Clinical sub-categorization of minimally conscious state according to resting functional connectivity

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Disclosures

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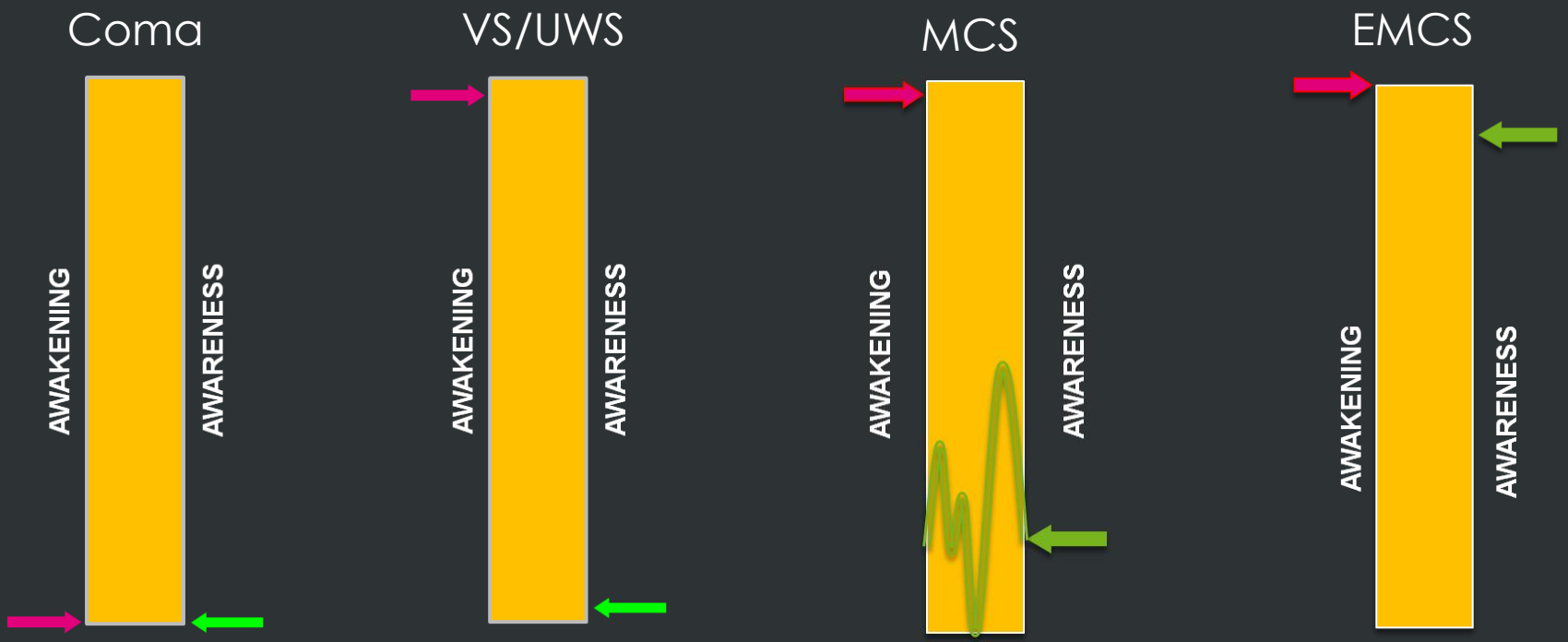
Disorders of consciousness



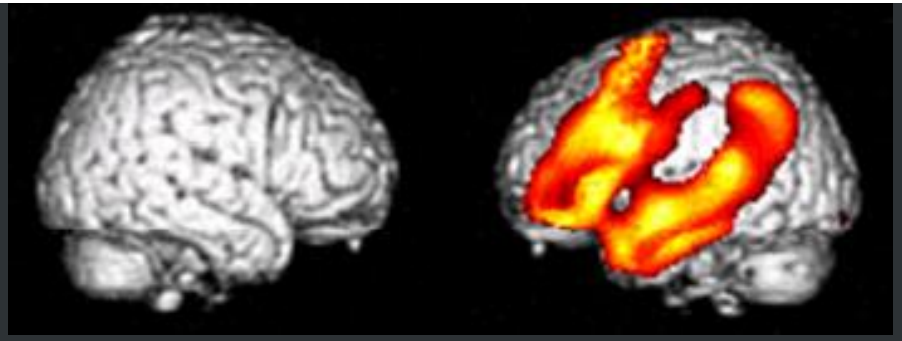
Minimally Conscious State

MCS -	MCS +
▫ Oriented (contextualized) behaviors ▫ Visual pursuit or fixation ▫ Orientation to noxious stimulation ▫ Reaching for objects ▫ Contingent behaviors (emotional)	**+** ▫ **Following simple commands** ▫ Intentional communication ▫ Intelligible verbalization

Giacino et al., *Neurology,* 2002; Bruno et al., *J Neurol,* 2012

Theoretical background

- Bruno et al., *J Neurol*, 2012:
  - FDG PET – Resting state



MCS-

- No response to command
- Metabolic impairment in a bilateral subcortical and cortical (fronto-temporo-parietal) network

MCS+

- Able to respond to command
- **Metabolism = preserved in language related areas** → Broca's and Wernicke's areas

Aims

1. Differenciate MCS- and MCS+ by means of resting state fMRI
2. Characterize the residual command-following ability

- Hypothesis:
  - Higher functional connectivity in MCS+ as compared to MCS- in language-related networks
    - → Left fronto-parietal network

