

Les corrélats neuronaux de la conscience

Sarah Wannez

Doctorante

Coma Science Group

Centre de Recherche du Cyclotron & Service de Neurologie

Université & Centre Hospitalier Universitaire de Liège



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CHU
de Liège

Plan



Terry Schiavo * 1963, vegetative 1990, † 2005



Eluana Englaro * 1970, vegetative 1992, † 2009



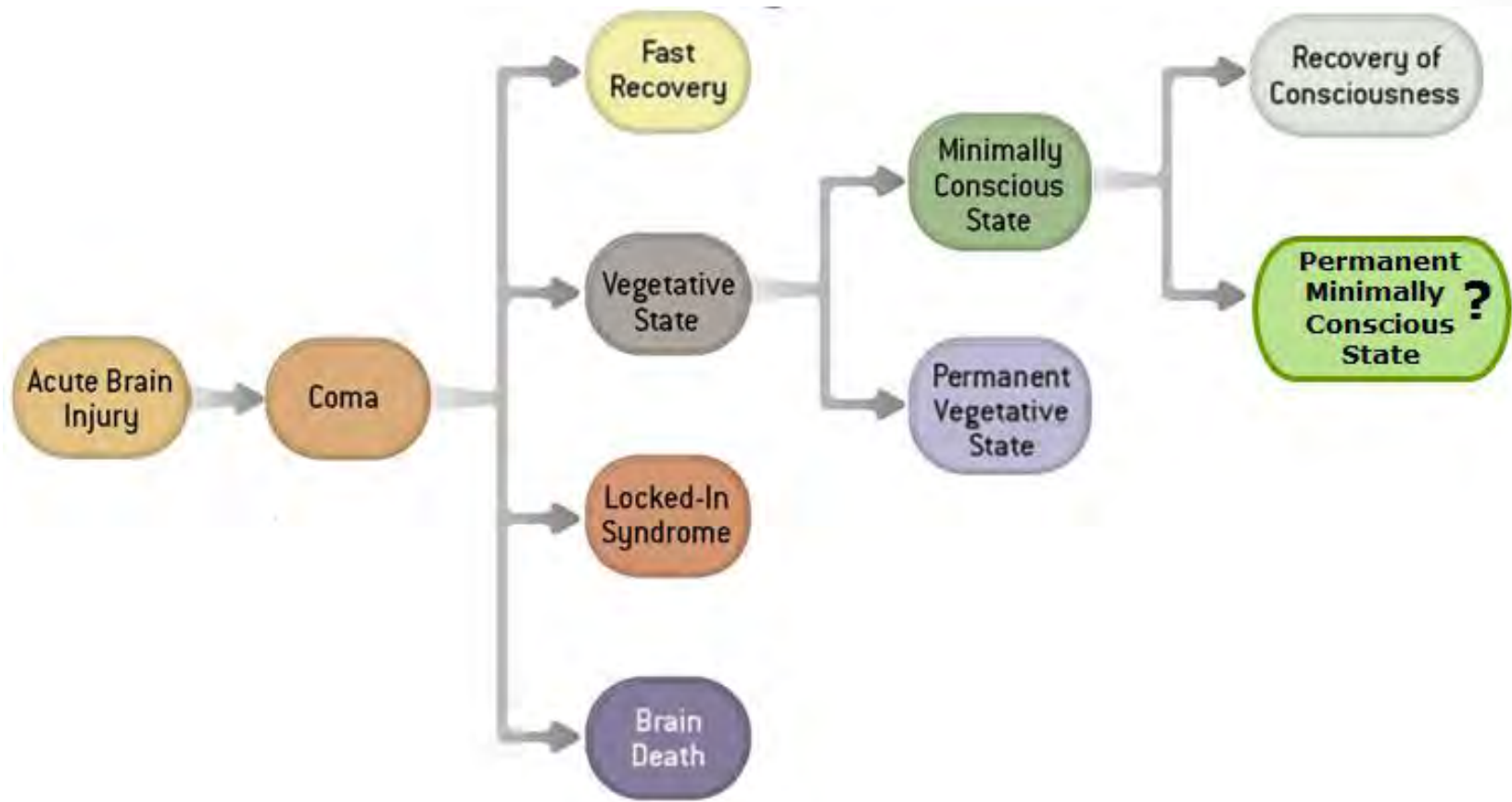
Rom Houben * 1969, LIS 1983

- Conscience
- Corrélats neuronaux
- Diagnostic
- Douleur et émotions
- Pronostic
- Traitement
- Conclusion



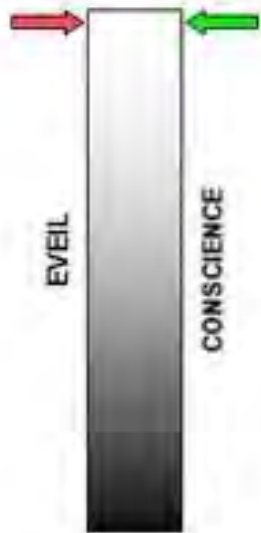
CONSCIENCE

Altération de la conscience

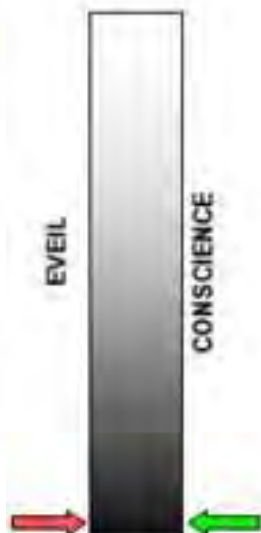


Les deux composantes de la conscience

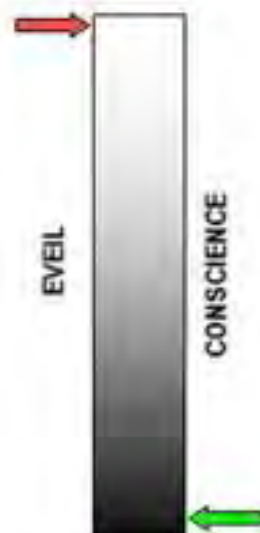
NORMAL CONSCIOUSNESS



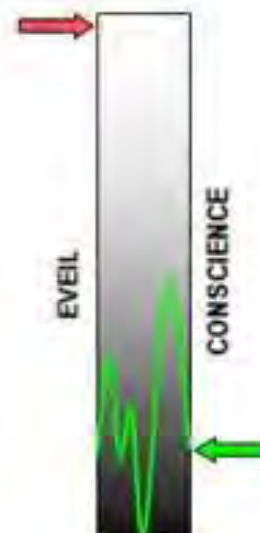
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VEGETATIVE STATE



MINIMALLY CONSCIOUS STATE

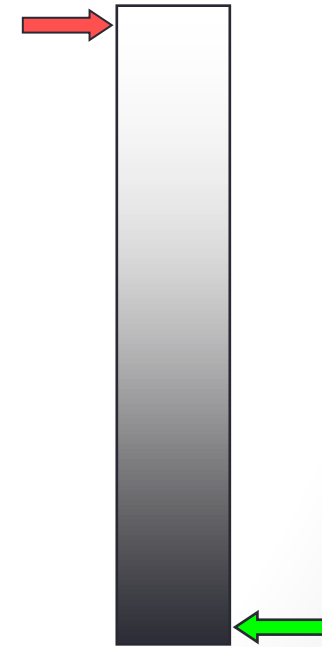


LOCKED IN SYNDROME



Syndrome d'éveil non répondant / État végétatif

- Pas de signe de conscience
- Pas d'interaction avec l'environnement
- Pas de comportement volontaire en réponse à des stimuli visuels, auditifs, tactiles ou douloureux
- Pas de compréhension ou d'expression langagière
- Cycles veille-sommeil



Un nouveau nom pour « végétatif »

BMC Medicine

Highly accessed Open Access

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

Steven Laureys¹, Gastone G. Celesia², Francois Colzani³, Jan Lavrijsen⁴, José León-Carrión⁵, Walter G. Sannita^{6,7}, Leon Szabon⁸, Erich Schmutzhard⁹, Klaus R. von Wild^{10,11}, Adam Zeman^{1,2} and Giuliano Dolce^{1,2} for the European Task Force on Disorders of Consciousness

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



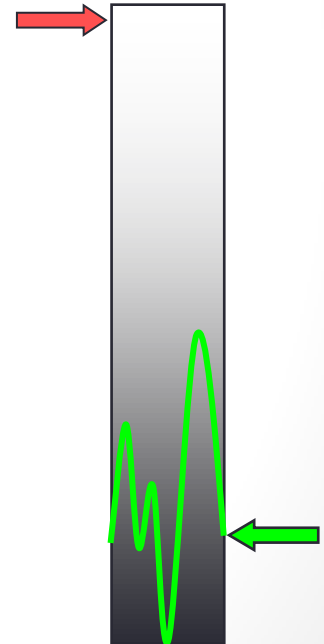
"There's nothing we can do...
he'll always be a vegetable."



État de conscience minimale

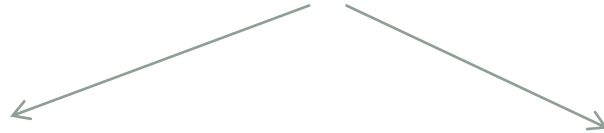
Preuves limitées mais clairement discernables de conscience de soi ou de l'environnement

- Réponse à la commande
- Réponse oui/non (gestuelle ou verbale, sans tenir compte de l'exactitude)
- Verbalisation intelligible
- Comportement dirigé vers un but:
 - Sourires appropriés
 - Vocalisations ou gestes appropriés
 - Chercher à atteindre des objets
 - Toucher ou tenir des objets
 - Poursuite visuelle ou fixation visuelle
- Emergence de l'état de conscience minimale
 - Communication fonctionnelle interactive
 - Utilisation fonctionnelle de deux objets différents



