

Intrinsic connectivity as a means to differentiate patients with disorders of consciousness

19th ASSC tutorial

7 July 2015
Paris, France

Athena Demertzi, PhD
Institut du Cerveau et de la Moelle épinière – ICM
Paris, France
&
Coma Science Group
Cyclotron Research Centre & Neurology Department
University & University Hospital of Liège, Belgium



Université
de Liège



LA LIBERTÉ DE CHERCHER

www.comascience.org

A clinical-ethical imperative

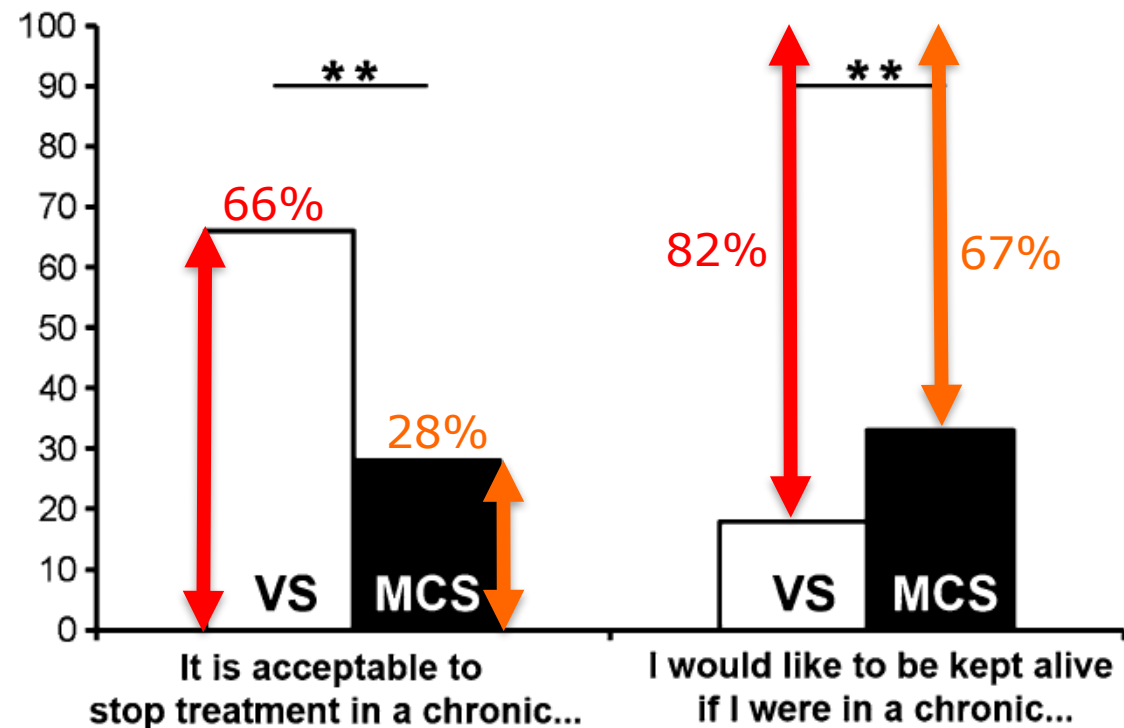
Attitudes towards end-of-life issues in disorders of consciousness: a European survey



A. Demertzi · D. Ledoux · M.-A. Bruno ·
A. Vanhaudenhuyse · O. Gosseries · A. Soddu ·
C. Schnakers · G. Moonen · S. Laureys

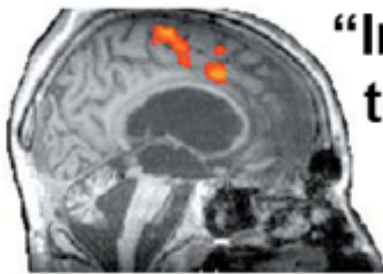


2,475 medical professionals

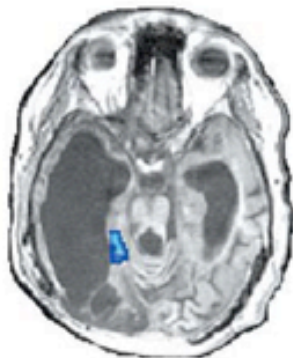


Neuroimaging paradigms

Active paradigms



“Imagine playing tennis”

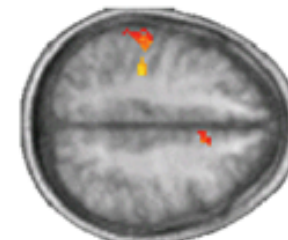
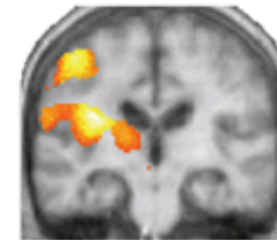
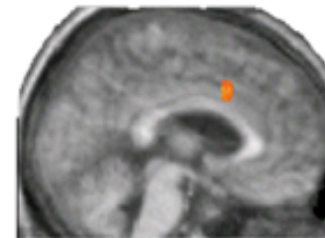


“Imagine visiting the rooms of your house”

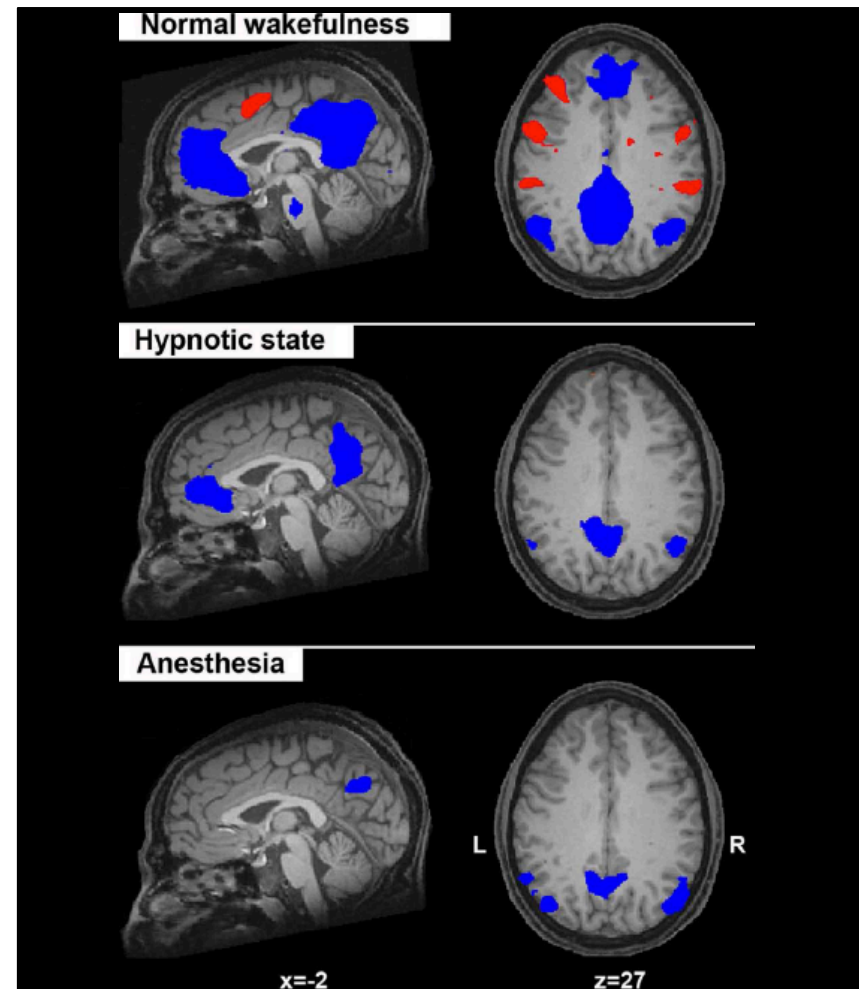
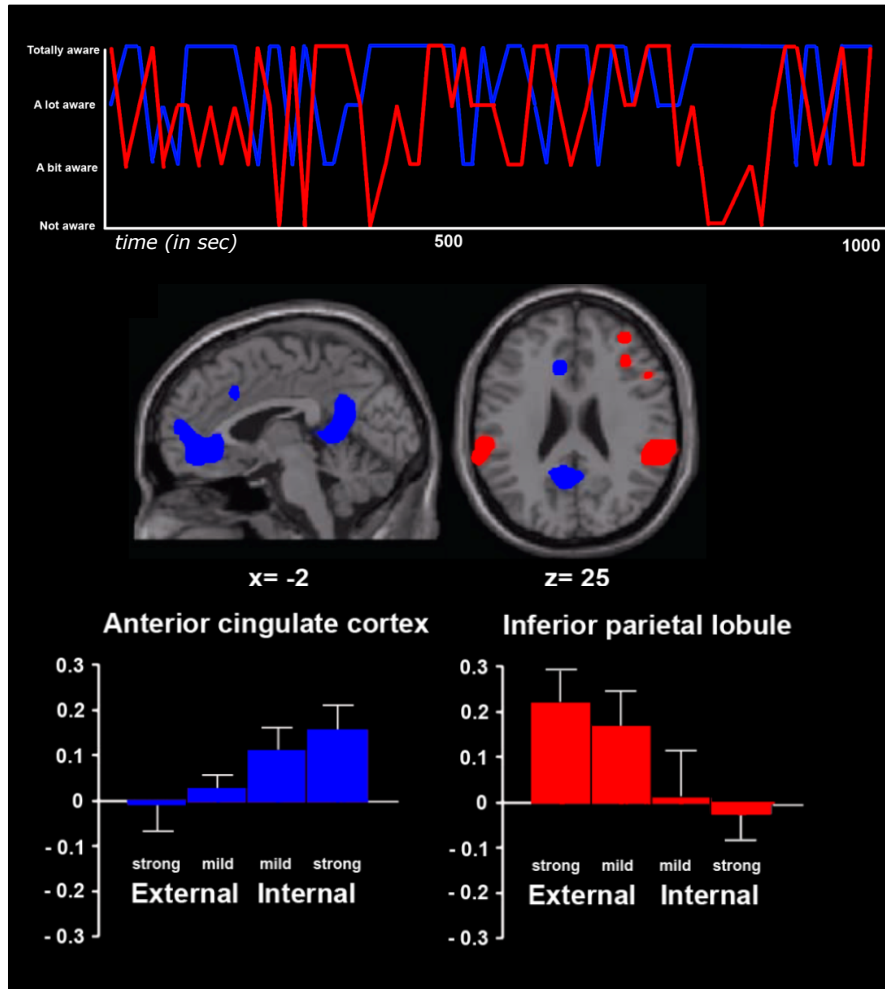
Passive paradigms