Laird & al., *J Cogn Neurosci*, 2011;
Smith & al., *Proc Natl Acad Sci*, 2009

Participants

Final sample:
MCS patients
n = 19

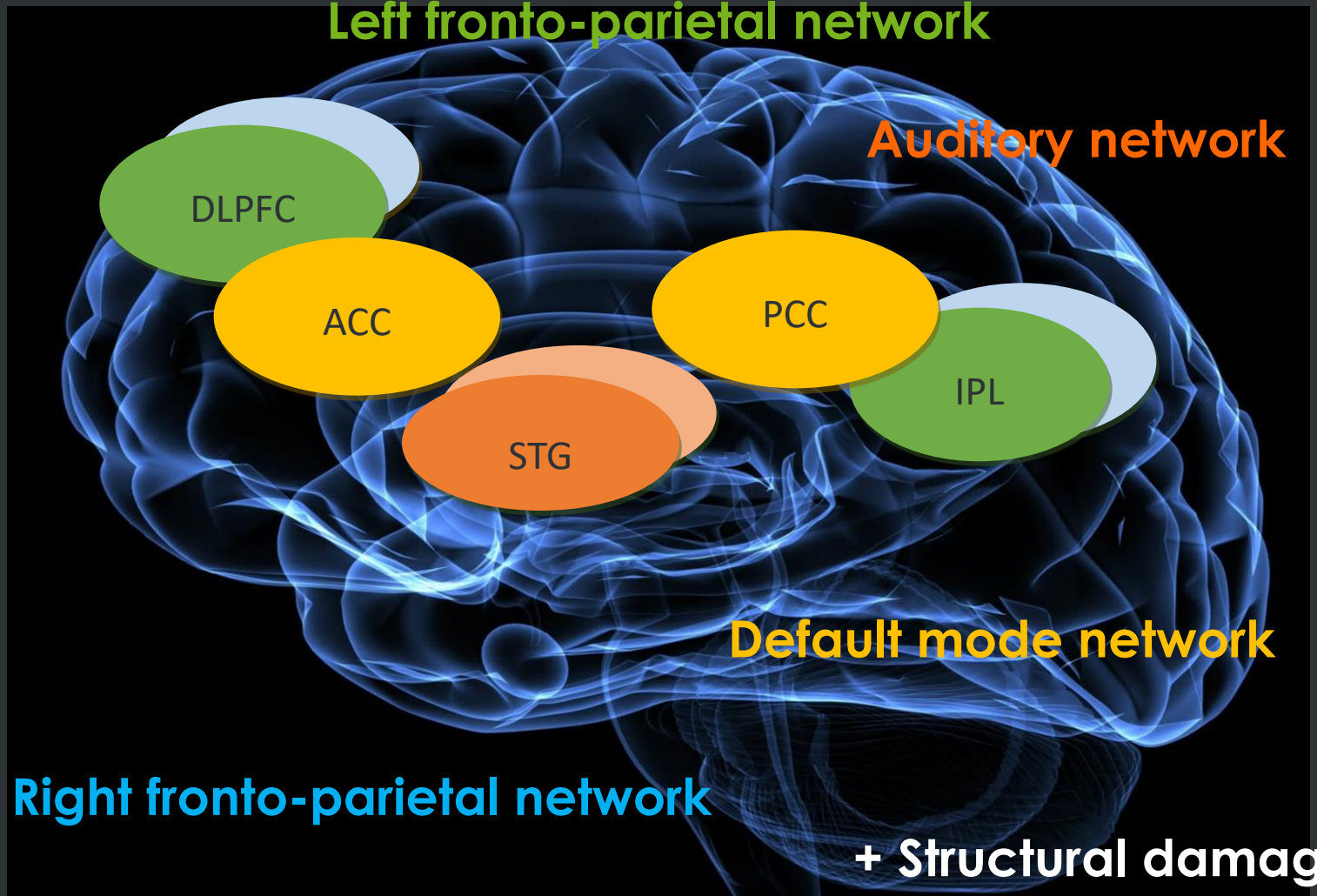
- MCS+
