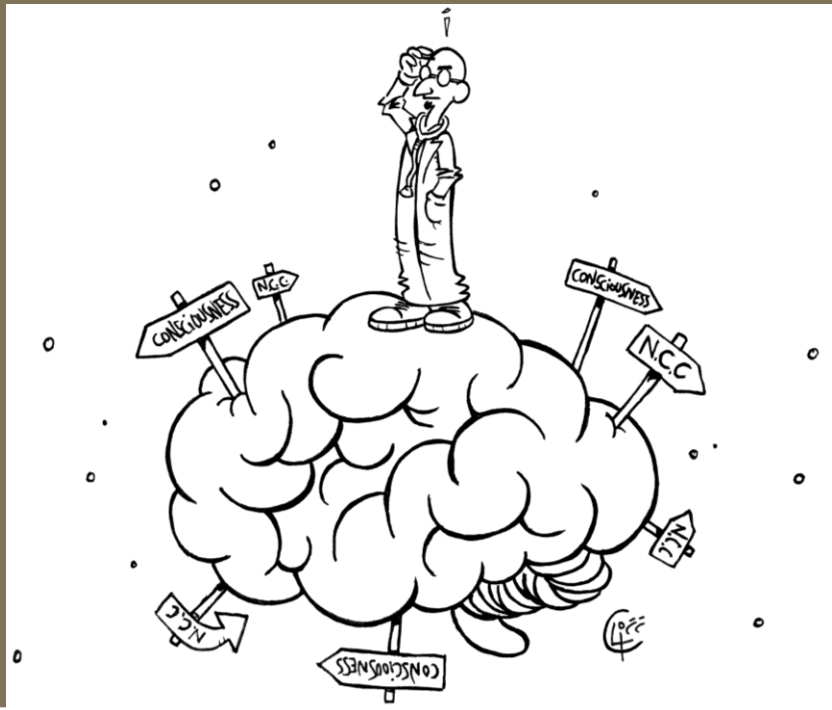
Quelle conscience dans le coma et les états de conscience altérée?

Aurore Thibaut
Kinésithérapeute, PhD Candidate

Coma Science Group
Cyclotron Research Centre
Université de Liège
CHU, Sart-Tilman

www.comascience.org

Conscience



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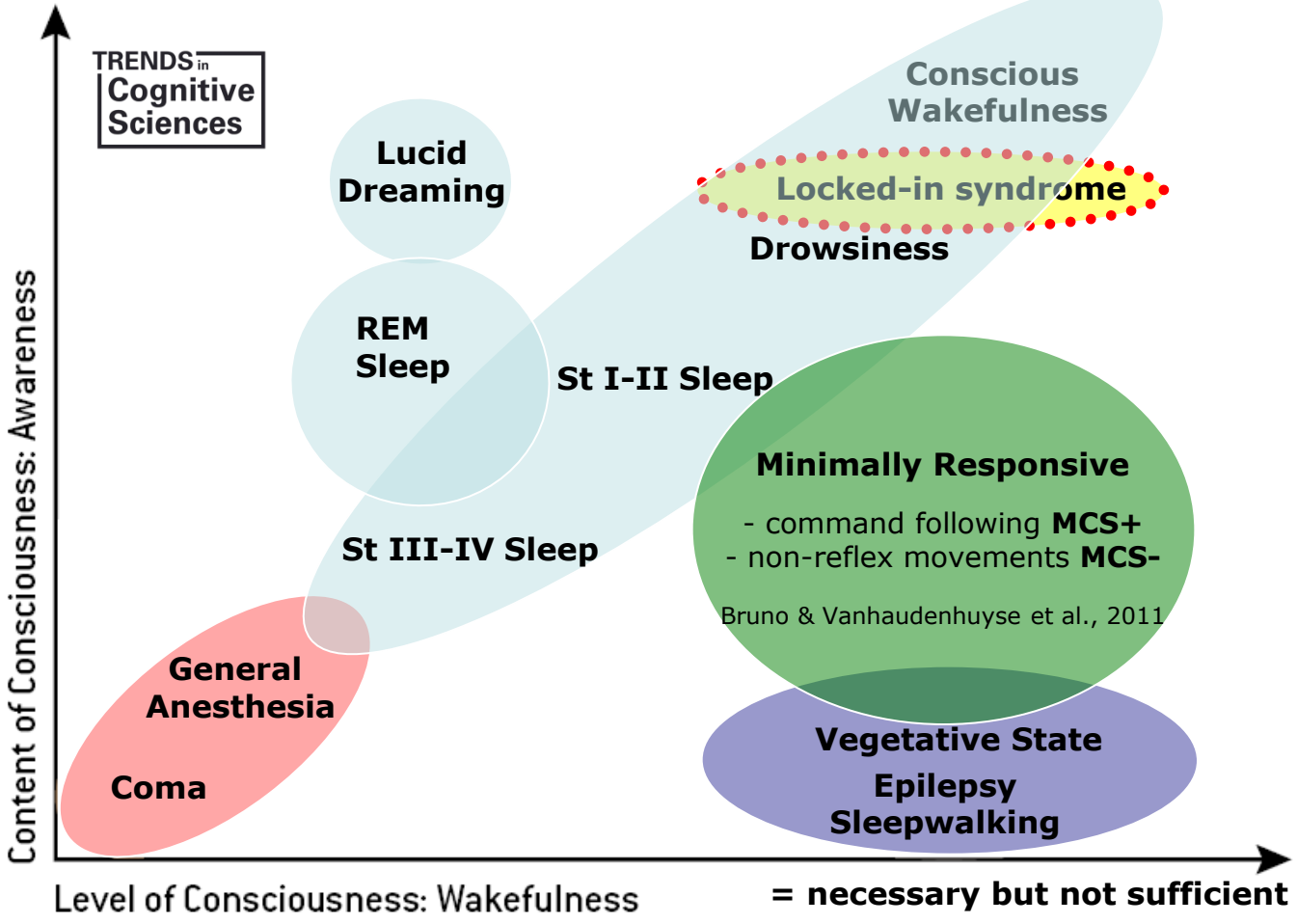
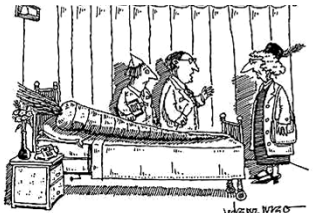
Conscience: 2 composantes



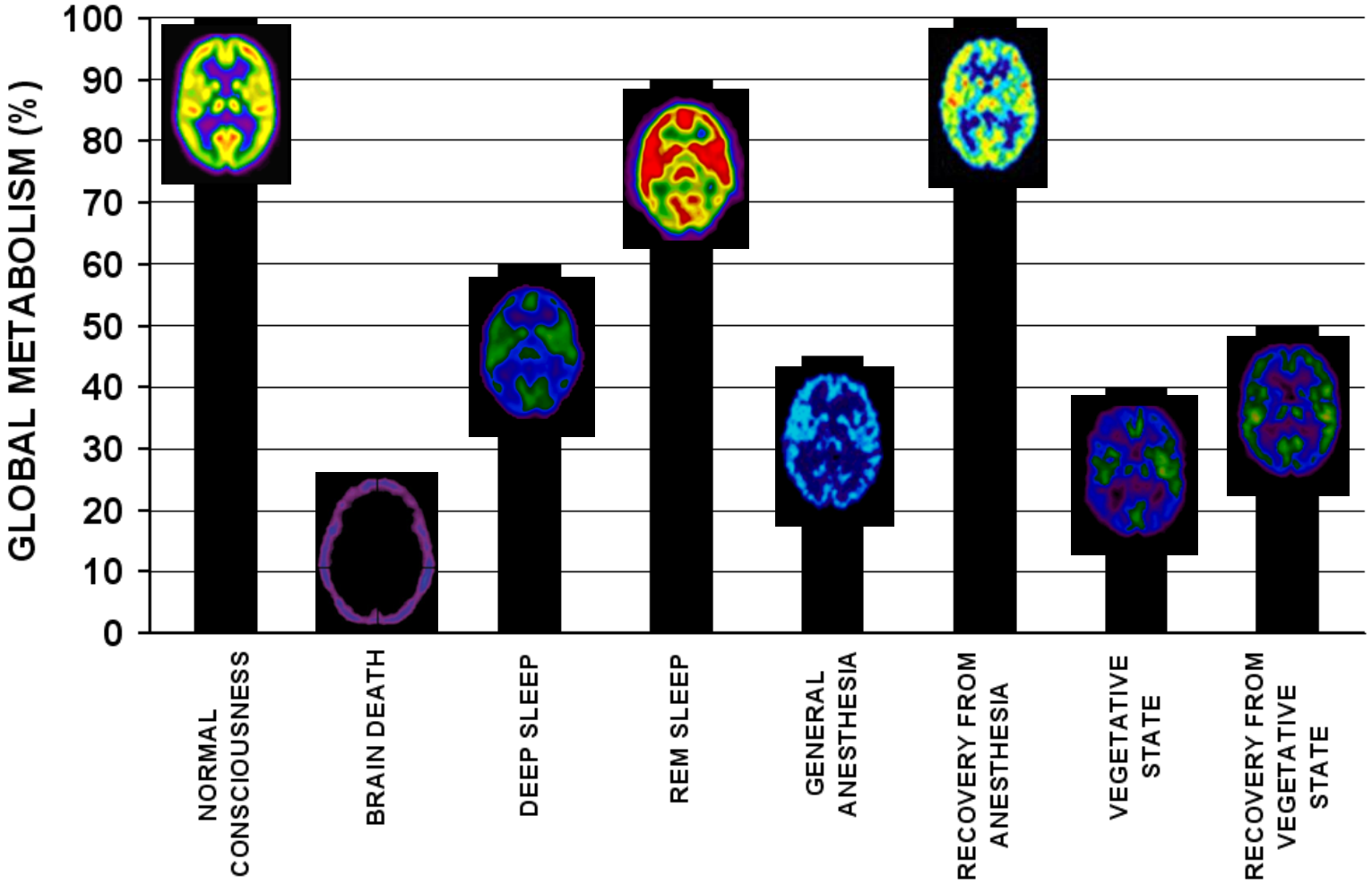
Unresponsive Wakefulness Syndrome
Laureys et al., 2010



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

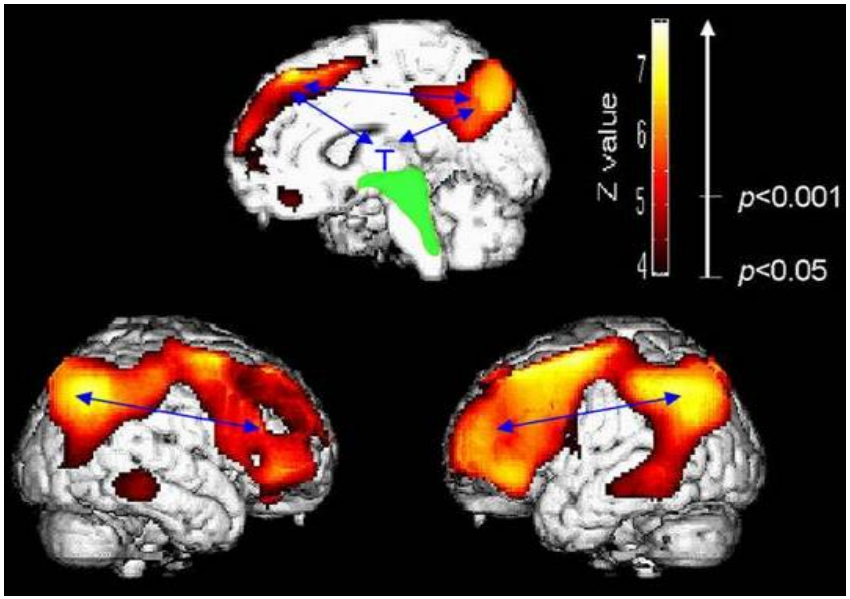
Laureys, *Trends in Cognitive Sciences*, 2005

Conscience ≠ cerveau entier

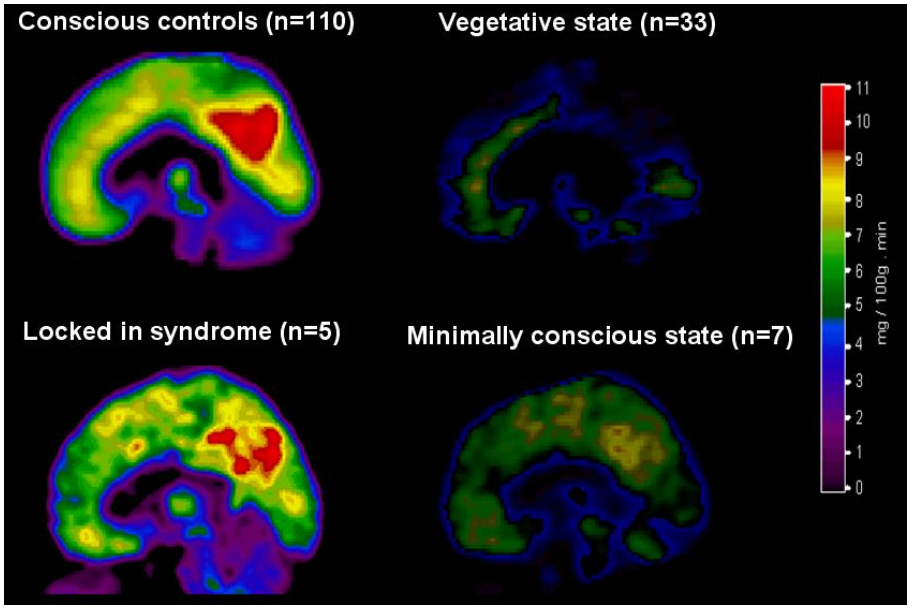


Laureys *et al, Lancet Neurology,* 2004

Consciousness ≈ frontoparietal

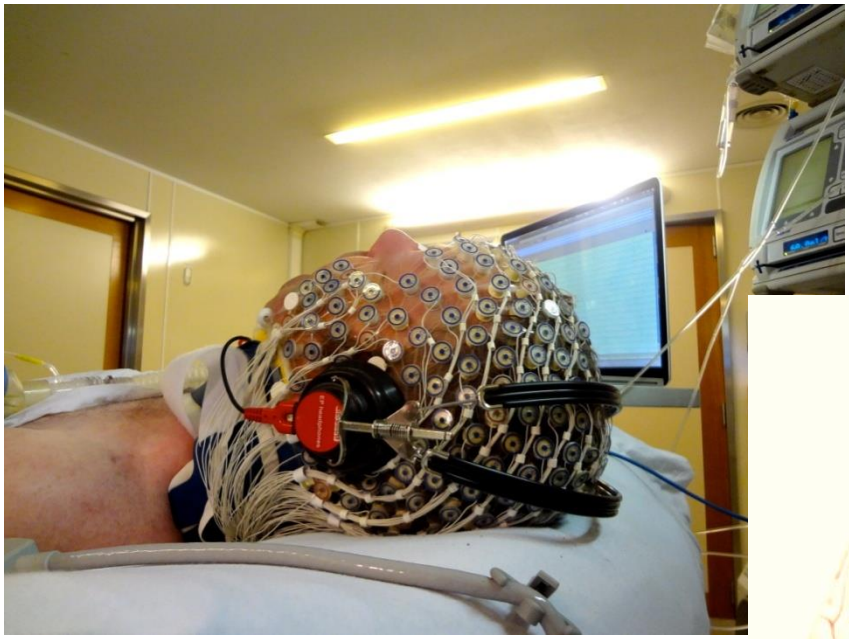


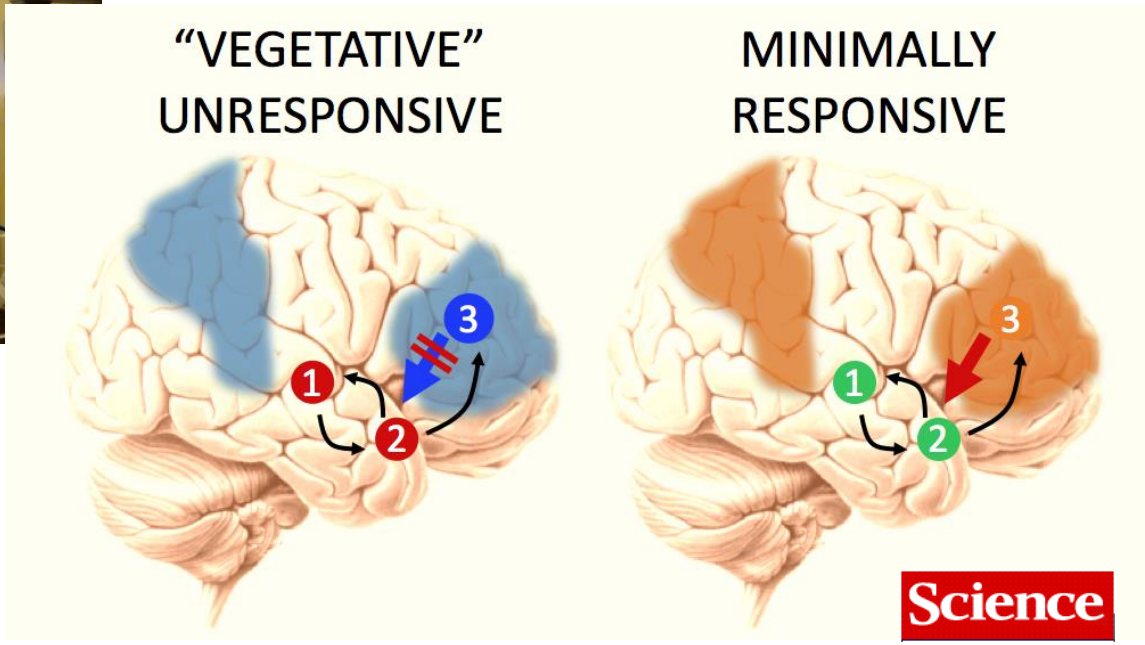
Laureys et al, Neuroimage 1999



Laureys et al, Lancet Neurology, 2004

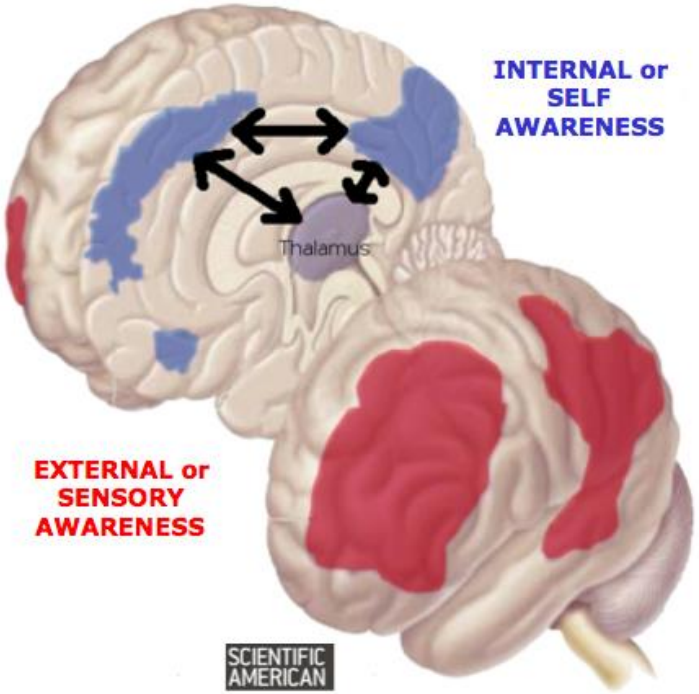
Conscience ≈ connectivité





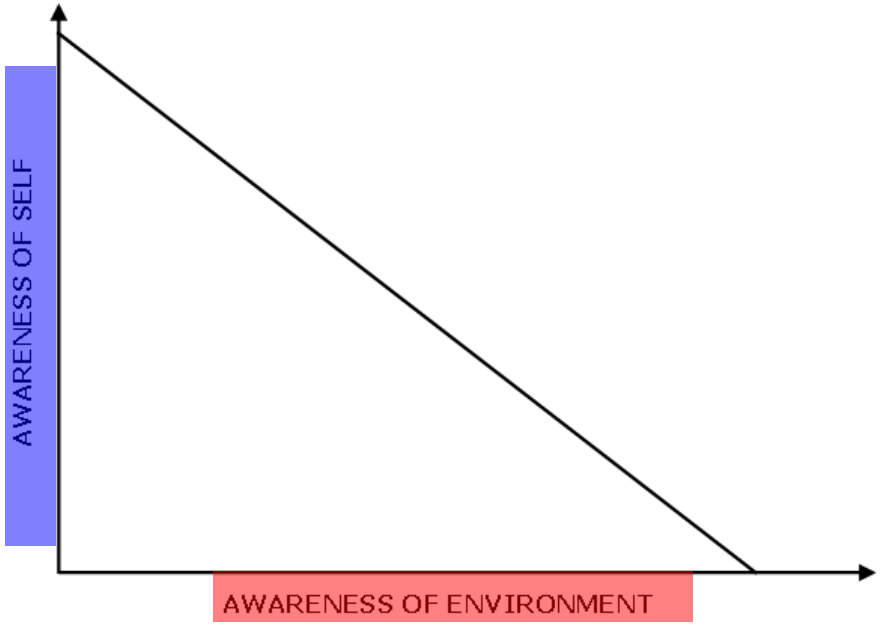
Boly, Garrido, Gosseries, Bruno, Schnakers, Massimini, Litvak, Laureys, Friston, *Science*, 2011

Interne *vs* Externe



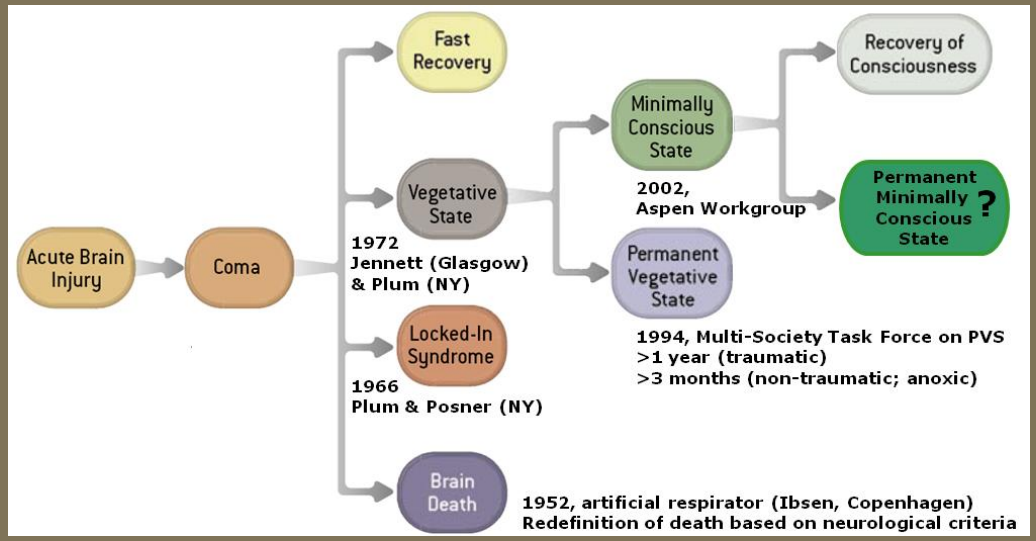
Conscience EXTERNE: sensorielle environnement

