A HEARTBEAT AWAY FROM CONSCIOUSNESS:
HEART RATE ENTROPY CAN ASSESS CONSCIOUSNESS

Stephen Karl Larroque[1]*, Francesco Riganello[1,2]*, Mohamed Ali Bahri[3], Lizette Heine[4], Charlotte Martial[1], Manon Carrière[1], Vanessa Charland-Verville[1], Charlène Aubinet[1], Audrey Vanhaudenhuyse[5], Camille Chatelle[1], Steven Laureys[1], Carol Di Perri[1,6]

[1] Coma Science Group, GIGA-Consciousness, University & Hospital of Liege, Belgium ; [2] Research in Advanced NeuroRehabilitation, Istituto S. Anna, Crotone, Italy ; [3] GIGA-Cyclotron Research Center In Vivo Imaging, University of Liege, Belgium ; [4] Centre de Recherche en Neurosciences, Inserm U1028 - CNRS UMR5292, University of Lyon 1, France ; [5] Sensation & Perception research Group, GIGA-Consciousness, University & Hospital of Liege, Belgium ; [6] Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK ; * These authors contributed equally to this work.

stephen.larroque@uliege.be, f.riganello@istitutosantanna.it

1. Background

• Healthcare differs if patient is unresponsive (UWS) or minimally conscious (MCS)
• **~35% clinical diagnosis error** which can impact life and death decisions
• **Neuroimaging** helps, but **is expensive and difficult** in daily clinical setting
• Heart and brain's Central Autonomic Network (CAN) are connected in a two-way dynamic interaction through the Autonomic Nervous System (ANS):
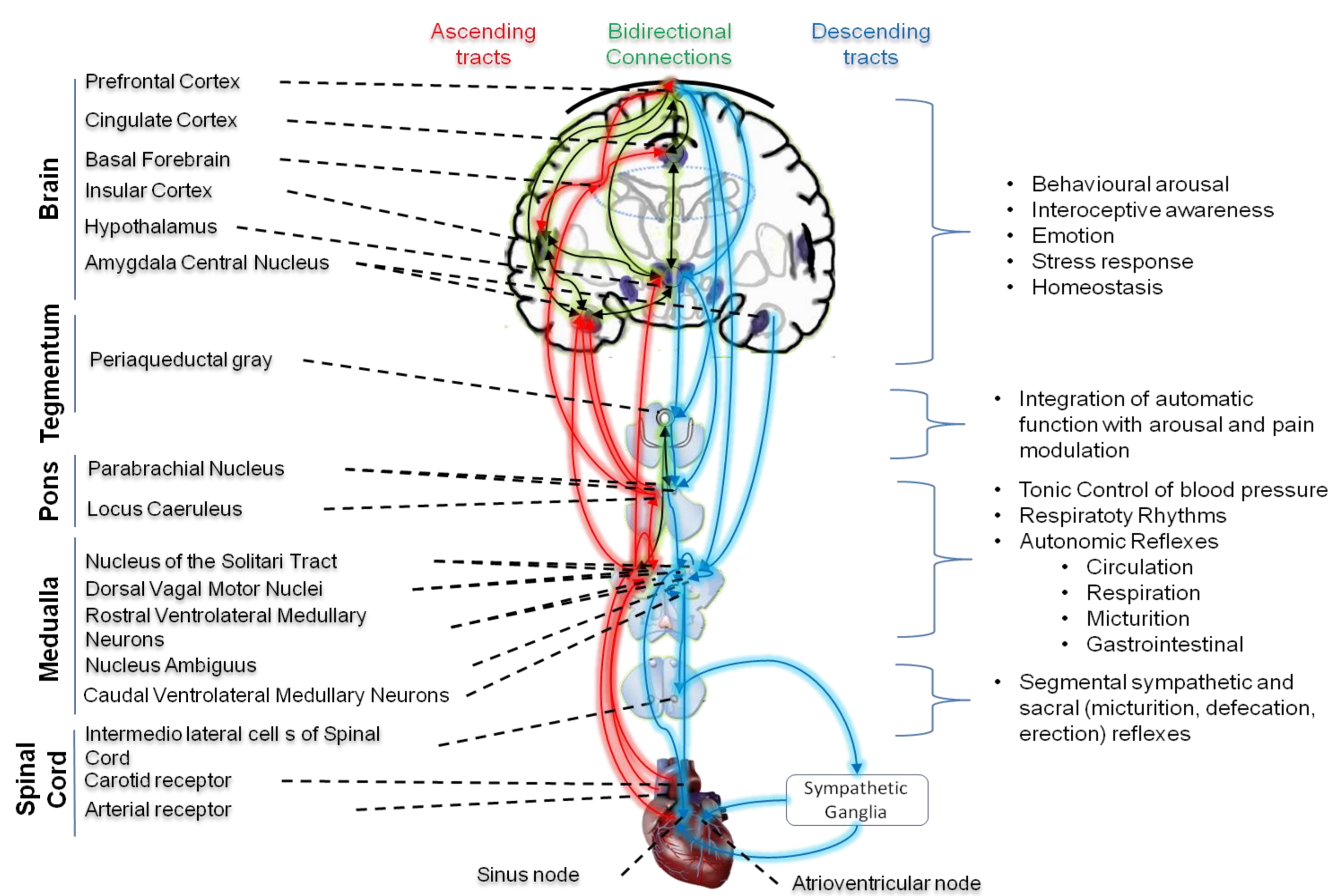
→ Can we better diagnose **by monitoring the heart**?