  n = 10
- MCS-
  n = 9

- Matched for:
  - age
  - gender
  - etiology
  - disease duration

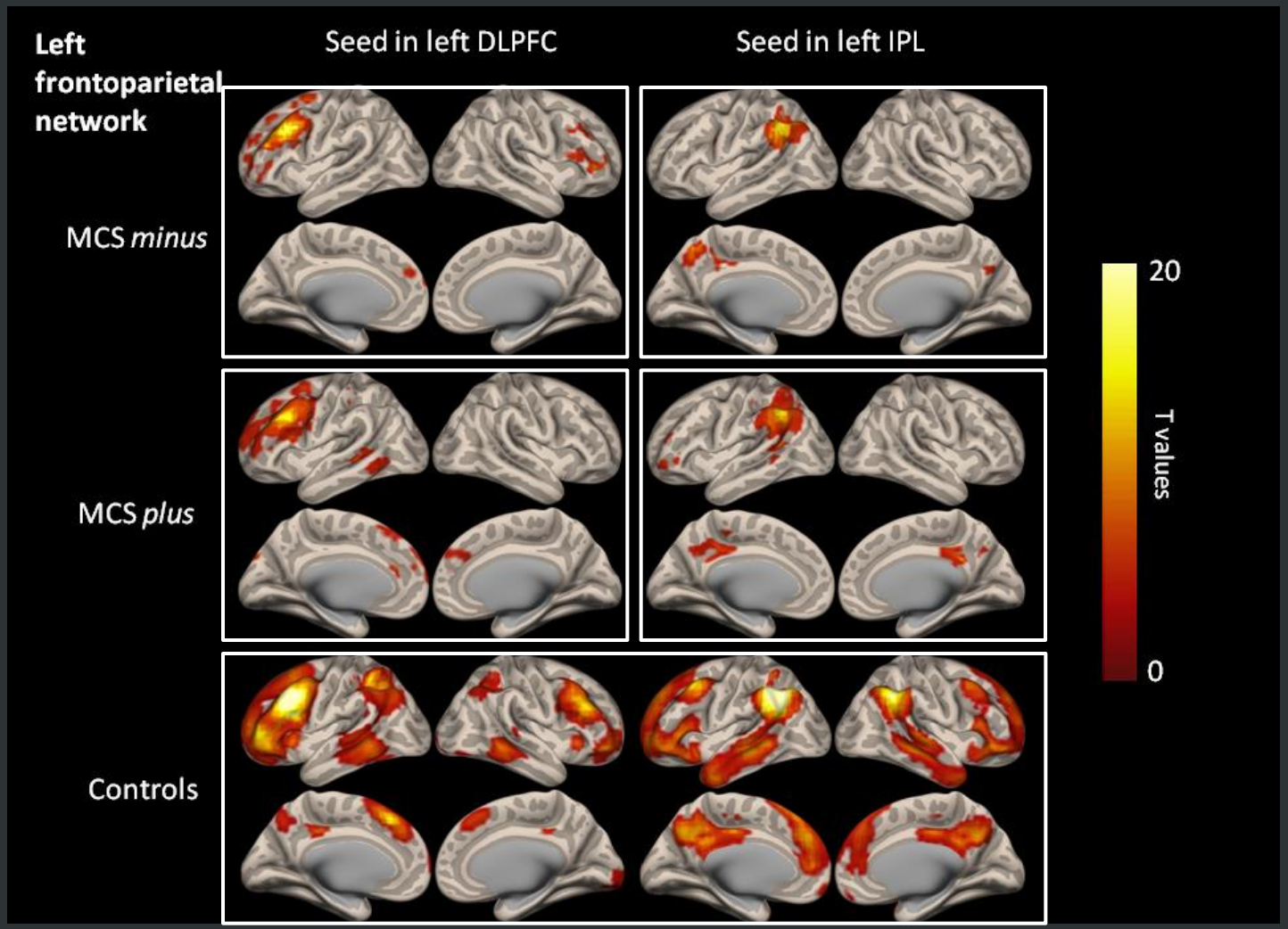
- **35 controls**

Methods

MCS- ≠ MCS+ ?