Conscience INTERNE: conscience de soi



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

Critères diagnostiques



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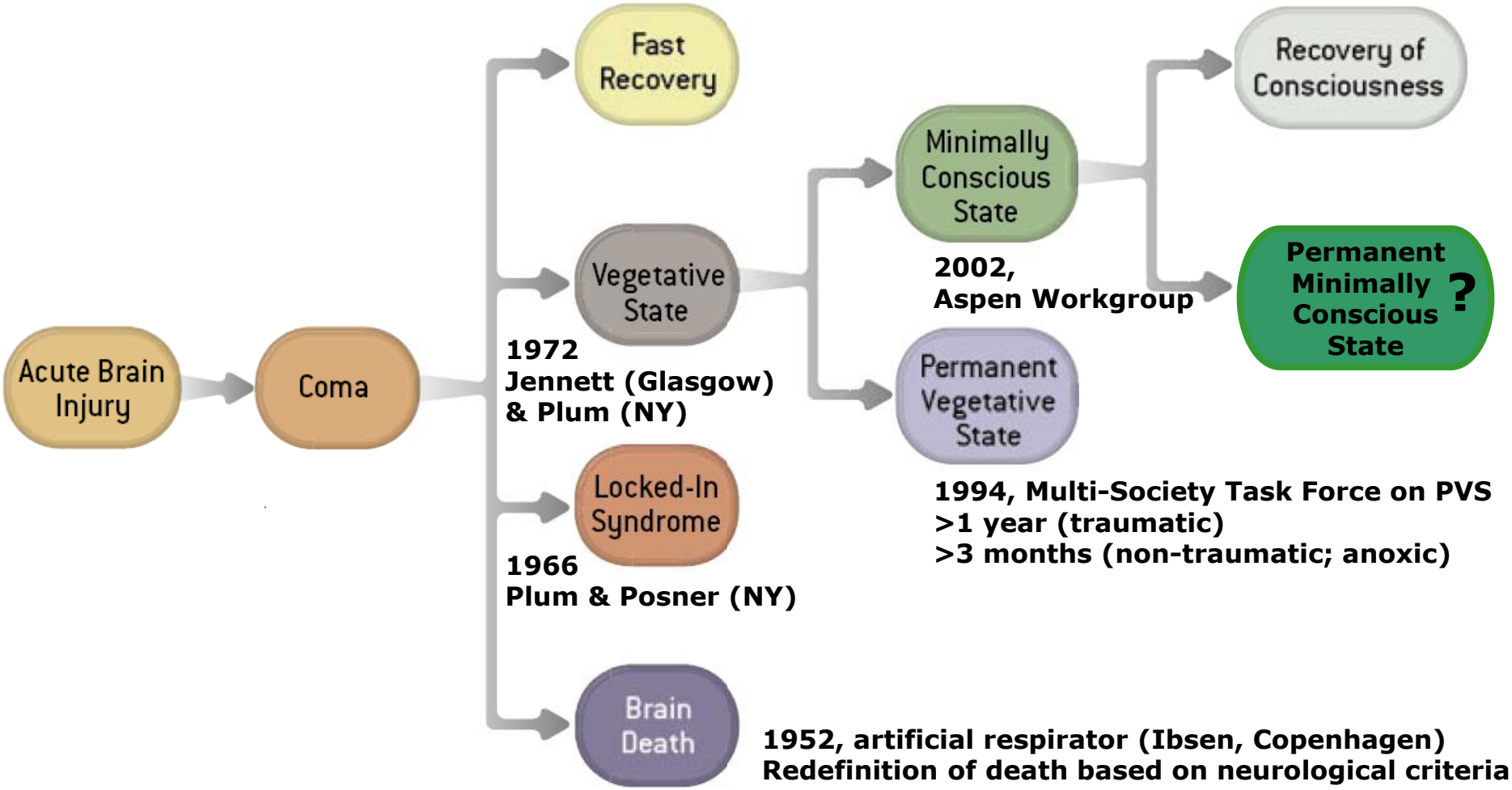
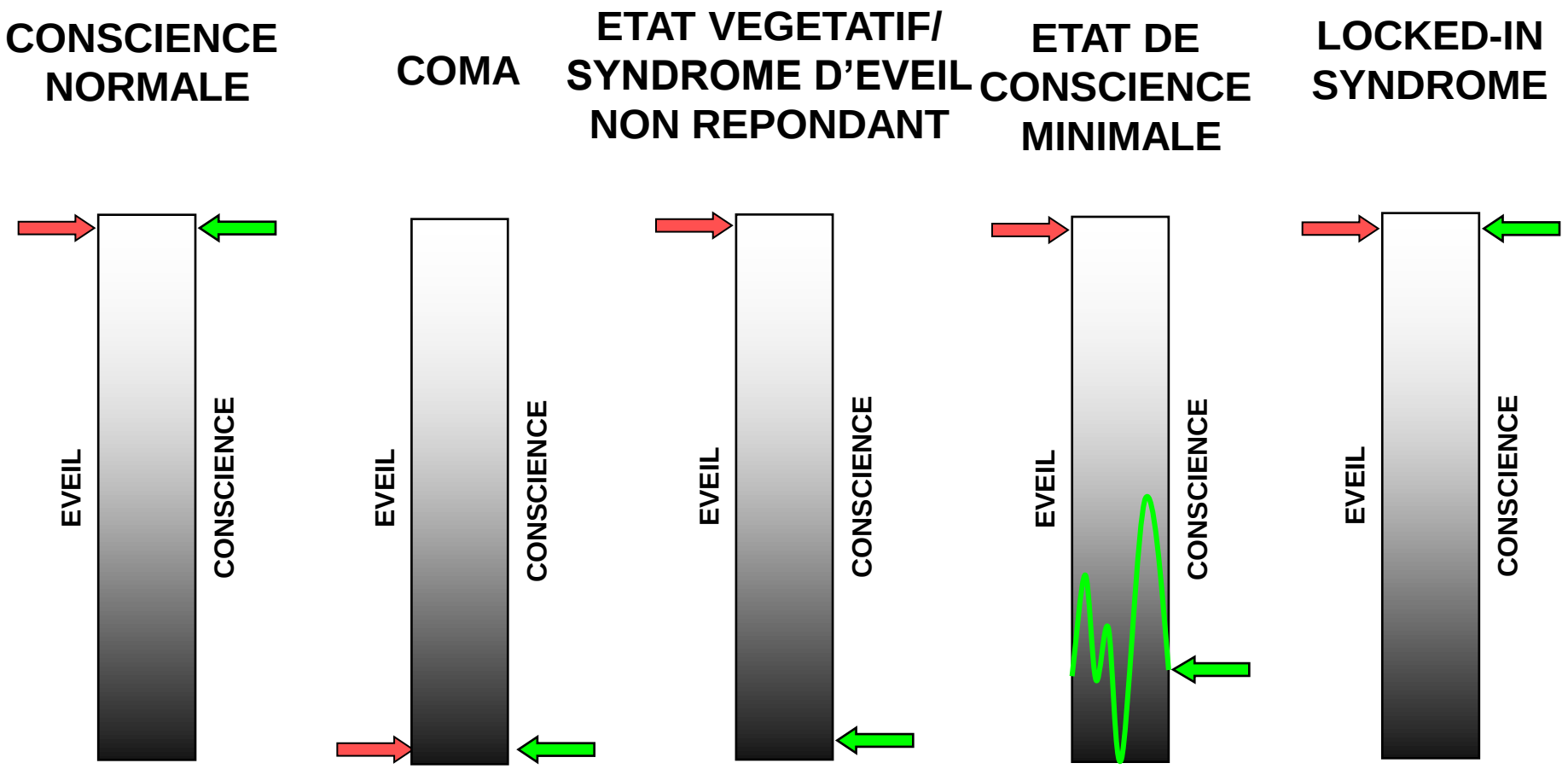
Etat de conscience altérée chronique



Laureys, Scientific American, 2007

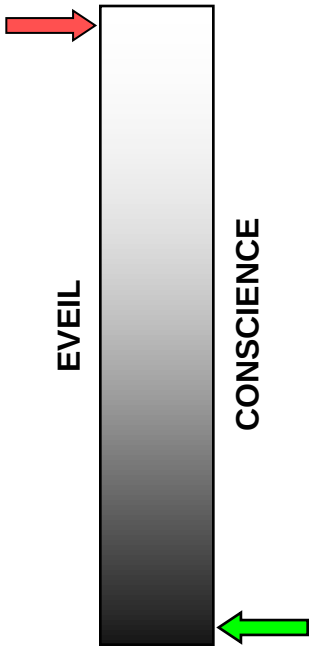
Conscience: 2 composantes



Laureys, Owen and Schiff, Lancet Neurology, 2005

Etat végétatif/non répondant

- Pas de signes de conscience
- Pas d'interaction avec l'environnement
- Pas de comportement volontaire en réponse à un stimulus visuel, auditif, tactile ou douloureux
- Pas de compréhension de langage ni expression
- Ouverture des yeux



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

Etat végétatif/éveil non répondant

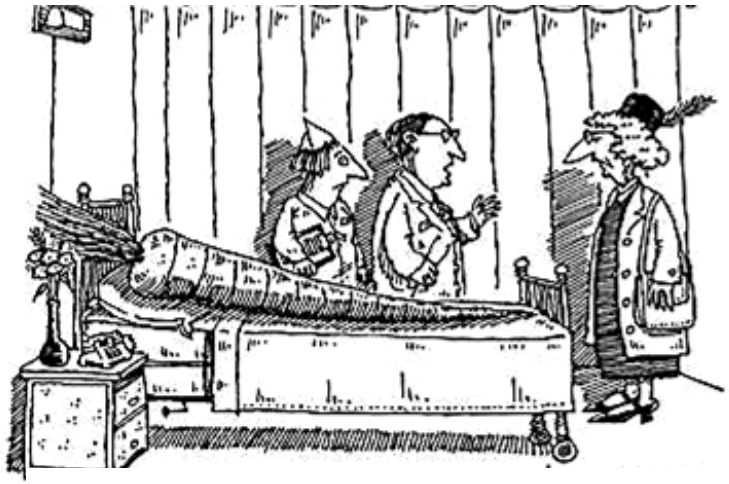
BMC Medicine

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]

http://www.biomedcentral.com/1741-7015/8/68



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

Laureys et al, *BMC Medicine* 2011

Etat de conscience minimale

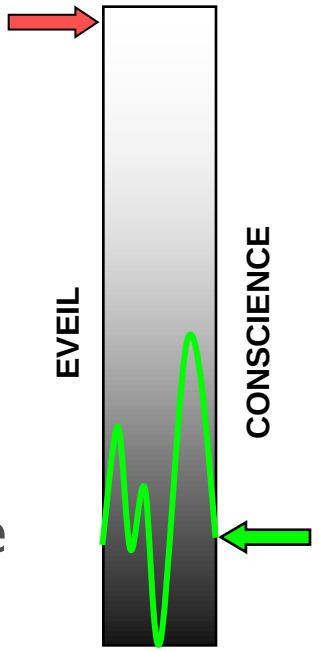
- Evidence claire d'une conscience :

- Poursuite visuelles
- Sourire ou pleurs appropriés
- Localisation d'objets
- Localisation de stimulations nociceptives
- Manipulation d'objets

MCS -

- Réponse à la commande
- Communication non fonctionnelle
- Verbalisations intelligibles

MCS +



L'émergence de l'ECM est caractérisée par le retour d'une communication ou d'une utilisation fonctionnelle d'objets

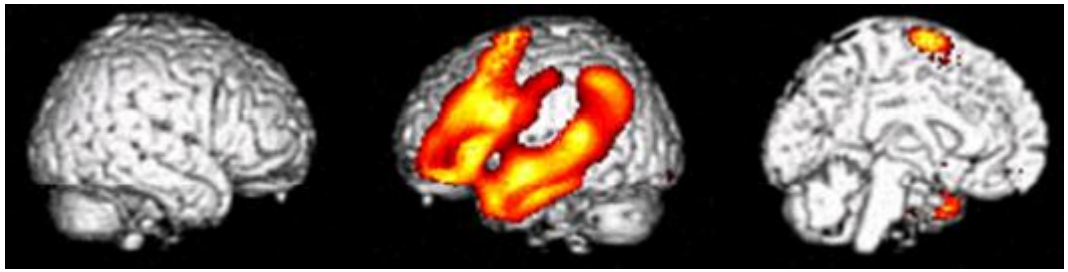
Aspen Workgroup, 2002;
Bruno & Vanhaudenhuyse et al., 2011

MCS: nouvelle terminologie

Minimally Conscious state

MCS +
Following simple command

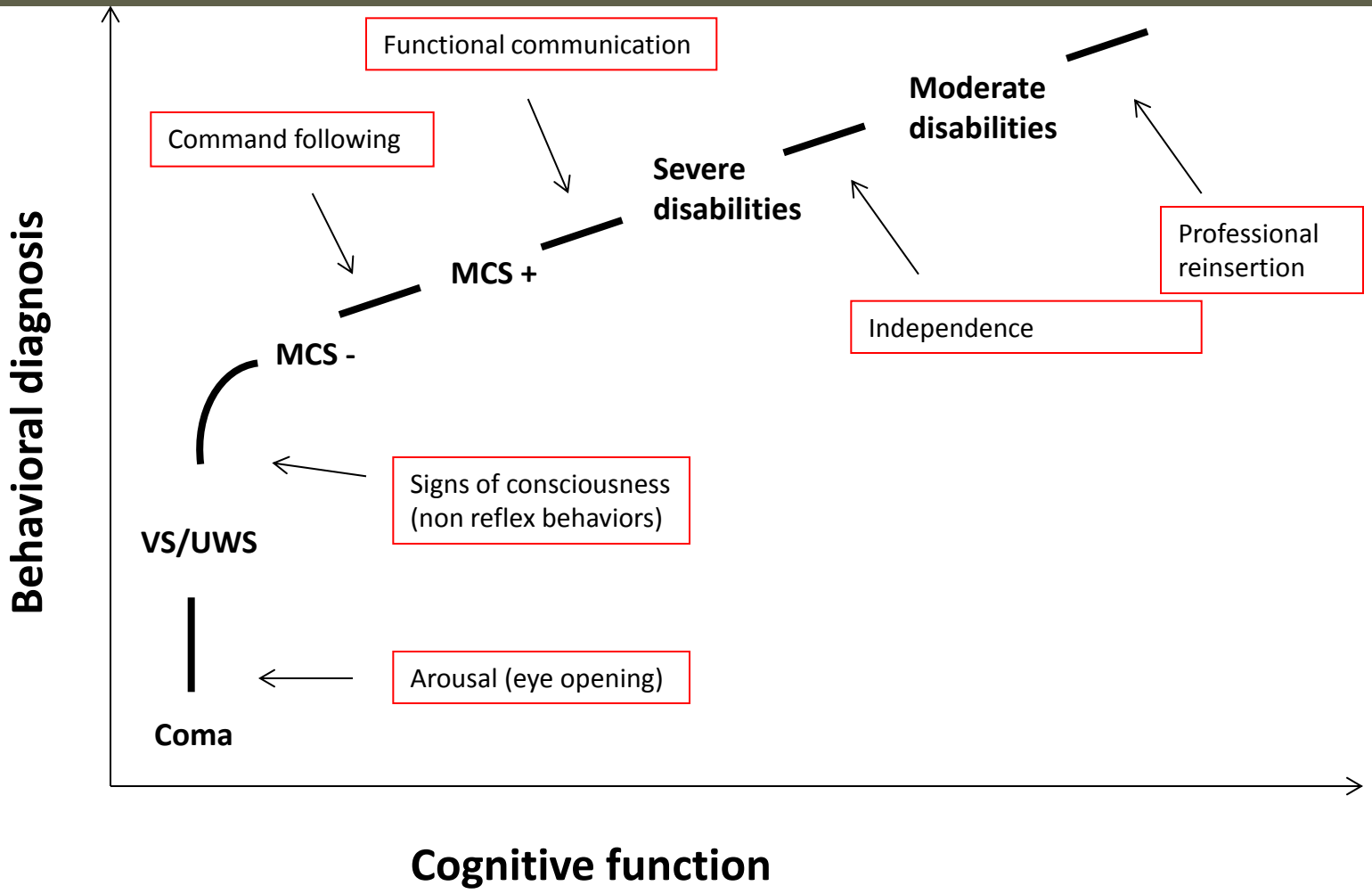
MCS+ > MCS-



MCS -
Pain localisation
Visual pursuit
Accurate smiling or crying

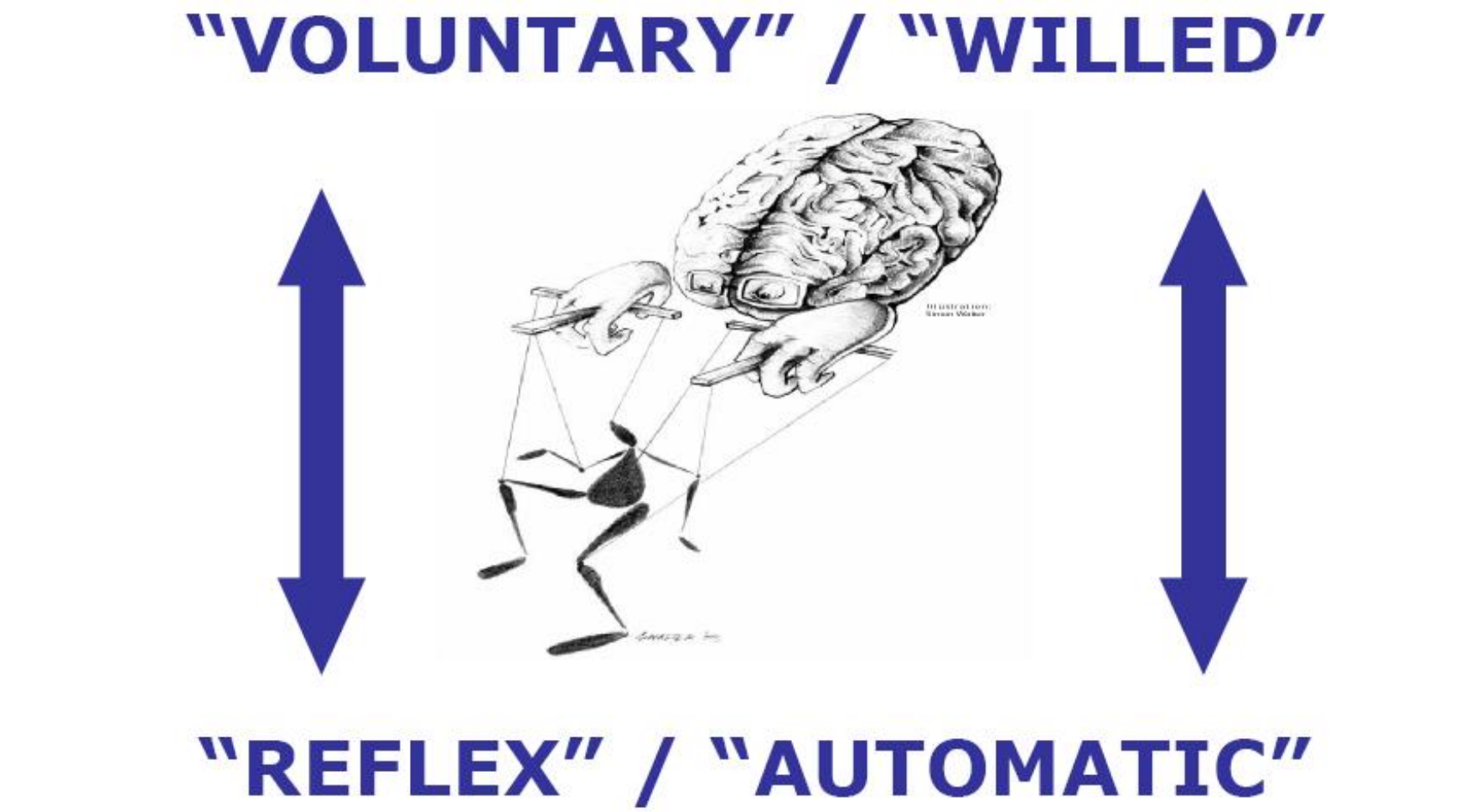
Bruno & Vanhaudenhuyse et al., 2011
Bruno et al., 2011

Récupération



Vanhaudenhuyse, Boly, Laureys. Scholarpedia (2009)

“Réflexe” versus “Volontaire”




©2000 Movement Disorder Society

Erreur diagno

n=103 patients post-coma

- 45 diagnostic d'état végétatif (
- 18 signes de conscience (Com

↳ **41% d'erreur diagnostique**

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								

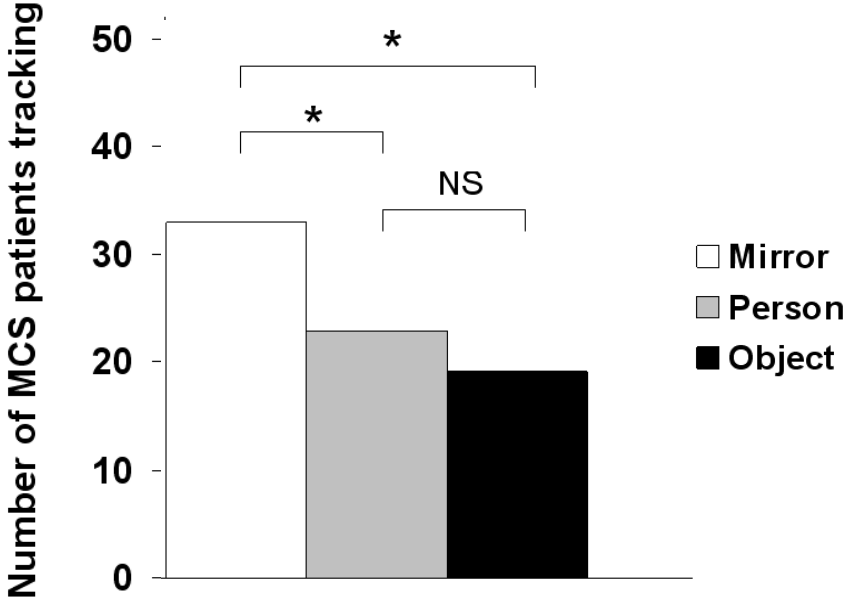
Denotes emergence from MCS †

Denotes MCS *

Schnakers et al, BMC Neurology 2009

Évaluation clinique

Vanhaudenhuyse et al., 2008

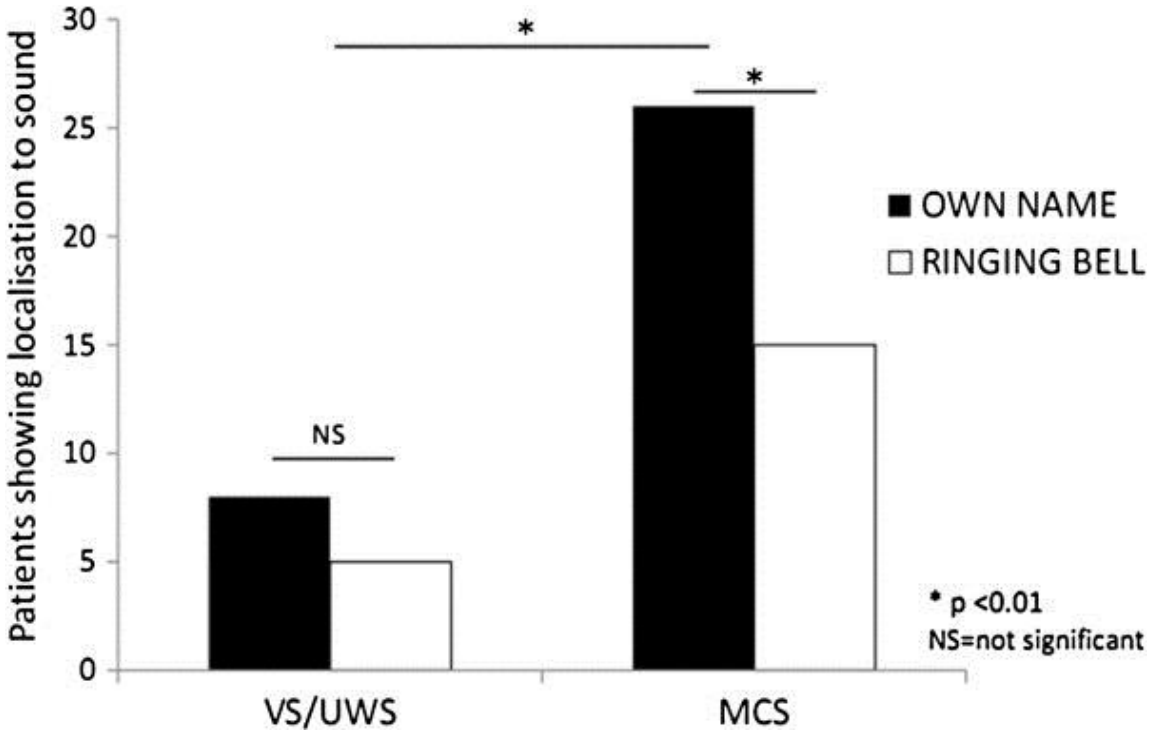


ÉCHELLE DE RÉCUPÉRATION DU COMA
VERSION REVUE FRANÇAISE ©2004
Formulaire de rapport

