Intrinsic functional connectivity changes along the spectrum of consciousness

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Consciousness

Materialism

Functionalism

Dualism

■ Edinburgh survey (n=250)
□ Liège survey (n=1858)
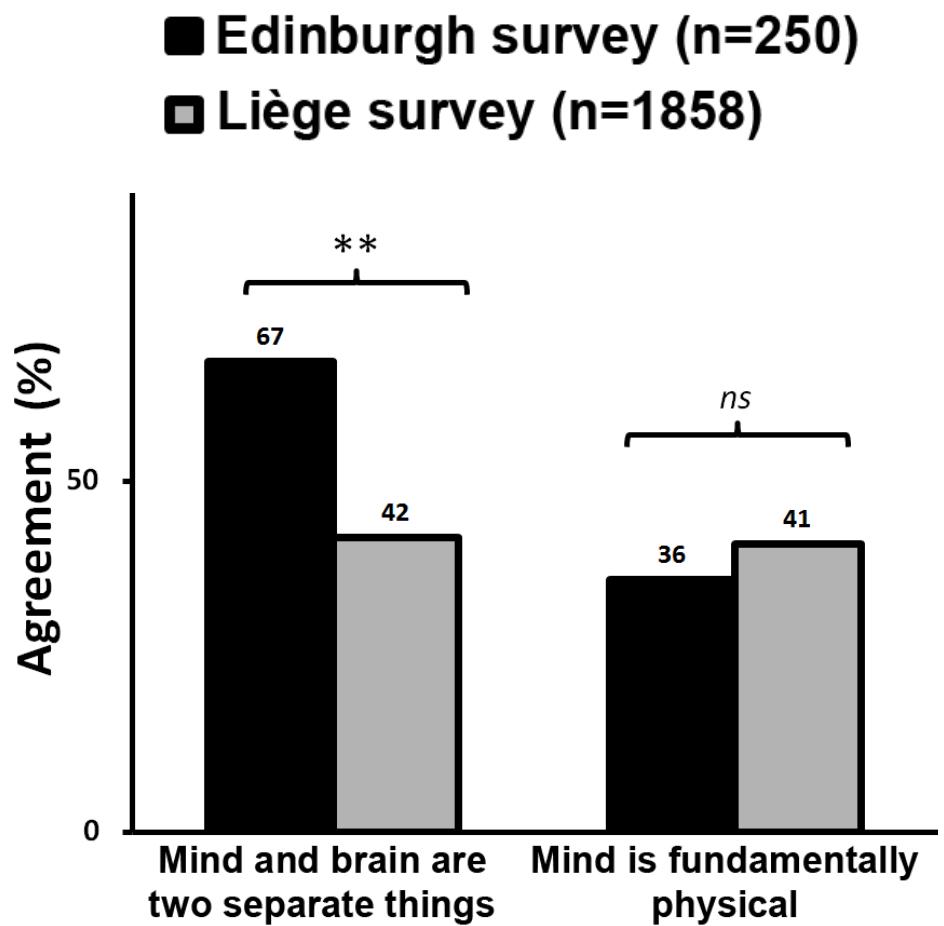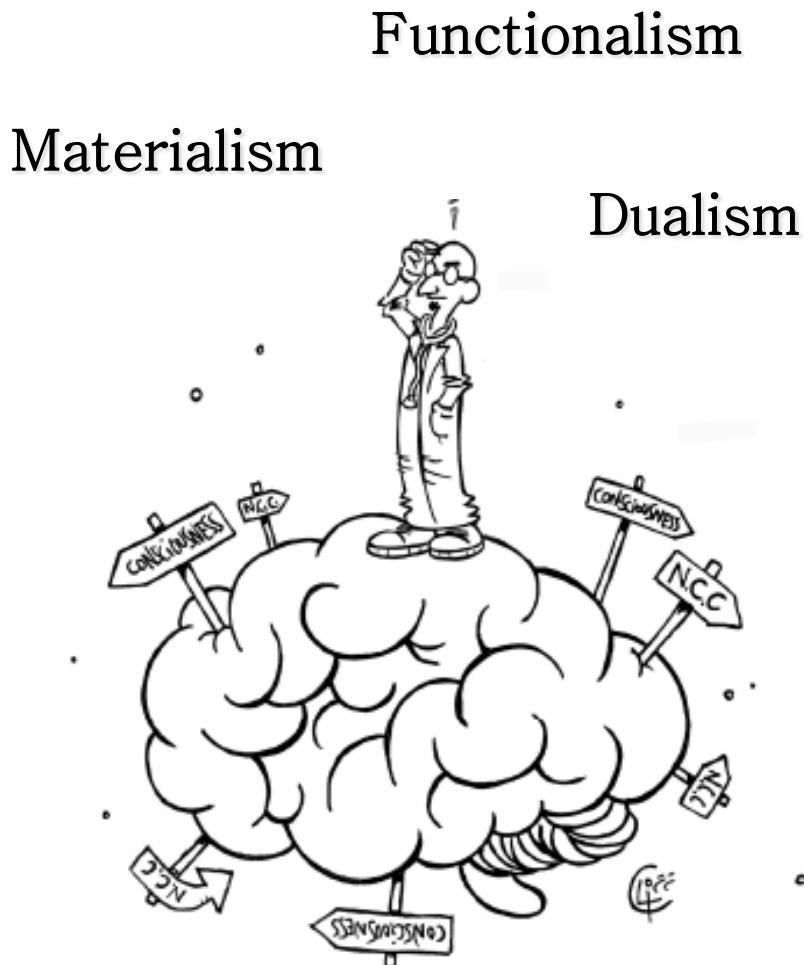
A clinical definition of consciousness

Demertzi et al, Encyclopedia of Consciousness 2009
Demertzi et al, Expert Review in Neurotherapeutics 2008
Laureys, Trends in Cognitive Sciences 2005
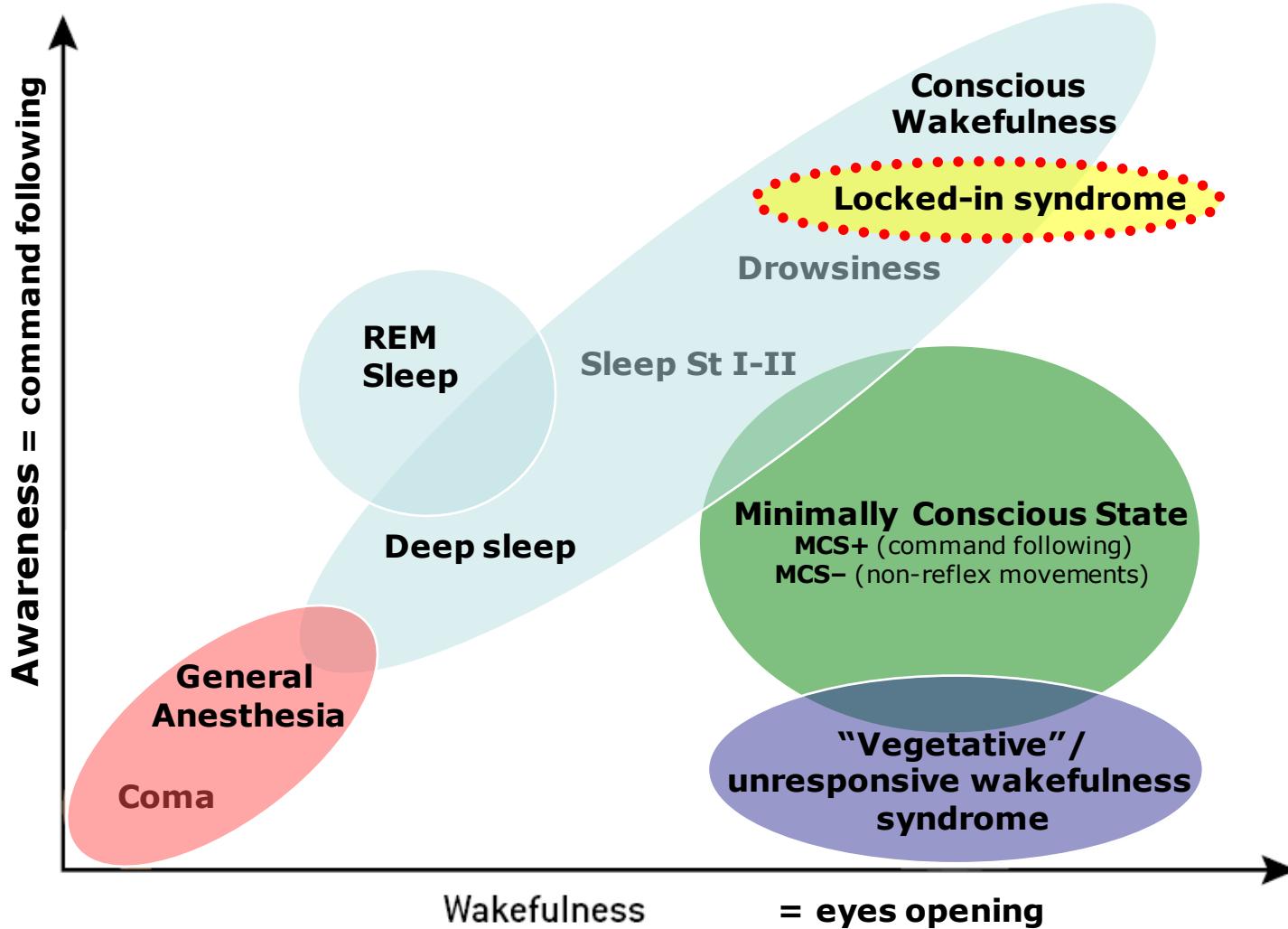
A clinical-ethical imperative

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

European Neurological Society
ENS

2,475 medical professionals

North
Central
South

VS MCS
It is acceptable to stop treatment in a chronic...

66%
28%

VS MCS
I would like to be kept alive if I were in a chronic...

82%
67%

** **

Demertzi et al, J Neurol 2011; Prog Brain Res 2009; Neuroethics 2013; Br Injury 2014
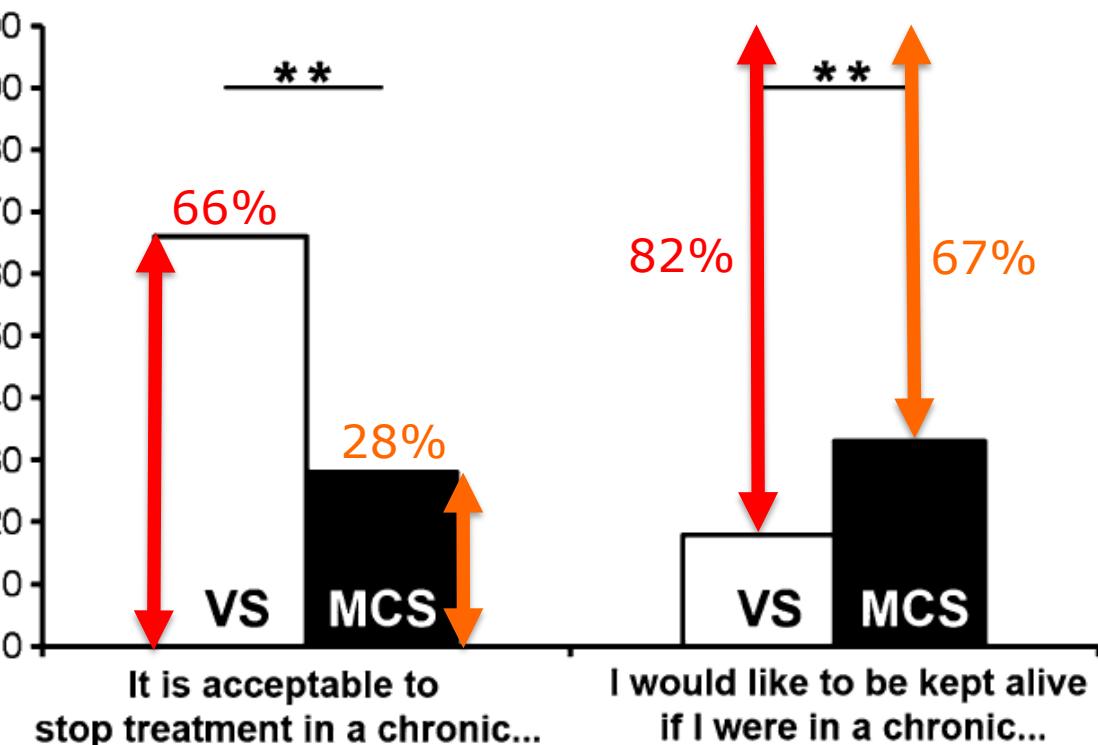
Neuroimaging paradigms

