Amplitude- and Phase-Based Brain Networks Provide Non-Redundant Information in the Classification of States of Consciousness.

Yacine Mahdid*[2,3], Catherine Duclos*[1,2], Kathleen Berkun[2], Matt Brookes[6], Jason da Silva Castanheira[3], Lucrezia Liuzzi[7], George Mashour[4], Stefanie Blain-Moraes[1,2]

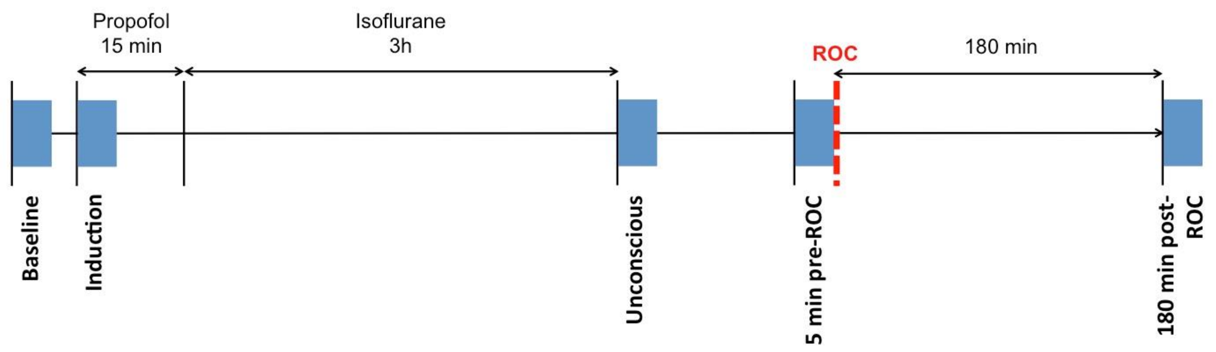
1. School of Physical and Occupational Therapy, McGill University, Montreal, Canada. 2. Montreal General Hospital, McGill University Health Center, Montreal, Canada. 3. Integrated Program in Neuroscience, McGill University, Montreal, Canada. 4. Center for Consciousness Science and Department of Anesthesiology University of Michigan Medical School, Ann Arbor, MI, USA. 6. School of Physics and Astronomy, University of Nottingham. 7. Sir Peter Mansfield Imaging Center, University of Nottingham

Introduction

Sophisticated tools to quantify changes in the brain's oscillatory dynamics across states of consciousness have investigated both phase- and amplitude-based measures of functional connectivity, but very rarely have they investigated both metrics concomitantly.

This study aims to compare the contributions of an amplitude-based measure (i.e. **Amplitude Envelope Correlation; AEC**) and a phase-based measure (i.e. **weighted Phase Lag Index; wPLI**) of functional connectivity in identifying **states of consciousness** using **machine learning**.

Methods



Participants: 9 healthy volunteers (5 men; 24.4 ± 1.0 years old).
Exclusion criteria: Class 1 or 2 physical status (American Society of Anesthesiologists), BMI < 30, Mallampati 1 or 2 airway classification, and no other factors predictive of difficult airways for anesthetic administration.

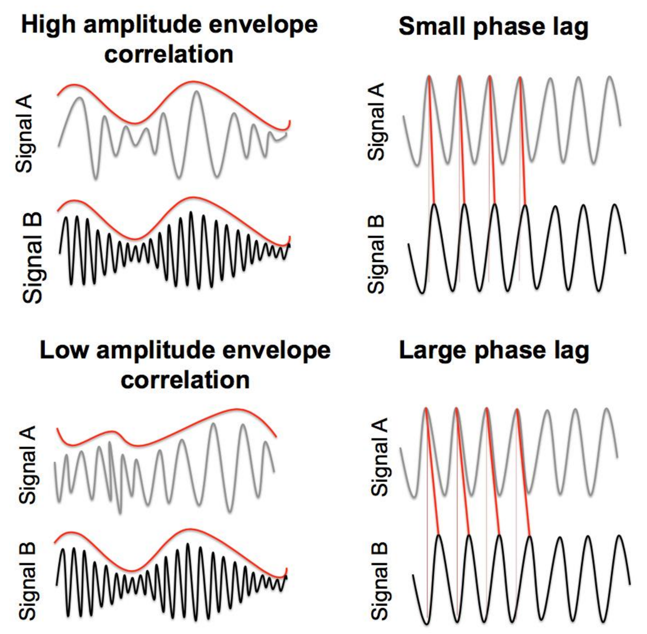
Anesthesia: Participants were pre-oxygenated with a face mask and received intravenous infusions of propofol in increasing amounts over three 5-minute periods for anesthetic induction (100 µg/kg/min, 200 µg/kg/min, and 300 µg/kg/min, respectively). After the 15-minute administration of propofol, participants were administered isoflurane at 1.3 minimum alveolar concentration (MAC) via mask inhalation for 3 hours.