median nerve



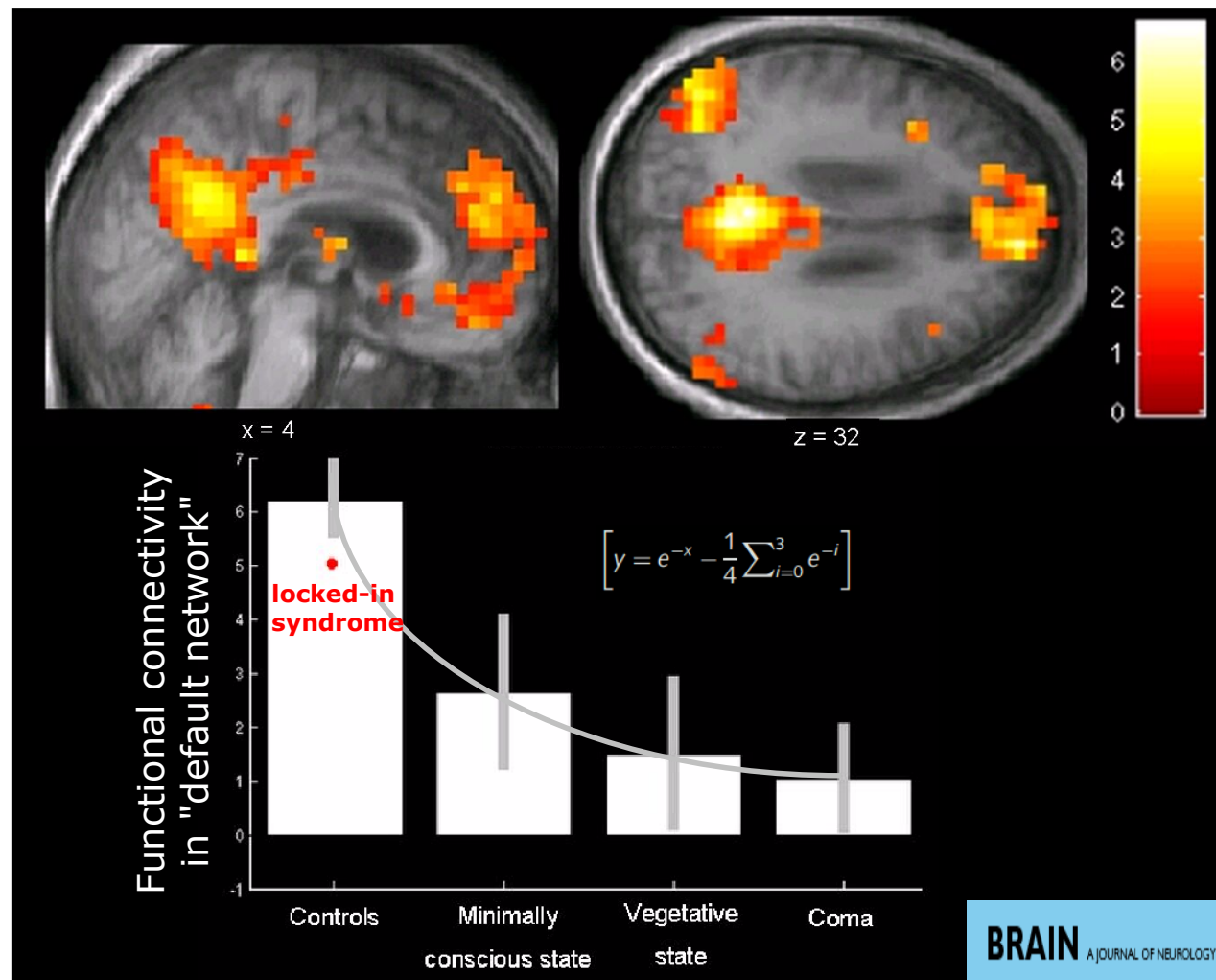
fMRI resting state and cognition



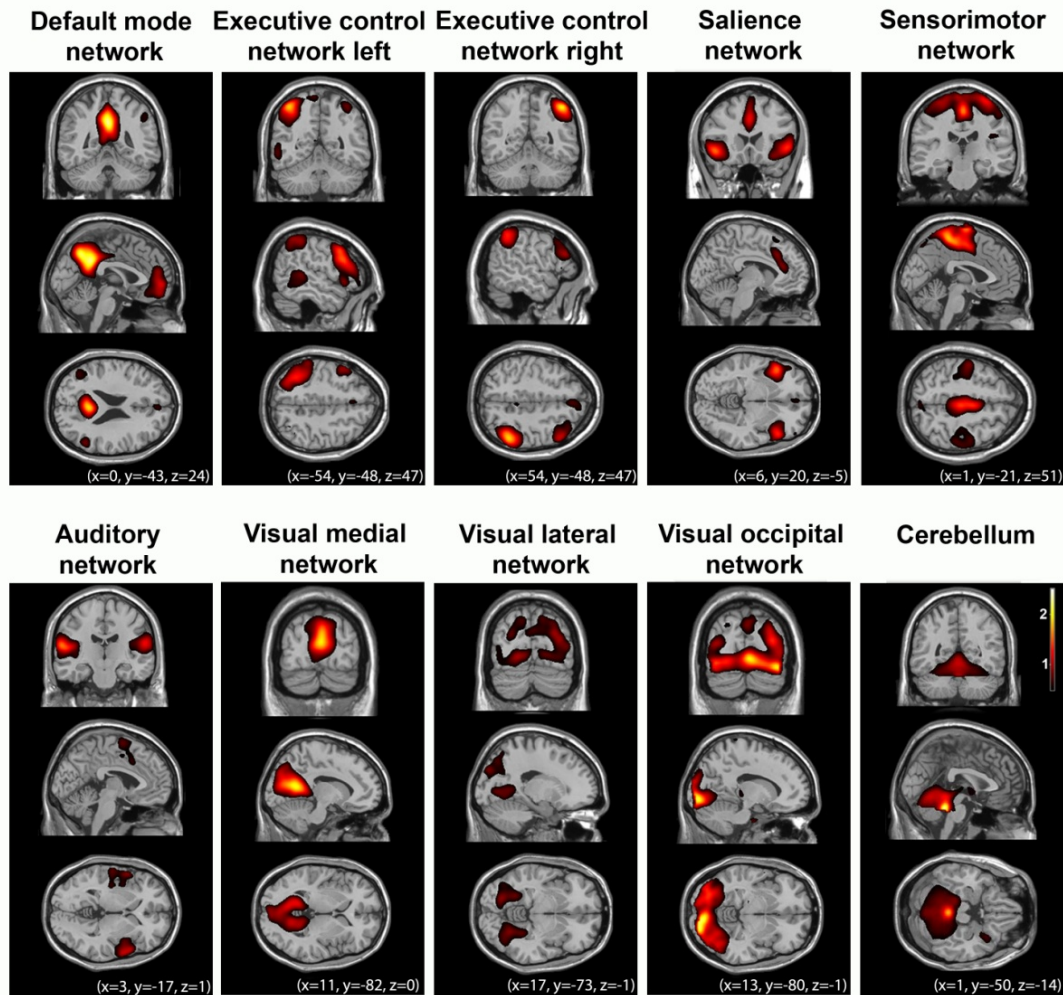
Vanhaudenhuyse & Demertzi et al, J Cogn Neurosci 2011

Demertzi & Whitfield-Gabrieli, in: *Neurology of Consciousness in press*
Demertzi, Soddu, Laureys, Curr Opin Neurobiol 2013
Demertzi et al, Front Hum Neurosci 2013
Demertzi et al, Prog Brain Res 2011

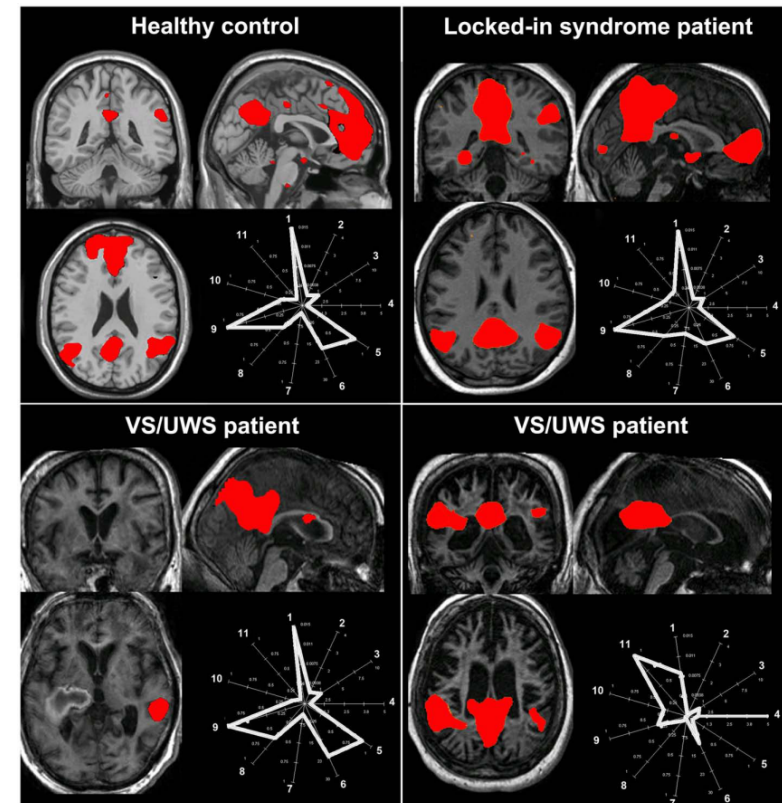
Disrupted DMN in patients



Multiple RSNs in DOC: issues

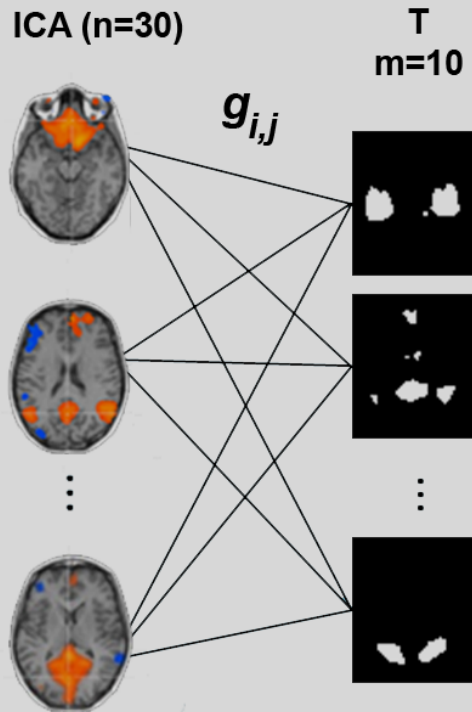


A challenge....

