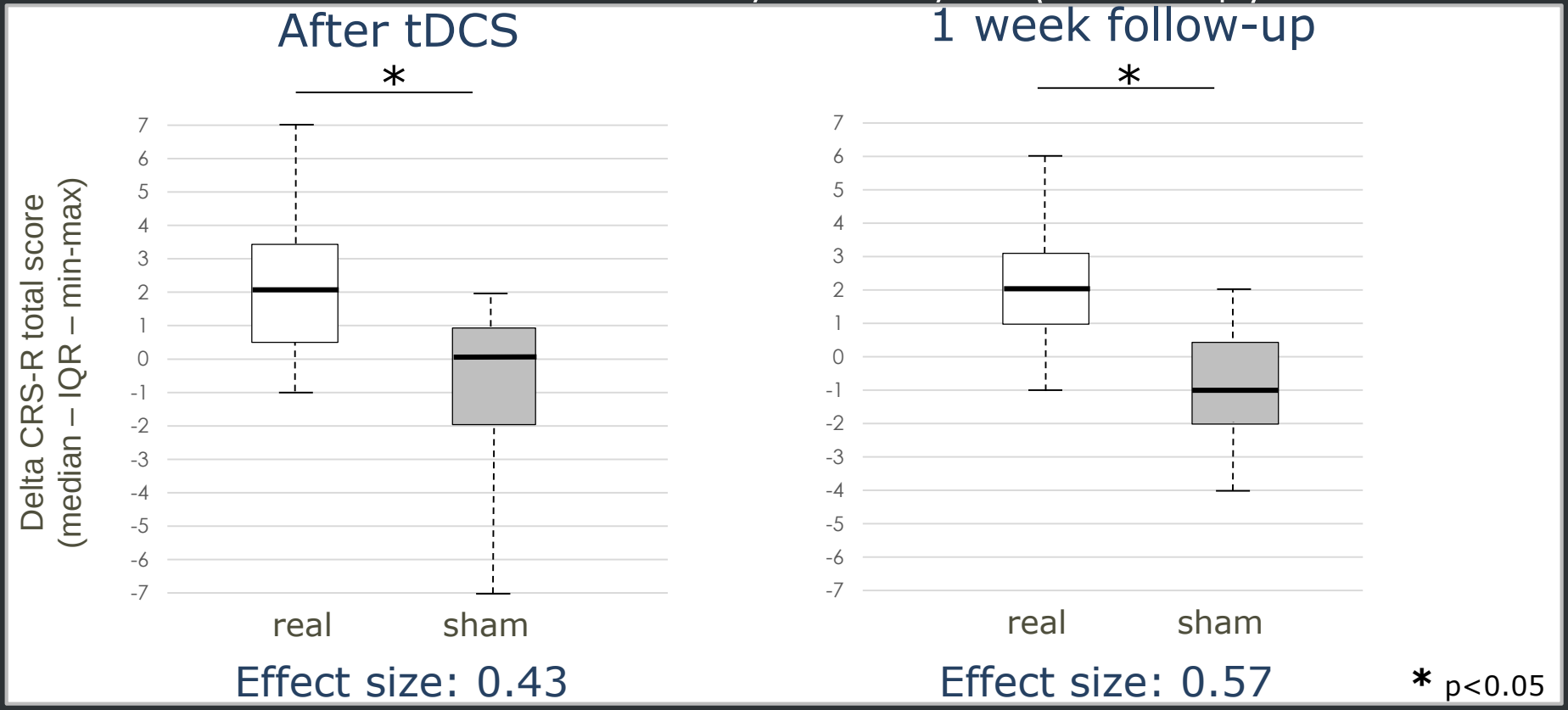
20 min tDCS

[1]Nitsche et *al.*, 2001; Thibaut *et al.*, 2017

tDCS – repeated sessions

16 patients in MCS (> 3months; 12 TBI; 47±16 y)

Treatment effect: delta CRS-R day 5 & day 12 (follow-up)

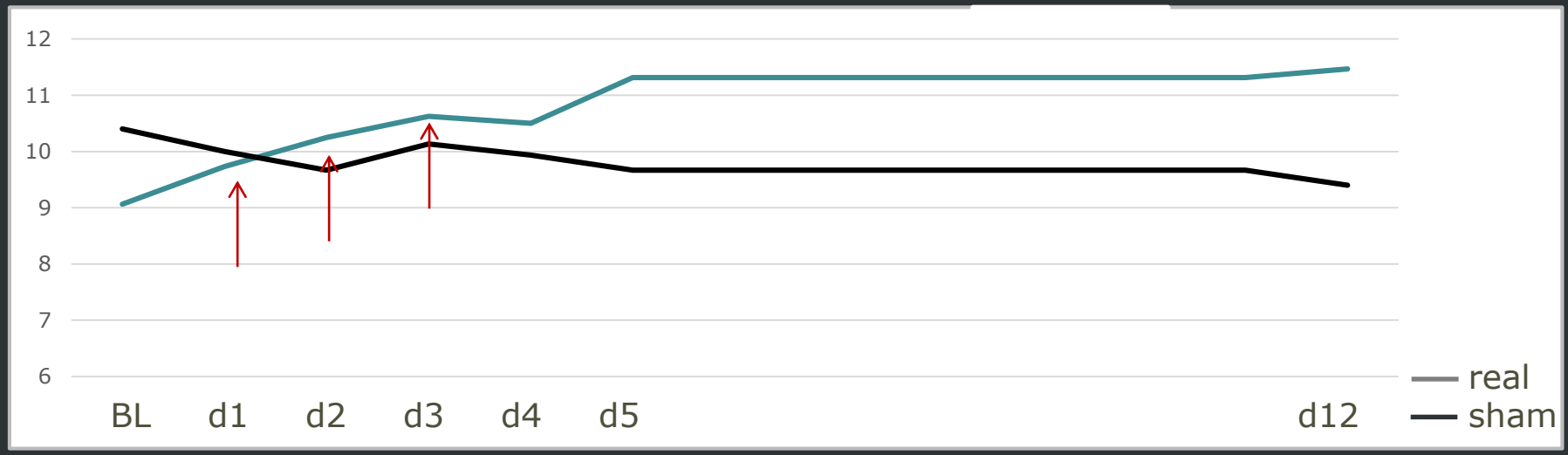


Thibaut *et al.*, 2016

tDCS – repeated sessions

Longitudinal analysis:

- Real session: significant + time evolution ($p<0.001$)
- Sham session: no evolution across time ($p=0.64$)



Some patients responded after 1, 2 or 3 days of tDCS

↗ responders (9/16 – 56%)

Single stim: 43% responders – effect size : 0.38 (versus 0.57)

Thibaut *et al.*, 2016

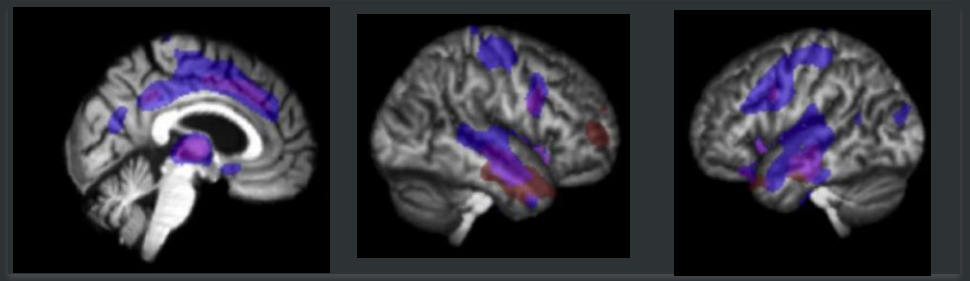
Predicting clinical response

tDCS responders ≠ non-responders

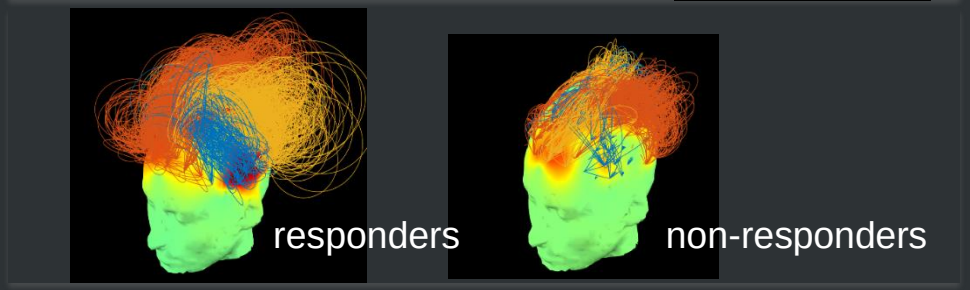
Brain metabolism (PET-scan)
≠ responders & non-responders

Grey matter atrophy (MRI)

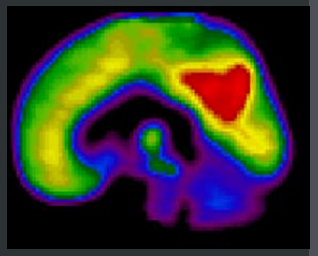
Grey matter atrophy
in responders
in non-responders

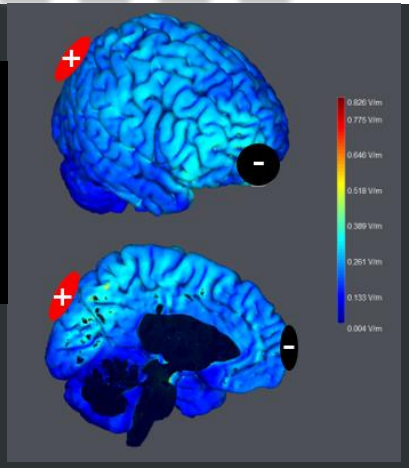


Brain connectivity (hd-EEG)
theta centrality



tDCS – Precuneus





Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Repeated stimulation of the posterior parietal cortex in patients in minimally conscious state: A sham-controlled randomized clinical trial

