Intrinsic functional architecture reflects the level of consciousness and differentiates non-communicating patients

5th BIENNIAL CONFERENCE ON RESTING STATE AND BRAIN CONNECTIVITY

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GIGA Research & Neurology Department
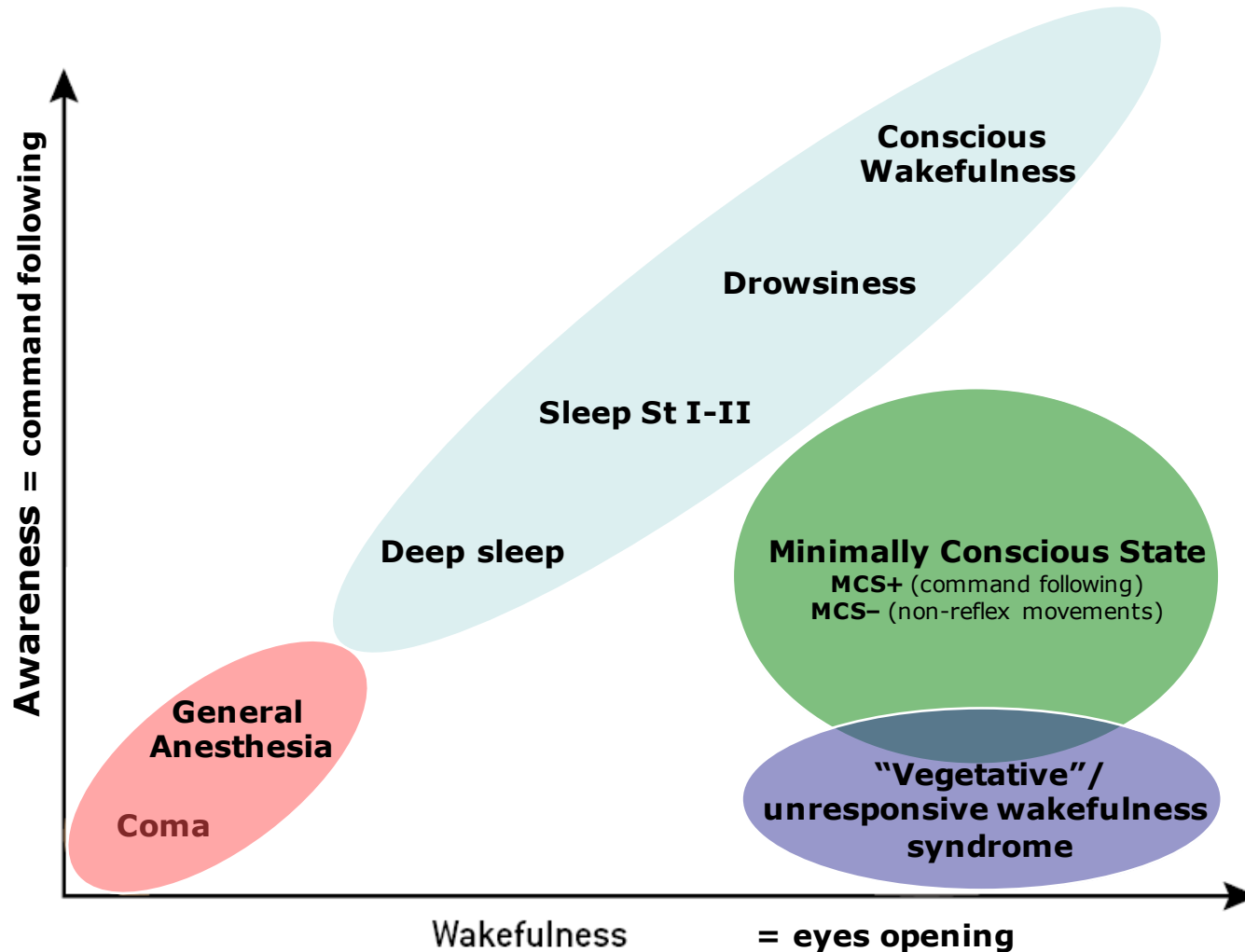**University & University Hospital of Liège, Belgium**
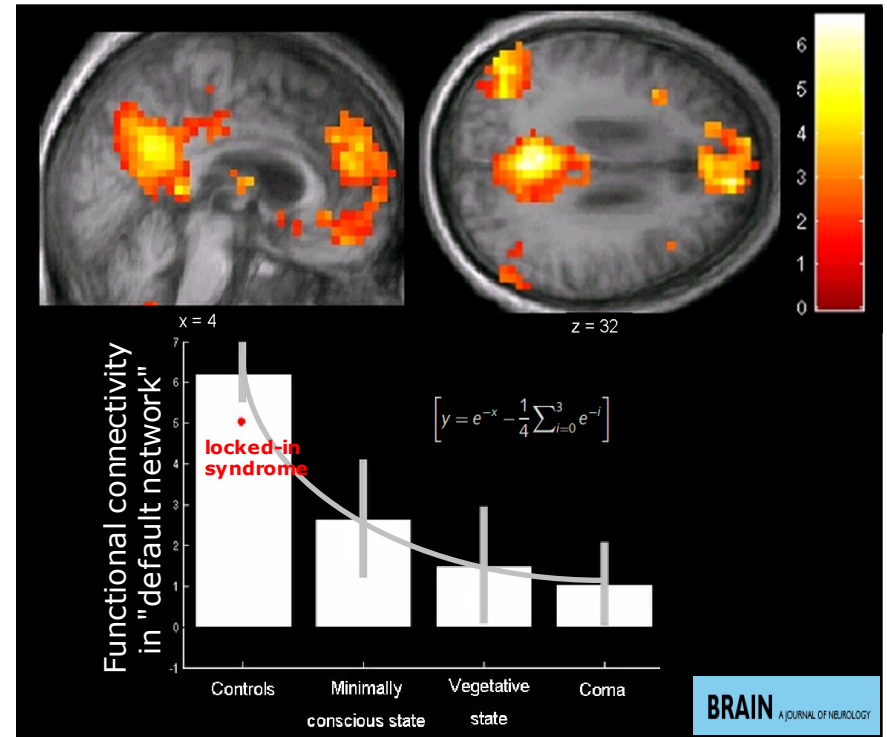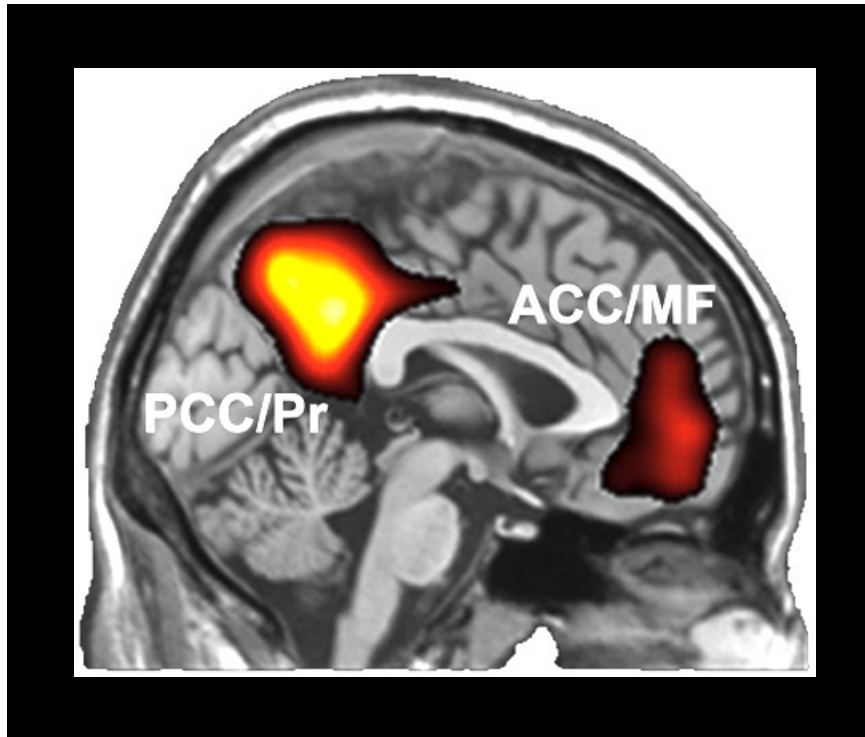
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LA LIBERTÉ DE CHERCHER

CHERCHER, TROUVER, GUÉRIR, POUR VOUS & AVEC VOUS.