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								
ÉVEIL								
3 – Attention								
2 – Ouverture des yeux sans stimulation								
1 – Ouverture des yeux avec stimulation								
0 – Aucun éveil								
SCORE TOTAL								

Évaluation clinique

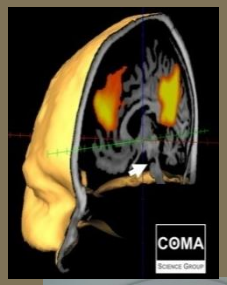
Auditory stimulation

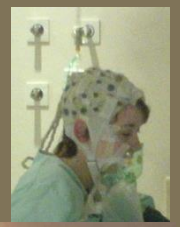


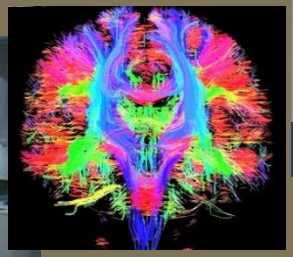
Own name ➔ Autoreferential stimulus

Cheng & Gosseries et al, BMC Neurology 2013

Diagnostic paraclinique







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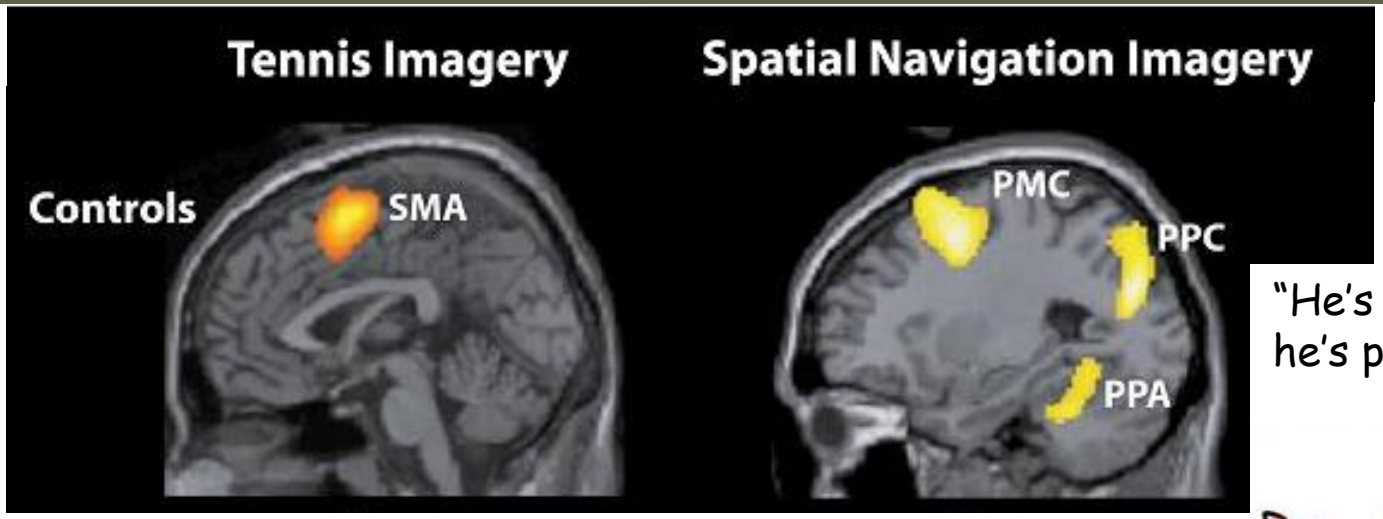
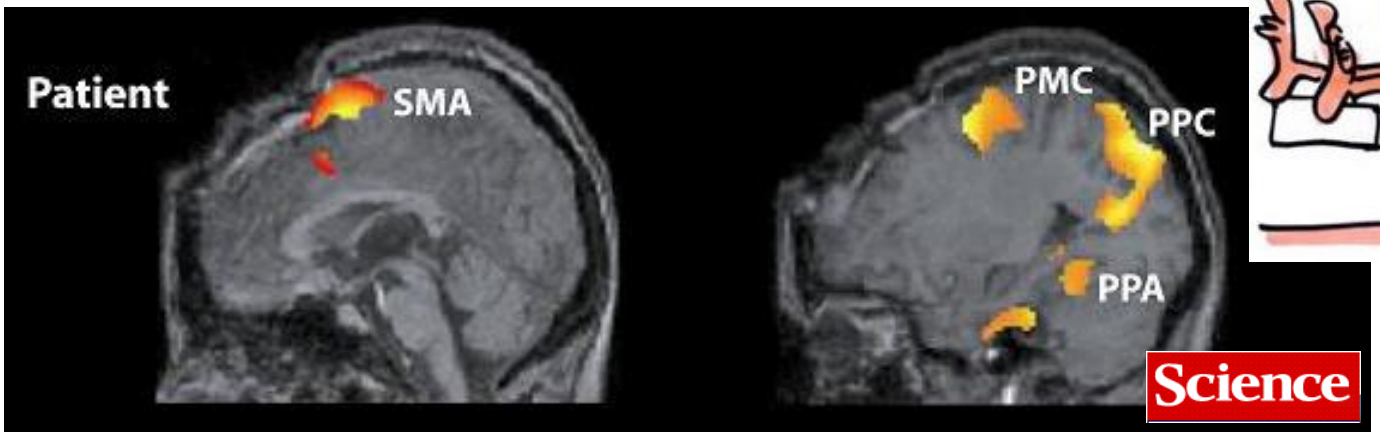
Signes de conscience avec l'IRMf



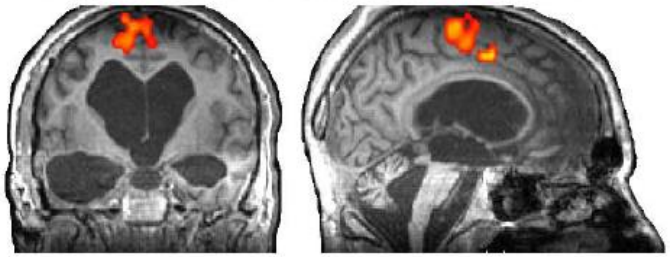


Monti & Vanhaudenhuyse, et al., *New England J Med* 2010

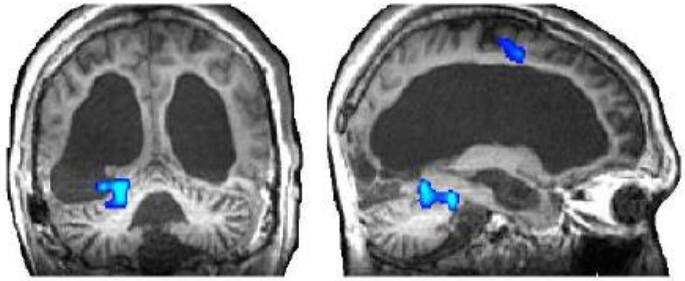
Communication oui/non avec l'IRMf

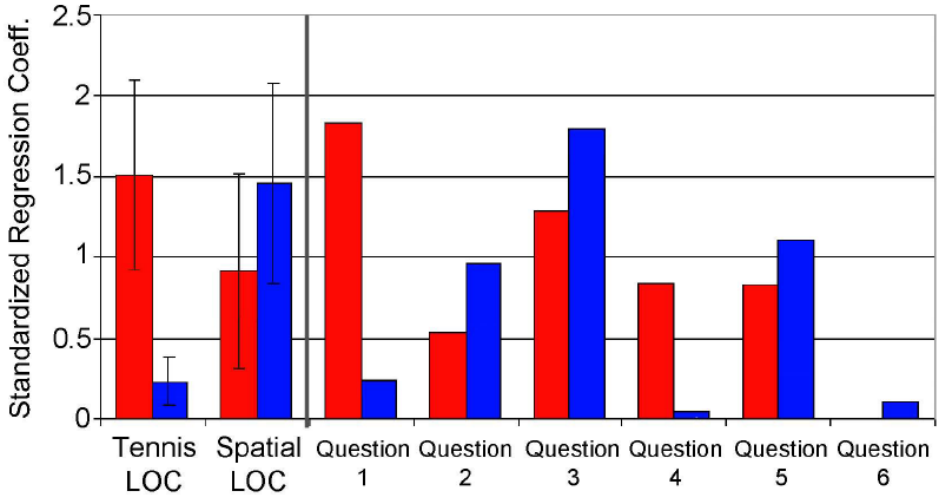
Imagine Tennis to answer 'YES'
Imagine Navigating to answer 'NO'

Is your father's name Alexander ?



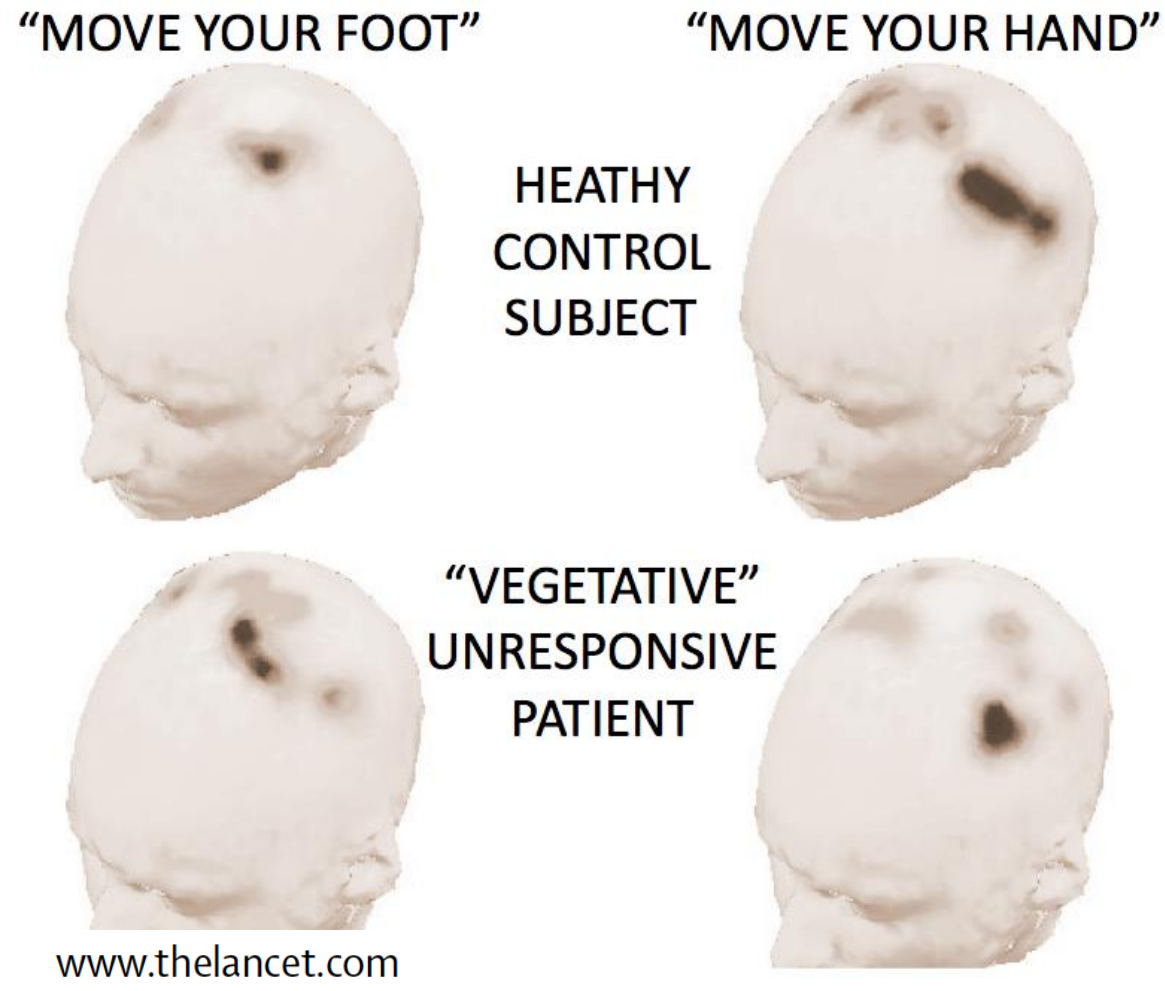
Is your father's name Thomas ?





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

Interface cerveau ordinateur : EEG



Brain and Mind
The University of Western Ontario

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UNIVERSITY OF CAMBRIDGE

CHU de Liège

Cruse et al, *Lancet* 2012

3/16 VS/UWS (19%)

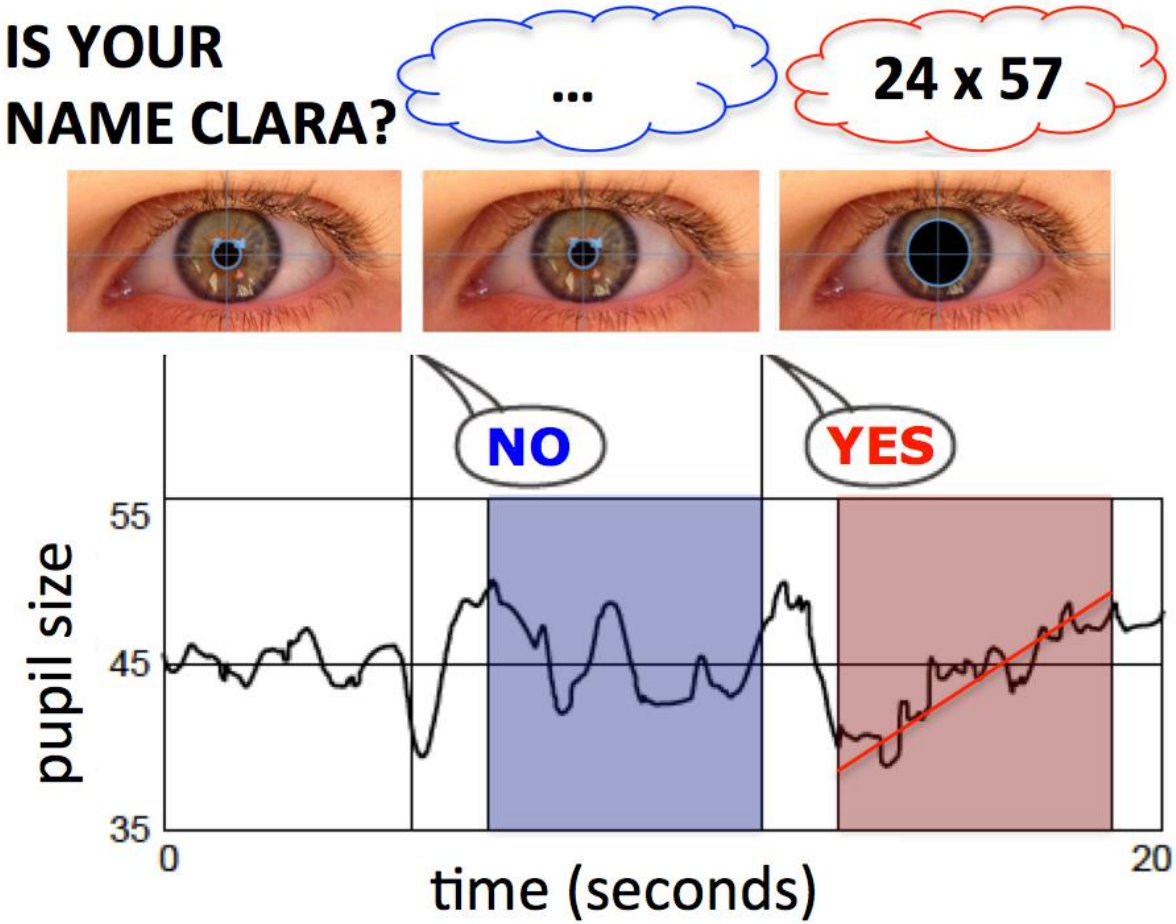
- 2/5 traumatic (40%)
- 1/11 non-traumatic (9%)

Cruse et al, *Neurology* 2012

7/23 MCS (30%)

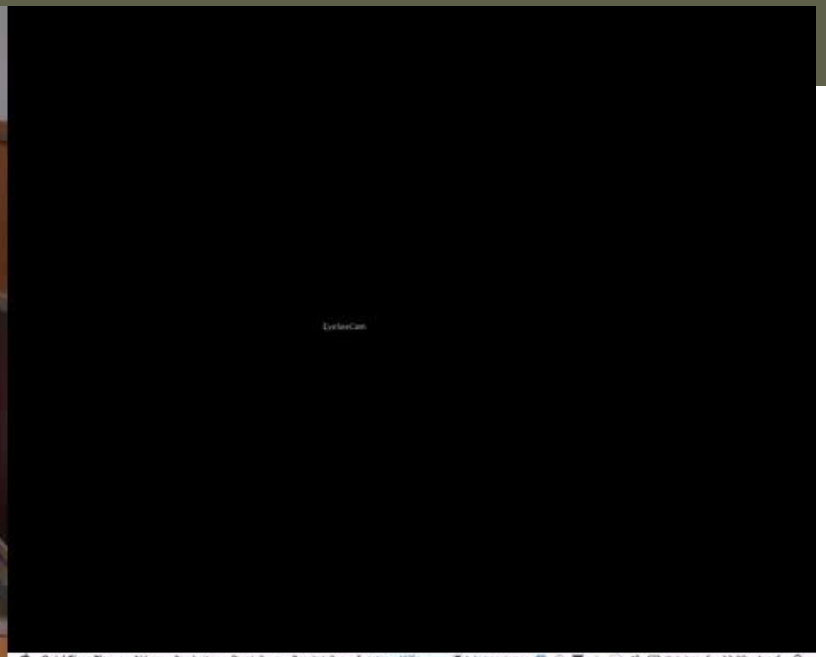
- 7/15 traumatic (49%)
- 0/8 non-traumatic (0%)

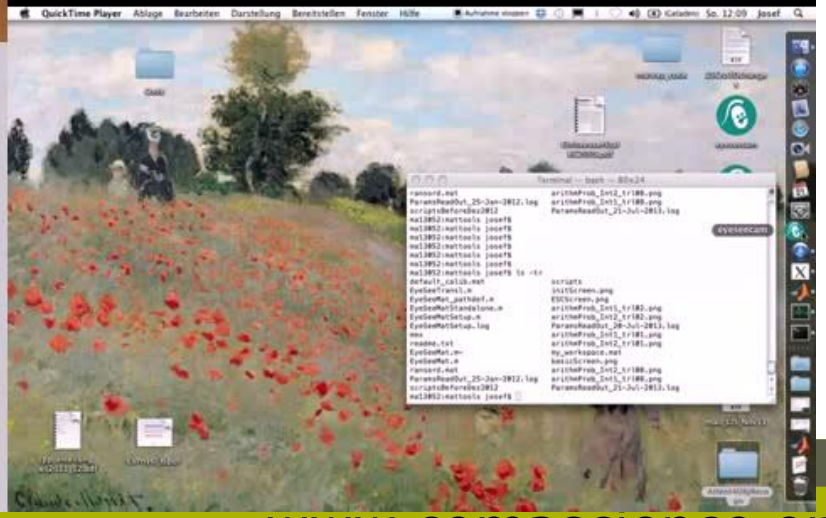
Interface cerveau ordinateur : pupil



Chatelle et al. Current Biology 2013

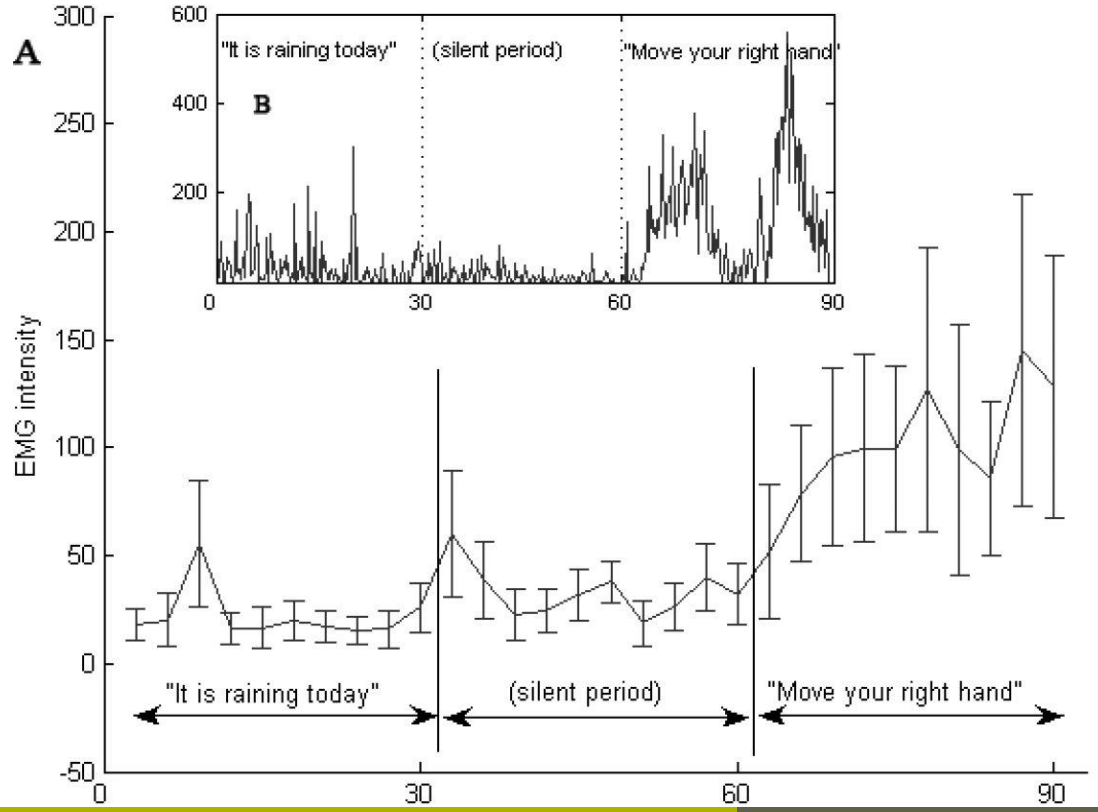
Interface cerveau ordinateur : pupil





Interface cerveau ordinateur : EMG

« Bougez la main droite »