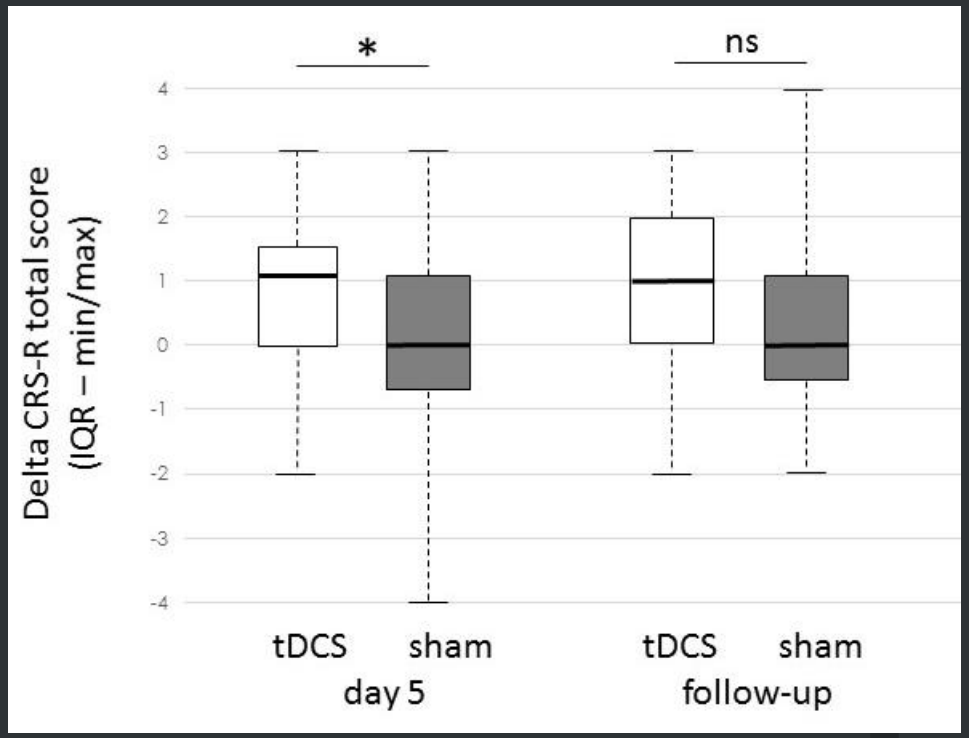
RCT crossover – 5 sessions

33 MCS >3 months post-insult (57±11y; 20 TBI)

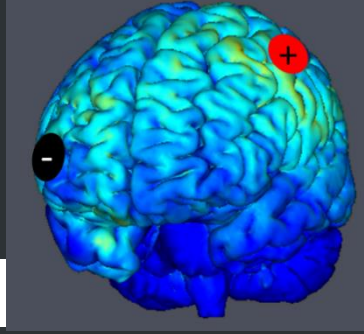
9 responders (27%)
Sub-acute > chronic

No effect at follow-up

Effect size : 0.31



tDCS – motor cortex



Motor cortex: common & efficient tDCS target

For patients with DOC?

→Immobilization, paresis…

→Improve behavioral responsiveness

→Covert consciousness

Group level (n=10): no significant improvement (p=0.55; ES=0.10)

Single-subject level: 2 responders

Single stimulation & small sample size

Martens et al., *Brain Injury* 2019

JFK COMA RECOVERY SCALE - REVISED ©2004

Record Form

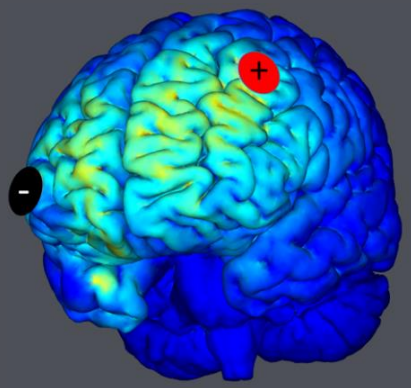
Patient: Date:								
AUDITORY FUNCTION SCALE								
4 - Consistent Movement to Command *								
3 - Reproducible Movement to Command *								
2 - Localization to Sound								
1 - Auditory Startle								
0 - None								
VISUAL FUNCTION SCALE								
5 - Object Recognition *								
4 - Object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