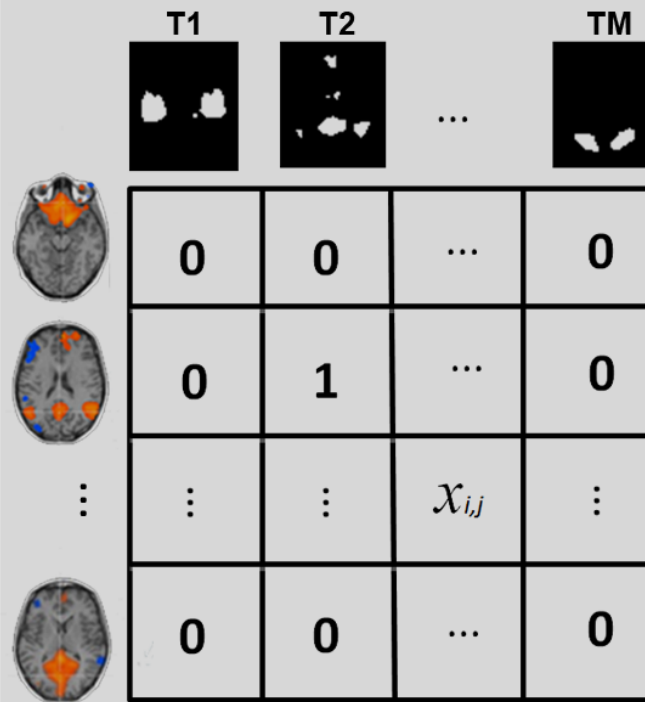


Multiple RSNs in DOC: an approach

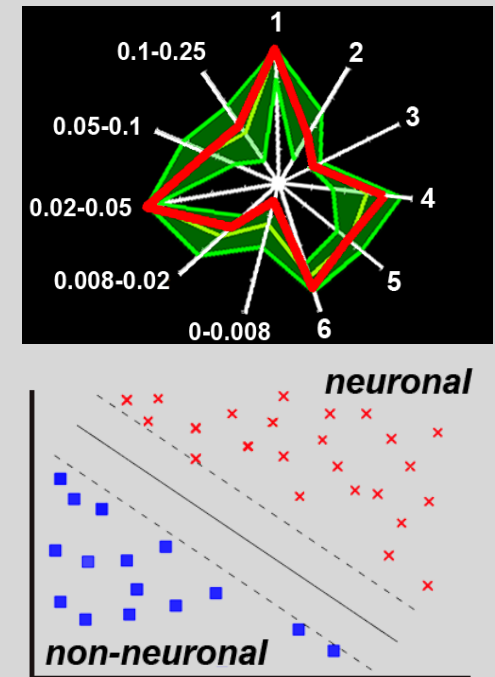
1. Goodness-of-fit calculation



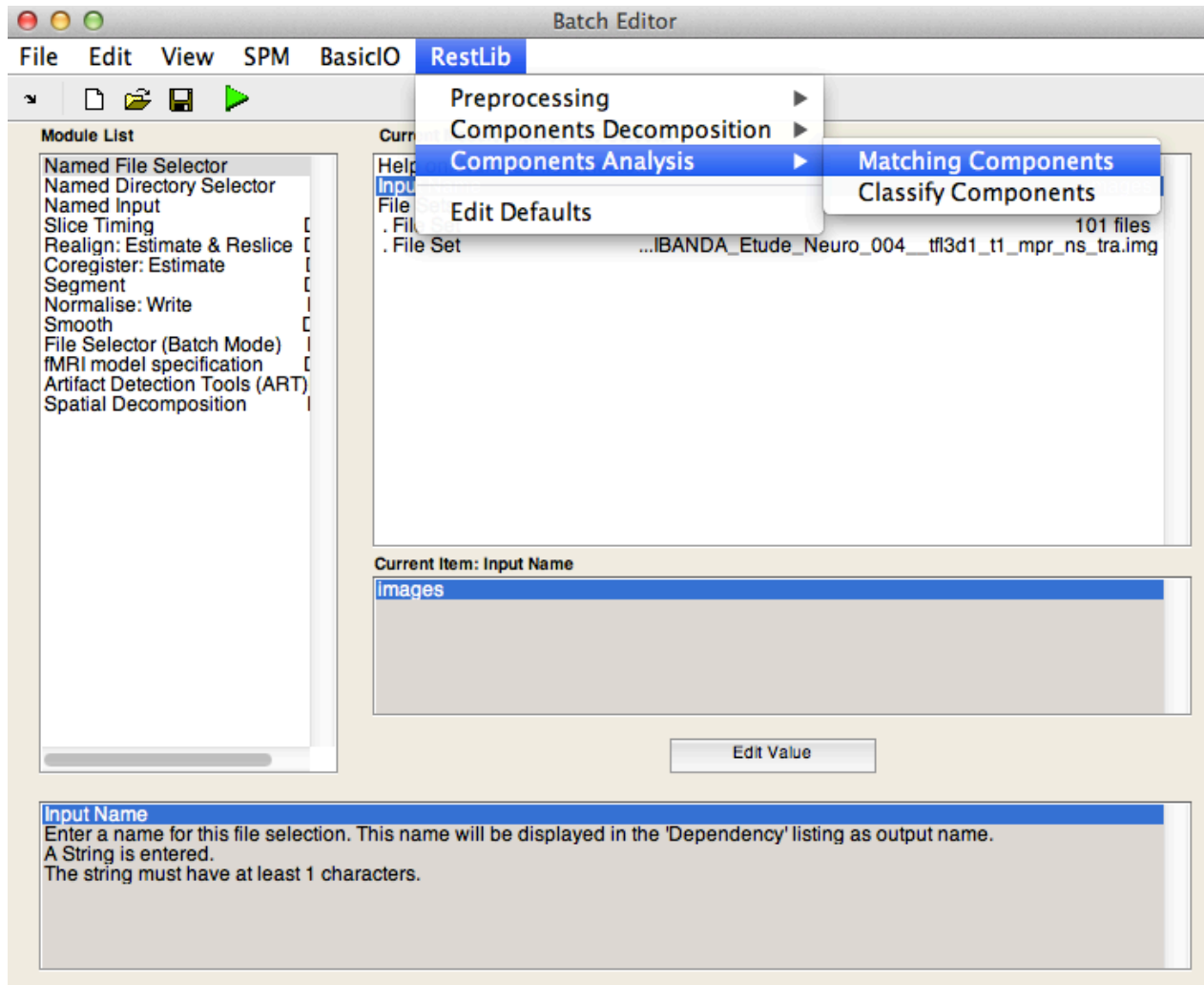
2. Multiple template assignment



3. "Neurality" test



The Coma RestLib



UNIVERSIDAD
CENTRAL

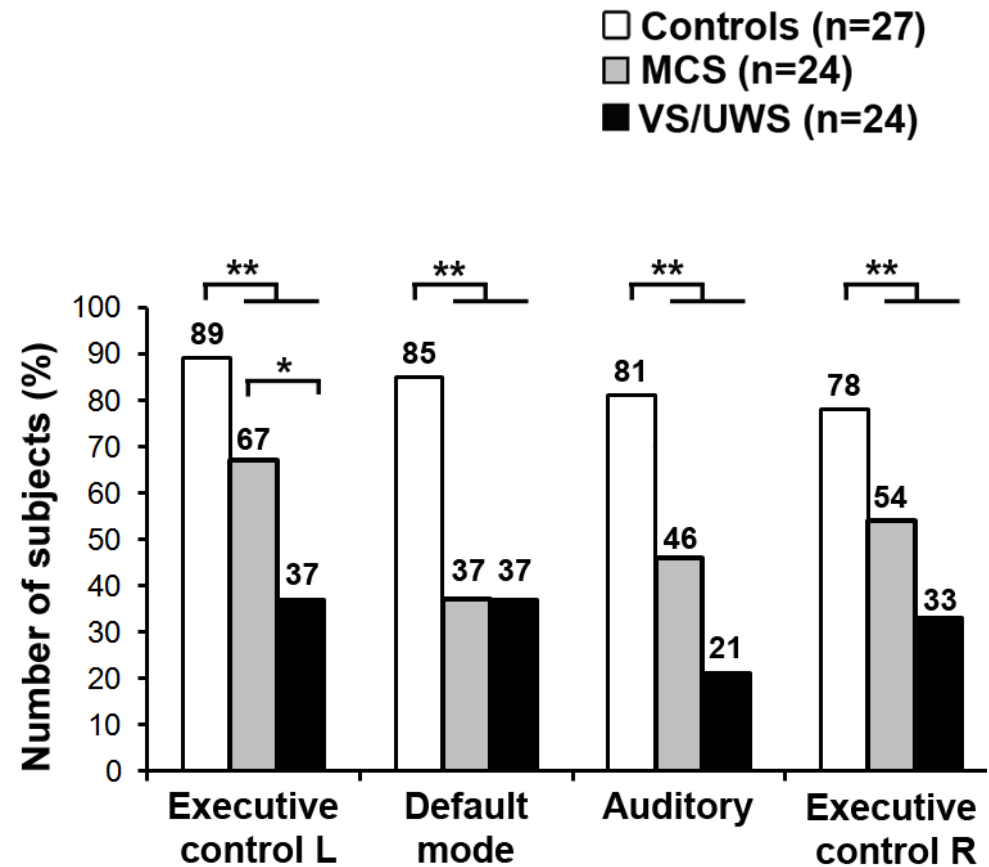
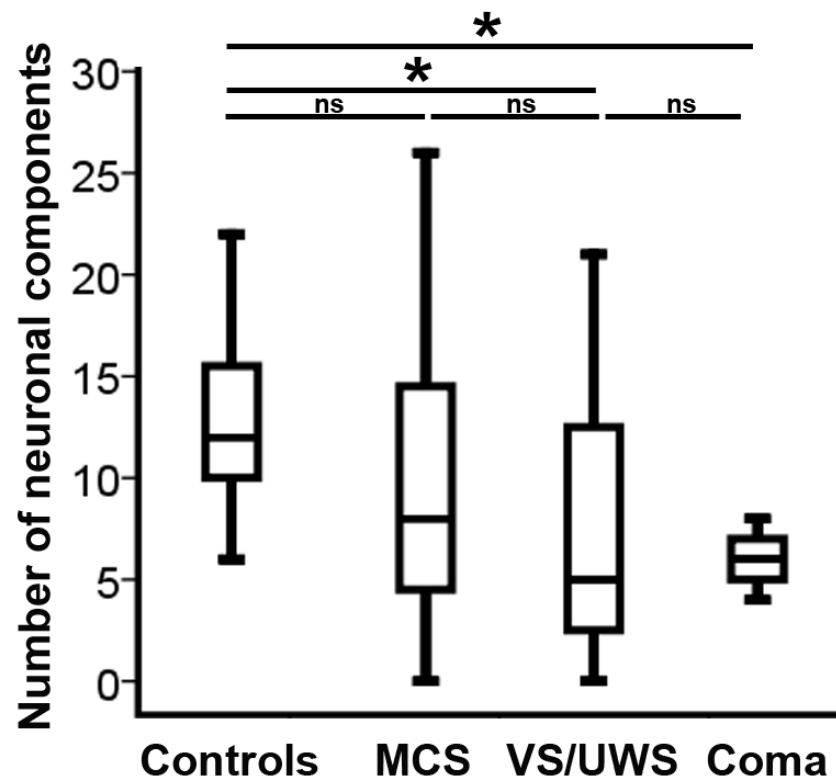
High Performance Computing Lab