EEG: Acquisition: 128-channel EEG (500 Hz sampling rate) referenced to Cz was collected during the entire duration of the anesthetic protocol. Pre-processing: Data were bandpass filtered from 0.1 to 50 Hz and averaged referenced. After cleaning, 5-minute segments were extracted for the 6 states of interest and filtered at alpha.

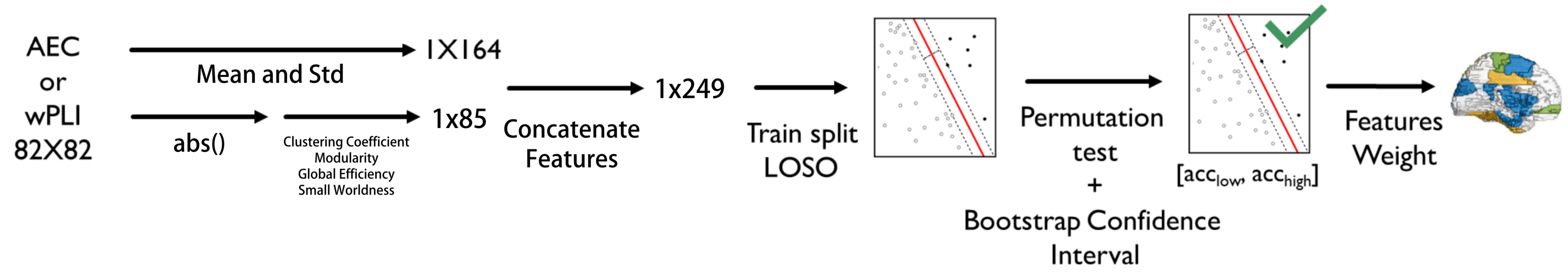
Source Localization: Forward model: 45,000 unconstrained dipoles (15,000 vertices x 3 orientations). A symmetric Boundary Element Model was used for the forward model. Inverse model: Source activity was estimated using linearly constrained minimum variance (LCMV) beamformers. The covariance matrix was regularized using the median eigenvalue. The mean source activity at 82 cortical regions of interest (ROIs; Automated Anatomical Labeling Atlas) was extracted to generate a time series.

AEC: A Hilbert transform was applied on the source localized time series; the instantaneous phase was discarded. The amplitude envelope was then calculated on 10 s windows of the amplitude time series and Pearson correlation was computed between ROI pairs.

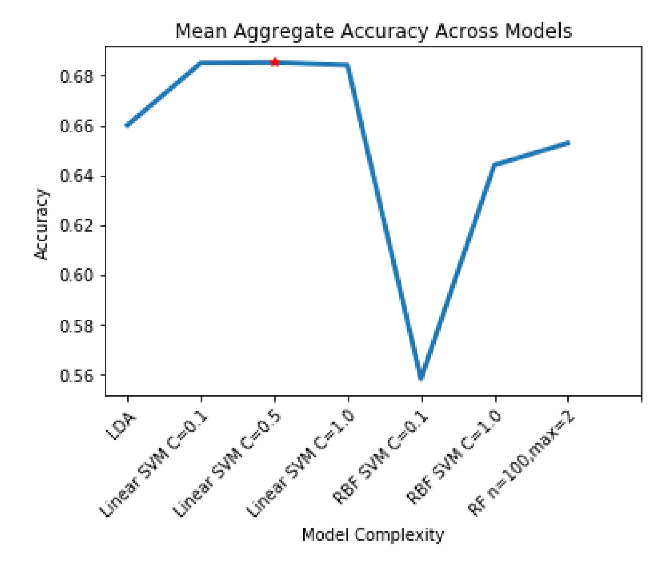
wPLI: A Hilbert transform was applied on the source localized time series; the instantaneous amplitude was discarded. The phase difference between signal pairs was then calculated and wPLI was computed using the imaginary part of the cross-spectrum.