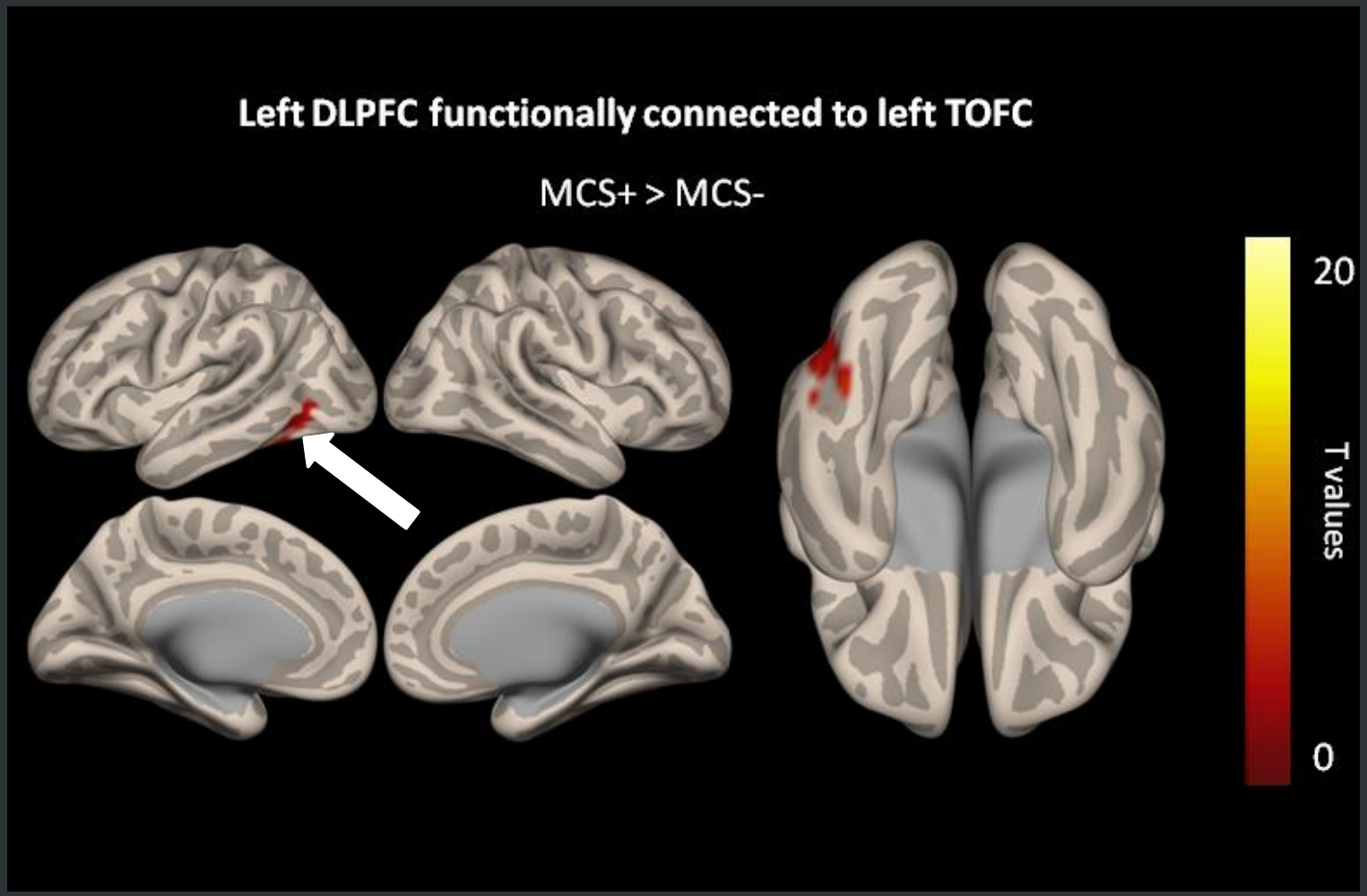
Results



p<0.05 FWE corrected at cluster level

Cluster made of voxels surviving a *p*<0.001

Results

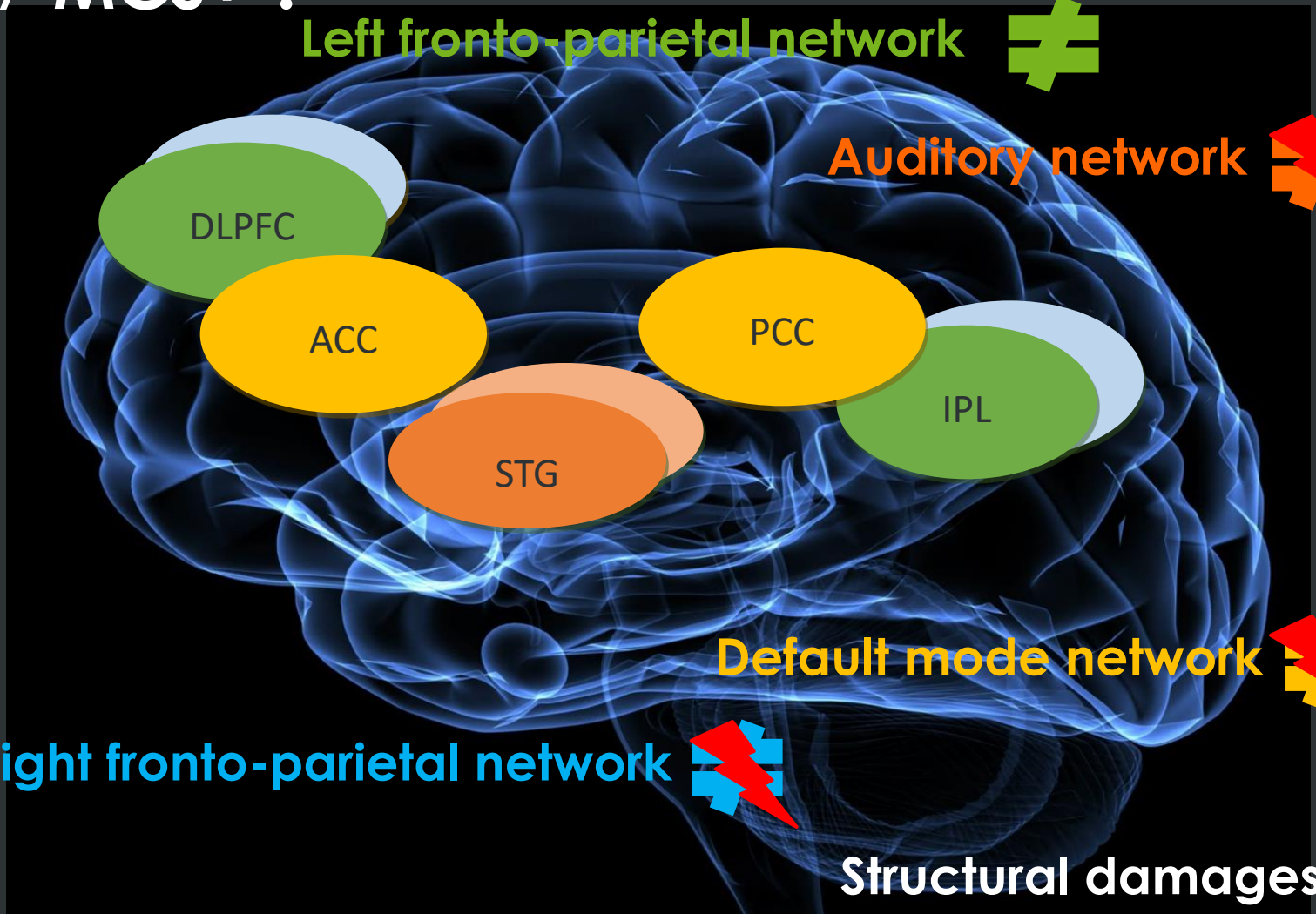


$p<0.05$ FWE corrected at cluster level

Cluster made of voxels surviving a $p<0.001$

Results

MCS- ≠ MCS+ ?