Active paradigms
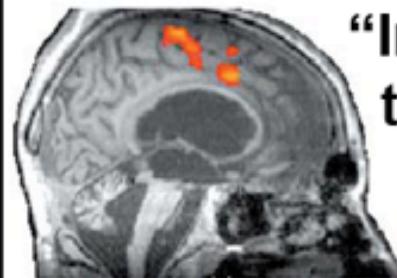
"Imagine playing tennis"

"Imagine visiting the rooms of your house"

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

Passive paradigms

median nerve
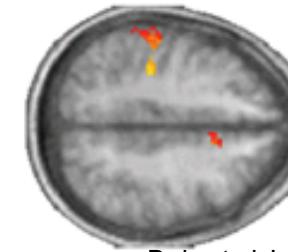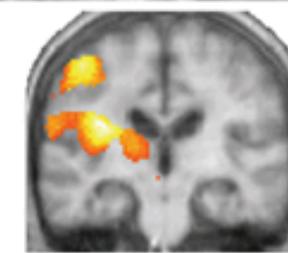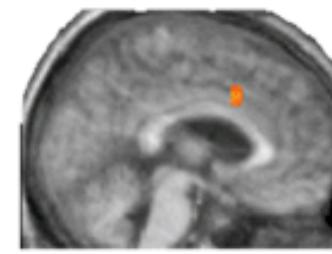
Boly et al, Lancet Neurol 2008

Intrinsic brain activity & awareness

External awareness
or **anticorrelated network**
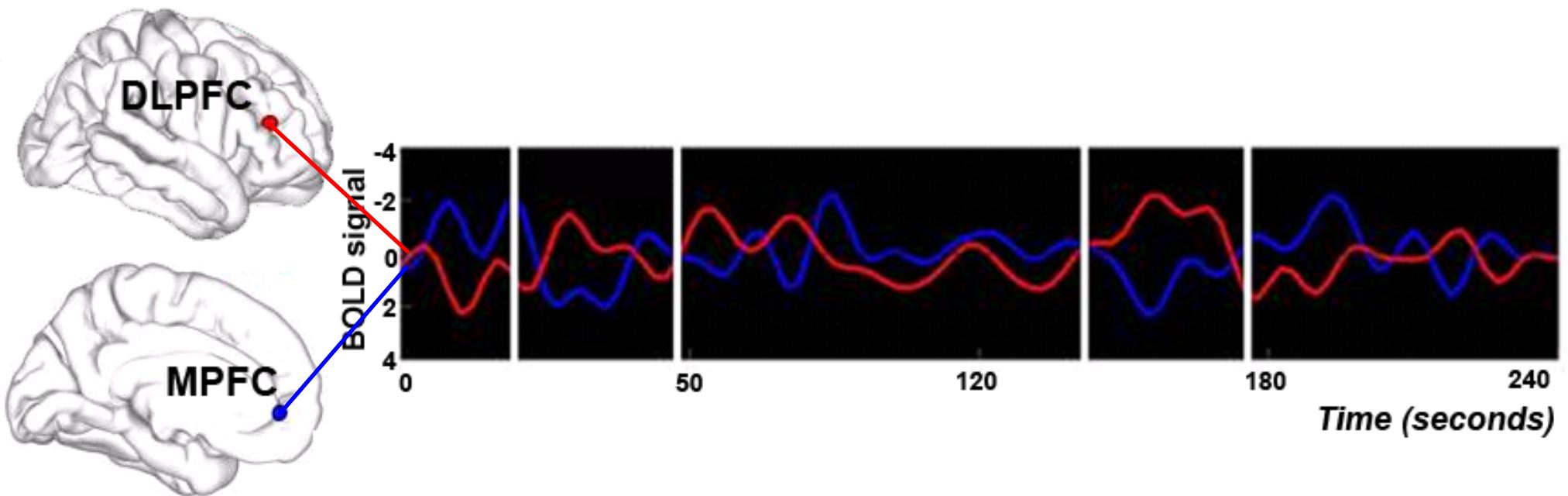
Internal awareness
or **Default mode network**

Demertzi & Whitfield-Gabrieli, in: *Neurology of Consciousness* 2nd ed. *2015*
Demertzi, Soddu, Laureys, Curr Opin Neurobiology 2013
Demertzi et al, Front Hum Neurosci 2013
Laureys, Scientific American 2007

Cognitive counterpart of intrinsic activity: the task

The cognitive counterpart of intrinsic activity
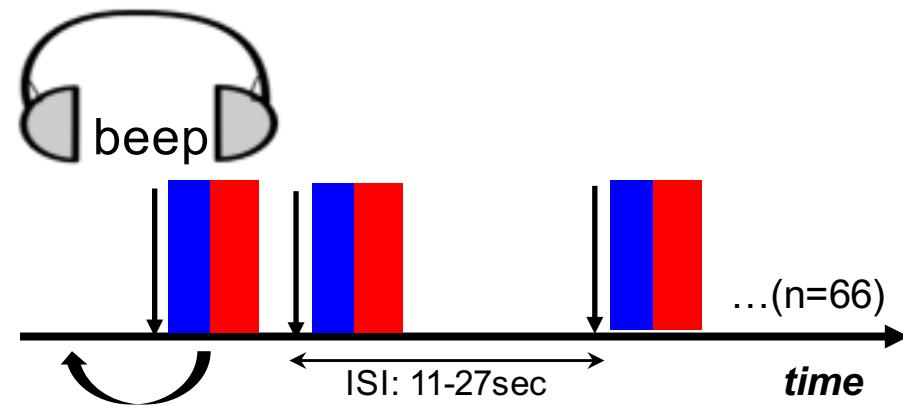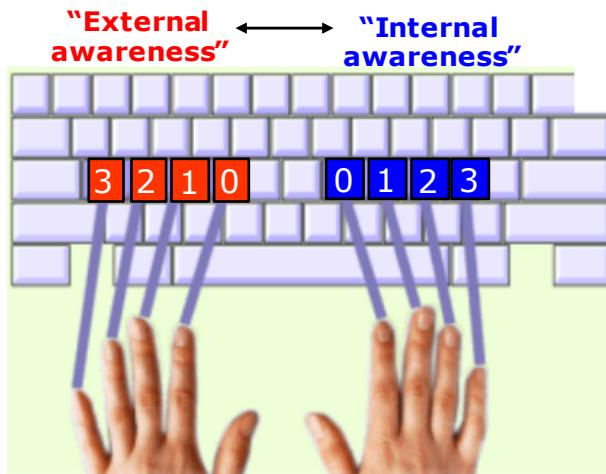
External-internal: r=-0.44, p<.02
Mean switch: 0.05Hz (range: 0.01-0.1)

Internal awareness
External awareness

Awareness: Totally aware / A lot aware / A bit aware / Not aware

time (in sec) — 500 — 1000

x= -2   FDR p<0.05   z= 25   SVC p<0.05

Anterior cingulate cortex

strong mild mild strong
External Internal

Inferior parietal lobule

strong mild mild strong
Extern   Interne

Vanhaudenhuyse & Demertzi et al, Journal of Cognitive Neuroscience 2011
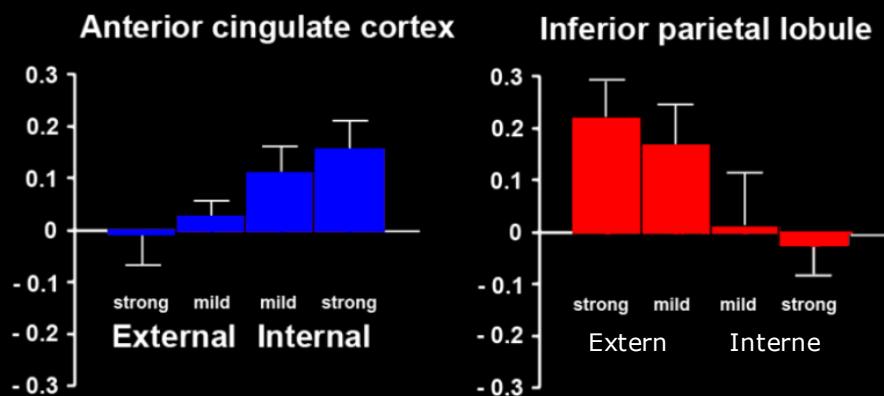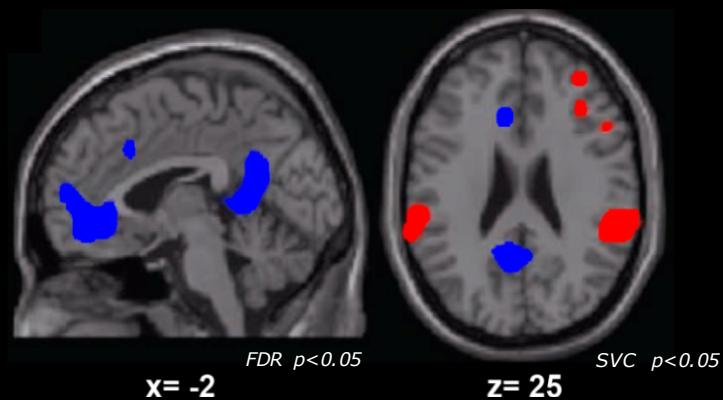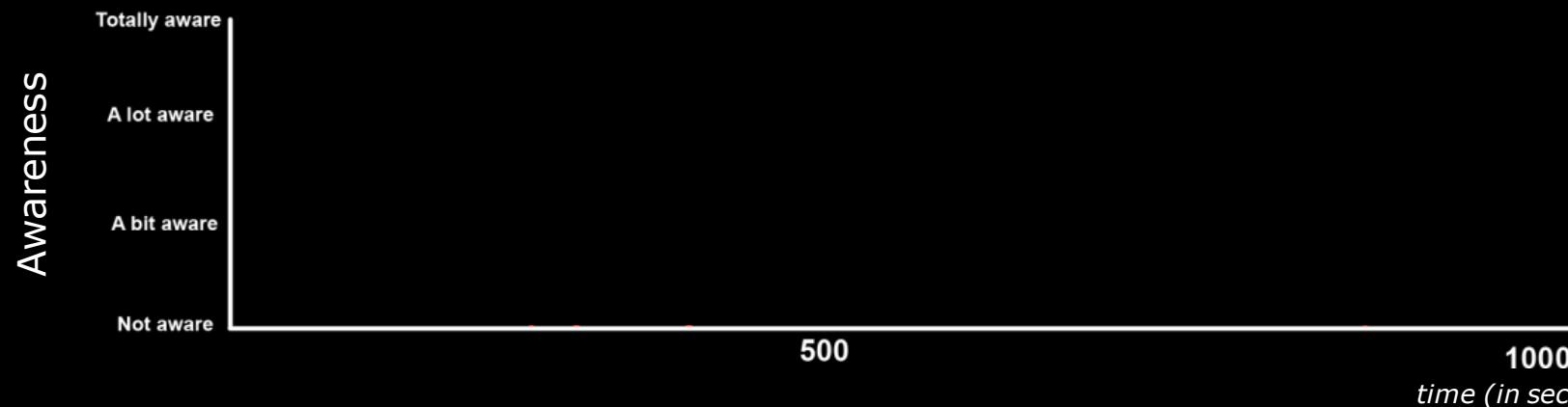
Anticorrelated brain connectivity is modified in hypnosis