ICM
Institut du Cerveau et de la Moelle épinière

# An operational definition of C

The brain's default mode at rest

Demertzi & Whitfield-Gabrieli, in: Neurology of Consciousness 2nd ed. 2015
Demertzi, Soddu, Laureys, Curr Opin Neurobiology 2013
Demertzi et al, Front Hum Neurosci 2013
Raichle et al, PNAS 2001

Vanhaudenhuyse & Noirhomme et al, Brain 2010
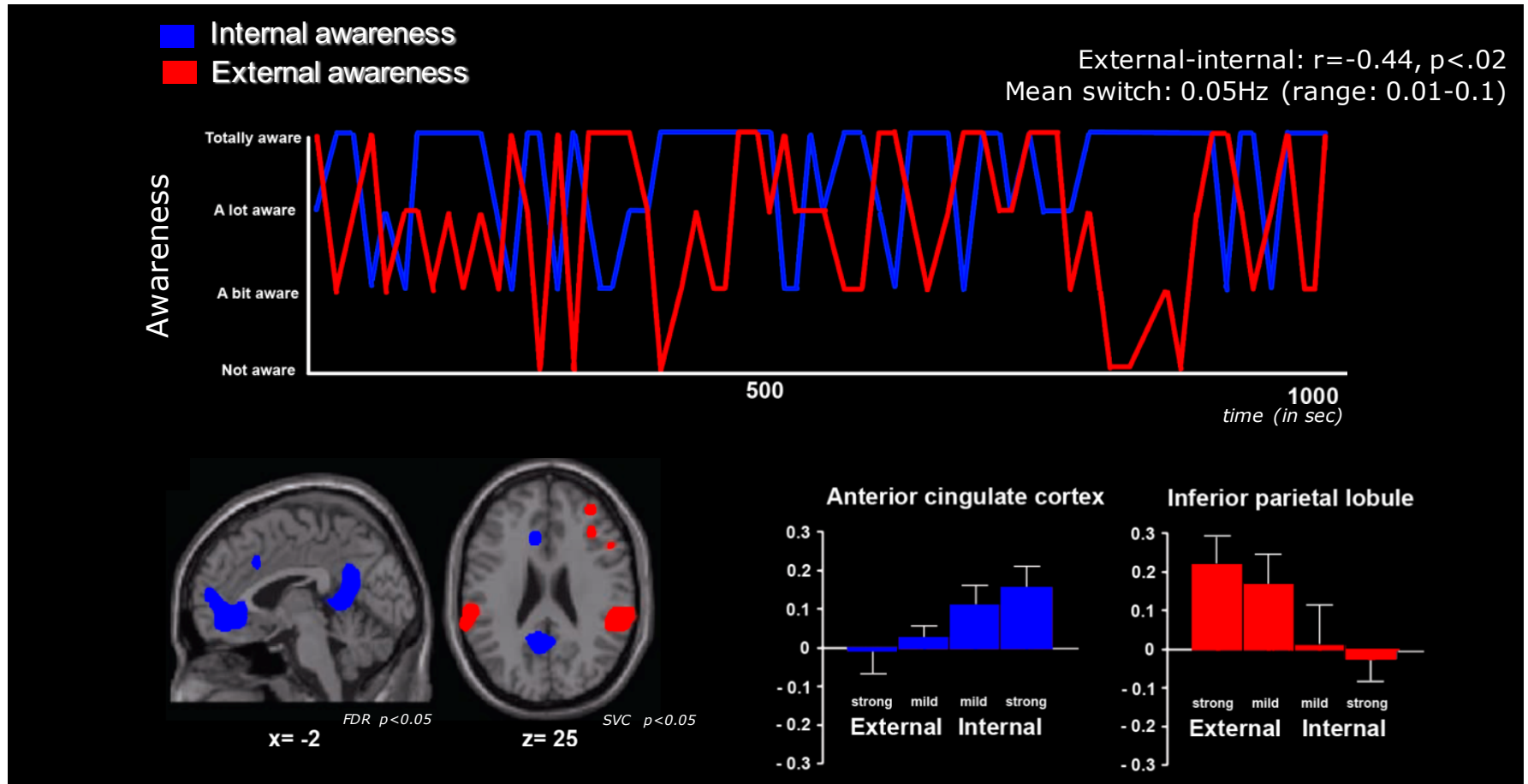
Default mode anticorrelations

DMN anticorrelated network

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; Fox et al, PNAS 2005; Fransson et al, HBM 2005
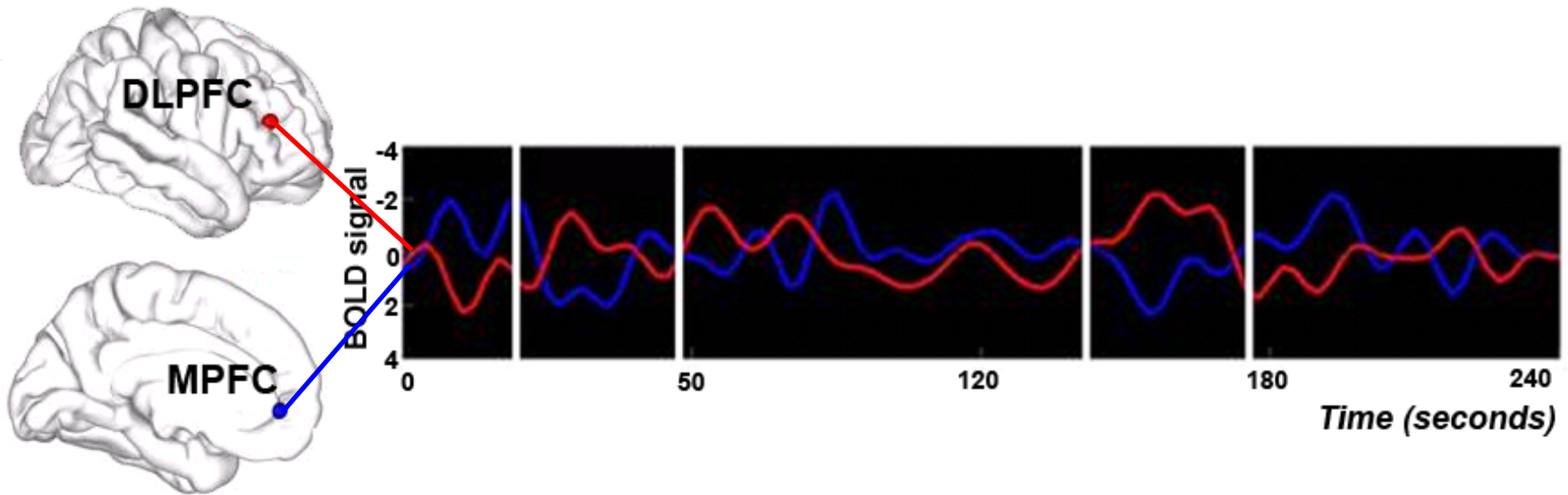
The cognitive counterpart of resting state

Anticorrelated activity is modified in hypnosis

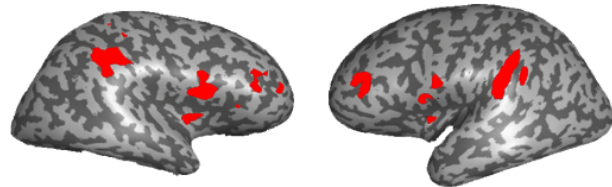- □ **Normal consciousness**
- ▣ **Autobiographical mental imagery**
- ■ **Hypnosis**
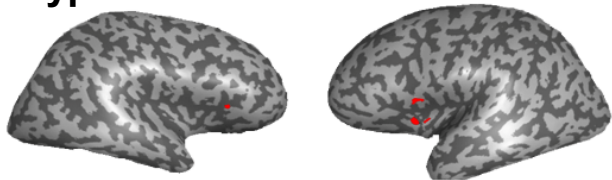
*p<.05
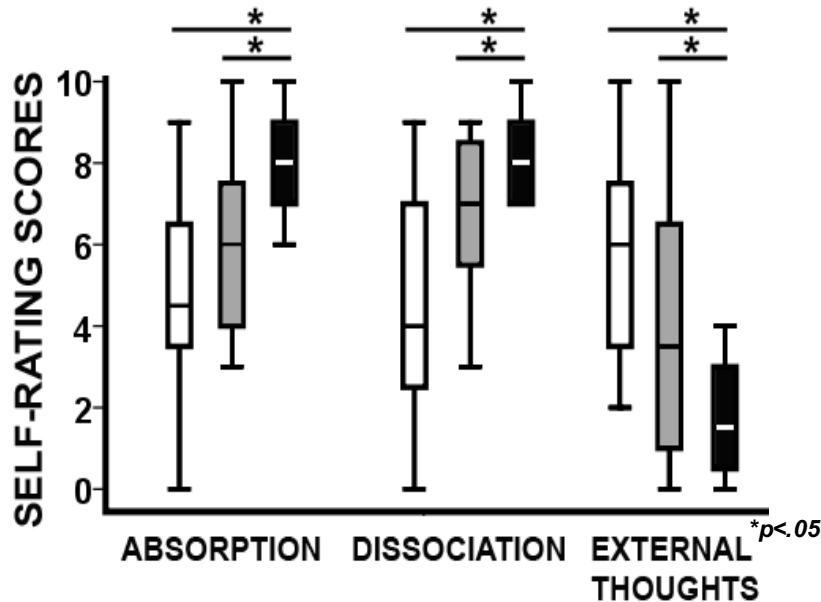
EXTRINSIC SYSTEM

