

Functional neuroimaging in patients with disorders of consciousness: What to care about?

Neuroethics Day
ETHICS OF NEUROSCIENCE, NEUROSCIENCE OF ETHICS

Friday 20 May 2016
Aix-Marseille University, France

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Paris, France
&
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GIGA Research & Neurology Department
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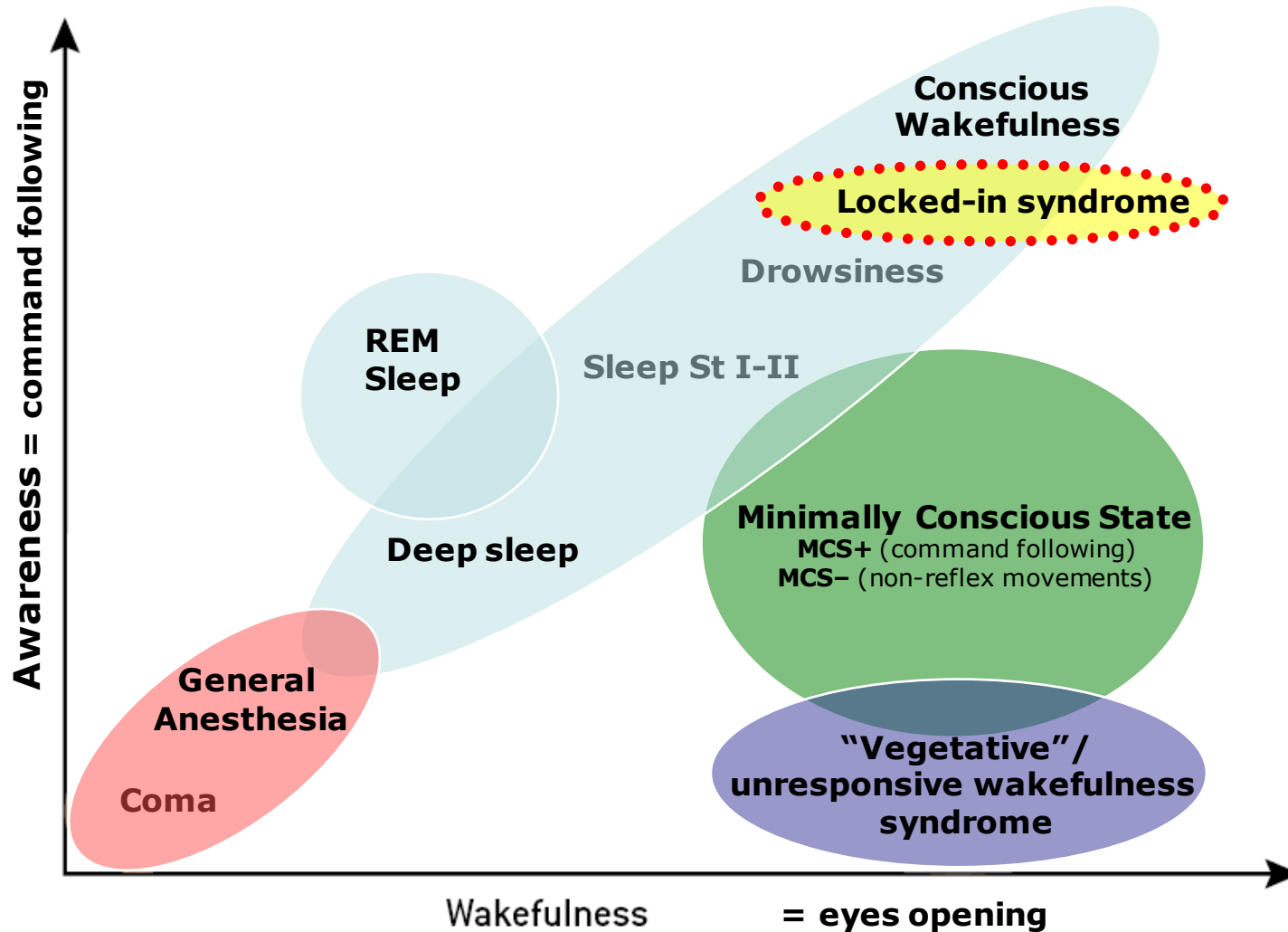


James S. McDonnell Foundation



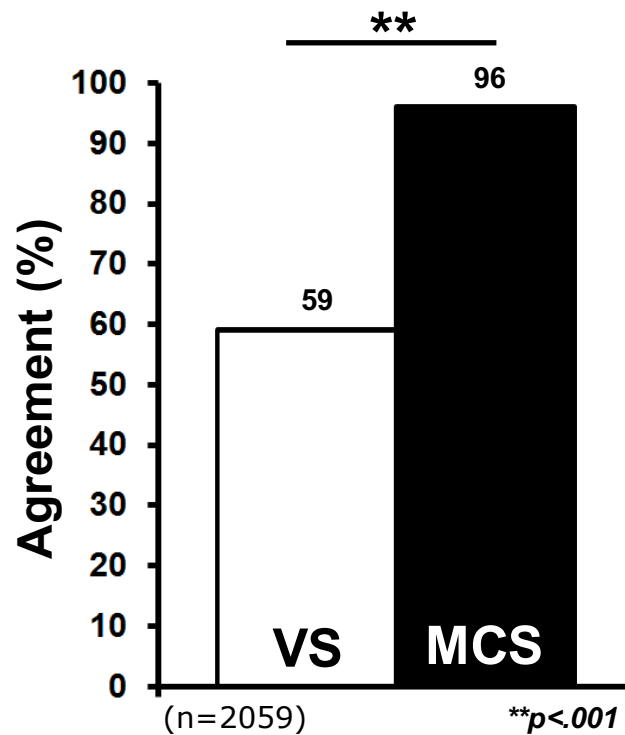
www.comascience.org

A clinical definition of consciousness



Attitudes towards pain

Do you think patients in a ...
can feel pain?



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

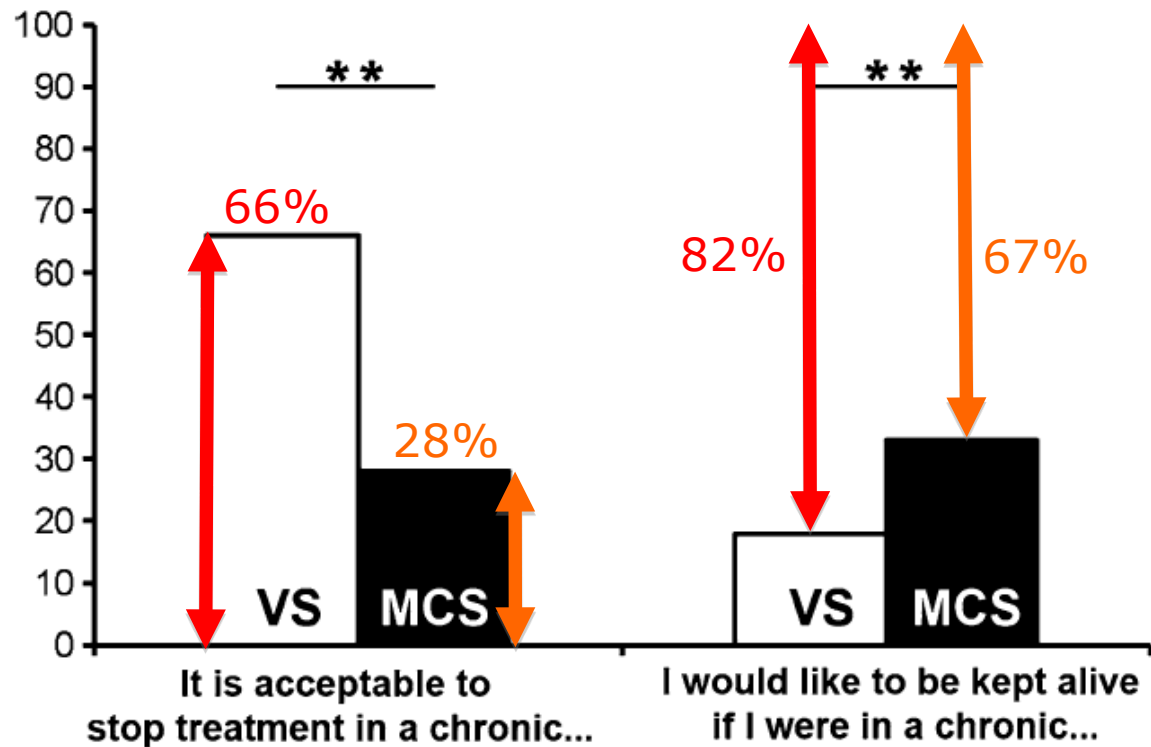
Predicted response: "agreement"

End-of-life issues

- VS worse than death for the patient: 55%
- VS worse than death for their families: 80%
- MCS worse than VS for the patient: 54%
- MCS worse than VS for their families: 42%

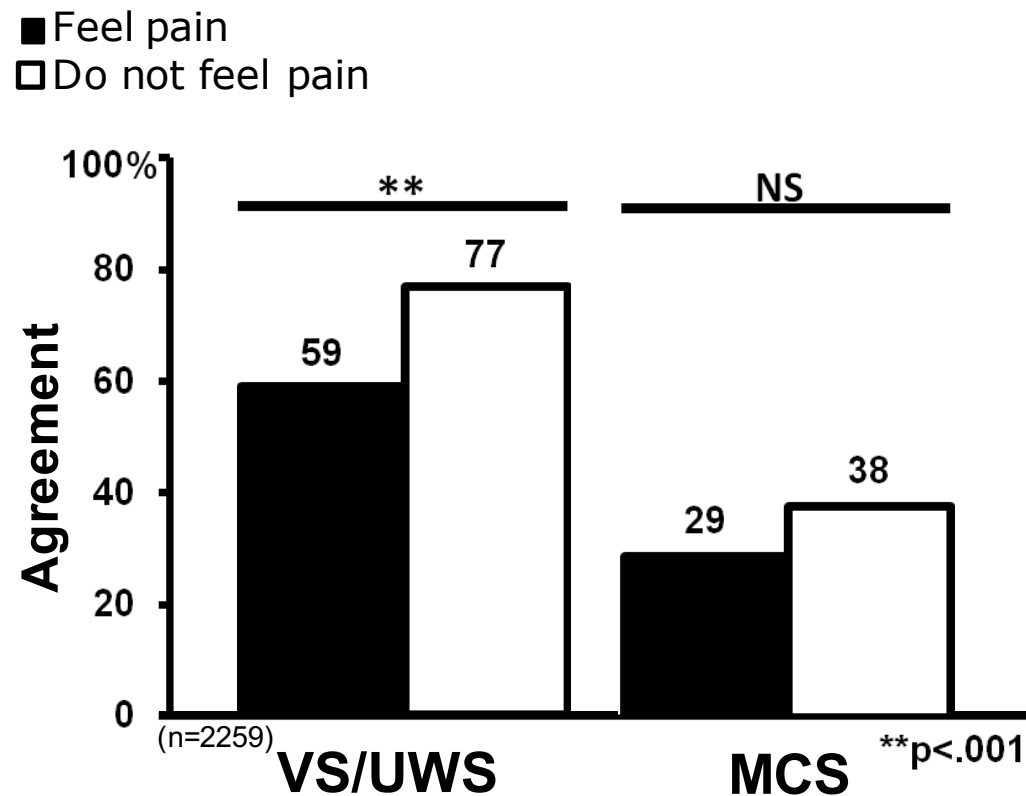


2,475 medical professionals



Attitudes towards pain & end-of-life

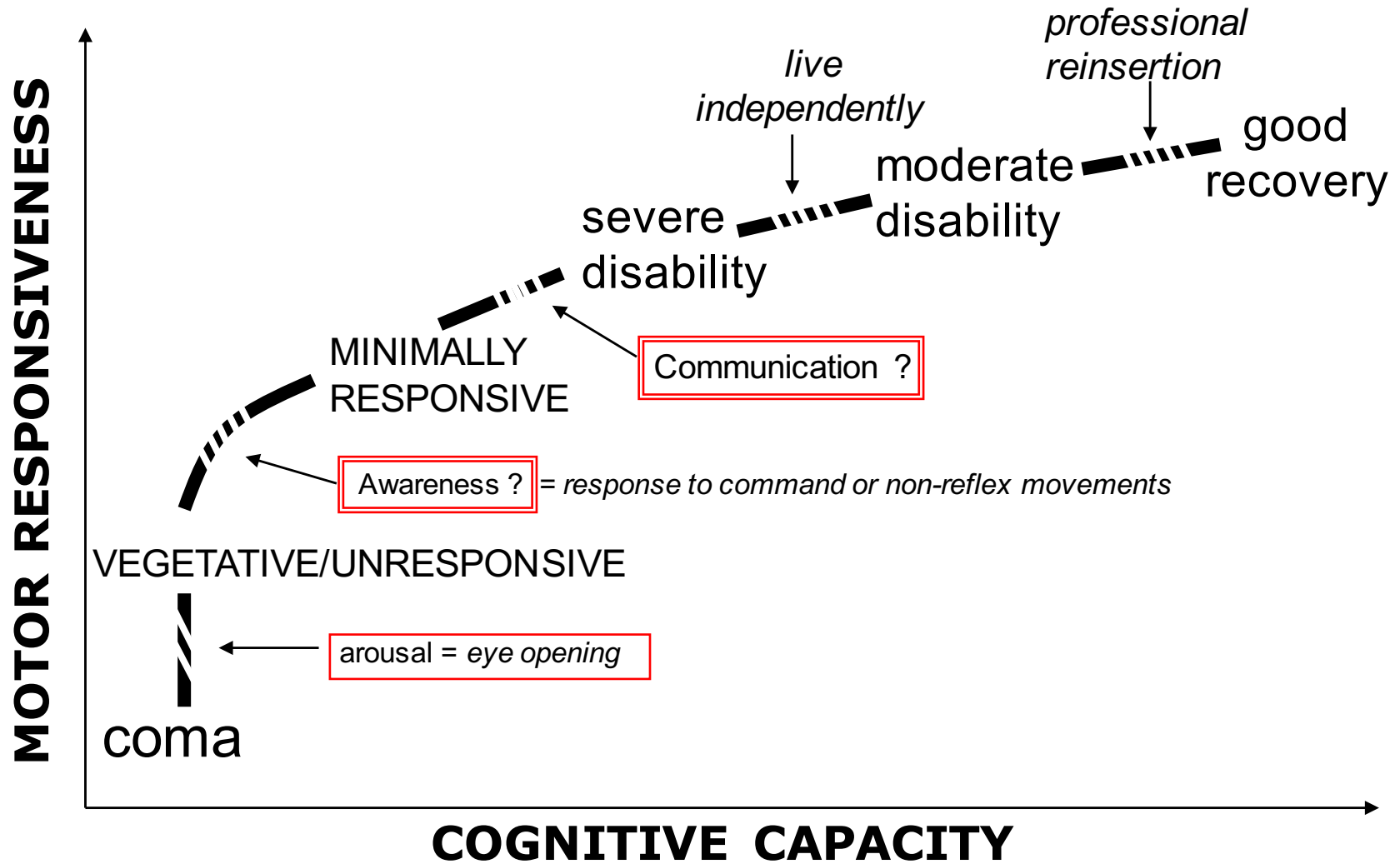
Treatment can be stopped in chronic...