2. Methods

From heart rate to multi-scale entropy to **COMPLEXITY INDEX** in the short term (CI_s) and long term (CI_l):
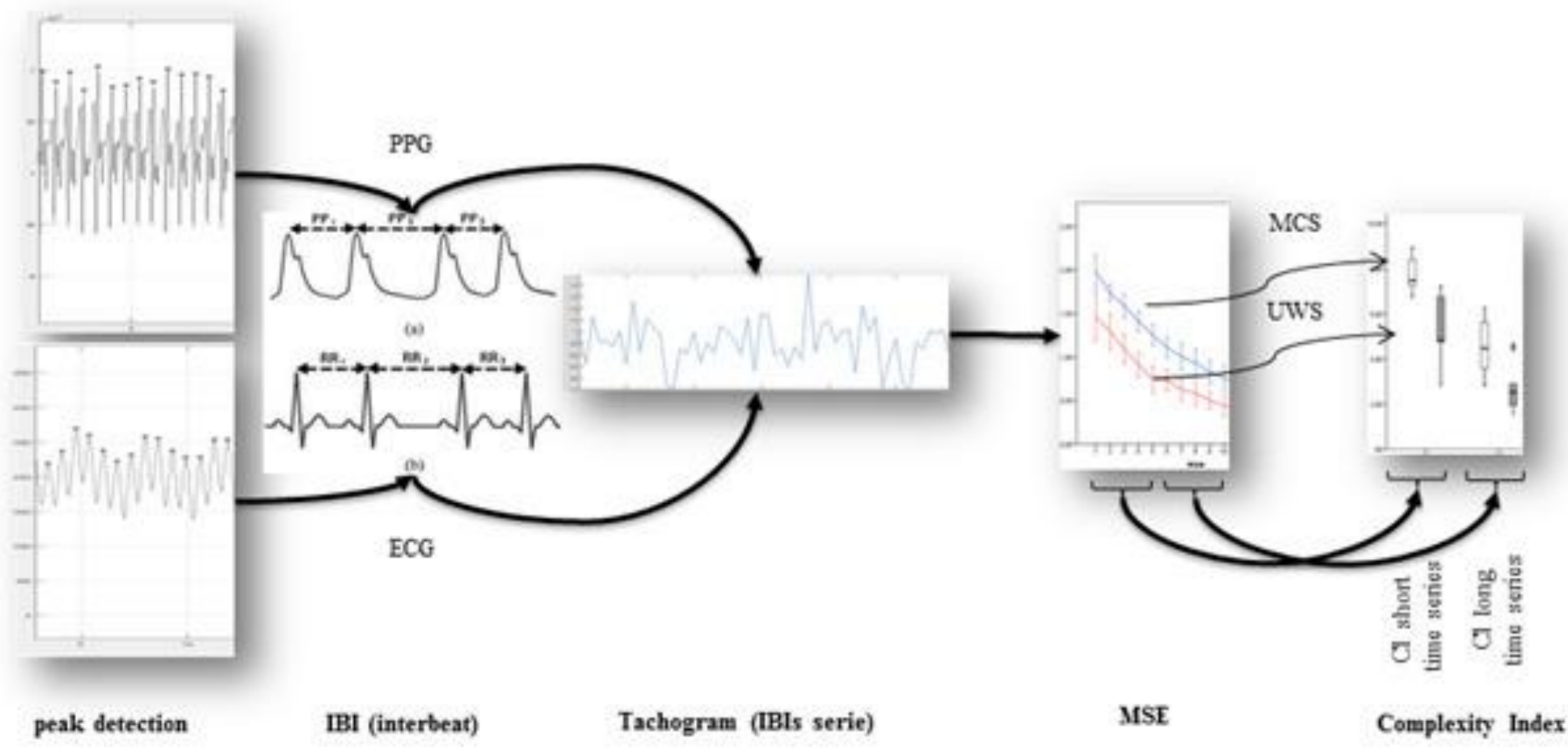
• Conducted on 14 UWS and 16 MCS sedated patients as assessed by the Coma Recovery Scale – Revised (CRS-R) acquired since 2008 up to 2017.
• Patients were matched for age, gender, etiology and onset.
• Electrocardiographic activity (ECG) and photoplethysmographic sensor (PPG) were acquired for 10 minutes, simultaneously with MRI (3T Siemens Magnetom TrioTim).
• PPG and ECG were cleaned with a Fourier Transform (SigView software) and multi-scale entropy was calculated (HRV Advanced Analysis software v2.2). CI was calculated as the area under the sample entropy timescale curve.
• MRI T1 and EPI BOLD were preprocessed with SPM12 and 2nd-level correlation analyses were calculated with CONN 17f with CI_s & CI_l as covariates of interest in a parametric regression.