Normal consciousness
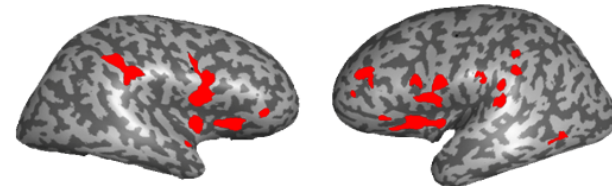
Autobiographical mental imagery
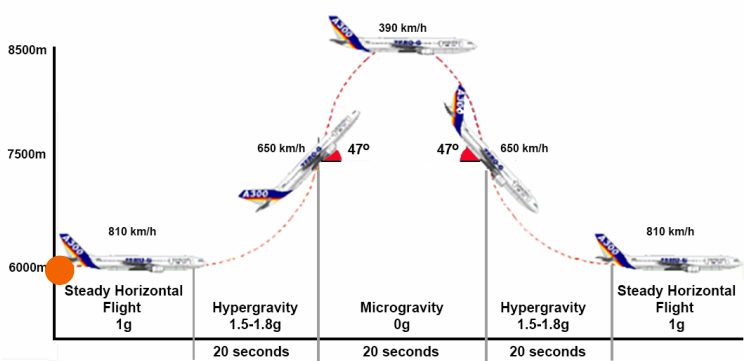
Hypnosis

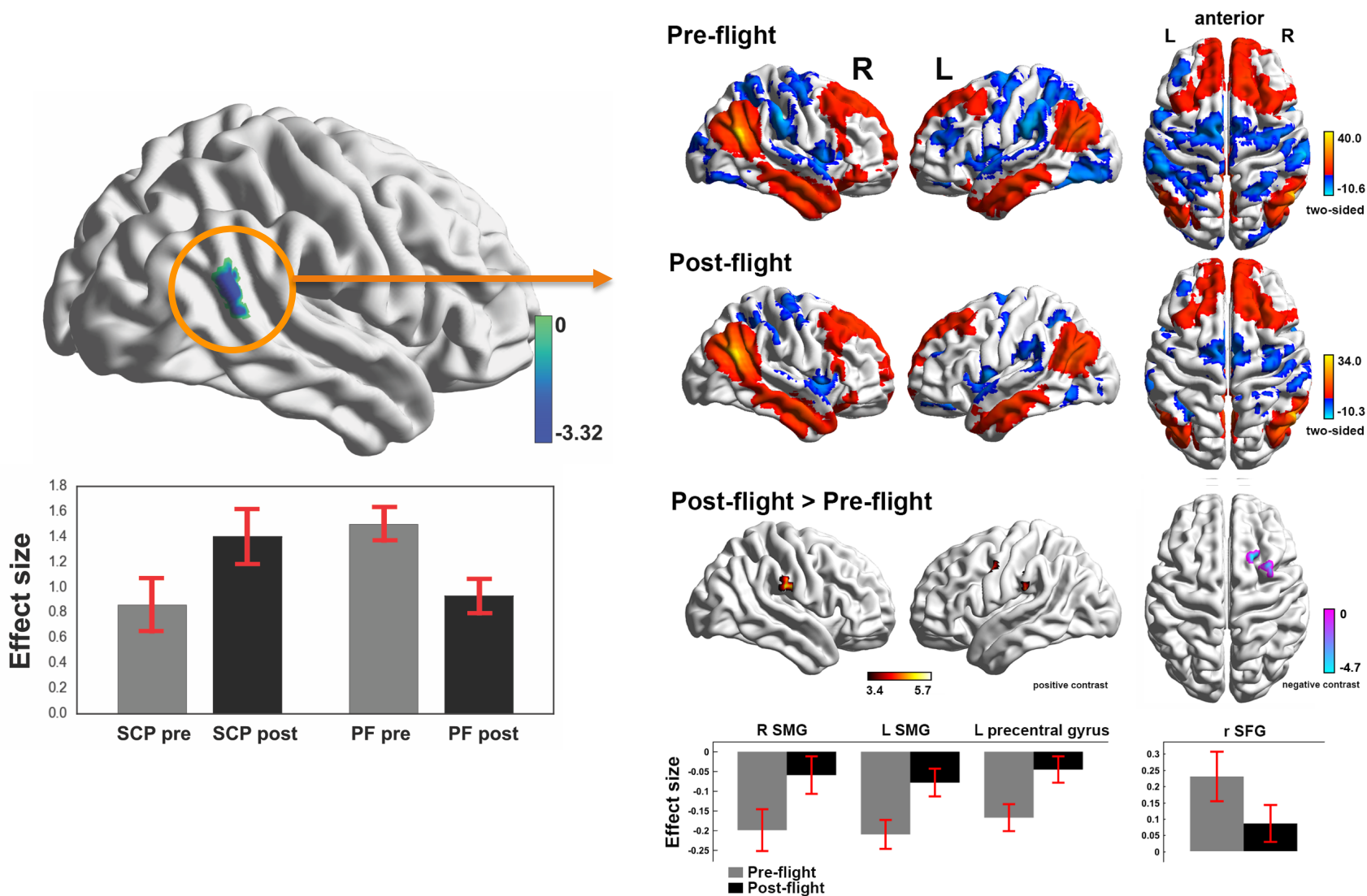*p<0.05 corrected for multiple comparisons*

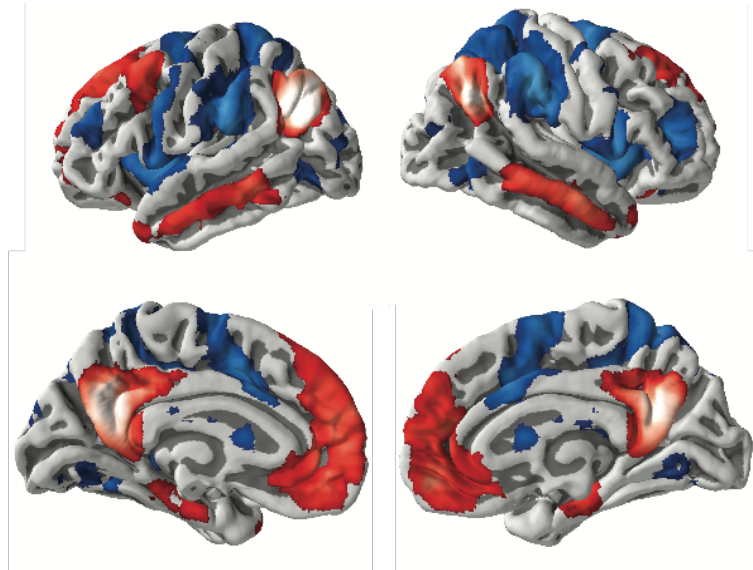# Less anticorrelated activity after exposure to microgravity