Universidad Central - Facultad de Ingeniería

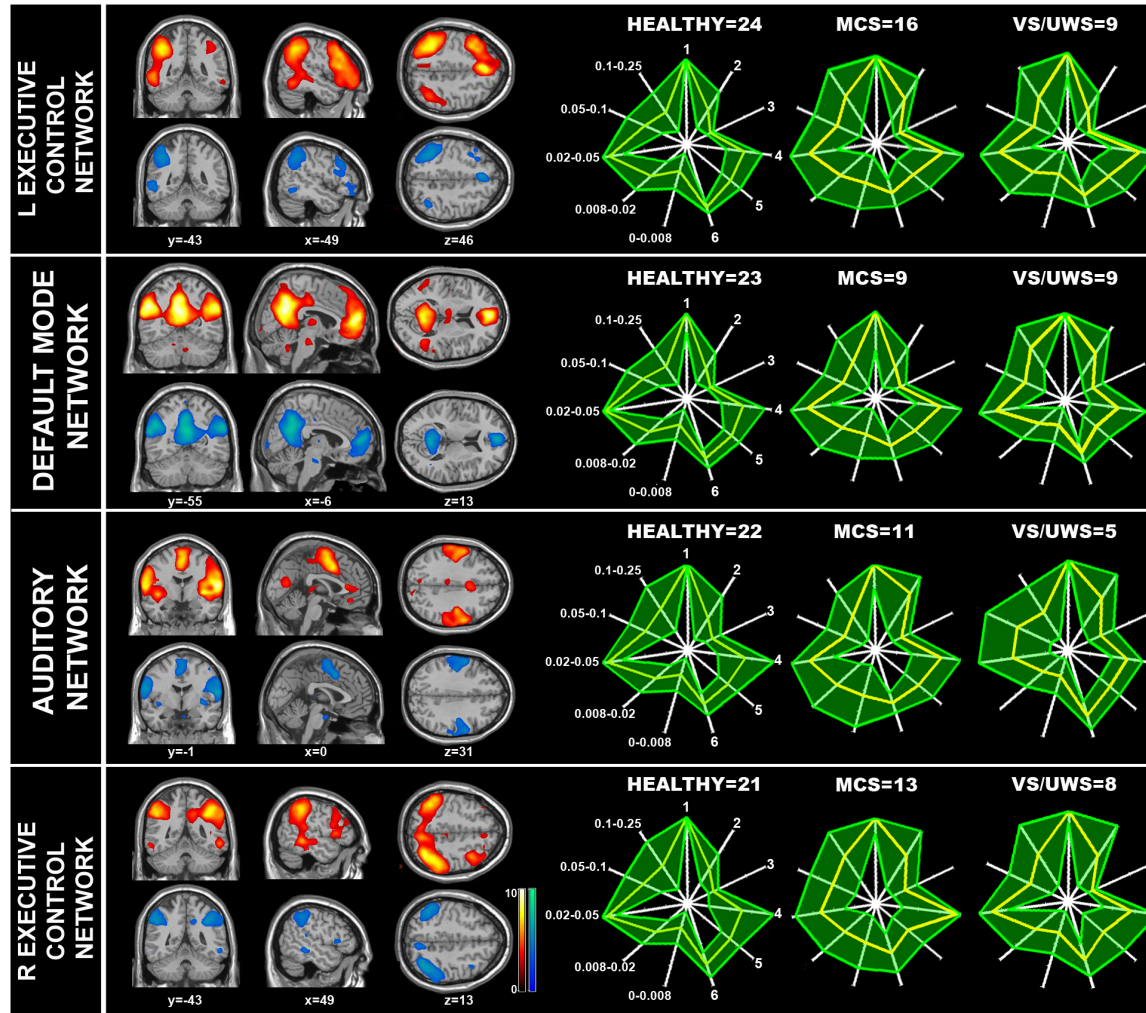
Dr. Francisco Gómez
Javier Guaje

**Email to Javier Guaje:
jrguajeg@unal.edu**

Fewer "neuronal" networks in DOC



Voxel-wise group comparisons

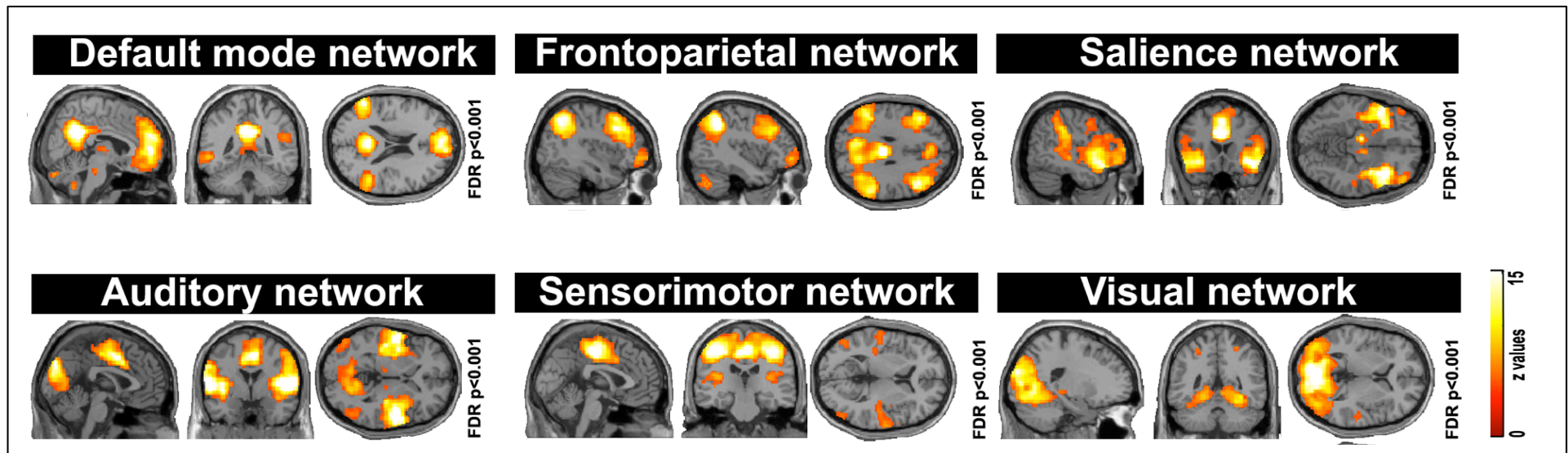


Controls N=27
MCS N=24
VS/UWS N=24

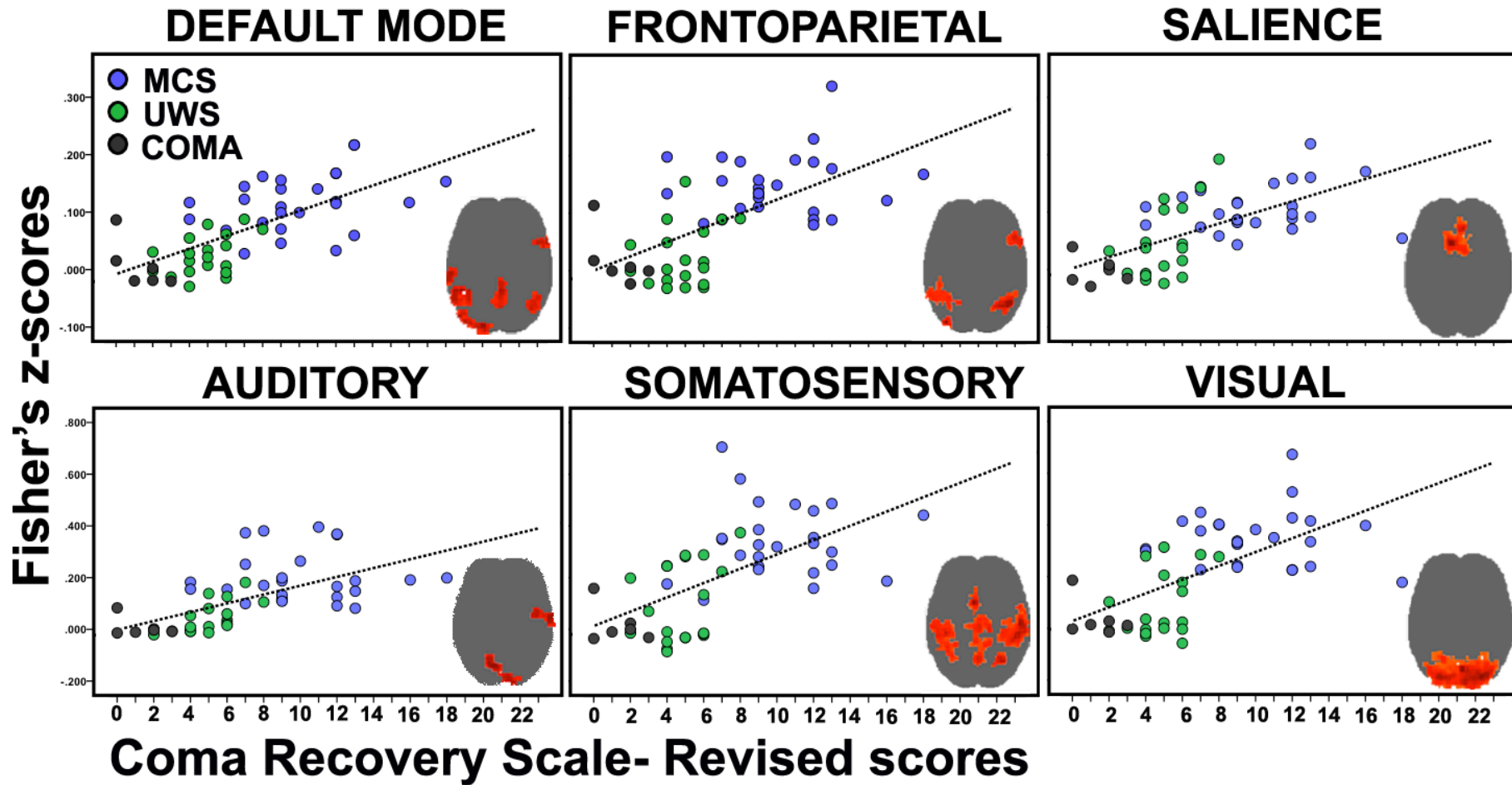
Classification feature: "neuronality"