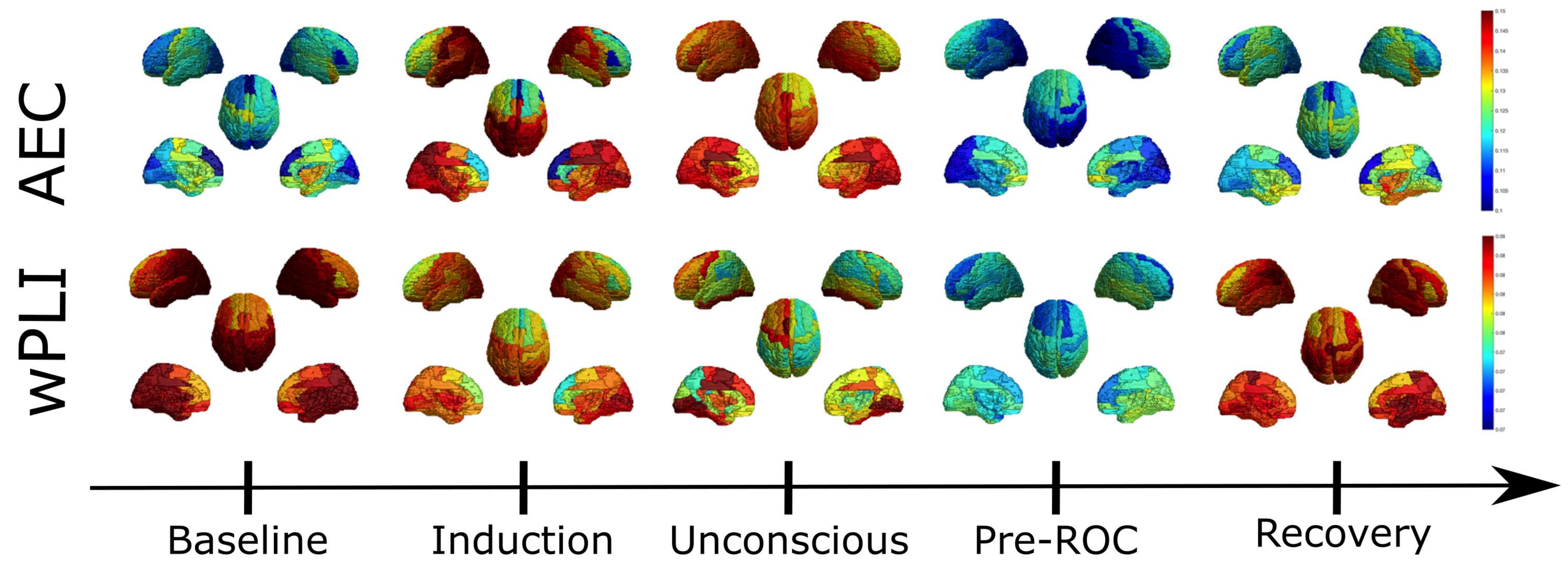
Machine Learning Pipeline



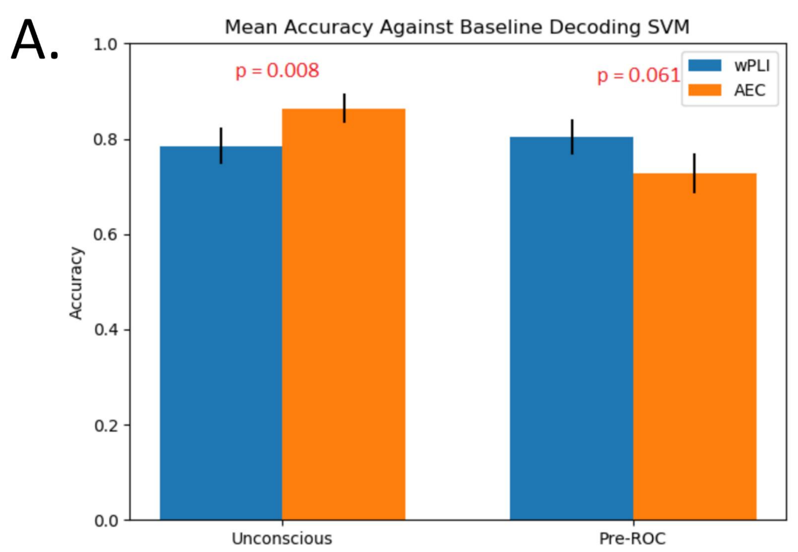
This Linear SVM with C=0.5 was selected for further analysis as it showed the highest decoding performance on average across analysis technique and epoch. More complex models were excluded to allow for simple interpretation of the results.