Parabolic flight

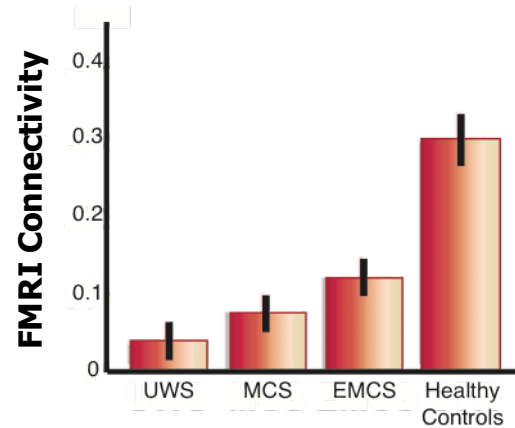

Parabolic flight trajectory

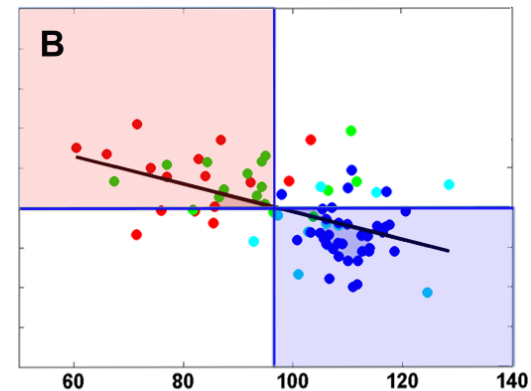# Less anticorrelated activity after exposure to microgravity
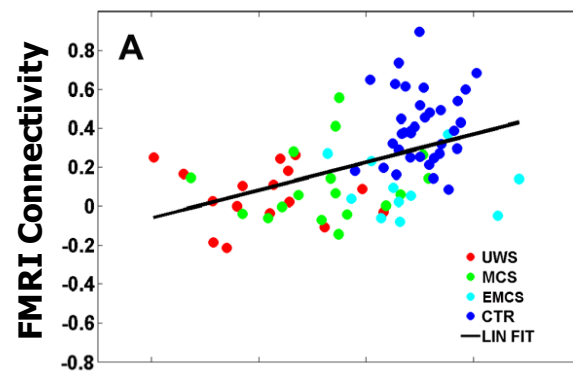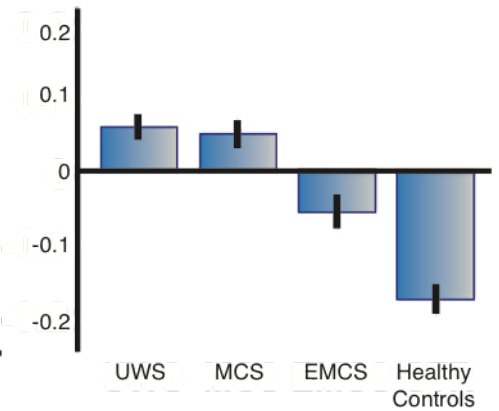
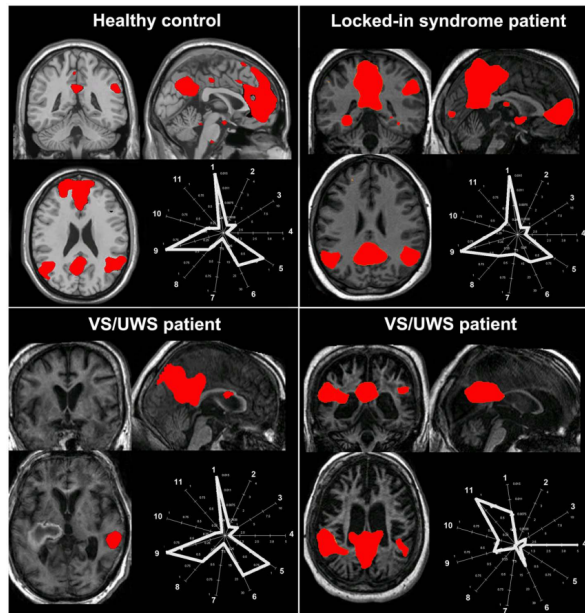# Anticorrelated activity is absent in DOC

DMN CORRELATIONS

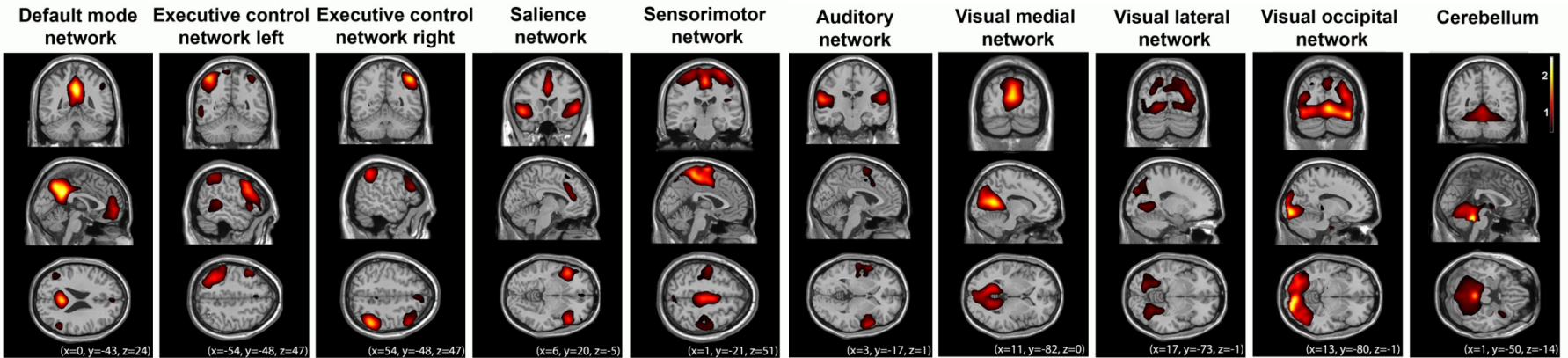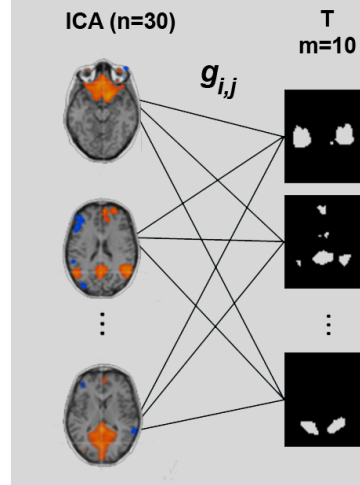**DMN ANTICORRELATIONS**

Systems-level intrinsic connectivity

Default mode network | Executive control network left | Executive control network right | Salience network | Sensorimotor network | Auditory network | Visual medial network | Visual lateral network | Visual occipital network | Cerebellum

(x=0, y=-43, z=24) | (x=-54, y=-48, z=47) | (x=54, y=-48, z=47) | (x=6, y=20, z=-5) | (x=1, y=-21, z=51) | (x=3, y=-17, z=1) | (x=11, y=-82, z=0) | (x=17, y=-73, z=-1) | (x=13, y=-80, z=-1) | (x=1, y=-50, z=-14)

Healthy control | Locked-in syndrome patient
VS/UWS patient | VS/UWS patient

1. Goodness-of-fit calculation — ICA (n=30), T m=10, $g_{i,j}$

2. Multiple template assignation — T1, T2, TM, $x_{i,j}$

3. "Neuronality" test — 0.1-0.25, 0.05-0.1, 0.02-0.05, 0.008-0.02, 0-0.008, neuronal, non-neuronal

Demertzi & Gómez et al, Cortex 2014
Heine et al, Front Psychol 2012; Smith et al, PNAS 2009; Beckmann et al, Phil. Trans. R. Soc. B 2005; Damoiseaux PNAS 2006
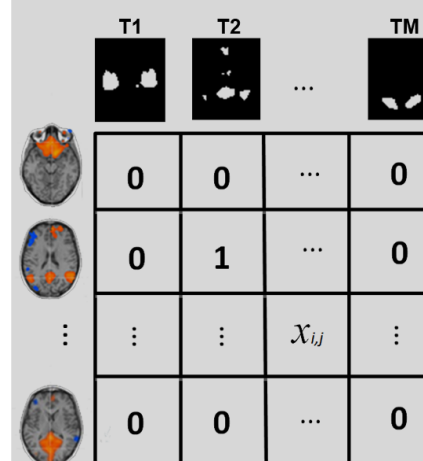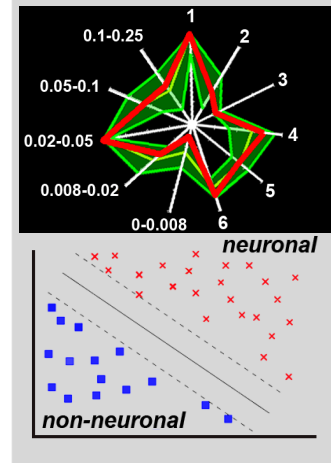
Fewer "neuronal" networks in DOC

Number of subjects (%) with neuronal networks
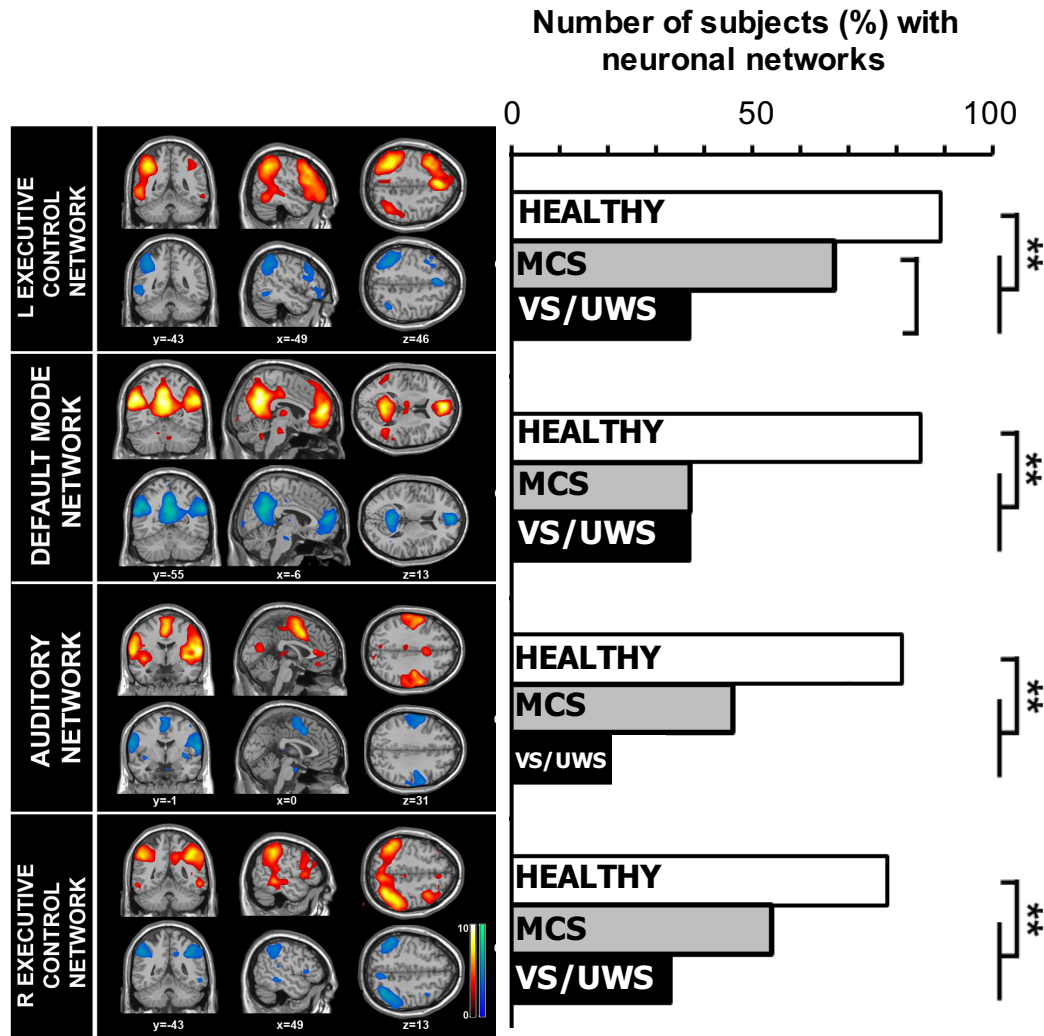
Single-patient classification