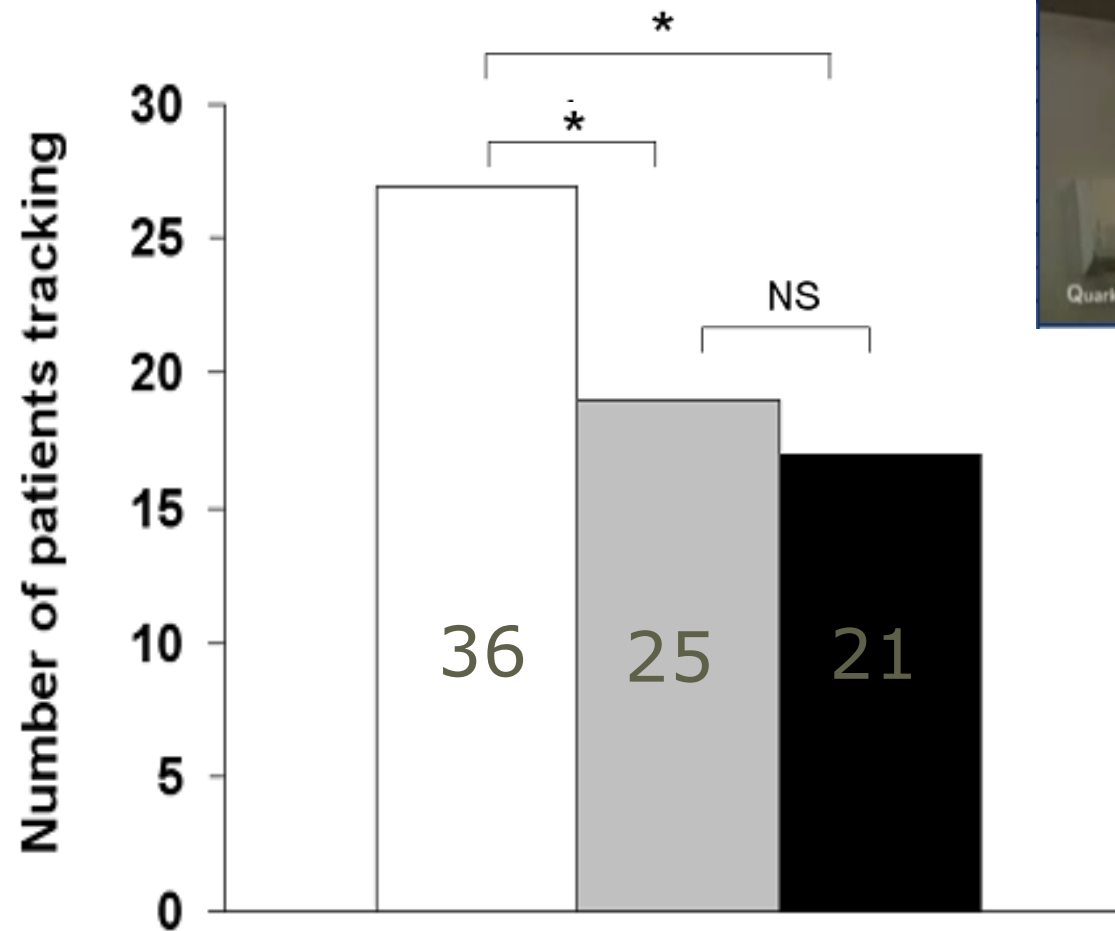
What is to diagnose as conscious?



Evaluating consciousness



Visual pursuit



- Mirror
- Person
- Object

$p < .05$

Misdiagnosis of vegetative state

n=103 post-comatose patients

45 Clinical diagnosis of “vegetative state”

27 Coma Recovery Scale diagnosis

↙ ↘ 40% misdiagnosis

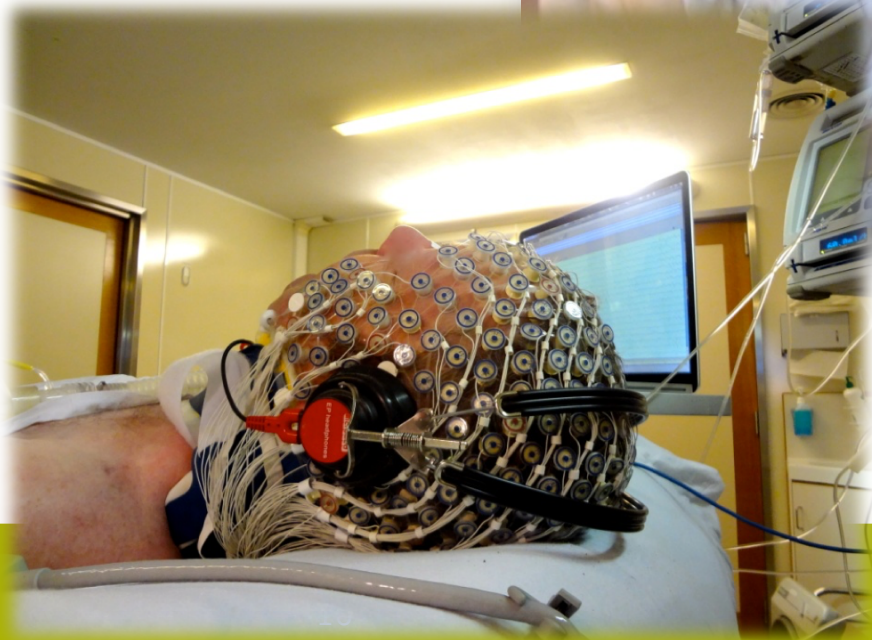


38% Schnakers et al Ann Neurol 2006; BMC Neurology 2009

37% Childs et al Neurology 1993

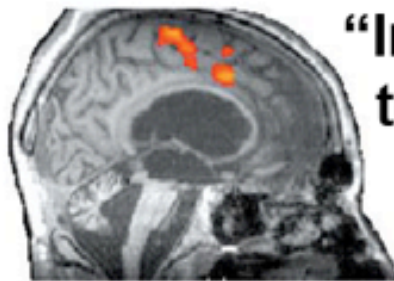
43% Andrews et al BMJ 1996

Complementary methodologies

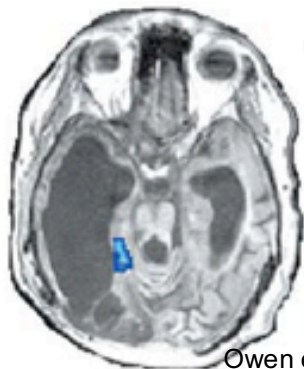


Neuroimaging paradigms

Active paradigms



“Imagine playing tennis”



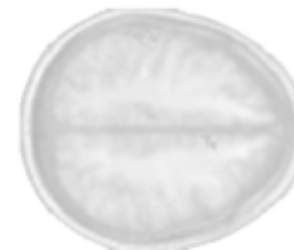
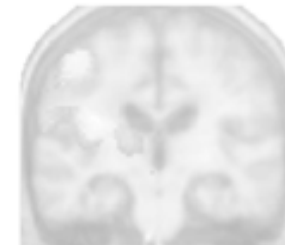
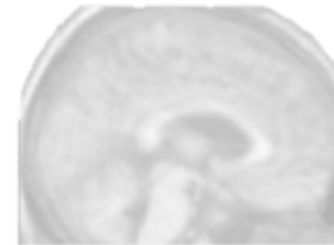
“Imagine visiting the rooms of your house”

Owen et al, Science 2006
Monti & Vanhaudenhuyse et al, NEJM 2010

Passive paradigms



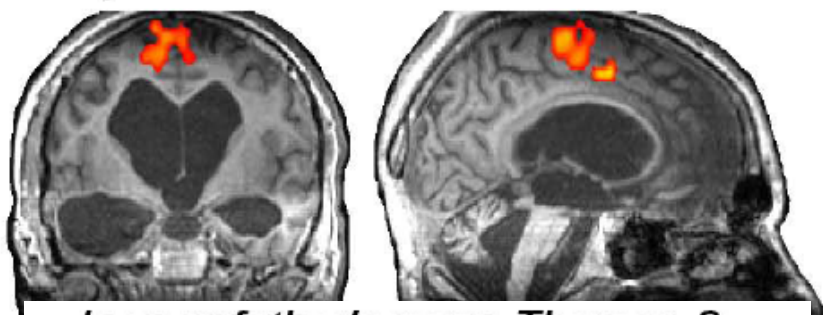
median nerve



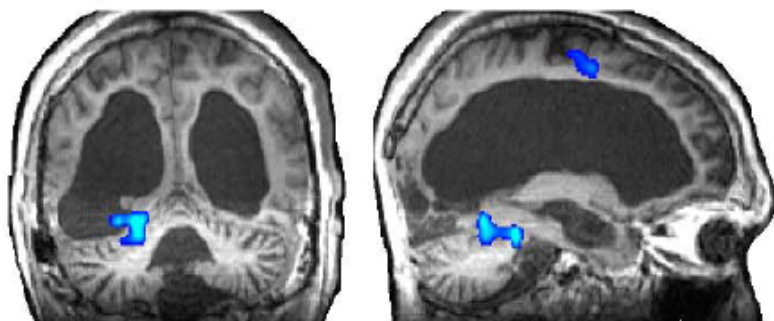
Yes-No communication with fMRI



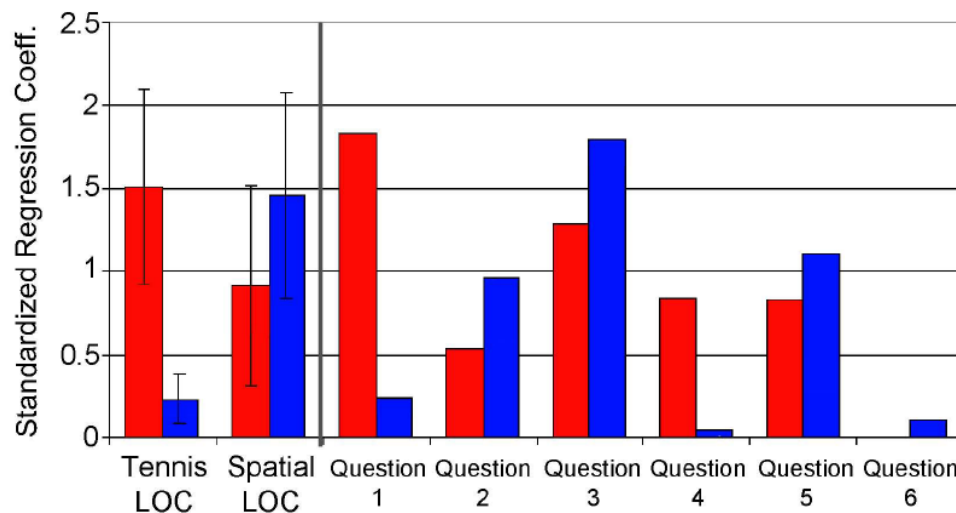
Is your father's name Alexander ?



Is your father's name Thomas ?