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

Network connectivity in healthy

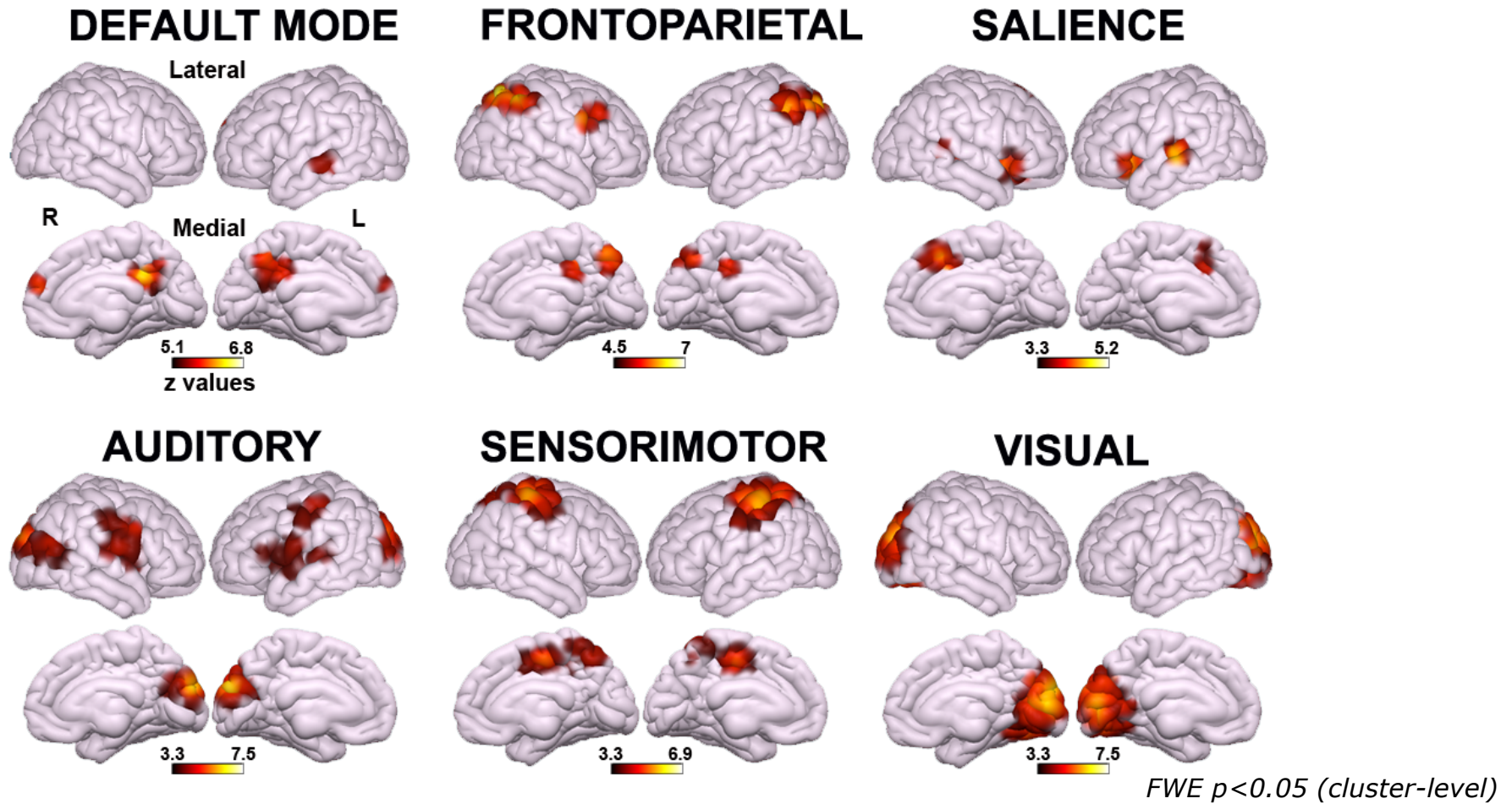


Intrinsic connectivity reflects level of C



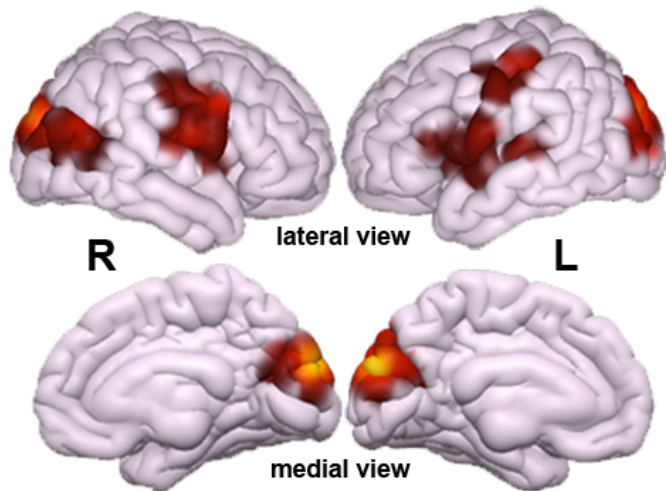
Finding the discriminative features

MCS > VS/UWS

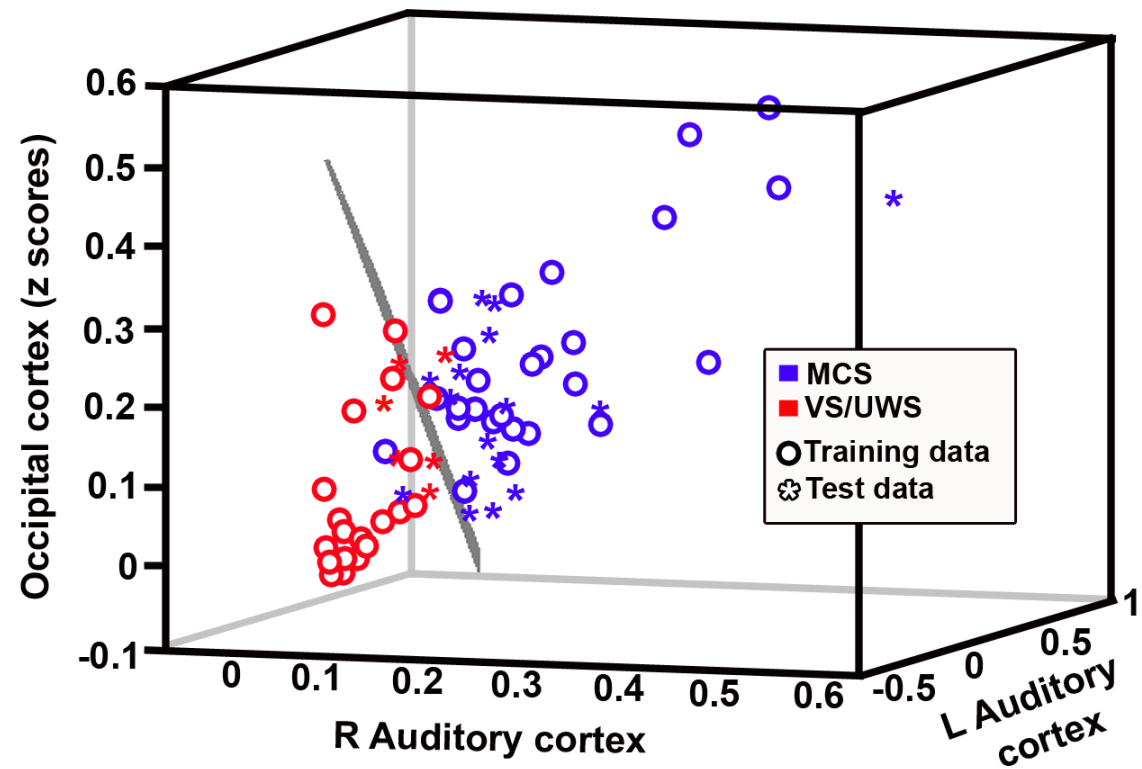


Training dataset: patients (Lg)

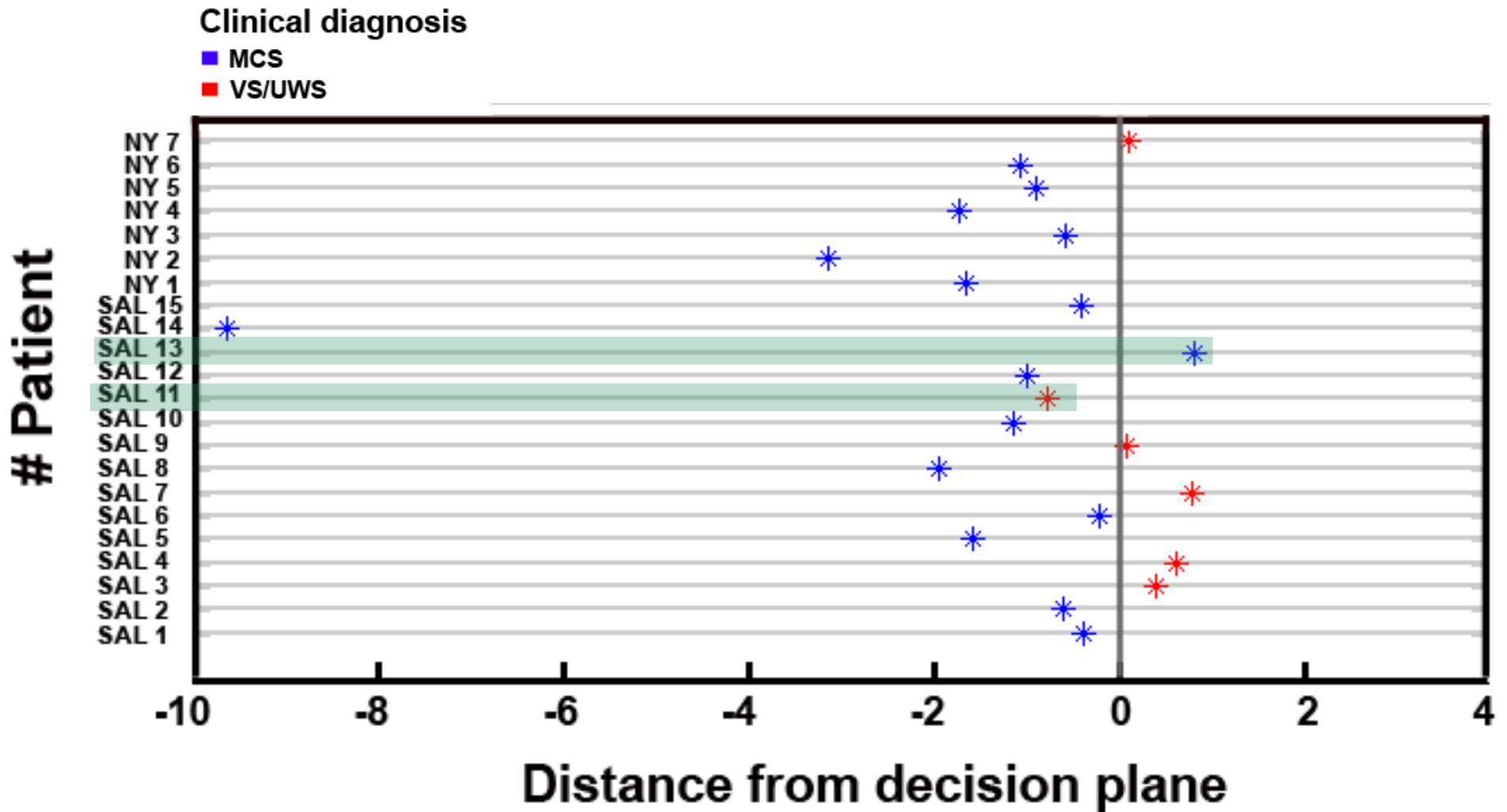
- 26 MCS, 19 VS/UWS
- 14 trauma, 28 non-trauma, 3 mixed
- 34 patients assessed >1m post-insult