☐ **Normal consciousness**
☐ **Autobiographical mental imagery**
■ **Hypnosis**
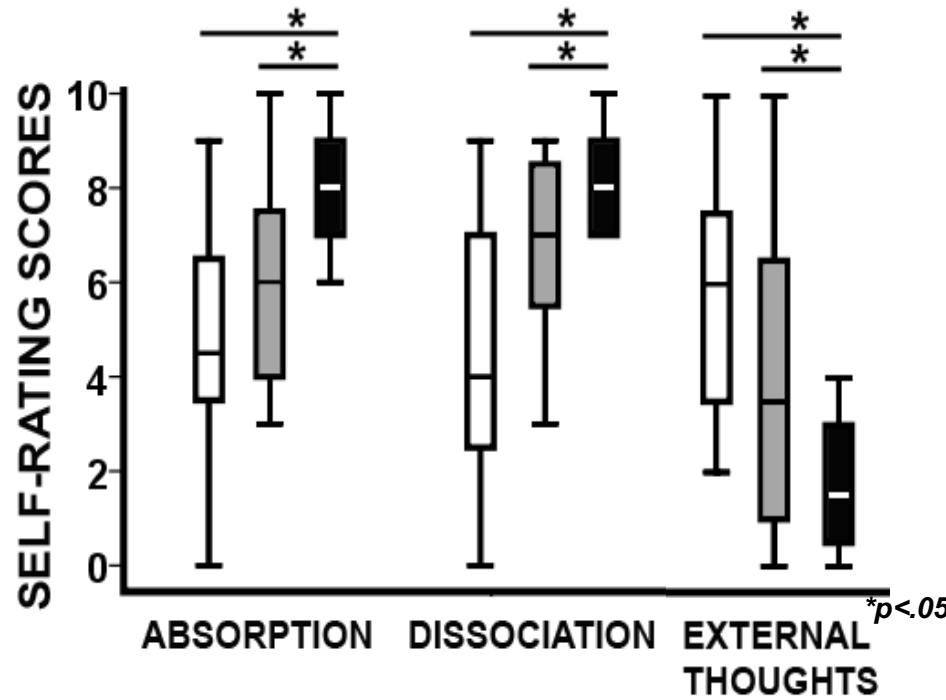
EXTRINSIC SYSTEM

Normal consciousness
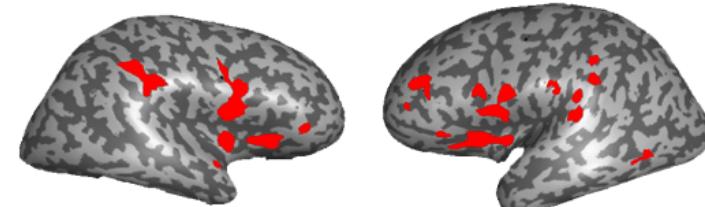
Autobiographical mental imagery
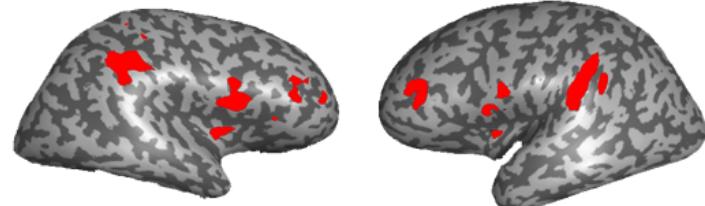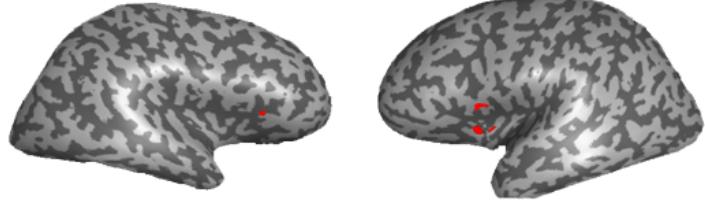
**Hypnosis**

p<0.05 corrected for multiple comparisons

*p<.05

Demertzi, Soddu, Faymonville et al, Progress in Brain Research 2011

Behavior is modified in hypnosis

Demertzi, Vanhaudenhuyse, Noirhomme, Faymonville, Laureys, in press