Denotes emergence from MCS †

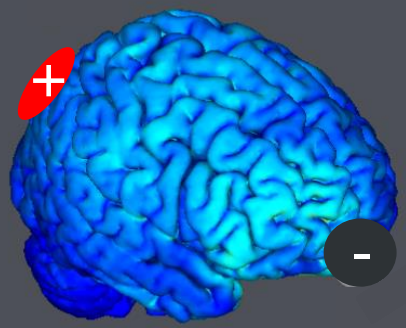
Denotes MCS *

Stimulating different brain areas

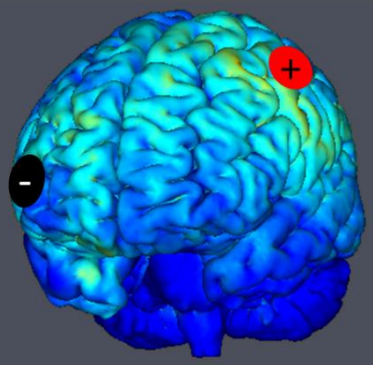
Prefrontal



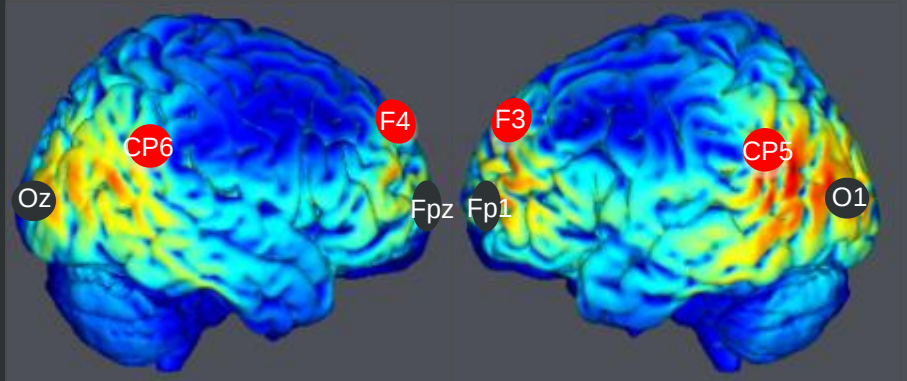
Precuneus



Motor



Multichannel frontoparietal

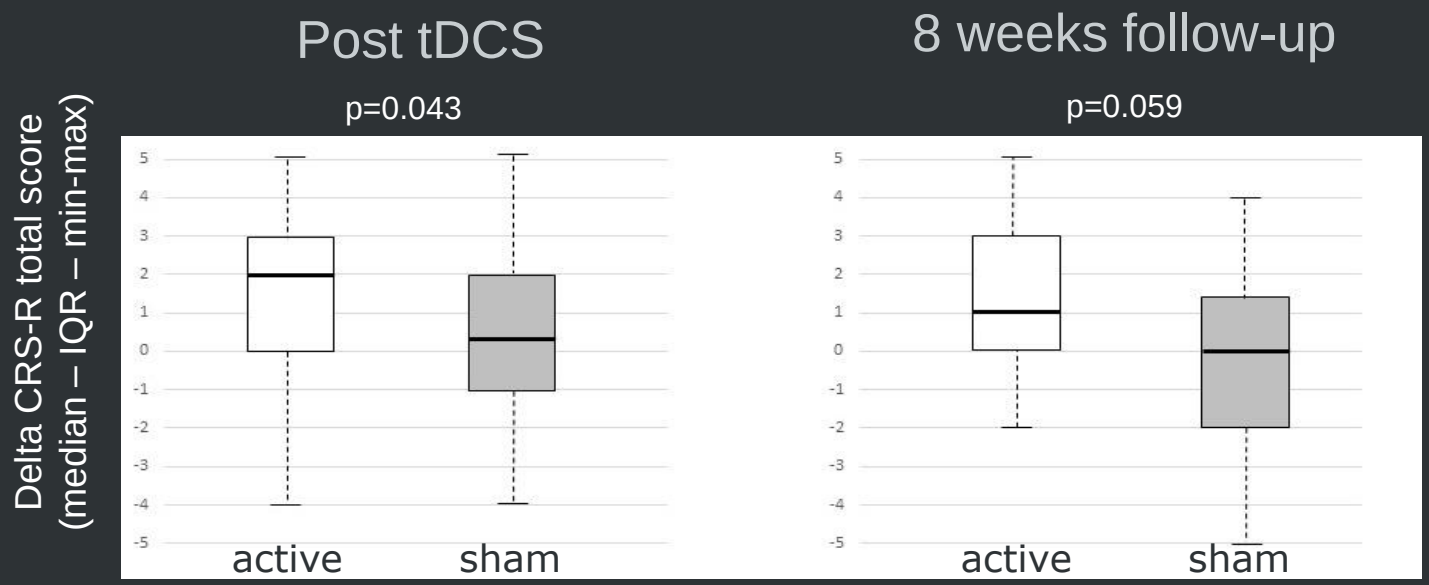


Group level: Prefrontal tDCS best area to target

Single-subject level: Patient's tailored montage

Clinical translation

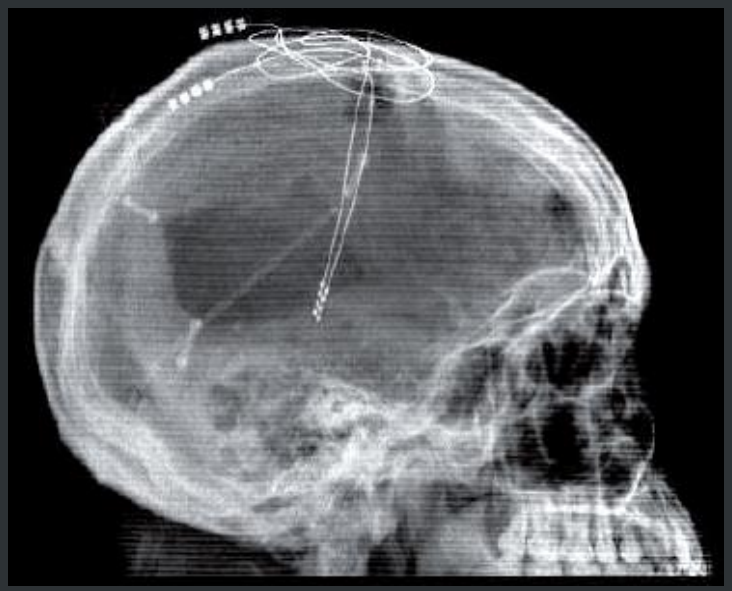
- **Feasibility of tDCS for daily use**
  - By relatives/caregivers (20 sessions)
  - 27 MCS patients – compliance: **93±14%**
  - No clinical effects
  - 22 MCS patients received ≥80% tDCS sessions
  - Significant effects & trend at 8-week follow-up – no AE

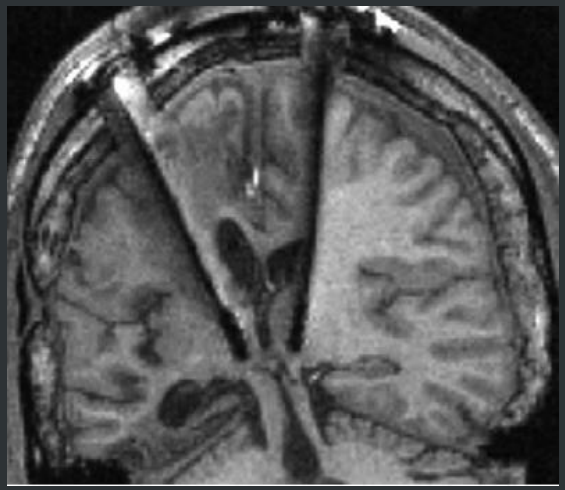


Martens et al, *Brain Stimulation* 2018

Deep Brain Stimulation

Intralaminar nuclei stimulation
induces “recovery” from
minimally responsive state

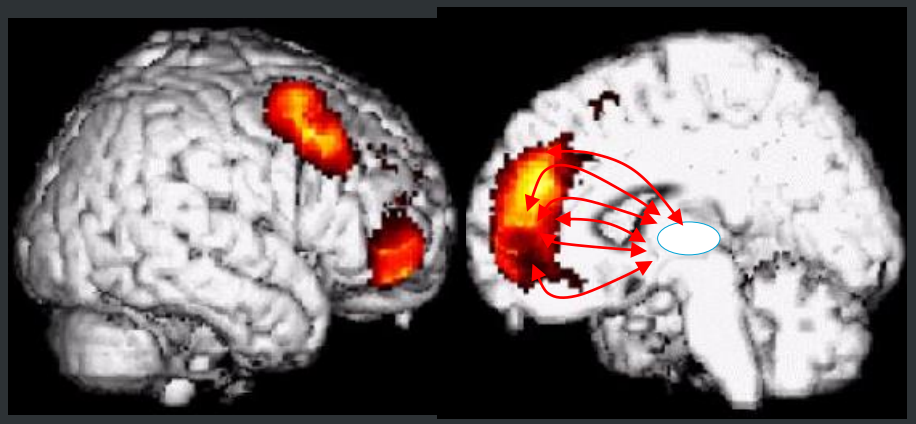




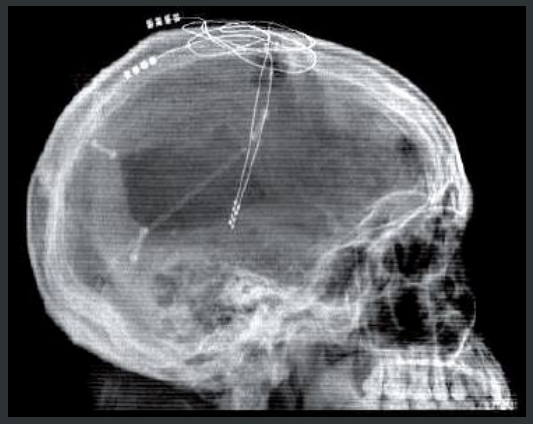
Schiff et al, Nature, 2007

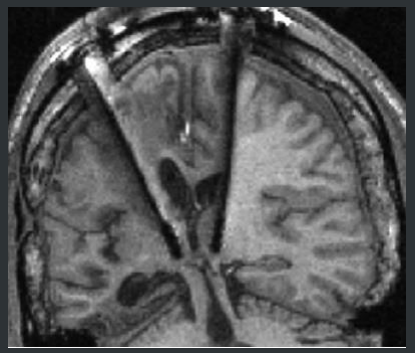
Deep Brain Stimulation

Intralaminar nuclei “reconnections” in spontaneous recovery from “vegetative” unresponsive state



Laureys et al, *Lancet* 2000





Schiff et al, *Nature* 2007

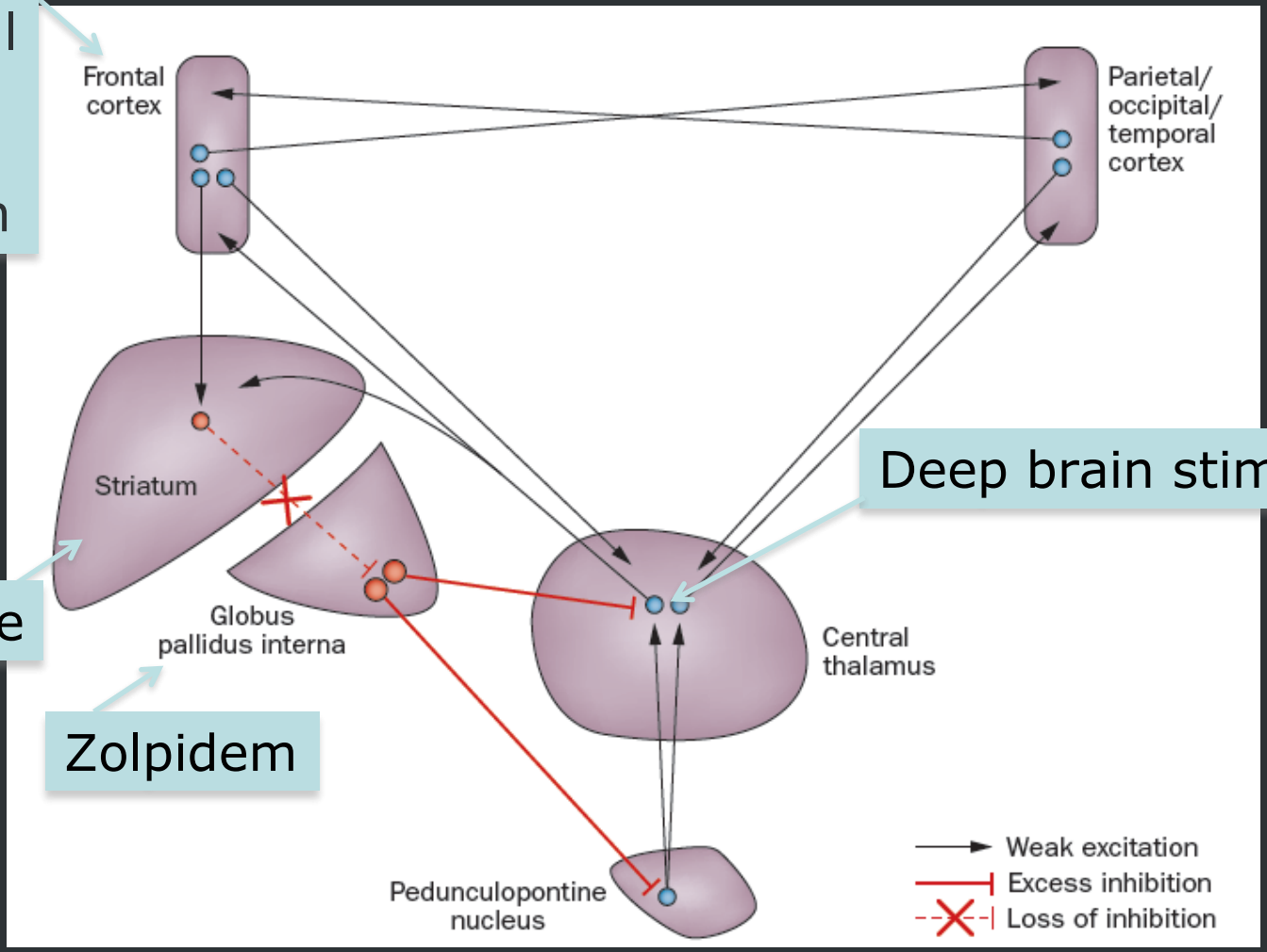
MCS ➔ emerged – prolonged effects

sustained attention, intelligible words, functional objects use

No RCT & side-effects

Combined treatment: potential solution?