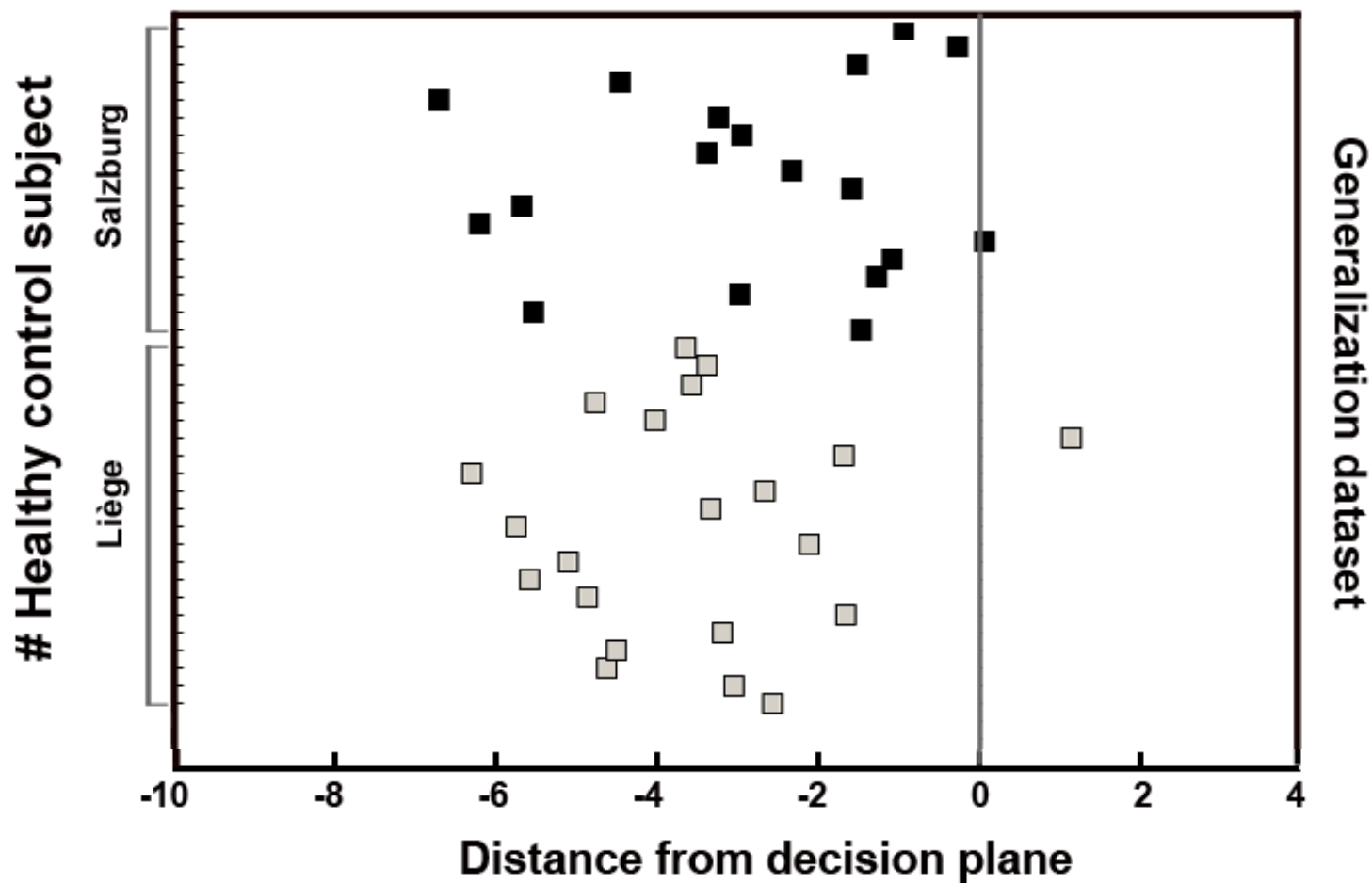
R auditory $w = -1.7890$
L auditory $w = -0.4002$
Occipital $w = -0.7362$



Validation dataset: patients (NY, Sal)

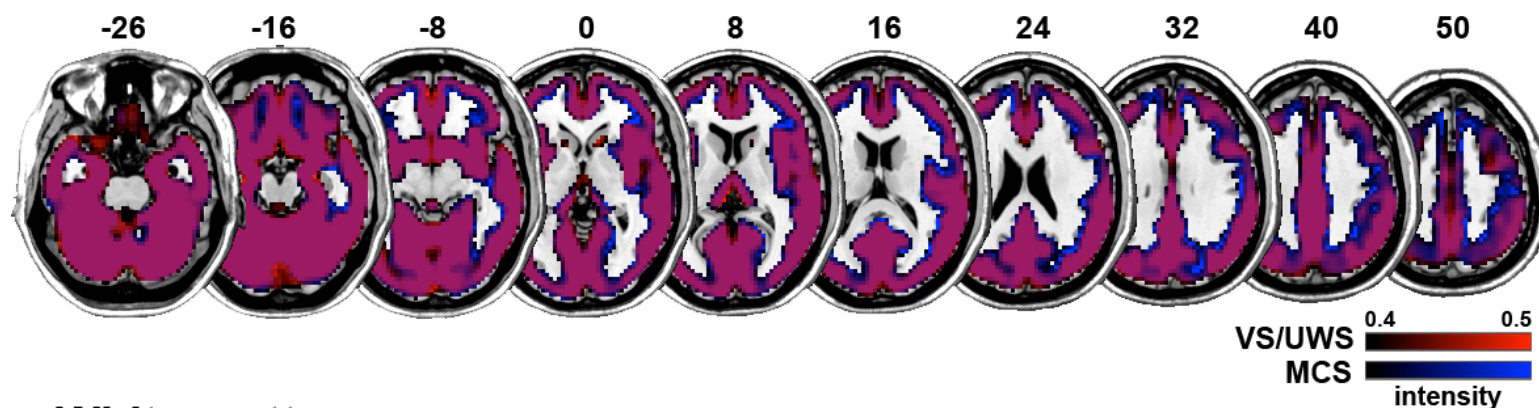


Generalization dataset: healthy

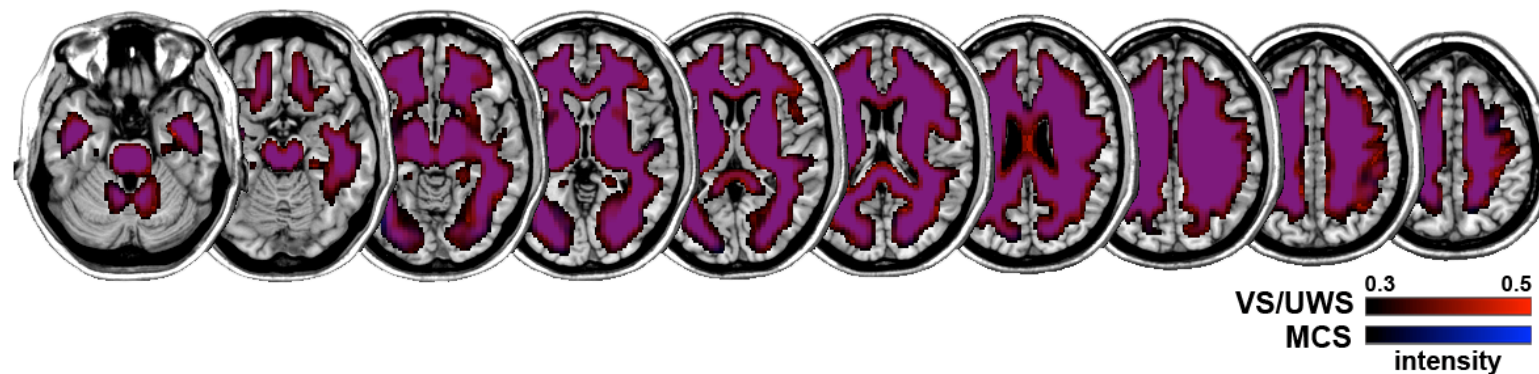


Echoes from structural connectivity?