3. Results

3.1. MCS have higher CI than UWS on average

Group-wise, MCS show higher CI_s (z=-3.346, p<0.001) and CI_l (z=-4.095, p<0.0001) compared to UWS using a Mann-Whitney's test.
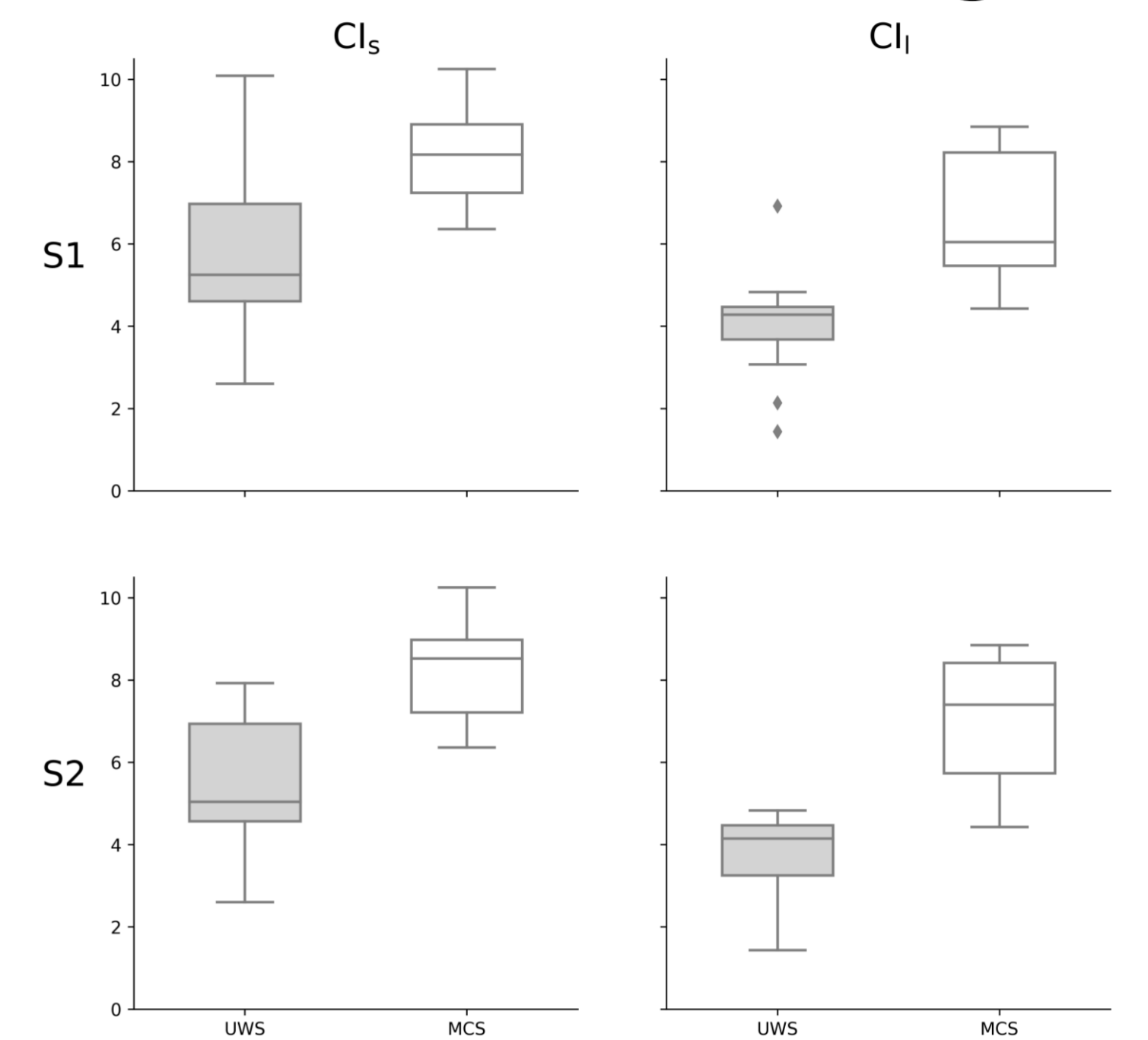
S1 includes all patients (n=30), S2 fMRI included (n=21)