Performance measures	Accuracy	TPR healthy	TPR patients	Selected RSNs
Healthy vs. all patients				
Neuronal	85.3	.82	.87	Auditory, DMN

Seed-based connectivity networks

Default mode network
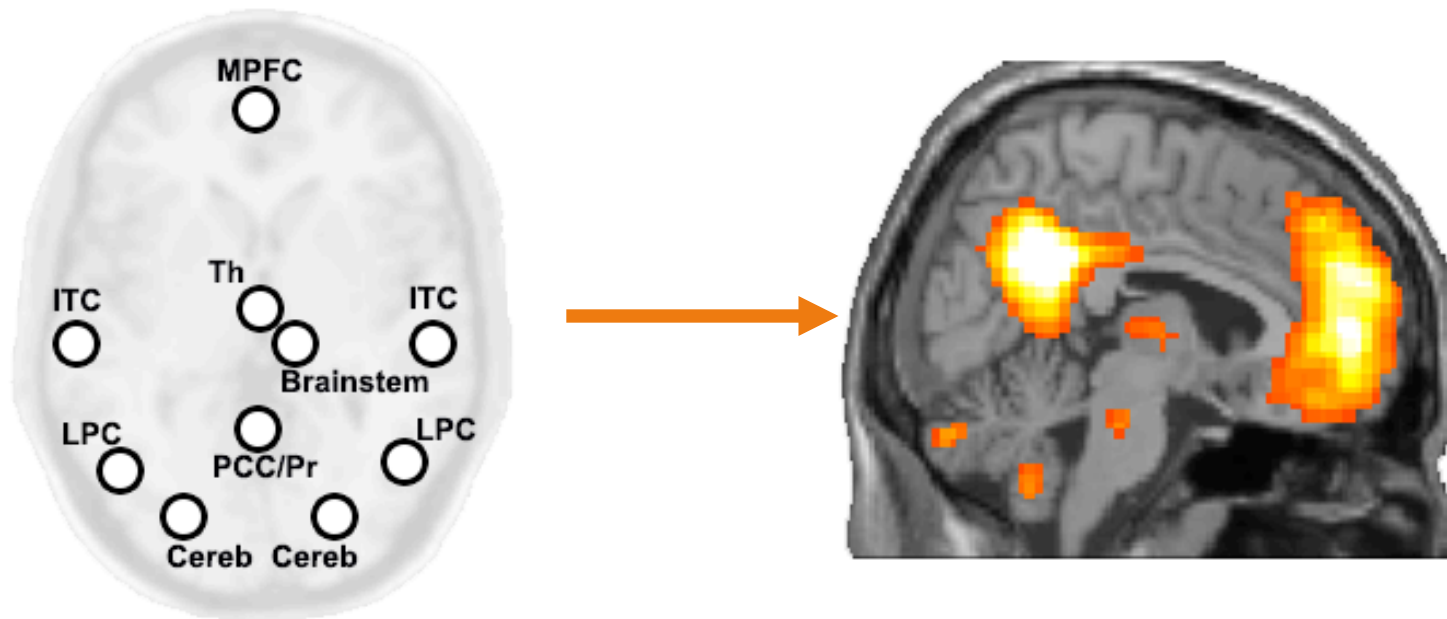
Intrinsic connectivity reflects the level of C
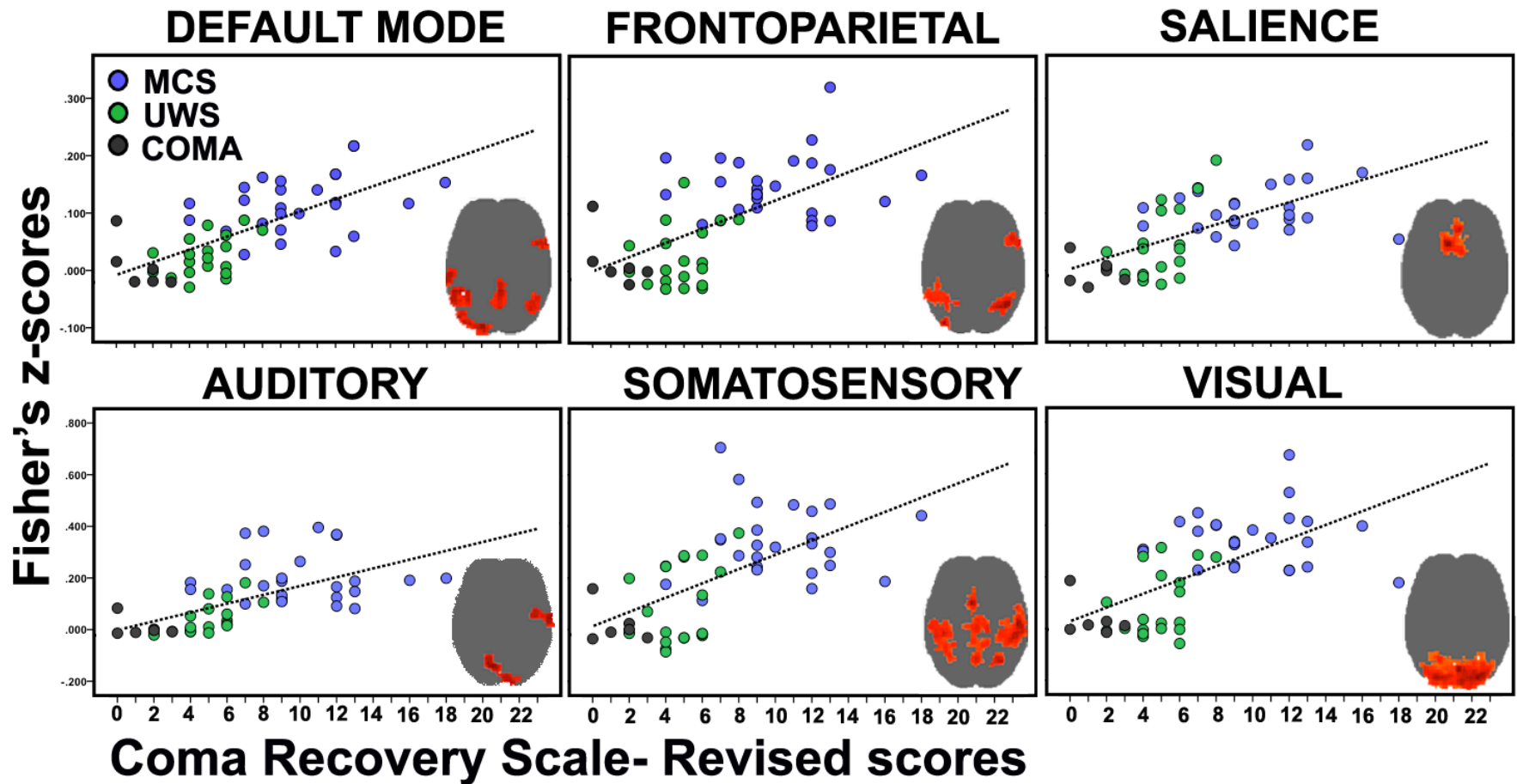
Which network discriminates best?