Awareness is modified in hypnosis (1)

Demertzi, Vanhaudenhuyse, Noirhomme, Faymonville, Laureys, in press

Awareness is modified in hypnosis (2)

Demertzi, Vanhaudenhuyse, Noirhomme, Faymonville, Laureys, J Physiol Paris in press
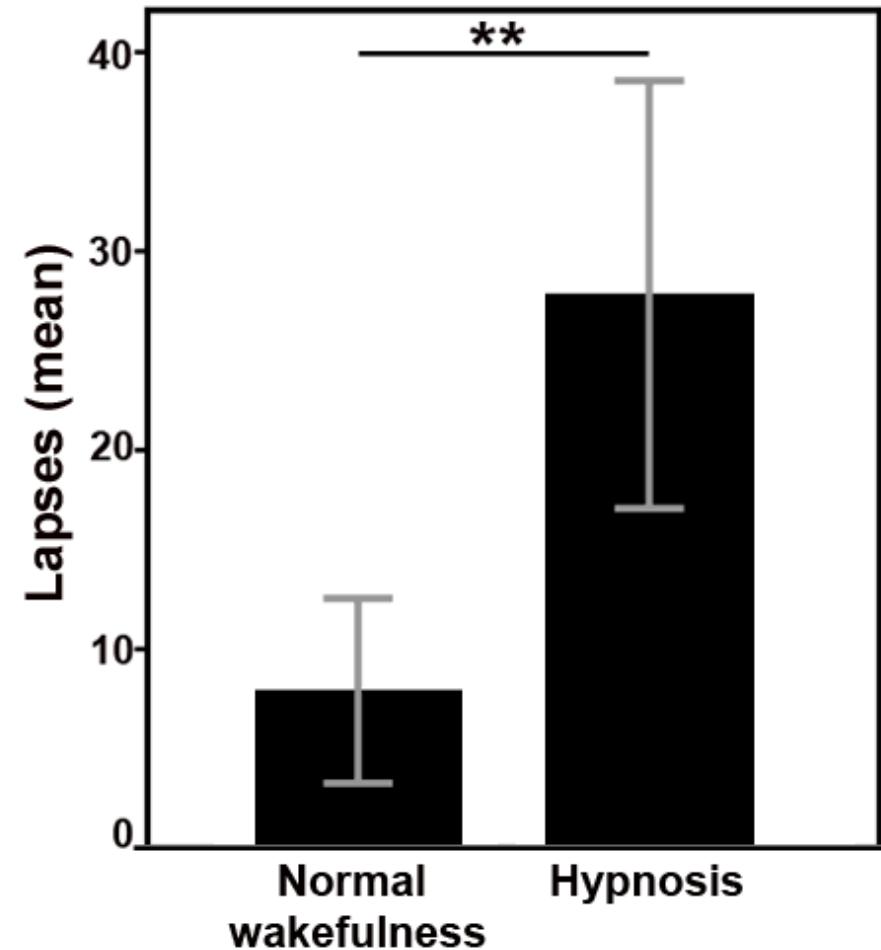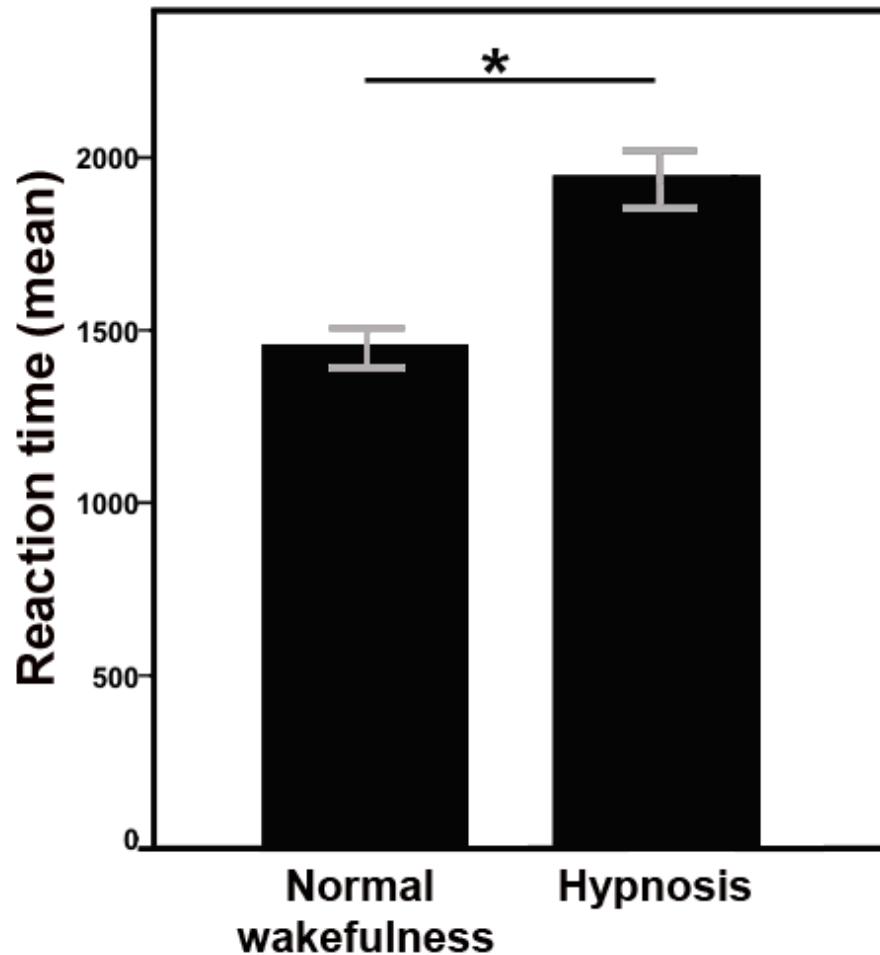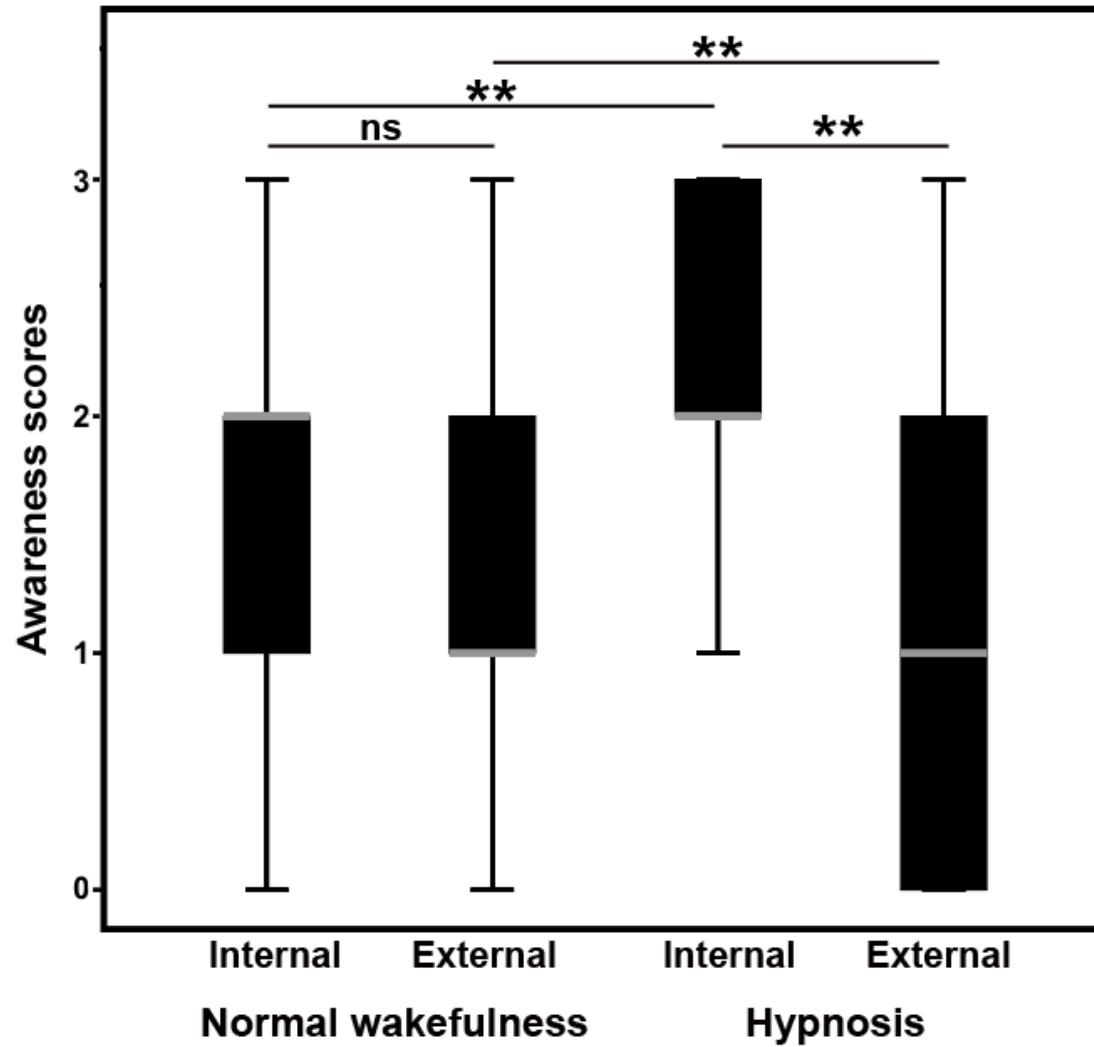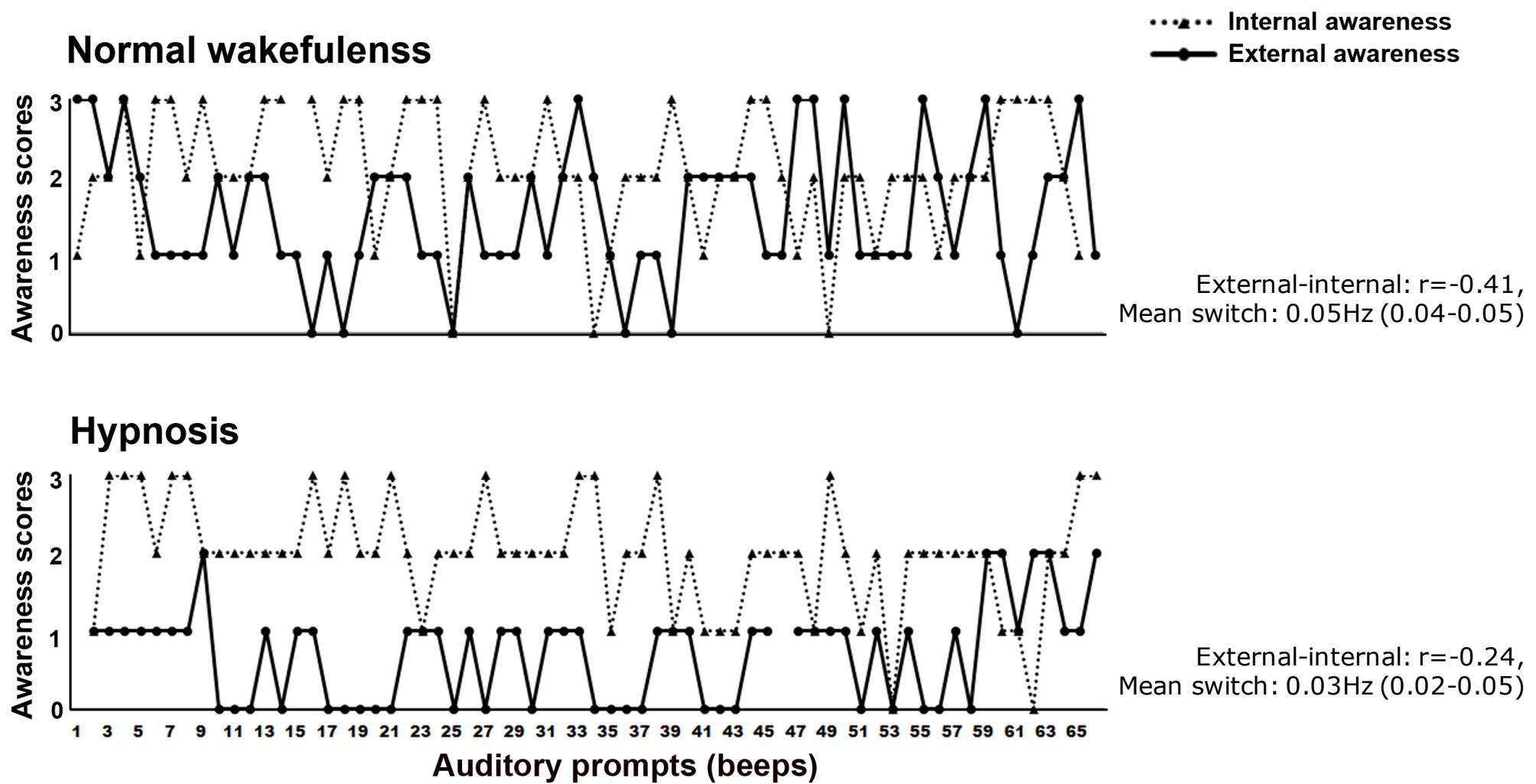
Disrupted DMN in patients
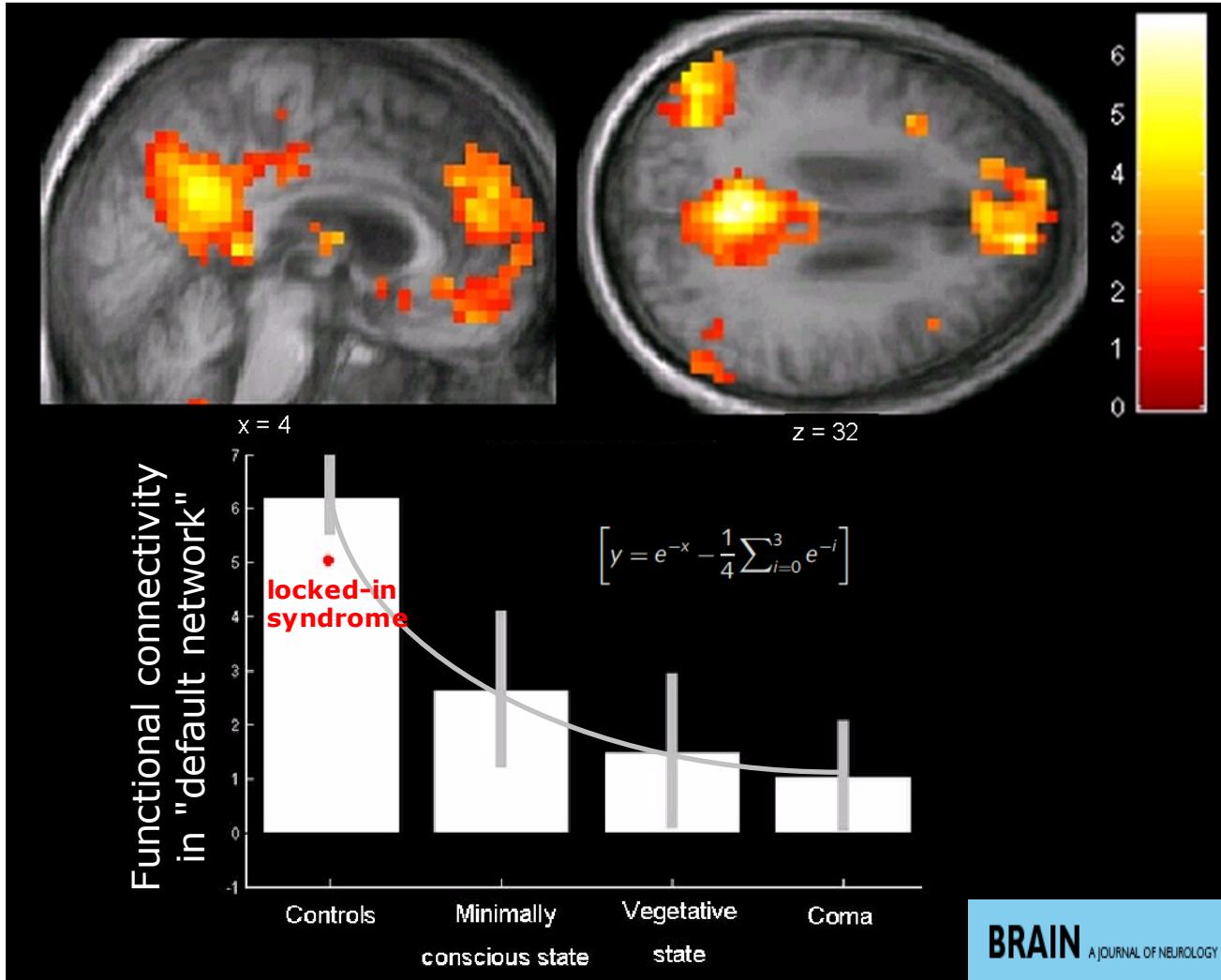
Multiple RSNs in DOC: issues