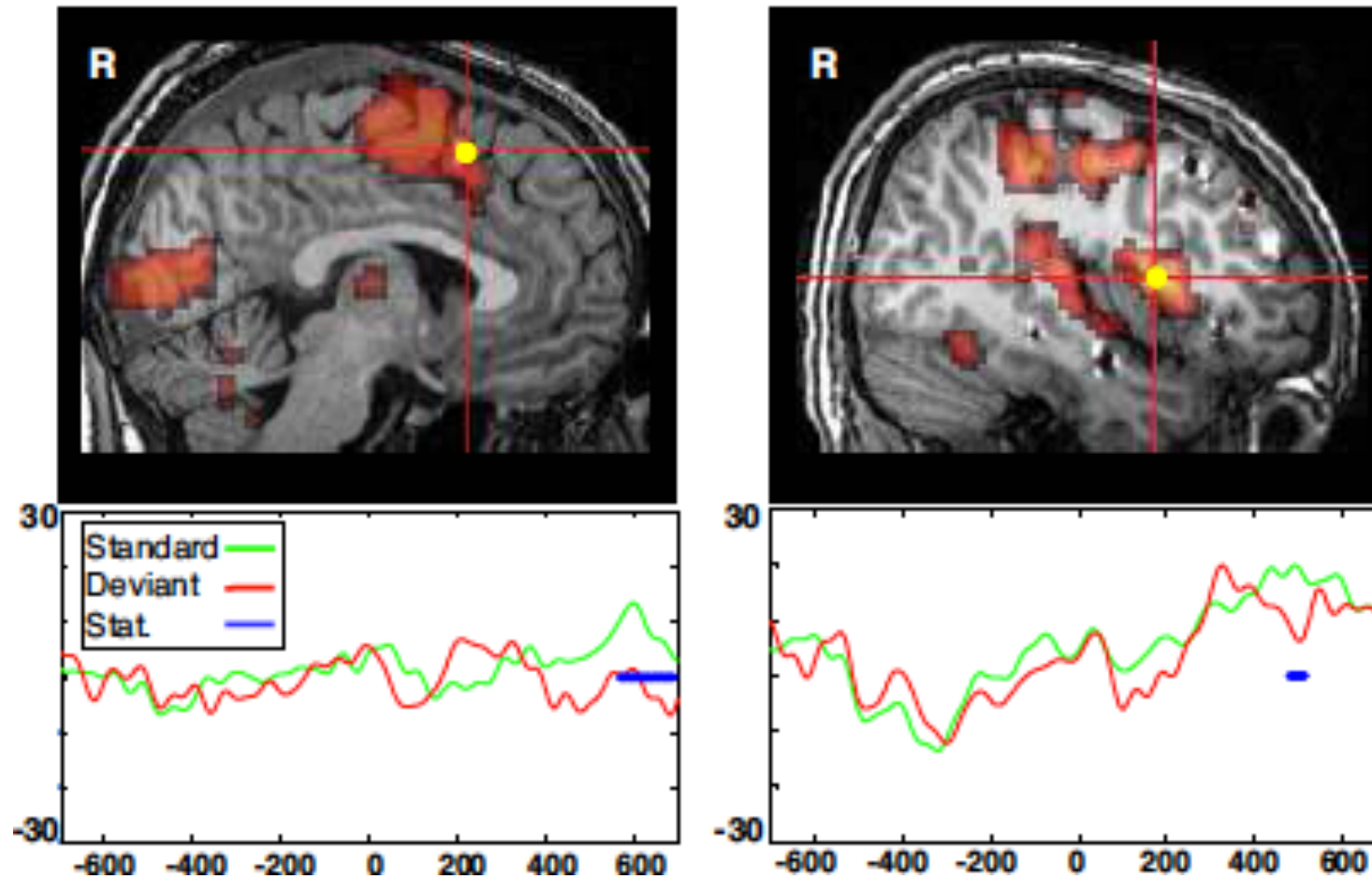
Gray matter



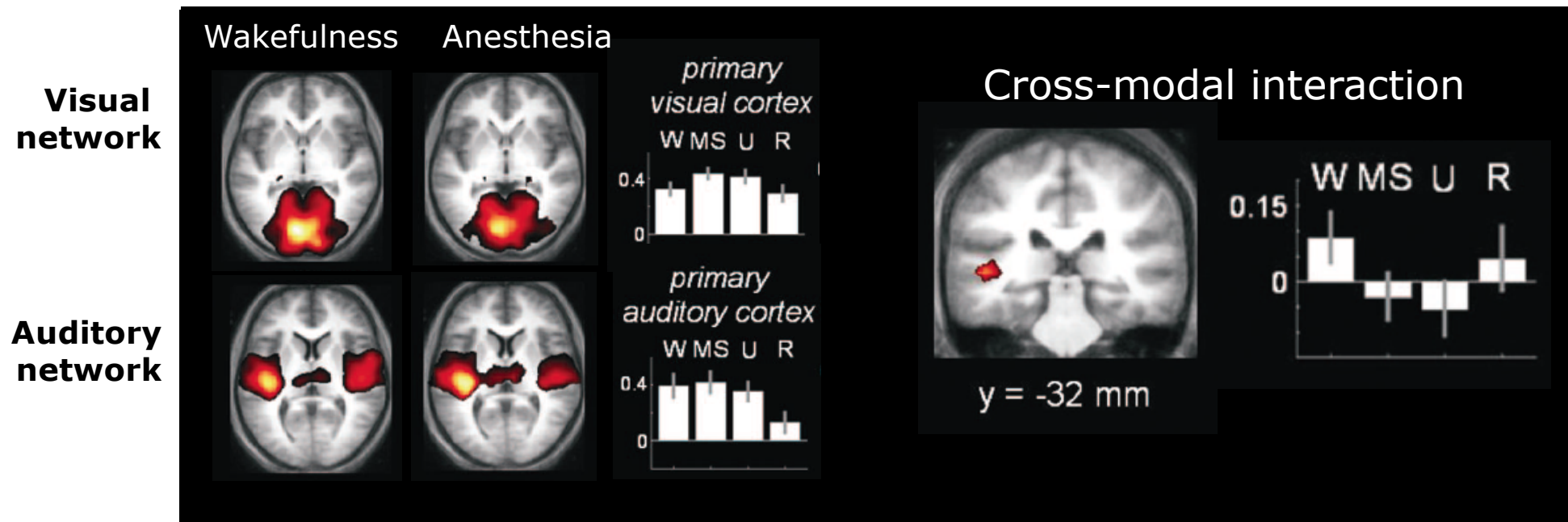
White matter



Cross-modal interaction during conscious processing



Cross-modal interaction demolishes under propofol anesthesia



Translational research

rsfMRI Biomarkers



Diagnostic & prognostic use



Medico-ethical issues in DOC

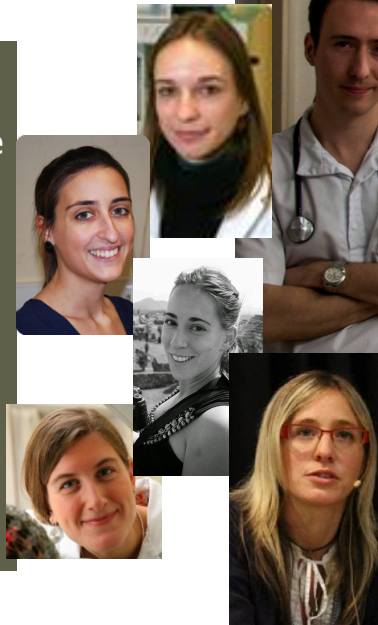


Niko Schiff & Henning Voss,
Weill Cornell Medical College

Julia Sophia Crone & the
Salzburg team

The departments of
Neurology and Radiology in
Liege and Paris

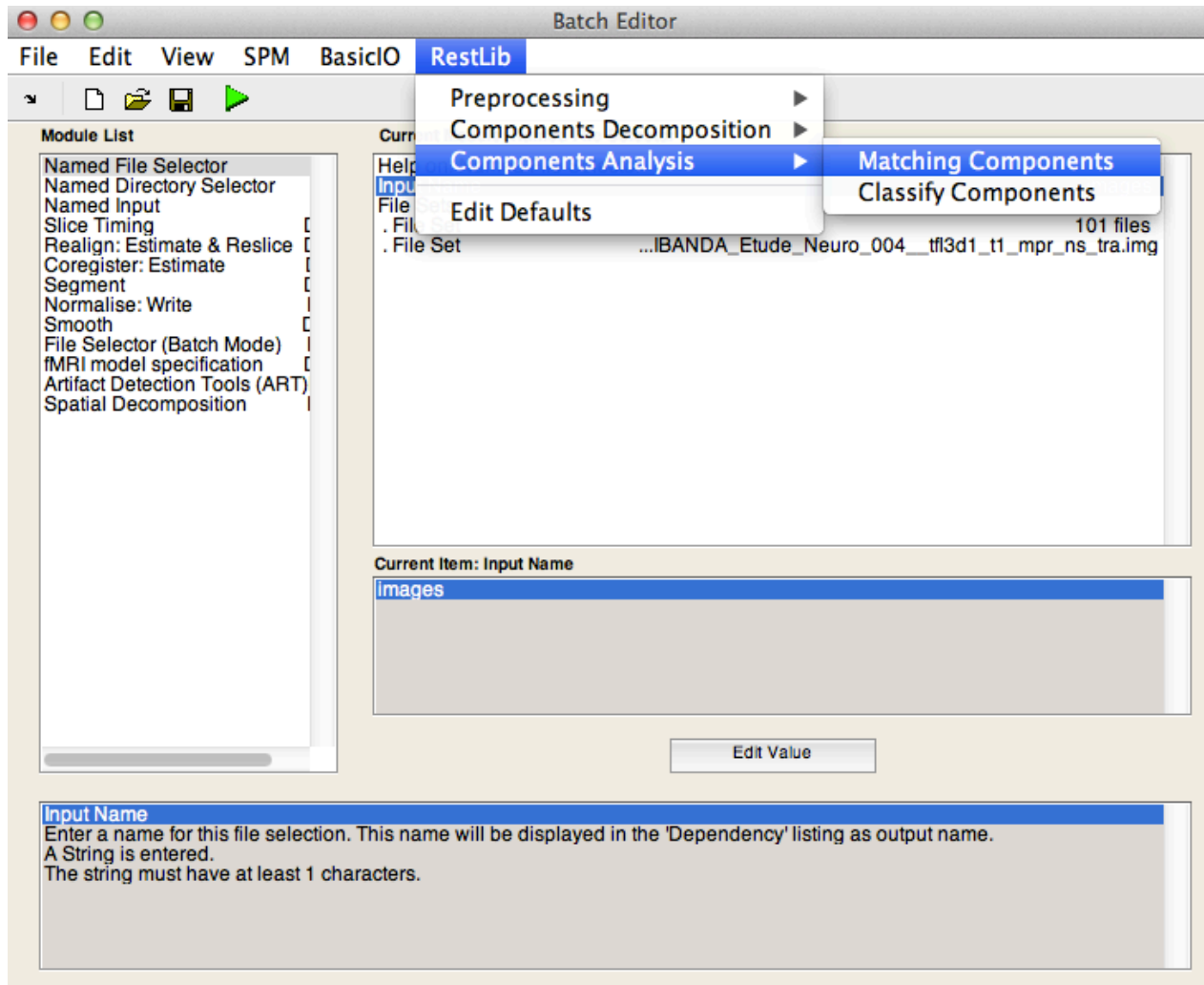
**...but mostly patients
and their families!**



James S. McDonnell Foundation 

athina.demertzi@icm-institute.org

The Coma RestLib



UNIVERSIDAD
CENTRAL

High Performance Computing Lab

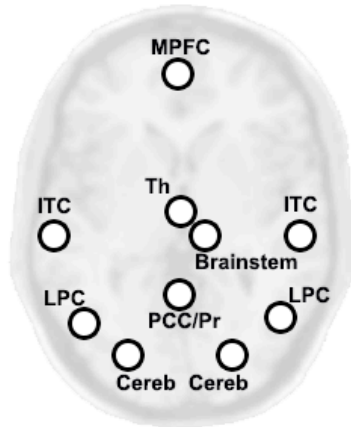
Universidad Central - Facultad de Ingeniería

Dr. Francisco Gómez
Javier Guaje

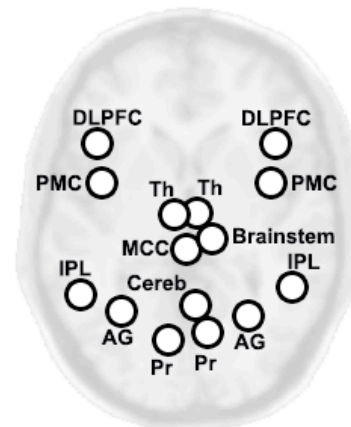
**Email to Javier Guaje:
jrguajeg@unal.edu**