transcranial Direct Current Stimulation



Deep brain stimulation

Amantadine

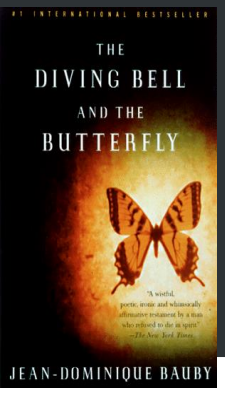
Zolpidem

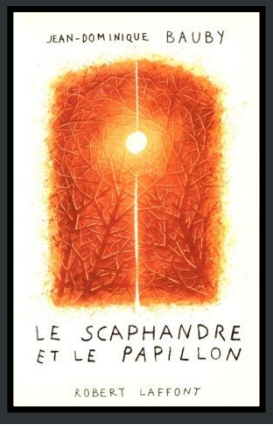
Giacino, Fins, Laureys, Schiff, Nature Rev Neurol 2014

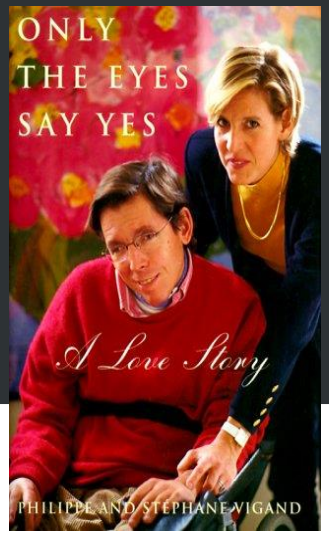
Conclusion

- Potential interest of pharmacological…
  - Zolpidem
  - Amantadine
- and non pharmacological treatments
  - tDCS
  - DBS

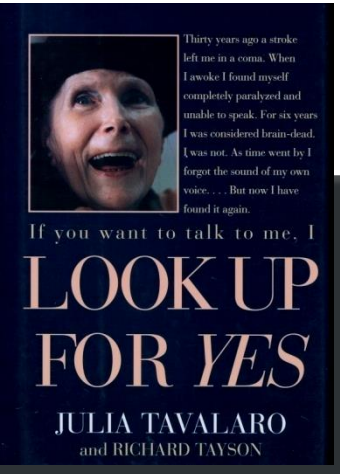
- More validation studies are needed
- Assessment of the daily use in clinical setting







Locked-In Syndrome



ALIS
Association du Locked-in Syndrome

LIÈGE université
GIGA institute

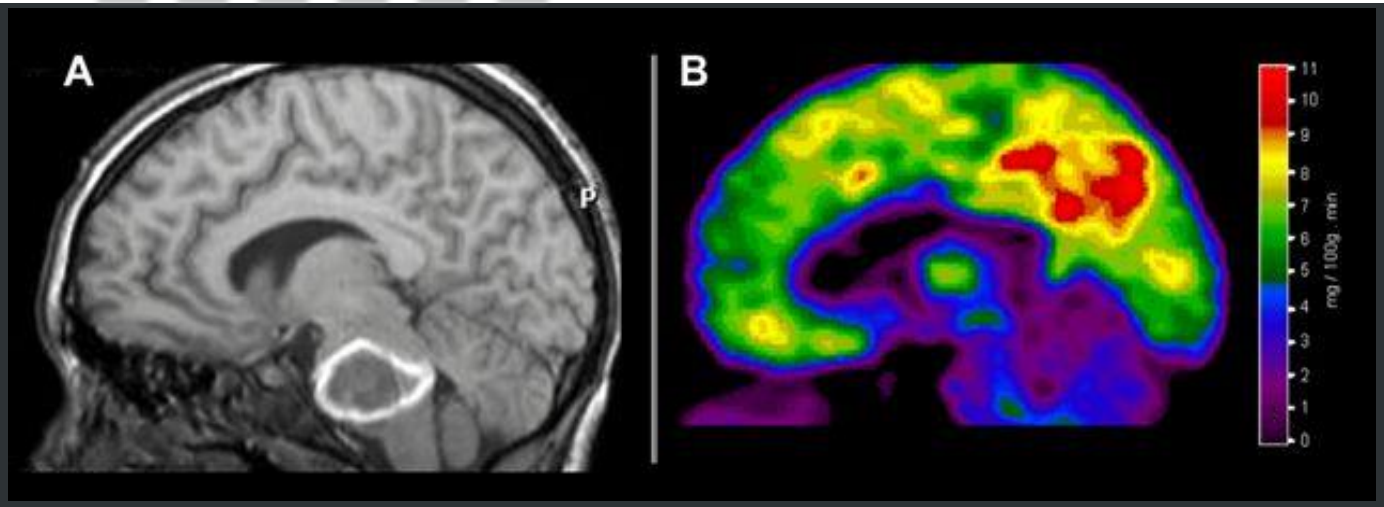
LIS - Definition

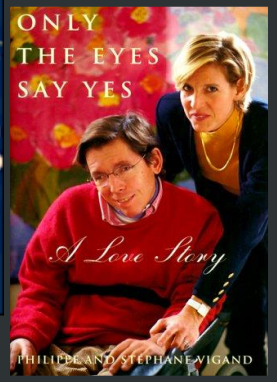
Bauer et al. (1989) :

- Classical LIS
  - Complete immobility except for vertical eye movements and blinks.
- Incomplete LIS
  - Some preserved voluntary motricity (head, superior or inferior limbs).
- Complete LIS
  - Total immobility including ocular motricity

Laureys, Pellas, Van Eeckhout, Ghorbel, Schnakers, Perrin et al., Prog Brain Res, 2005

LIS - Diagnosis

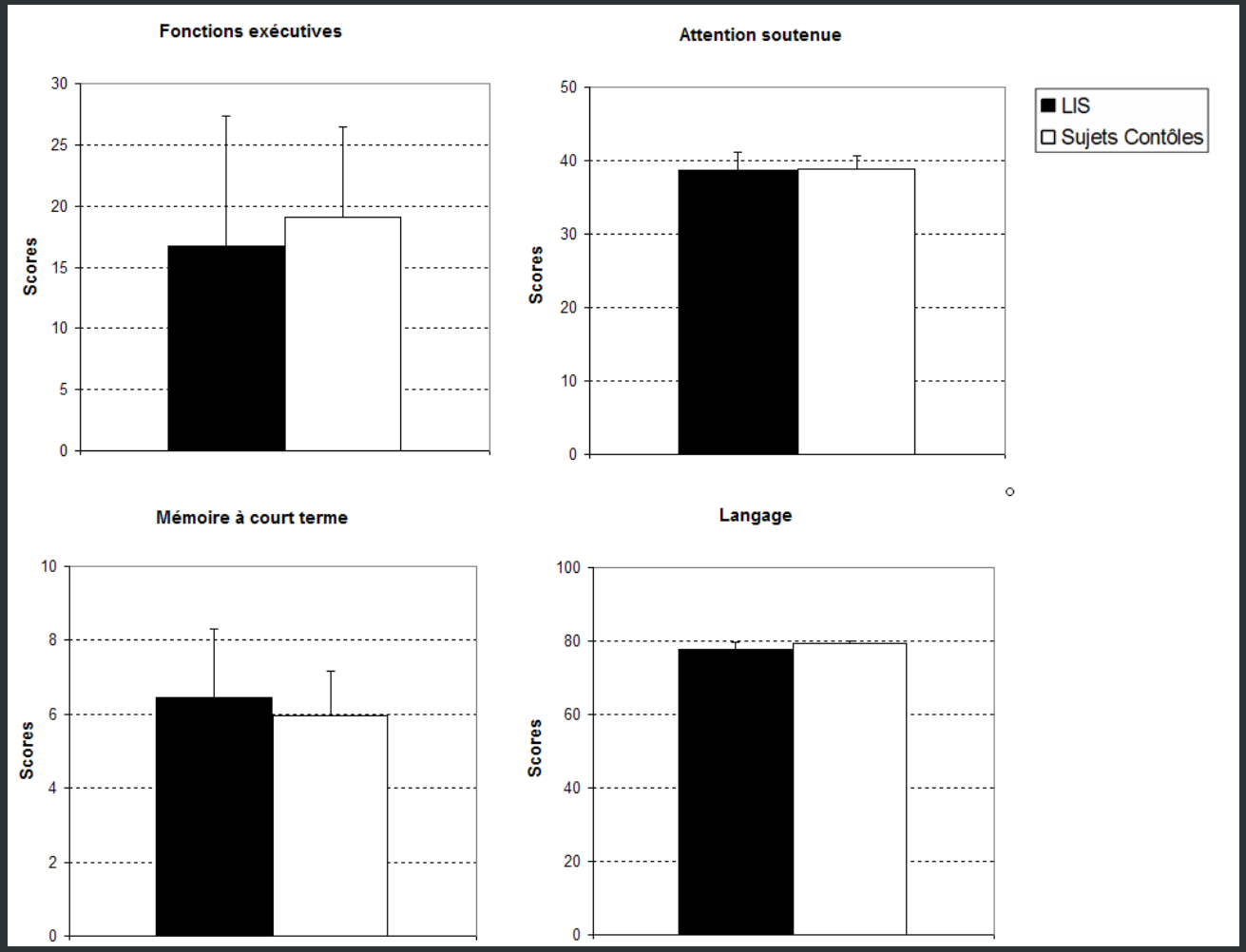




Person who gave the LIS diagnosis	Number of patients (n=84) (%)
Medical doctor	52 (62%)
Family member	28 (33%)
Other	4 (5%)