A challenge….

Heine et al, Frontiers in Psychology 2012
Smith et al, PNAS 2009
Beckmann et al, Phil. Trans. R. Soc. B 2005
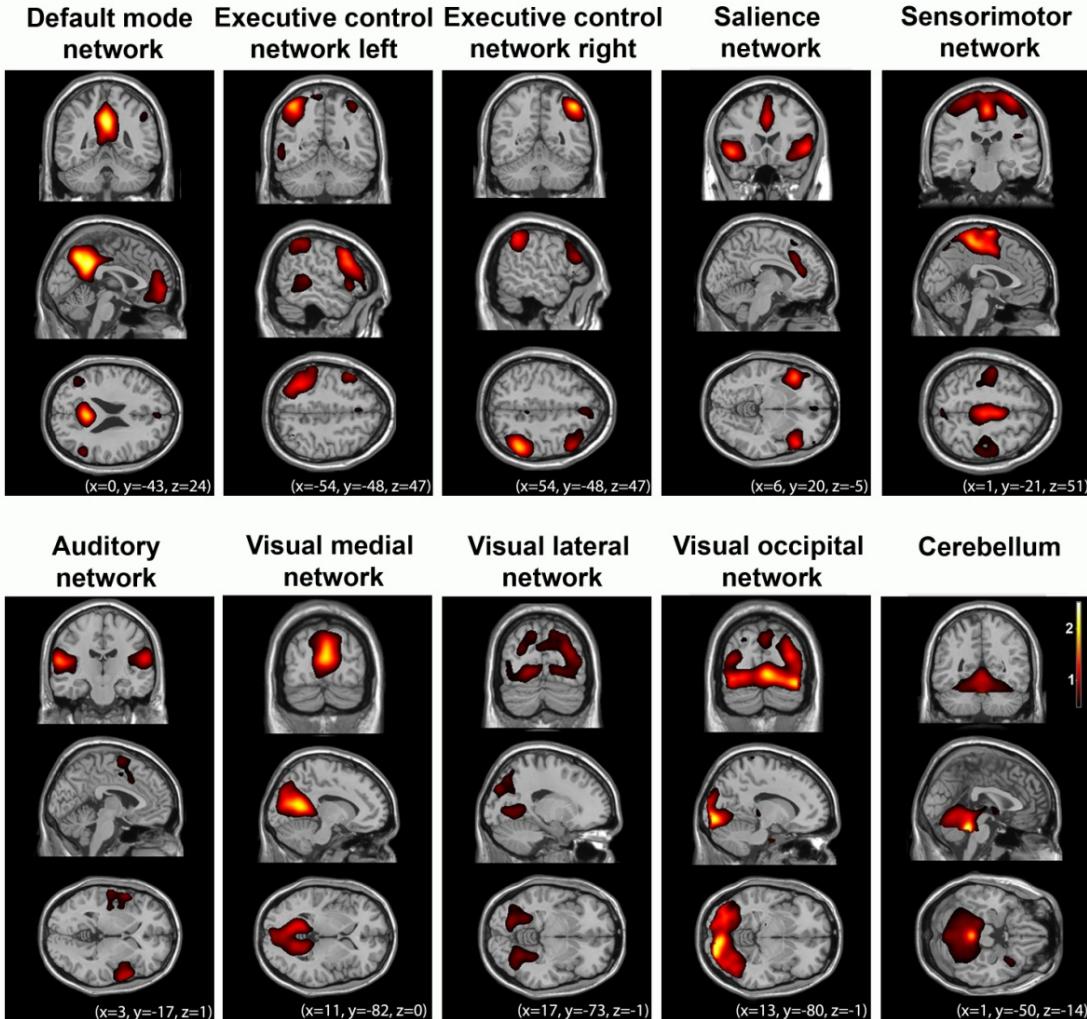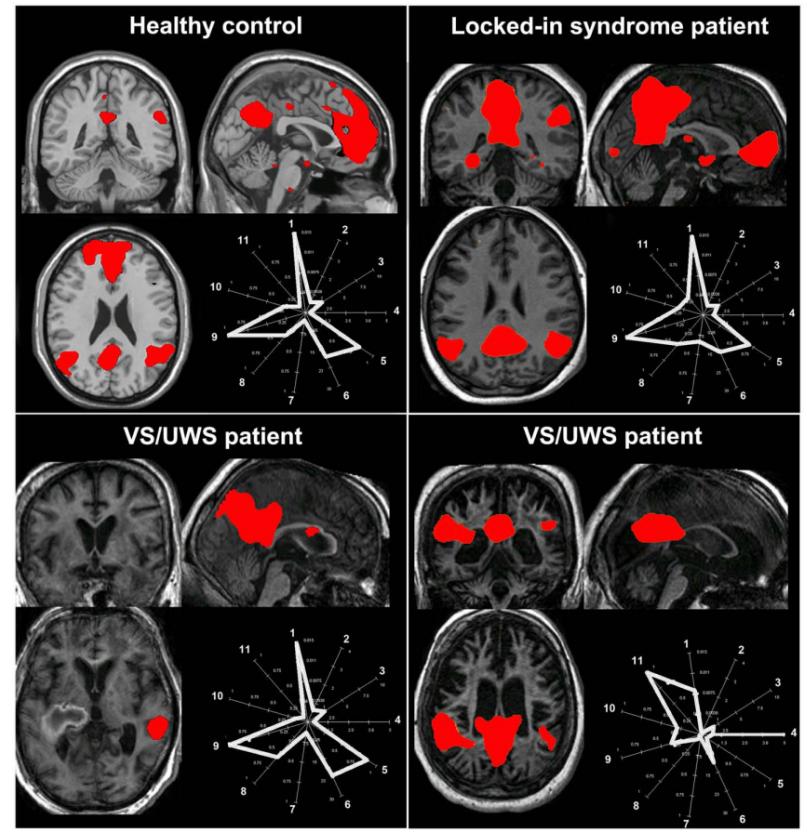
Multiple RSNs in DOC: an approach
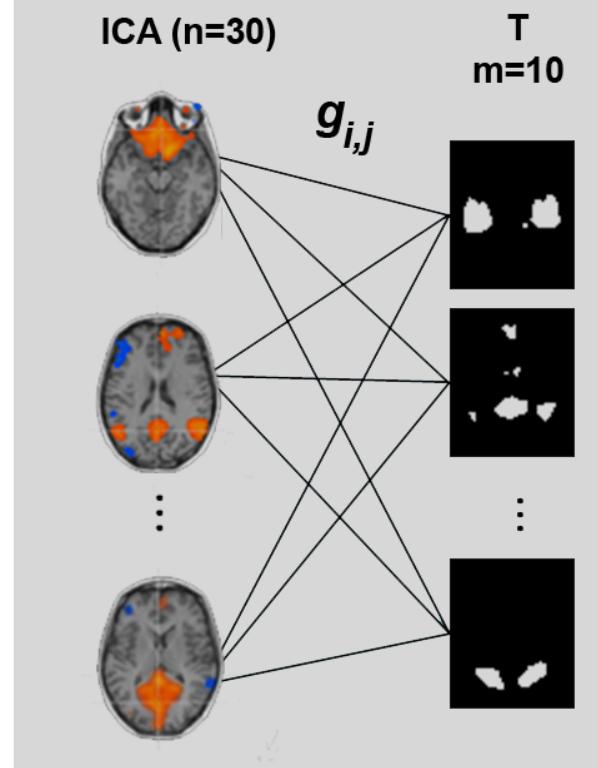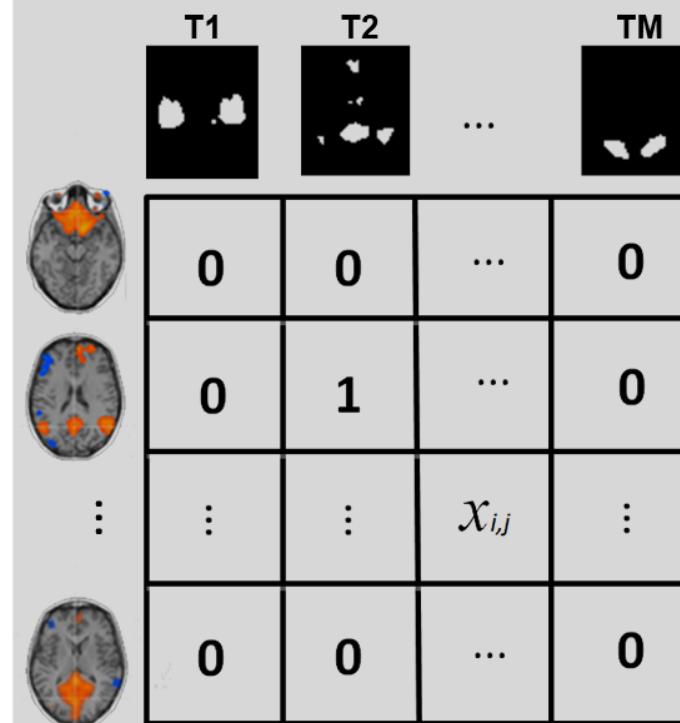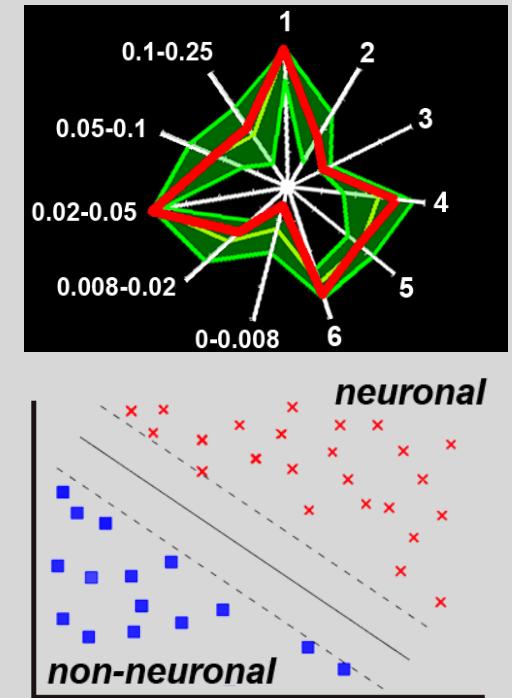
Fewer "neuronal" networks in DOC
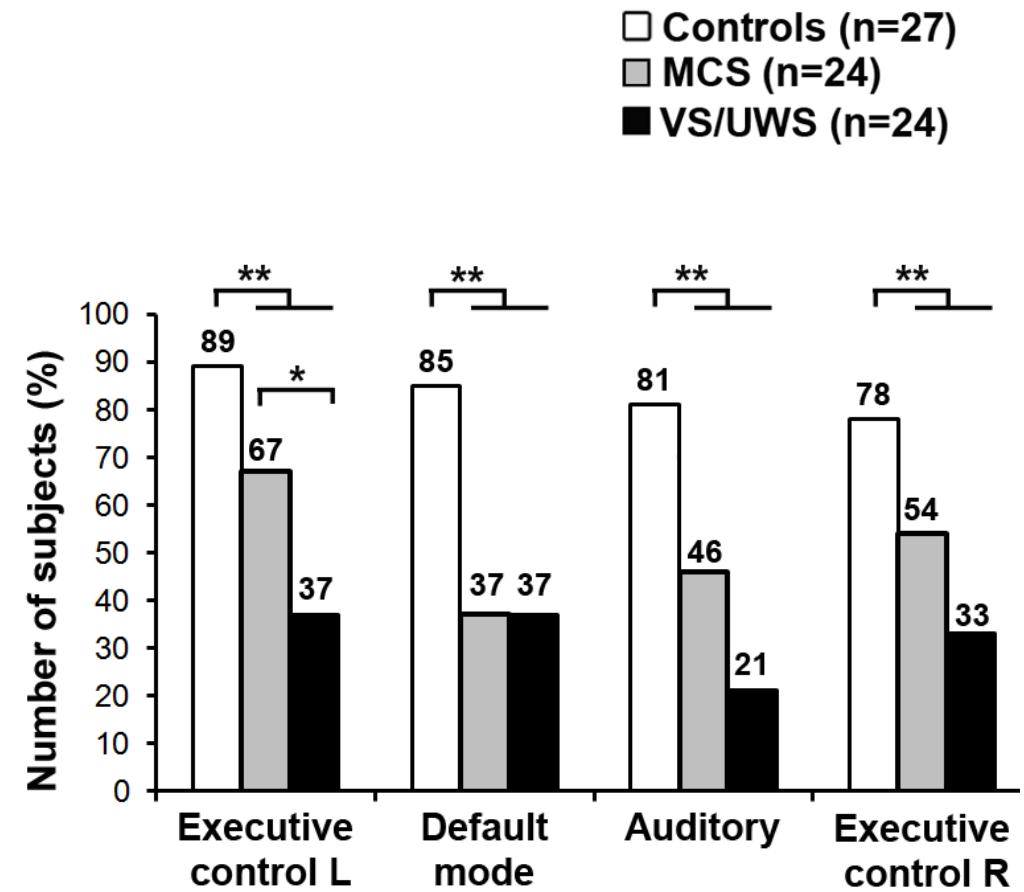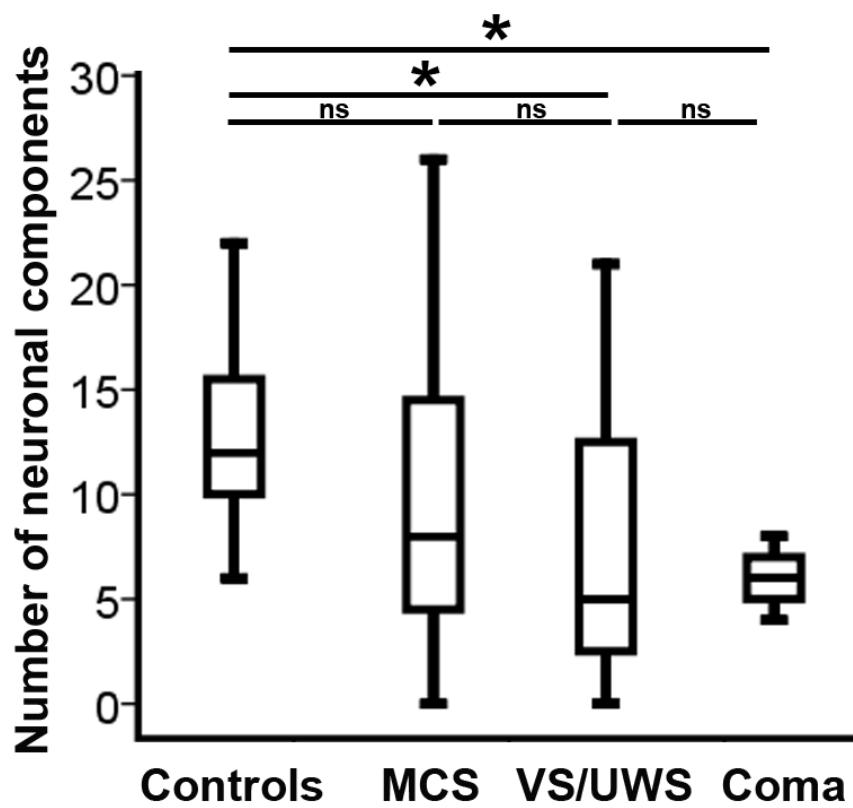
# Voxel-wise group comparisons
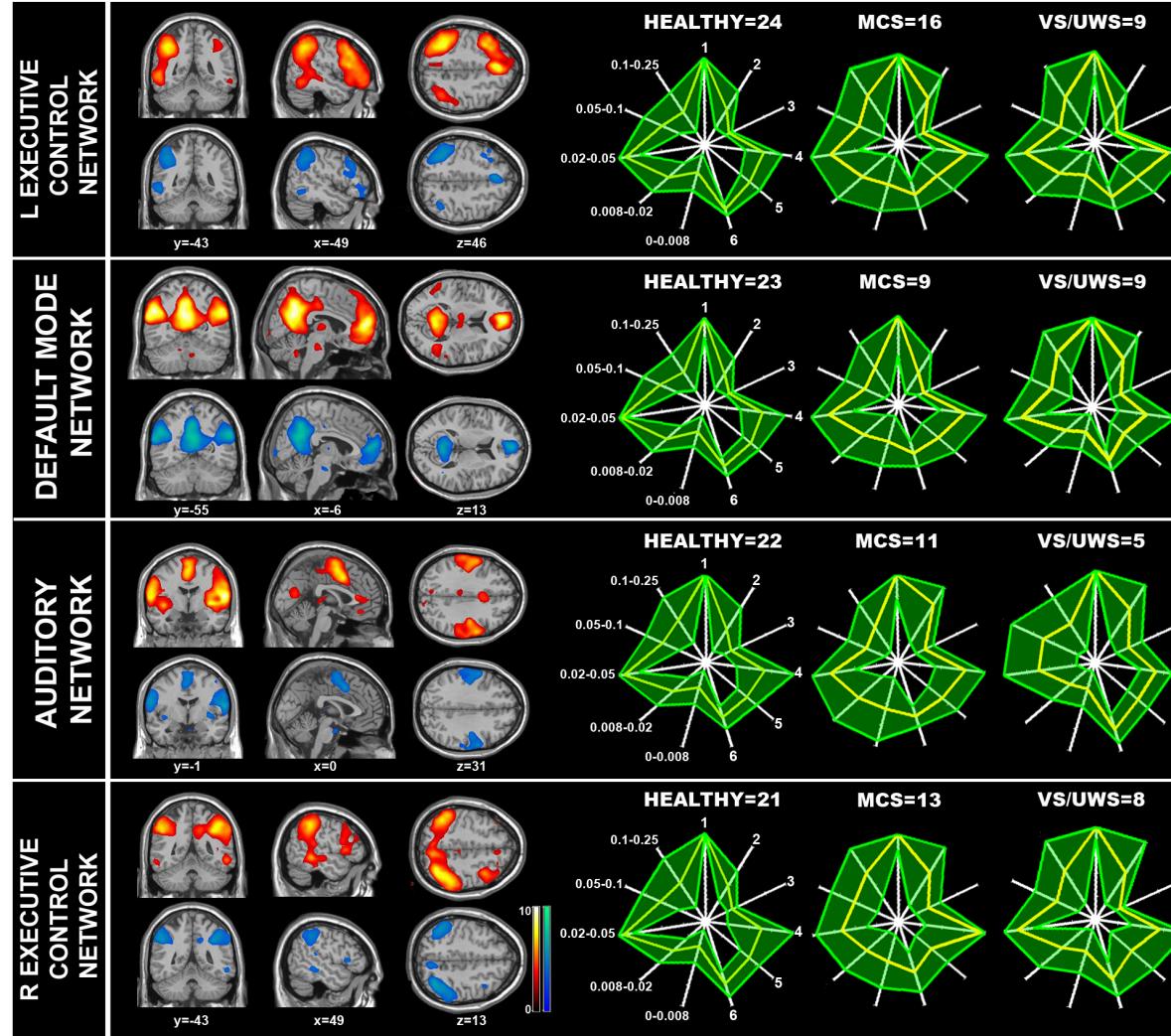
Controls N=27
MCS N=24
VS/UWS N=24