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

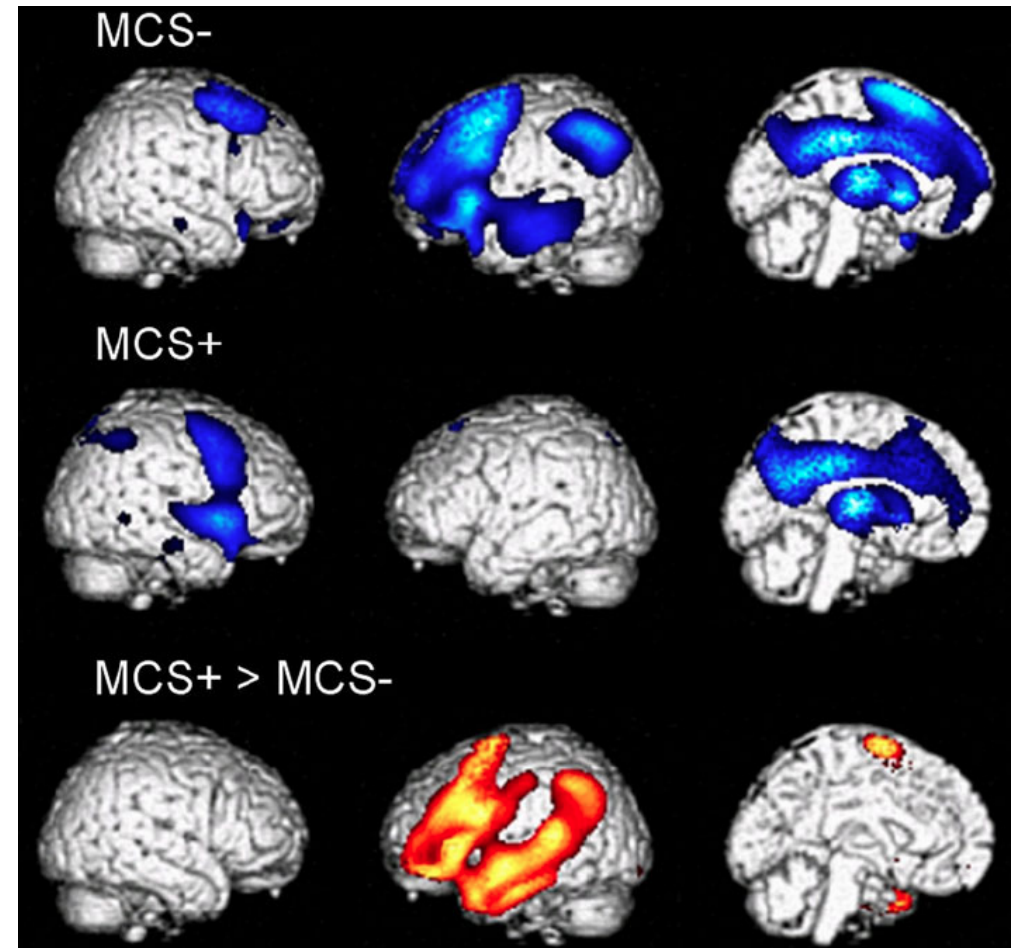
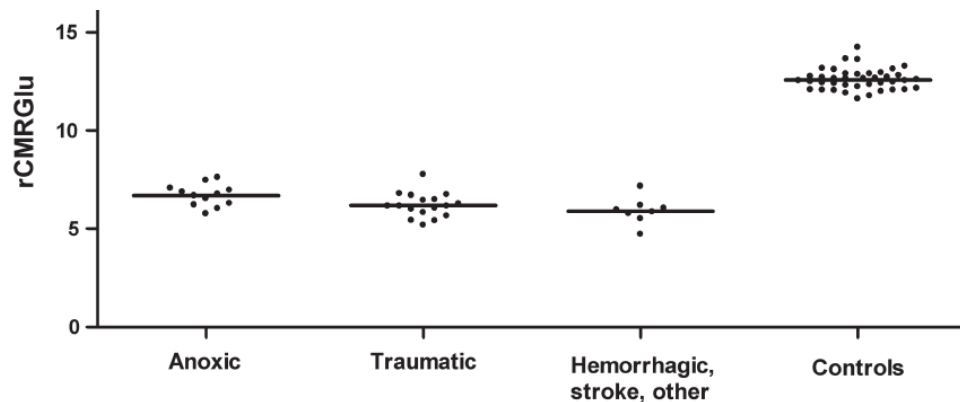


Aphasia as a confound

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

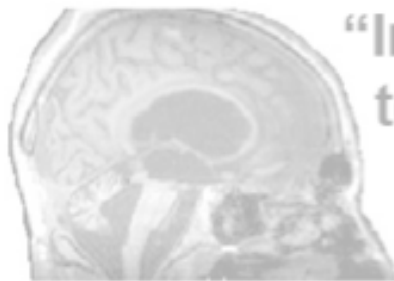
Steve Majerus^{1,3}, Marie-Aur lie Bruno^{2,3}, Caroline Schnakers²,
Joseph T. Giacino⁴ and Steven Laureys^{2,3,*}

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Neuroimaging paradigms

Active paradigms



“Imagine playing tennis”

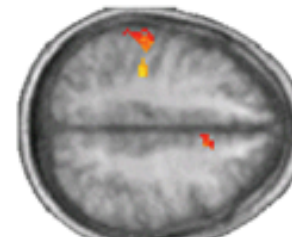
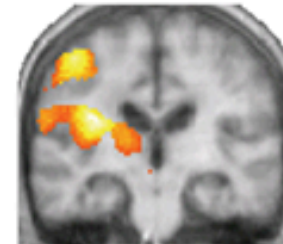
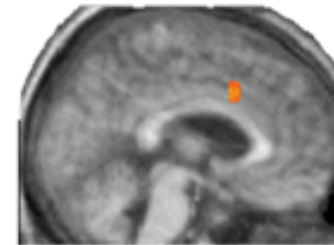


“Imagine visiting the rooms of your house”

Passive paradigms



median nerve

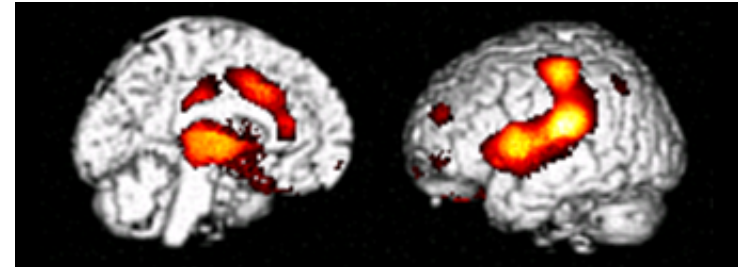


Boly et al, Lancet Neurol 2008

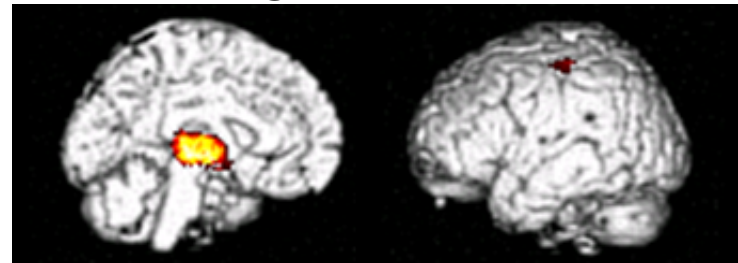
Noxious stimulation



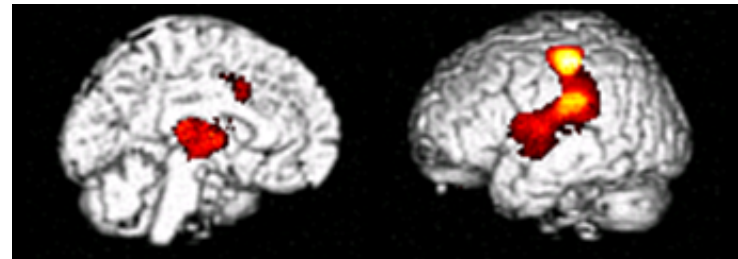
HEALTHY



« VEGETATIVE »

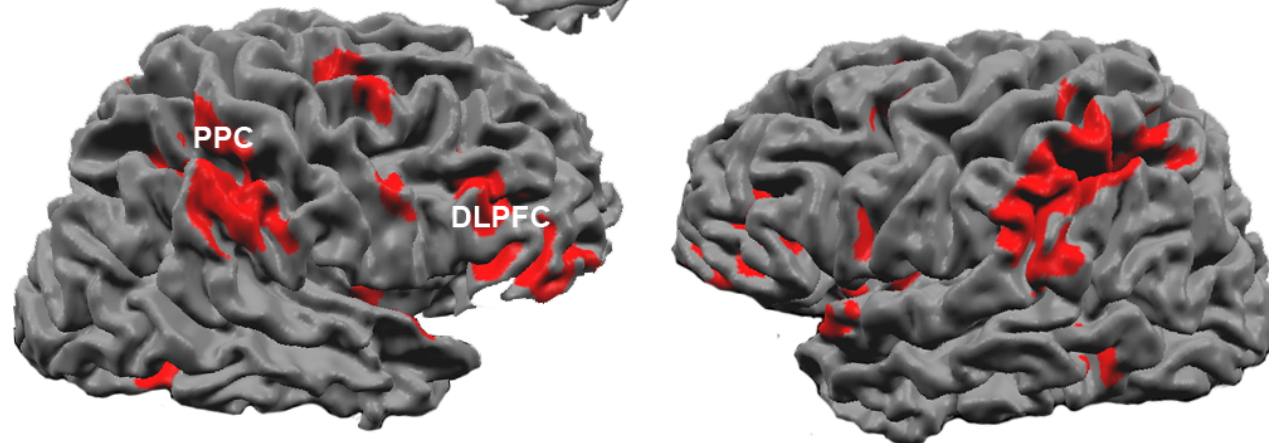
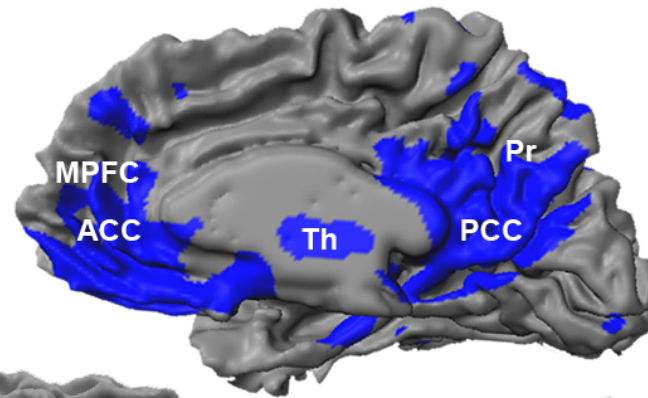


