Connectivity via magnetoencephalography

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The capacity engendered by the fusion of imaging, neurophysiological recording, and complex data analysis to provide new insights into disease processes and recovery of the nervous system continues to expand. In their article “Resting state magnetoencephalography functional connectivity in traumatic brain injury,” Tarapore and colleagues offer a preliminary look into what is now possible with this approach, and how it may change our understanding of recovery and, eventually, allow us to monitor the effects of specific interventions.

The authors describe 21 patients with various types and clinical severities of traumatic brain injuries (TBIs) who underwent functional connectivity studies via magnetoencephalography (MEG) between 4 and 42 months after injury, along with structural imaging. Five patients also had a second MEG study at intervals ranging from 21 to 31 months after the initial MEG study. Using a beamformer source analysis in combination with the imaginary coherence (IC) from a resting-state MEG measurement, the authors found a reduction in the IC in the alpha band in specific areas of the cortex compared with age-matched, healthy controls. The authors concluded that specific aspects of functional connectivity were decreased in patients compared with controls and that those with serial measurements had improvement (fewer regions with decreased connectivity) on average over time. Although this is a pilot study, if the findings are valid, it is a fascinating result that has implications for the treatment of patients with TBI.

The paper contains striking images. On the more technical imaging side, although the results are likely complimentary and may be due to differences in analytic technique, it would be important to know whether these changes in functional connectivity correspond to the findings in other studies. For example, Huang with various authors1,2 and Lewine et al.3 found focal slowing (low-frequency discharges) that was not found with simultaneous surface electroencephalography. These were found with simple bandpass filtering and sequential equivalent current dipole (ECD) analysis or by using the distributed source analysis method (for example, VESTAL). The frequency of the focal slowing found in these studies was much lower in spectral frequency than the alpha frequencies used for the IC reductions found in this study. These apparent differences are likely reflections of cortical disconnections from white matter. From a practical standpoint, it would be important to know whether the changes in IC correspond to areas of focal slowing, since the focal slowing can be identified with the widely implemented ECD analysis of filtered data, without the need for a comparison with an age-matched control or advanced analysis of IC.

There are some limitations of this study, including the use of IC for the functional connectivity. As the authors point out, using only the imaginary projection of coherence reduces overestimation of crosstalk that may occur locally due to the source analysis. It is worth pointing out that in the case of using a source analysis method, this is not due to volume conduction effects; this would be true in electroencephalography electrodes, but that is not the case in this study. As has been pointed out in other studies, IC requires a higher signal-to-noise ratio and also will suppress actual brain activity that has no phase lag, even if it occurs over long distances. There is evidence that this does occur over long distances in the human brain but perhaps is less likely in the alpha frequency band. It seems that the authors used the alpha band with the highest spectral power to mitigate the issue of requiring high signal-to-noise ratio for robust IC measures.

The authors also speculate that increased functional connectivity in some of the 5 patients who underwent sequential MEG examinations suggests plasticity in the brain. If true, this would be an important observation that would allow for a biomarker of neuroplasticity in patients with TBI that could supplement traditional measures of neurocognitive improvement and that might indicate the mechanisms of recovery or response to intervention in an individual patient. These techniques show promise, and the authors are to be congratulated on exploring these new methods to further understand the common but frustratingly treatment-elusive condition of TBI.

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Disclosure

The authors report no conflict of interest.

References

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Editorial


Response

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We appreciate the enthusiasm raised about our article. In this article, we documented resting-state alpha band functional connectivity decrements in TBI, which were robust across our sample of 21 patients. In a small subset of 5 patients, we observed improvements in functional connectivity associated with recovery.

Our alpha band (8- to 12-Hz) functional connectivity was based on resting-state activity measured using a 1-minute segment of data collected in our patients with their eyes closed. Whereas our efforts have focused on the overall connectivity patterns, others have examined abnormal power during episodic events, such as abnormal slowing in the delta band (1- to 4-Hz) range, as reported by Huang et al. 1 and Lewine et al. 2 in TBI cohorts.

Magnetoencephalography evaluation of slowing originally required manual identification of episodes of slow waves and ECD fitting of such events, which is operator dependent in all cases and also quite subjective if parameters are extracted for more than 1 dipole. Indeed, recently automated procedures have been developed for examining slower frequency delta oscillatory power. Similar to this approach, our procedure is also almost completely objective; it only requires selection of an overt artifact-free contiguous 1-minute segment of data for processing. Reconstructions are then automatically obtained using adaptive spatial filtering methods. Computation of global imaginary coherence within patient-specific alpha band frequencies requires no manual intervention. We agree that a larger cohort study comparing the 2 methods would be noteworthy. In particular, we agree that it will be interesting to examine whether regions of reduced alpha band functional connectivity correspond to those with reduced power and focal slowing in the delta band.

Concerning the choice of our metric of IC, a recent paper has shown that IC significantly reduces the effect of “seed blur” that is typically observed with magnitude coherence. 3 Furthermore, the use of IC with higher-resolution adaptive spatial filters further improves performance and sensitivity. We agree that magnitude coherence can extract some long-range connectivity that may have zero phase lags. However, given that many such correlations can be spurious due to either lead-field or spatial weight correlations or due to other artifacts, caution should be applied to the interpretation of zero-phase-lag correlations.

In general, we agree that it will be interesting to look at other connectivity metrics that are immune to spurious correlations and to examine not only other frequency bands of interest but also the coupling between the different oscillatory bands. Furthermore, we believe that novel imaging biomarkers for TBI should include a multimodal imaging approach with structural and functional connectivity data, as well as network-level analysis of such data.

References


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