Questionnaire ALIS 2007 ; Bruno, et al., 2010

LIS – Cognitive functions



Schnakers, Majerus, Goldman, Boly, Van Eeckhout, Gay et al, J Neurol, 2008

Ethical issues

Attitudes towards end-of-life issues in disorders of consciousness: a European survey

A. Demertzi · D. Ledoux · M.-A. Bruno · A. Vanhaudenhuyse · O. Gosseries · A. Soddu · C. Schnakers · G. Moonen · S. Laureys

2,475 medical professionals

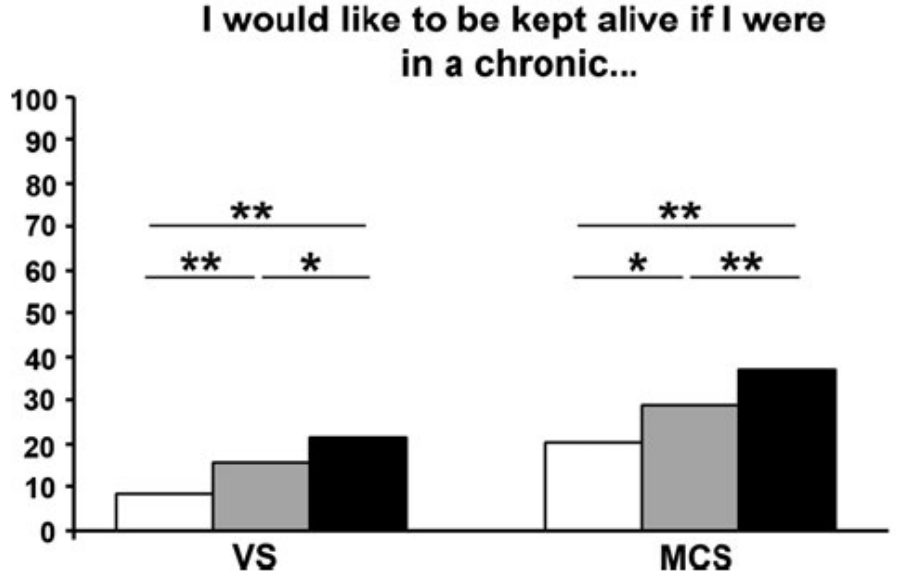


Fig. 2 End-of-life attitudes towards the vegetative state (*VS*) and minimally conscious states (*MCS*) depending on geographic region. Bars represent % agreement (*white*: Northern, *grey*: Central, *black*: Southern Europe; $*P < 0.05$, $**P < 0.001$)

Demertzi et al, *J Neurology* 2011

Ethical issues: what about LIS?

Open Access Research

BMJ open

A survey on self-assessed well-being in a cohort of chronic locked-in syndrome patients: happy majority, miserable minority

Marie-Aurélie Bruno,[1] Jan L Bernheim,[2] Didier Ledoux,[1] Frédéric Pellas,[3] Athena Demertzi,[1] Steven Laureys[1]

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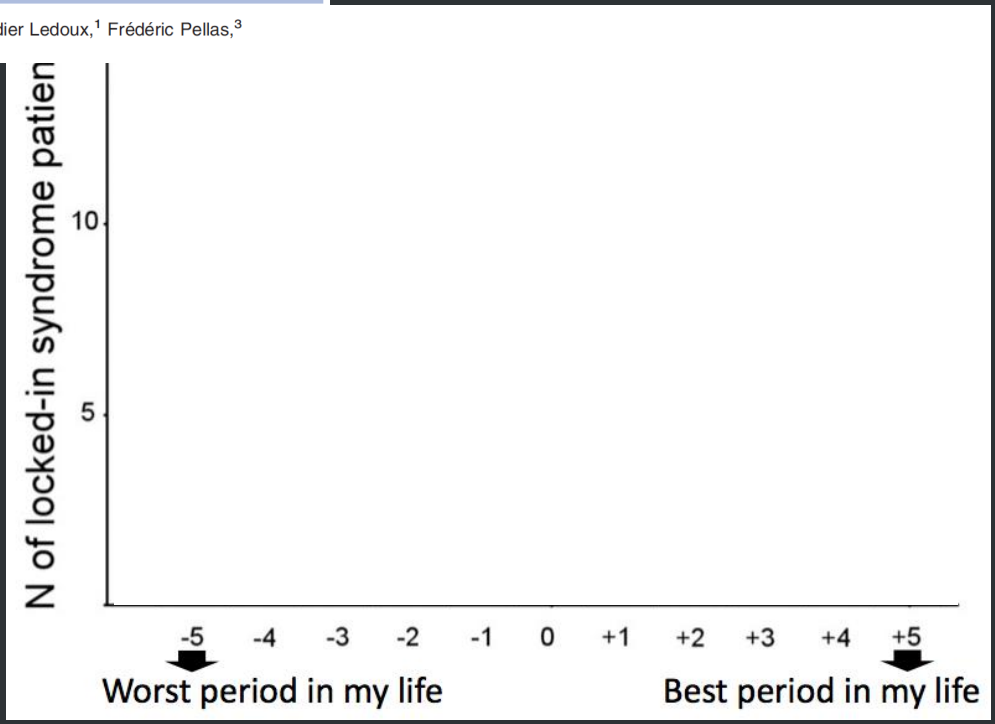

Bruno et al, *BMJ Open*, 2011

Ethical issues

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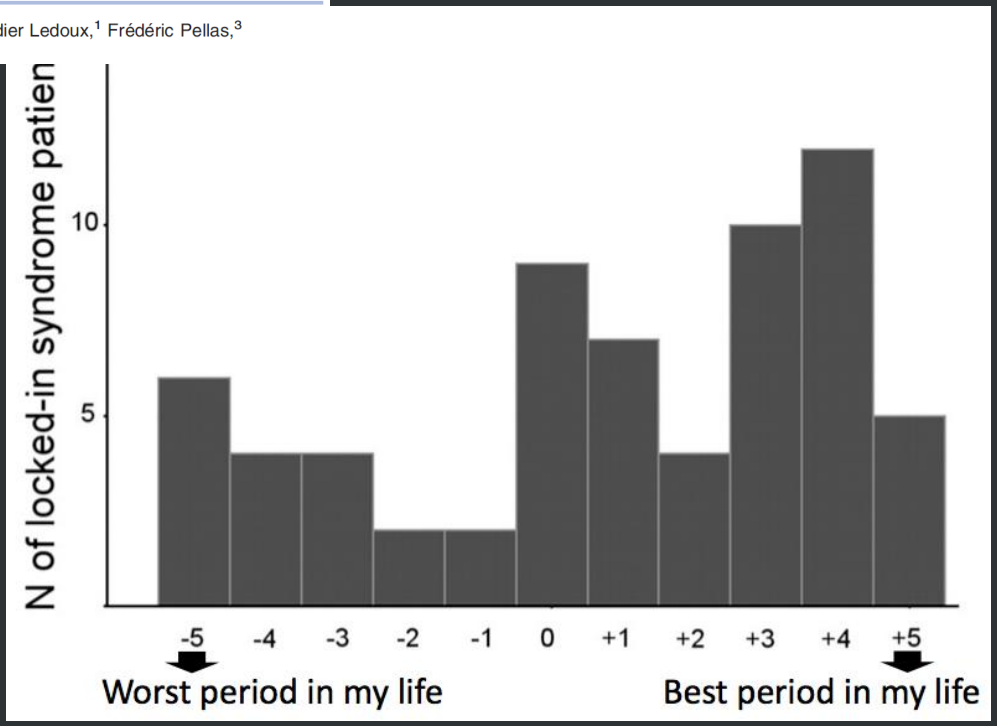

Bruno et al, *BMJ Open*, 2011

Conclusion

- LIS # DOC in terms of brain lesions and level of consciousness
- Preserved cognitive abilities
- Happy majority?
  - Pain
  - Communication
  - Don’t forget the minority!

Near-death experiences

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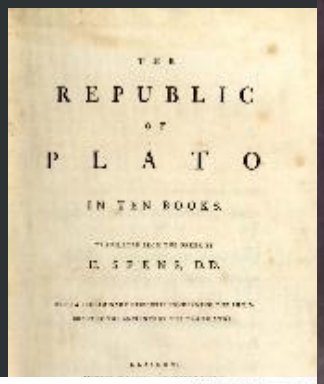
Near-death experiences: definition

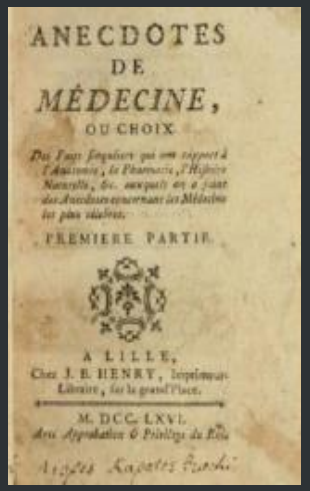
- **Near-Death Experience (NDE):** "*Profound psychological events with transcendental & mystical elements typically occurring to individuals close to death or in situations of intense physical or emotional danger*".