MINIMALY CONSCIOUS STATE



Two awareness networks

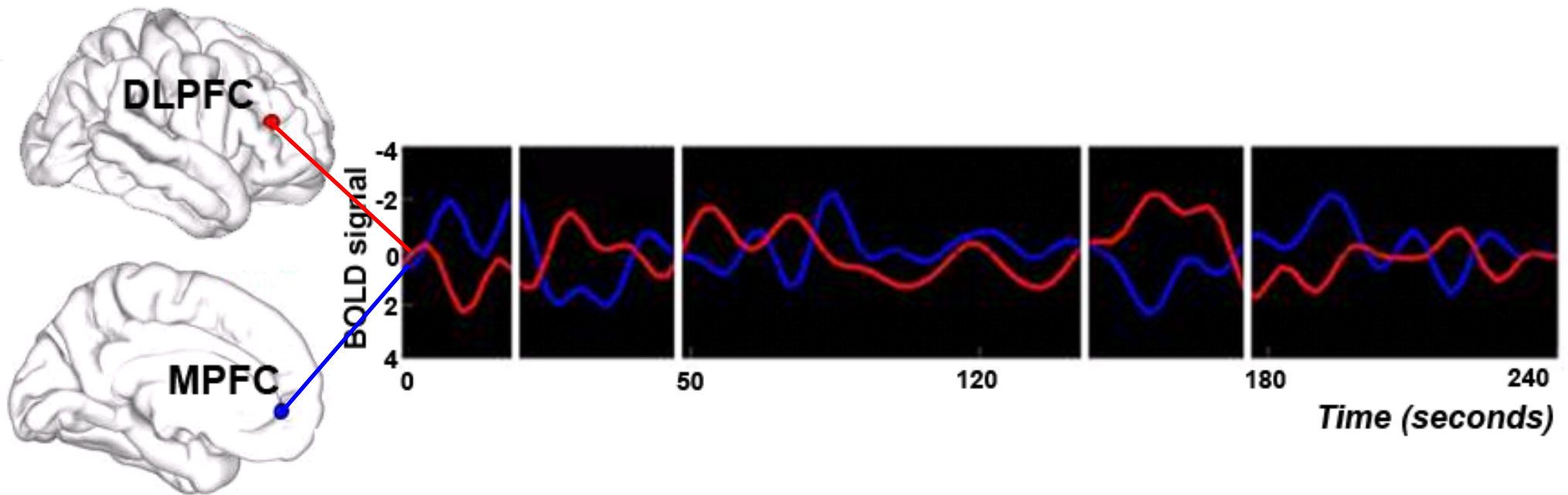
Internal awareness network



External awareness network

Intrinsic brain activity & awareness

**External awareness
or anticorrelated network**

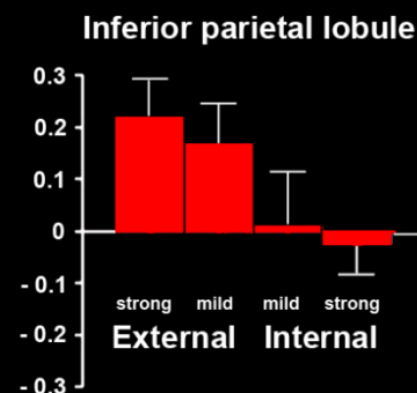
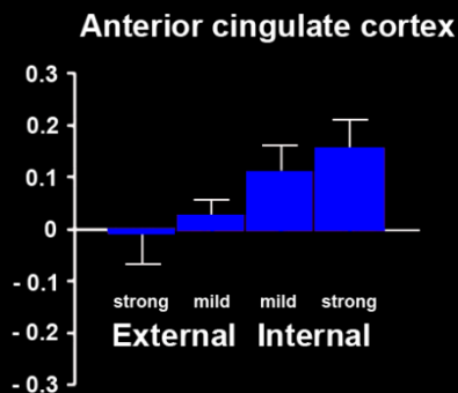
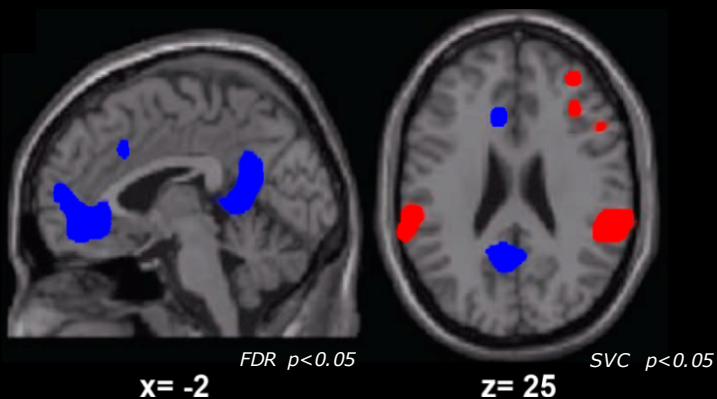
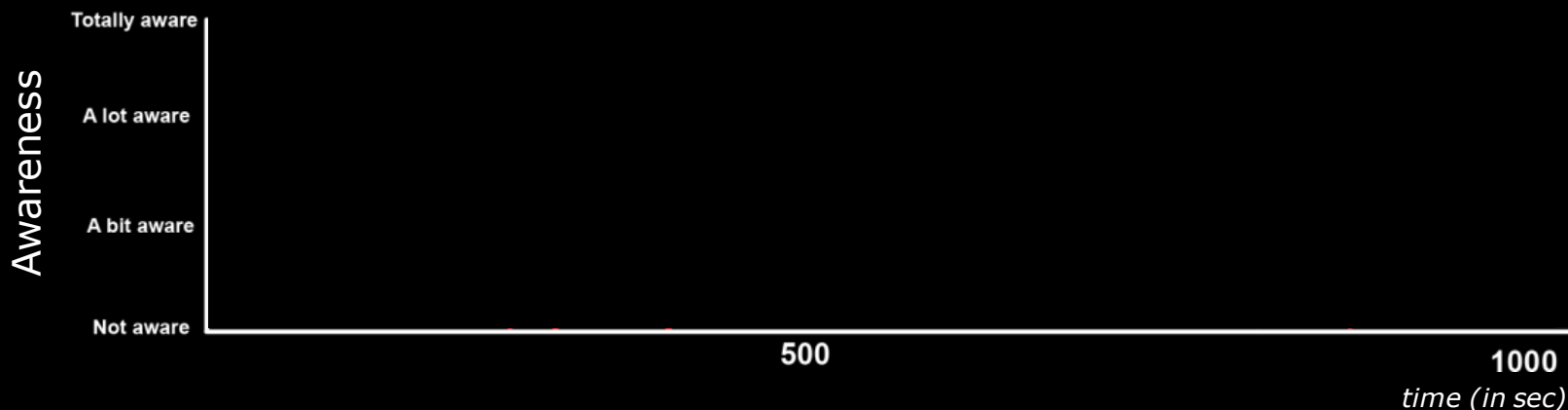


**Internal awareness
or Default mode network**

Cognitive-behavioral coupling at "resting" state

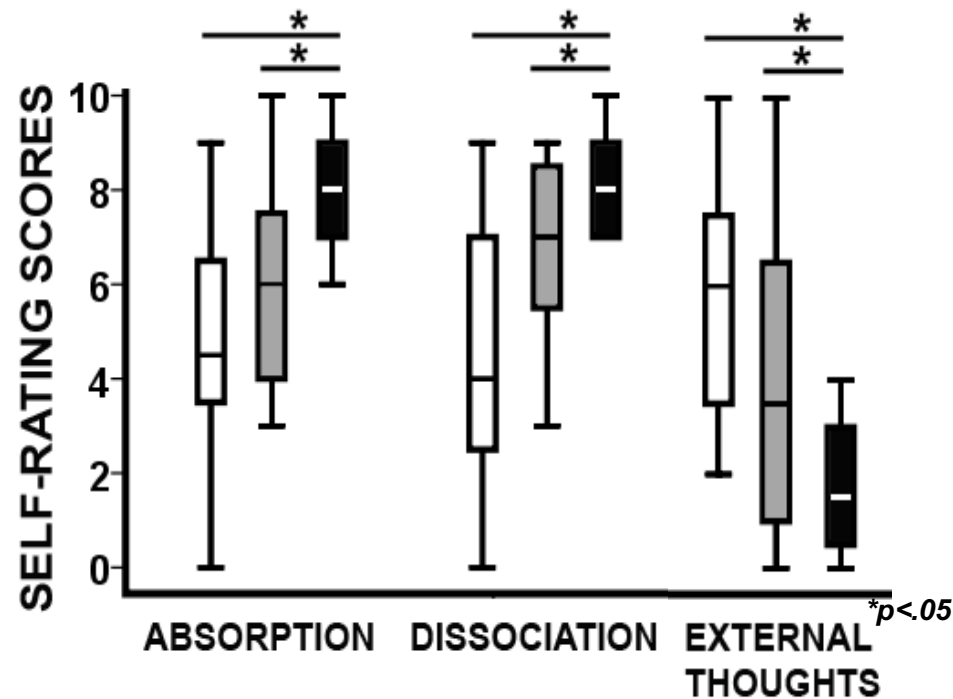
■ External
■ Internal

External-internal: $r = -0.44, p < .02$
Mean switch: 0.05Hz (range: 0.01-0.1)



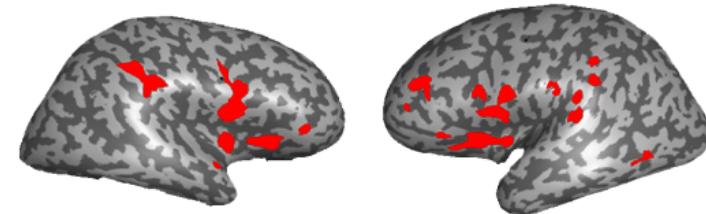
Hypnotic modulation of resting state

- Normal wakefulness
- ▒ Autobiographical mental imagery
- Hypnosis

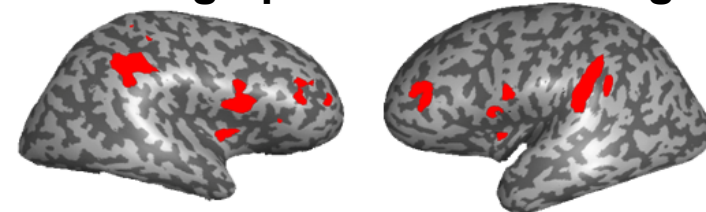


EXTRINSIC SYSTEM

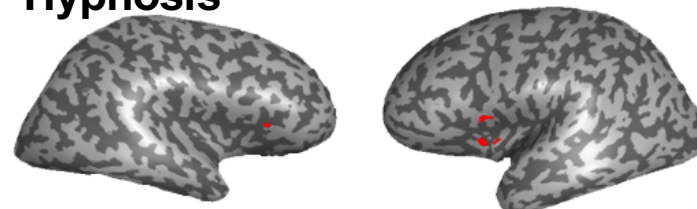
Normal wakefulness



Autobiographical mental imagery

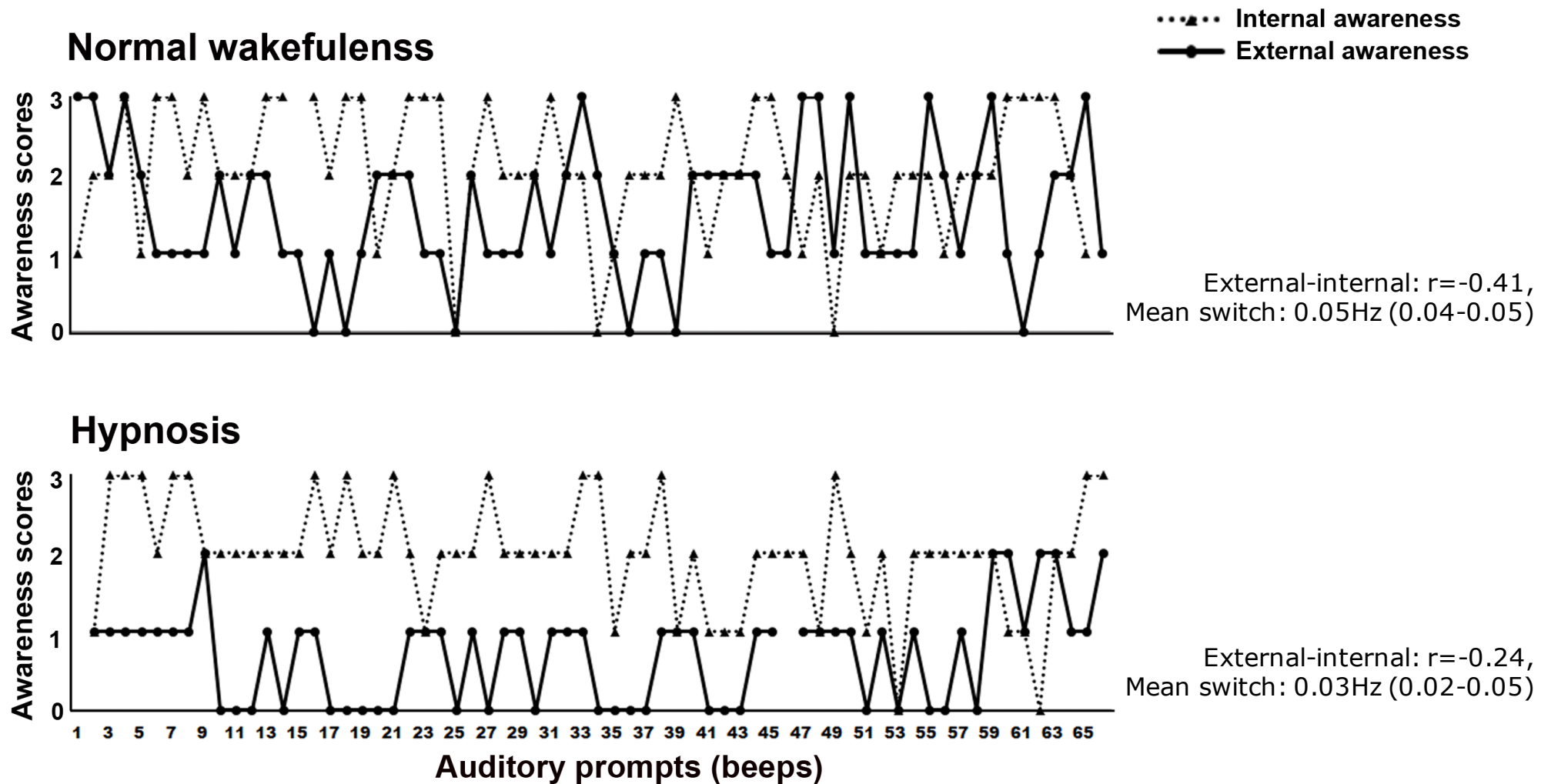


Hypnosis

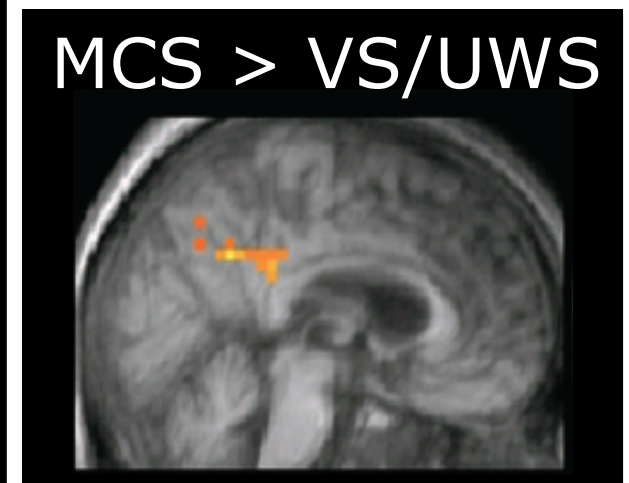
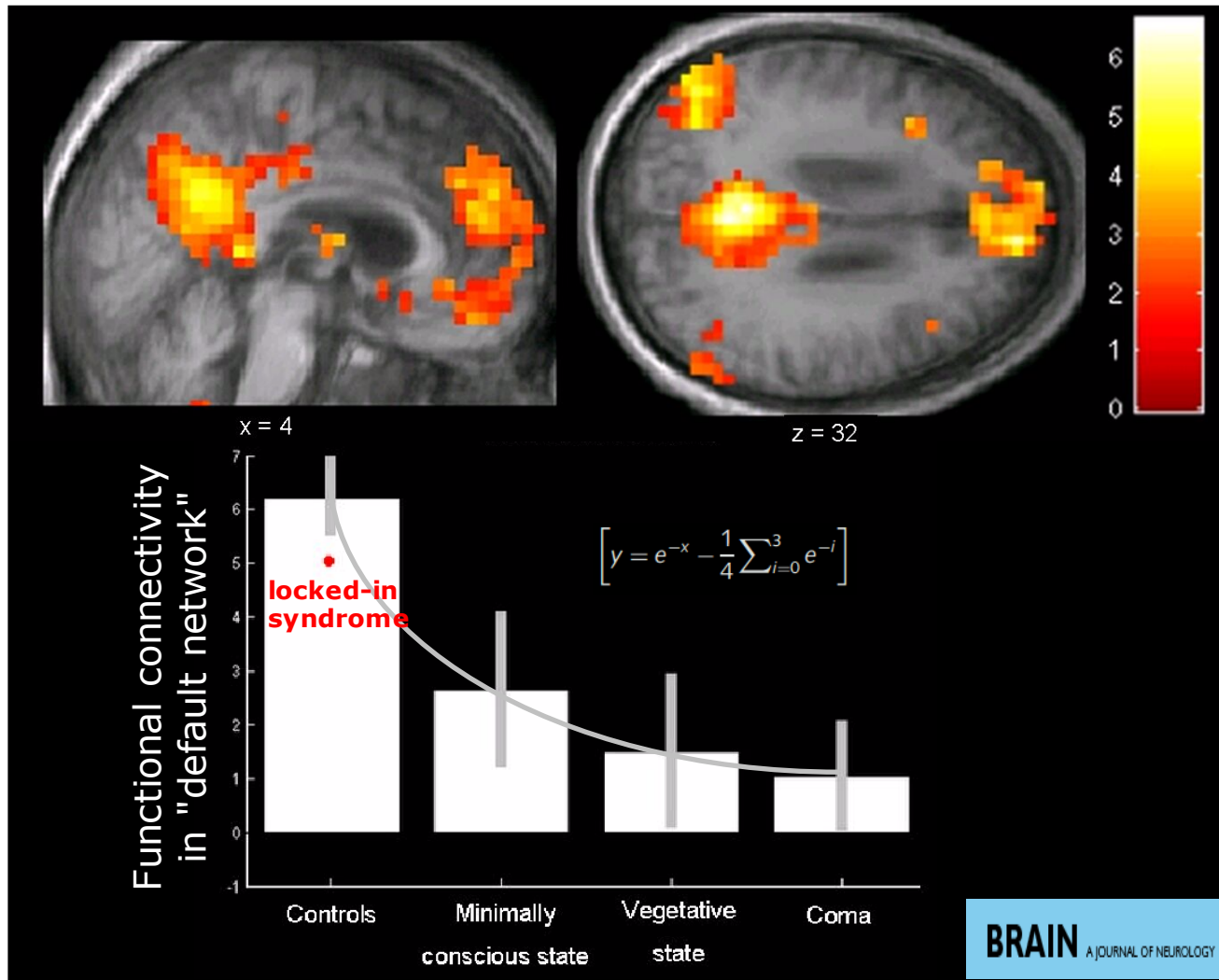