Conclusions

- Clinical subcategorization of MCS is sustained by connectivity differences in left FPN
  - Linked to language comprehension processes
- Command following is seemingly not influenced by:
  - auditory capacities
  - perception of external world
  - internal thoughts
  - structural abnormalities

→ Clinical perspective: integration and improvement of clinical assessment of patients with disorders of consciousness

Thank you for your attention!

Submitted paper

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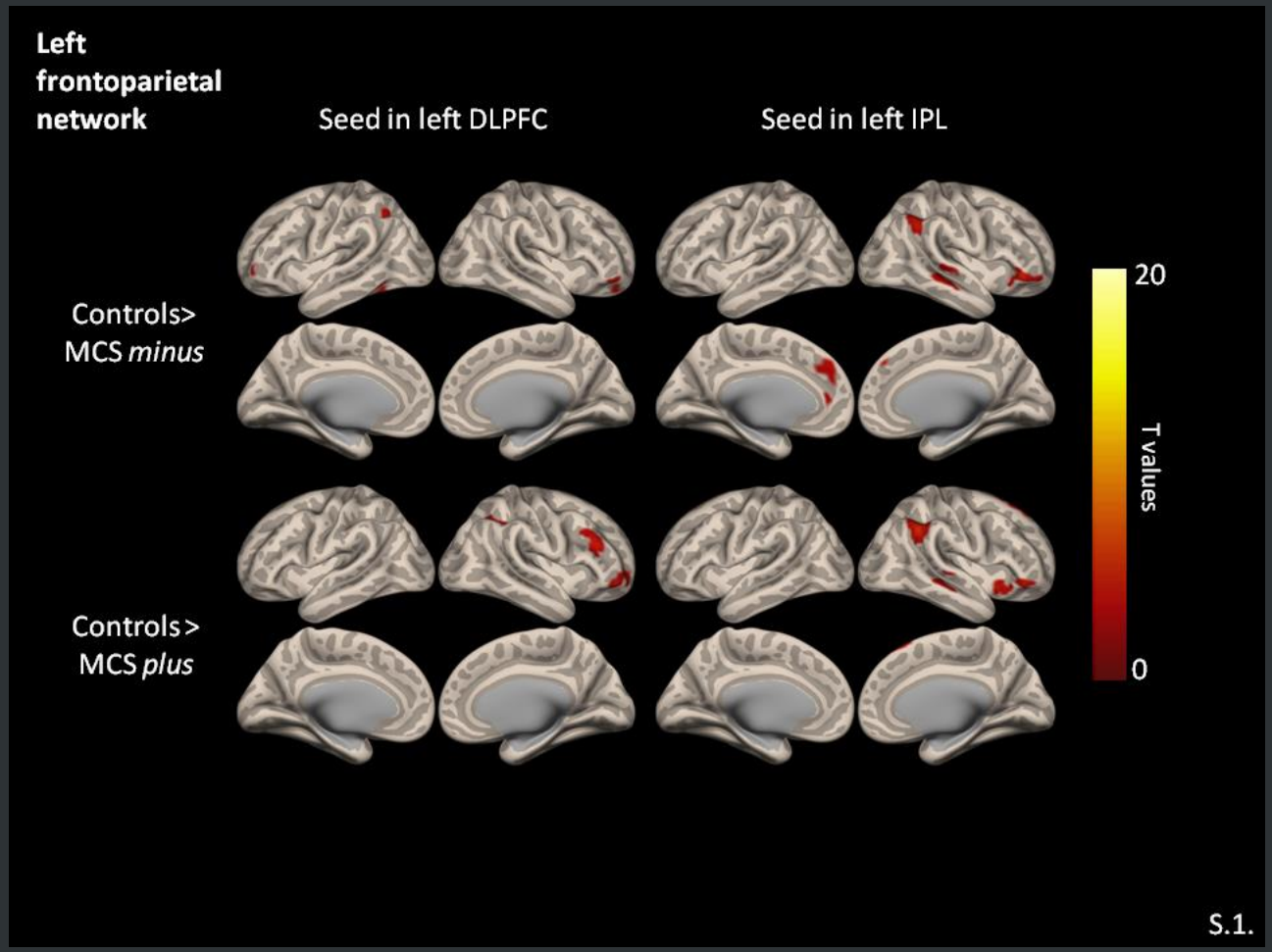
- The Coma Science Group
- Our co-authors,
- The patients and their families,
- Everybody involved

Supplementary

Patient	Age	Sex	Etiology	Months since onset	CRS-R best score	Auditory functions	Visual functions	Motor functions	Oro-motor functions	Final diagnosis
1	66	M	CVA	1,5	12	2	3	5	2	MCS-
2	27	M	TBI	12	9	1	3	2	2	MCS-
3	19	F	TBI	26	10	1	3	2	2	MCS-
4	37	M	CVA	60	10	1	3	3	2	MCS-
5	30	M	TBI & Anoxia	14	9	0	1	5	2	MCS-
6	28	M	TBI & Anoxia	3	7	1	3	2	1	MCS-
7	43	M	Anoxia	21	8	2	3	1	2	MCS-
8	45	F	TBI	8	8	2	3	2	1	MCS-
9	38	M	Anoxia	9	9	1	4	1	1	MCS-
10	34	F	TBI	96	12	3	3	2	2	MCS+
11	29	M	TBI	8	11	3	3	3	2	MCS+
12	50	M	TBI	8	13	3	4	2	2	MCS+
13	51	M	Epilepsy	2	14	3	5	2	3	MCS+
14	54	M	TBI	1,5	12	3	3	4	3	MCS+
15	29	M	TBI	1,5	9	3	4	5	2	MCS+
16	57	M	Anoxia	15	7	3	0	2	2	MCS+
17	30	F	TBI	90	8	3	0	2	2	MCS+
18	34	M	TBI	44	8	3	0	2	2	MCS+
19	23	M	TBI	22	10	3	3	3	3	MCS+