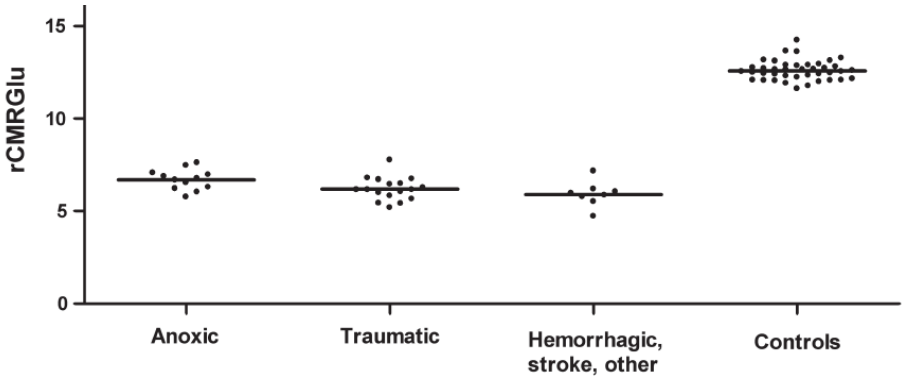
Bekinschtein et al JNNP 2008

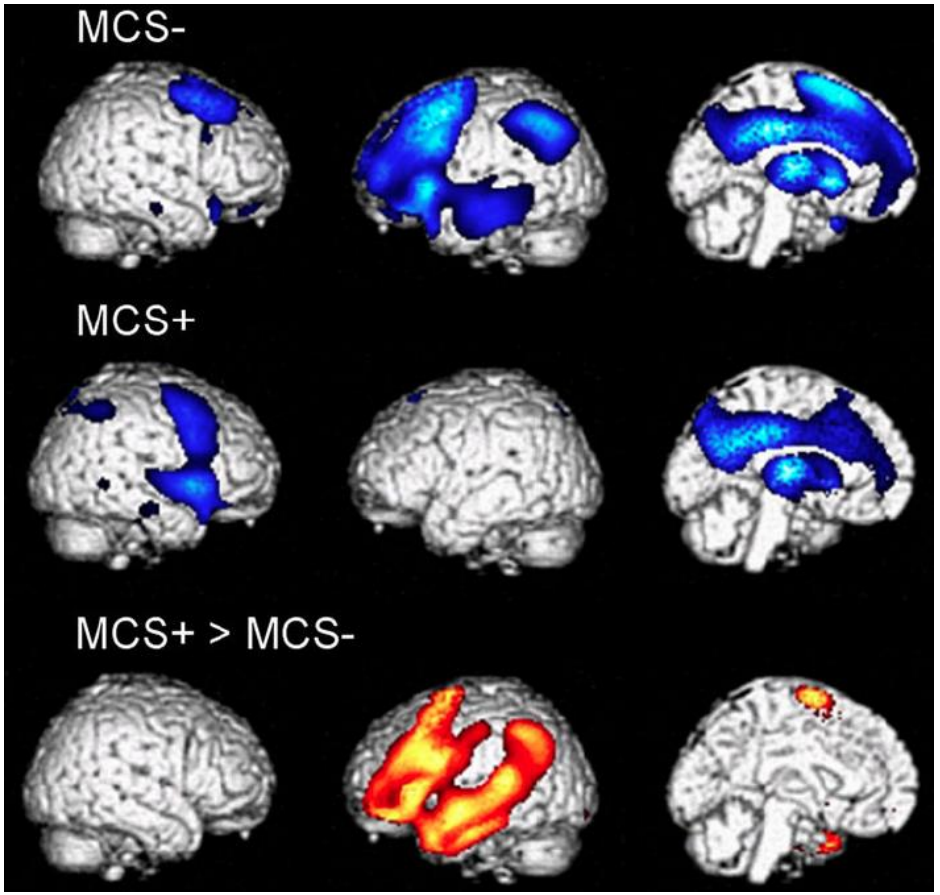
Aphasie

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

Steve Majerus[1,3], Marie-Aurélie Bruno[2,3], Caroline Schnakers[2], Joseph T. Giacino[4] and Steven Laureys[2,3,*]