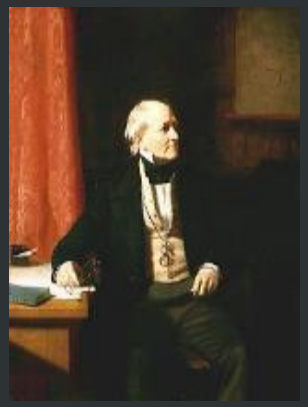
- a set of mental events with highly emotional, self-related, mystical & spiritual aspects
- recurrent "features" (e.g., feeling of peacefulness, out-of-body experiences, …)
- classically occurring in an altered state of consciousness

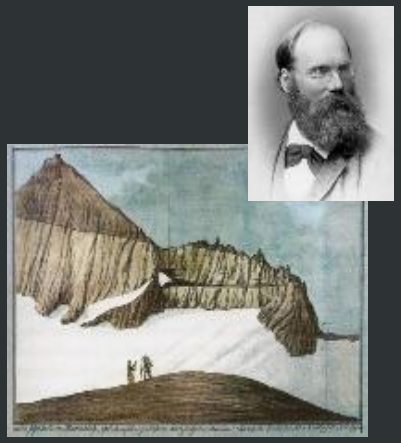
Greyson, 2000

Near-death experiences: historical background









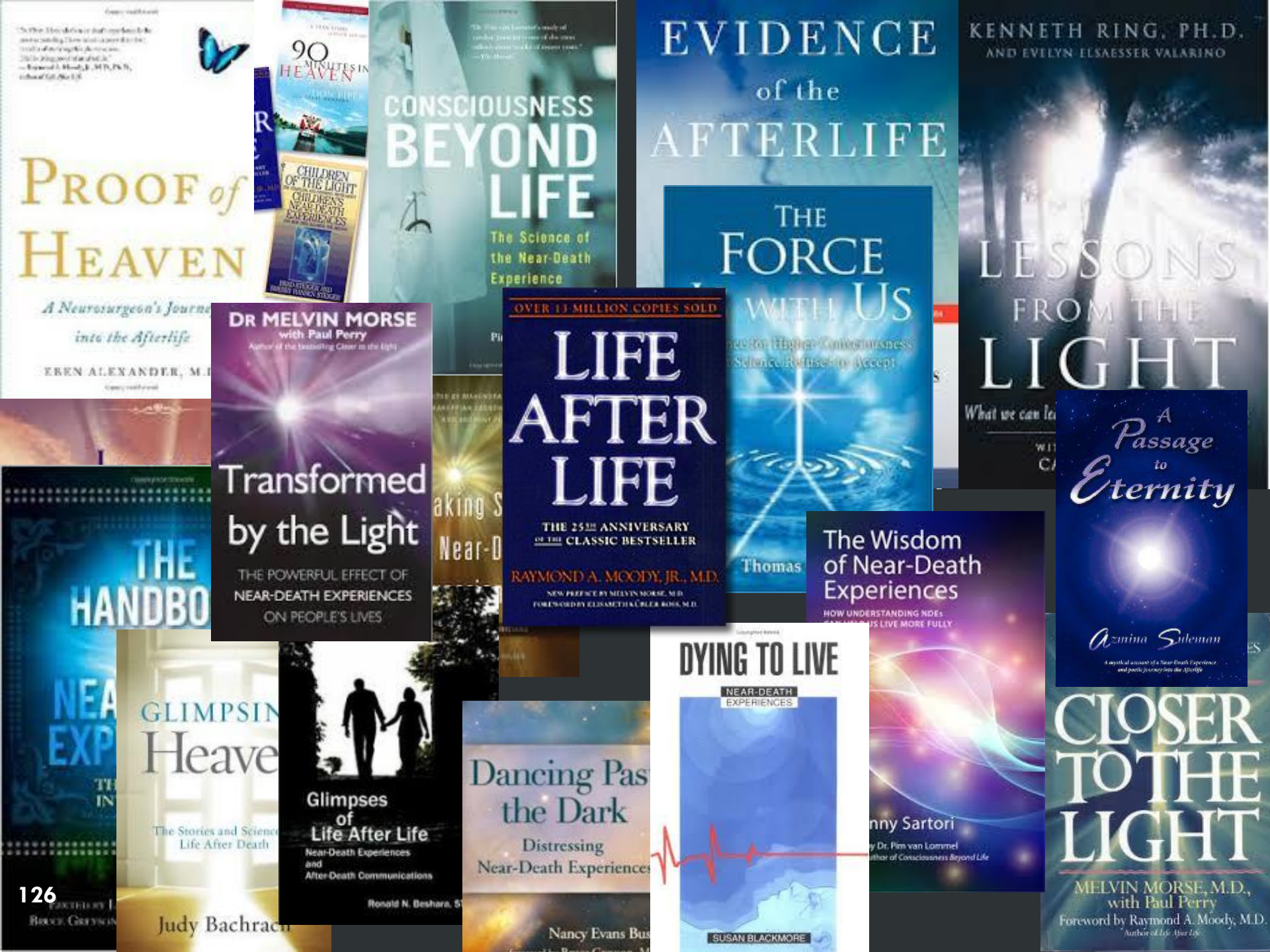
Platon's Republic
315 B.C.

Jerome Hieronymus Bosch
1516

Pierre Jean du Monchaux
1740

Amiral Beaufort
1795

Albert Heim
1892


PROOF of HEAVEN
A Neurosurgeon's Journey into the Afterlife
EBEN ALEXANDER, M.D.
90 MINUTES IN HEAVEN
CHILDREN OF THE LIGHT
CHILDREN'S NEAR-DEATH EXPERIENCES
CONSCIOUSNESS BEYOND LIFE
The Science of the Near-Death Experience
EVIDENCE of the AFTERLIFE
THE FORCE WITH US
KENNETH RING, PH.D.
AND EVELYN ELSAESSER VALARINO
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SUSAN BLACKMORE
nny Sartori
CLOSER TO THE LIGHT
MELVIN MORSE, M.D.,
with Paul Perry
Foreword by Raymond A. Moody, M.D.

Near-death experiences

- **Main explanatory models**

- *Spiritual theories* ▸ ▸"dualistic" approach toward the mind–brain relationship
- *Neurobiological theories* ▸ ▸ brain mechanisms might underlie NDEs
- *Psychological theories* ▸ ▸ psychological reaction to impending death

Near-death experiences: Identification

Greyson NDE scale: Scores ≥7 = NDE experiencer

Cognitive

(1) Did time seem to speed up or slow down?
- 0 = No
- 1 = Time seemed to go faster or slower than usual
- 2 = Everything seemed to be happening at once; or time stopped or lost all meaning

(2) Were your thoughts speeded up?
- 0 = No
- 1 = Faster than usual
- 2 = Incredibly fast

(3) Did scenes from your past come back to you?
- 0 = No
- 1 = I remembered many past events
- 2 = My past flashed before me, out of my control

(4) Did you suddenly seem to understand everything?
- 0 = No
- 1 = Everything about myself or others
- 2 = Everything about the universe

Affective

(5) Did you have a feeling of peace or pleasantness?
- 0 = No
- 1 = Relief or calmness
- 2 = Incredible peace or pleasantness

(6) Did you have a feeling of joy?
- 0 = No
- 1 = Happiness
- 2 = Incredible joy

(7) Did you feel a sense of harmony or unity with the universe?
- 0 = No
- 1 = I felt no longer in conflict with nature
- 2 = I felt united or one with the world

(8) Did you see, or feel surrounded by, a brilliant light?
- 0 = No
- 1 = An unusually bright light
- 2 = A light clearly of mystical or other-worldly origin

Greyson, 1983

Near-death experiences: Identification

Greyson NDE scale: Scores ≥7 = NDE experiencer

Paranormal

(9) Were your senses more vivid than usual?
0 = No
1 = More vivid than usual
2 = Incredibly more vivid

(10) Did you seem to be aware of things going on elsewhere, as if by ESP?
0 = No
1 = Yes, but the facts have not been checked out
2 = Yes, and the facts have been checked out

(11) Did scenes from the future come to you?
0 = No
1 = Scenes from my personal future
2 = Scenes from the world's future

(12) Did you feel separated from your body?
0 = No
1 = I lost awareness of my body
2 = I clearly left my body and existed outside i

Transcendental

(13) Did you seem to enter some other, unearthly world?
0 = No
1 = Some unfamiliar and strange place
2 = A clearly mystical or unearthly realm