Nouvelle terminologie

ETAT DE CONSCIENCE MINIMALE



ECM +

Réponse à la commande

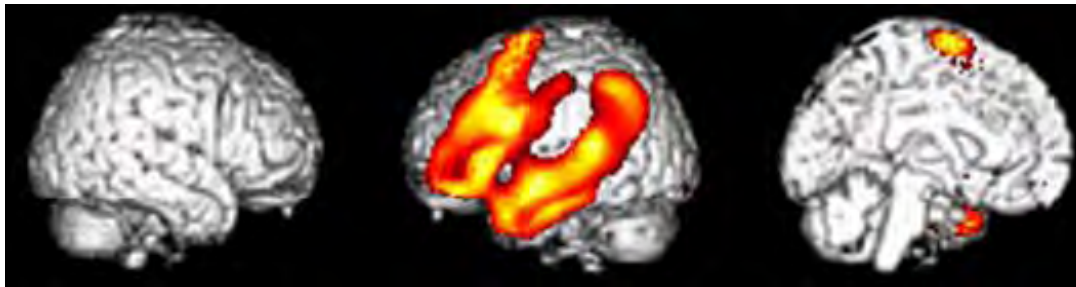
ECM –

Localisation à la douleur

Poursuite visuelle

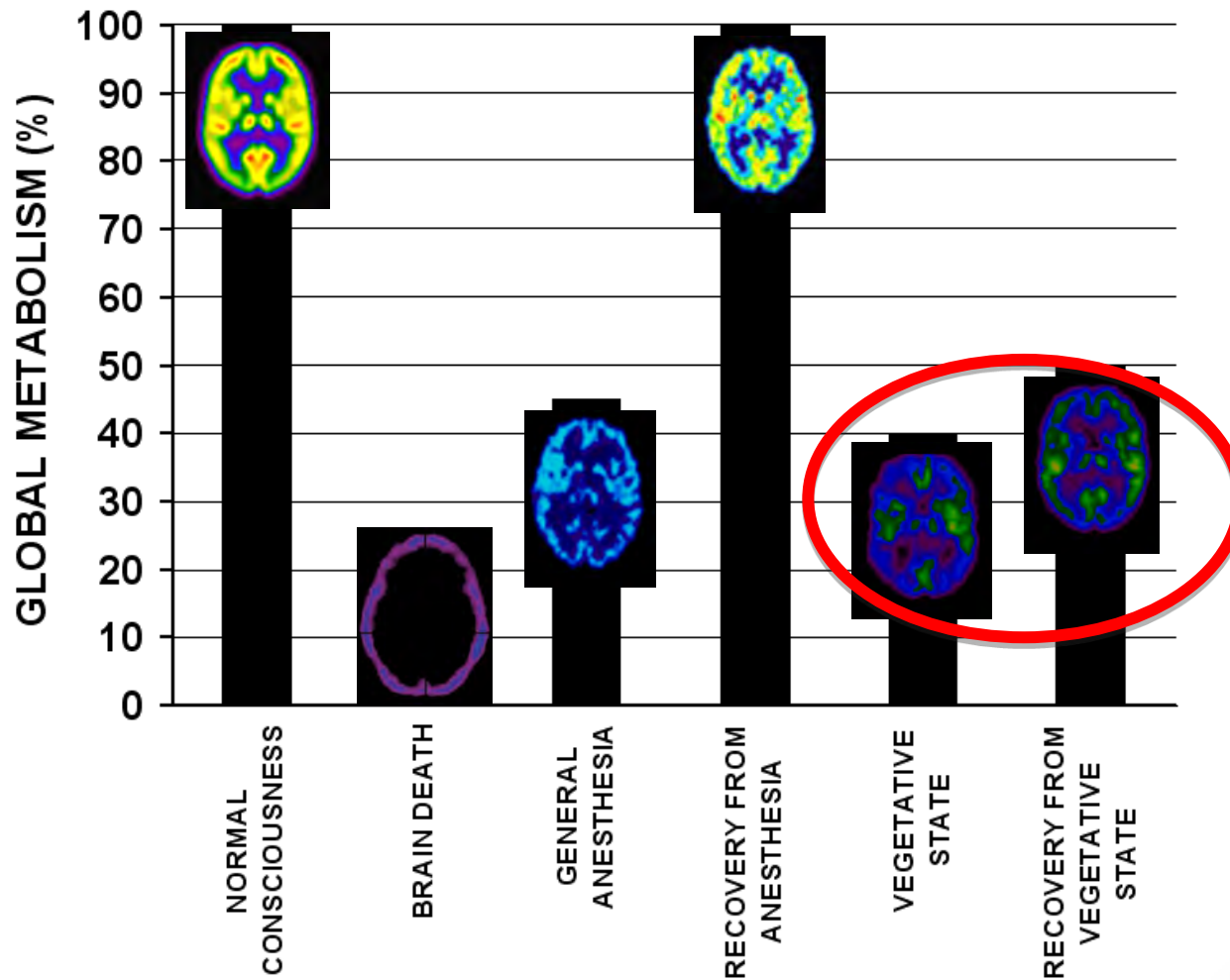
Sourires et pleurs
contextualisés

ECM+ > ECM -



CORRÉLATS NEURONAUX

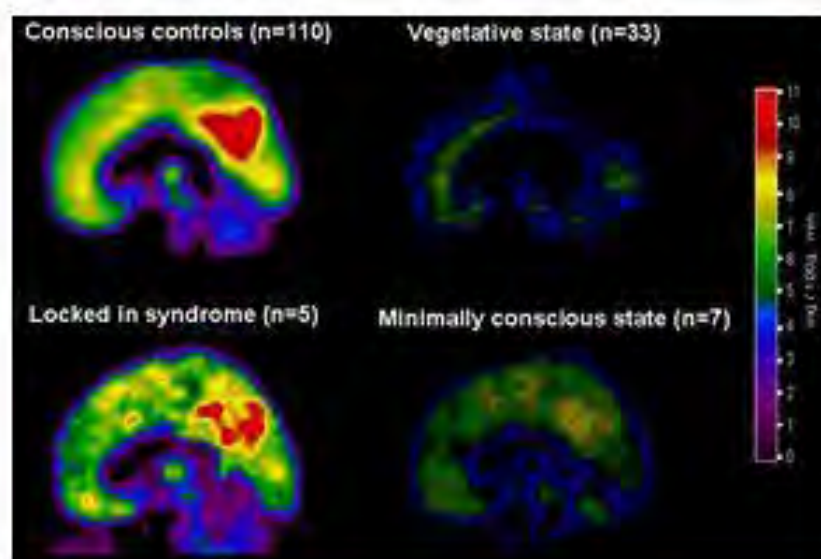
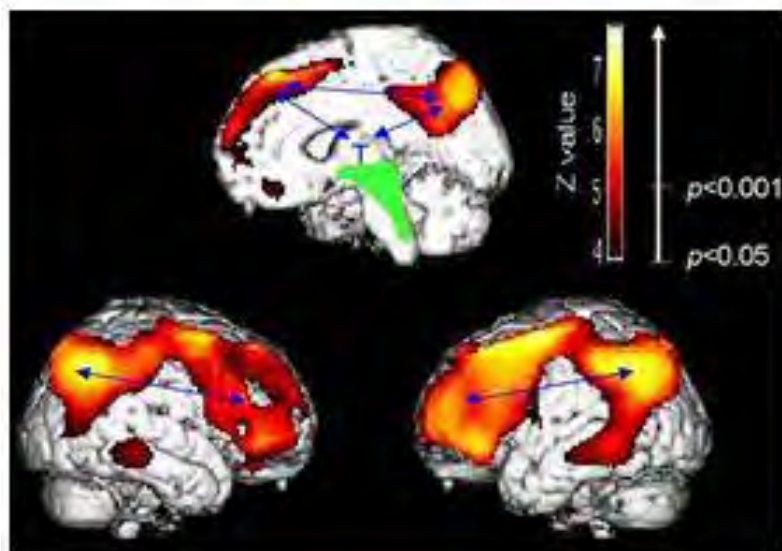
Conscience ≠ Fonction cérébrale globale



Conscience \approx Fronto-pariétal

Aires systématiquement dysfonctionnelles chez les patients en syndrome d'éveil non répondant et récupérant une activité après récupération de la conscience

Le précuneus est une aire critique dans la connectivité fronto-pariétale

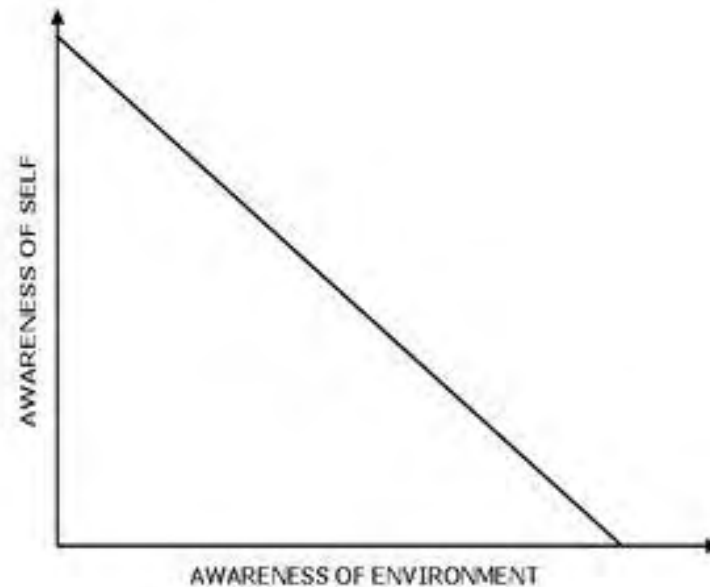
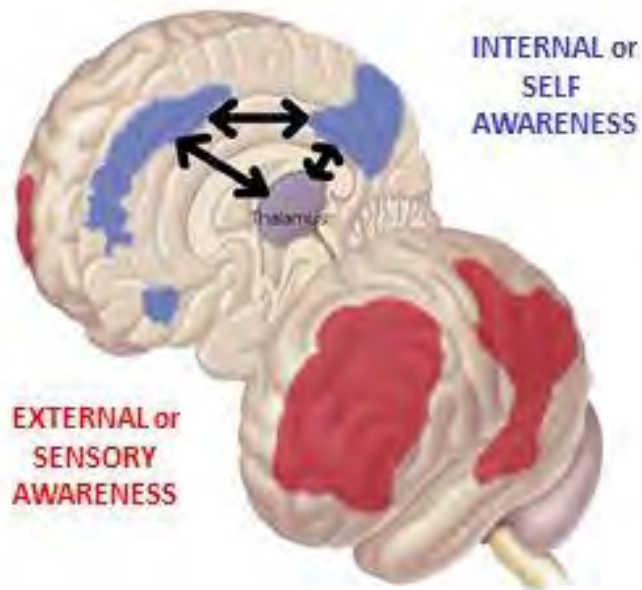


Laureys et al., *Neuroimage*, 1999

Laureys et al., *J Neurol Neurosurg Psychiatry*, 1999

Laureys et al., *Lancet Neurology*, 2004

Les deux réseaux de la conscience



DIAGNOSTIC

Erreurs diagnostiques

N= 103 patients cérébro-lésés

- 45 diagnostiqués par le corps médical comme « végétatifs »
- 18 présentaient des signes de conscience (Coma Recovery Scale- Revised)