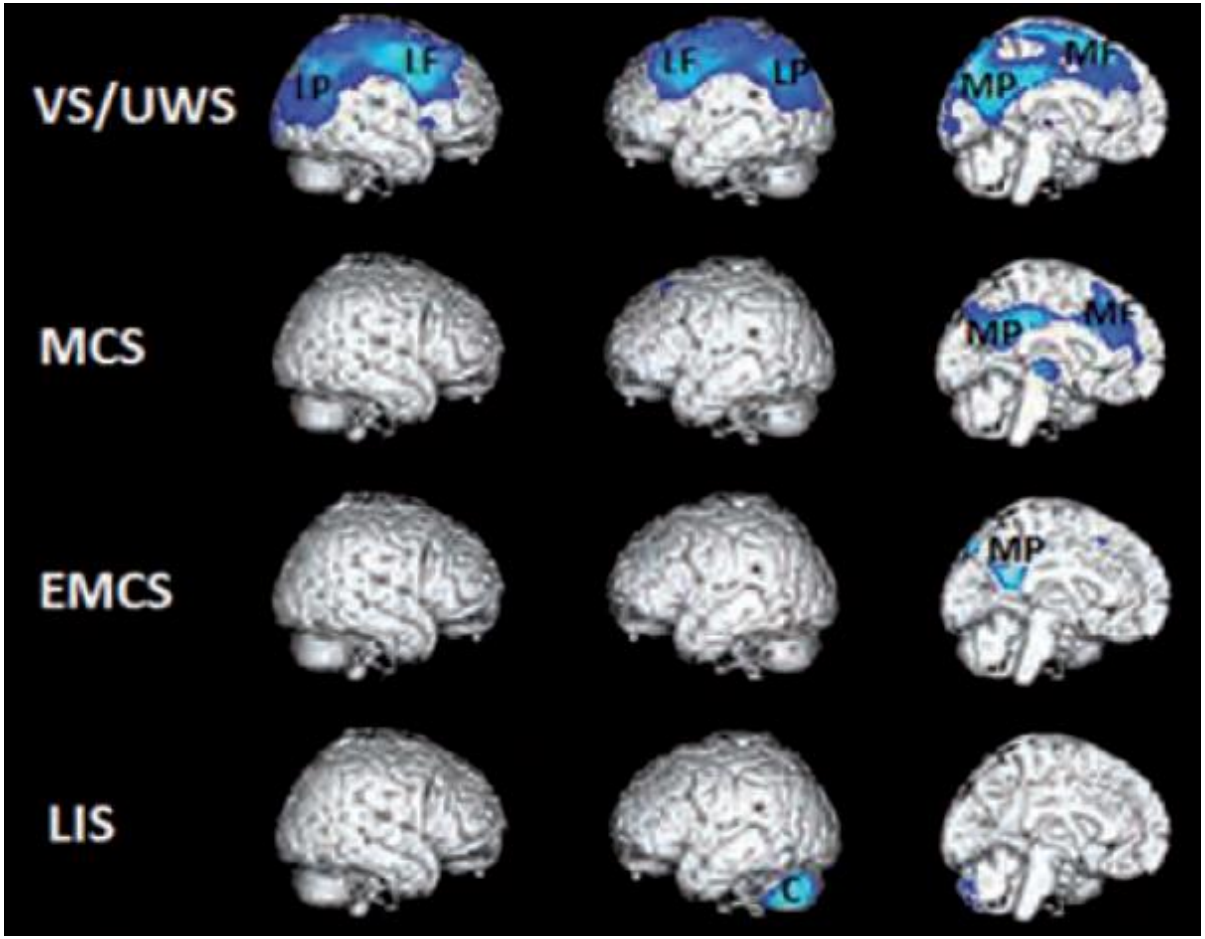
Progress in Brain Research, Vol. 177





Bruno et al, J Neurology 2012

Metabolisme cérébral – PET scan

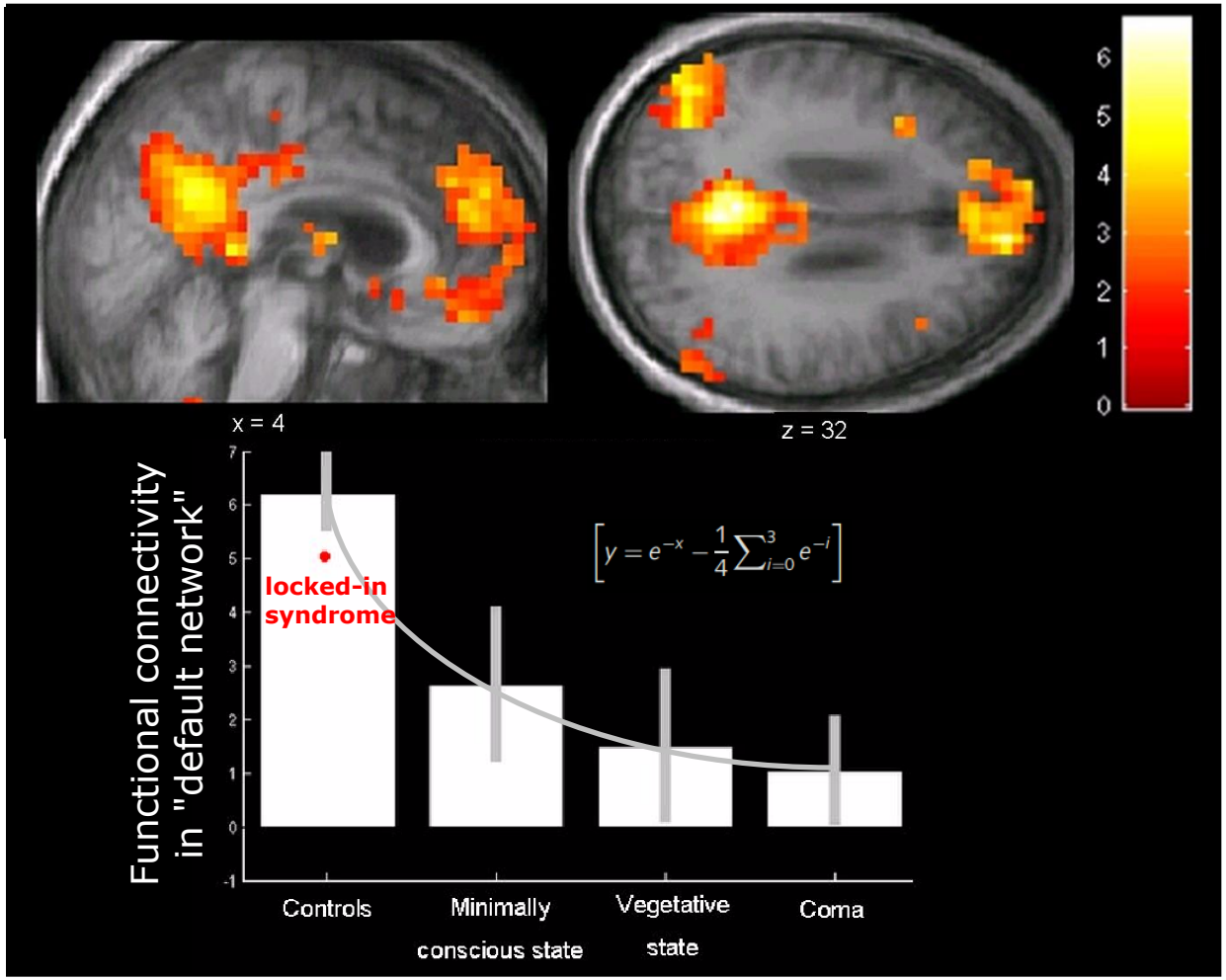


➔ Réseaux conscience interne ET externe

➔ Réseaux conscience interne

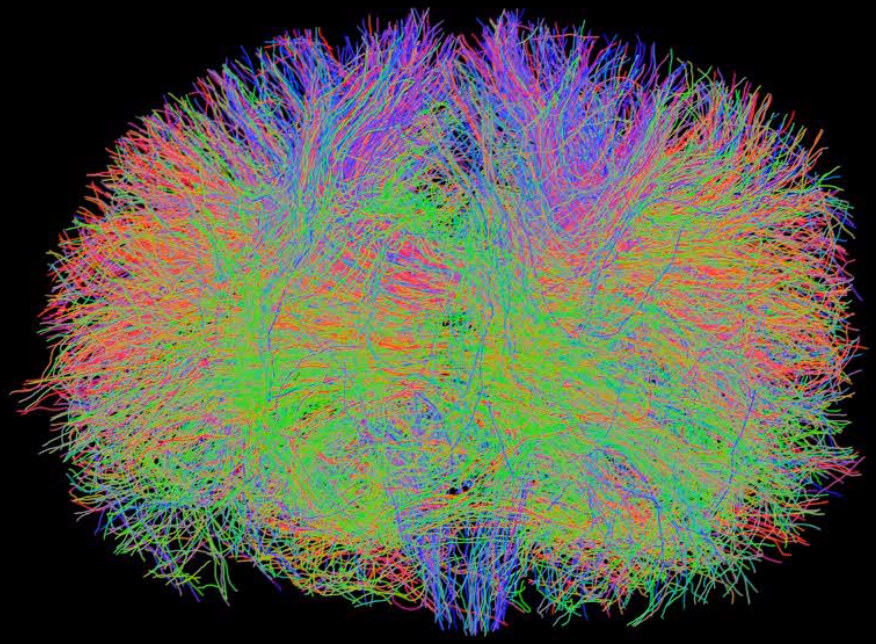
Thibaut et al, J Rehabil Med 2012

Réseau du mode par défaut : IRMf



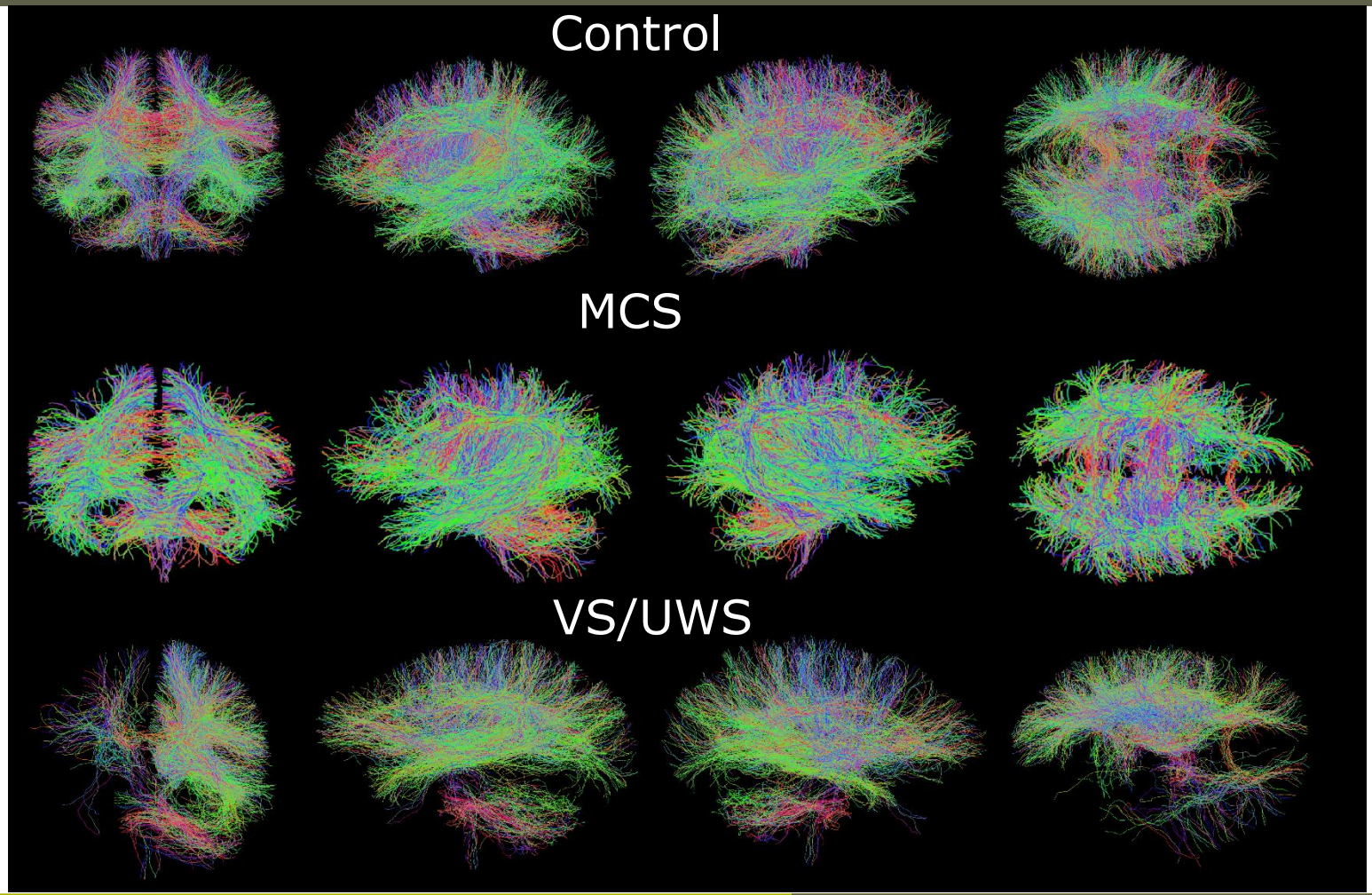
Vanhaudenhuyse et al, *Brain*, 2010

Imagerie par tenseur de diffusion



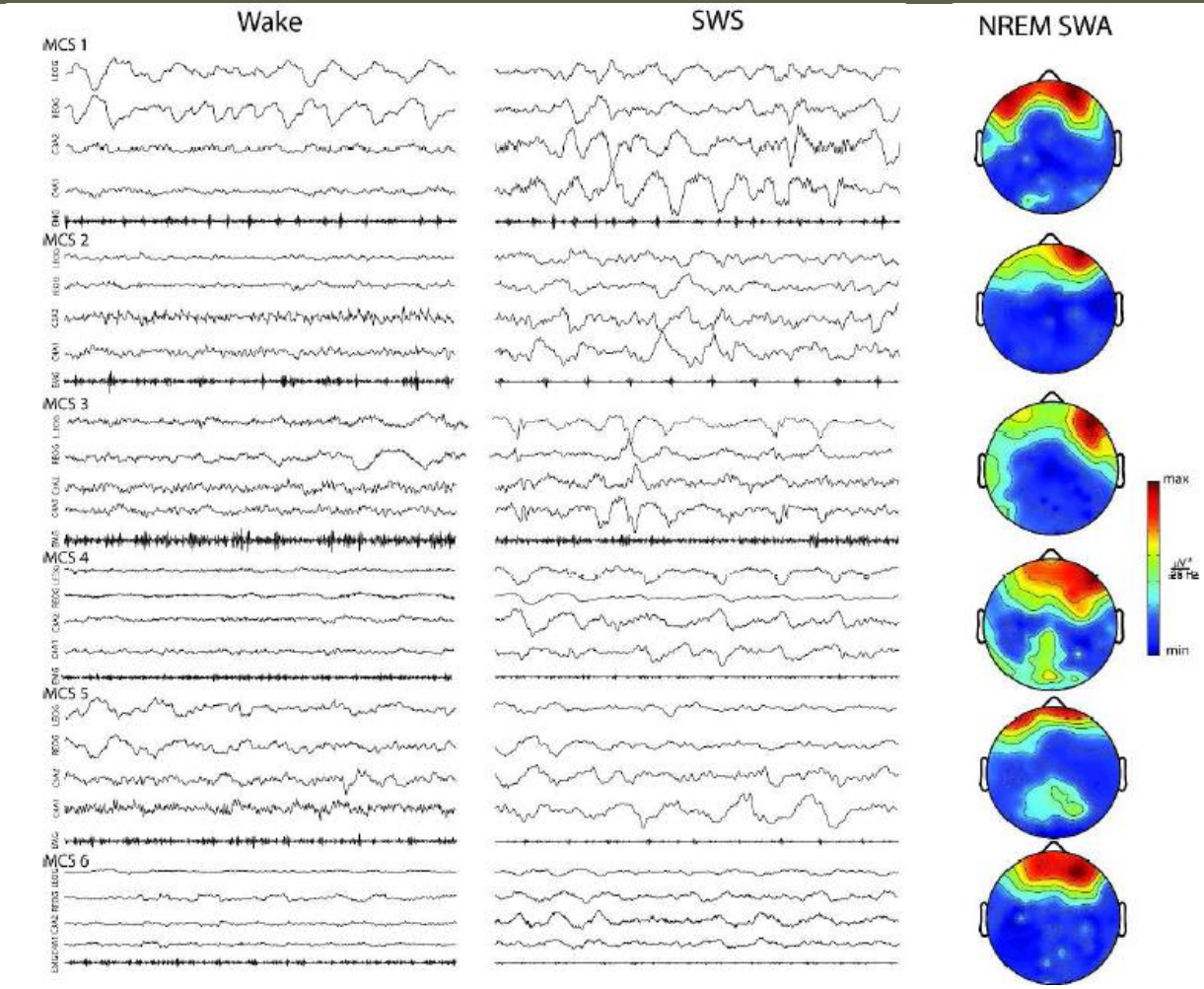
Gomez et al., 2012

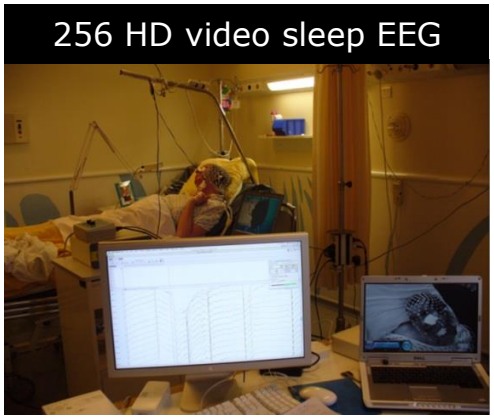
Imagerie par tenseur de diffusion



Gomez et al., 2012

Sommeil

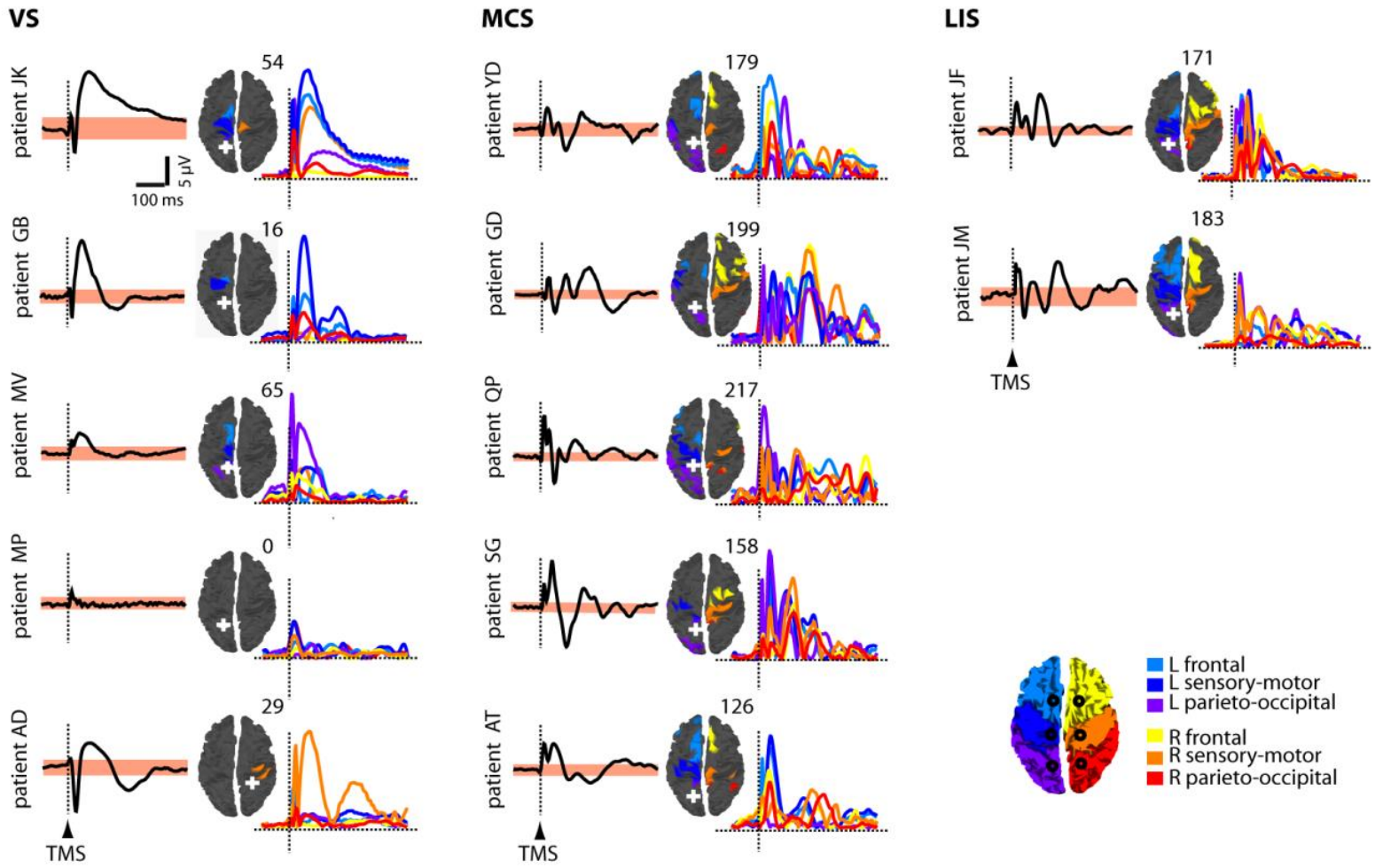




MCS : périodes de rêves

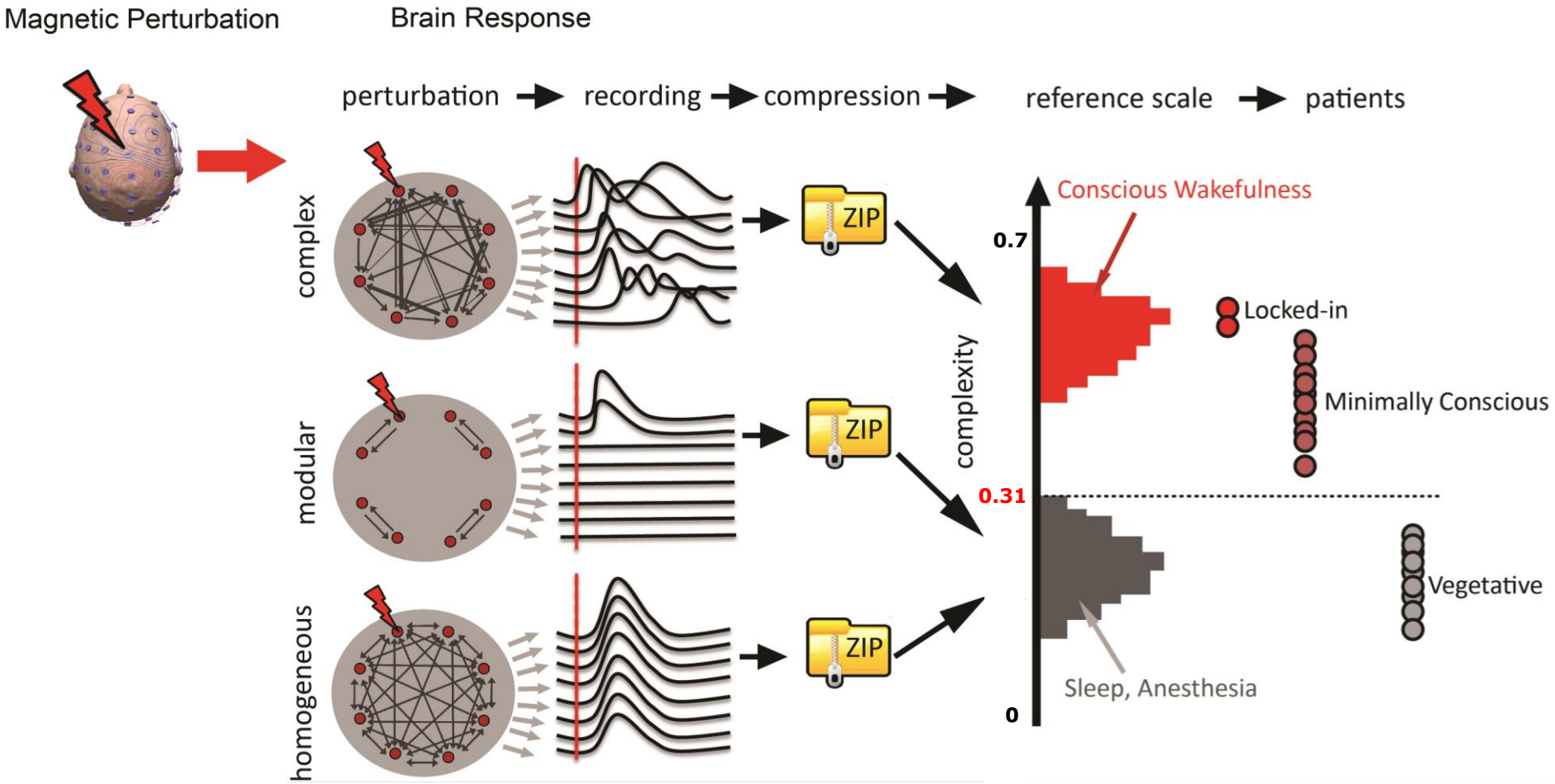
Landnes and Bruno et al, *Brain*, 2011

Stimulation Magnétique Transcranienne



Rosanova and Gosseries et al, Brain, 2012

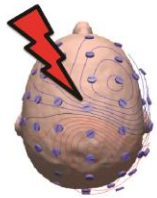
Perturbational Complexity Index (PCI)



Casali and Gosseries et al, Sci Transl Med, 2013

Perturbational Complexity Index (PCI)

Magnetic Pertu



tients

n

Minimally Conscious

Vegetative

Casali and Gosseries et al, Sci Transl Med, 2013

Douleur et émotions

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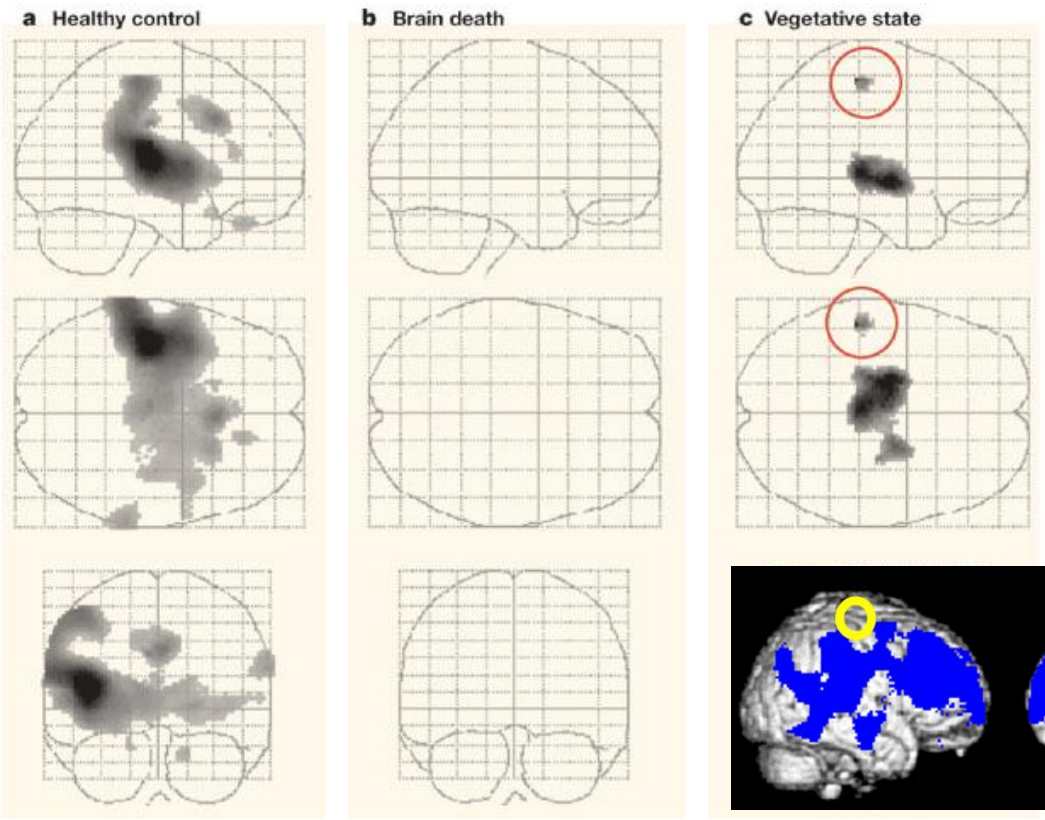
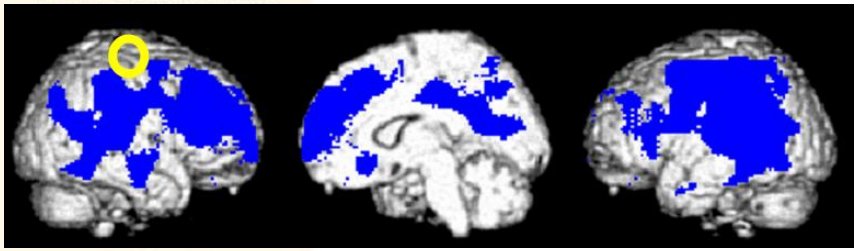
Douleur : mort cerebrale et VS

Noxious electrical stimulation

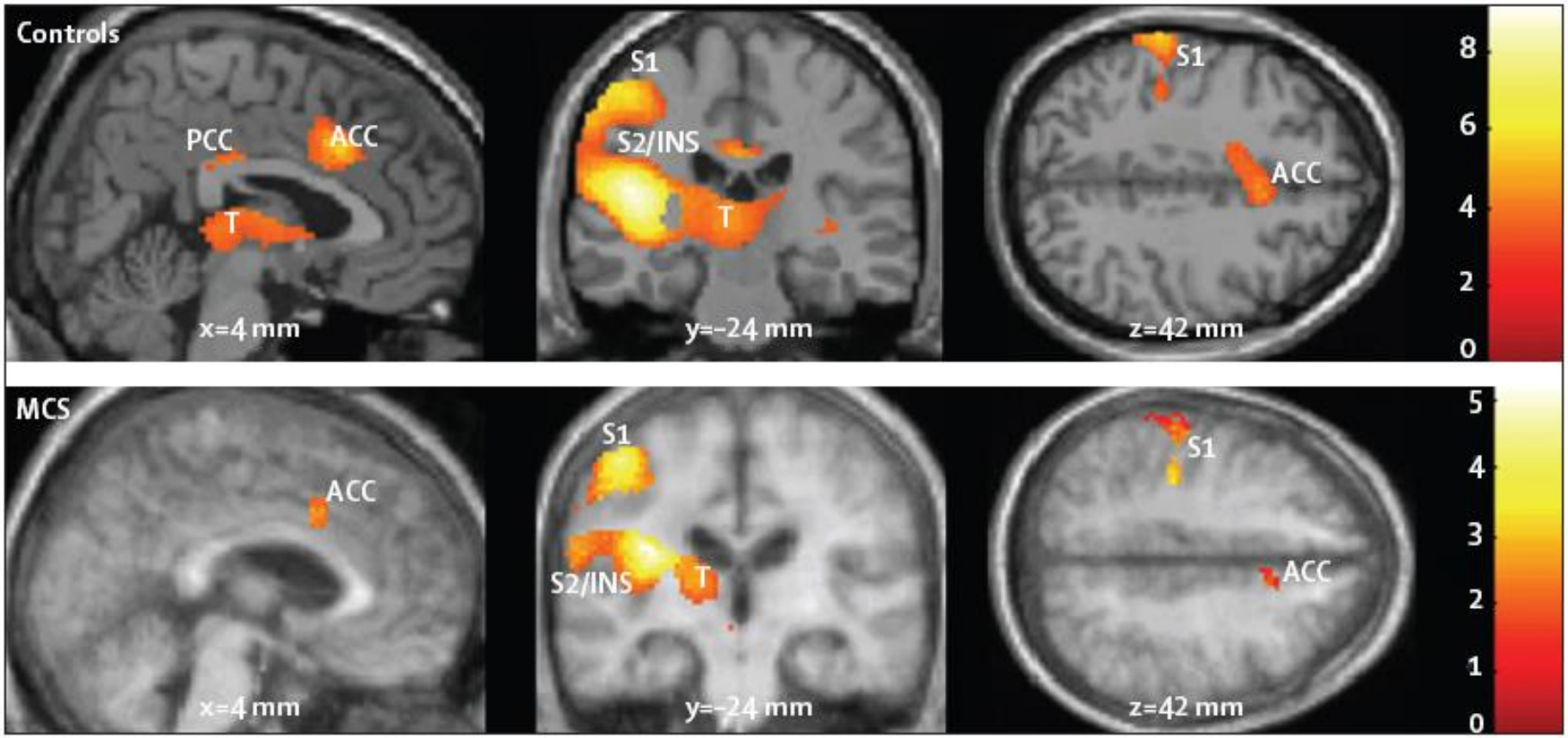


Low level disconnected cortical activation



Laureys et al, *Neuroimage,* 2002
Laureys, *Nature Reviews Neuroscience,* 2005

Douleur : MCS



Boly et al, *Lancet Neurology,* 2008

Evaluer la douleur

Nociception Coma Scale - Revised

Motor response
3 – Localization to noxious stimulation
2 – Flexion withdrawal
1 – Abnormal posturing
0 – None/flaccid

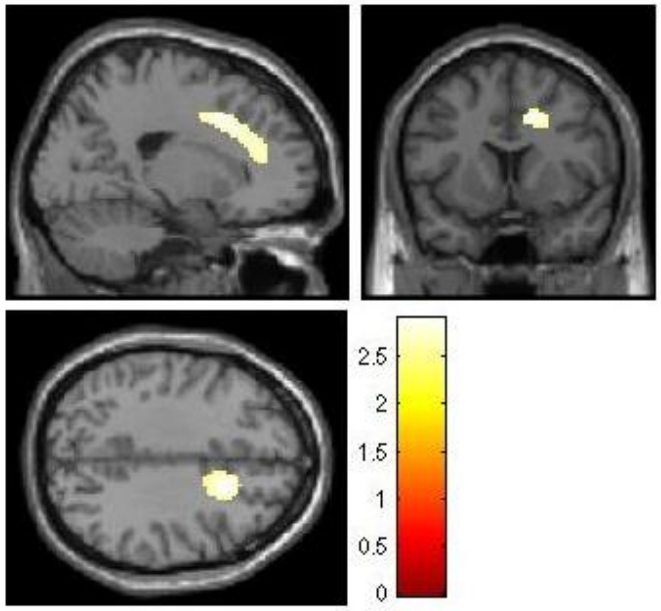
Verbal response
3 – Verbalisation (intelligible)
2 – Vocalisation
1 – Groaning
0 – None

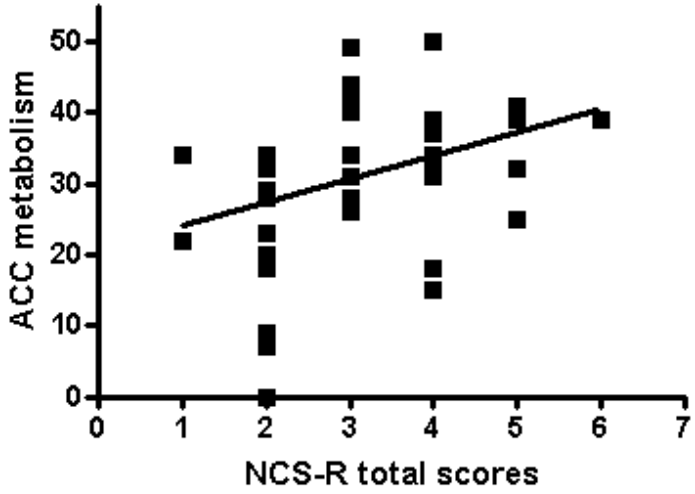
Facial expression
3 – Cry
2 – Grimace
1 – Oral reflexive movement/startle response
0 – None

Score >3/9 = traitement antalgique

Chatelle et al, *JNNP,* 2012

Evaluer la douleur





Corrélation entre le métabolisme du cortex cingulaire antérieur (ACC – pain matrix) et le score à l'échelle d'évaluation de la douleur (NCS-R)

Chatelle, Thibaut et al. NNR, 2013

Spasticité

➔ Exagération du réflexe myotatique qui induit une contraction musculaire involontaire lors d'un mouvement ou de manière permanente

Facteurs aggravants: Vitesse d'étirement
Fatigue et stress

Effets secondaires: Rétraction musculaire
Fixation irréductibles
Position vicieuses et douleur

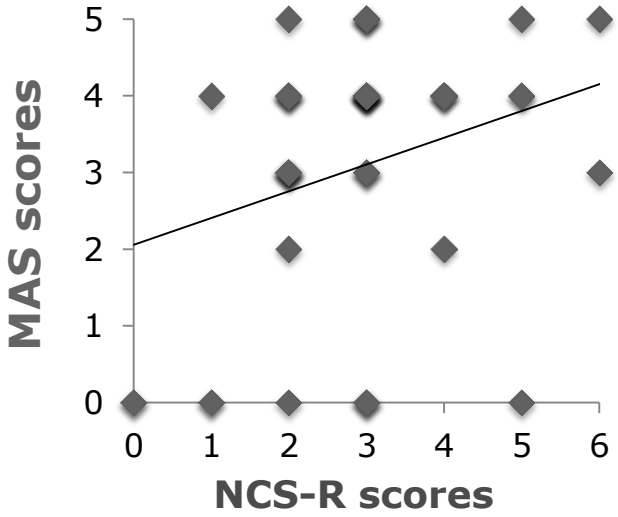
Physiopathologie pas encore entièrement comprise
Pas de guidelines claires pour le traitement

Thibaut et al, *Brain Injuy,* 2013

Spasticité

Evaluation de la spasticité* chez VS/UWS & MCS (n=65)

- **89%** (n=58) spastiques
  60% (n=39) spasticité sévère
- **Durée depuis l'accident**: corrélation positive avec la spasticité
- **Douleur** (*Nociception Coma Scale Revised*) : corrélation positive



* Evaluation avec l'échelle d'Ashworth modifiée

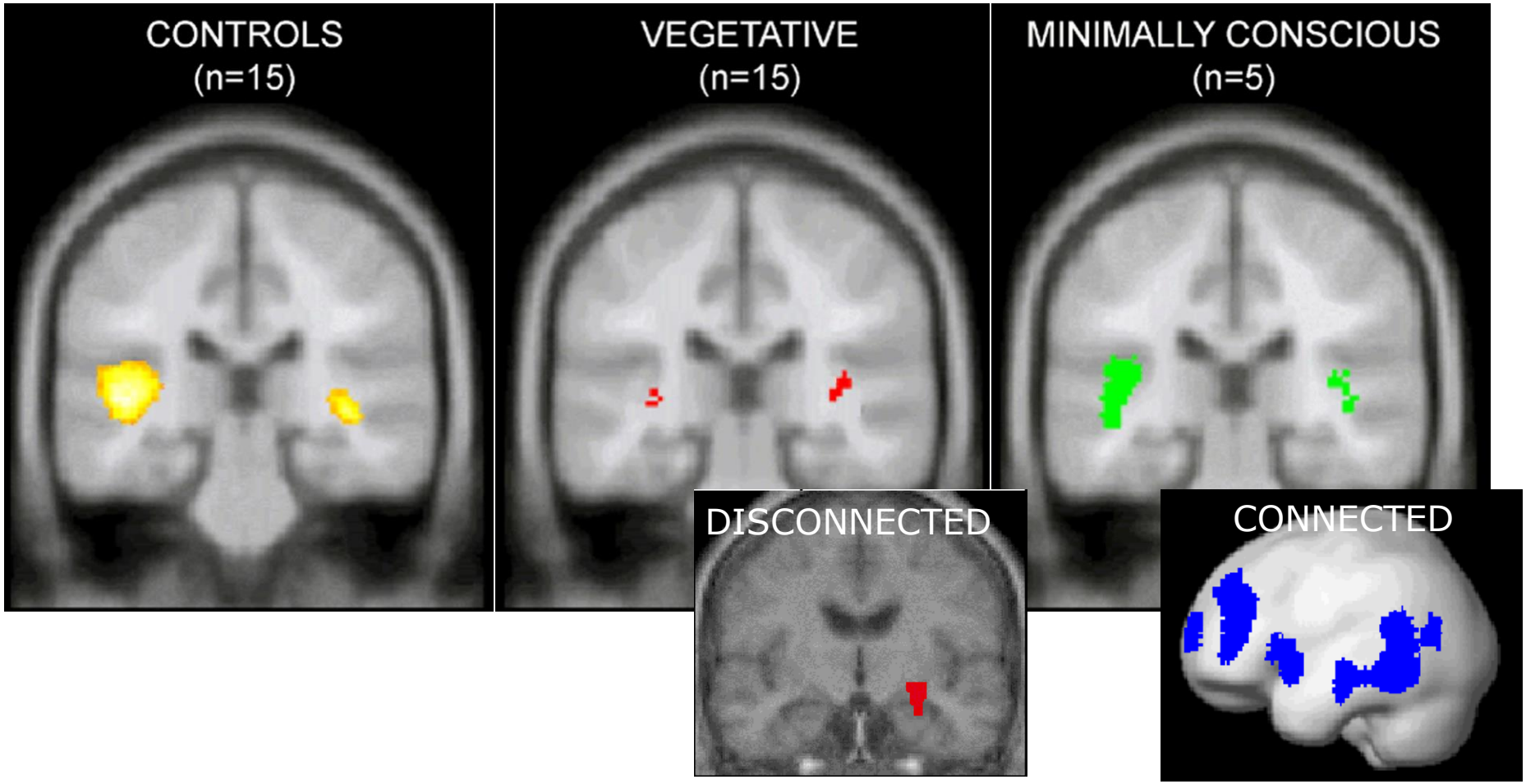
Thibaut et al, *Eur J Rehabil*

Nous entendent-ils?

"Parle avec elle" (Hable con Ella)
Pedro Almodóvar

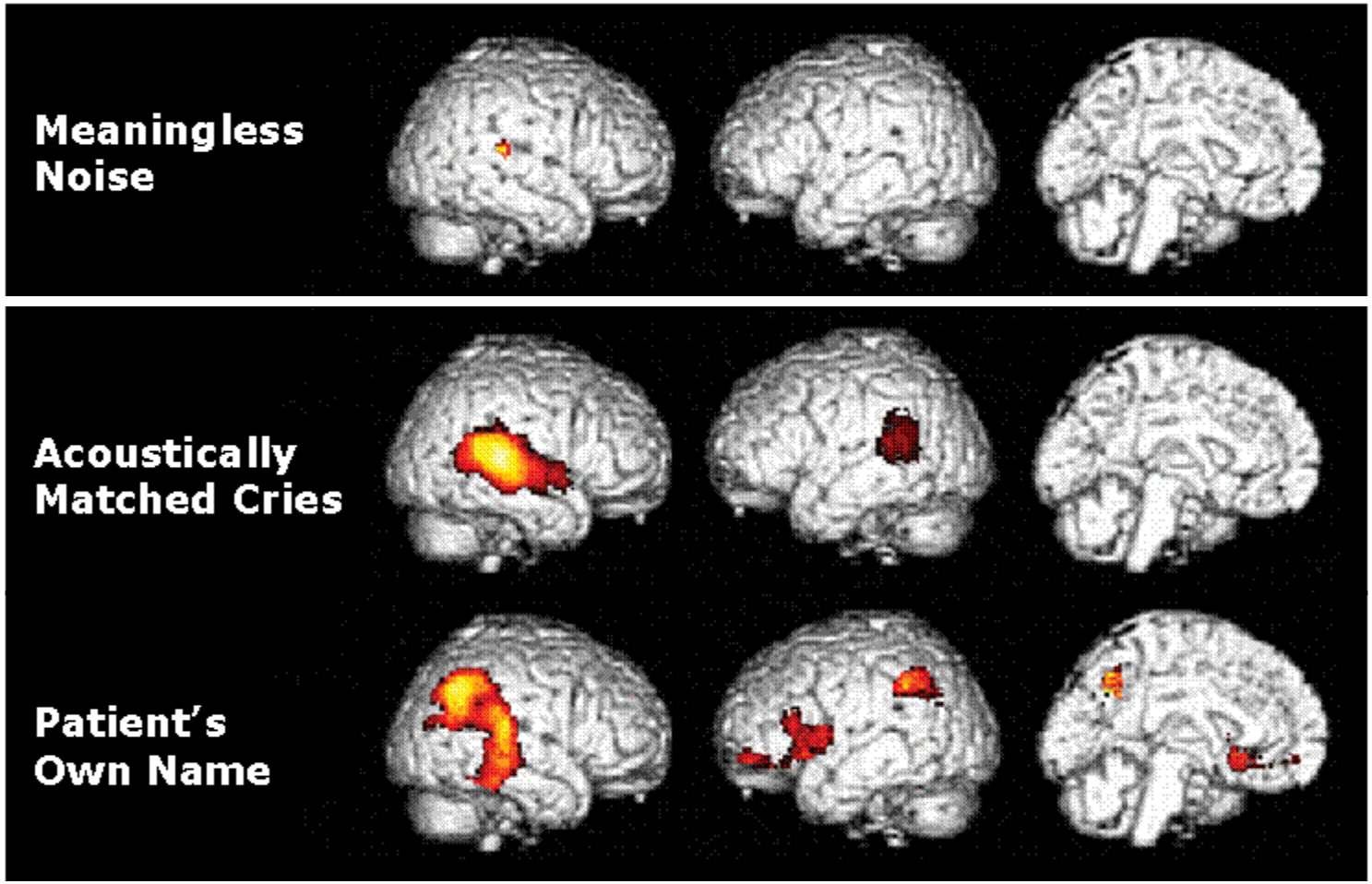
"…a (wo)men's brain is a mystery...
and even more so in this state."