3.2. CI correlates with CAN fMRI connectivity recovery
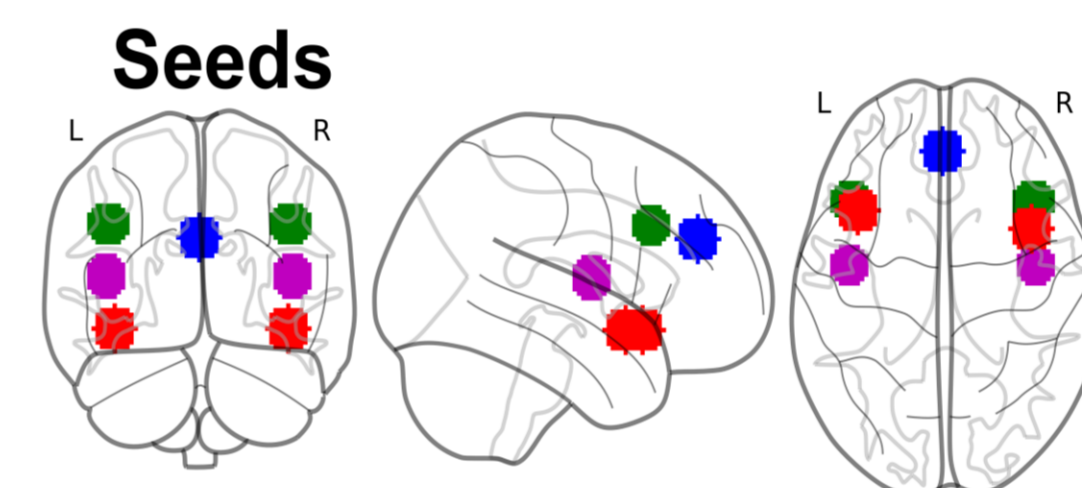
Red: Fronto-Insular   Magenta: STG
Blue: Paracingulate   Green: DLPFC
n=21