41% d'erreurs diagnostiques

Coma Recovery Scale - Revised

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 | | | | | | | | | |



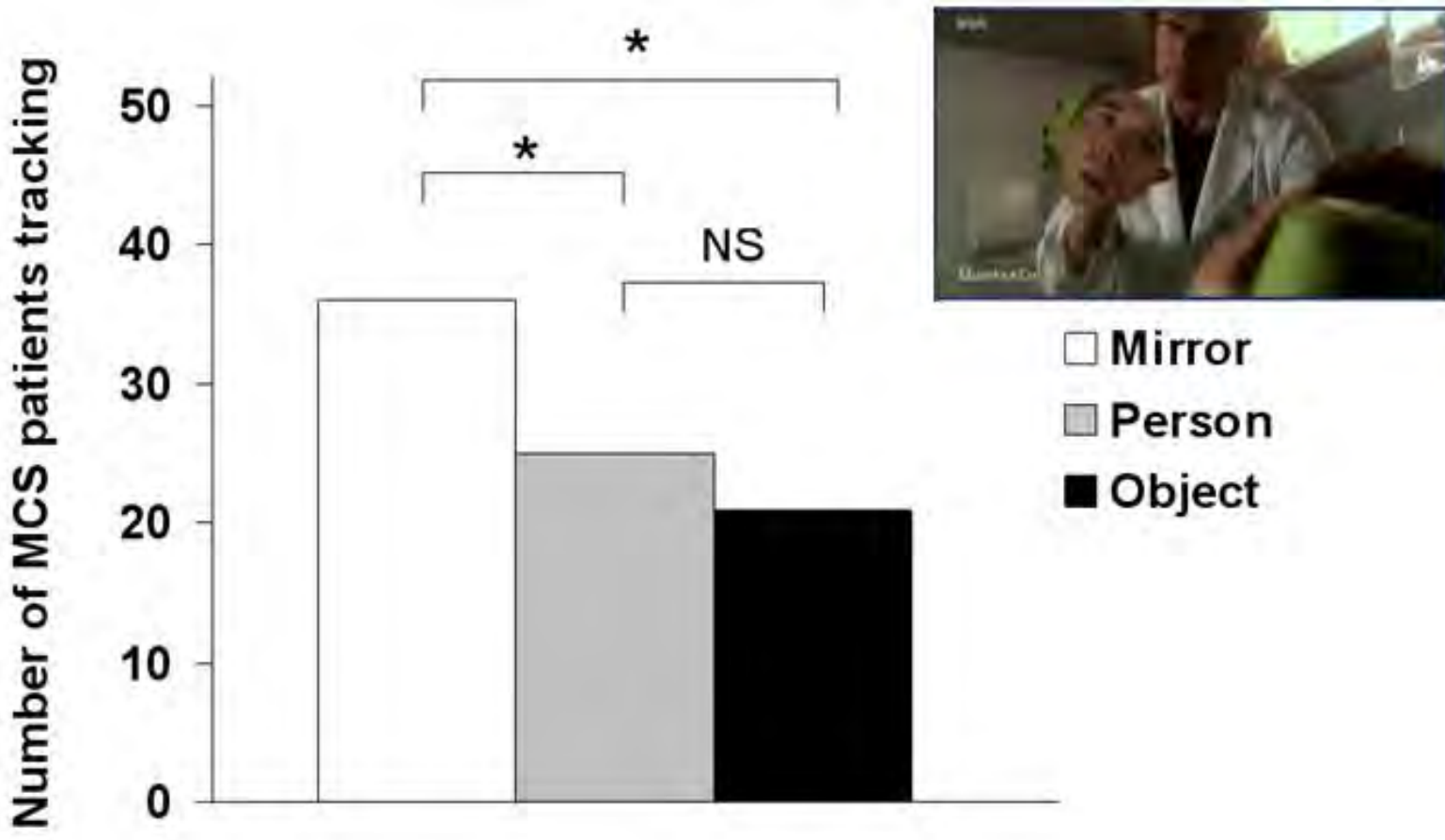
SELF-STUDY DVD OFFER

**COMA RECOVERY SCALE - REVISED:
GUIDELINES FOR ADMINISTRATION AND
SCORING**

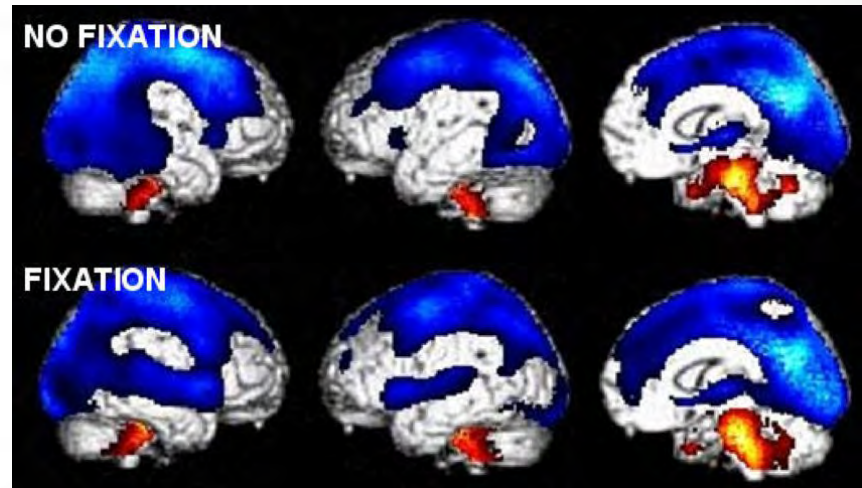
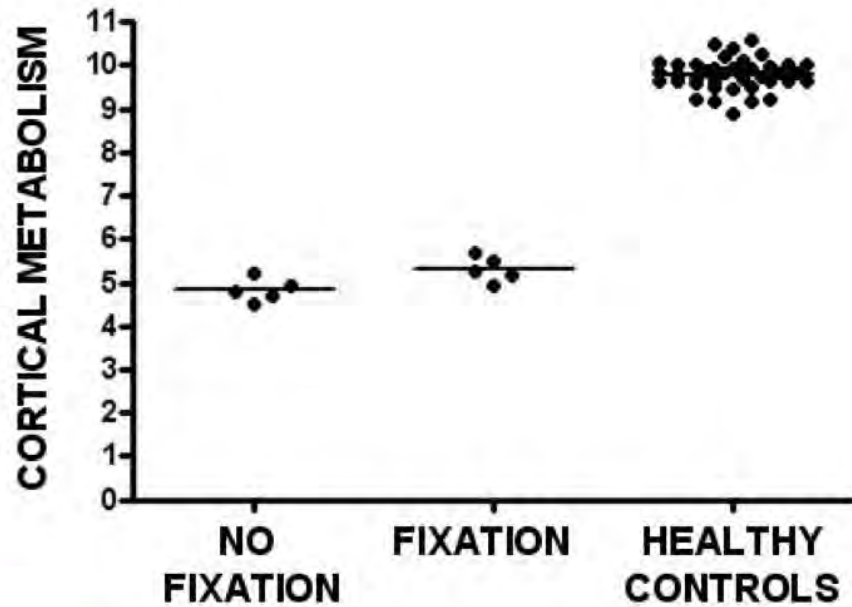


coma@chu.ulg.ac.be

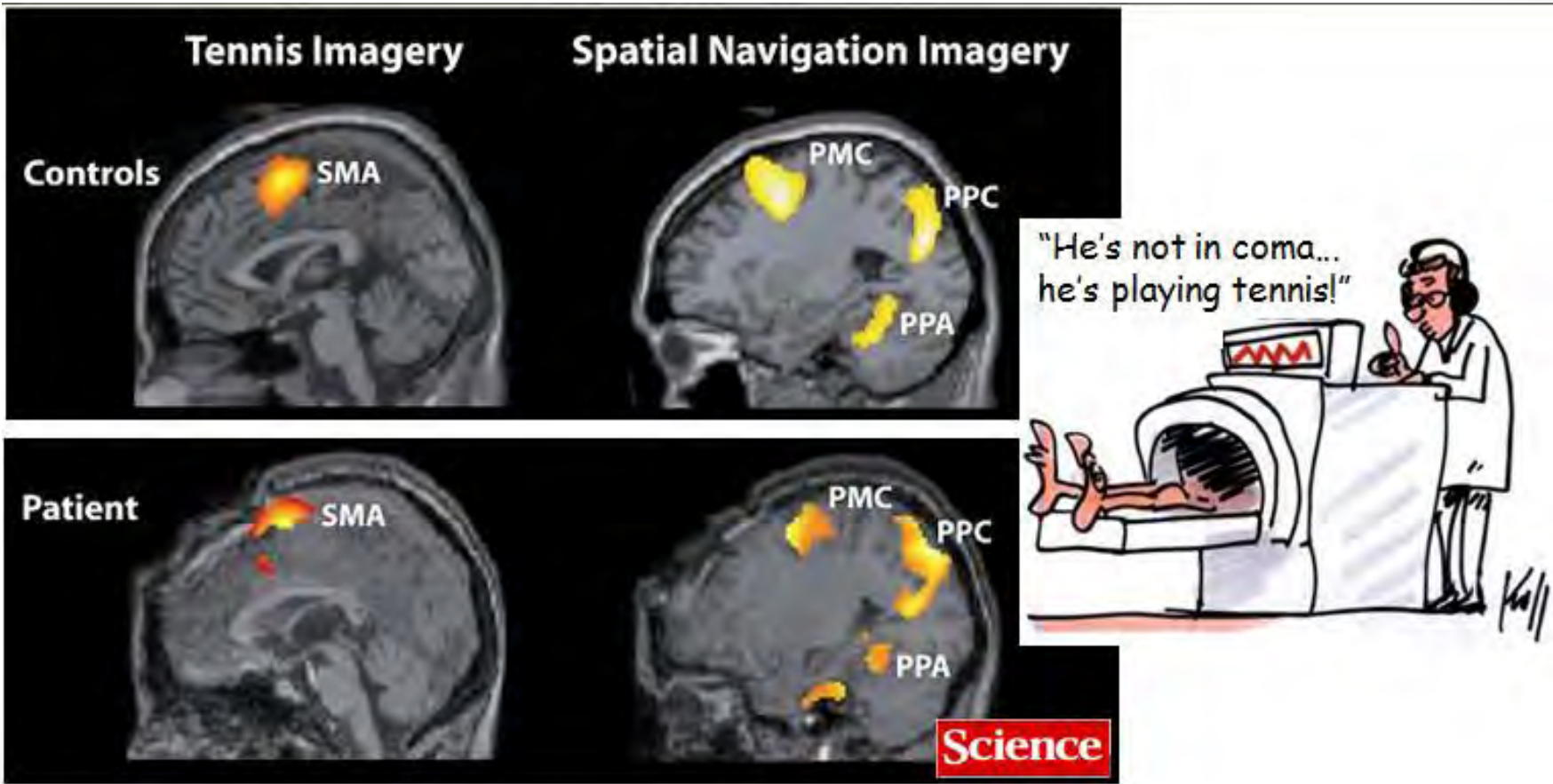
Poursuite visuelle : miroir !



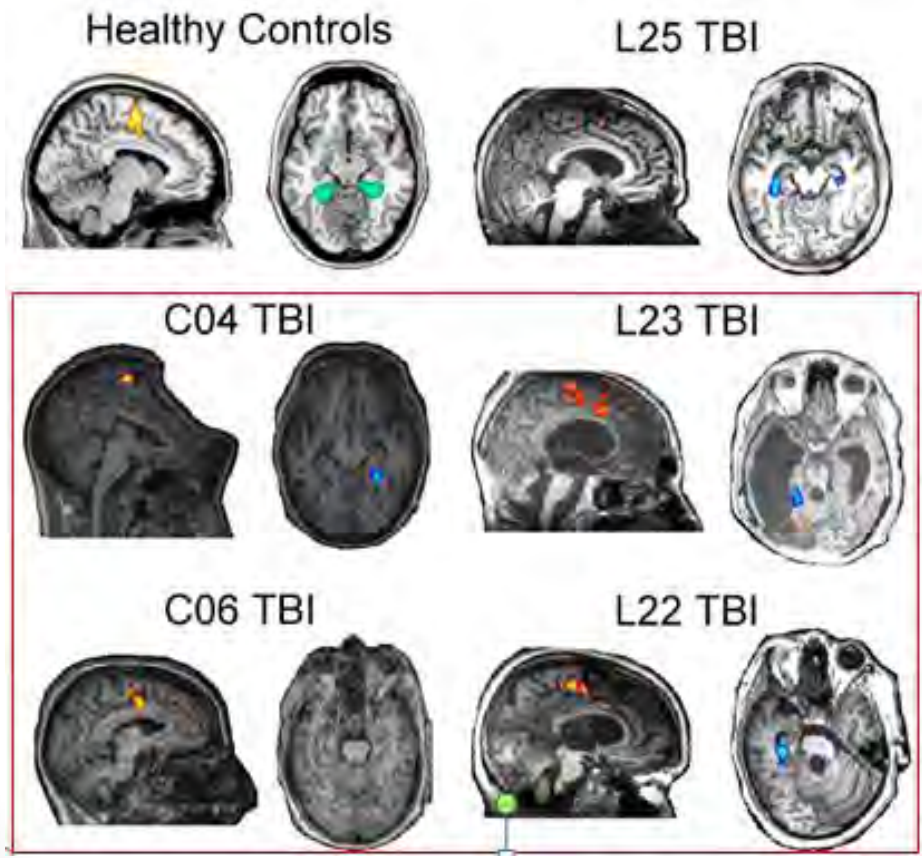
La fixation visuelle est un réflexe



Signes de conscience en IRMf

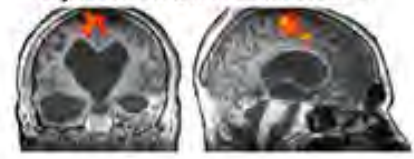


Communication oui/non par IRMf

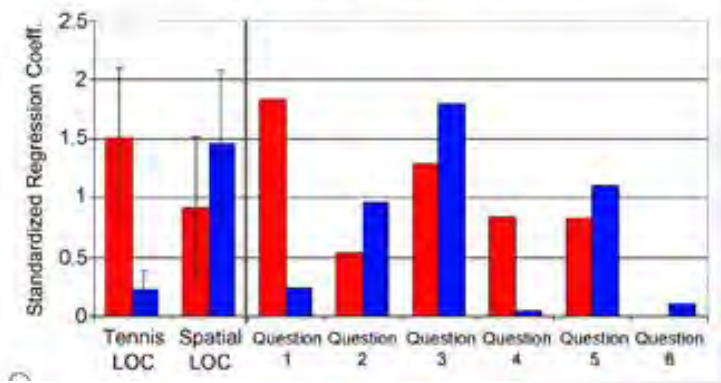


Imagine **Tennis** to answer 'YES'
 Imagine **Navigating** to answer 'NO'

Is your father's name Alexander ?



Is your father's name Thomas ?



Interface cerveau/ordinateur par EEG

“MOVE YOUR FOOT”



“MOVE YOUR HAND”