Seed positions

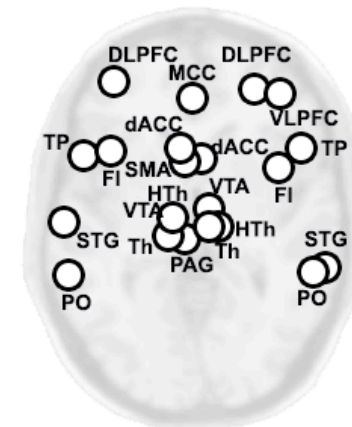
Default mode network



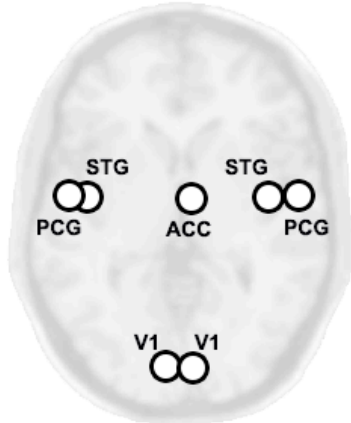
Frontoparietal network



Salience network



Auditory network



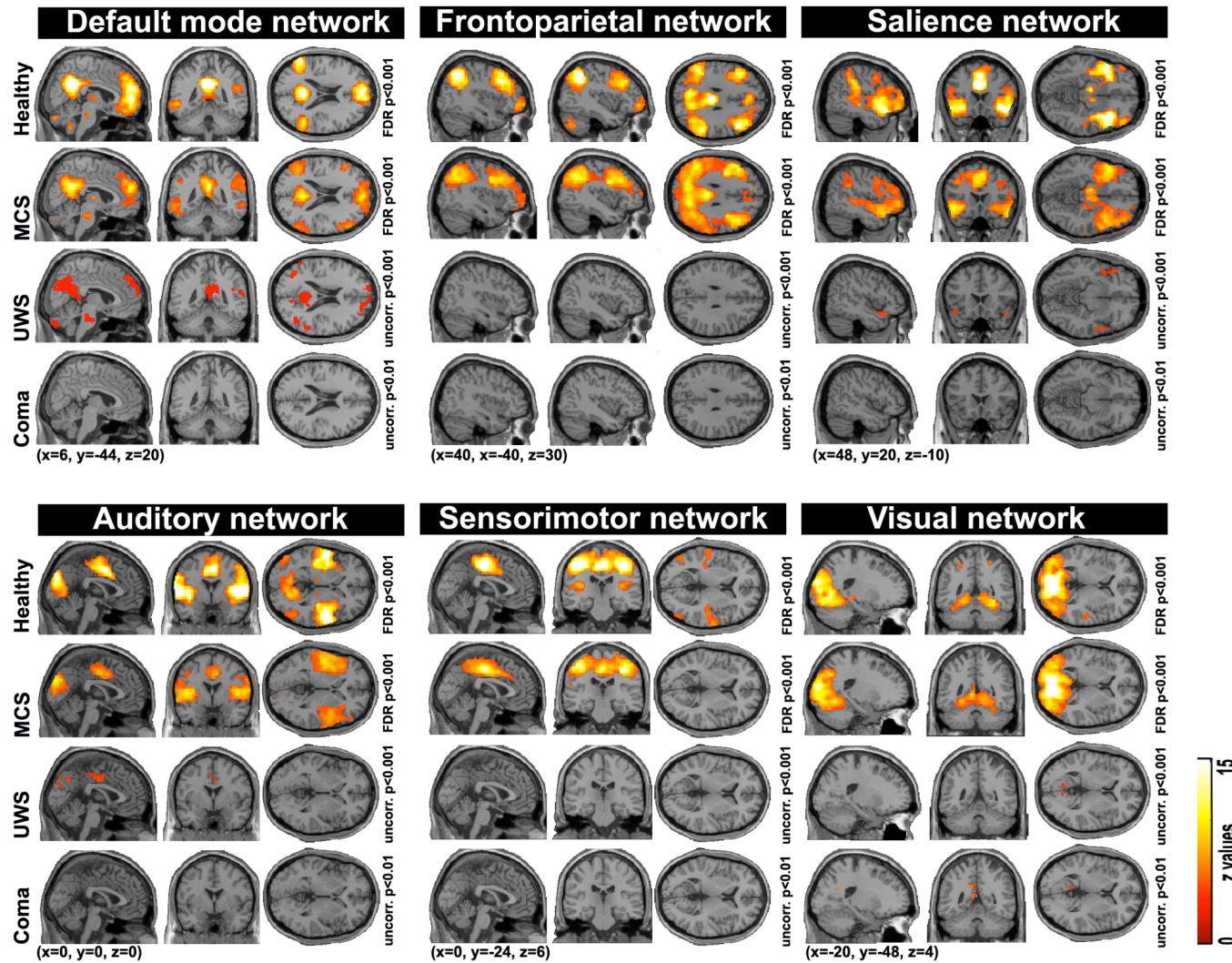
Somatosensory network



Visual network

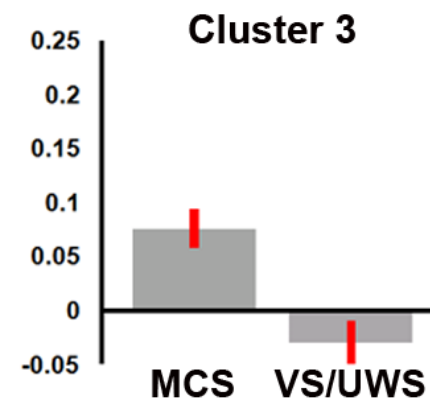
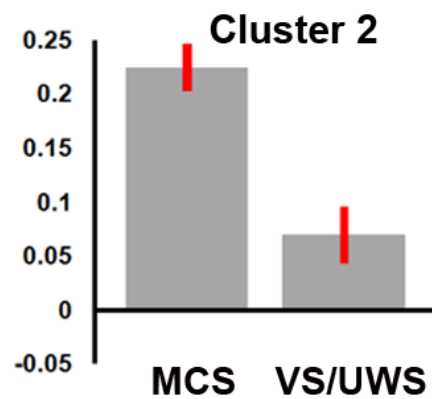
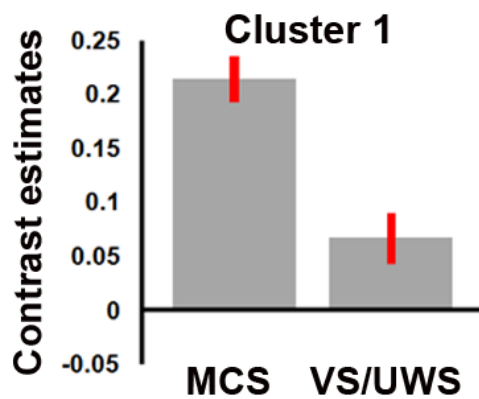
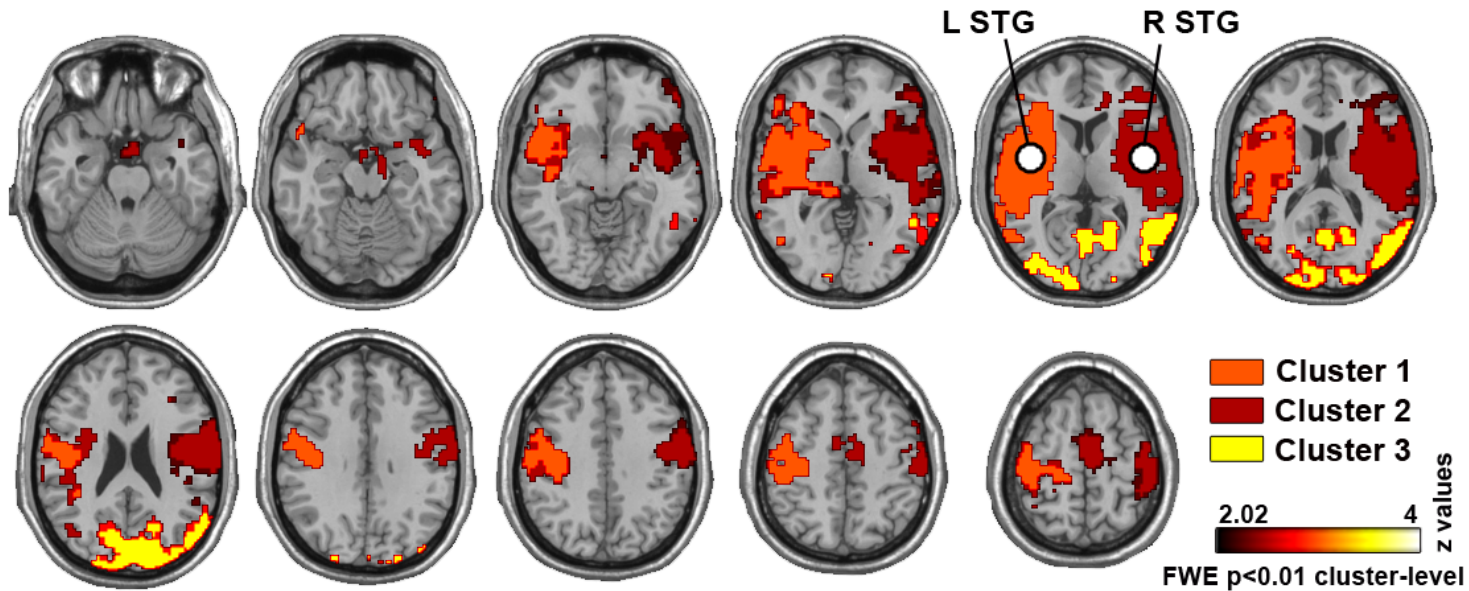


The studied RSNs



Controls N=21
MCS N=26
VS/UWS N=19
Coma=6

Disentangling the crossmodal interaction

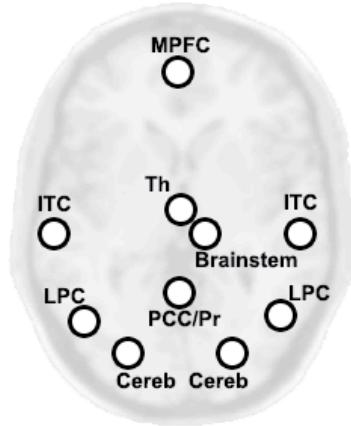


Feature ranking

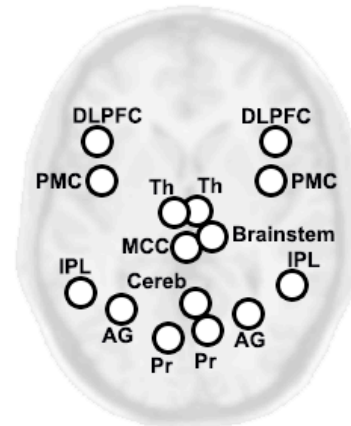
	Feature selection criterion (t-test)			Single-feature classification		
	t value	Rank	p value	True positives (MCS)	True negatives (VS/UWS)	Performance accuracy
Auditory	8.32	1	<.001	25	18	43/45
Visual	7.79	2	<.001	23	15	38/45
Default mode	6.95	3	<.001	23	15	38/45
Frontoparietal	6.82	4	<.001	23	15	38/45
Saliency	6.21	5	<.001	24	15	39/45
Sensorimotor	5.87	6	<.001	24	13	37/45

The studied networks

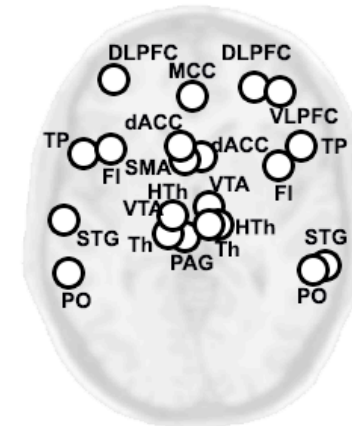
Default mode network



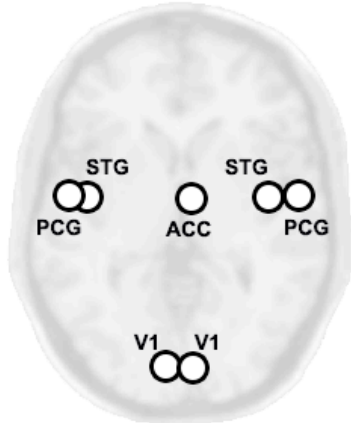
Frontoparietal network



Salience network



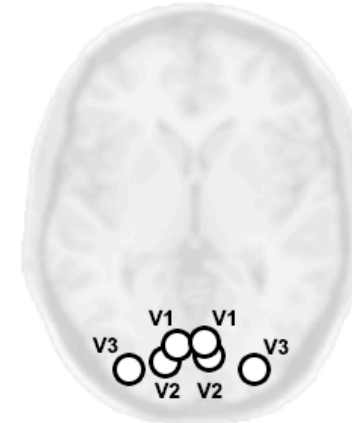
Auditory network



Somatosensory network



Visual network



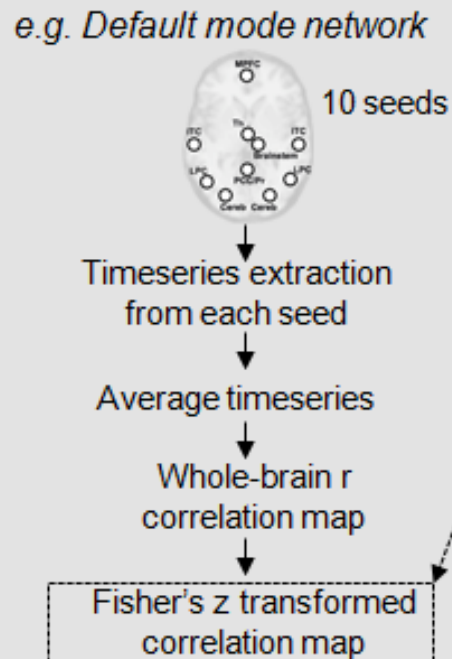
Analysis pipeline

Subject-level analysis

Preprocessing

1. Slice time correction, realignment, segmentation, normalization, smoothing
2. Noise reduction
 - Detection of motion outliers (ART)
 - aCompCor
 - Regressing out motion parameters and their derivatives, and motion outliers
3. Band-pass filtering (0.008-0.09Hz)

Extraction of intrinsic connectivity networks *e.g. Default mode network*



All data sets n=73

Liège data set

Salzburg & New York data set

Group-level analysis

One-sample t-tests

CRS-R regression

Two-sample t-tests
(MCS>VS/UWS)

binary masks to extract individual patient mean z-values (features)

Network ranking and selection

most highly ranked network

Classification of independently assessed patients