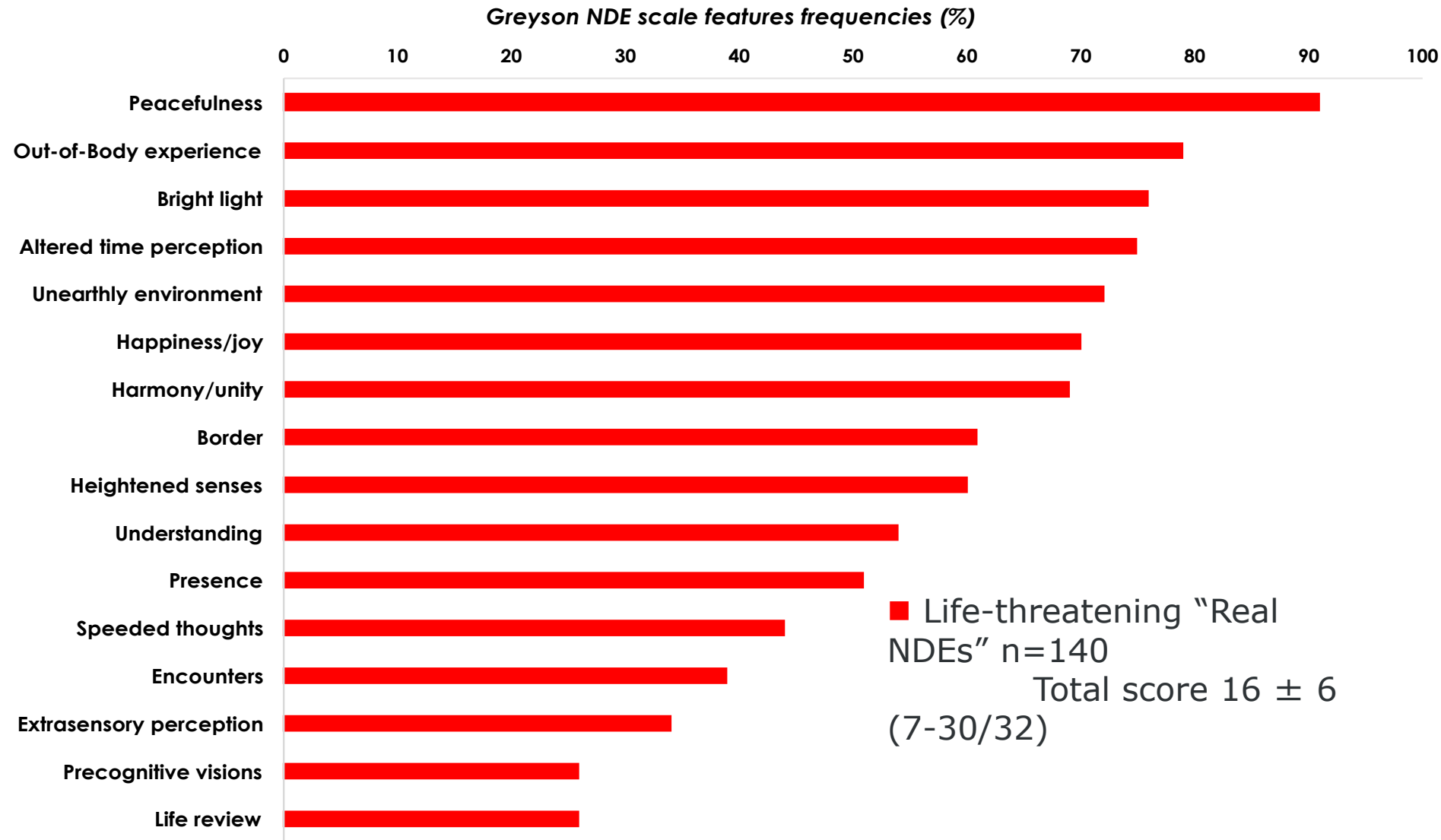
(14) Did you seem to encounter a mystical being or presence, or hear an unidentifiable voice?
0 = No
1 = I heard a voice I could not identify
2 = I encountered a definite being, or a voice clearly of mystical or unearthly origin

(15) Did you see deceased or religious spirits?
0 = No
1 = I sensed their presence
2 = I actually saw them

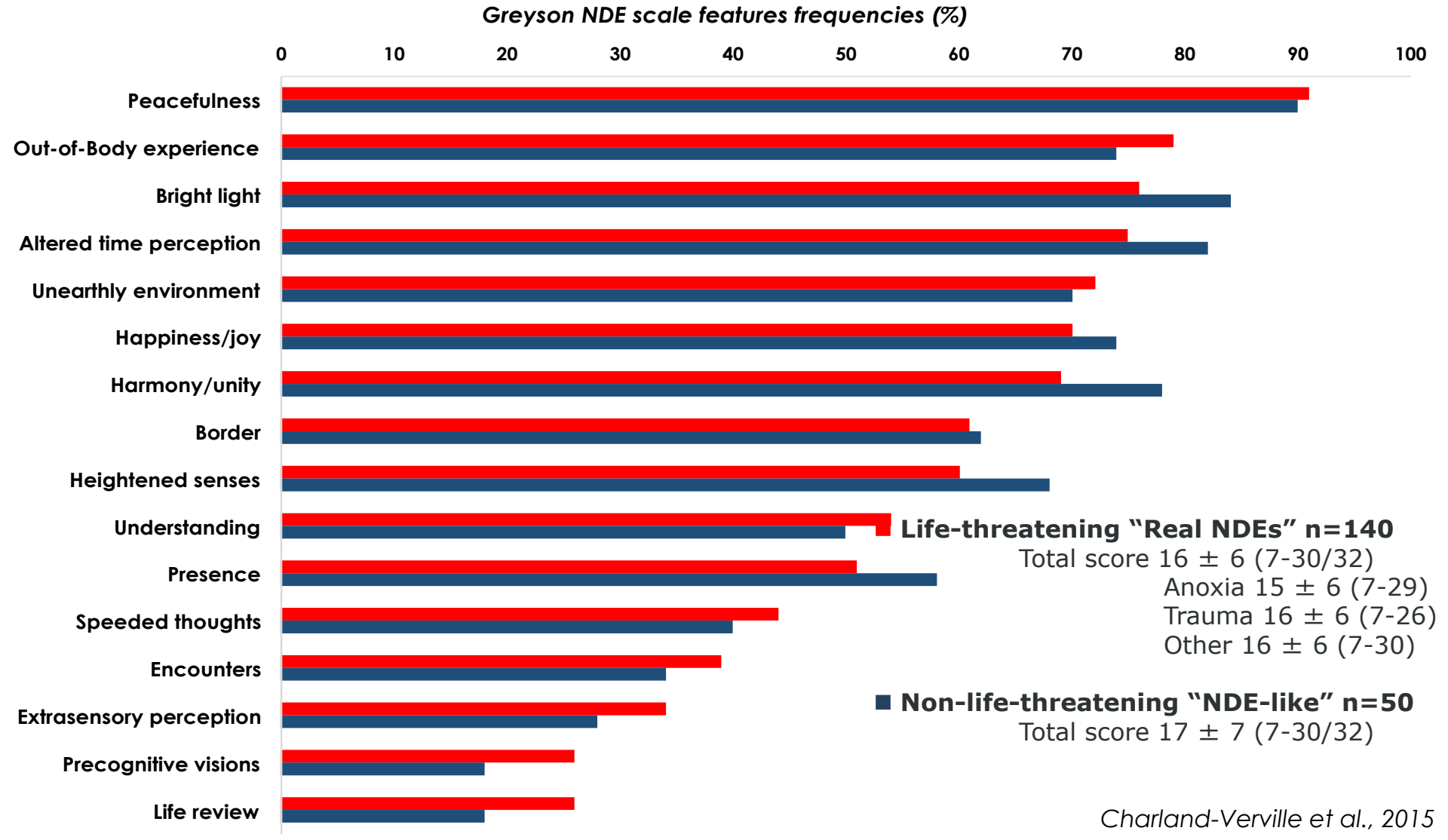
(16) Did you come to a border or point of no return?
0 = No
1 = I came to a definite conscious decision to return to life
2 = I came to a barrier that I was not permitted to cross; or was sent back against my will

Greyson, 1983

Near-death experiences: features



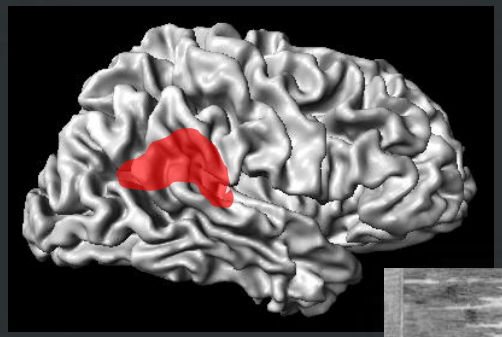
Near-death experiences: features

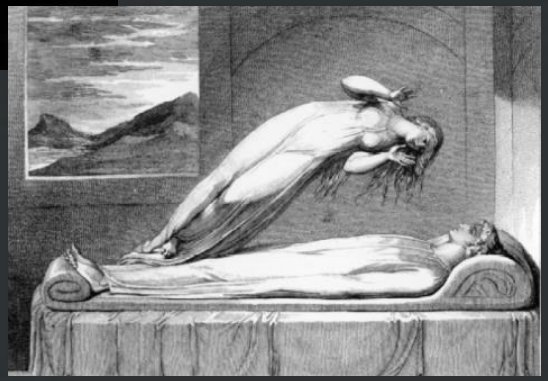


Charland-Verville et al., 2015

Near-death experiences: neural correlates

Right temporo-parietal stimulation





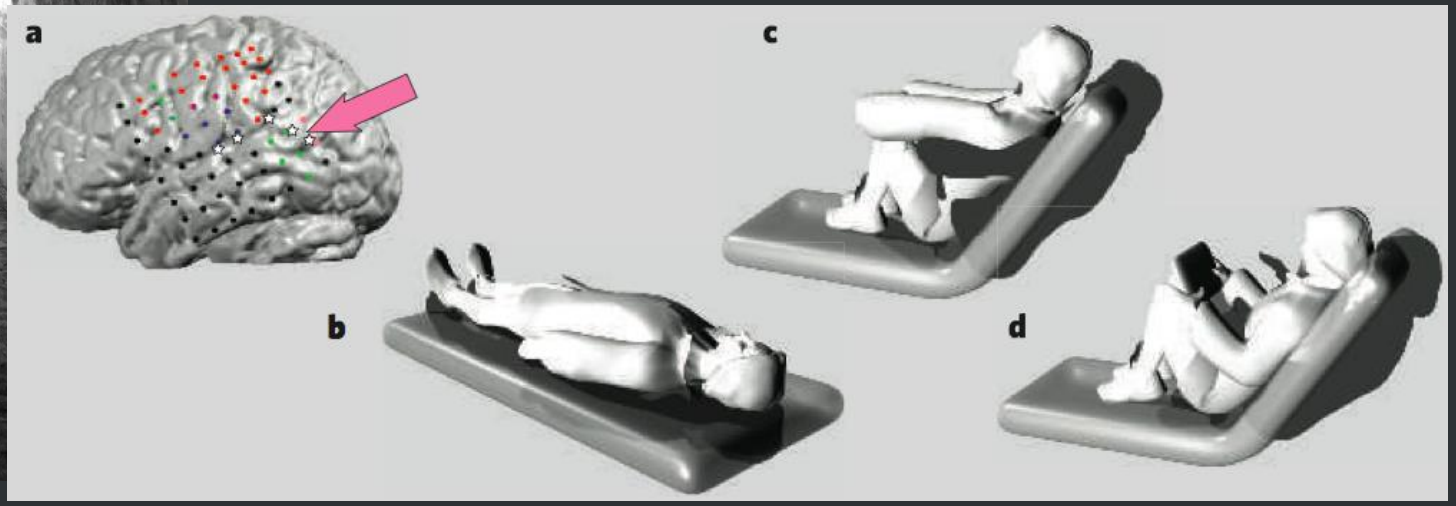
Hypercarbia (Meduna, 1950)