p < 0.05 corrected for multiple comparisons

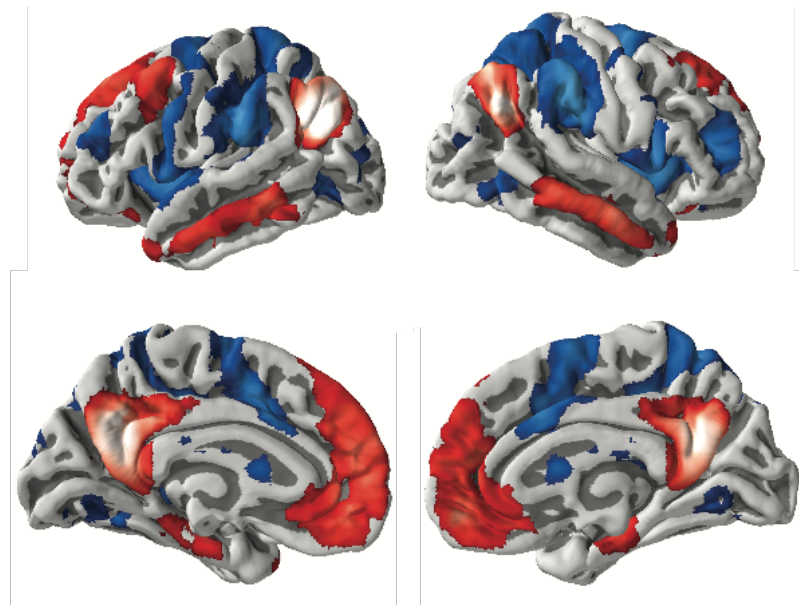
Awareness is modified in hypnosis



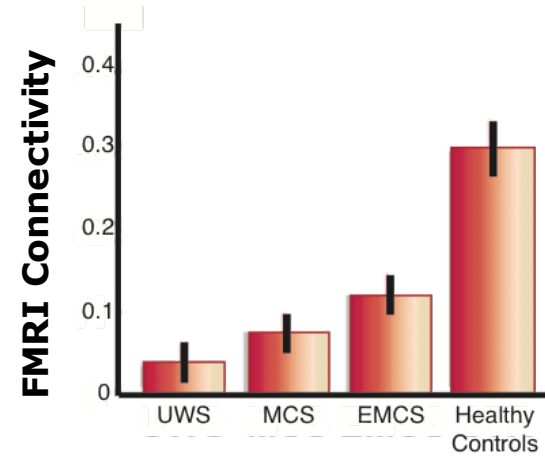
Default connectivity in patients



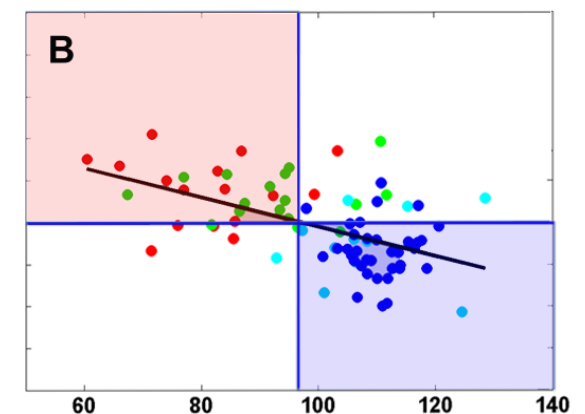
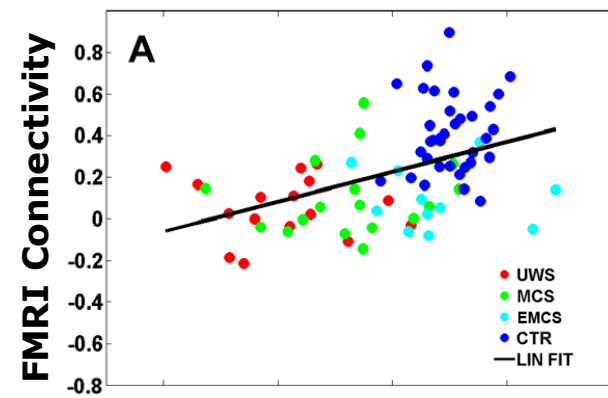
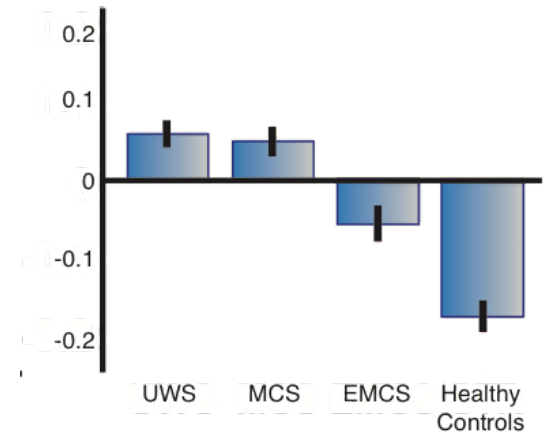
Two awareness networks in DOC



POSITIVE CONNECTIVITY



NEGATIVE CONNECTIVITY

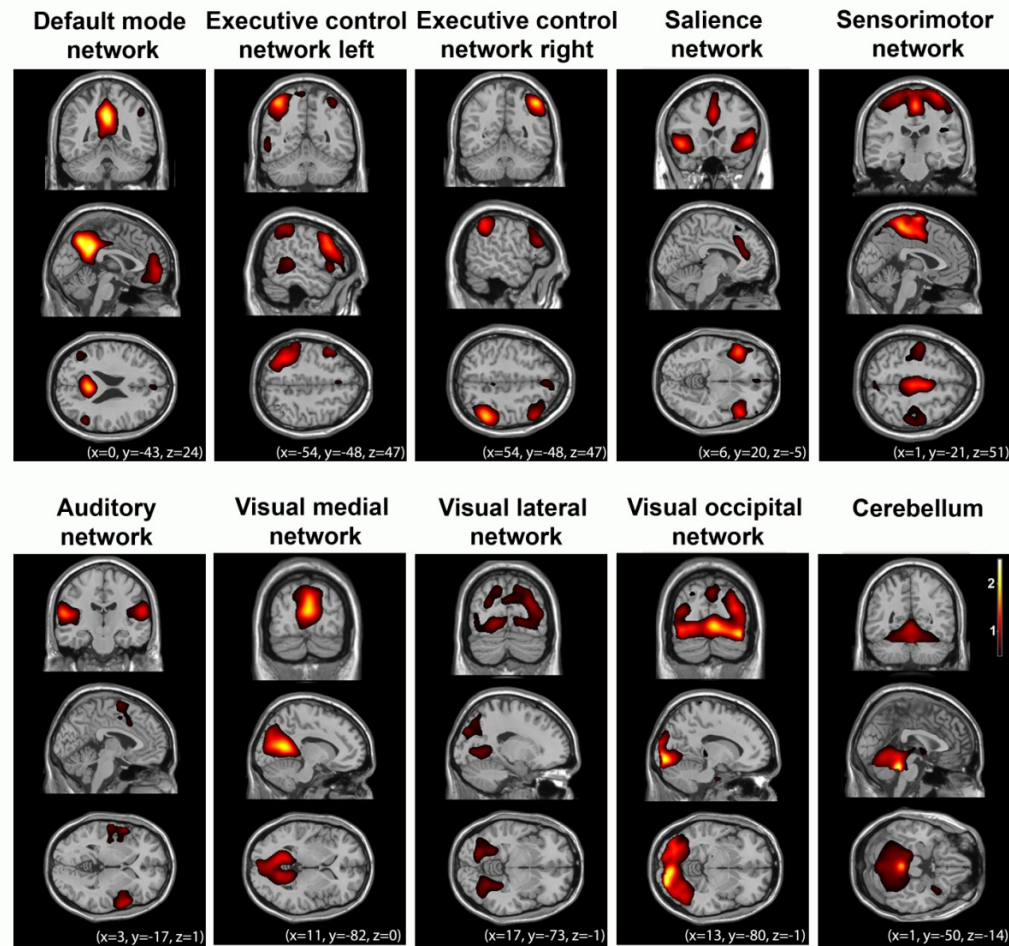


Brain metabolism

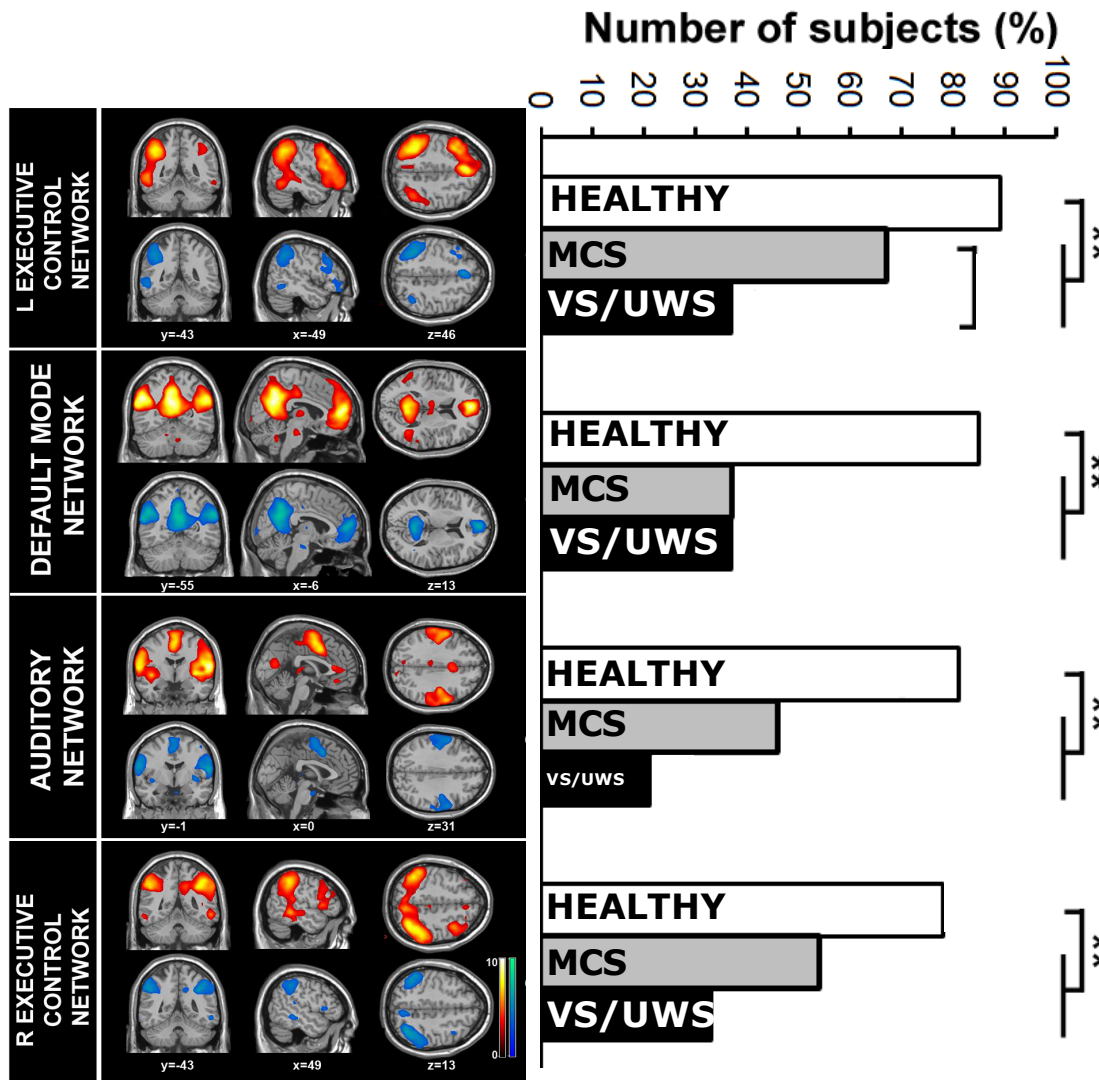
Multiple networks

Resting state networks and consciousness

Alterations of multiple resting state network connectivity in physiological, pharmacological, and pathological consciousness states