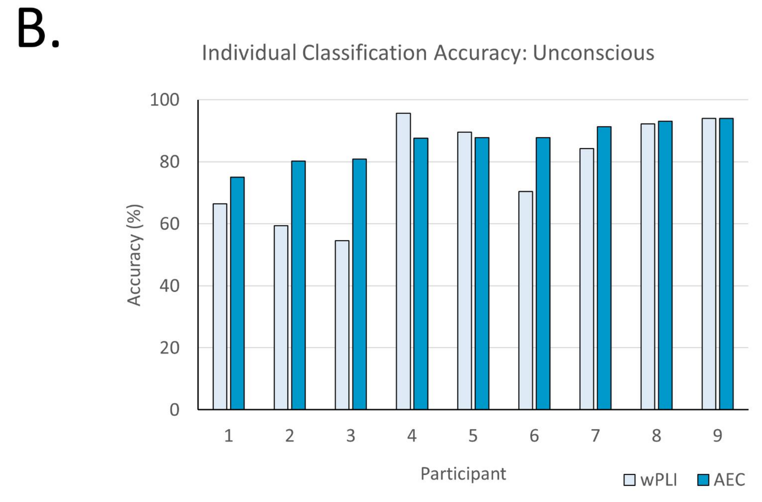
Functional Connectivity Result



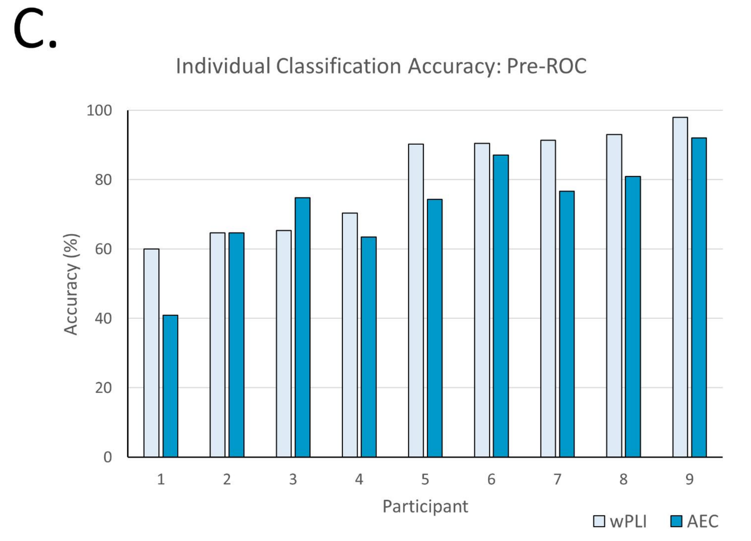
A.



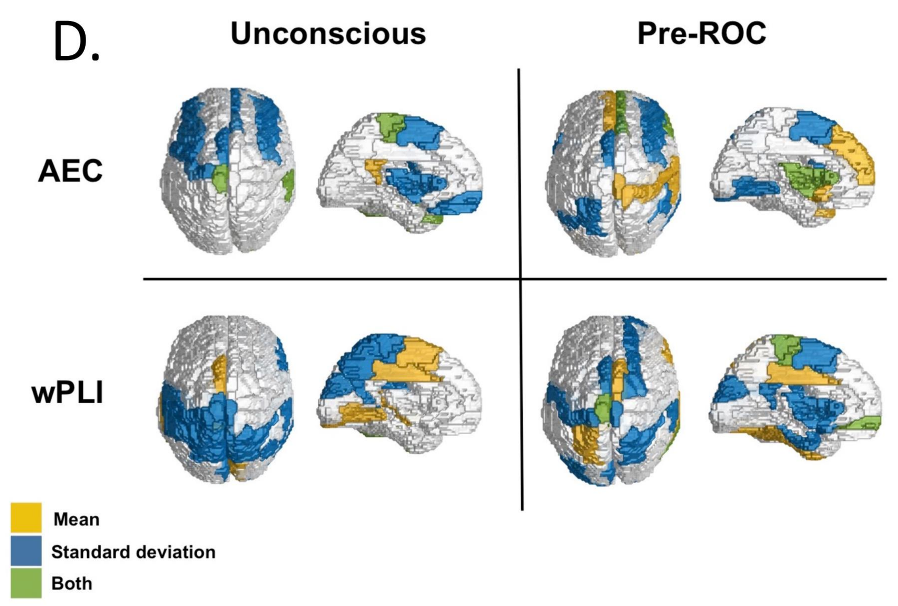
B.