Perception auditive



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

Emotions chez les MCS



Laureys et al., Neurology, 2004

Pronostic

Laureys & Boly
What is it like to be vegetative or minimally conscious?
Curr Opin Neurol 20 (2007) 609-13

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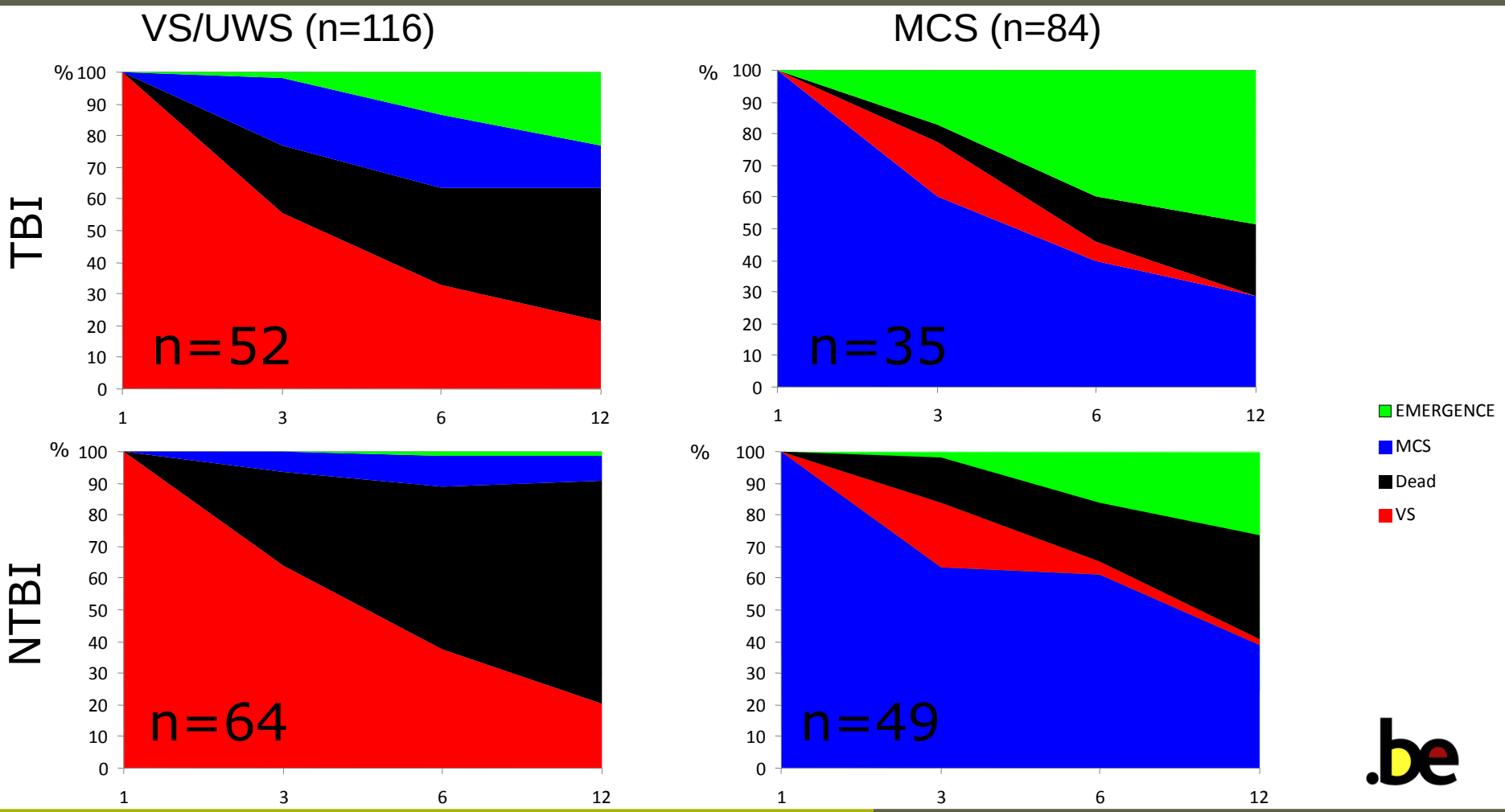
Pronostic (Projet fédéral belge)

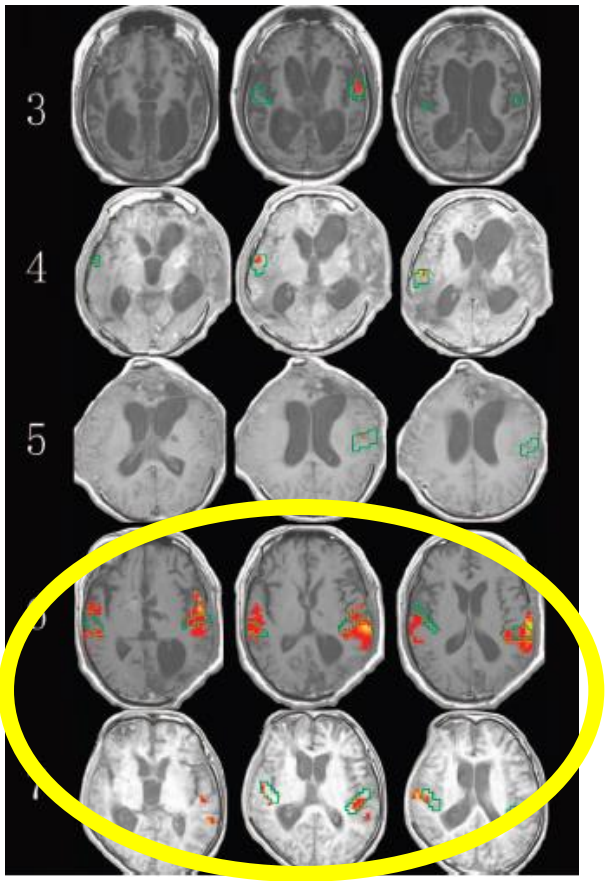


Bruno et al., 2011

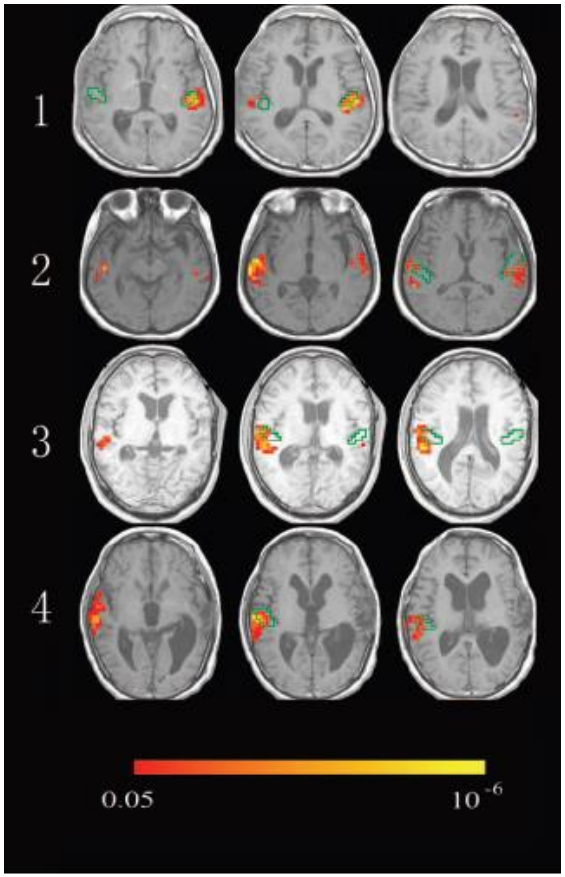
Valeur pronostique de l'IRMf

Activité corticale atypique ➔ meilleur pronostic

VS/UWS

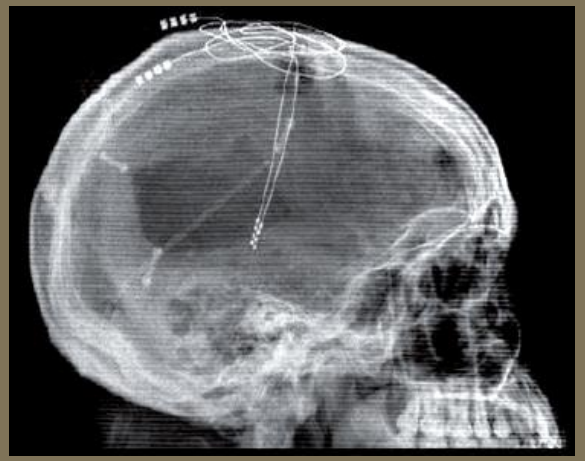


MCS



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

Traitements



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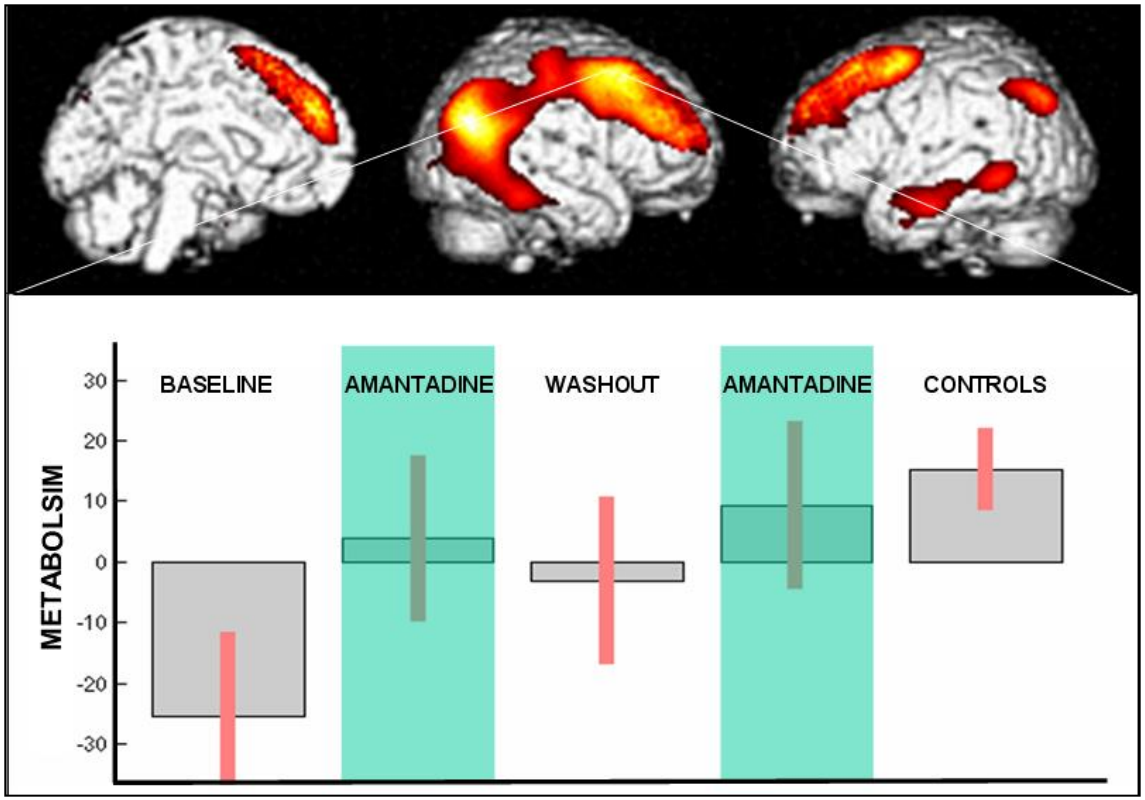
Traitements pharmacologiques

Drugs	Study (first author, year)	Number of patients and etiology	Diagnosis	Placebo control	Reported functional outcome
Dopaminergic agents					
Amantadine	Giacino (2012)	184 TBI	MCS/VS	Yes	Positive
	Schnakers (2008)	1 anoxic	MCS	No	Positive
	Patrick (2006)	10 TBI	Low responsive level	No	No effect
	Hughes (2005)	123 TBI	Coma	NA	No effect
	Saniova (2004)	41 TBI	'Persistent unconsciousness'	NA	Positive
	Meythaler (2002)	35 TBI	MCS	Yes	Positive
Bromocriptine	Brahmi (2004)	4 intoxication	Coma	No	Positive
Levodopa	Matsuda (2003)	3 TBI	VS	No	Positive
Nonbenzodiazepine sedative					
Zolpidem	Cohen (2008)	1 anoxic	Lethargic	No	Positive
	Shames (2008)	1 anoxic	MCS	No	Positive
	Singh (2008)	1 TBI	MCS	No	No effect
	Brefel-Courbon (2007)	1 hypoxic	Akinetic mutism	Yes	Positive
	Clauss (2006)	2 TBI, 1 anoxic	VS	No	Positive
	Clauss (2000)	1 TBI	Semi-comatose	No	Positive
GABA agonist					
Baclofen	Sarà (2007)	1 non-TBI	VS	No	Positive

Adapted from Demertzi et al, *Expert Rev Neurotherapeutics*, 2008

Amantadine

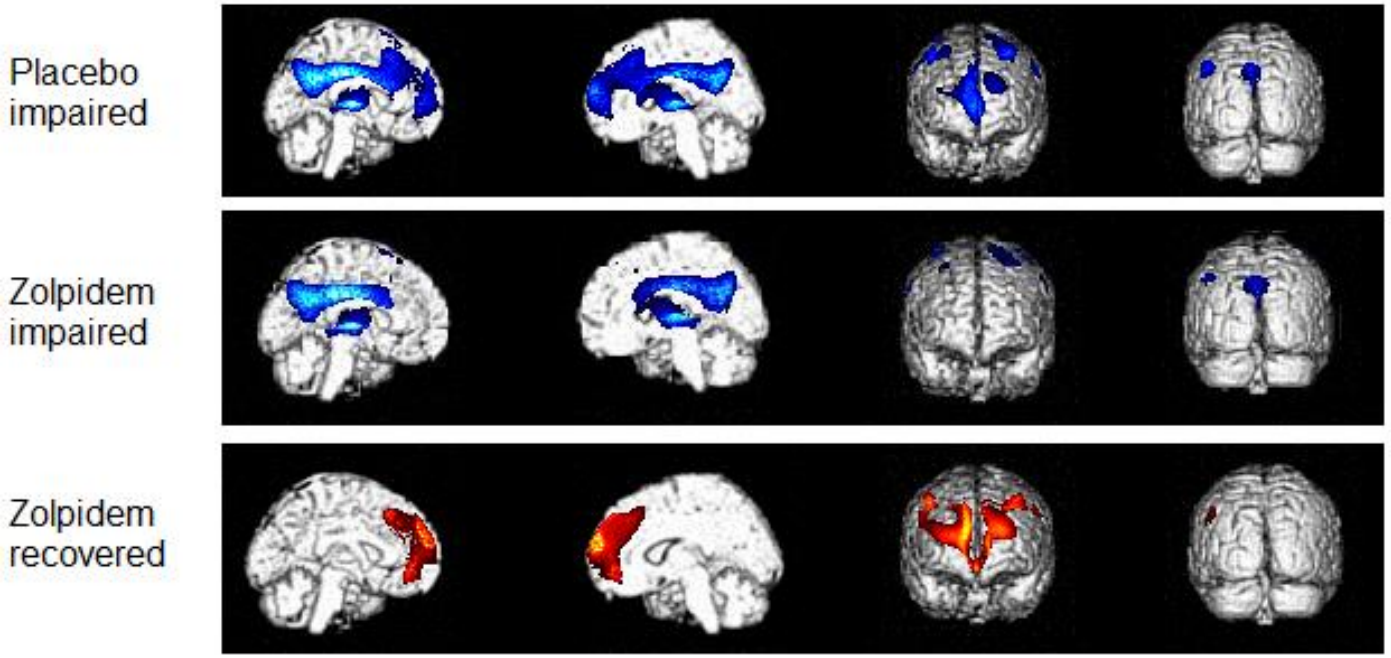
Agent dopaminergique (Parkinson)



Schnakers et al, *JNNP,* 2008

Zolpidem

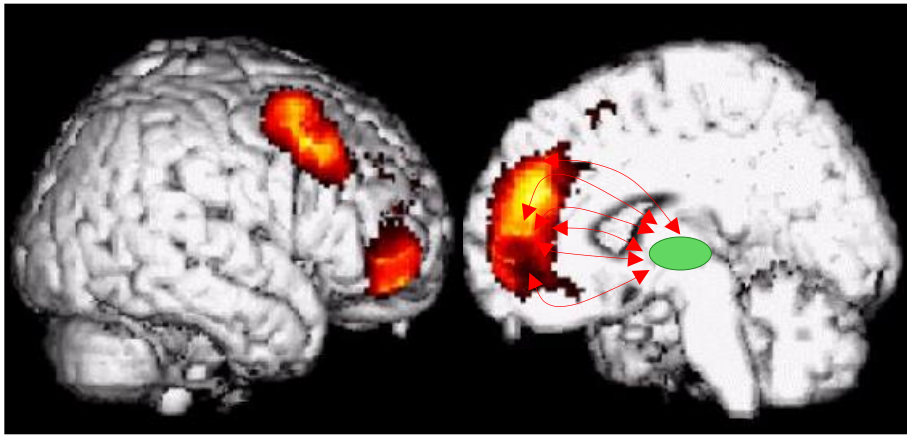
Agent sédatif (insomnie)



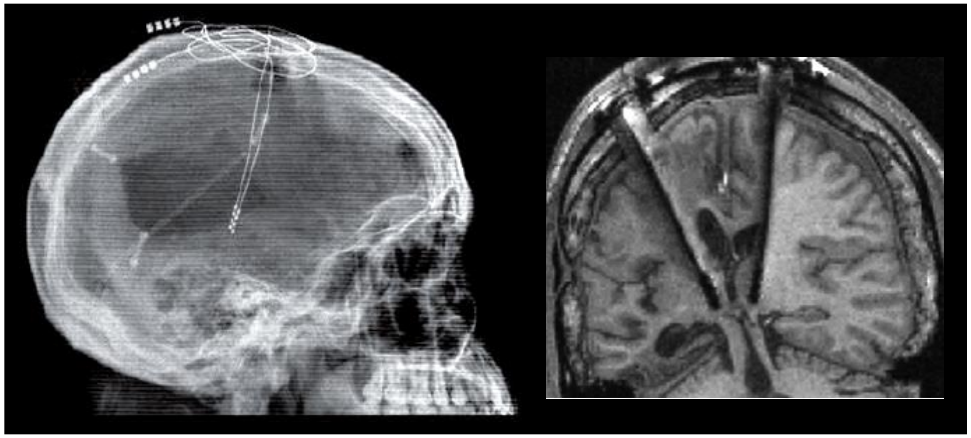
Chatelle & Thibaut, et al., Frontiers 2014

Stimulations cérébrales profondes

Recovery of consciousness = recovery of thalamo-cortical (prefrontal) connectivity

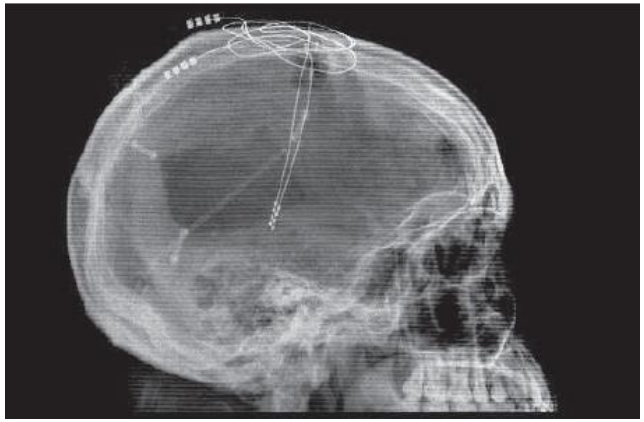


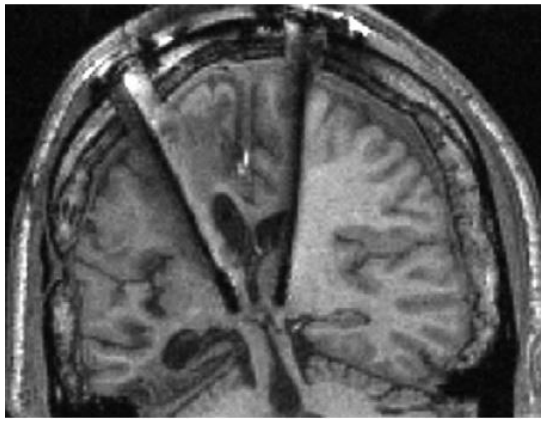
Intralaminar nuclei stimulation induces “recovery” from minimally responsive state

