Whole-brain analyses reveal the impairment of posterior integration and thalamo-frontotemporal broadcasting in disorders of consciousness

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ABSTRACT

Patients with severe brain injury can fall into a coma, which is characterized by the absence of both wakefulness and awareness. Patients surviving coma often recover signs of wakefulness, i.e. eye opening, but without manifestation of awareness of the self nor of the environment. Such state is known as *unresponsive wakefulness syndrome* (UWS). Some of these patients gradually regain awareness and progress into the so-called *minimally conscious state* (MCS), showing a range of non-reflexive behaviors such as visual pursuit, localization to pain or response to simple commands, although their ability to communicate remains hampered.

Clinical assessment of the state and the cognitive abilities of these patients is a challenging endeavour. Up to date, behavioural assessments based on the responses of the patients to sensory stimuli, pain or simple commands constitutes still the first line of action taken at bedside. However, the study of the brain's dynamical activity is opening a new window for the assistance in diagnosis of patients with disorders of consciousness (DoC). For example, the dysfunctional spread of naturalistic or synthetic stimuli has proven useful to characterize hampered consciousness. Beyond classification, understanding of the mechanisms leading to traumatic loss of consciousness is fundamental.

Here we study the propagation of endogenous and exogenous perturbations in the neural activity of patients with DoC, based upon directed and causal interactions estimated from resting-state fMRI. First we investigate the intrinsic ignition properties of the neural activity. Resting-state activity in healthy awake subjects contains spontaneous local events whose global propagation can be followed to identify the capacity of the network to transmit information. We find that in patients with DoC, specially in those with UWS, the number of spontaneous local events is very much reduced and their propagation hampered, with local events failing to give rise to global activity.

Then, we simulate the propagation of exogenous perturbations on the network. Therefore whole-brain effective connectivity is inferred from the resting-state activity of each subject, assuming the multivariate Ornstein-Uhlenbeck as the generative model of the fMRI signals. The effective connectivity quantifies the interaction strength between every pair of brain areas, allowing for the estimation of the directional causal influences as well. Considering the effective connectivity as the underlying network on which perturbations are propagated, we unfold the global spatio-temporal responses of local perturbations.This allows us to characterise both the broadcasting capacity of a brain region (i.e., how a perturbation on region *i*, affects all other regions *j*) and their integrative capacity (i.e., the response of a brain region to perturbations somewhere else.

Our results show that the mechanisms leading to traumatic loss of consciousness are the combination of several factors: the broadcasting capacity of fronto-parietal networks is hampered while for posterior regions see their integrative capacity affected (see Fig. 1). Regarding much debated theories of consciousness, integrated information theory and the global neuronal workspace, our results indicate that both theories focus on distinctive aspects of consciousness, representing two sides of the same coin.

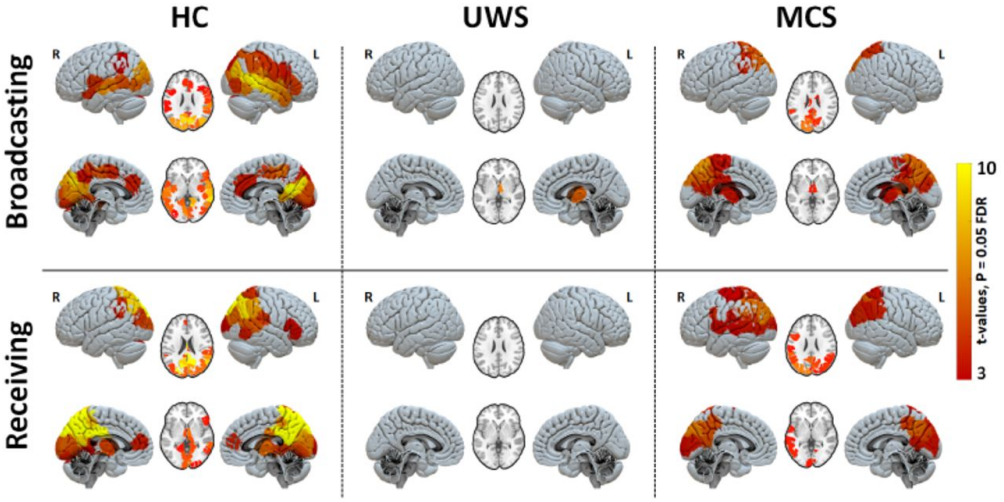

FIGURE 1. Region-wise broadcasting and receiving capacities due to exogenous perturbations.
Maps of significantly large broadcasting and receiving capacities for the three study groups (healthy controls, HC; unresponsive wakefulness syndrome, UWS; and minimally conscious state, MCS). The color code represents the t-values. Only regions with significantly high values are presented in each case (FDR corrected p-values <0.05 for 214 tests (ROIs)).