Multi-modal modeling of disorders of consciousness at the single patient level

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Disorders of consciousness (DoC) refer to a scope of conditions that can occur after patients that suffered various types of brain damage (e.g. traumatic brain injury, stroke, cardiac arrest) fall into a coma from which they only partially recover. Doctors have defined several categories to classify the DoC patients: the Unresponsive Wakefulness Syndrome (UWS) corresponds to patients who do not show any conscious responses to sensory stimulation; the Minimally Conscious State (MCS) describes patients who show limited but clear evidence of awareness while the locked-in syndrome describes patients that are aware of their environment but remain unable to move or communicate. However, in practice, these categories consider highly heterogeneous populations of patients in terms of pathology, behavior and cognitive ability, yielding a need for individualized diagnosis and treatment approaches.

Here, we develop patient-specific, biologically interpretable, whole-brain models[1] using multi-modal data (EEG and fMRI), aiming to investigate the cause of each patient's DoC individually and seek new therapeutic protocols.

One of the main challenges of building such models is the need to work in very high dimensional spaces (hundreds to thousands of dimensions), which leads to a prohibitive number of model parameters to fit (up to thousands) and heavy computations. Recent studies have unveiled the existence of a lower dimensional space, (or latent manifold), that can encompass the complexity of the brain resting-state activity in tractable dimensions. However, there is no consensus nor systematic description of this manifold or their optimal dimension. We compare here two different dimensionality reduction methods (PCA and auto-encoders) to define the optimal dimension needed to explain the data without losing the complexity of the brain's response, nor the ability to classify between the different DoC diagnosis (UWS/MCS/locked-in). We show that both methods yield to the same optimal dimension thus suggesting a biological relevance of this latent manifold.

Further, we build patients specific models using the resulting latent manifold. The reduced dimension allows us to investigate different models of increasing complexity, with a particular focus on the regulation of the neuronal activity by the astrocytic network[2, 3]. Indeed, several recent studies have shown the importance of astrocyte activity in different types of unconscious states such as dreamless (slow wave) sleep and general anesthesia[4] as opposed to REM sleep or wake. Moreover astrocytes are known to play a crucial role in regulation of the neuronal bursting activity[5], which underlies the emergence of specific neuronal oscillations observed in EEG in such states. We show the first results provided by such models and their fitting at the individual patient level.

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