A Heartbeat Away From Consciousness: Heart Rate Variability Entropy can discriminate disorders of consciousness and is correlated with resting-state fMRI brain connectivity of the Central Autonomic Network

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Motivation:
Heart rate variability (HRV) reflects the heart-brain two-way dynamic interactions[1-5]. HRV entropy analysis quantifies the unpredictability and complexity of the heart rate beats intervals and over multiple time scales using multiscale entropy (MSE)[6-8]. The complexity index (CI) provides a score of a system’s complexity by aggregating the MSE measures over a range of time scales[8]. Most HRV entropy studies have focused on acute traumatic patients using task-based designs[9]. We here investigate the CI and its discriminative power in chronic patients with unresponsive wakefulness syndrome (UWS) and minimally conscious state (MCS) at rest, and its relation to brain functional connectivity.

Methods:
We investigated the CI in short (CIs) and long (CIl) time scales in 16 UWS and 17 MCS sedated. CI for MCS and UWS groups were compared using a Mann-Whitney exact test. Spearman’s correlation tests were conducted between the Coma Recovery Scale-revised (CRS-R) and both CI. Discriminative power of both CI was assessed with One-R machine learning model. Correlation between CI and brain connectivity (detected with functional magnetic resonance imagery using seed-based and hypothesis-free intrinsic connectivity) was investigated using a linear regression in a subgroup of 12 UWS and 12 MCS patients with sufficient image quality.

Results and Discussion:
Significant differences were found between MCS and UWS for CIs and CI (0.0001 ≤ p ≤ 0.006). Significant correlations were found between CRS-R and CIs and CI (0.0001 ≤ p ≤ 0.026). The One-R classifier selected CI as the best discriminator between UWS and MCS with 85% accuracy, 19% false positive rate and 12% false negative rate after a 10-fold cross-validation test. Positive correlations were observed between CI and brain areas belonging to the autonomic system. CI was found to be significantly higher in MCS compared to UWS patients, with high discriminative power and lower false negative rate than the reported misdiagnosis rate of human assessors, providing an easy, inexpensive and non-invasive diagnosis tool. CI is correlated to functional connectivity changes in brain regions belonging to the autonomic nervous system, suggesting that CI can provide an indirect way to screen and monitor connectivity changes in this neural system. Future studies should investigate further the extent of CI’s predictive power for other pathologies in the disorders of consciousness spectrum.

Figure 1

Figure 2
A Heartbeat Away From Consciousness: Heart Rate Variability Entropy can discriminate disorders of consciousness and is correlated with resting-state fMRI brain connectivity of the Central Autonomic Network.


Keywords: disorders of consciousness (DOC), fMRI – functional magnetic resonance imaging, ECG, heart rate variability (HRV) analysis, machine learning (artificial intelligence), unresponsive wakefulness syndrome (UWS), minimally conscious state (MCS), Central autonomic network, coma recovery scale-revised (CRS-R)


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Figure 3

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References