Supplementary



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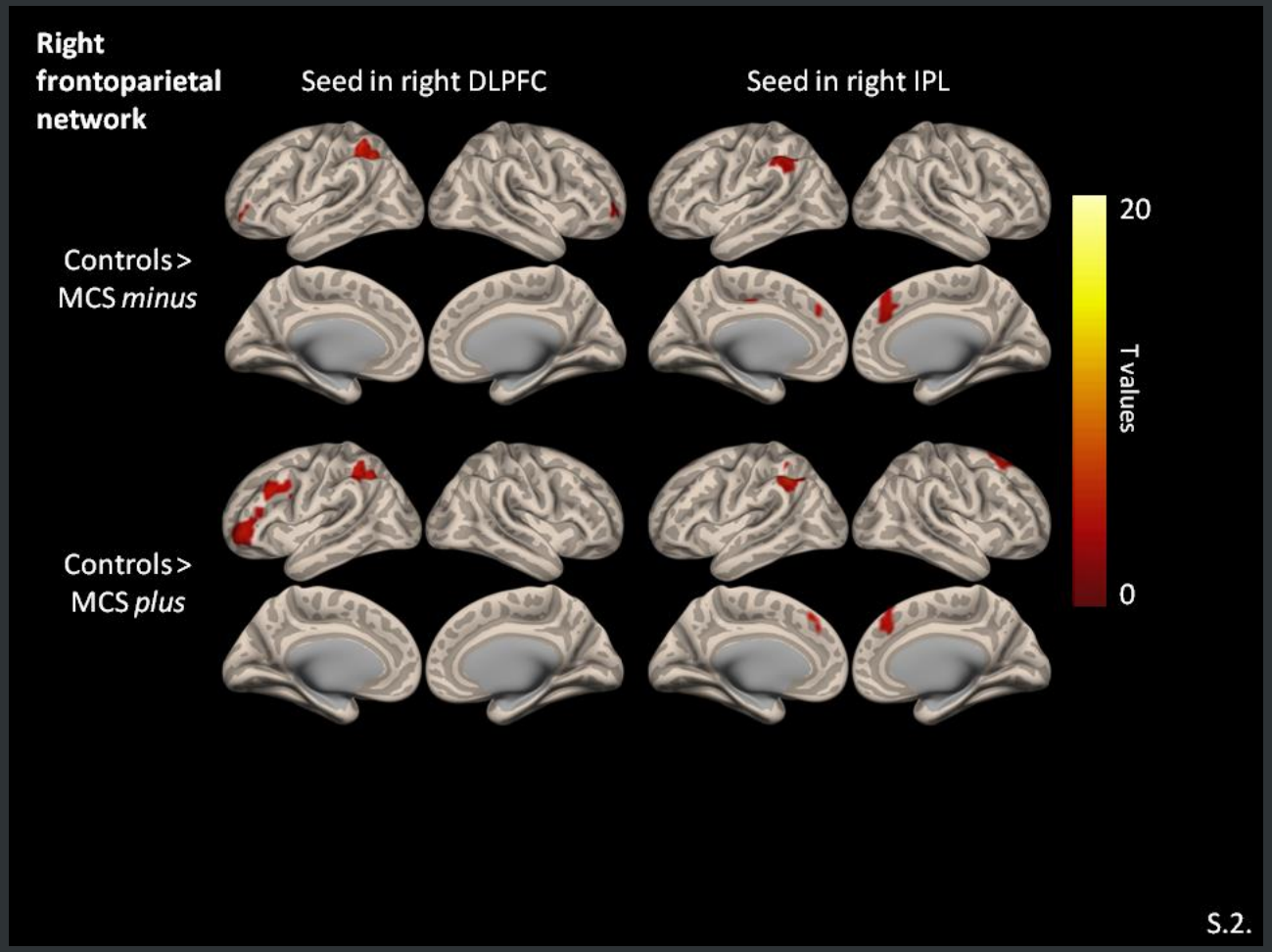