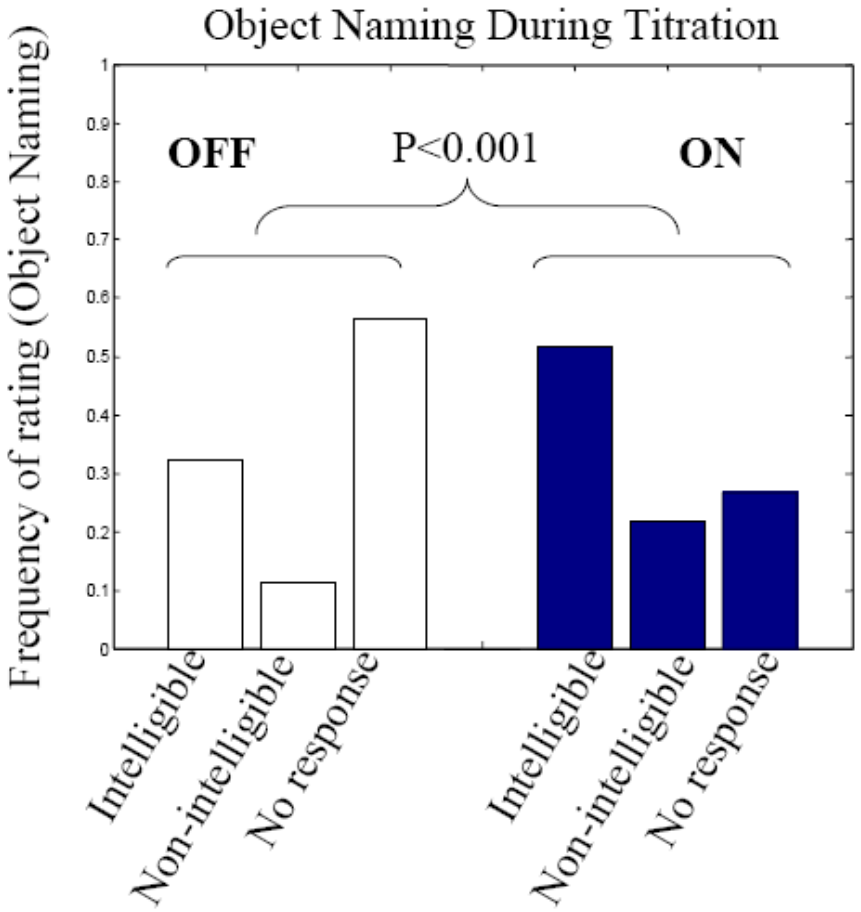


Laureys et al, *Lancet,* 2000
Schiff et al, *Nature*, 2007

Stimulations cérébrales profondes



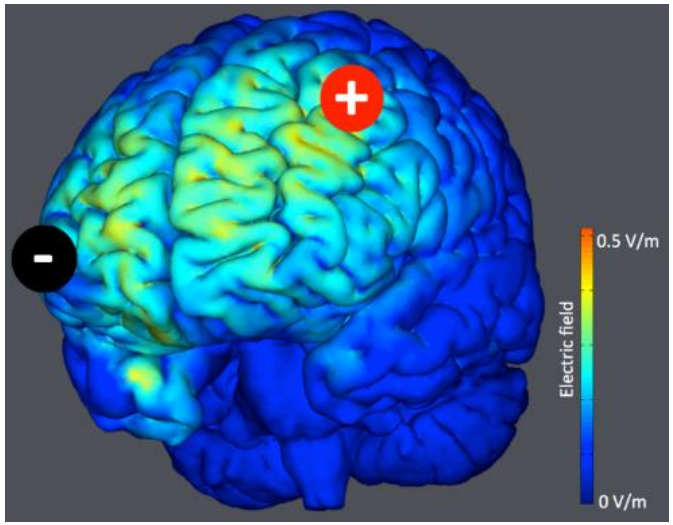




Schiff et al, *Nature*, 2007

Stimulations non-invasives

Stimulations transcraniennes à courant continu



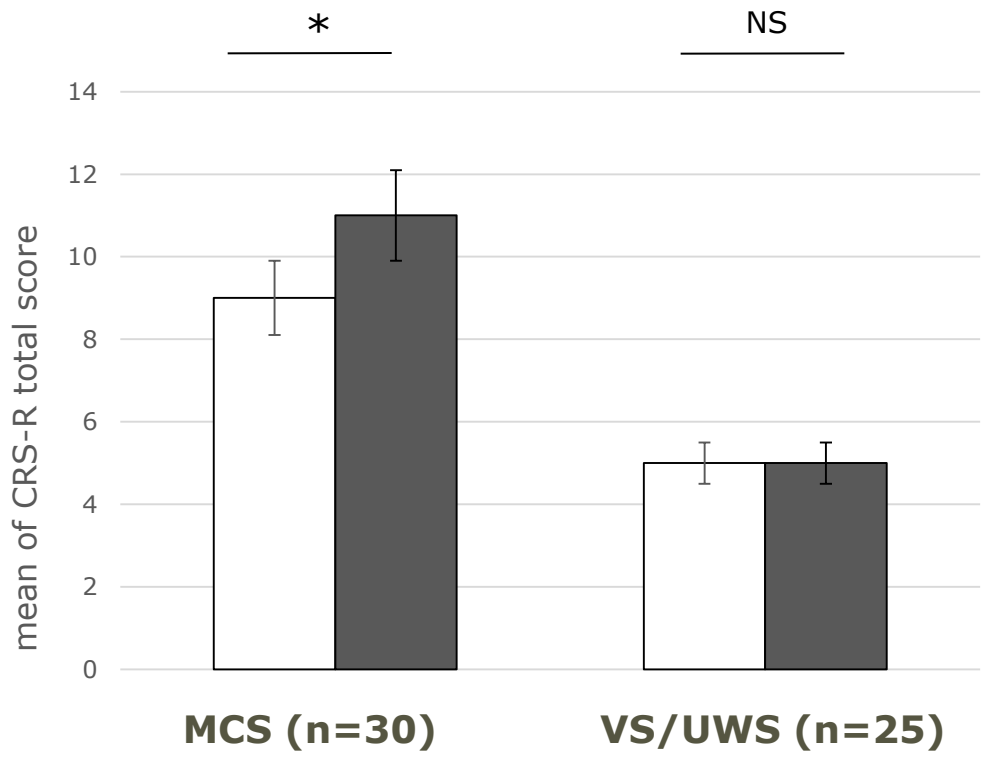
Courant continu de 2mA

20minutes sur le cortex préfrontal gauche

Thibaut et al, *Neurology, 2014*

Stimulations non-invasives

Stimulations transcraniennes à courant continu



➔ **15/55 répondants**

- 2 UWS; acute
- 13 MCS
  ➔ 43% of MCS
  5>1y post insult

* p<0.001

Thibaut et al, *Neurology, 2014*

Stimulations non-invasives

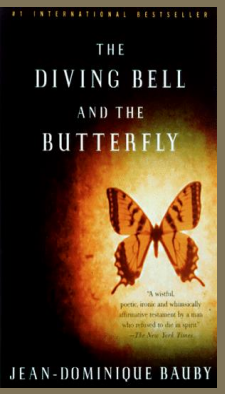
Stimulations transcraniennes à courant continu

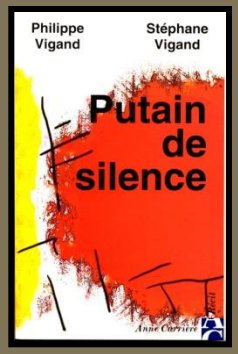
Utilisation d'une cuillère après une stimulation tDCS

Avant

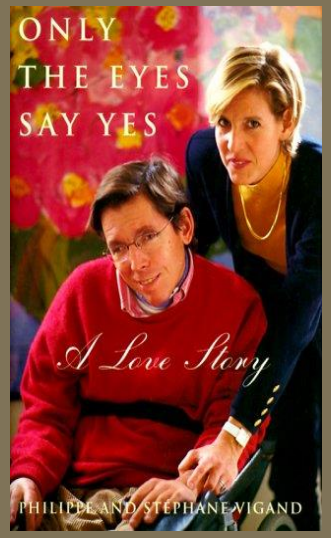
Après

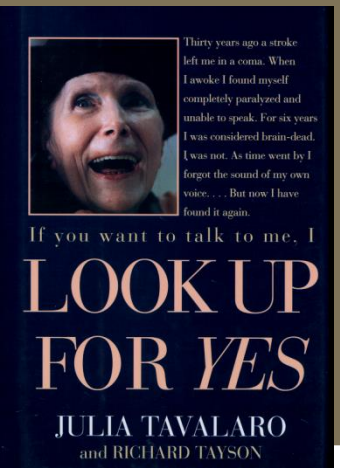
Thibaut et al, *Neurology, 2014*

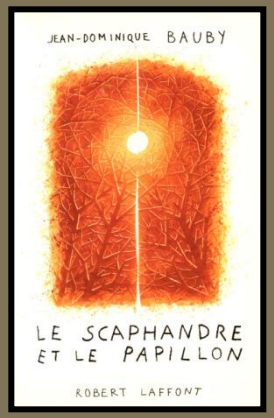




Locked-In Syndrome







ALIS
Association du Locked-in Syndrome

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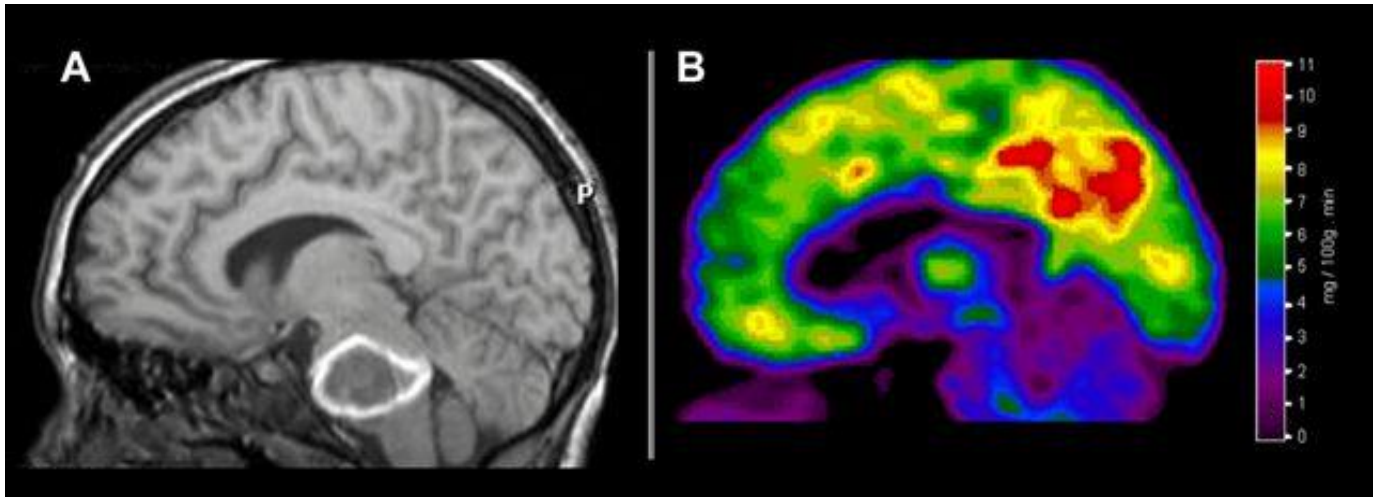
Locked-in syndrome

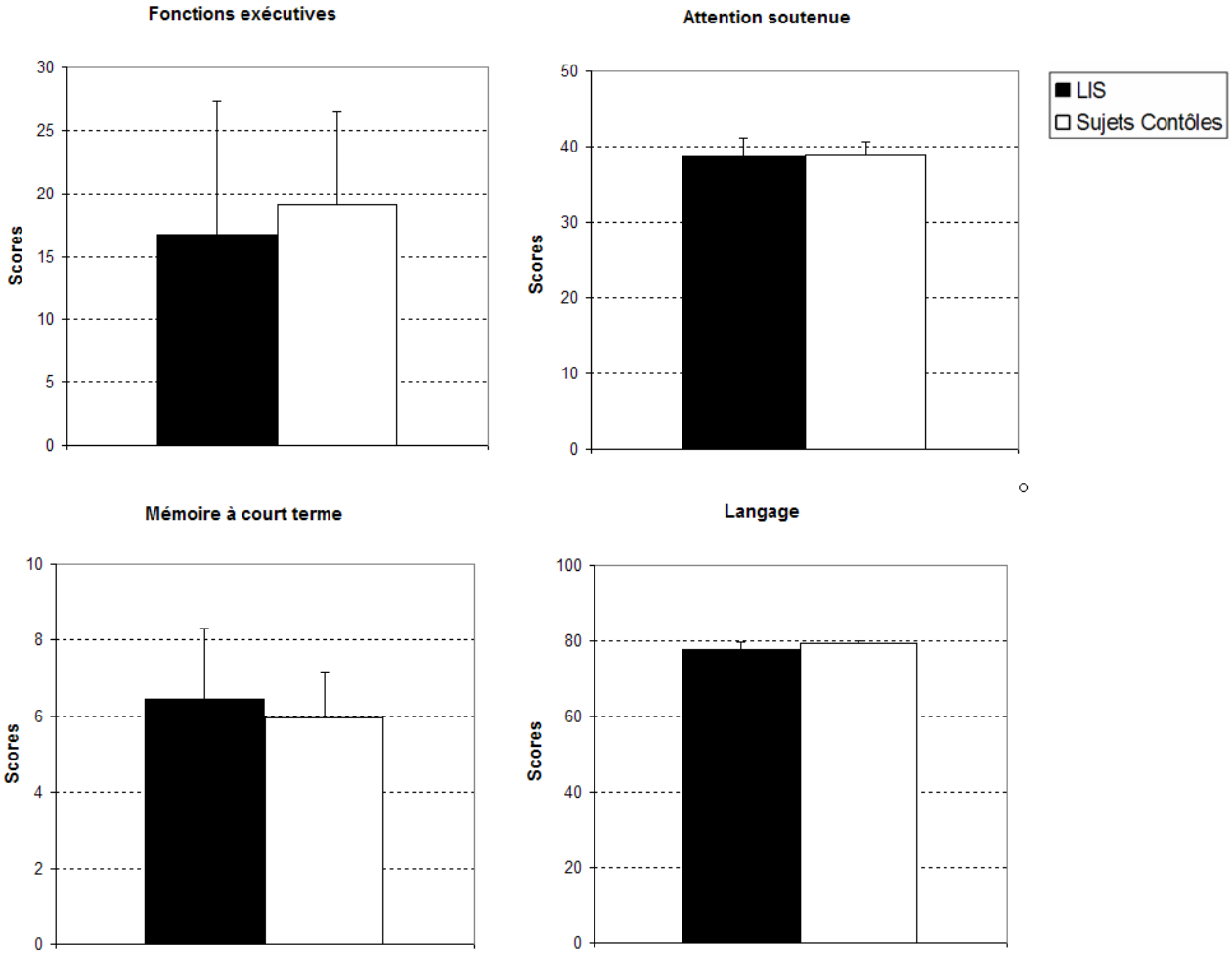
LIS - diagnostique



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

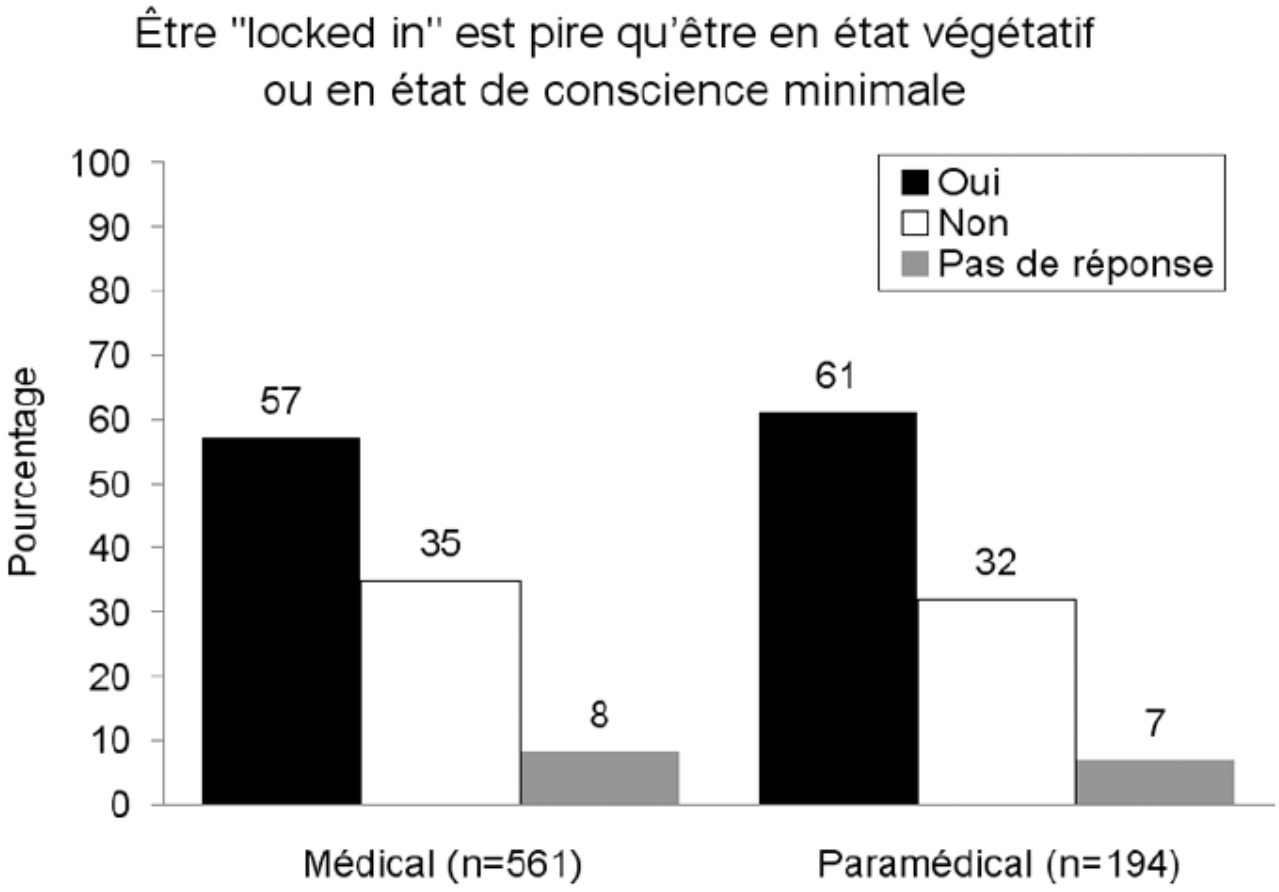
Laureys, Pellas et al., Progress in Brain Research, 2005

Fonctions cognitives



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

Qualité de vie & LIS



Bruno et al., Revue médicale de Liège, 2008

Qualité de vie & LIS

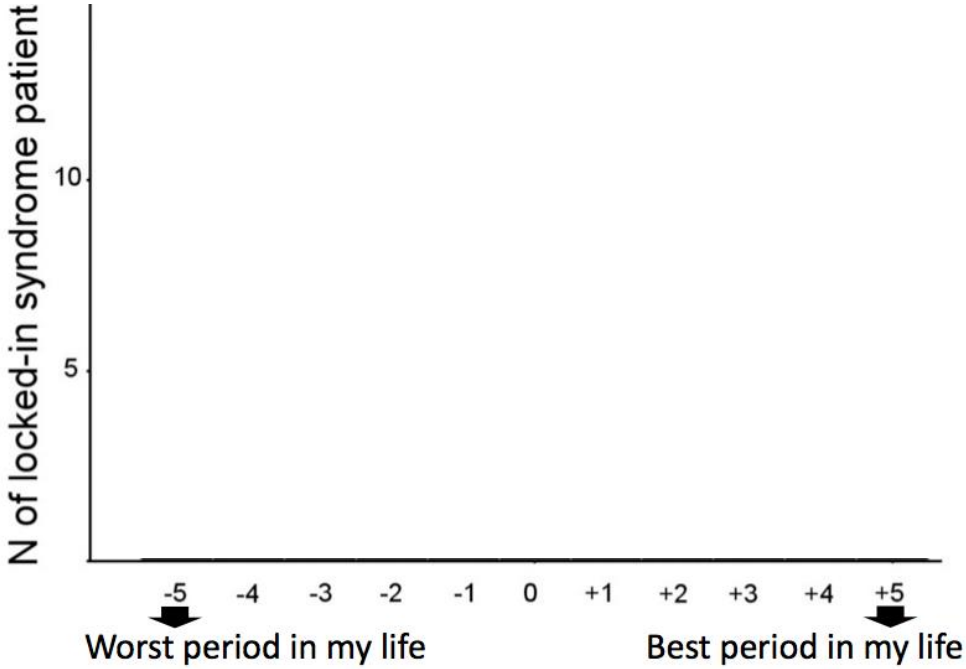
Open Access Research

BMJ open accessible medical research

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]

ALIS Association du Locked-in Syndrome



Bruno et al, *BMJ Open*, 2011

Qualité de vie & LIS

Open Access Research

BMJ open

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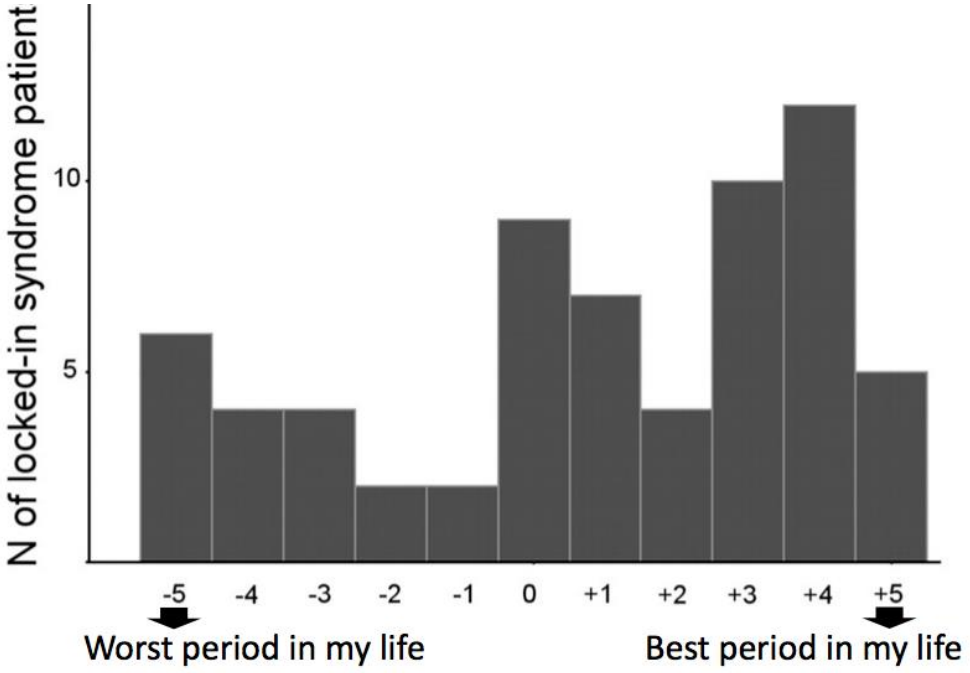
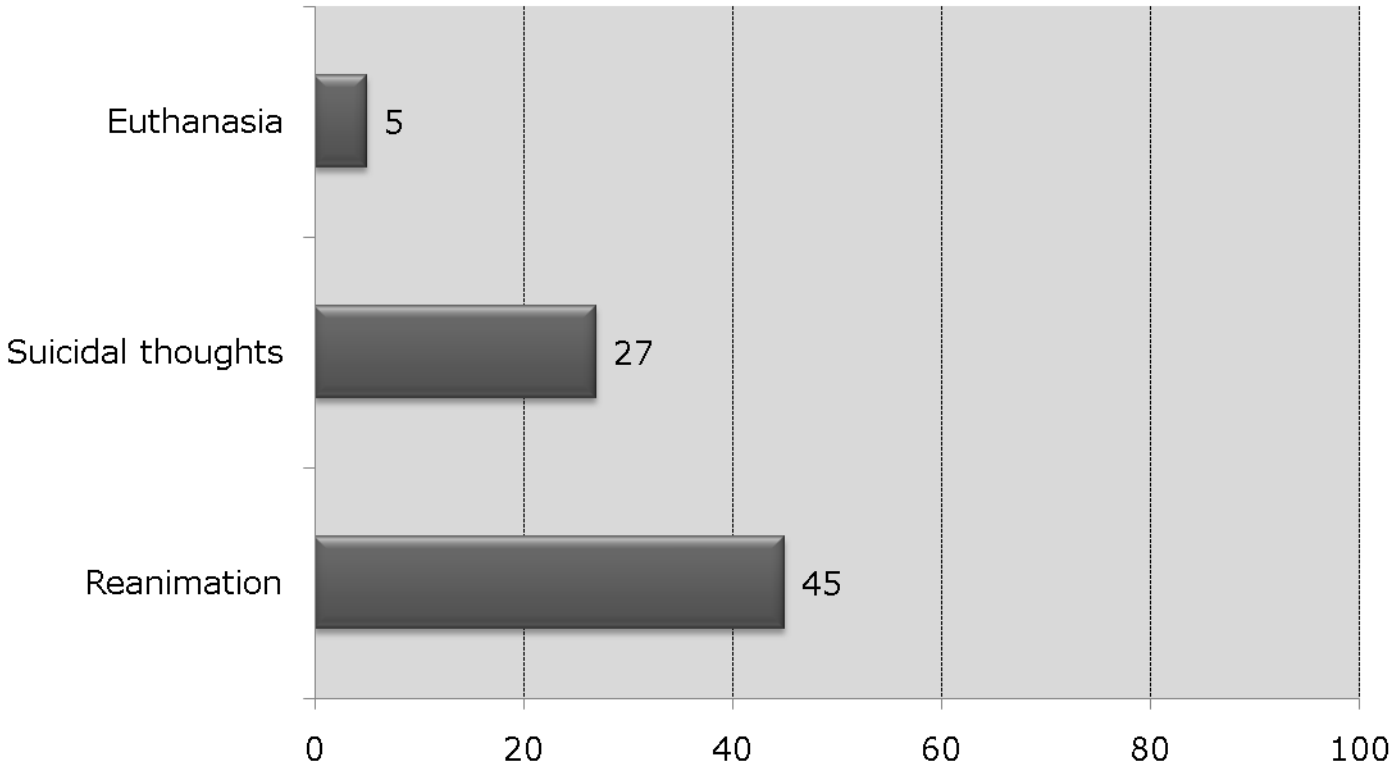
ALIS Association du Locked-in Syndrome

No ≠
between LIS and controls



Bruno et al, *BMJ Open*, 2011

Qualité de vie & LIS

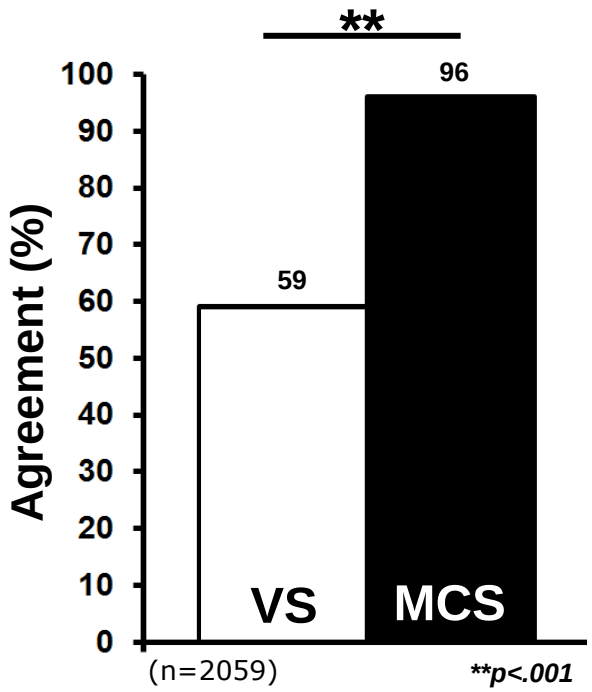


Questionnaire ALIS 2007

Questions éthiques

Prise en charge de la douleur

Pensez vous que les patients en … ressentent la douleur?