MCS> VS/UWS
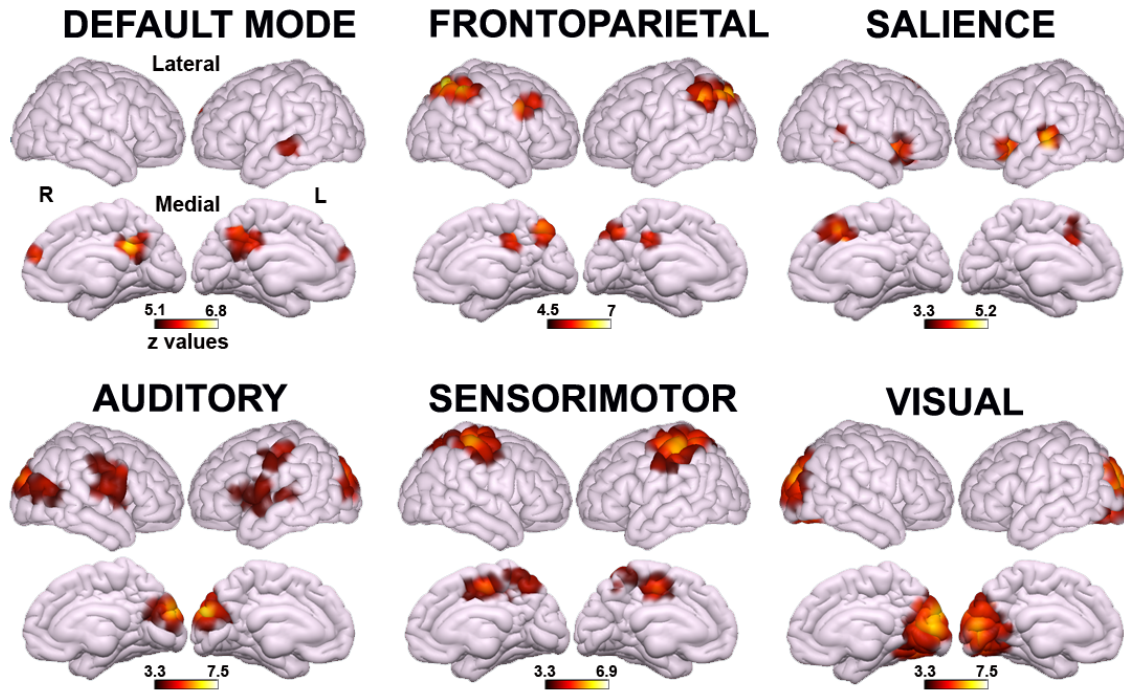
| Network	Feature selection criterion (t-test)			Single-feature classification		
	t value	Rank	p value	TP MCS	TN VS/UWS	Accuracy
Auditory	8.32	1	<.001	25	18	43/45
Visual	7.79	2	<.001	23	15	38/45
Default mode	6.95	3	<.001	23	15	38/45
Frontoparietal	6.82	4	<.001	23	15	38/45
Salience	6.21	5	<.001	24	15	39/45
Sensorimotor	5.87	6	<.001	24	13	37/45

FWE p<0.05 (cluster-level)

Crossmodal connectivity classifies independently assessed patients

- Training set: 45 DOC (26 MCS, 19 VS/UWS)
  - 14 trauma, 28 non-trauma, 3 mixed
  - 34 patients assessed >1m post-insult
- Test set:
  - **16 MCS**, **6 VS/UWS** (M_{age}: 43y, 15 non-trauma; all chronic)
  - From 2 different centers

Demertzi & Antonopoulos… Whitfield-Gabrieli & Laureys, Brain 2015
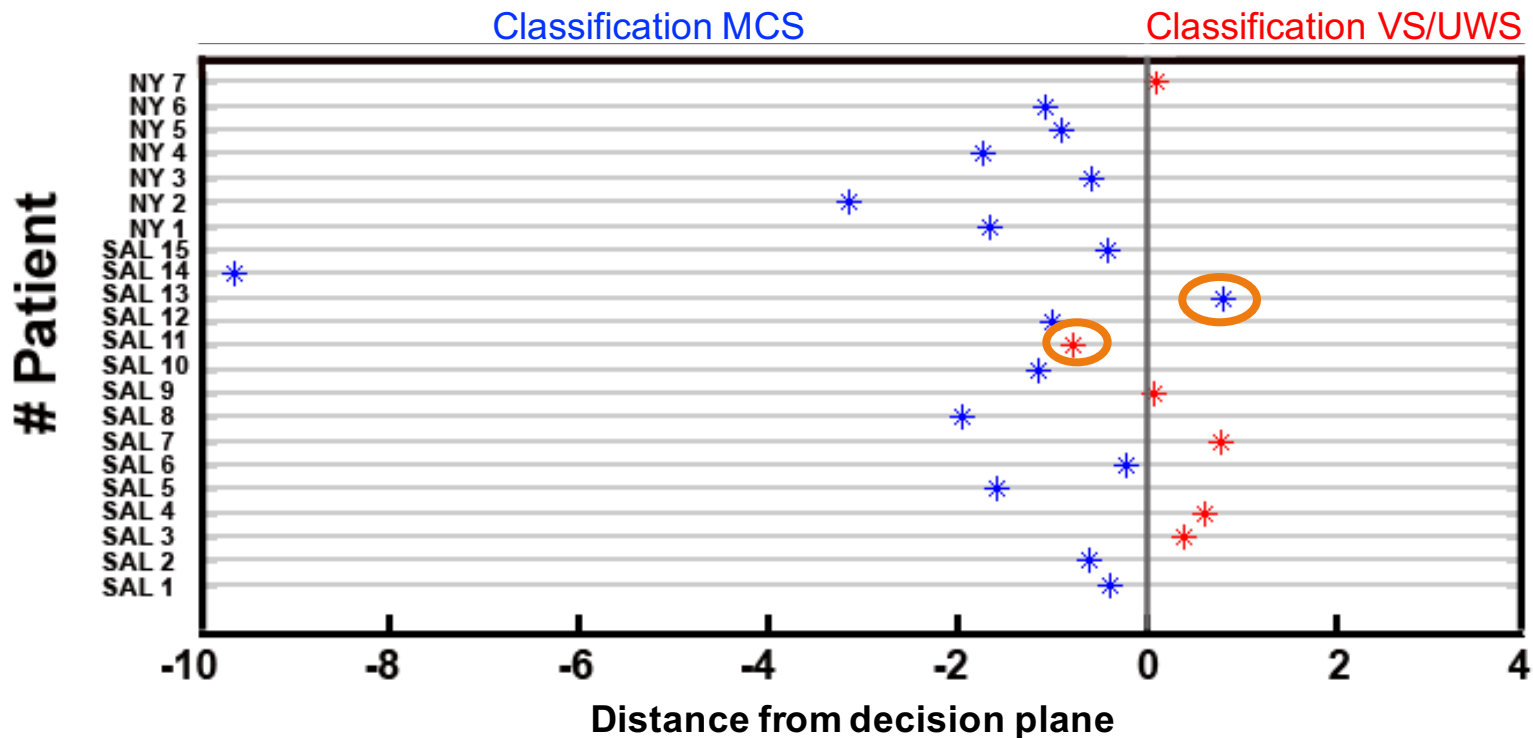
Conclusions

- DMN anticorrelations have a cognitive counterpart, which can be modulated under psychological and physiological conditions

- Clinical objective: to separate unconscious from (minimally) conscious patients

- The most discriminative feature is the connectivity between occipital, parietal, insular and superior temporal regions

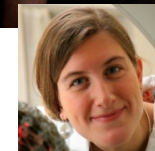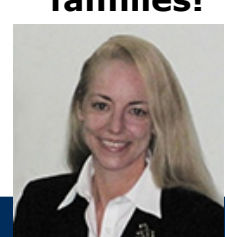➤ Anesthetized patients?

➤ Prognostic value?

R   lateral view   L

medial view
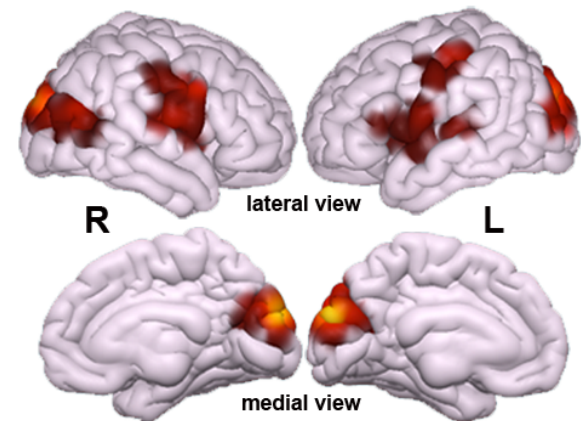
Thank you!

Coma Science Group & PICNIC Lab

The deparments of Neurology and Radiology in Liège and Paris

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

a.demertzi@ulg.ac.be

CHERCHER, TROUVER, GUÉRIR, POUR VOUS & AVEC VOUS.