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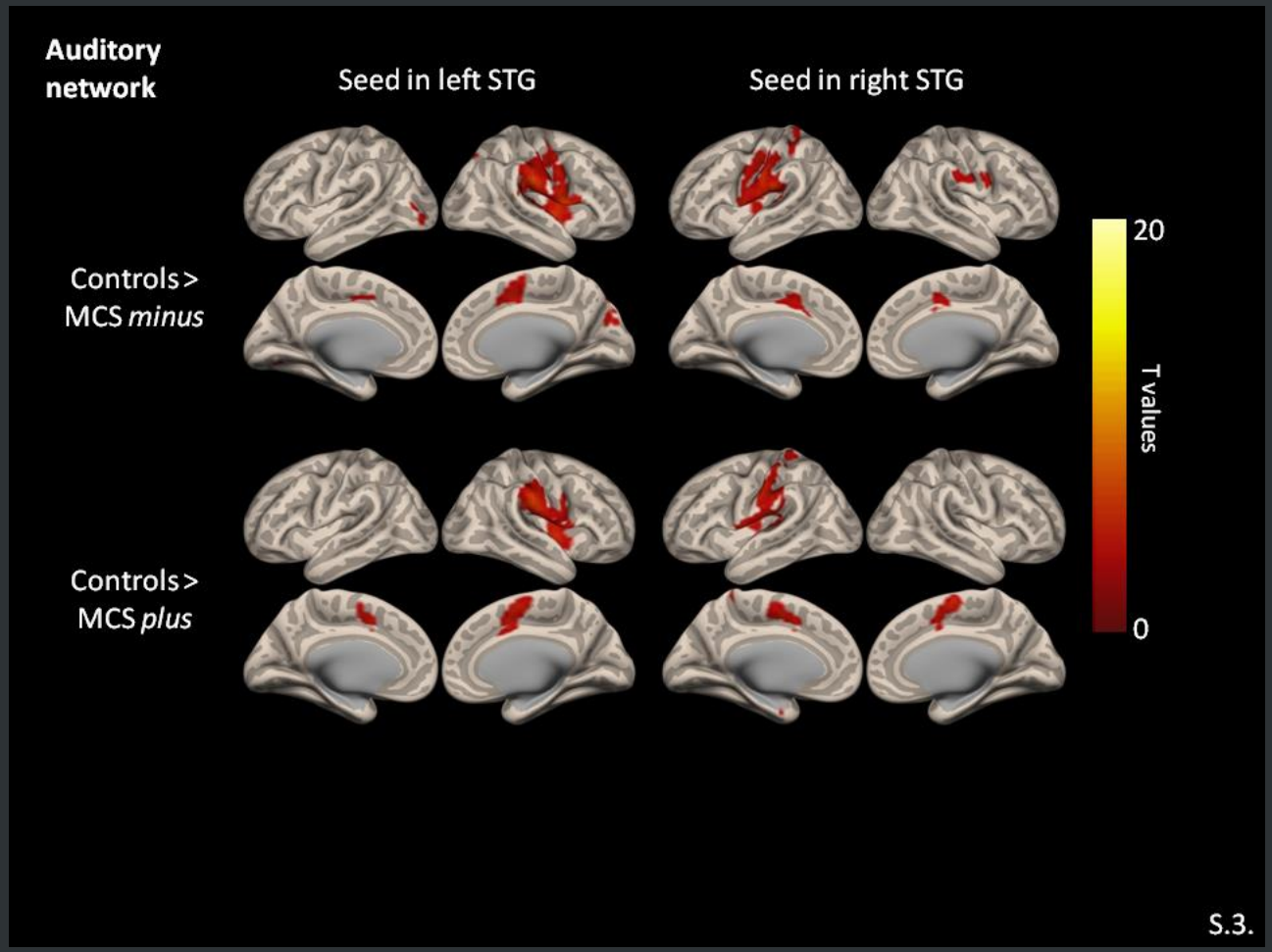

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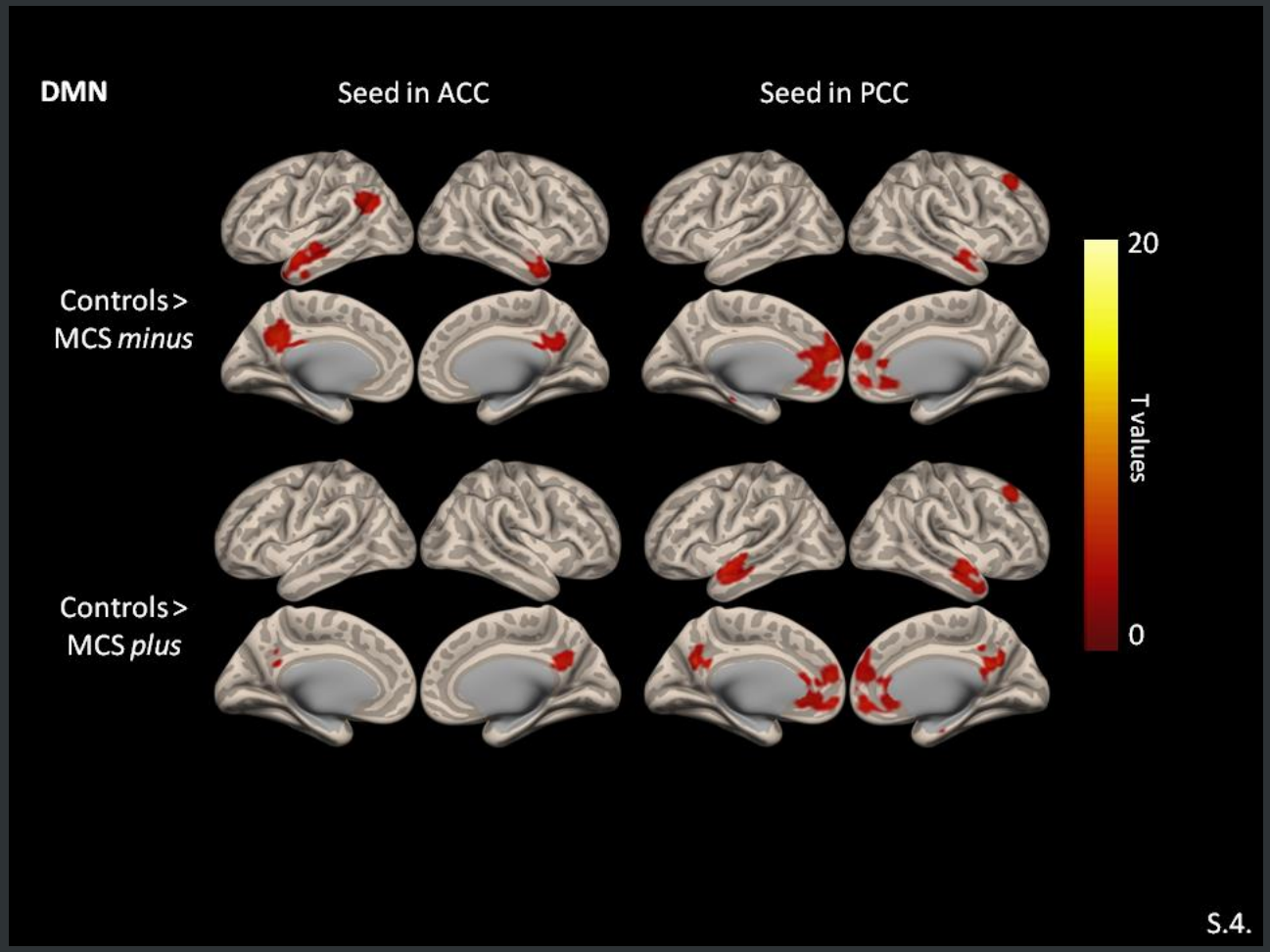

