A HEARTBEAT AWAY FROM CONSCIOUSNESS:

HEART RATE VARIABILITY ENTROPY CAN DISCRIMINATE DISORDERS OF CONSCIOUSNESS

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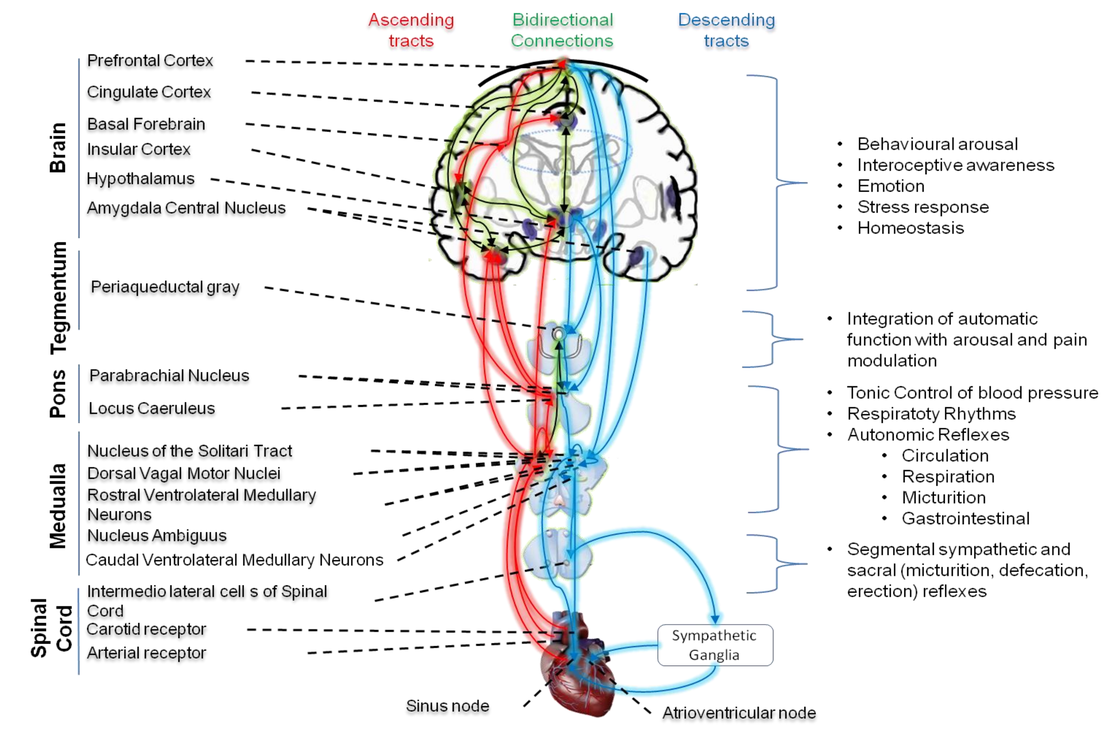
1. Background

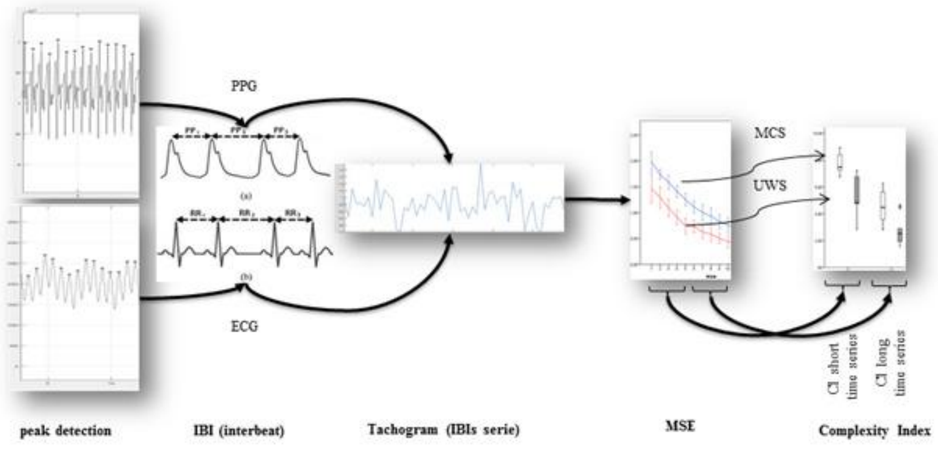
- Healthcare differs if patient is unresponsive (UWS) or minimally conscious (MCS)
- **~35% clinical diagnosis error** which can impact life and death decisions
- **Neuroimaging** helps, but **is expensive and difficult** in daily clinical setting
- Heart and brain's Central Autonomic Network (CAN) are 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):