Question Predictors	Odds Ratio	95% Confidence Interval		p value
Do you think VS patients feel pain?				
Age	1.01	1.00	1.02	.050
Women	1.25	.99	1.58	.060
Northern Europe	1.00			
Central Europe	.81	.58	1.14	.240
Southern Europe	1.10	.76	1.60	.600
Paramedical professionals	1.56	1.20	2.00	<.001
Religious respondents	1.37	1.10	1.70	.004
Do you think MCS patients feel pain?				
Women	2.38	1.33	4.26	.003
Religious respondents	1.83	1.05	3.18	.031

Predicted response: "agreement"

Demertzi et al, Progress in Brain Research 2009
Demertzi & Racine et al, Neuroethics 2013

Douleur et fin de vie

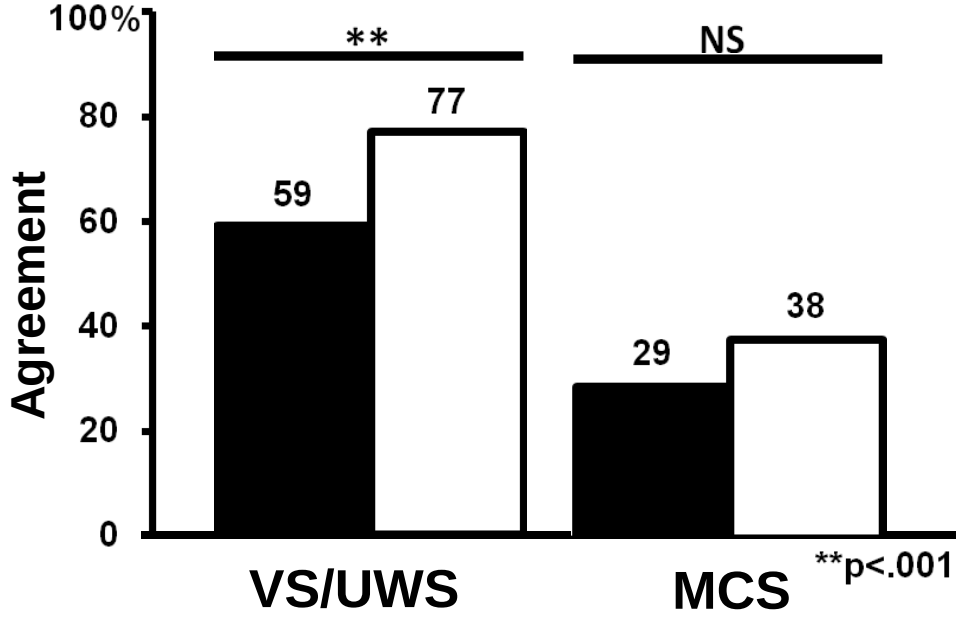
Pain Perception in Disorders of Consciousness: Neuroscience, Clinical Care, and Ethics in Dialogue

A. Demertzi · E. Racine · M-A. Bruno · D. Ledoux · O. Gosseries · A. Vanhaudenhuyse · M. Thonnard · A. Soddu · G. Moonen · S. Laureys

European Neurological Society

ENS

Le traitement peut être arrêter chez un patient chronique



(n=2259)

- Ressentent la douleur
- Ne ressentent pas la douleur

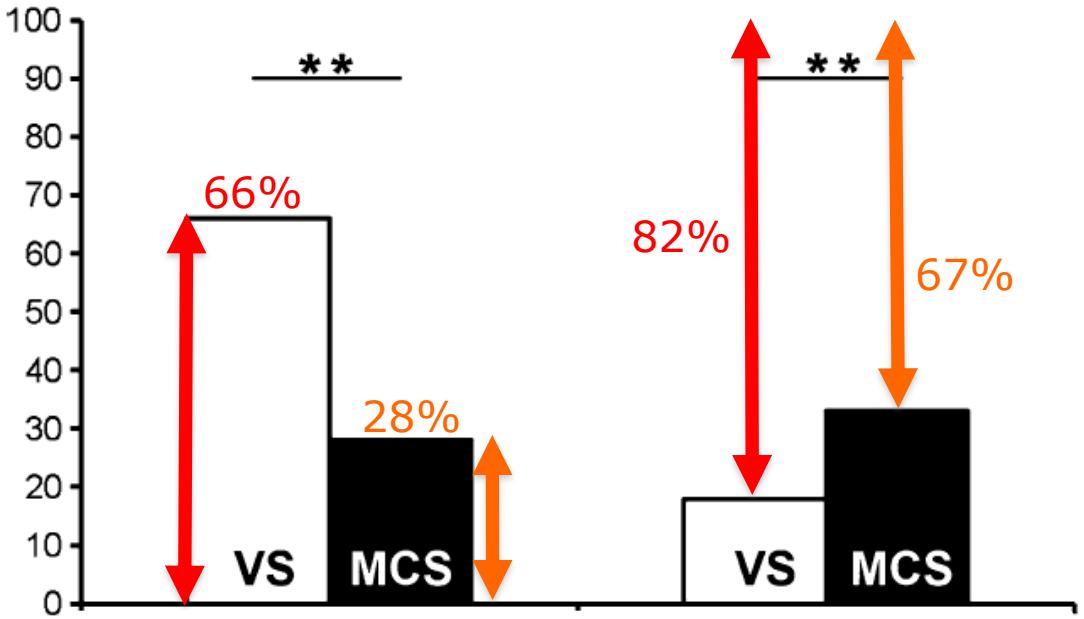
Demertzi & Racine et al, *Neuroethics* 2012

Décision de fin de vie

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 professionels médicaux



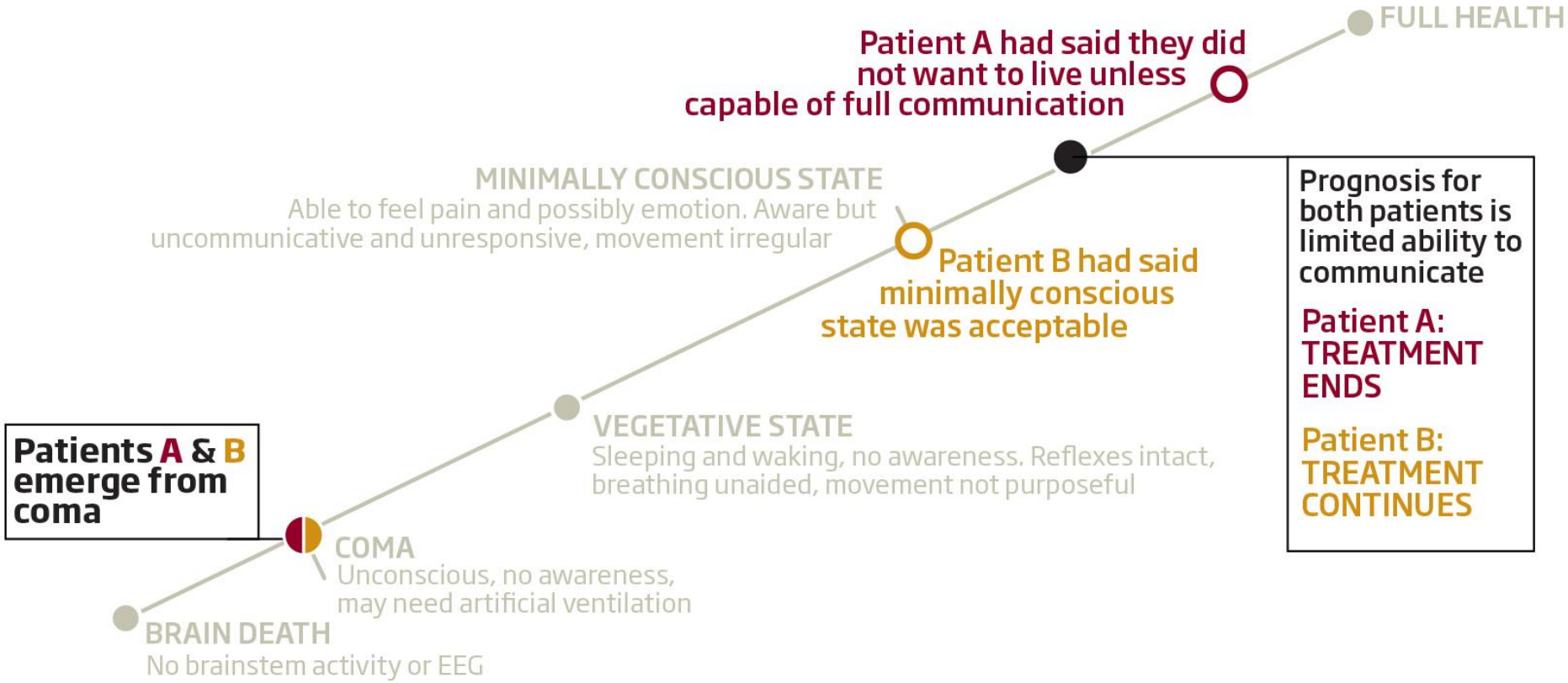
Est-il acceptable d'arrêter le traitement chez un patient chronique VS ou MCS?

Voudriez-vous être maintenu en vie si vous étiez dans un état chronique VS ou MVS?

European Neurological Society

Demertzi et al, *J Neurology* 2011

Identifier un proxy



Conclusion

Translational research

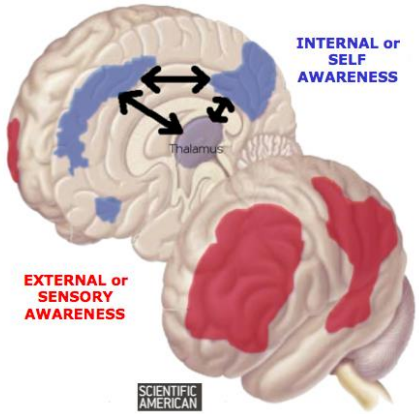
Corrélats neuronaux de la conscience
≈ connectivité au sein d'un réseau frontopariétal

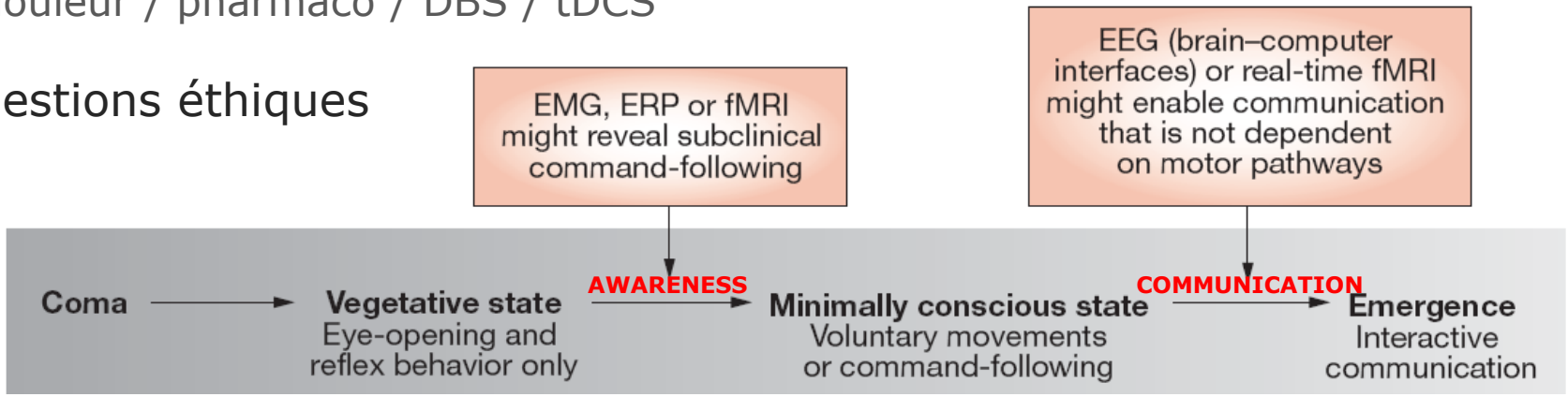
Echelles cliniques
CRS-R, NCS-R

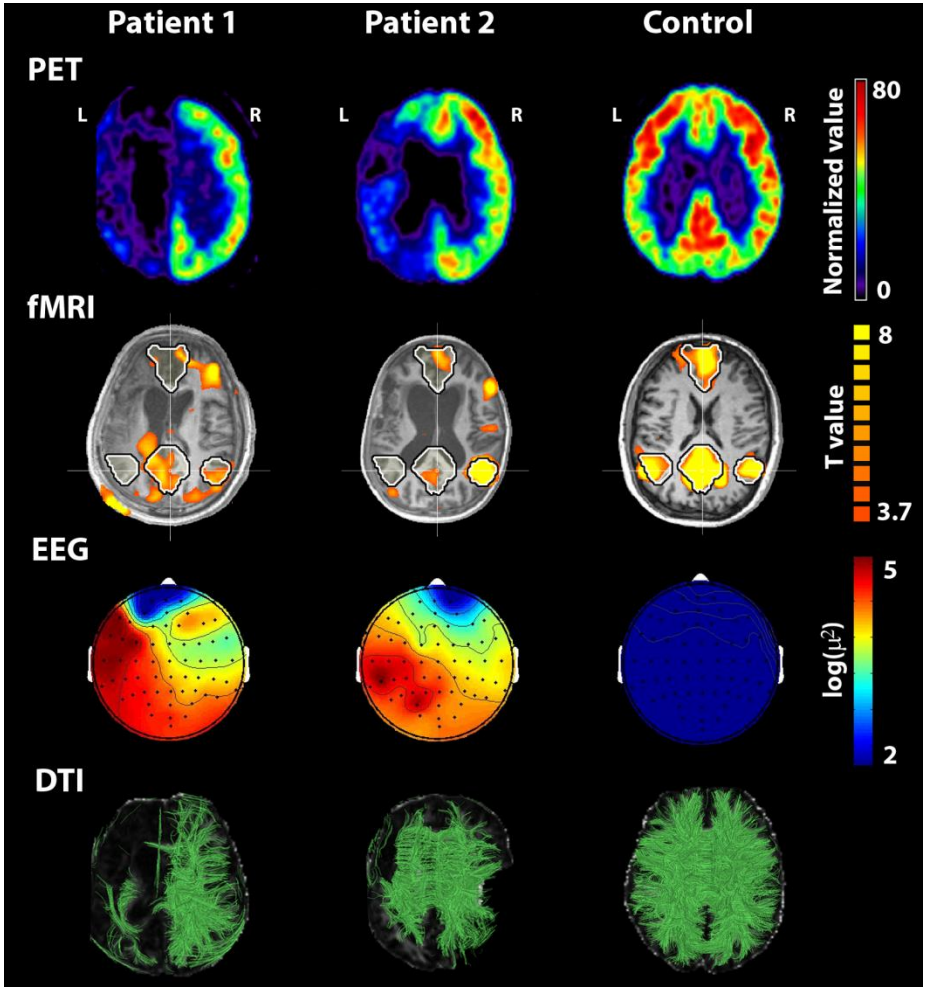
Outils paracliniques
fMRI, PET-scan, EEG, BCIs

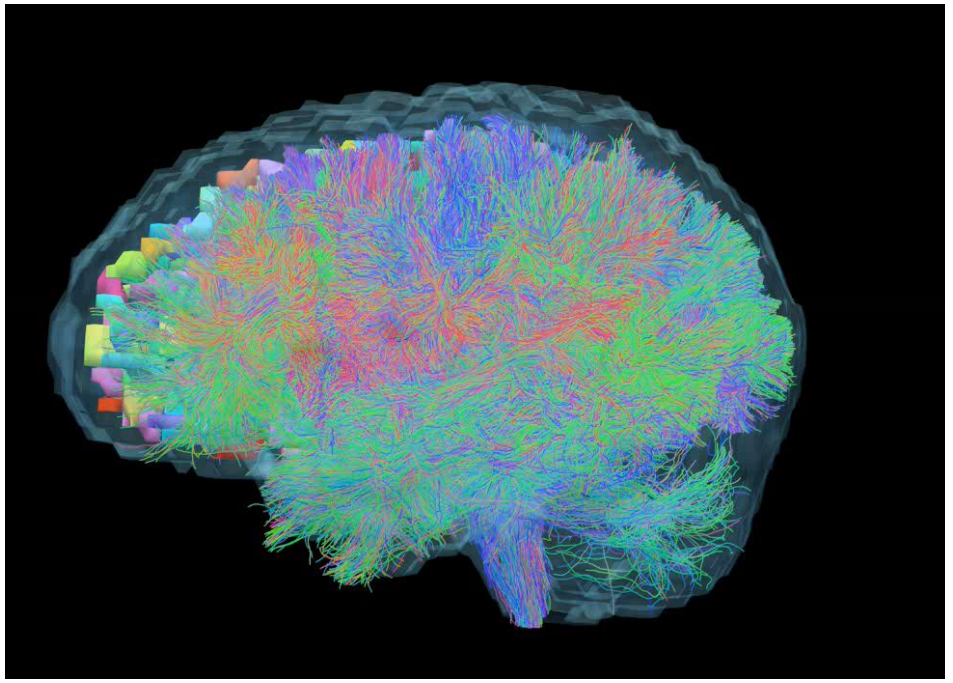
Traitements
douleur / pharmaco / DBS / tDCS

Questions éthiques









Erik Ziegler, *Cyclotron Art Committee*

Bruno et al, *Prog Brain Res,* 2011

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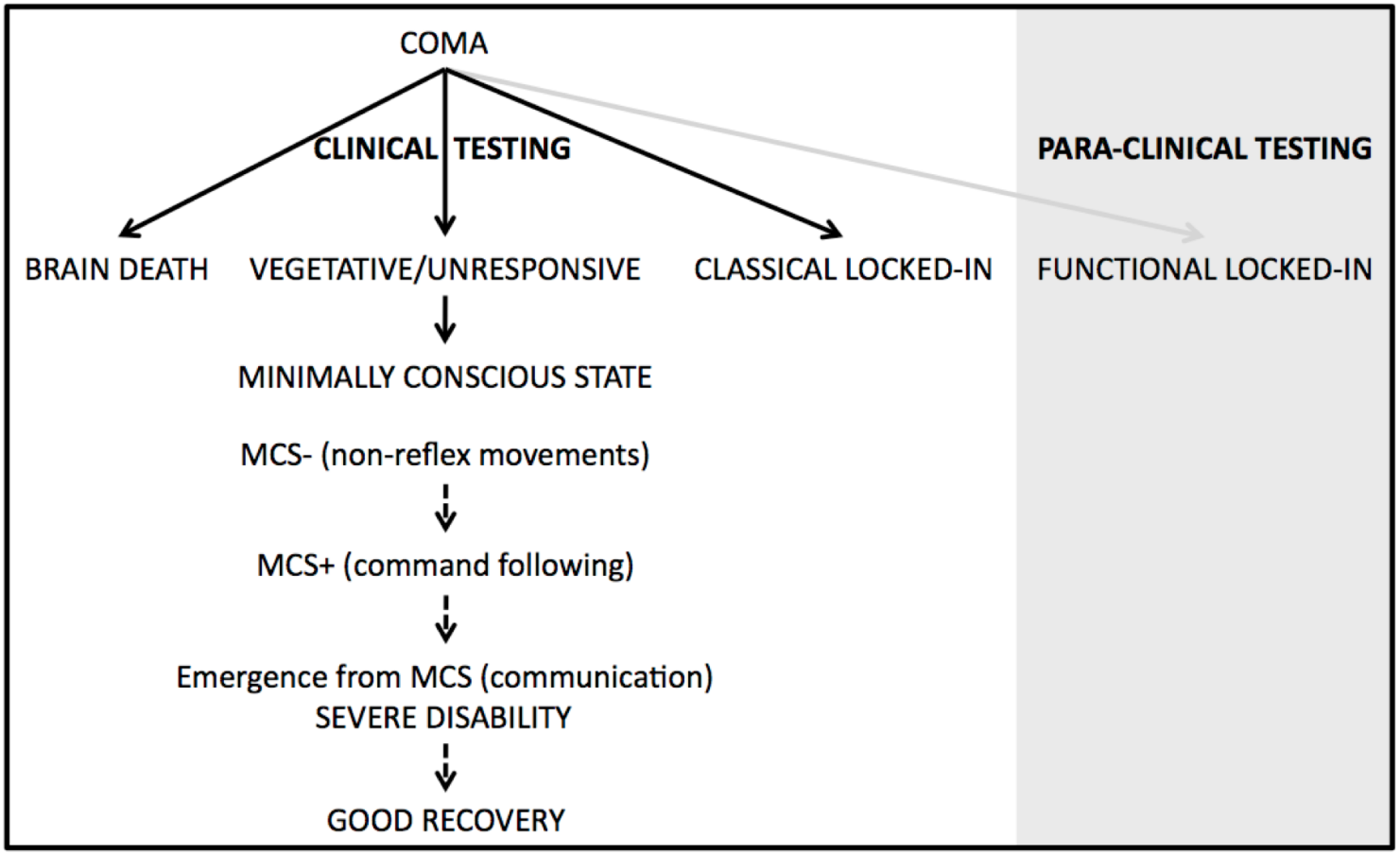

Bruno, Vanhaudenhuyse et al *J Neurology,* 2011