Classification feature: "neuronality"

Performance measures	Accuracy	TPR healthy	TPR patients	Selected RSNs
Healthy vs. all patients				
Occurrence	85.3	.82	.87	Auditory, DMN
Occurrence & GOF	82.6	.70	.89	Auditory, DMN, Visual lateral
GOF	80	.78	.81	Auditory, DMN, ECNL, Visual lateral
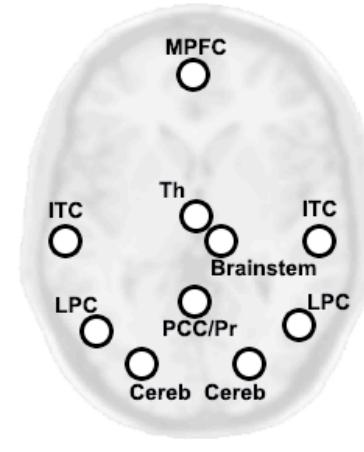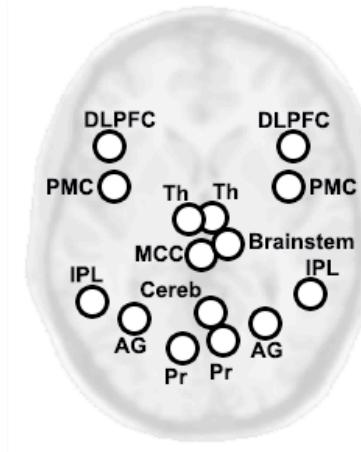
Demertzi & Gómez et al, Cortex 2014

The studied networks
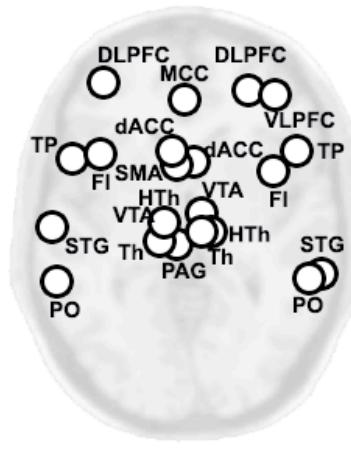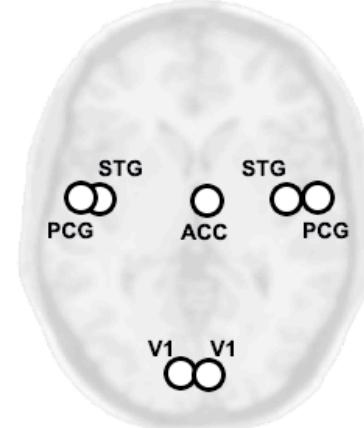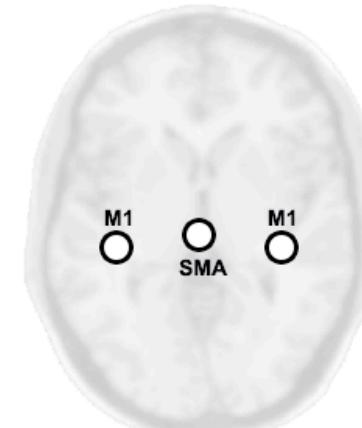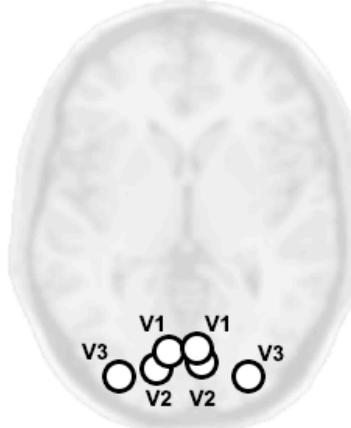
Network connectivity in healthy
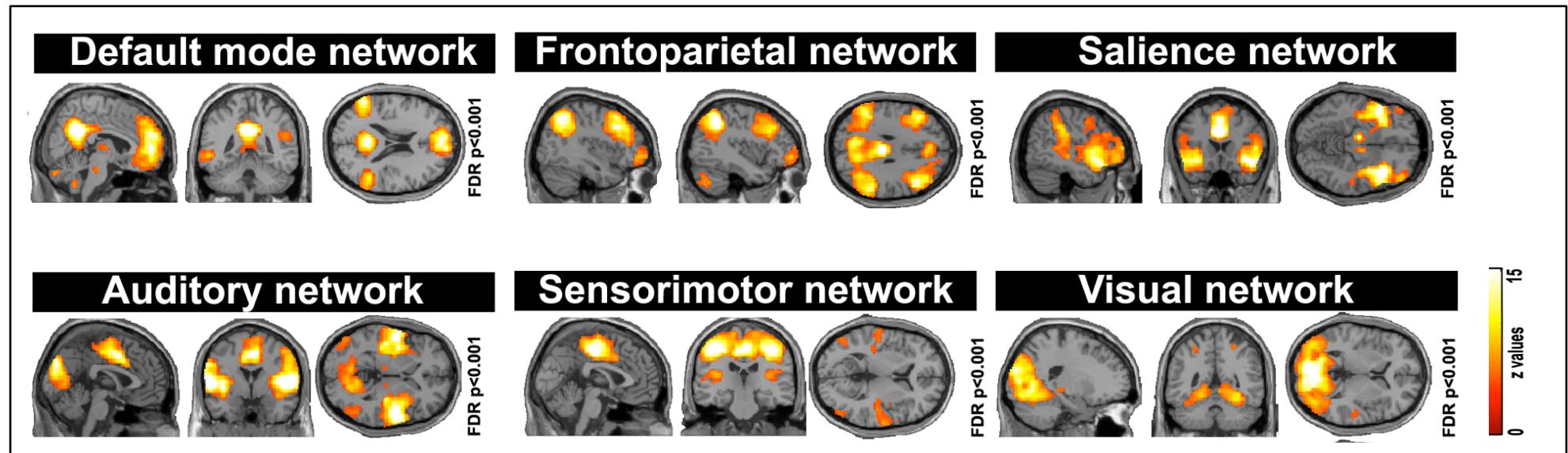
Intrinsic connectivity reflects level of C

Demertzi & Antonopoulos et al, Brain 2015
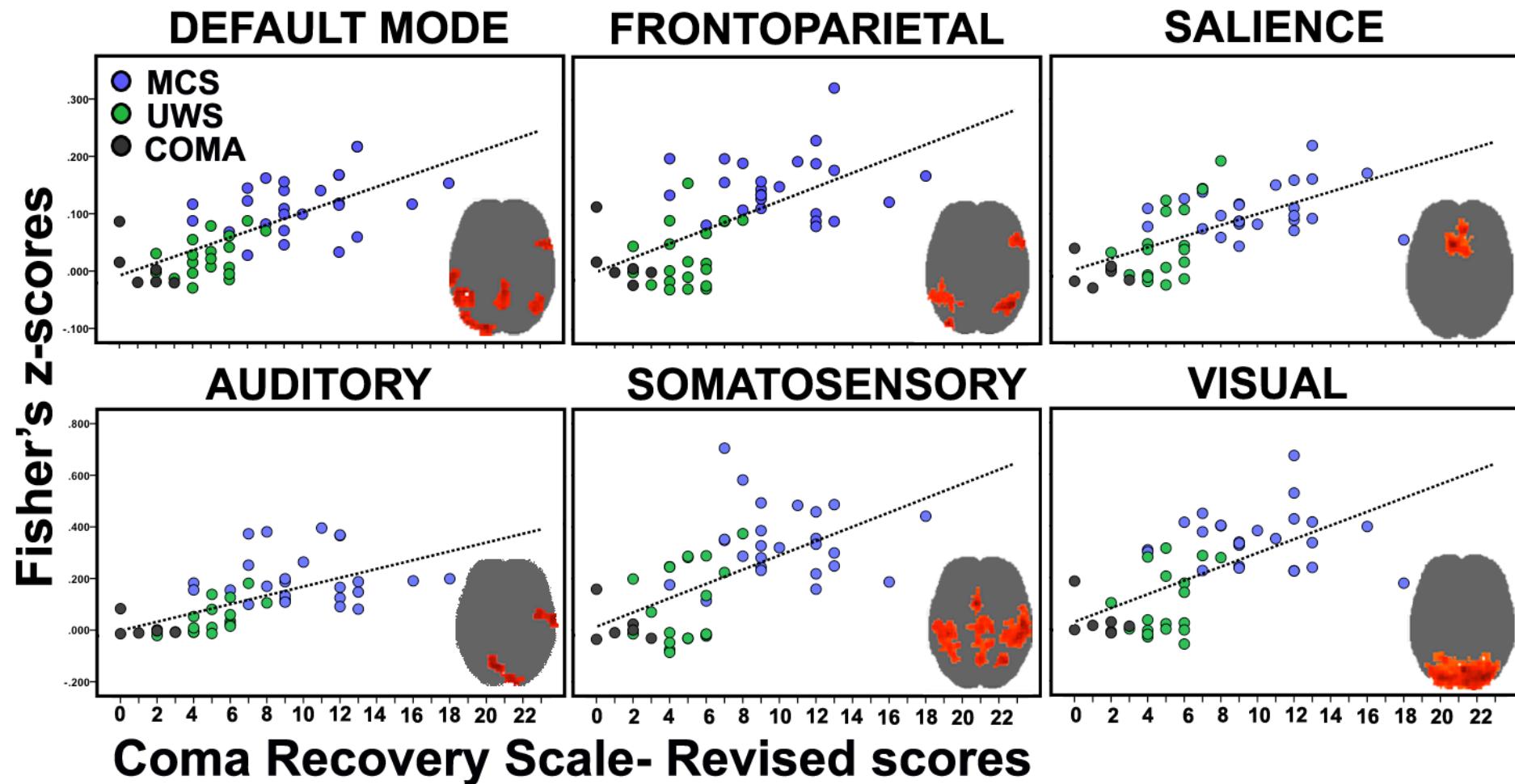
Finding the discriminative features

MCS > VS/UWS
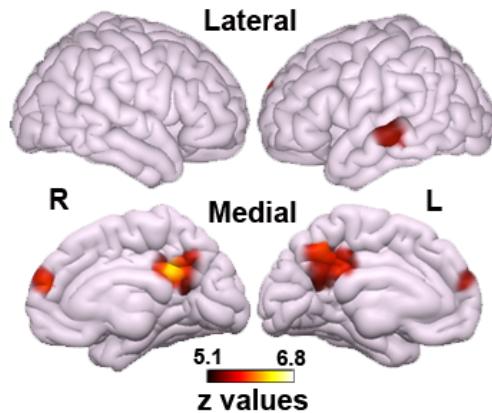
FWE p<0.05 (cluster-level)