Non-parametric cluster-mass p-FWE < 0.05 (voxel p-uncorrected < 0.001)
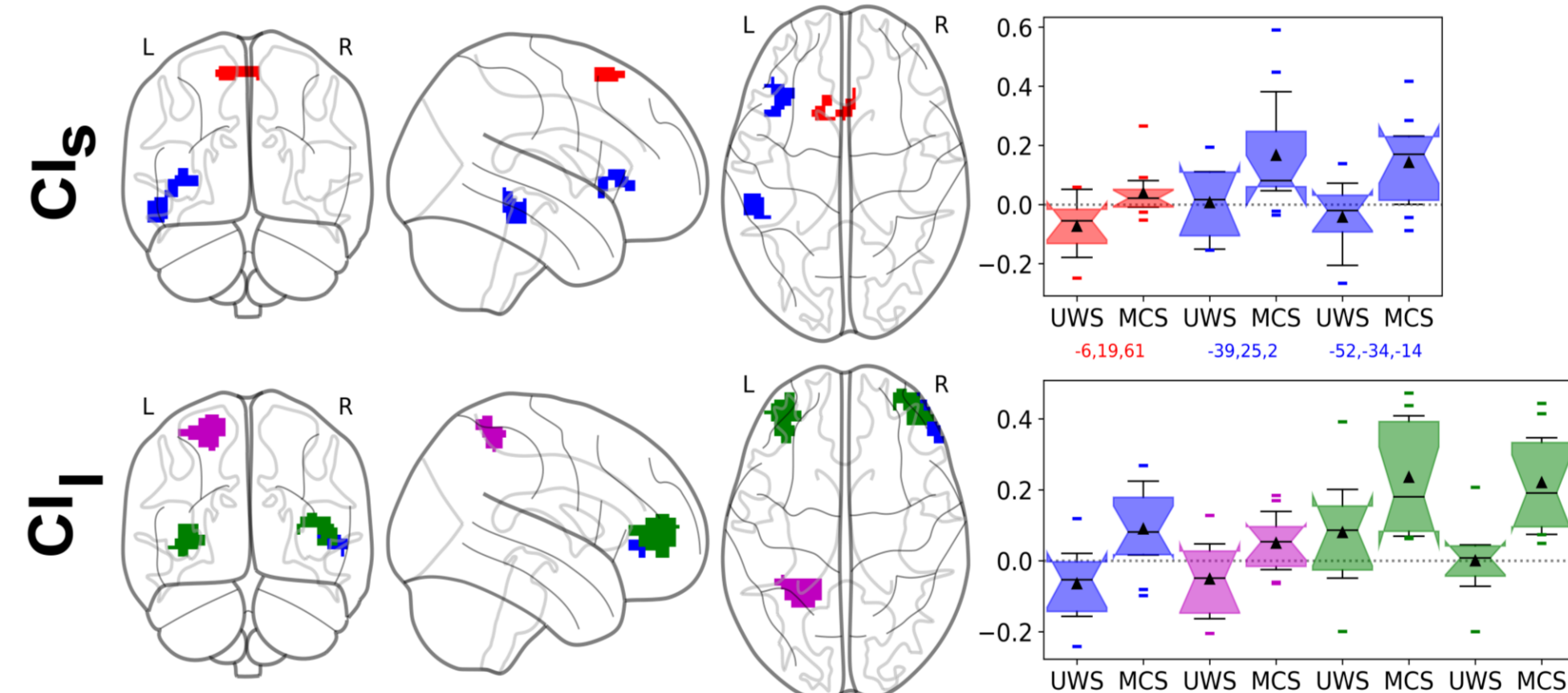
• CI_s correlates with FI <–> Superior Frontal Gyrus (red), PC <–> Temporal Gyrus & Insula (blue) connectivities.

• CI_l correlates with PC <–> left Fronal Pole (blue), STG <–> Superior Parietal Lobule (magenta), DLPFC <–> Frontal Poles (green) connectivities

• CI_s correlates with an increase of intrinsic connectivity in pMTG and pSTG

• CI_l correlates with an increase in MFG

3.3. CI reliably discriminates MCS from UWS

One-R classifier with 10-fold cross-validation:
→ CI_l selected as the best predictor
→ **90% accuracy**, 7% false positive and **13% false negative rates**
→ In comparison, Zero-R (always predicting MCS) has 53% accuracy
→ **Lower error than clinical consensus**

| Confusion Matrix	
MCS (true)	MCS as UWS (false negative)
15	1
1	13
UWS as MCS (false positive)	UWS (true)