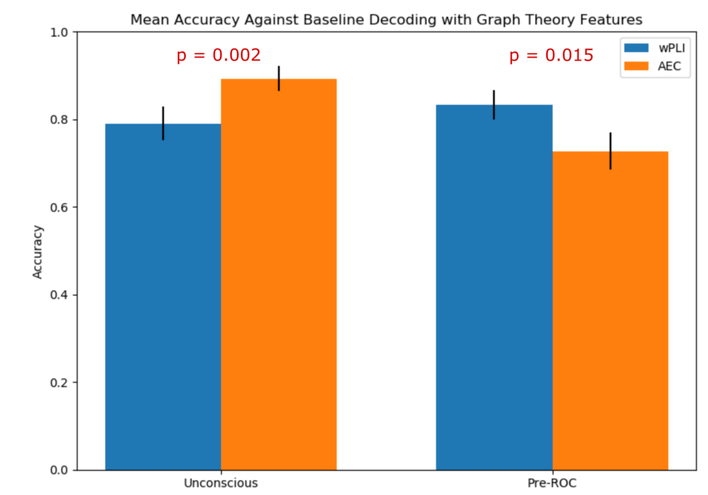
C.

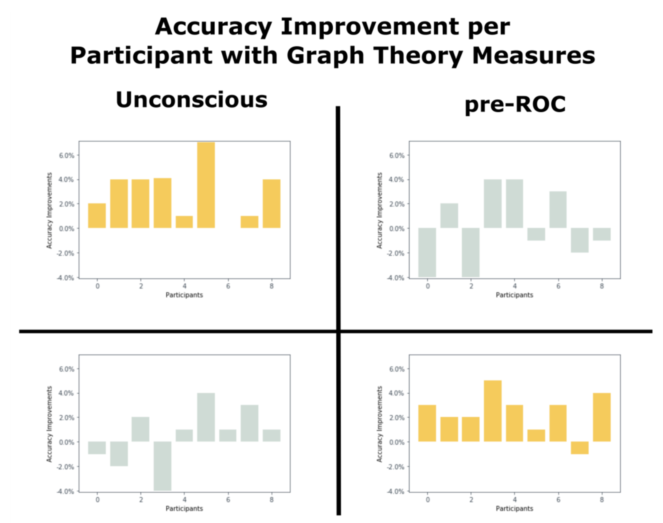


D.



Graph Theory Result





The addition of the clustering coefficients (for each channel), modularity, global efficiency and small worldness **improved the classification of the already dominant modality** (AEC in Unconscious and wPLI in pre-ROC) by **~2.7%.** This **increase in accuracy in the dominant modality was manifested in most participants** (yellow bars), while the other modality didn't beneficiate as clearly from the addition of graph theory features (grey bars).

Conclusion

This study provides evidence that **envelope and phase-based brain networks provide non-redundant information in the classification of states of consciousness**. Phase-based functional connectivity contributed more to the prediction of "light" states of unconsciousness, while amplitude-based functional connectivity contributed more strongly to the prediction of "deep" states of unconsciousness. Furthermore, the two measures of functional connectivity demonstrated **differential predictive contributions across participants** and **involved different brain regions**. Finally, graph properties like clustering coefficient, modularity, global efficiency and small-worldness augment the classification power of envelope and phase-based brain networks in their respective best state of consciousness. This hint towards a **dynamic state of unconsciousness as envelope and phase-based brain networks contribute in different proportions through time to the consciousness states.**

Contact: yacine.mahdid@mail.mcgill.ca