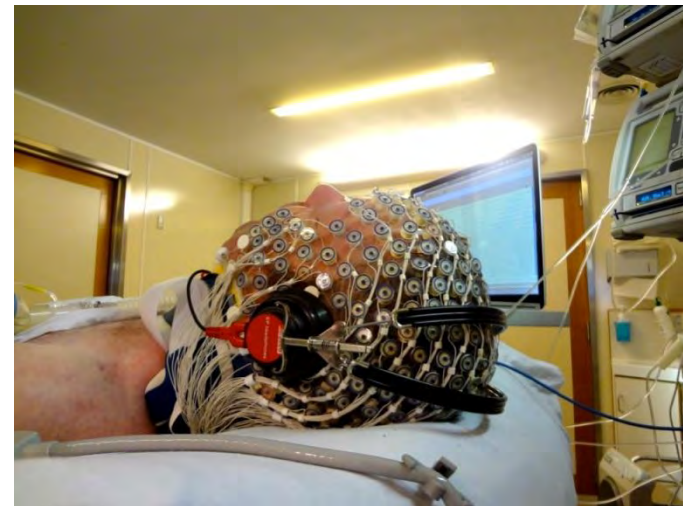
HEALTHY
CONTROL
SUBJECT

“VEGETATIVE”
UNRESPONSIVE
PATIENT

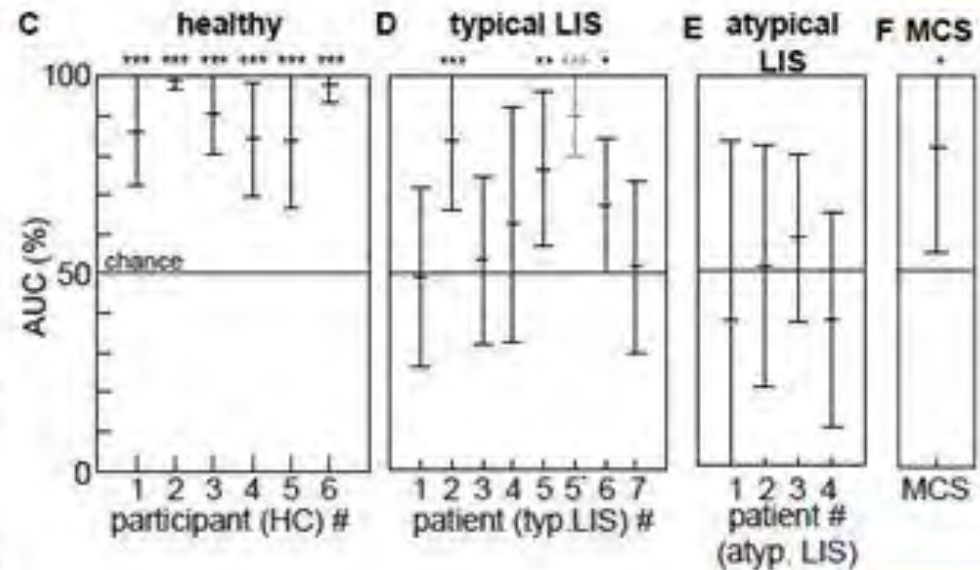
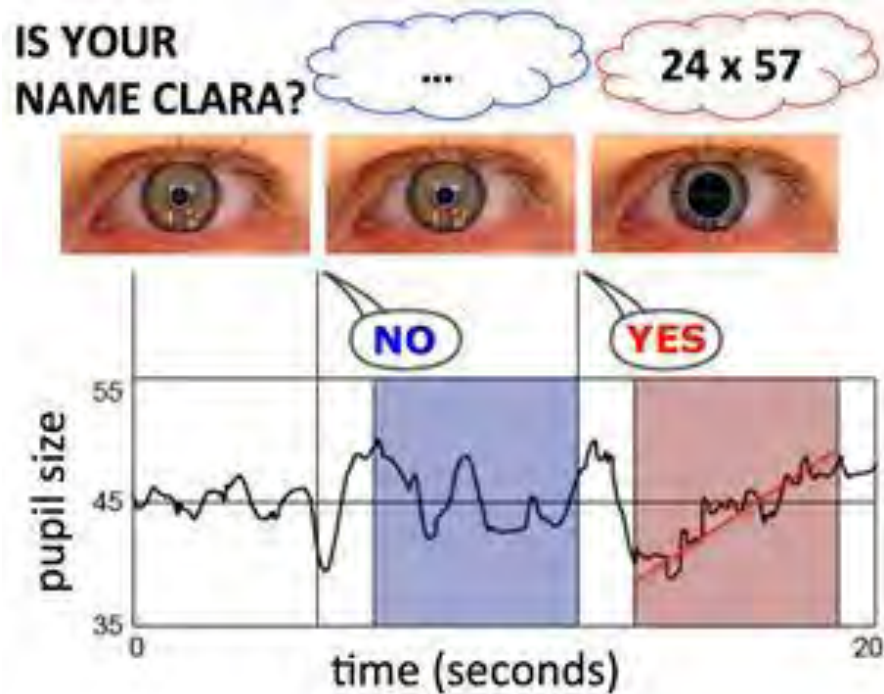


3/16 ENR (19%) ont fait la tâche

Mais seulement 7/23 ECM (30%) (faux négatifs)

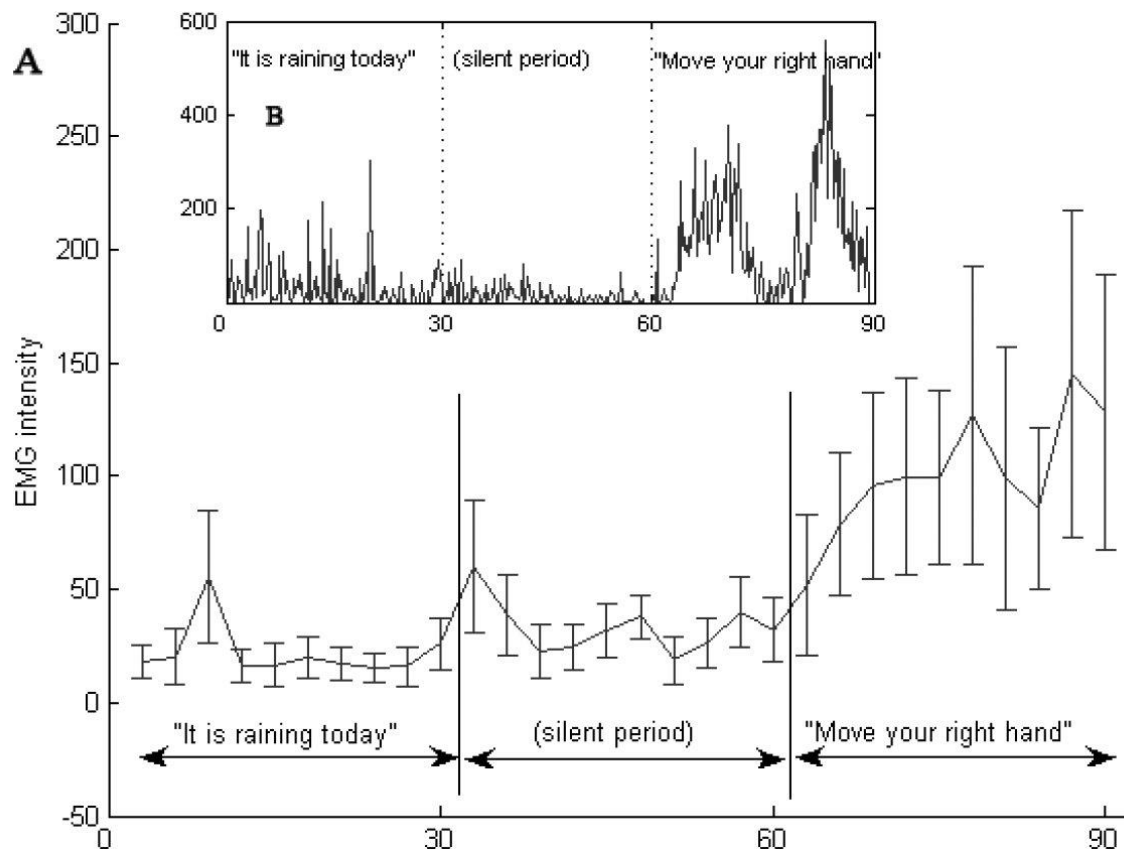


Interface cerveau/ordinateur basée sur la pupille



Électromyogramme actif

« Bougez votre main droite »



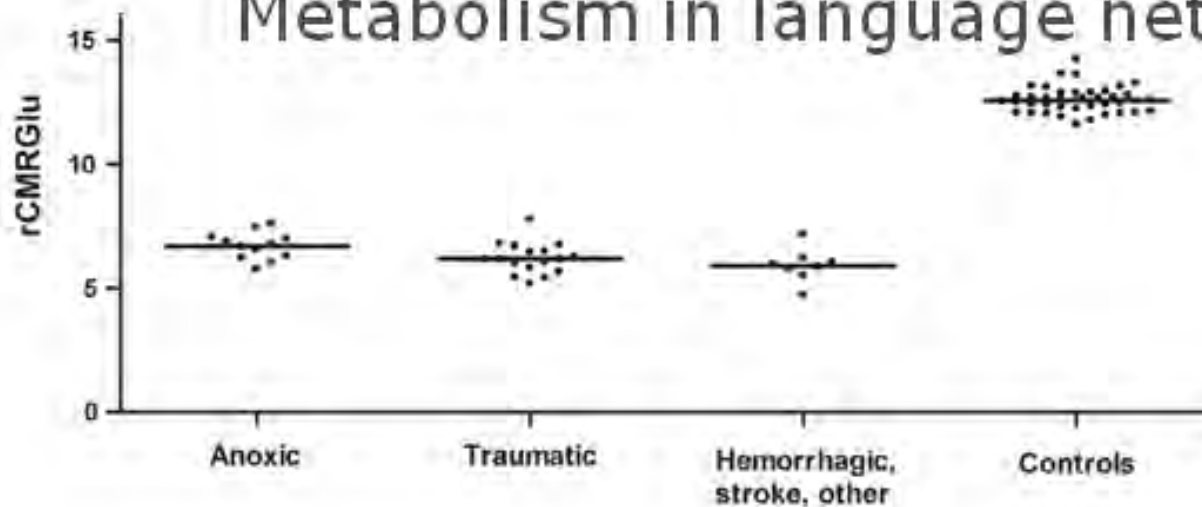
Réponse à la commande et aphasie

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

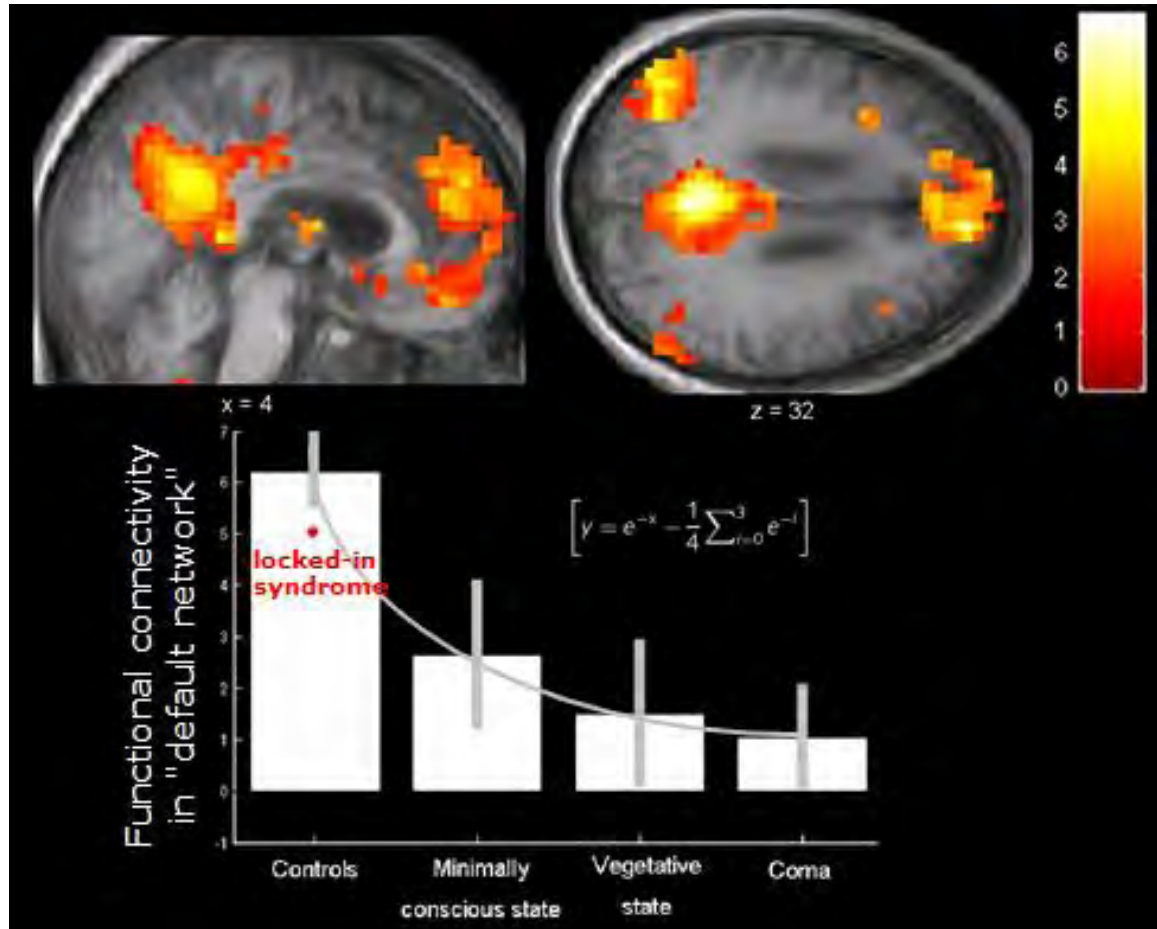
Steve Majerus^{1,3}, Marie-Aurélie Bruno^{2,3}, Caroline Schnakers²,
Joseph T. Giacino⁴ and Steven Laureys^{2,3,*}

