Spatio-temporal Brain Dynamics Across Consciousness Levels in Clinical and Healthy Populations

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Symposium

The quest for the neural underpinning of consciousness and the main organizational principles characterizing the neural dynamics in conscious and unconscious states represent one the most challenging and unsolved problems in science. In this symposium, we will present novel findings providing complementary evidence across varieties of unconscious states supporting the view that loss of consciousness is accompanied by global changes in intrinsic brain dynamics, such as perturbation of scale-free properties of the brain, changes in background non-oscillatory neural activity, and processing of bodily signals.

The first presentation investigates the link between consciousness and complexity of electroencephalography (EEG) responses to transcranial magnetic stimulation (TMS) in sleep, anaesthesia and patients with disorders of consciousness. The second presentation will quantify background neural activity to delineate wakefulness from states of reduced consciousness -NREM & REM sleep, anesthesia and epileptic seizures-, in scalp and intracranial EEG. The third talk will investigate how the coordination, complexity and background non-oscillatory properties of neural responses to external stimuli are affected by the loss of consciousness in acute coma, proposing markers of outcome prognostication. Last, the fourth talk will examine the link between heartbeat signals and auditory processing in healthy participants and coma, proposing a novel mechanism for processing the timing of auditory sequences in conscious and unconscious states.

Taken together, these presentations will reveal the distinct role of background neural activity, complexity and bodily signals in supporting conscious processing in health and disease.

Learning outcomes:
1. Present novel approaches to study the neural correlates of consciousness in healthy and pathological conditions based on evidence from sleep, anaesthesia, epilepsy and patients with disorders of consciousness
2. Familiarise the audience with methodological approaches including TMS, scalp and intracranial EEG
3. Present clinical applications and neural markers of conscious processing

Objective

- Becoming familiar with novel approaches to study intrinsic dynamics and interoceptive processing across consciousness levels
- Launching a dialogue between basic and clinical research, approaching consciousness in health and disease, taking examples from sleep, anaesthesia and patients with disorders of consciousness or epilepsy
- Present an interdisciplinary view on applying computational techniques for quantifying brain dynamics in the field of human brain mapping

Target Audience

Our symposium is targeting an interdisciplinary audience of researchers and clinicians in the field of human brain mapping, interested in the organization of brain dynamics and their perturbation in states of reduced consciousness.

Moreover, our target audience will include OHBM members interested in methodological approaches to advance basic and clinical electrophysiology research.

Presentations

Consciousness and Complexity: An empirical perturbational approach

The clinical evaluation of disorders of consciousness in severely brain-injured patients relies on their ability to connect to the surrounding environment and demonstrate their subjective experience through motor behavior. However, some patients may become unable to respond to stimuli despite still having conscious experiences. This may happen because of motor or executive function impairments and/or because of sensory disconnection from the environment. States of disconnected consciousness can occur in healthy subjects during dreaming and some forms of anesthesia and may result from severe brain injury. In the latter case, covertly conscious patients may be misdiagnosed as being in a vegetative state (VS). This discrepancy advocates the development of brain-based measures of consciousness that are independent of sensory processing as well as from explicit motor outputs. With this in mind, a novel metric— the Perturbational Complexity Index (PCI)—has recently been developed based on a quantification of the electroencephalographic (EEG) responses to transcranial magnetic stimulation (TMS). Inspired by theoretical considerations, PCI directly gauges the ability of many functionally specialized modules of the thalamocortical system (differentiation) to interact rapidly and effectively (integration), thus producing complex patterns of activity in response to a direct perturbation. I will review a decade of experimental evidence demonstrating the ability of such approach in distinguishing between conscious and unconscious subjects under controlled experimental physiological (wakefulness, NREM sleep, REM sleep) as well as pharmacologically induced conditions (general anesthesia with propofol, xenon and ketamine). I will then discuss the effectiveness of PCI when tested at the bedside of severely brain-injured patients with disorders of consciousness, highlighting potential mechanistic insights responsible for the collapse of brain complexity. I will finally discuss some practical diagnostic, therapeutic and patient management perspectives, as well as prognostic implications derived by this empirical perturbational approach.

Presenter

Simone Sarasso, University of Milan, Italy

Neural Correlates of Unconsciousness: Complementary roles of oscillatory and aperiodic EEG activity

States of unconsciousness such as non-rapid eye movement sleep, general anesthesia with propofol or epileptic seizures are linked to the occurrence of prominent synchronized oscillations in the electroencephalogram (EEG), such as slow oscillations. However, other states of altered consciousness like coma, rapid eye movement sleep or ketamine anesthesia are characterized by a desynchronized EEG, lacking pronounced rhythmic patterns. Despite the sparsity of oscillations, these conditions display a behavioral state consisting of amnesia, akinesia and hypnosis that is similar to unconsciousness found in 'oscillatory' states. Previously, it has been debated whether highly synchronized slow oscillations decrease information processing capacity in the human brain, thus, effectively mediating unconsciousness by limiting processing resources. However, given that several states of these states are not necessarily defined by synchronous oscillations, I predict that these states might exhibit strong changes in their aperiodic or 1/f-like behavior. Critically, several lines of research indicated that 1/f activity reflects the lion's share of the EEG power spectrum. While non-oscillatory background activity has often been disregarded as electrophysiological and therefore, discarded prior to analysis, I specifically addressed whether it contains behaviorally-relevant information. In this talk, I discuss recent progresses in using 1/f dynamics to delineate wakefulness from states of altered consciousness such as sleep, coma, epileptic seizures or anesthesia. First, I will survey the origin and definition of 1/f-like behavior in the human brain and briefly review recent advances in understanding aperiodic neural activity. Then I will present empirical data from both scalp and intracranial EEG, which dissociates the role of 1/f activity and neuronal oscillations. I will specifically address the relationship of aperiodic activity and oscillatory network features and discuss how the temporally coordinated interplay of both signatures mediates unconsciousness. Lastly, I will provide an outlook on the neurophysiologic basis of the 1/f behavior and its relationship to population firing. Taken together, I will provide converging evidence suggesting that 1/f activity directly reflects behaviorally-relevant population activity and thus, constitutes a powerful marker to address both neuroscientific as well as clinical questions regarding the neuronal basis of unconsciousness.

