The seesaw brain: why do anti-correlated functional networks underlie the recovery of consciousness after brain injury?

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The article by Di Perri et al.1 in the current issue brings novel functional neuroimaging evidence to bear upon the challenge of understanding the complex process of recovery of consciousness from the so-called vegetative/unresponsive wakeful (VS/UWS) and minimally conscious states (MCS), collectively referred to as disorders of consciousness (DoC). The authors used functional magnetic resonance imaging (fMRI) to study the resting brain activity in patients who have emerged from a minimally conscious states (EMCS), placing the results along a spectrum extending from the vegetative state to normal consciousness. In particular, they focused on the ‘dominant modes’ of activity observable at rest in the healthy brain. These modes of activity are known to be anti-correlated, ‘seesawing’ over time between increases in the so-called default mode and task positive networks, which have been postulated to correspond to internally and externally focused processes, respectively. The results of their analysis replicate a previously reported pattern: as behavioural signs of consciousness in patients become increasingly evident, overall levels of correlated brain activity within these networks also increase linearly. The authors also confirm that this linear increase is mirrored by increases in brain metabolism measured by [18F]fluorodeoxyglucose positron emission tomography (PET). However, their core observation, that between-network anti-correlations are observed only in EMCS patients and healthy controls, represents an important step forward in understanding the recovery of consciousness after brain injury. Their findings also provide a potentially novel imaging marker of pathological unconsciousness, where the correlations between these networks are positive, rather than reciprocal.

Taken together, a key theme emerges from these findings, which is in keeping with emerging data from cognitive neuroscience: the recovery of consciousness after injury is supported not only by increases in positive correlations within key brain networks, but also by complex interactions between these networks. Such reciprocal interactions between the default mode and anticoorrelated networks may provide the substrate for neural integration that has been postulated to support conscious processing. Within this process, the DMN is thought to contribute internal/associative information which is scrutinised/manipulated by frontoparietal networks. These interactions may be more complex than simple reciprocity: we have shown that hubs conventionally associated with the DMN may facilitate task execution by changing their network membership to task positive networks.

This manuscript generates additional clinical research opportunities. We may be able to use modern neuroimaging to understand the structural substrates that underlie re-emergence of between-network anti-correlations that accompany recovery of consciousness in EMCS patients. Such data might also explain why anti-correlations are not observed in MCS patients, who present positive (albeit inconsistent) signs of awareness at the bedside, but in this regard, resemble behaviourally unresponsive VS patients. Such knowledge might also allow us to identify options that accelerate recovery - imaging biomarkers could help explore the mechanisms and efficacy of “arousal” interventions that have been employed in DoC. An additional attractive option would be to identify electroencephalographic (EEG) markers that also provide robust evidence of such
anticorrelations, and could hence provide a means of detecting their existence that is more accessible and cost-effective than fMRI. Indeed, we\textsuperscript{11} and other groups\textsuperscript{12} have previously identified abnormally robust low-frequency connectivity in resting EEG of DoC patients, but the link between such EEG-based signatures and underlying BOLD correlations remains to be conclusively made.

This work by Di Perri et al.\textsuperscript{1} contributes new knowledge to the growing body of recent literature about the neuroscience of DoC. In a marked step change, this and other recent publications in this field have increasingly aggregated data from relatively large patient cohorts, in some cases pulling together datasets from multiple research sites. This positive trend represents an important advance towards consolidating viable markers and tools from translational neuroscience for developing diagnostic and prognostic applications. To bring benefits of this research to patients, their carers and families, future work will need to validate these markers in prospective clinical studies.

While careful behavioural evaluation by trained experts remain the accepted gold standard for assessing patients with DoC\textsuperscript{13}, a growing body of fMRI\textsuperscript{14} and EEG\textsuperscript{11,12} literature show characteristic differences in resting brain activity between VS, MCS, and normal consciousness. However, definitive neural signatures of the potential for, and recovery of, normal consciousness after brain injury are yet to be conclusively identified. Di Perri et al take us a bit further along this path, and are to be complimented on gathering the large cohorts of patients and the outstanding methodological expertise that enables the generation of these results. However, we need to find ways in which these methods can be implemented in less expert contexts, and for decision support in individual patients.

References