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

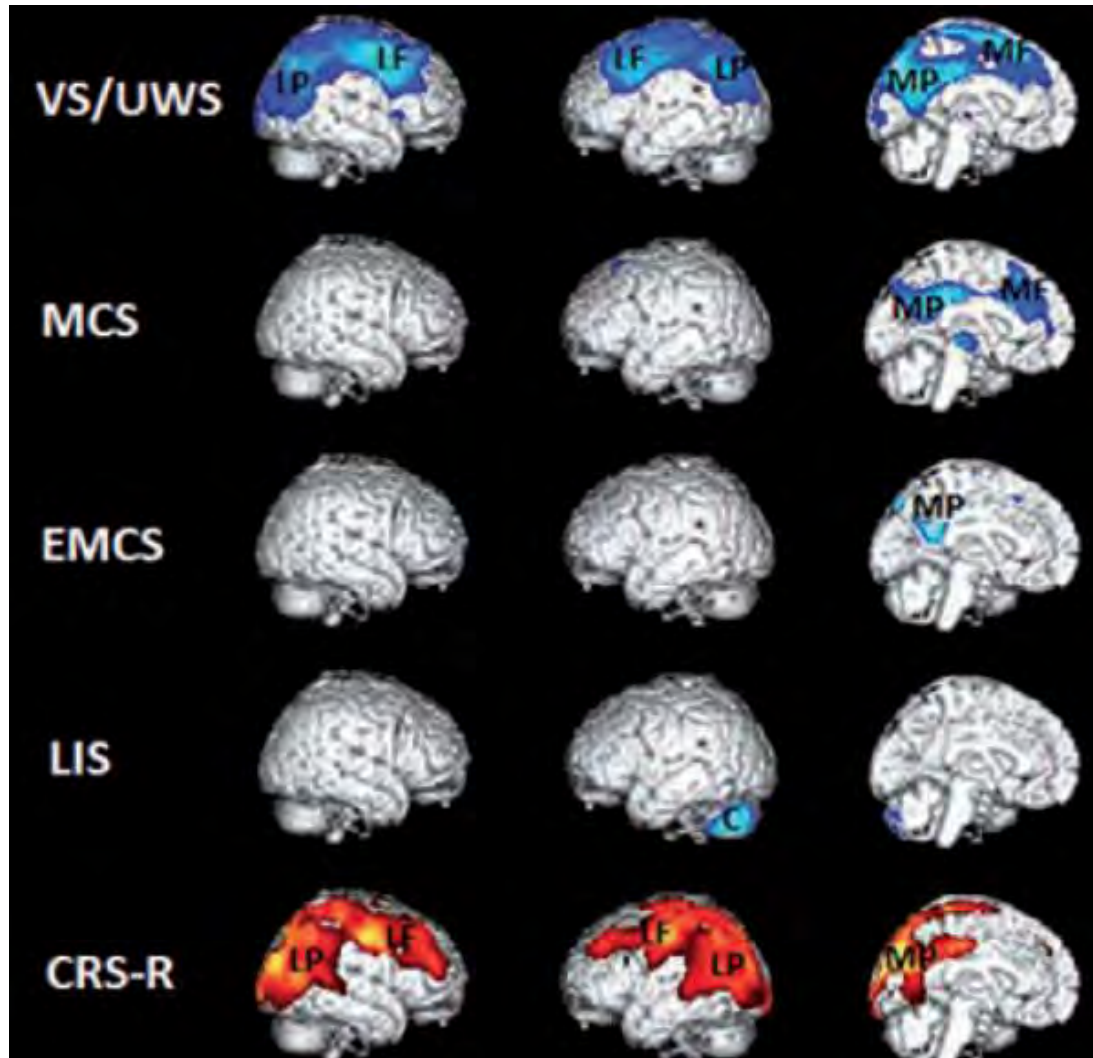
Metabolism in language network



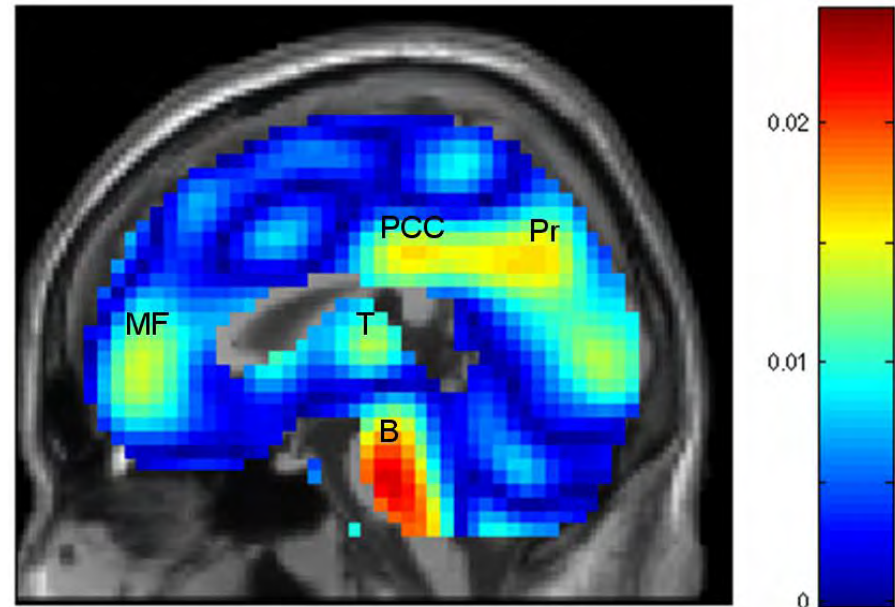
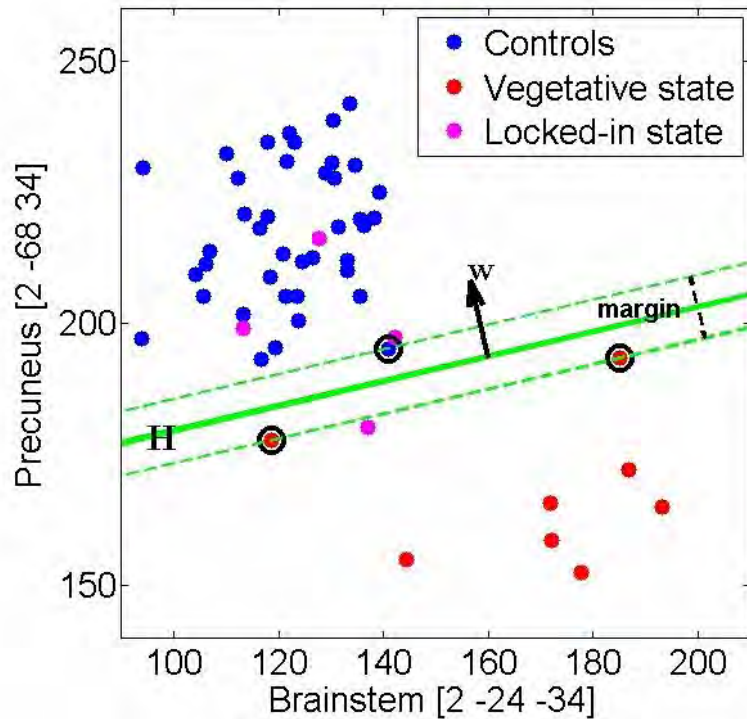
« Resting state » : Réseau du mode par défaut



Métabolisme cérébral au repos – PET Scan

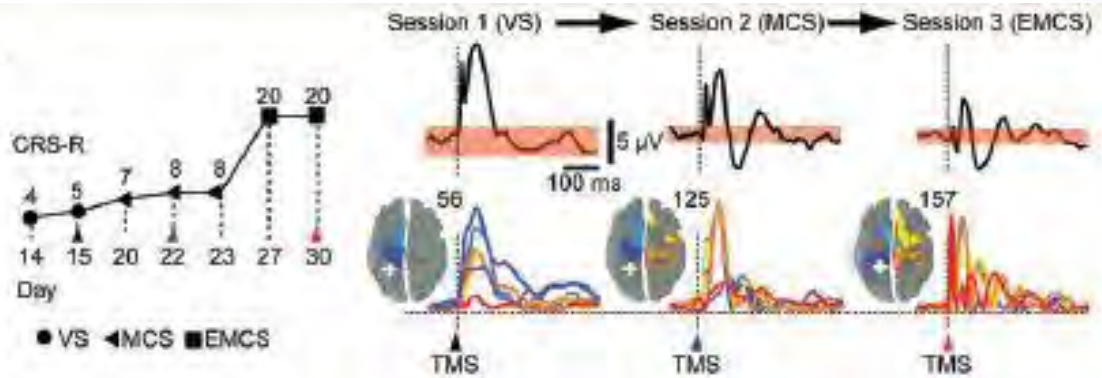
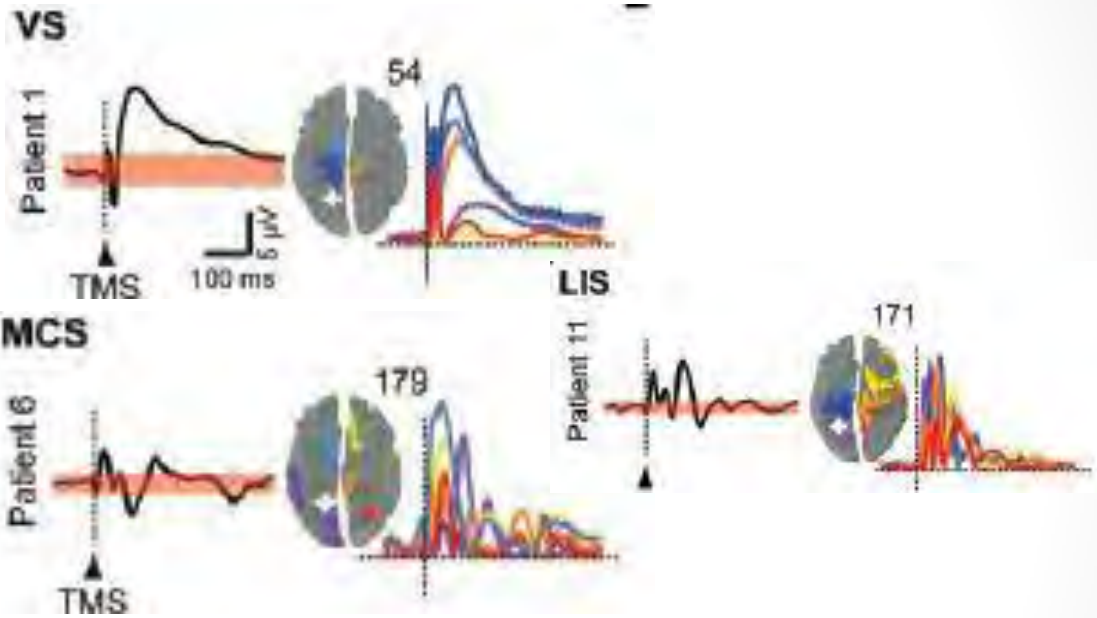