Supplementary

ROI to ROI analysis

Controls > MCS-

Analysis Unit	Statistic	p-unc	p-FDR
Seed ACC	F(39) = 8.08	0.0000	0.0000
	Intensity = 11.76		
	Size = 3		
ACC-PCC	T(45) = 4.72	0.0000	0.0002
ACC-DLPFC_L	T(45) = -3.82	0.0004	0.0014
ACC-DLPFC_R	T(45) = -3.22	0.0024	0.0056
Seed STG_R	F(39) = 5.39	0.0002	0.0009
	Intensity = 5.30		
	Size = 1		
STG_R-STG_L	T(45) = 5.30	0.0000	0.0000
Seed PCC	F(39) = 4.32	0.0013	0.0031
	Intensity = 4.72		
	Size = 1		
PCC-ACC	T(45) = 4.72	0.0000	0.0002
Seed STG_L	F(39) = 4.21	0.0015	0.0031
	Intensity = 5.30		
	Size = 1		
STG_L-STG_R	T(45) = 5.30	0.0000	0.0000
Seed DLPFC_R	F(39) = 3.69	0.0038	0.0060
	Intensity = 3.22		
	Size = 1		
DLPFC_R-ACC	T(45) = -3.22	0.0024	0.0167
Seed IPL_R	F(39) = 3.57	0.0046	0.0060
	Intensity = 4.09		
	Size = 1		
IPL_R-IPL_L	T(45) = 4.09	0.0002	0.0012
Seed IPL_L	F(39) = 3.50	0.0052	0.0060
	Intensity = 4.09		
	Size = 1		
IPL_L-IPL_R	T(45) = 4.09	0.0002	0.0012
Seed DLPFC_L	F(39) = 3.13	0.0102	0.0102
	Intensity = 3.82		
	Size = 1		

Controls > MCS+

Analysis Unit	Statistic	p-unc	p-FDR	p-
Seed ACC	F(40) = 7.32	0.0000	0.0001	
	Intensity = 9.90			
	Size = 3			
ACC-PCC	T(46) = 3.95	0.0003	0.0019	
ACC-DLPFC_L	T(46) = -3.18	0.0026	0.0092	
ACC-DLPFC_R	T(46) = -2.77	0.0081	0.0189	
Seed STG_L	F(40) = 6.30	0.0001	0.0002	
	Intensity = 5.53			
	Size = 1			
STG_L-STG_R	T(46) = 5.53	0.0000	0.0000	
Seed IPL_R	F(40) = 5.94	0.0001	0.0002	
	Intensity = 5.10			
	Size = 1			
IPL_R-IPL_L	T(46) = 5.10	0.0000	0.0000	
Seed DLPFC_R	F(40) = 5.38	0.0002	0.0004	
	Intensity = 7.21			
	Size = 2			
DLPFC_R-DLPFC_L	T(46) = 4.45	0.0001	0.0004	
DLPFC_R-ACC	T(46) = -2.77	0.0081	0.0284	
Seed IPL_L	F(40) = 4.84	0.0005	0.0008	
	Intensity = 5.10			
	Size = 1			
IPL_L-IPL_R	T(46) = 5.10	0.0000	0.0000	
Seed PCC	F(40) = 4.55	0.0008	0.0010	
	Intensity = 3.95			
	Size = 1			
PCC-ACC	T(46) = 3.95	0.0003	0.0019	
Seed DLPFC_L	F(40) = 4.46	0.0010	0.0010	
	Intensity = 7.63			
	Size = 2			
DLPFC_L-DLPFC_R	T(46) = 4.45	0.0001	0.0004	
DLPFC_L-ACC	T(46) = -3.18	0.0026	0.0092	
Seed STG_R	F(40) = 4.46	0.0010	0.0010	
	Intensity = 5.53			
	Size = 1			