4. Conclusion

→ Complexity Index has **high discriminative power** and low false negative rate
→ Might provide an inexpensive way to diagnose MCS & UWS and **screen/monitor** CAN connectivity changes
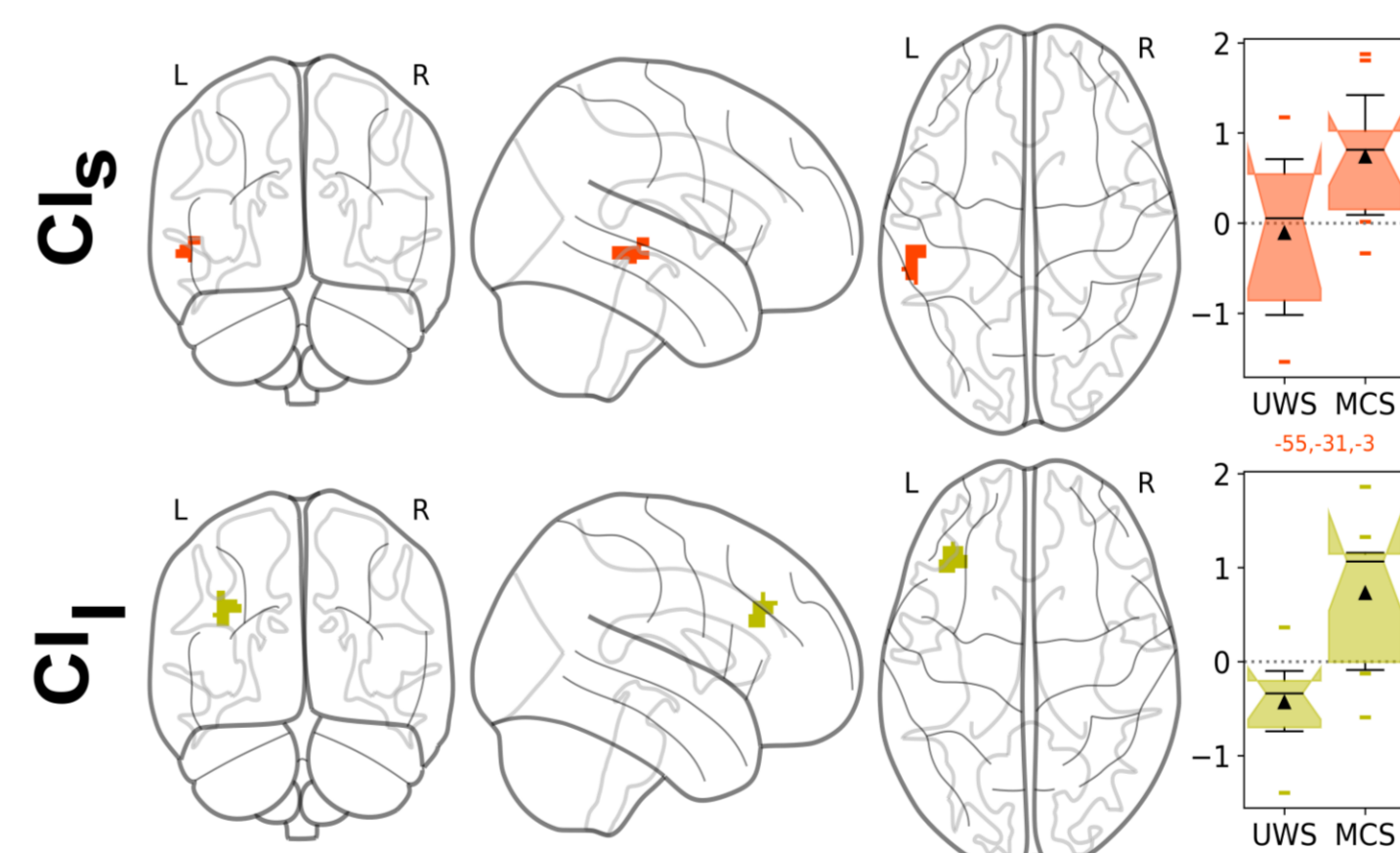→ Future: should investigate in a bigger cohort and in acute patients

5. Bibliography & Acknowledgements

• Porges SW. The polyvagal theory: New insights into adaptive reactions of the autonomic nervous system. Cleve Clin J Med (2009)
• Harrison NA, et al. Central autonomic network mediates cardiovascular responses to acute inflammation. Brain Behav Immun (2013)
• Costa M, et al. Multiscale entropy analysis of biological signals. Phys Rev E (2005)
• Riganello F, et al. Heart Rate Variability, Homeostasis, and Brain Function: A Tutorial and Review of Application. J Psychophysiol (2012)