Classificateur automatisé de la conscience

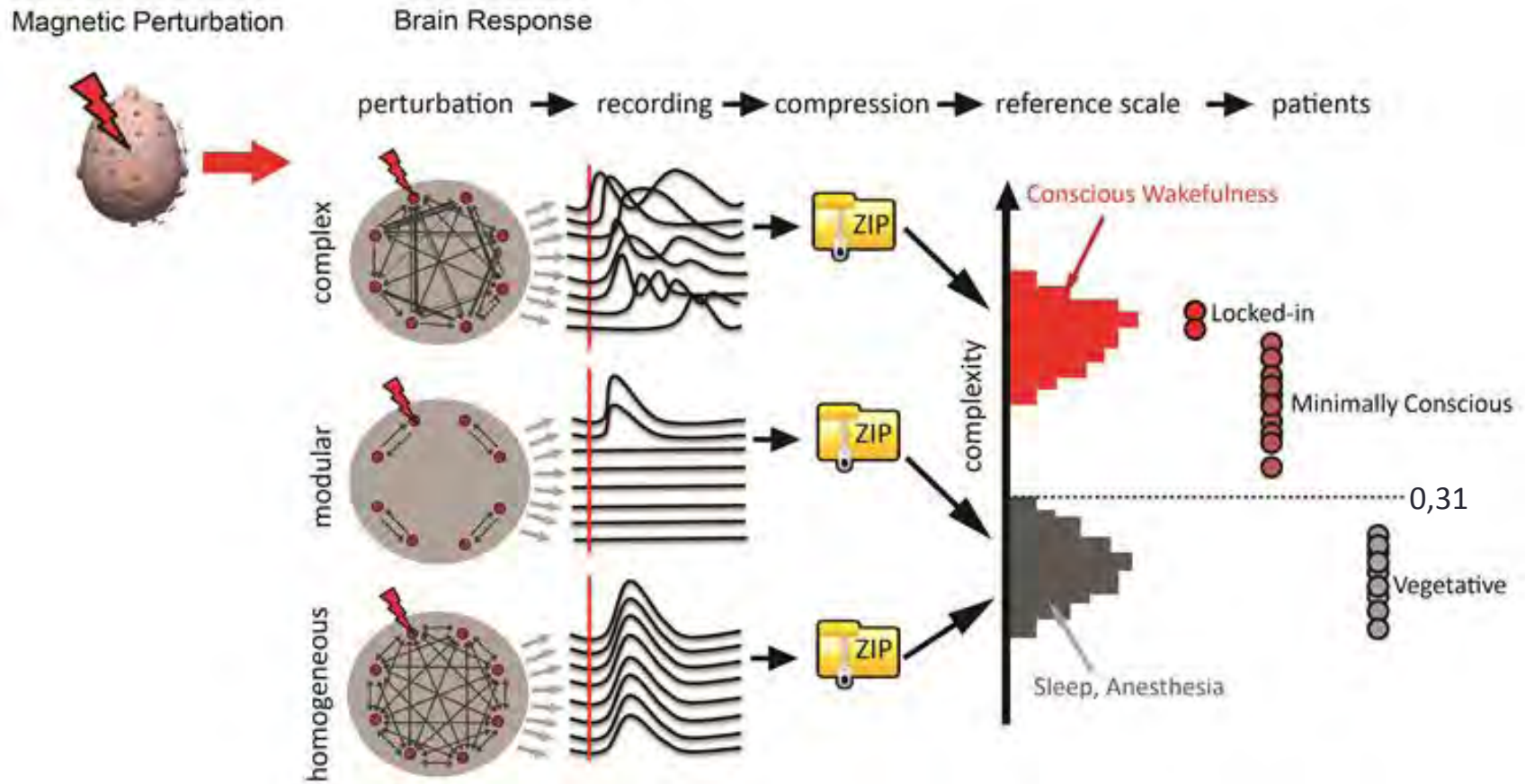


Stimulation magnétique transcrânienne

EEG-TMS



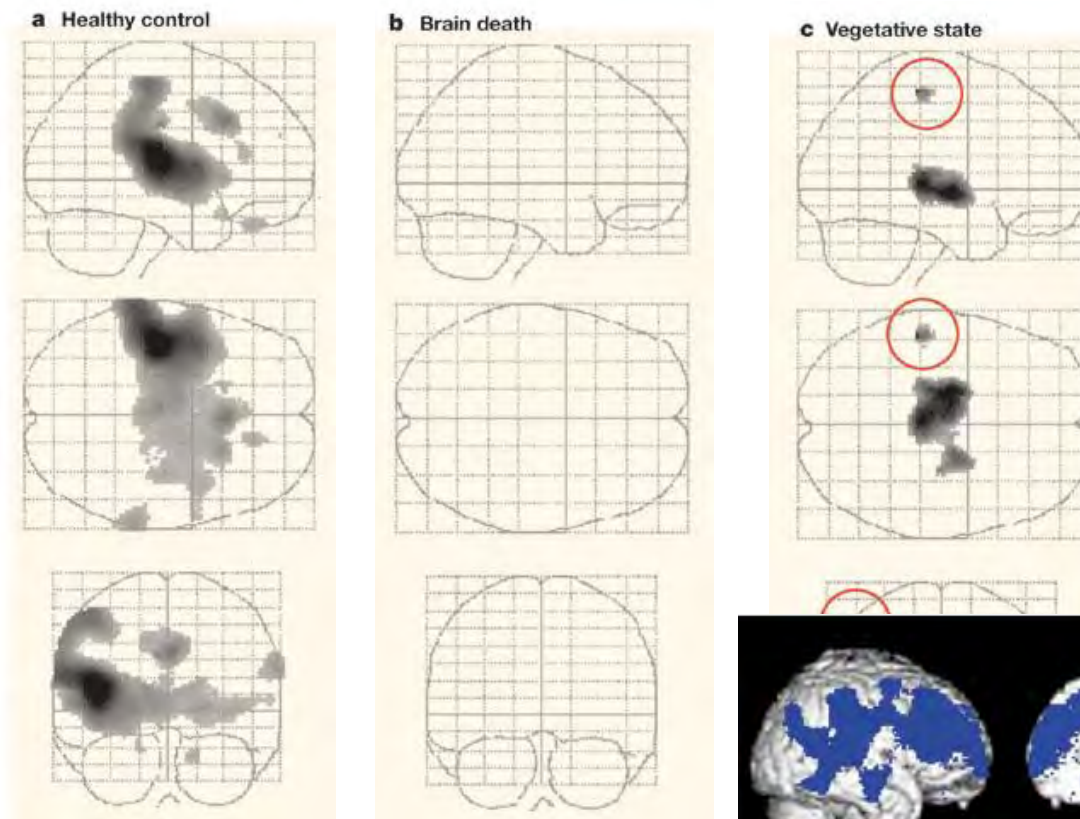
Stimulation magnétique transcrânienne



DOULEUR ET ÉMOTIONS

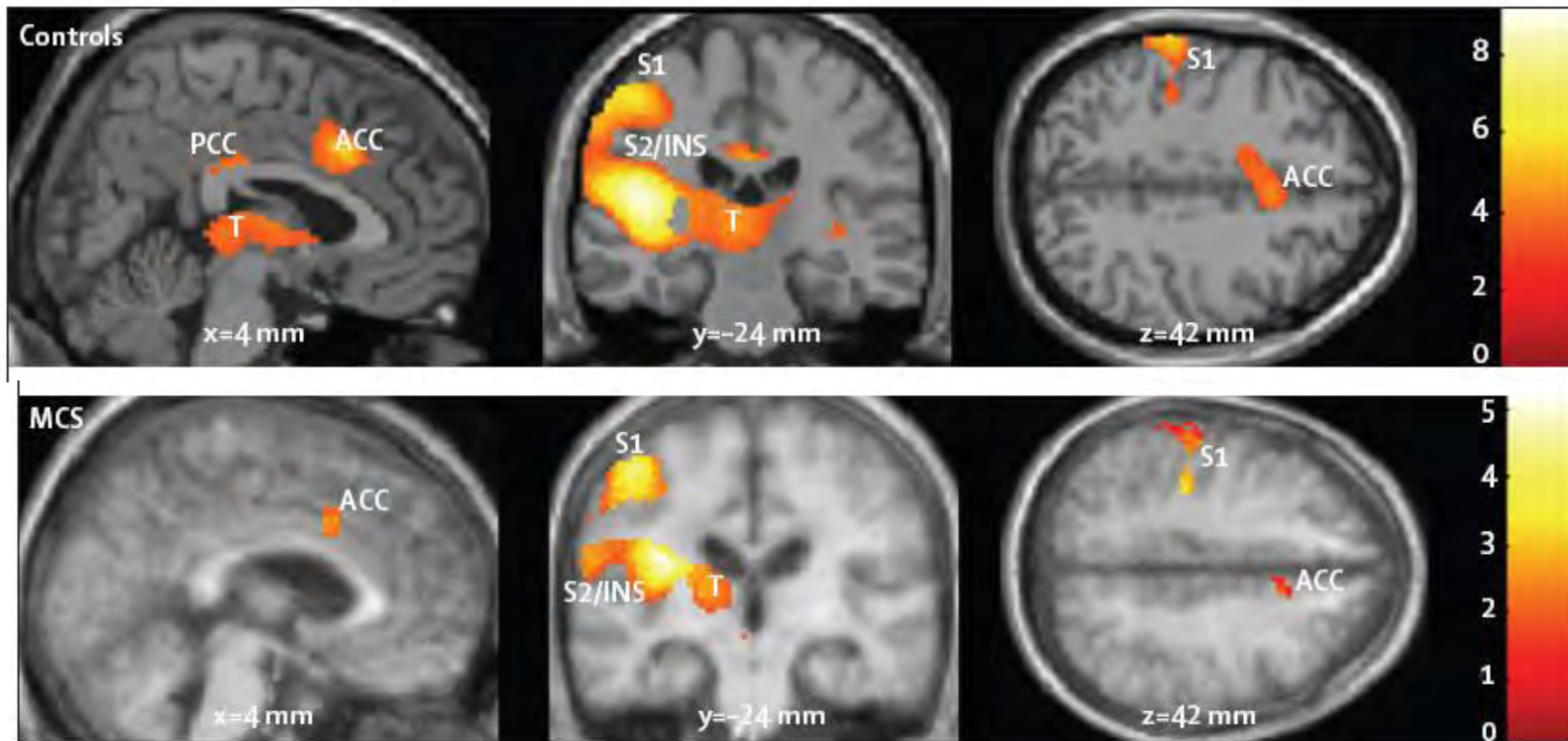
La douleur en mort cérébrale et en syndrome d'éveil non répondant