Fewer "neuronal" networks in DOC

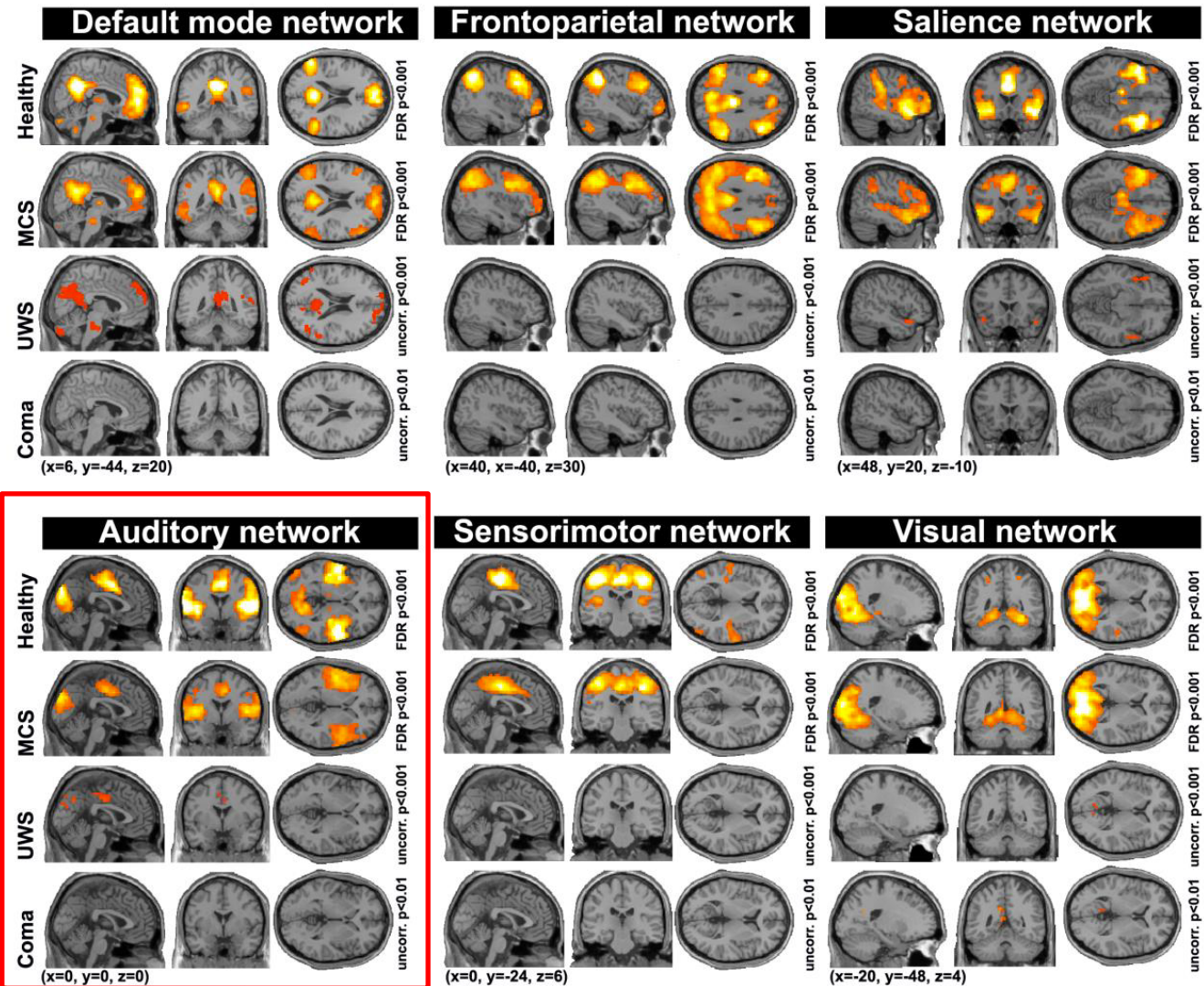


Single-patient classification

Performance measures	Accuracy	TPR healthy	TPR patients	Selected RSNs
Healthy vs. all patients				
Neuronal	85.3	.82	.87	Auditory, DMN
Neuronal & GOF	82.6	.70	.89	Auditory, DMN, Visual lateral
GOF	80	.78	.81	Auditory, DMN, ECNL, Visual lateral

Finding the discriminative features

BRAIN A JOURNAL OF NEUROLOGY

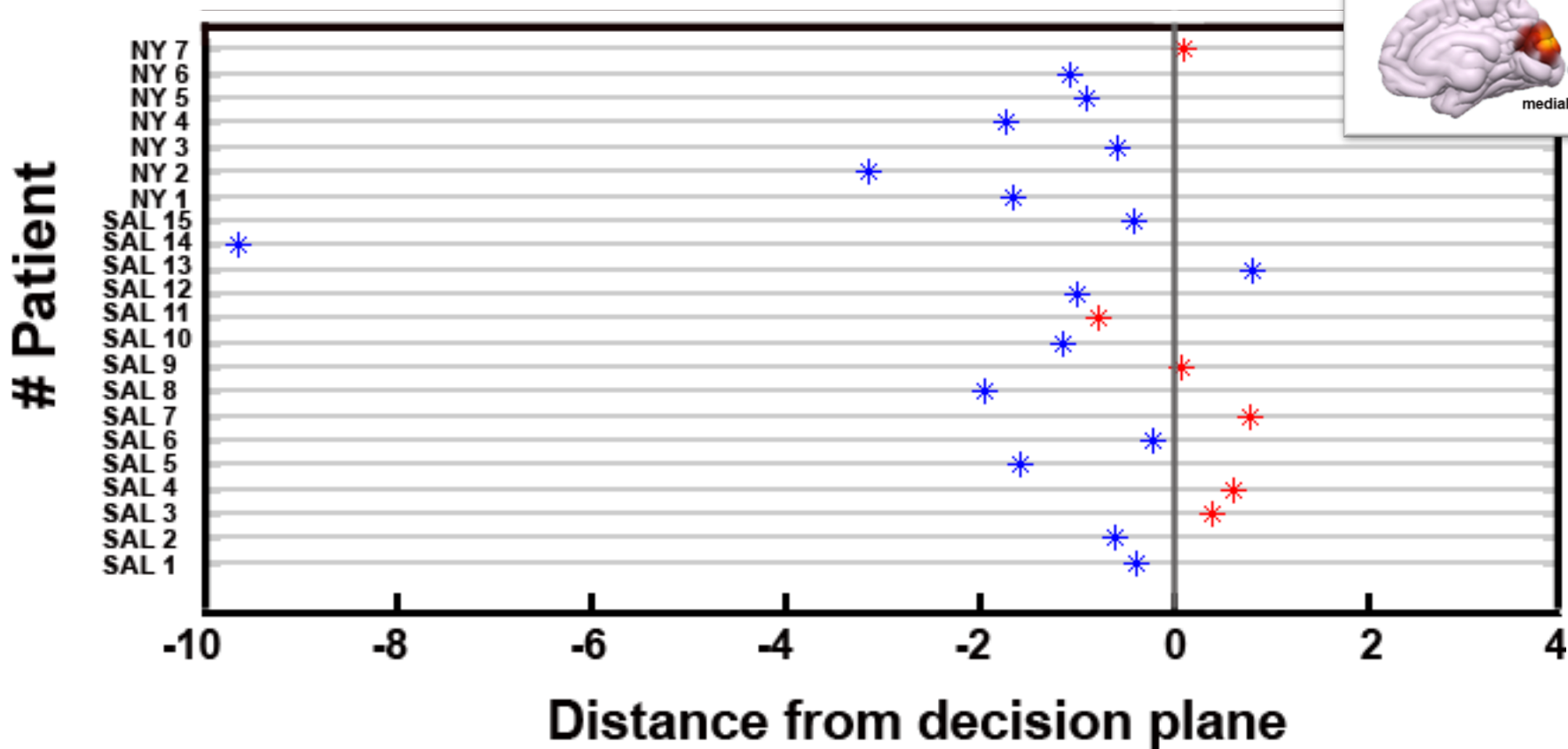
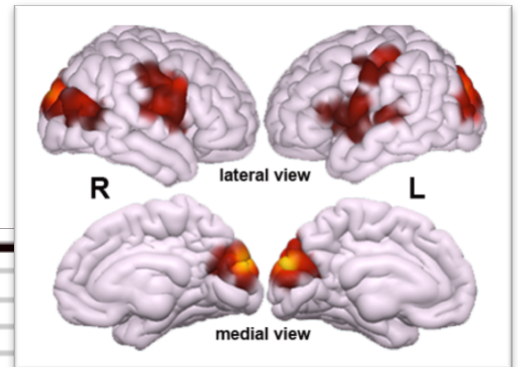


Classification of new patients

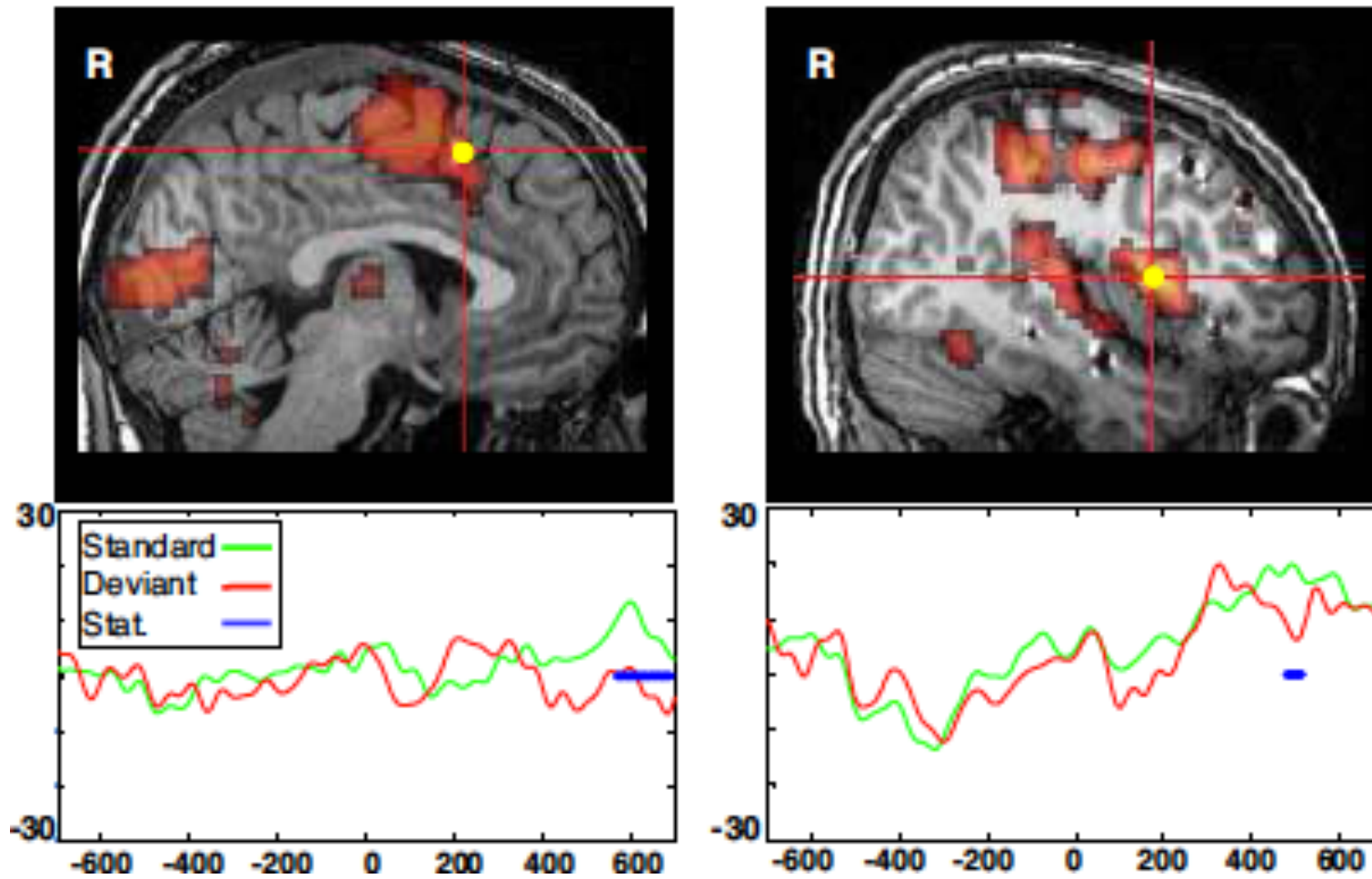
- 26 MCS, 19 VS/UWS
- 14 trauma, 28 non-trauma, 3 mixed
- 34 patients assessed >1m post-insult