Demertzi & Antonopoulos et al, Brain 2015
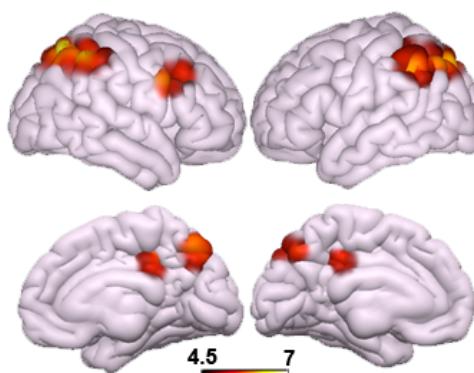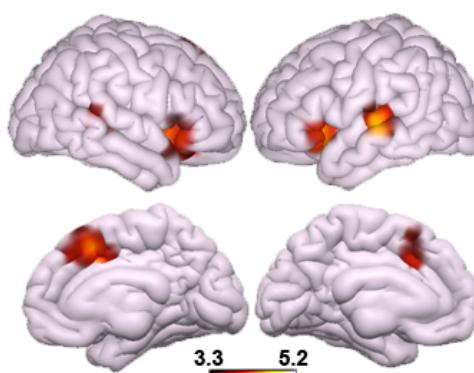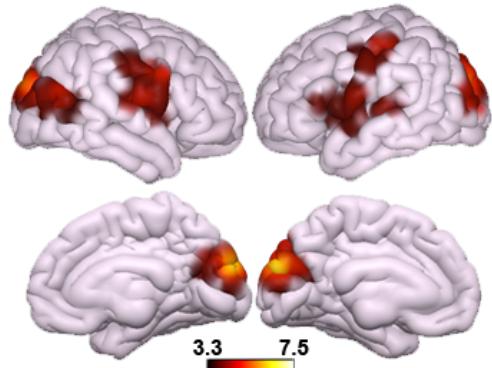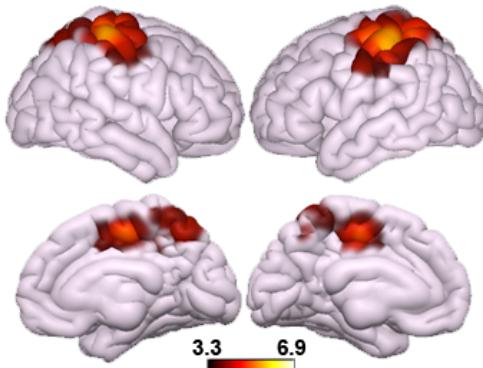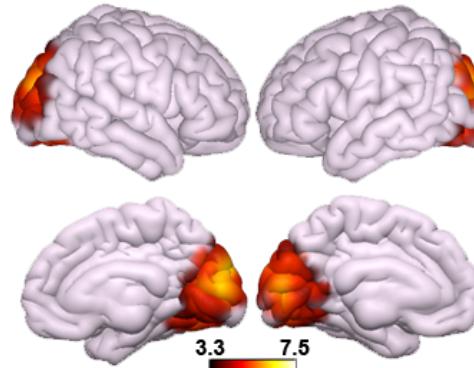
Training dataset: patients (Lg)

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

Demertzi & Antonopoulos et al, Brain 2015
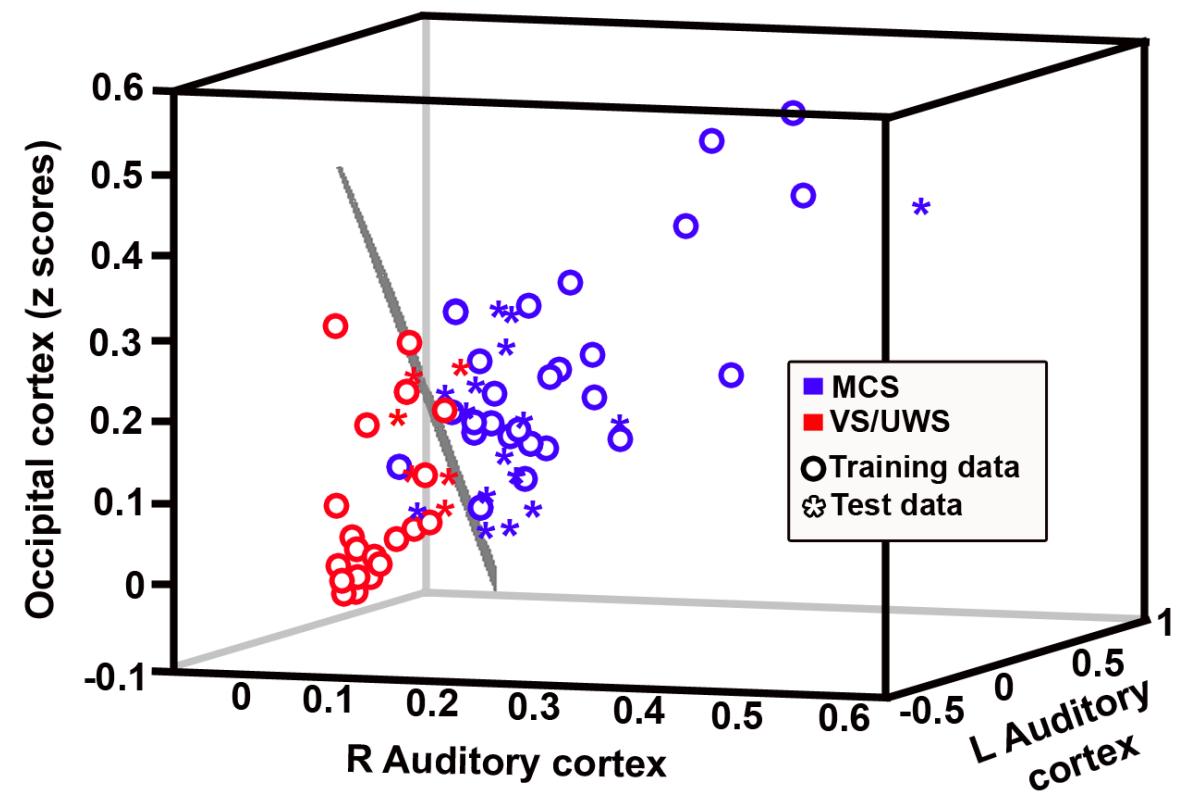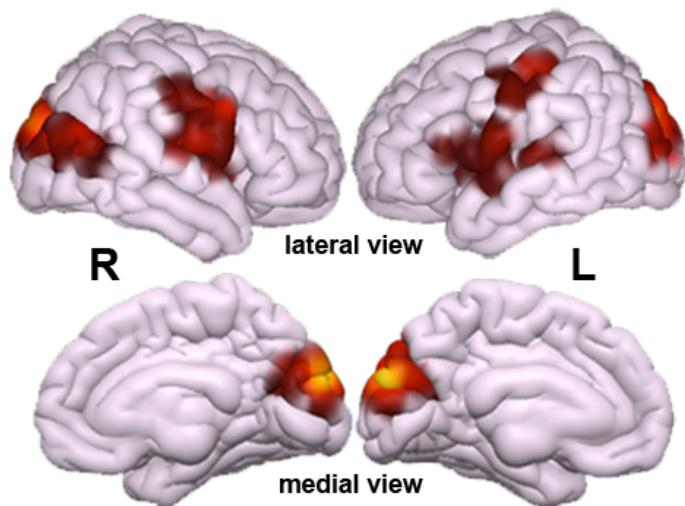
Validation dataset: patients (NY, Sal)

Demertzi & Antonopoulos et al, Brain 2015
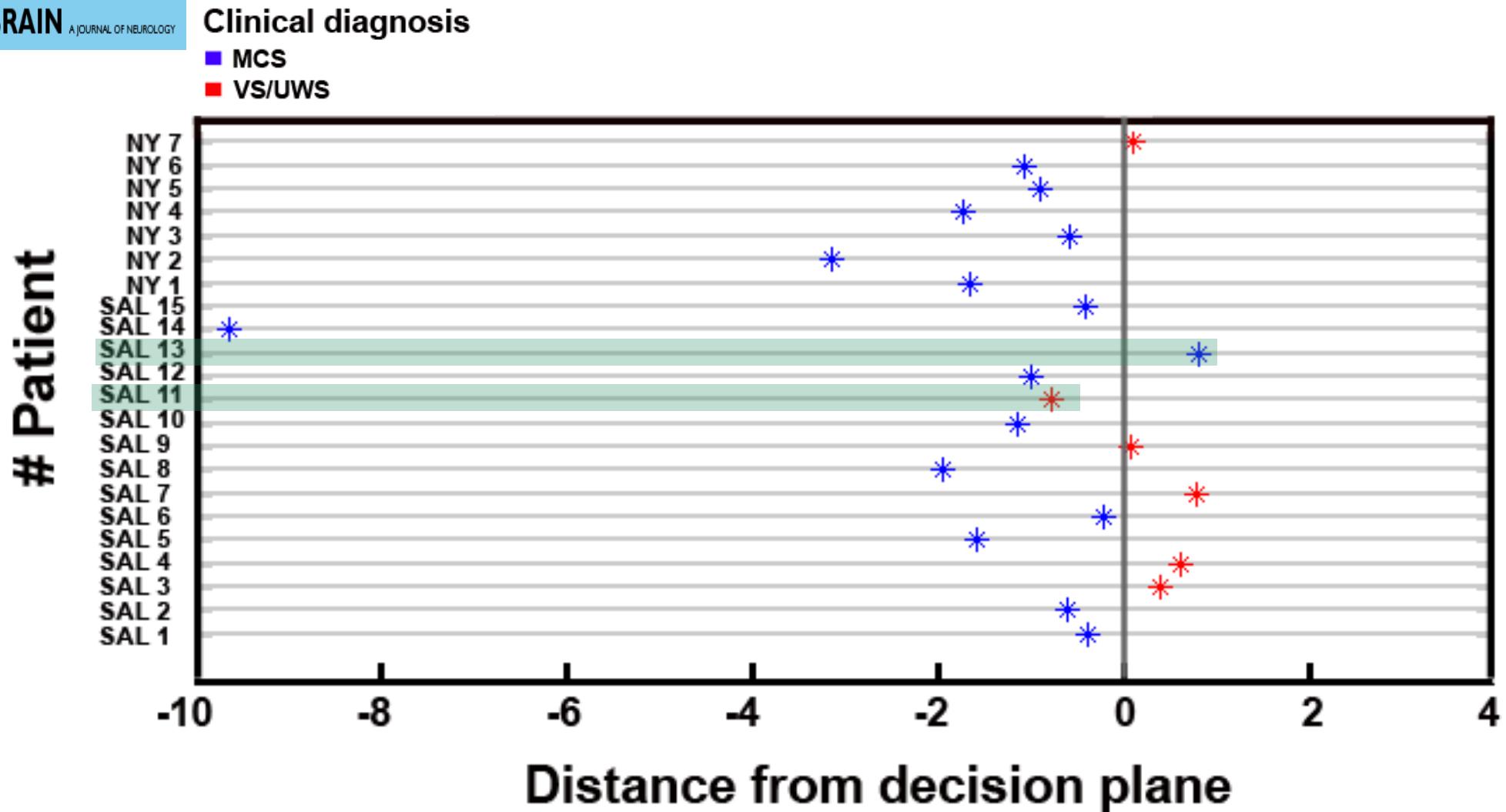
Generalization dataset: healthy
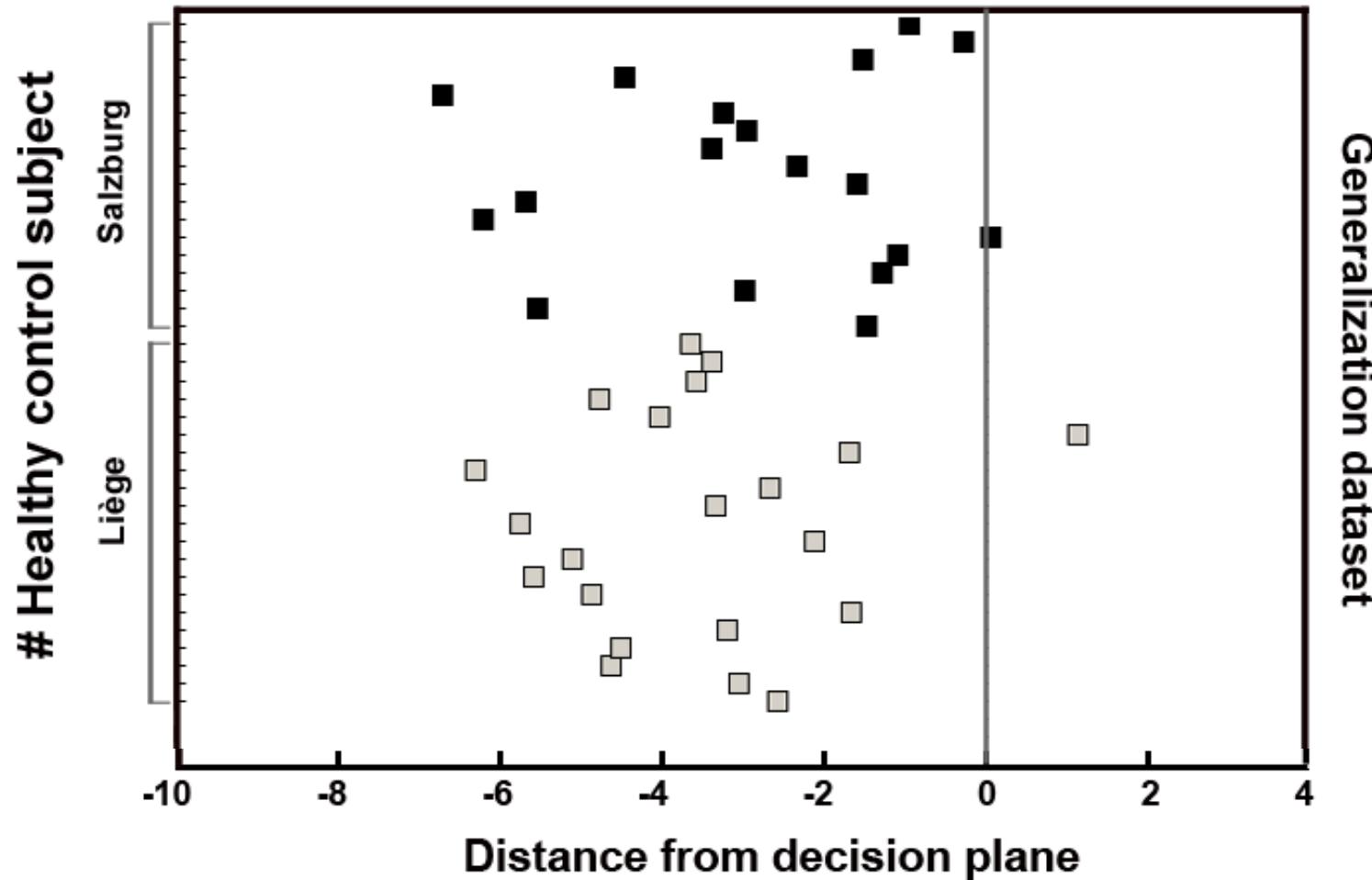
Echoes from structural connectivity?