- Bright light
- Recollection of memories
- OBEs
- Mystical insights

Blanke et al Stimulating illusory own-body perceptions. *Nature*, 2002
De Ridder et al Visualizing out-of-body experience in the brain. *N Engl J Med*, 2007

Near-death experiences: neural correlates

Presence ~ left temporoparietal



Arzy, S., *et al. (2006) Nature 443:287*
Induction of an illusory shadow person.

Near-death experiences: laboratory setting

Aim: Reproduce NDEs in controlled laboratory setting

Hypothesis: Induced hypoxic loss of consciousness produces NDE like memories (Lempert, 1994)

Charland-Verville et al., (in prep)

Near-death experiences: laboratory setting

33 heathy volunteers aged 25 ± 5 y (range 20-46); 19 women (58%)

Induction of vasovagal syncope:
45 s hyperventilation while squatting, fast rising, 10 s Valsalva maneuver

Simultaneous high-density video-EEG recordings
Greyson NDE scale & semi-structured recorded audio interviews

Induced loss of consciousness : 26/33 (79%)
Duration of loss of consciousness : 24 ± 7 s (range 14-45)

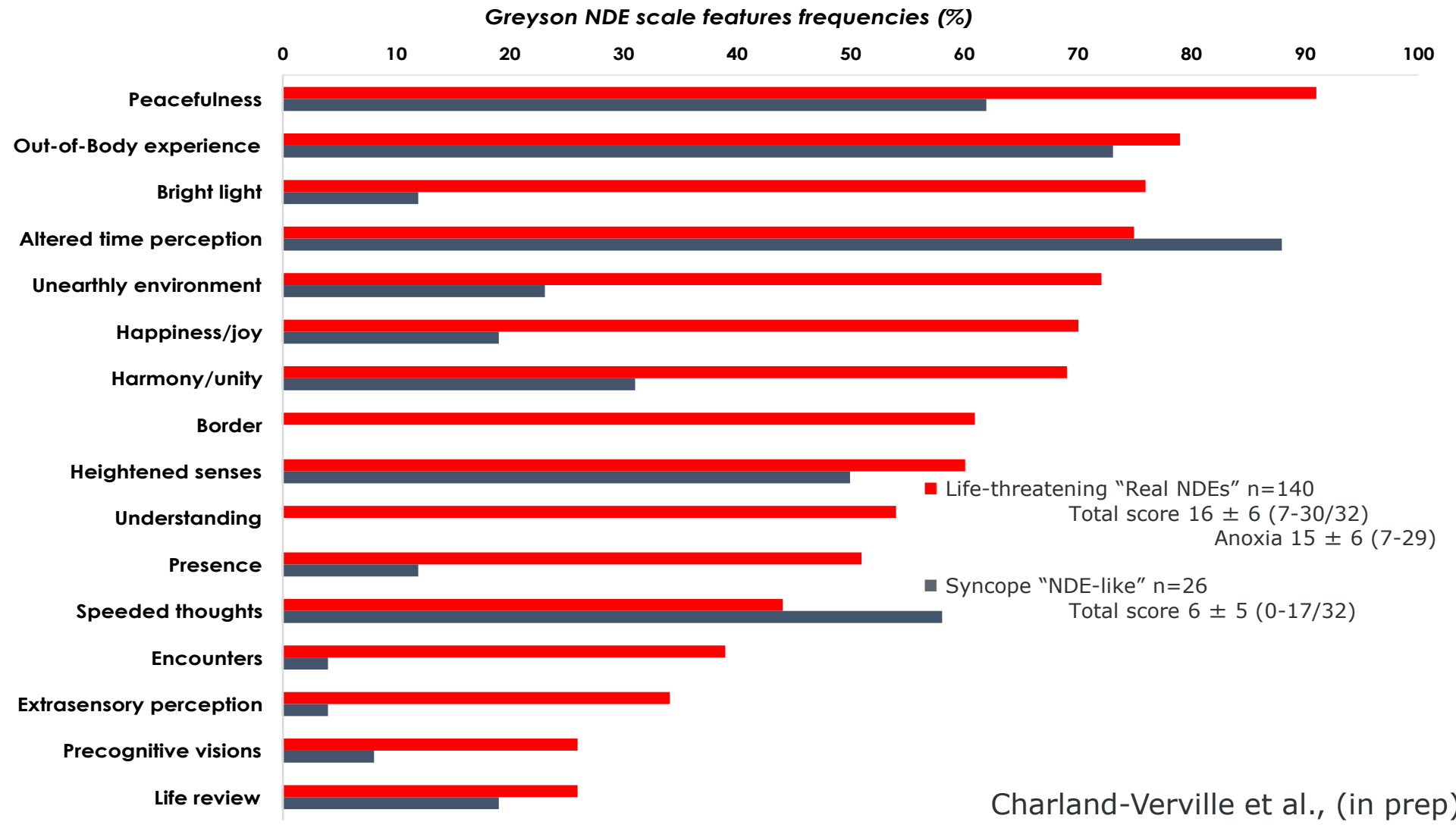
NDE total scores: 6 ± 4 (range 0-17)

Identified NDErs: 9/26 (35%)

1 subject excluded because of bad quality EEG recording

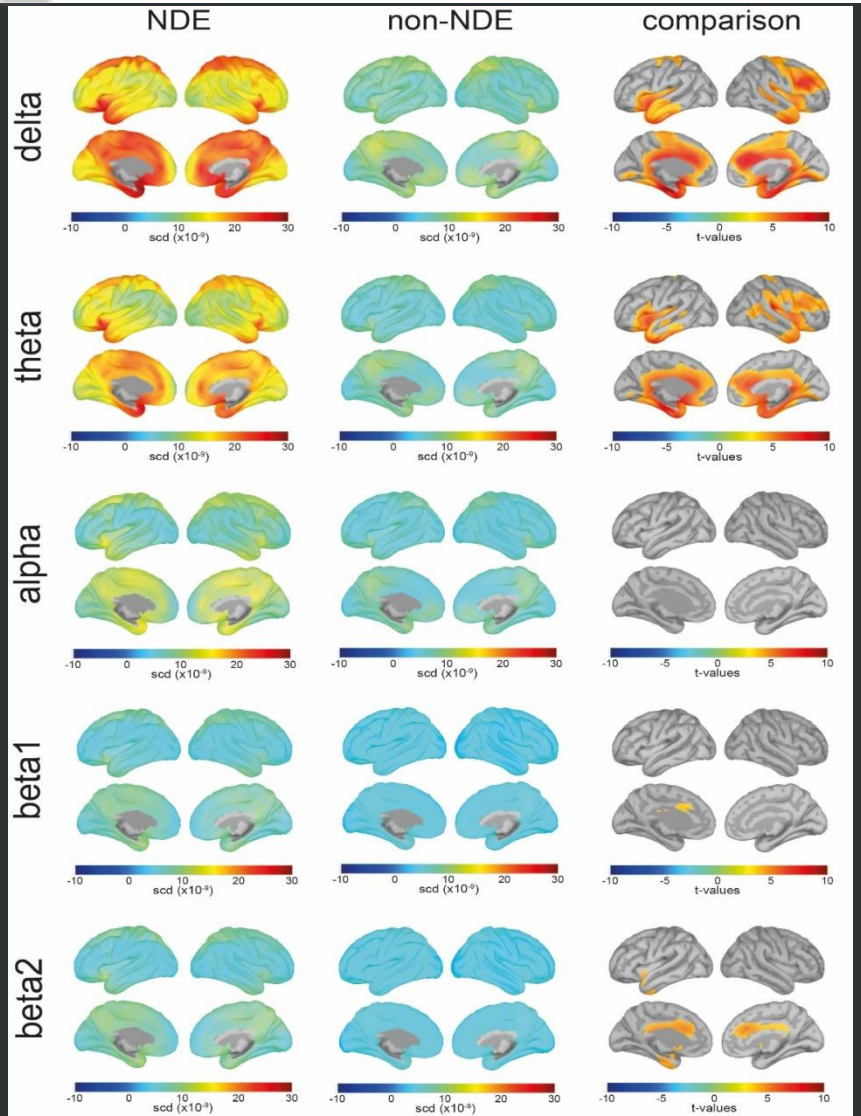
Charland-Verville et al., (in prep)

Near-death experiences: laboratory setting



Charland-Verville et al., (in prep)

Near-death experiences: laboratory setting



Charland-Verville et al., (in prep)

That's it folks!

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THANK YOU!

Geraldine.martens@uliege.be

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