Clinical diagnosis

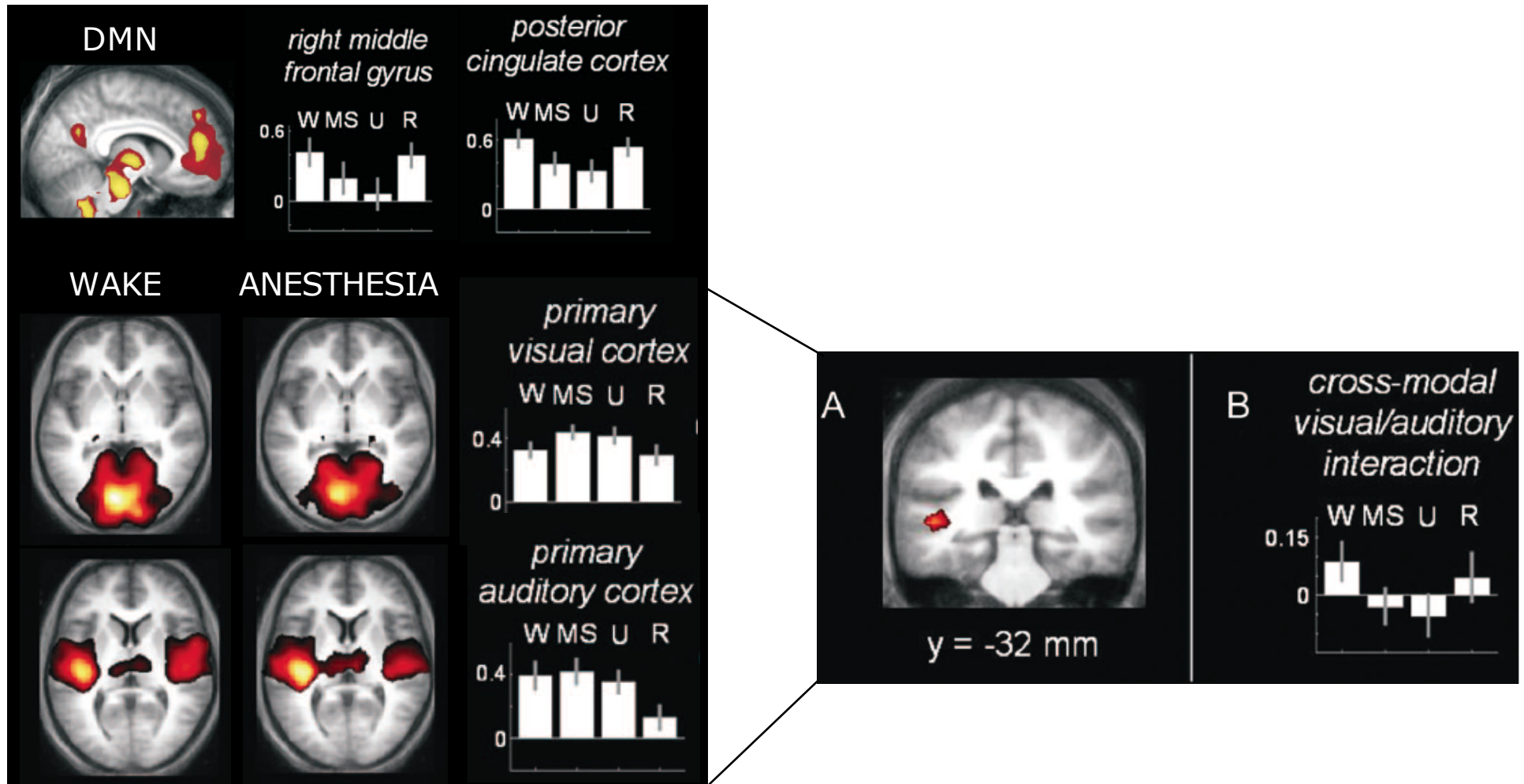
- MCS
- VS/UWS



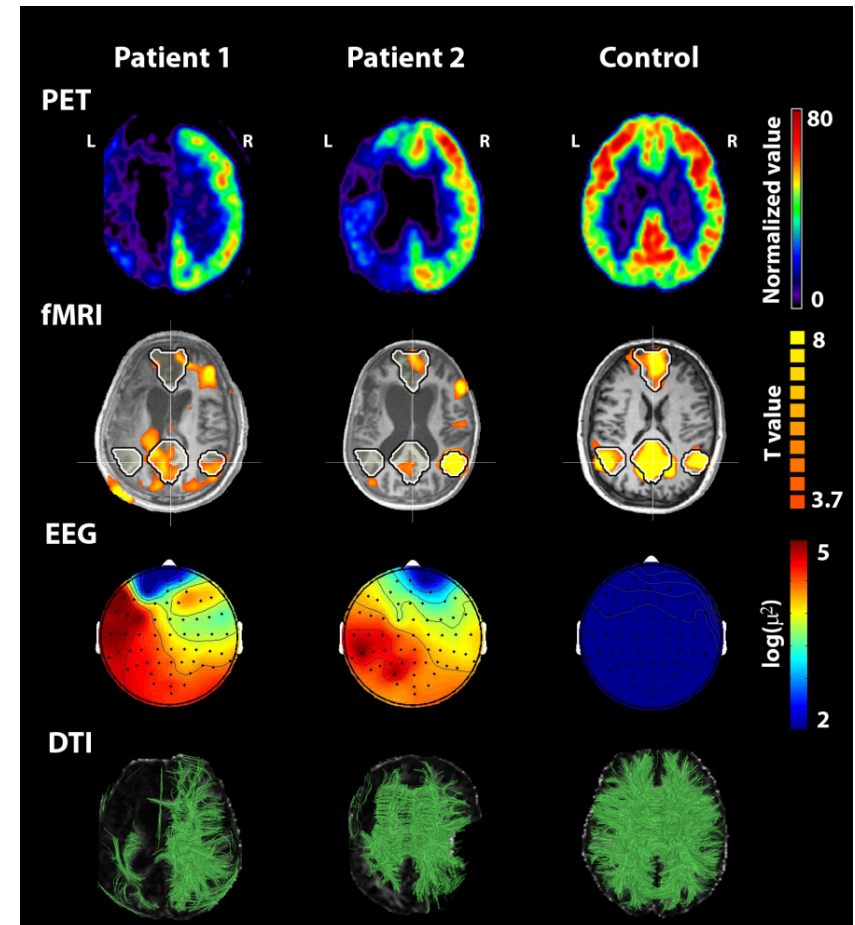
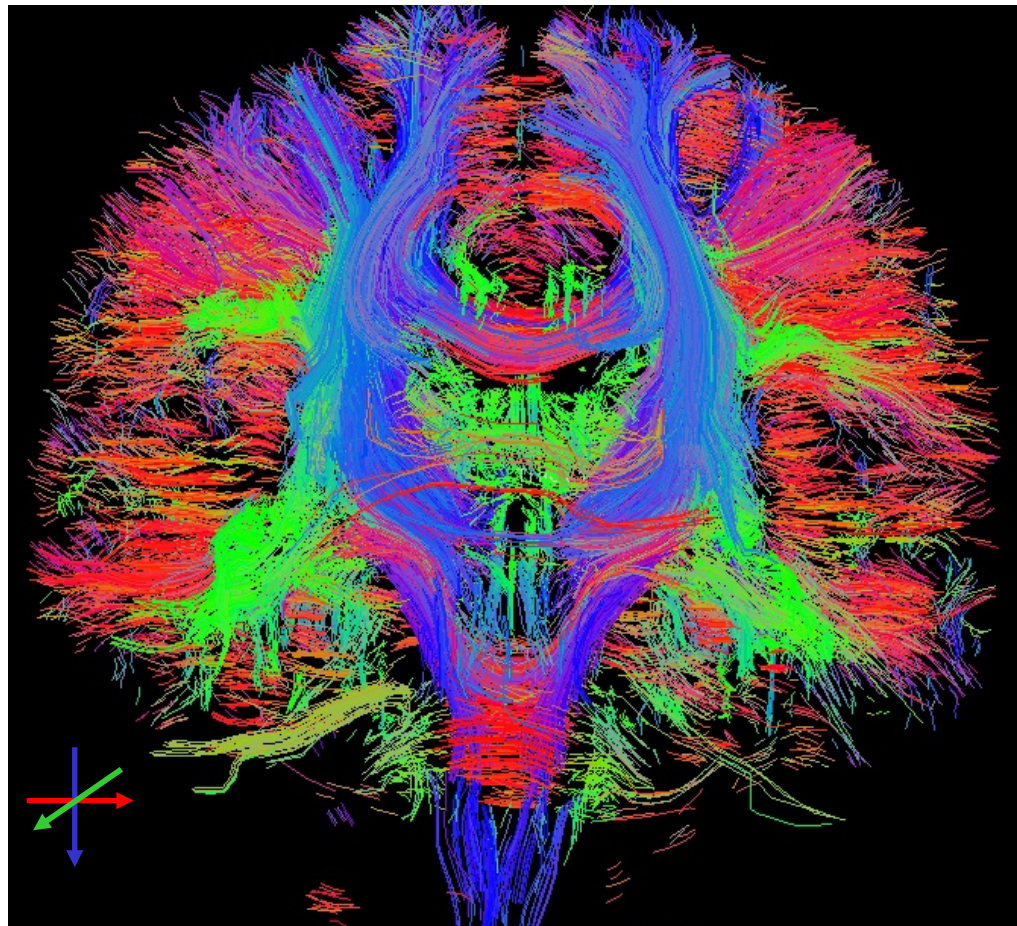
Cross-modal interaction in conscious processing



Default connectivity in anesthesia



Multimodal imaging



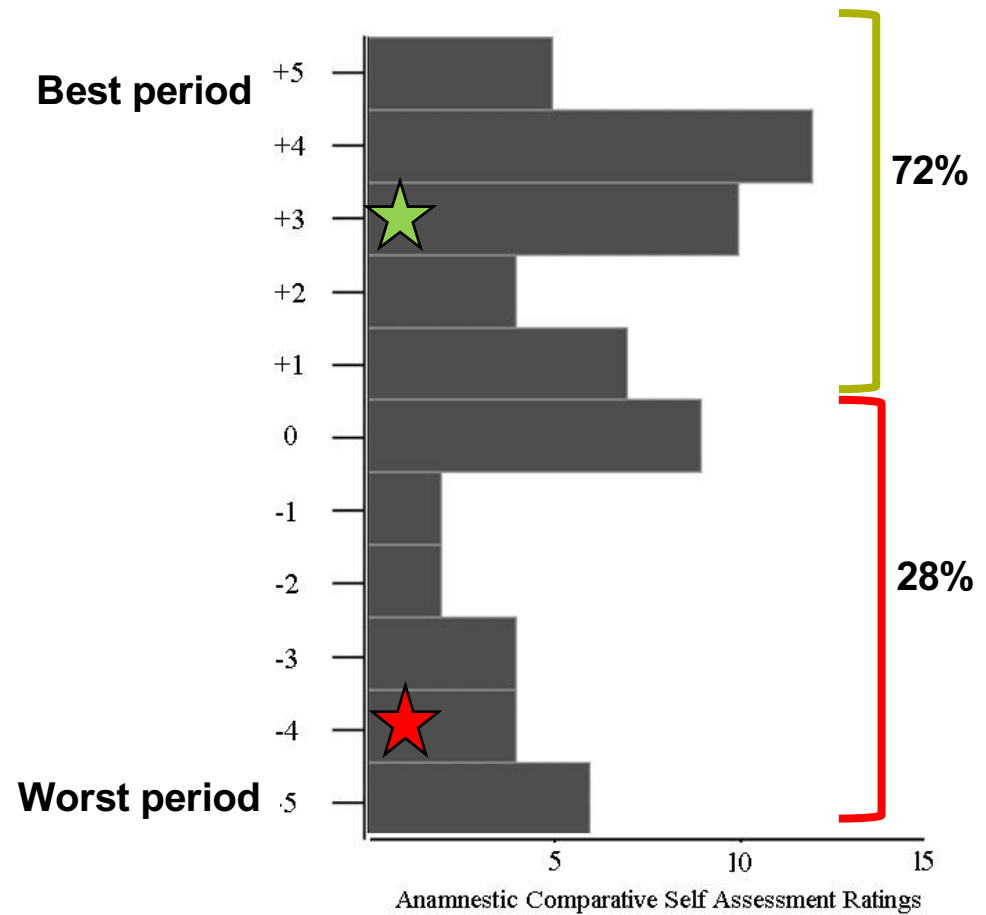
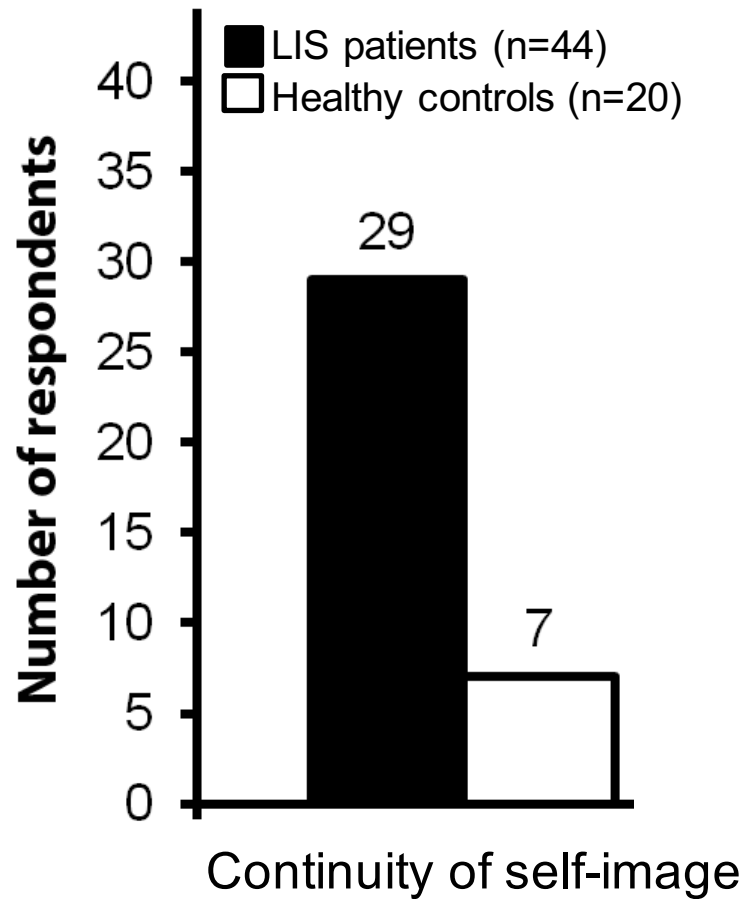
The ethical relevance of technology-based assessment