Stimulation électrique douloureuse



Activation
corticale de
bas niveau
déconnectée

La douleur en état de conscience minimale



Nociception et 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

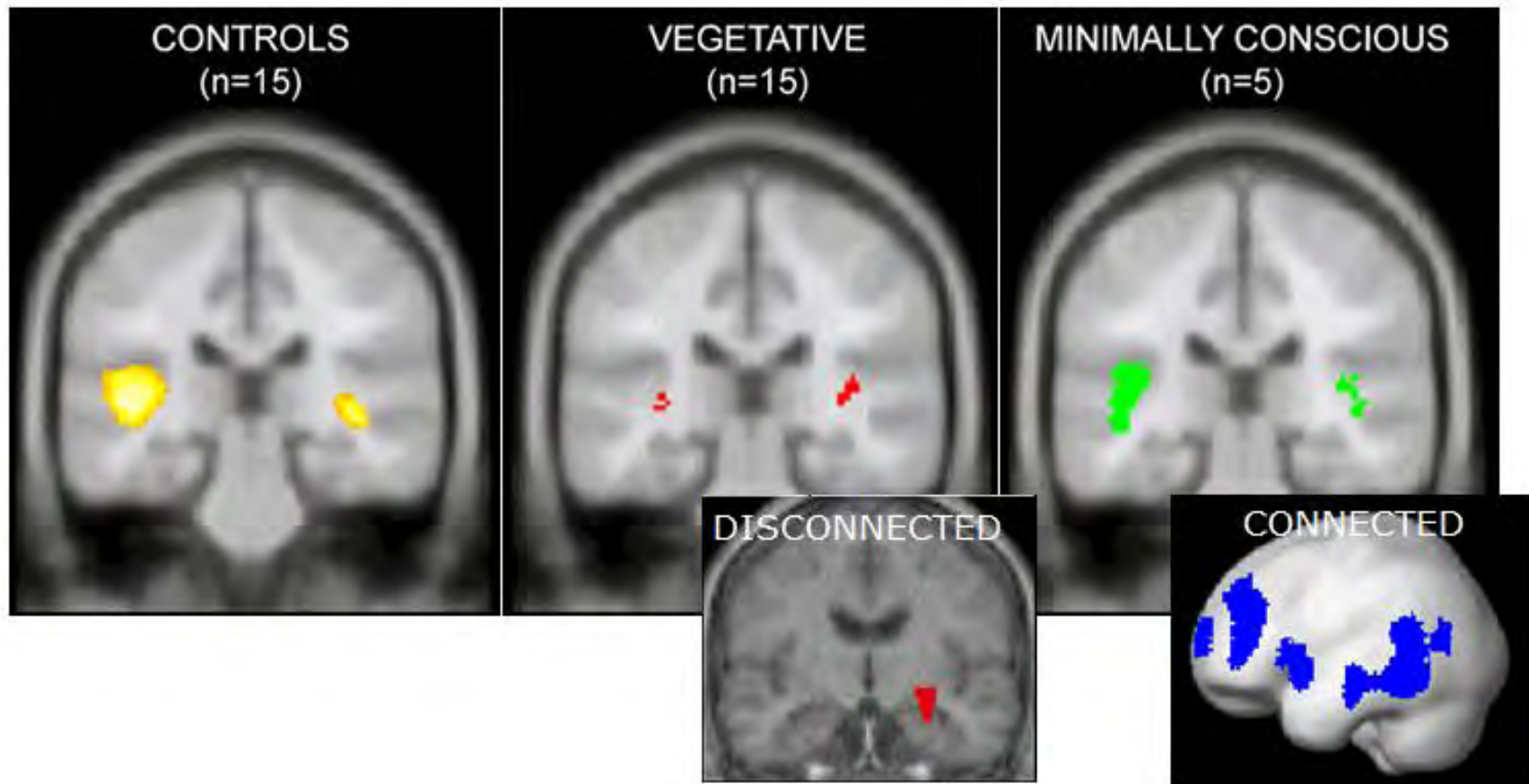
Facial expression

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

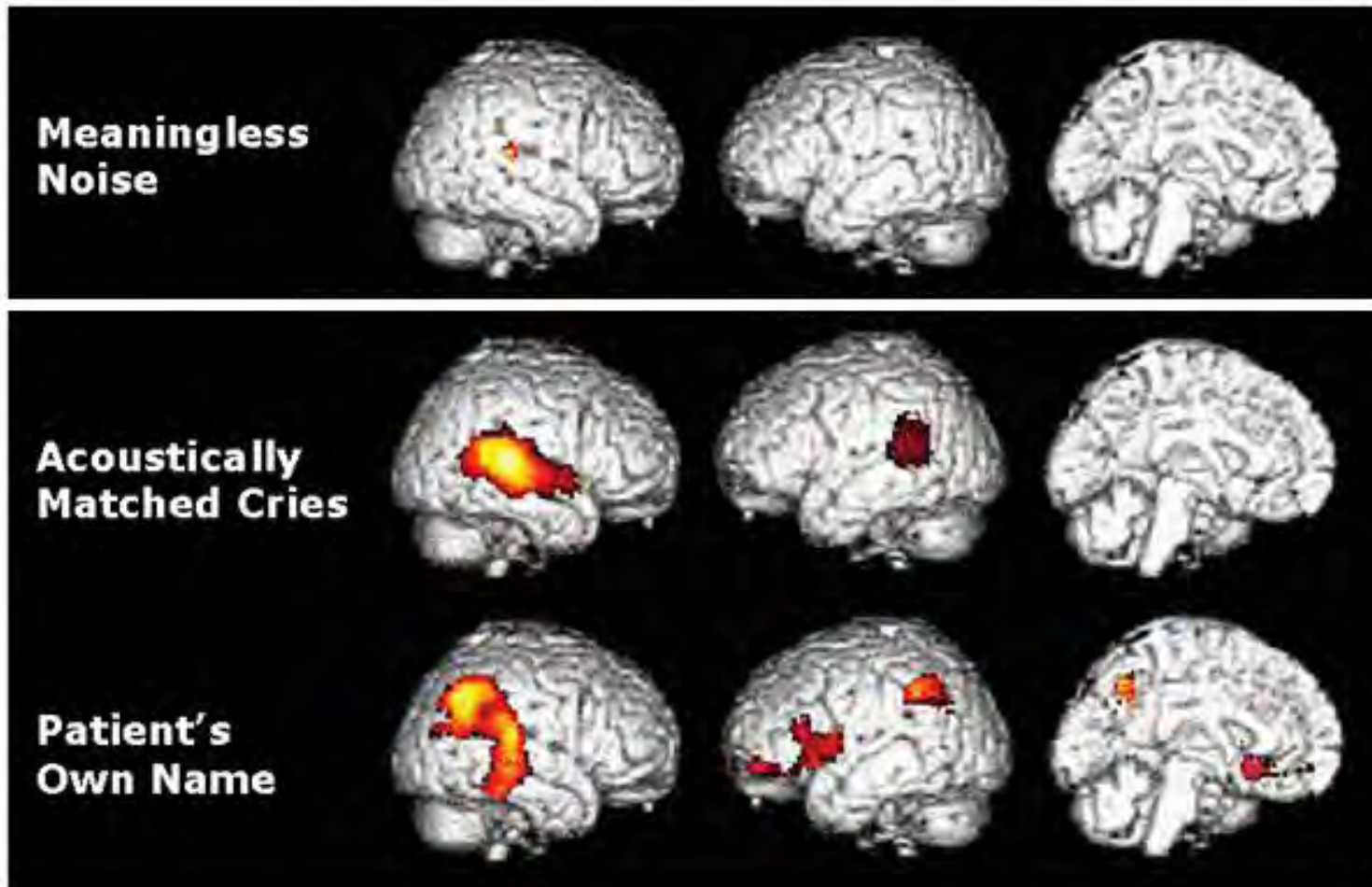
Score >3/9
= traitement
antalgique



Perception auditive



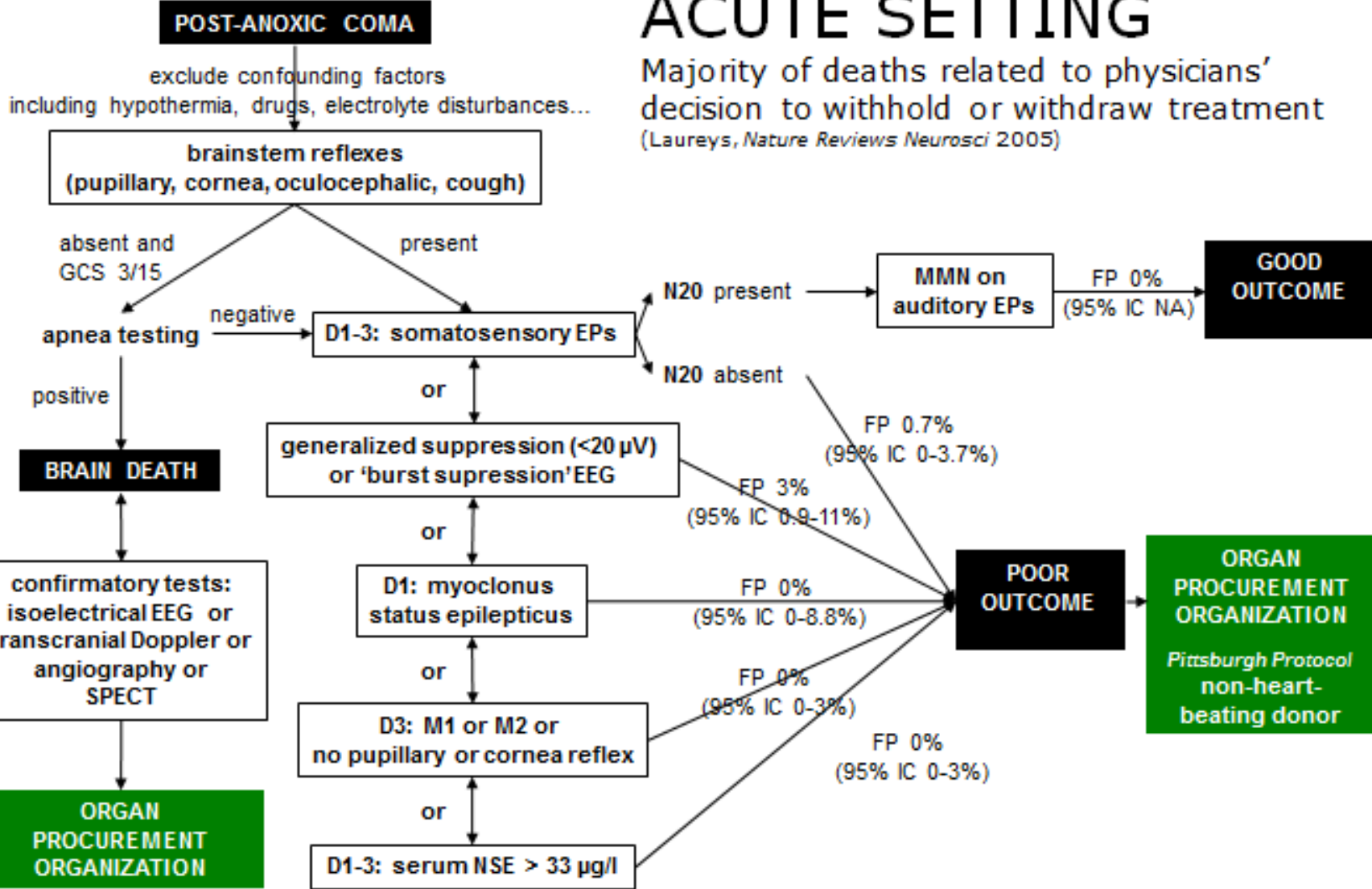
Émotions en état de conscience minimale



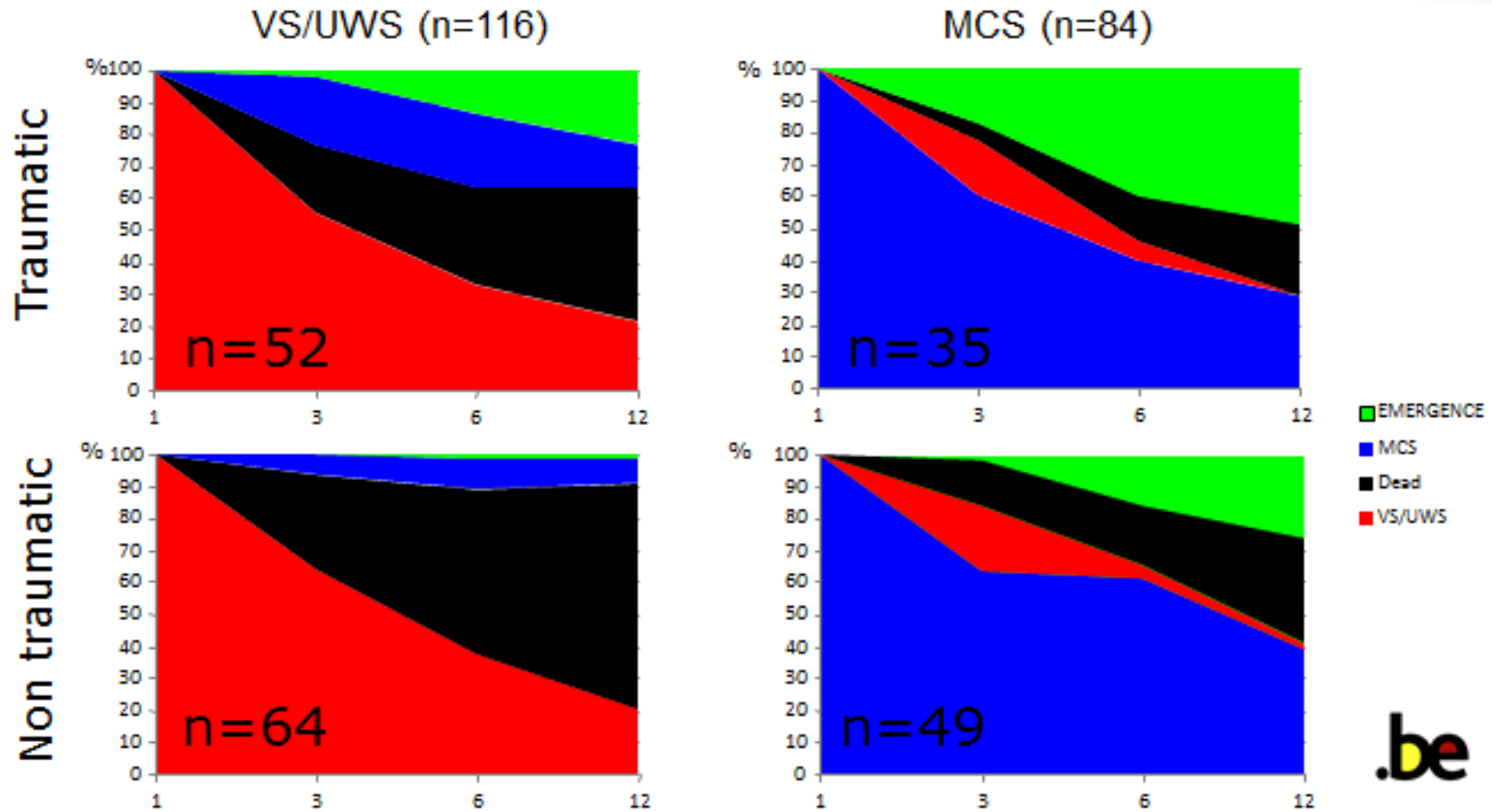
PRONOSTIC

ACUTE SETTING

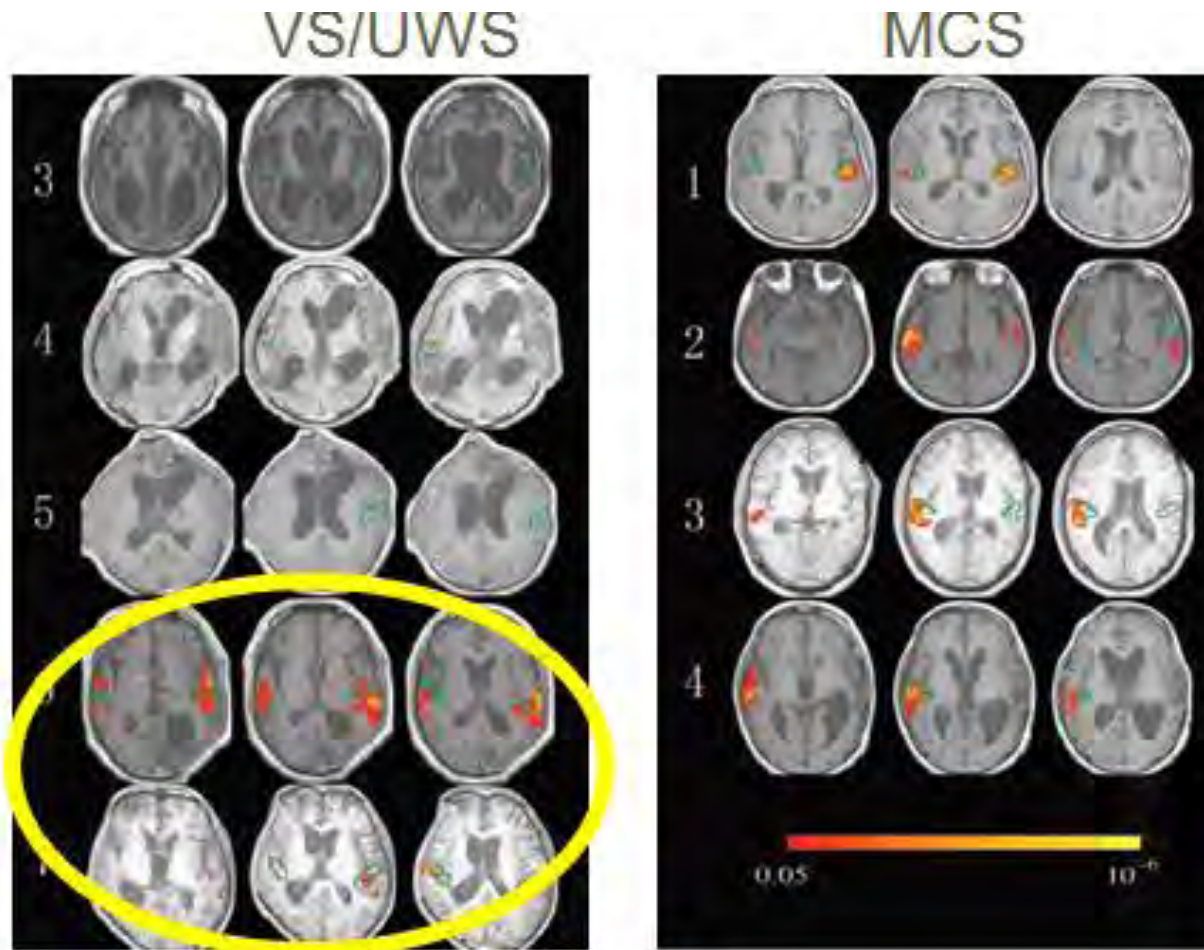
Majority of deaths related to physicians' decision to withhold or withdraw treatment
(Laureys, *Nature Reviews Neurosci* 2005)