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et de la Moelle épinière

Denoising functional volumes

Denoising (Chai et al, NeuroImage 2012):

1. Motion artifact detection (ART)
2. Regressing out the realignment parameters, their derivatives and the ART-detected outliers
3. Anatomical component-based noise correction method (aCompCor) which models the influence of noise as a voxel-specific linear combination of multiple empirically estimated noise sources (WM, GM and CSF)
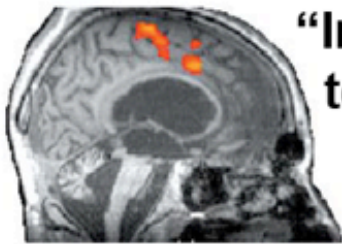4. Temporal band-pass filtering [0.008-0.09Hz]
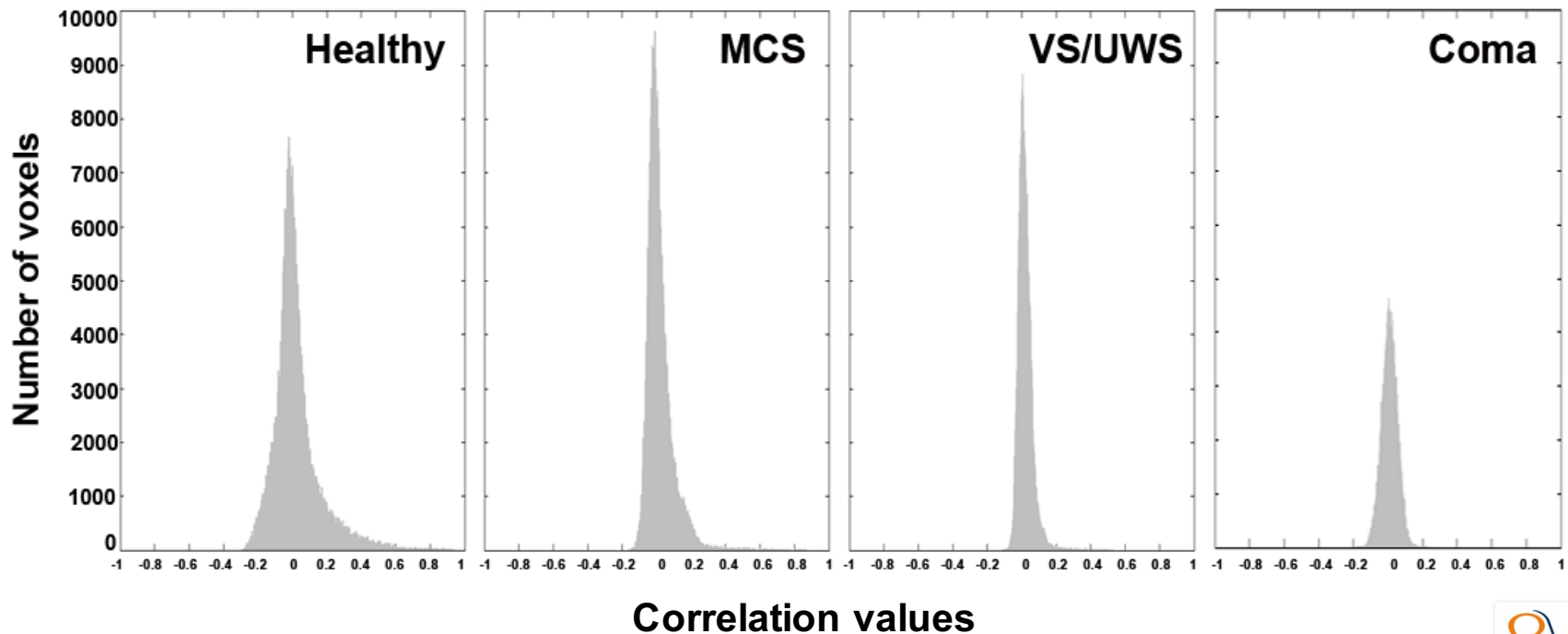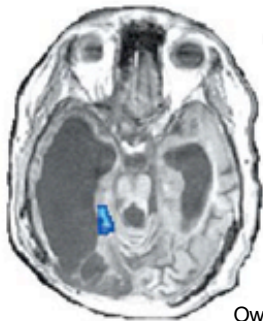
Classifier generalizes to healthy
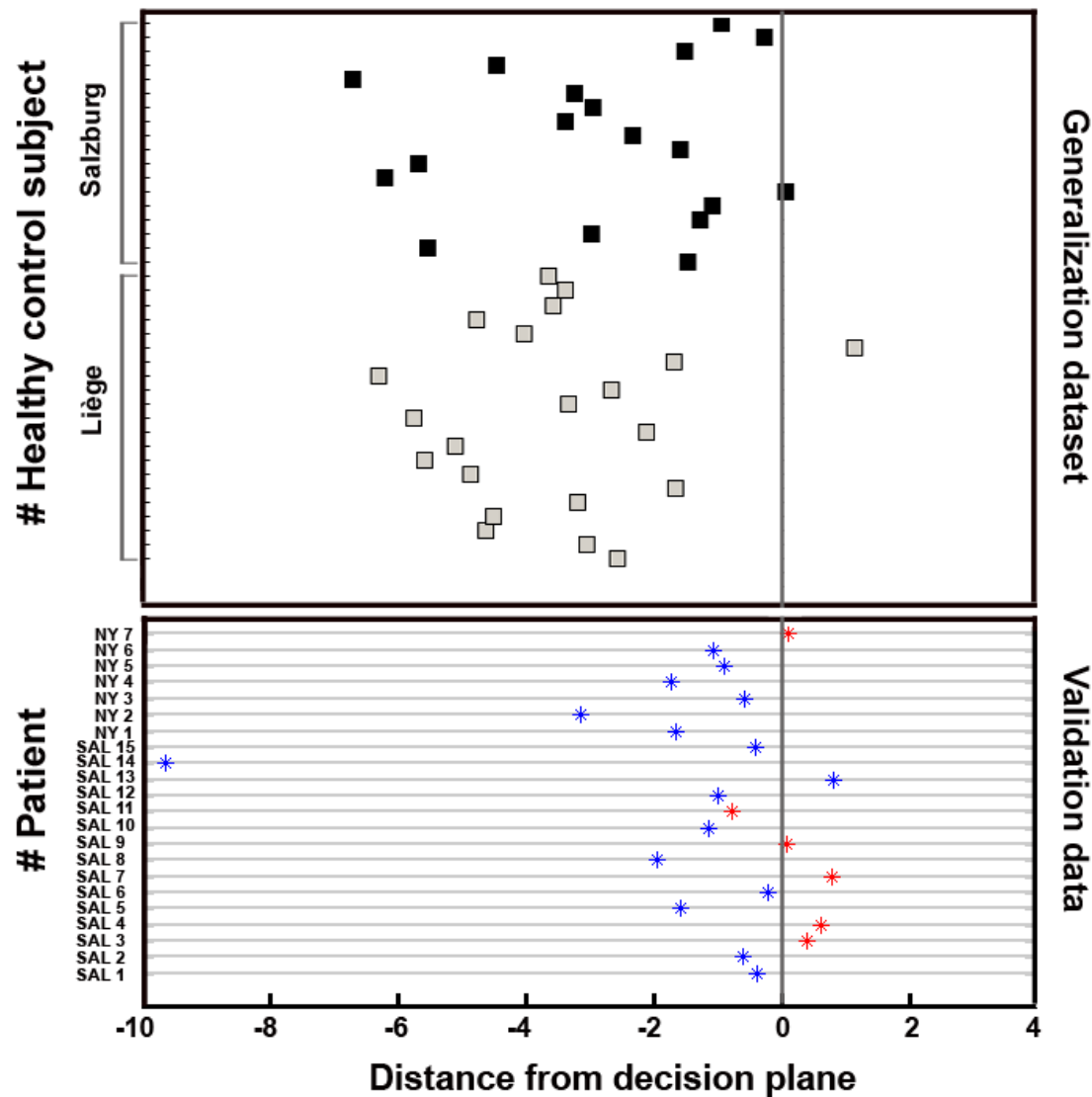
Detecting awareness with fMRI
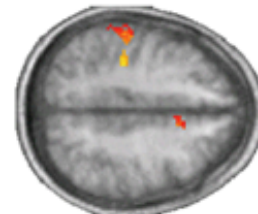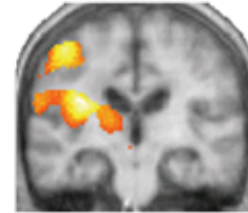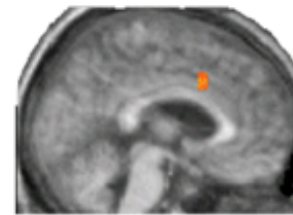

Active paradigms

"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

Heine, Di Perri, Soddu, Laureys, Demertzi
In: *Clinical Neurophysiology in Disorders of Consciousness,* Springer-Verlag 2015