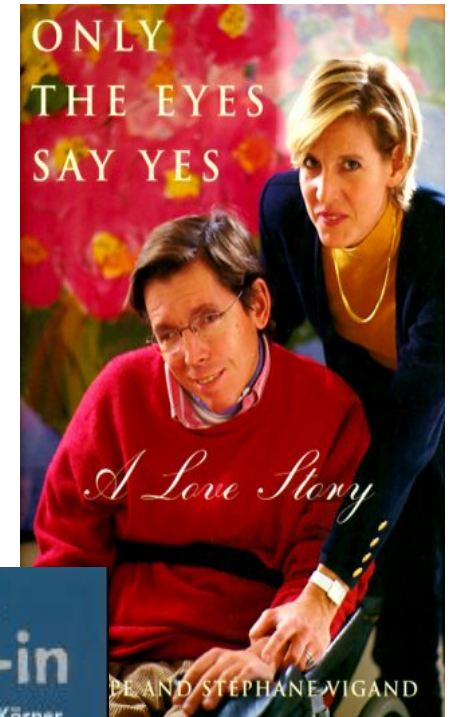
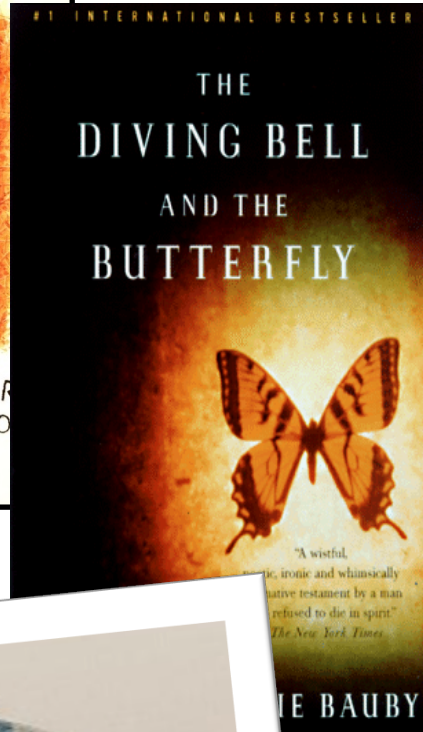
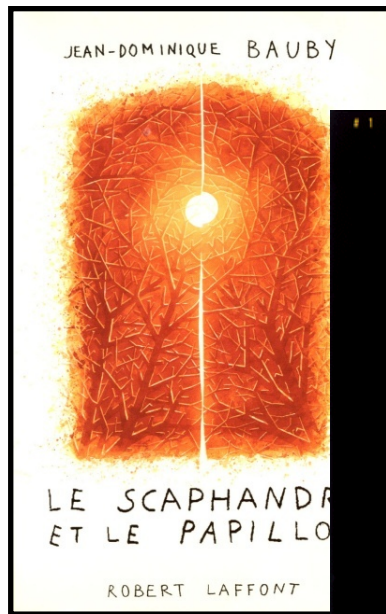
Results of Tests	Beneficial Effects	Harmful Effects
- brain activity than neurological examination	Relatives: decisions to limit life-sustaining treatment	Relatives: may lose hope, purpose, and meaning in life
+ brain activity than neurological examination	Clinical management: may be intensified by the chance of further recovery	Relatives: false hopes
Same as neurological examination	Clinicians & relatives: may be affirmed in their decision about the level of treatment	Clinicians & relatives: may be disappointed & treatment cost/effectiveness may be poor

Communication in LIS

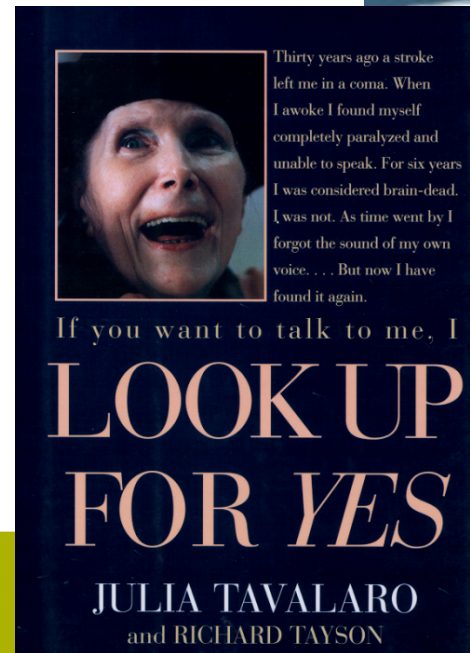


Third vs. first-person perspective

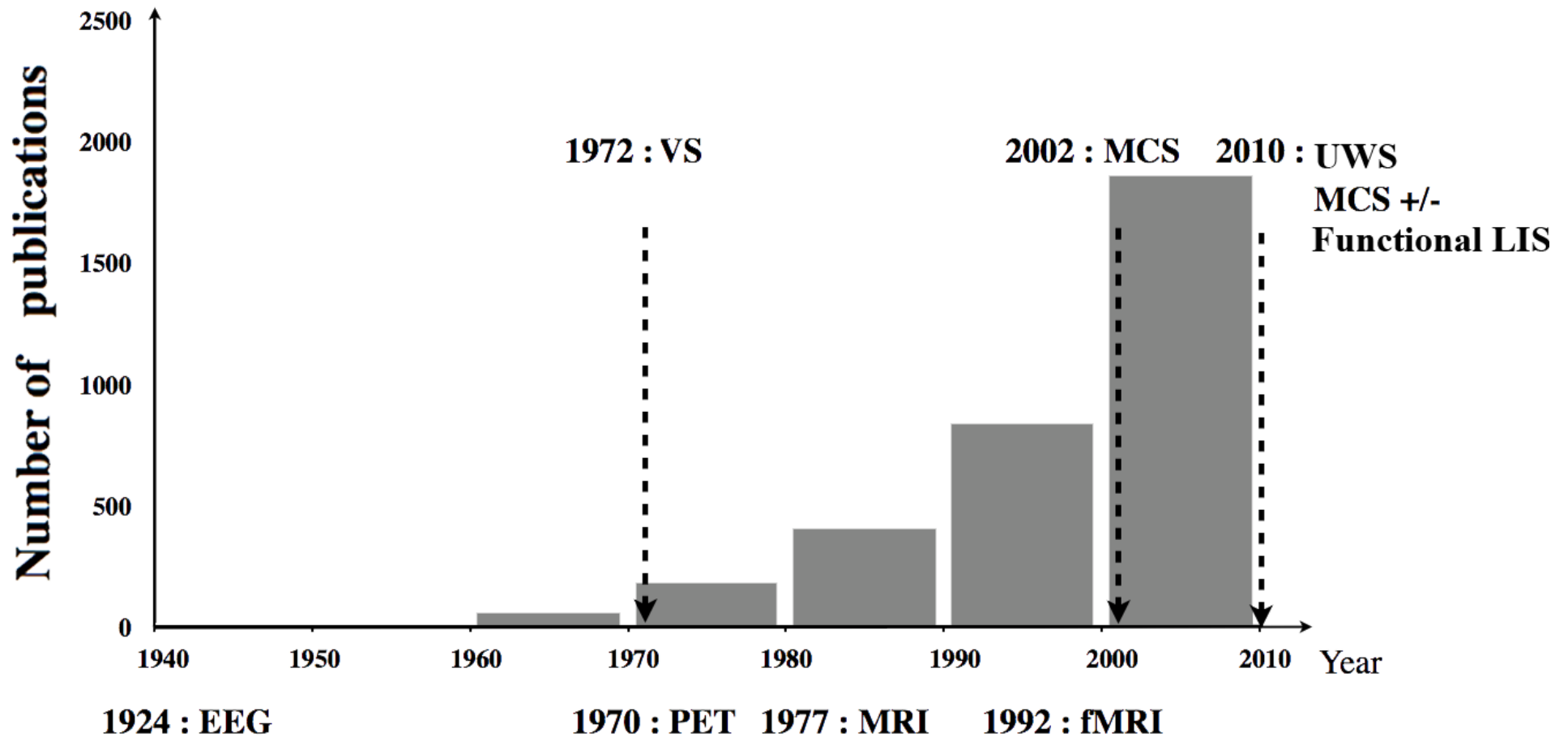




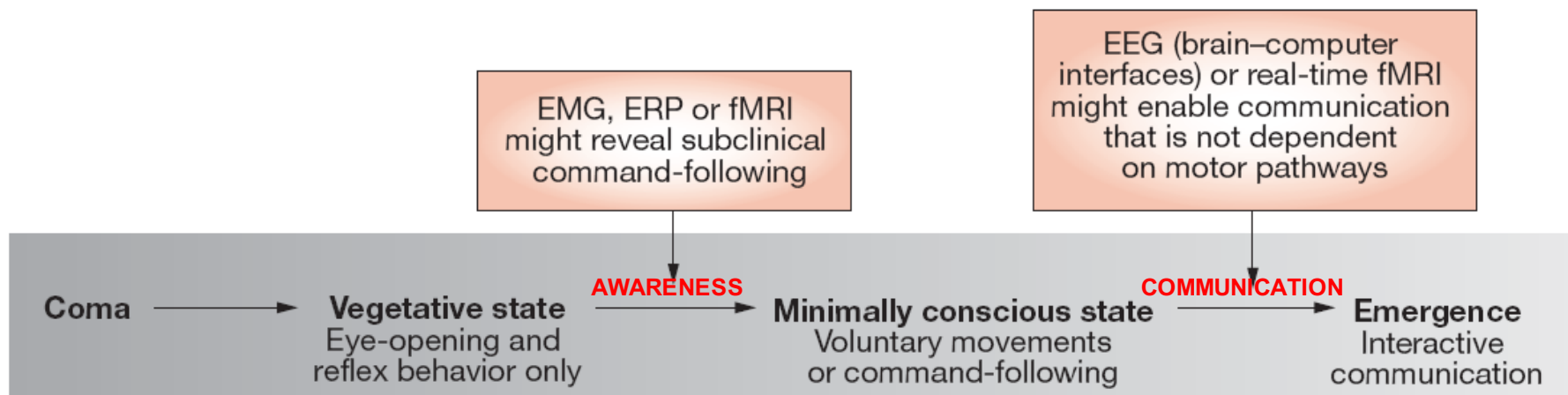
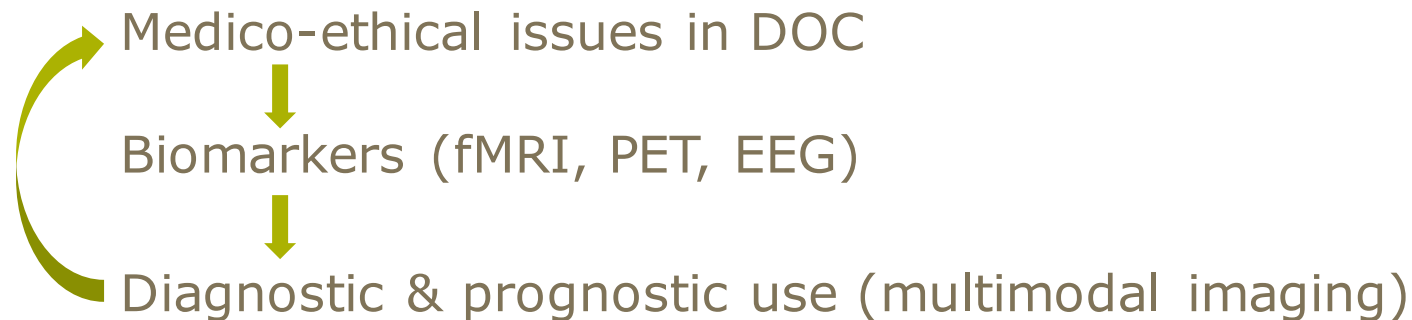
'Le scaphandre et le papillon' (2007)
Direction: Julian Schnabel



New knowledge, new nosology



Translational research



www.nature.com/clinicalpractice/neuro

Neuro-ethical issues to consider:

- The moral significance of Consciousness
 - ontological understanding: consciousness = personhood = moral agency
 - relational or contextual understanding: patients have value for others
- Legal challenges: responses to critical questions with NI
- Cognitive neuroscience is about brain/mind reading
 - to what degree do we neuroscientists have the right to interfere with a patient's intimacy, such as cognitive contents, in the absence of their consent?
 - in essence, where do we draw the limits of deciphering another person's cognitive content, like dreams, ongoing mentation etc? What is the additive value of it to a societal level?

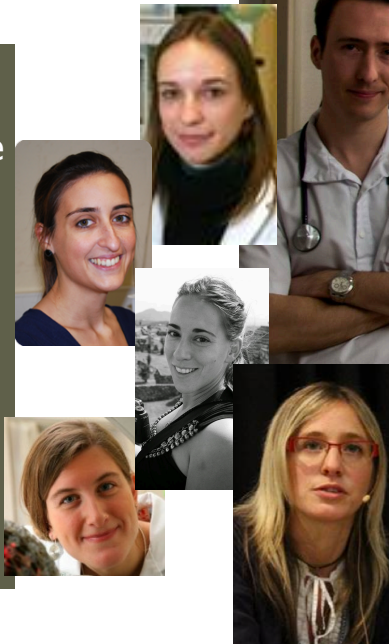


Niko Schiff & Henning Voss,
Weill Cornell Medical College

Julia Sophia Crone & the
Salzburg team

The departments of
Neurology and Radiology in
Liege and Paris

**...but mostly patients
and their families!**



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