Presenter

Janna Lendner, University Medical Center Tuebingen, Tuebingen, Germany

Spatio-temporal Structure and Complexity of Auditory Processing in Coma

There is converging evidence that the loss of consciousness is accompanied by a loss of coordinated neural responses to external stimuli and changes in the levels of background neuronal noise. One neural circuit that is particularly interesting for studying consciousness is that of processing environmental regularities, as it is often preserved even in the absence of conscious perception. Several studies have linked the integrity of this circuit, mainly evaluated by characterising scalp EEG responses to external stimuli, with conscious processing. However, the properties and neural dynamics that support processing of auditory stimuli in the absence of consciousness remain under-explored. In our recent work, we hypothesized that neural functions in coma, and in particular in patients that do not regain consciousness, degenerate already during the acute stage of coma. We tested this hypothesis using metrics that reflect the spatial structure of neural responses within the sensory processing network, and its levels of complexity and background neural activity. In this talk, I will present evidence suggesting that discrimination of auditory regularities is preserved in early coma, irrespective of patients' outcome, and that it deteriorates for patients who do regain consciousness already within the first few days of coma. Then, I will focus on the organization of electrophysiological responses to auditory stimuli in coma patients and awake volunteers, quantifying their spatial properties via phase locking, and also the complexity and levels of background neural activity. Our results show that neural responses to sounds in the first day of coma exhibit a lower phase locking for non-survivors compared to survivors or healthy controls, establishing possible markers of patients' outcome. Moreover, the levels of complexity of EEG responses and non oscillatory background neural activity differ between coma patients and healthy controls, such that patients that later survive have lower complexity and spectral exponent compared to awake control participants. Overall, this talk will present the view that intrinsic neural dynamics within the sensory processing network reflect conscious access to the environment and are indicative of the chances of regaining consciousness.

Presenter

Athina Tzovara, University of Bern, Switzerland

Keeping Track of Heartbeat Signal Induces Auditory Expectation in Conscious and Unconscious States

Exposure to sensory regularities in the environment induces the human brain to form expectations about 'which' and 'when' incoming stimuli occur in the future. Evidence comes from the neural response to violation of sensory regularities and in particular to unexpected omission in auditory series. Regularity in auditory series usually refer to fixed sound-to sound- intervals. Here we focused on auditory series where their temporal regularity is induced by interoceptive rhythms, i.e produced by the body. Specifically, we investigated how the human brain encodes temporal regularity induced by heartbeat by recording neural responses to sound omissions after repeated sound presentation synchronized to the ongoing heartbeat. We further investigated whether such omission response requires awareness of stimulus regularity and whether it can be elicited in the absence of consciousness. We recorded EEG in a group of healthy subjects (N=16), while delivering sounds via earphones. The experiment comprised four conditions: a 'baseline' condition during which we recorded neural activity at rest; 'synchronous', when sound onsets were synchronized with subjects' heartbeat; 'asynchronous', where sound onsets followed the heartbeat during baseline of the same participant. Sounds were randomly omitted within the auditory sequences 20% of the time. Participants were naïve to the cardio-audio coupling and none of them could report any perceived temporal relation between sound onset and heartbeat at the end of the experiment. The same experiment was carried out in a group of comatose patients (N=28) during their first day of coma, 17 of them had a long-term favorable outcome. During sound omission we extracted the neural response locked to the sound omission, which corresponds -by construction- to the Heartbeat Evoked Potentials (HEPs), the average evoked response locked to the heartbeat during the omission interval. We conducted all EEG analyses at group-level based on the cluster-based permutation test corrected in space and time for multiple comparisons. In healthy participants, an auditory omission induces a difference between HEPs in the synchronous vs asynchronous conditions at 153-278ms after onset of the omitted sounds. In comatose patients with favorable outcome we observed a significant difference between HEPs in the synchronous vs asynchronous condition at 238-349ms after onset of the omitted sound. No significant effect was observed when performing the same analysis in the group of patients with unfavorable outcome. Control analyses ruled out possible contributions of the pseudo regularity in the auditory sequence. We show that cardio-audio synchronicity within auditory sequences modulates the neural response to sound omission in the human brain. This provides evidence that the human brain can take advantage of the heartbeat signals for anticipating stimuli from the environment. This phenomenon does not require perceptual awareness of the synchronicity rule and remains preserved in an unconscious state of comatose patients at least in those with good prognosis. That the cardio audio response appears disrupted in comatose patients with unfavorable outcome encourages its investigation at the single patient level for evaluating its prognostic value for patient outcome.

Presenter

Marzia De Lucia, Lausanne University Hospital Lausanne, Vaud, Switzerland