Gray matter

White matter

Demertzi & Antonopoulos et al, Brain 2015
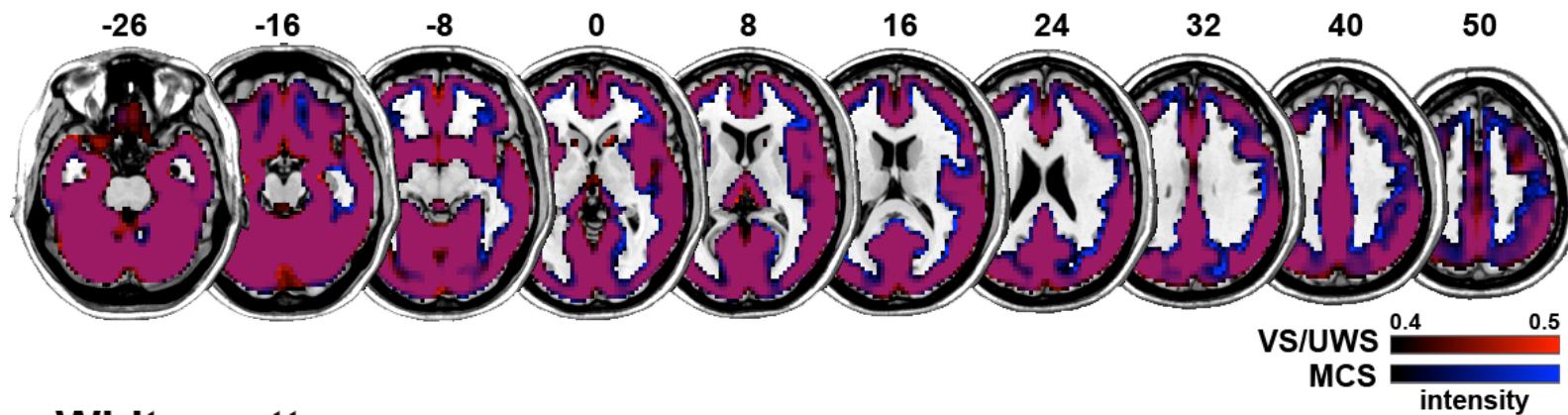
# Cross-modal interaction during conscious processing

Bekinschtein et al, PNAS 2009
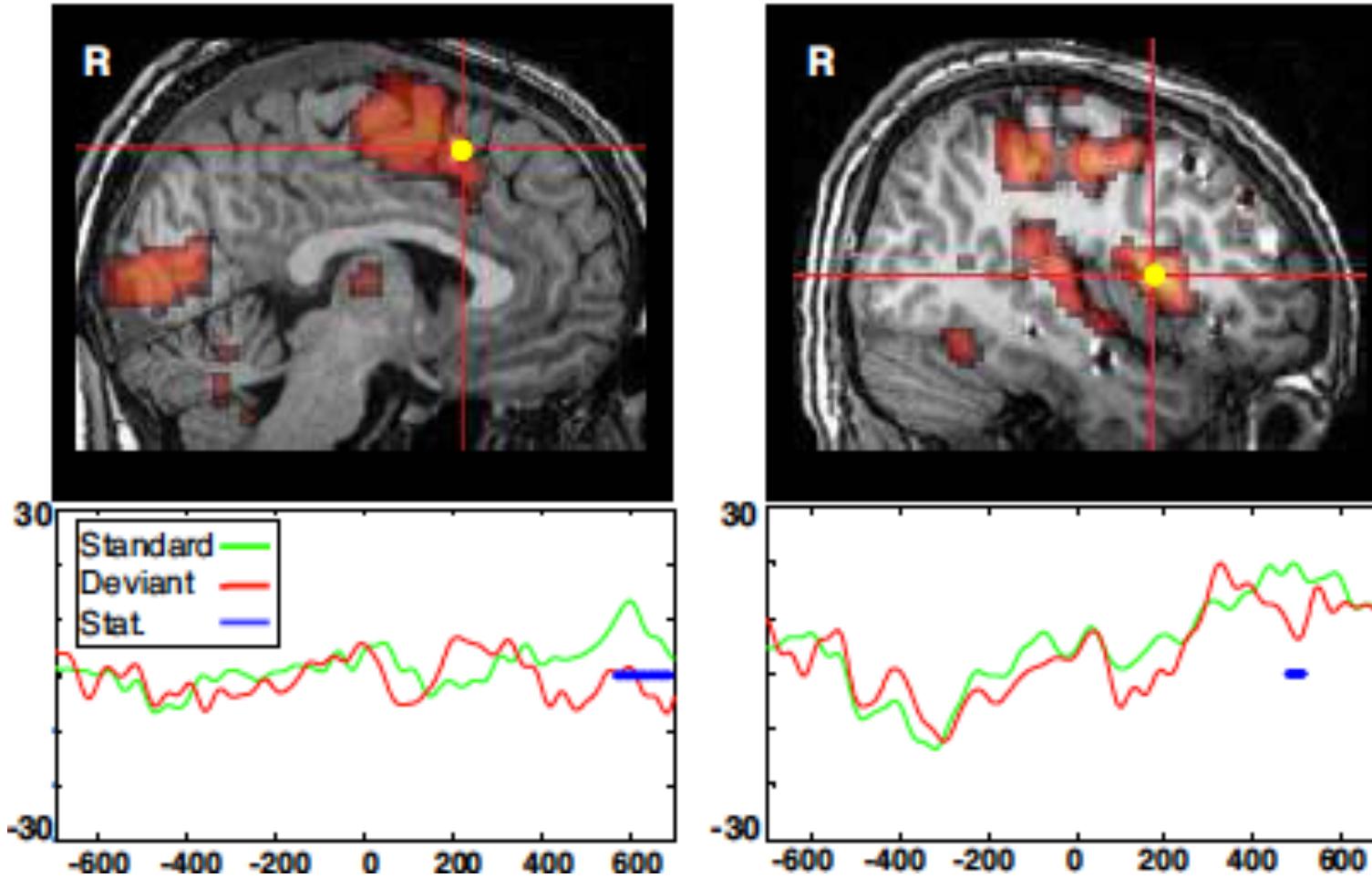
Cross-modal interaction demolishes under propofol anesthesia

Boveroux et al, Anesthesiology 2010
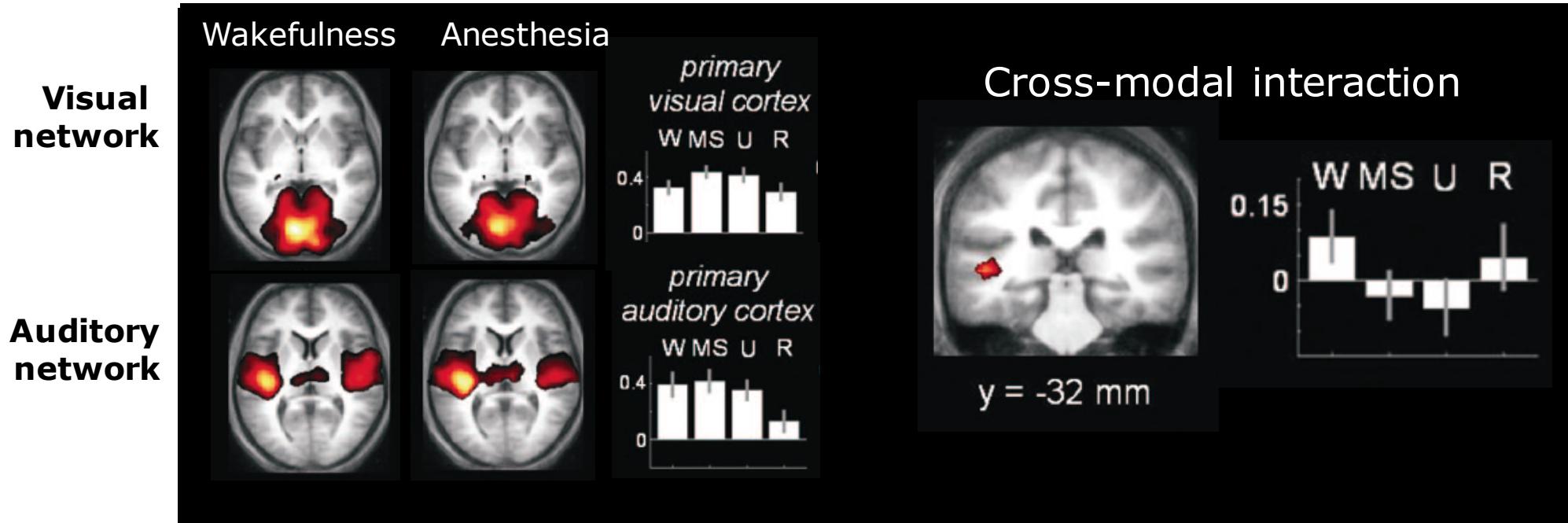
Translational research

Medico-ethical issues in DOC

Biomarkers (fMRI, PET, EEG)

Diagnostic & prognostic use (multimodal imaging)

EMG, ERP or fMRI might reveal subclinical command-following

EEG (brain–computer interfaces) or real-time fMRI might enable communication that is not dependent on motor pathways

AWARENESS

COMMUNICATION

Coma → **Vegetative state** Eye-opening and reflex behavior only → **Minimally conscious state** Voluntary movements or command-following → **Emergence** Interactive communication

www.nature.com/clinicalpractice/neuro

Laureys & Boly, Nature Clinical Practice 2008
Owen, Schiff & Laureys, Progress in Brain Research 2009
Jox, Bernat, Laureys and Racine, Lancet Neurology 2012

Niko Schiff & Henning Voss,
Weill Cornel Medical College

Julia Sophia Crone & the
Salzburg team

The deparments of
Neurology and Radiology in
Liege and Paris

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

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