Demertzi & Laureys, In: *I know what you are thinking: brain imaging and mental privacy*, Oxford University Press 2012
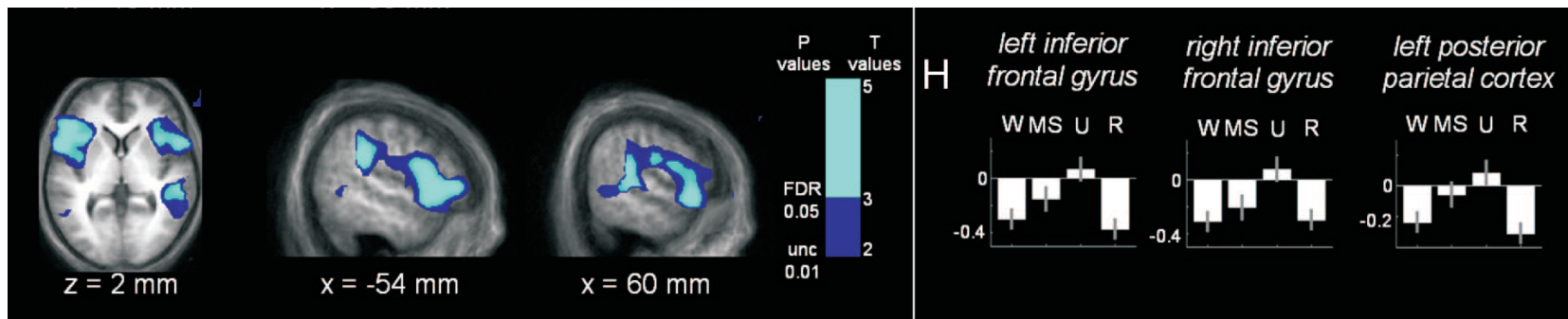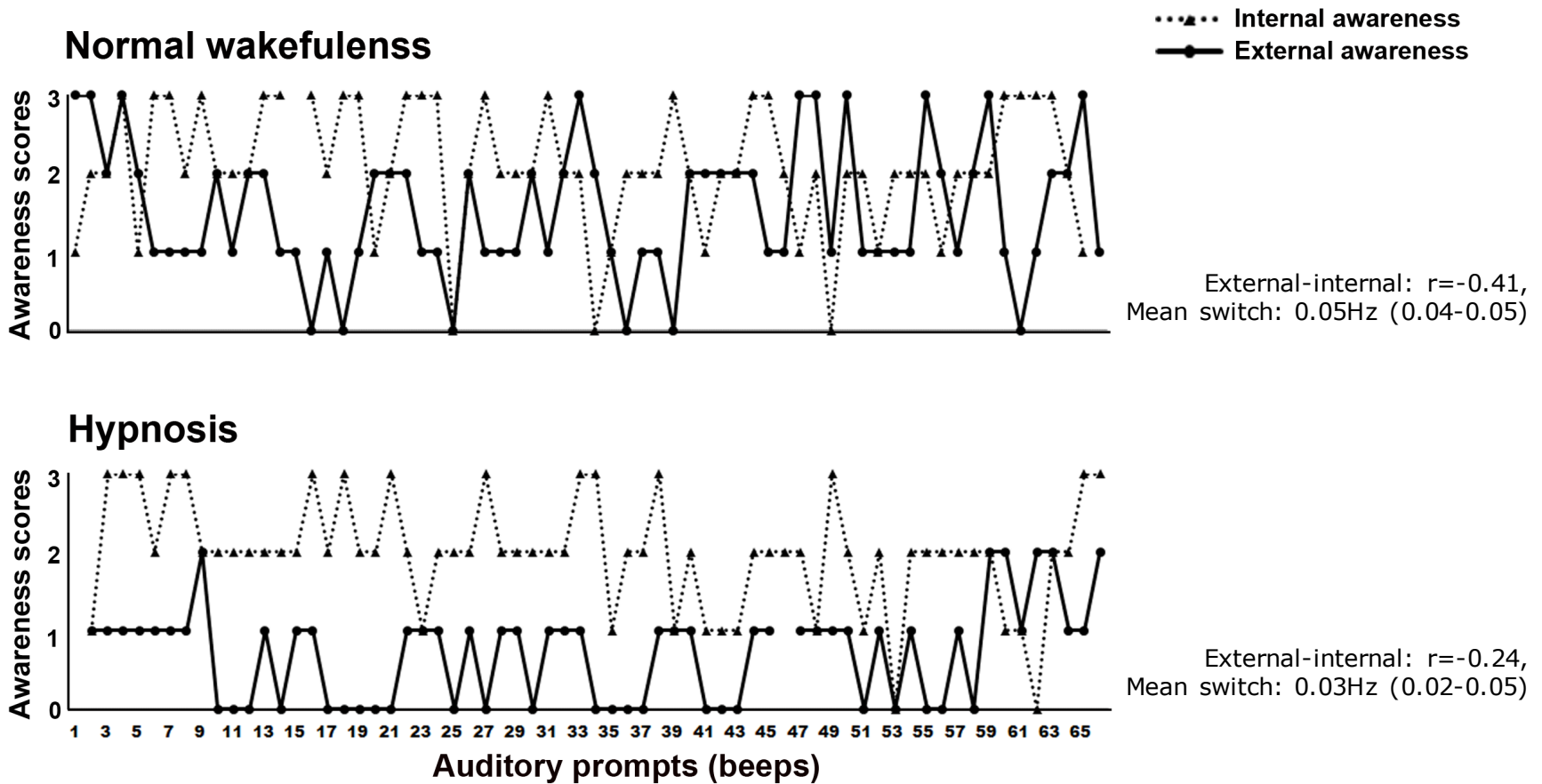
Propofol-induced anesthesia

Cross-modal interaction

DMN anticorrelations

Boveroux et al, Anesthesiology 2010
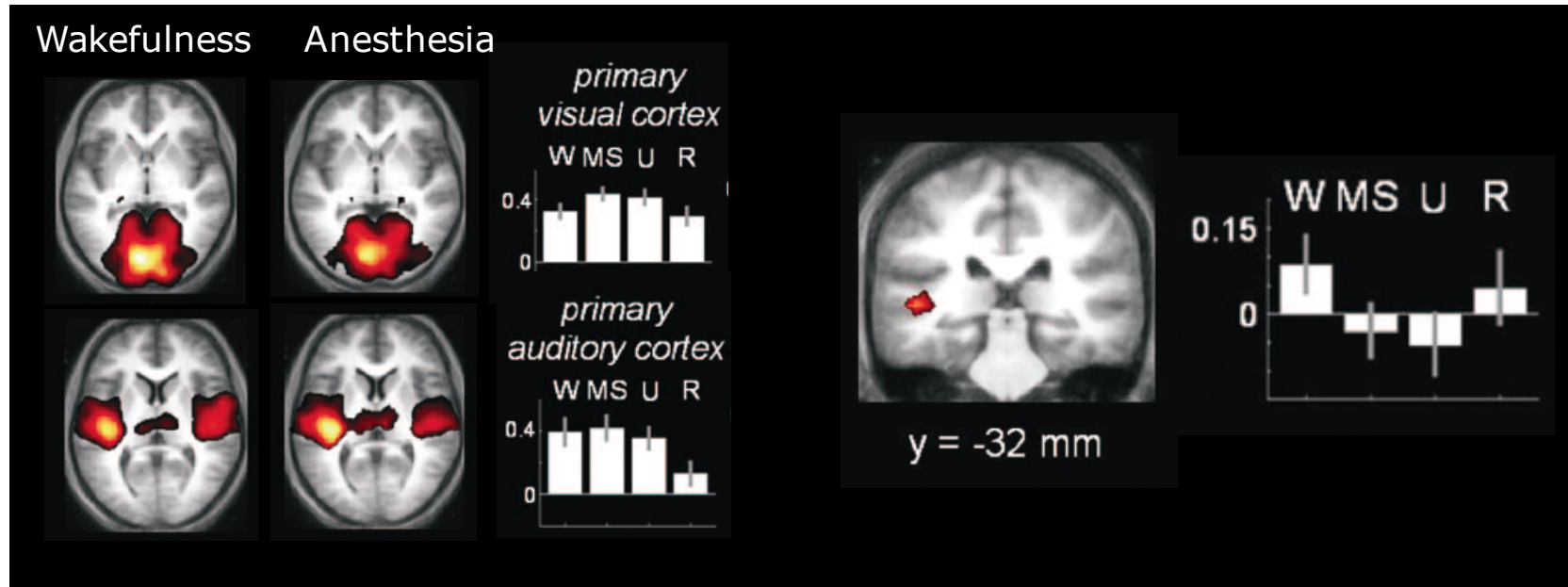
Awareness is modified in hypnosis

Demertzi, Vanhaudenhuyse, Noirhomme, Faymonville, Laureys, J Physiol Paris in press

Consciousness

Functionalism

Materialism

Dualism

■ Edinburgh survey (n=250)
□ Liège survey (n=1858)