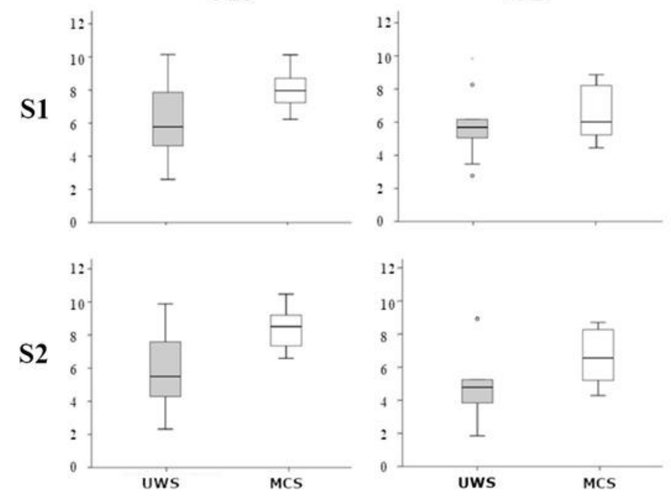
- Conducted on 16 UWS and 17 MCS sedated patients as assessed by the Coma Recovery Scale – Revised (CRS-R) acquired since 2008 up to 2017.
- Patients were matched for age, gender, etiology and onset.
- Electrocardiographic activity (ECG) and photoplethysmographic sensor (PPG) were acquired for 10 minutes, 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

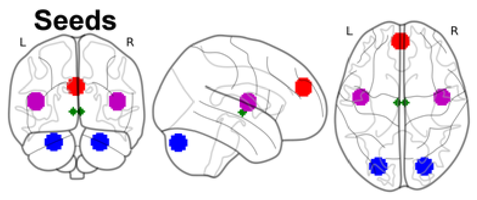
3.1. MCS have higher CI than UWS on average

Group-wise, MCS show higher CI_s ($z=-2.846$, $p=0.002$) and CI_l ($z=-3.386$, $p<0.0001$) compared to UWS using a Mann-Whitney's test.

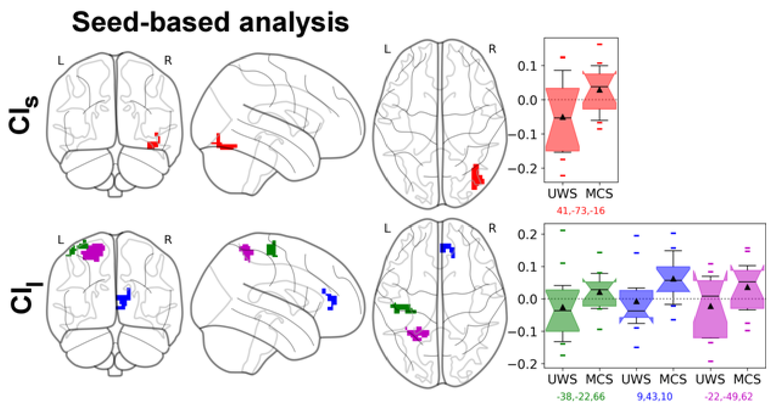
S1 represent all patients (n=33), S2 the subset who underwent fMRI analysis (n=24).



3.2. CI correlates with CAN fMRI connectivity recovery



Red: MPFC
Blue: Cerebellum
Magenta: STG
Green: Thalamus



- CI_s correlates with MPFC <–> Lateral Occipital Cortex/Occipital Fusiform Gyrus (red) connectivity,
- CI_l correlates with Thalamus <–> Sensorimotor (green), Cerebellum <–> AC/PC Gyri(blue), Auditory STG <–> SPL (magenta) connectivities

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

- CI_l correlates with an increase in MFG

Significance: voxel-wise p-uncorrected < 0.001, non-parametric permutation test cluster-mass p-FWE < 0.05.

3.3. CI reliably discriminates MCS from UWS

One-R classifier with 10-fold cross-validation:
→ CI_l selected as the best predictor
→ **85% accuracy**, 19% false positive and **12% false negative rates**
→ In comparison, Zero-R (always predicting MCS) has 52% accuracy
→ **Lower error than clinical consensus**

Confusion Matrix	
MCS (true) 16	MCS as UWS (false negative) 1
3 UWS as MCS (false positive)	13 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

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