Pronostic (Projet fédéral belge, 2004-2007)



Valeur pronostique de l'IRMf



Atypical
cortical
activity

TRAITEMENT

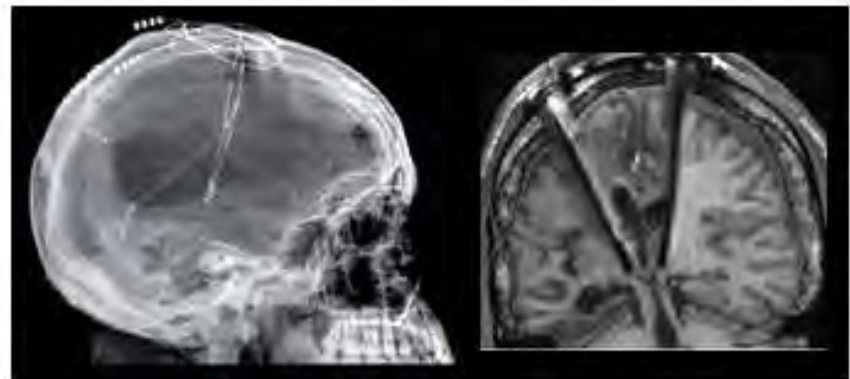
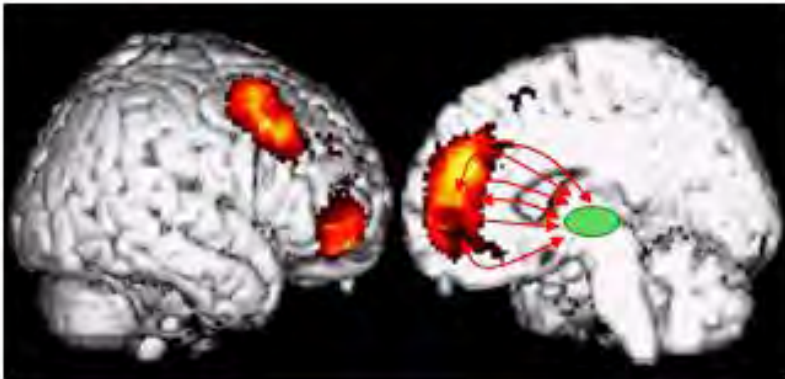
Traitement curatif : médicaments?

| Drug | Study (first author, year) | Number of patients and etiology | Diagnosis | Placebo control | Reported functional outcome |
|-----------------------------------|----------------------------|---------------------------------|------------------------------|-----------------|-----------------------------|
| <i>Dopaminergic agents</i> | | | | | |
| 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 |
| | Sanlova (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 |
| <i>Nonbenzodiazepine sedative</i> | | | | | |
| 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 |
| | <i>GABA agonist</i> | | | | |
| Baclofen | Sará (2007) | 1 non-TBI | VS | No | Positive |

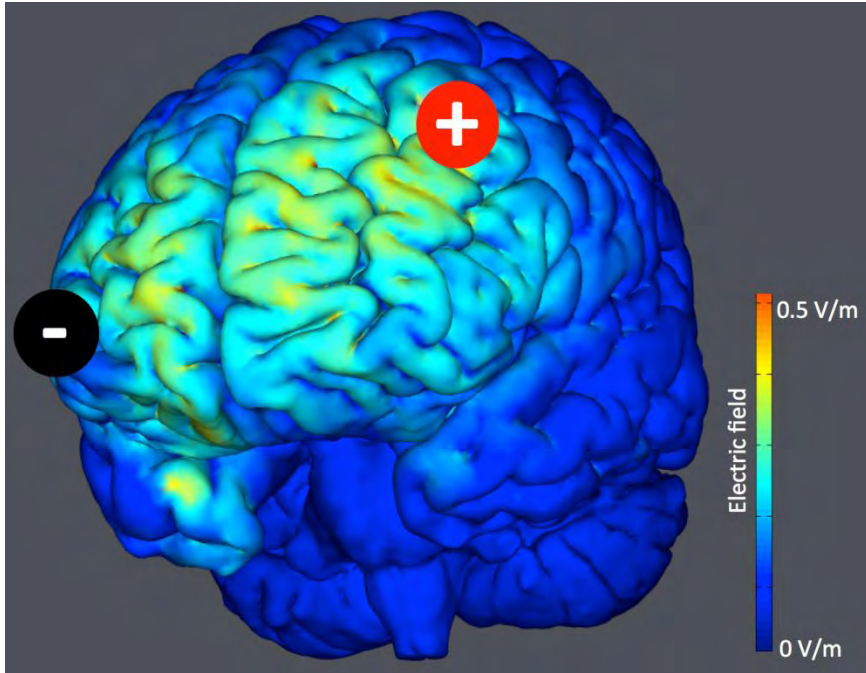
Stimulation cérébrale profonde

« Reconnexion » des noyaux intralaminaires dans la récupération spontanée de l'état « végétatif » (non répondant)

La stimulation des noyaux intralaminaires induit une « récupération » dans l'état de conscience minimale

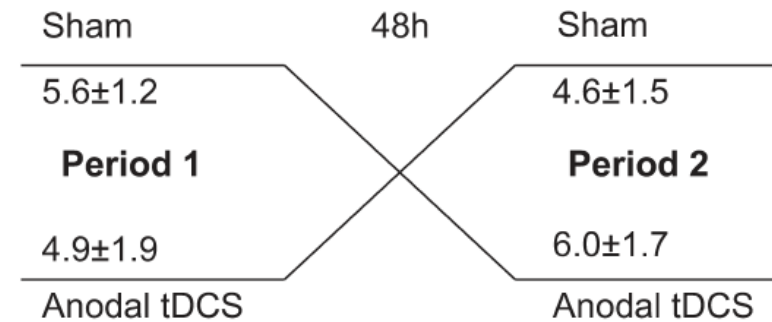


Stimulation transcrânienne à courant continu



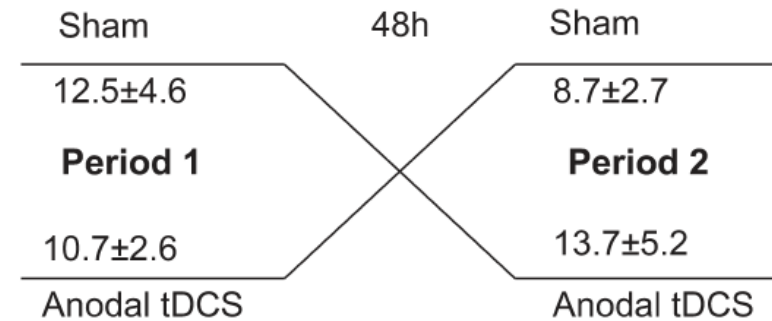
VS/UWS - CRS-R

(n=25)



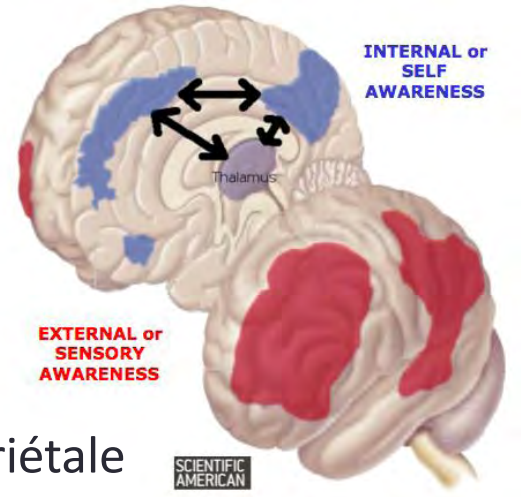
MCS - CRS-R

(n=30)

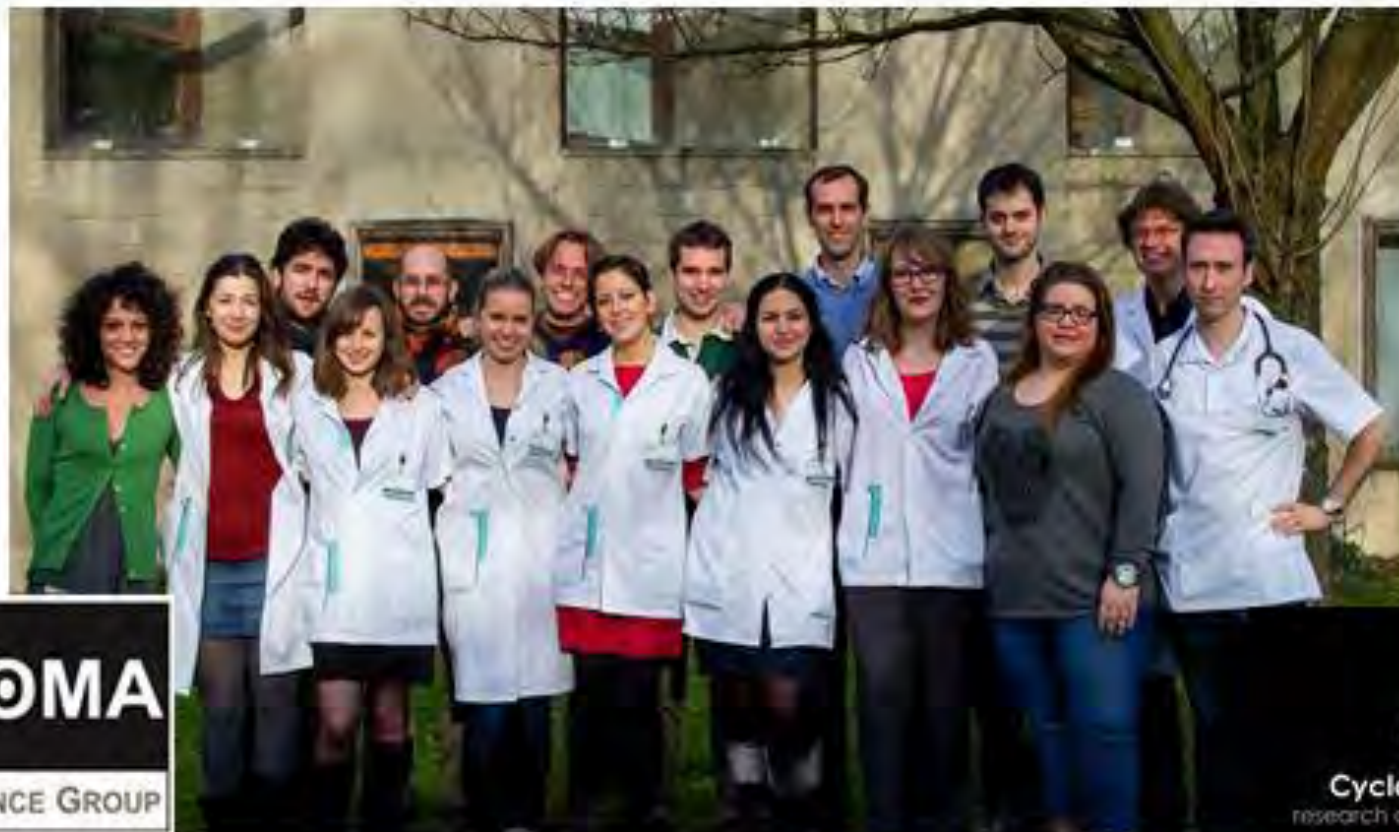


CONCLUSION

Conclusion

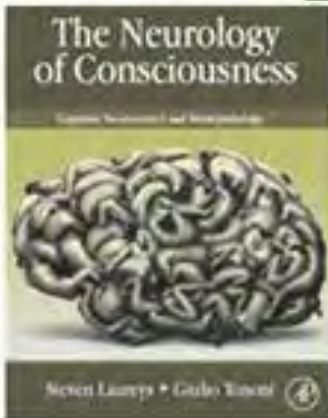


- Conscience humaine
≈ propriété émergente de la connectivité fronto-pariétale
- Pronostic : meilleur pour les patients en état de conscience minimale et en cas d'accident traumatique
- Diagnostic
 - ± 40% d'erreurs diagnostiques
 - Échelle clinique (CRS-R) et neuroimagerie
- Thérapeutique
 - Traitement de la douleur (NCS)
 - Stimulation cérébrale profonde – Stimulation à courant continu



COMA
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Cyclotron
research centre



James S. McDonnell Foundation

COMA@ULG.AC.BE



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