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THE USE OF EEG AND MRI TO EXPLORE ALTERATIONS IN COGNITIVE NETWORKS IN EPILEPSY.

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INTRODUCTION

The combined application of electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) has emerged as a key method for investigating the impact of epilepsy on cognitive networks. EEG-fMRI uniquely integrates the high temporal sensitivity of EEG with the spatial precision of fMRI, enabling researchers to capture both the timing and the localization of epileptiform discharges. This multimodal approach allows the mapping of how seizure activity influences neural circuits responsible for attention, working memory, language, and executive functioning.

Research demonstrates that epilepsy is increasingly understood as a disorder of brain networks rather than isolated cortical regions. EEG-fMRI studies have shown that interictal epileptiform discharges can cause transient disturbances in large-scale networks, such as the default mode network (DMN), fronto-parietal control systems, and hippocampal-prefrontal pathways. These alterations may explain the frequent cognitive comorbidities in patients, including memory deficits, impaired concentration, and slowed information processing. Importantly, the method also distinguishes between maladaptive network disruptions and compensatory mechanisms that support cognitive resilience in chronic epilepsy.

In clinical practice, EEG-fMRI contributes to presurgical evaluation by linking epileptic foci to functional brain networks, thereby balancing seizure control with preservation of cognitive functions. It also offers insights into disease progression, helping clinicians monitor how recurrent seizures affect long-term neural connectivity. Furthermore, EEG-fMRI provides a platform for the development of targeted interventions, including neurostimulation and cognitive rehabilitation strategies, by clarifying the network dynamics underlying cognitive decline.

The use of EEG-fMRI represents a transformative advance in epilepsy research and management, bridging the gap between seizure localization and the broader understanding of cognitive network dysfunction. Its continued integration into clinical and experimental frameworks promises not only more precise diagnostic outcomes but also the potential for personalized, network-based therapeutic approaches.

Key words:

- Electroencephalography (EEG)
- Magnetic Resonance Imaging (MRI)
- Functional MRI (fMRI)
- Epilepsy
- Cognitive networks
- Network alterations
- Interictal epileptiform discharges
- Brain connectivity
- Cognitive comorbidity

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Epileptic Activity Can Dynamically Affect Cognition

Different hypotheses have tried to explain these deficits. A disruptive role of interictal epileptic discharges (IEDs) during ongoing physiological activity has been shown even if these discharges do not result in clinical signs of a seizure; the occurrence of IEDs can therefore be related to transient cognitive impairment. Previous studies based on intracranial EEG have investigated how epileptic activity can alter normal cognitive processing through large-scale network disruption however, due to the low spatial sampling of electrophysiological recordings, it is often challenging to map these networks without prior assumptions on the relevant brain regions to be recorded. Although intracranial EEG has high temporal and spatial resolutions, it has a low spatial sampling, thus preventing this tool to be used alone to investigate large-scale networks.

Interactions Between Epileptic Activity and Cognitive Networks

Cognition engages large-scale brain networks . Resting-state fMRI (rsfMRI) investigates synchronous activity between regions in the absence of an explicit task and can be subdivided into Intrinsic Connectivity Networks (ICNs). The spatial organization of ICNs has been consistent with relevant cognitive tasks, however with subtle variations . As such, previous studies have implied that cognitive networks remain dynamically active even during periods of rest . The effect of interictal activity could explain part of the nature of cognitive dysfunction in patients with epilepsy. So far, studies have mostly focused on the cognitive disturbances associated with the occurrence of IEDs . However, the interactions between detailed spatio-temporal aspects of epileptic activity and changes in ICNs and task-related cognitive networks have not been greatly explored. Therefore, the current review will discuss the current applications of EEG-fMRI in relation to cognition in both human and animal studies.

EEG-fMRI in the Study of Cognition in Humans

Previous studies have commented on the relationship between cognition and ICNs extracted from traditional resting state fMRI, especially in relation to patients with epilepsy . ICNs can be ascribed to specific functions, such as self-awareness, attention, cognitive control, or perceptions such as visual, auditory, or motor. There is some spatial overlap between these networks in both patients and healthy controls; however the abnormal modulation of activity between these networks can be indicative of a patient's clinical syndrome.

Over the last 5 years there has been a substantial increase in the use of EEG-fMRI, especially for pre-surgical evaluations for patients with epilepsy. However, the effects of IEDs on cognitive networks were not often explored until recently. Following pioneering work relating IED-correlated decreases in Default Mode Network activity in temporal lobe epilepsy and generalized epilepsy , recent works have shown the possible impact of interictal activity on several ICNs in focal epilepsy in adults , focal epilepsy in children, children with idiopathic focal epilepsy [Benign Epilepsy with Centro-temporal Spikes (BECTS)], epileptic encephalopathy , as well as generalized epilepsies , including Childhood Absence Epilepsy (CAE), and even reflex epilepsies . The majority of recent EEG-fMRI studies who evaluate the interaction between interictal discharges, ICNs, and their relationship to neuropsychological outcome have been in BECTS patients; these studies found a negative correlation between cognitive functioning and Functional Connectivity (FC).

Transient Effects of IEDs On Epileptic and Cognitive Networks

Regarding cognition, Shamshiri et al. found connectivity differences in cognitive networks (related to attention) in a group of children with focal epilepsy compared to controls. However, no evidence remained for non-transient differences in network connectivity between patients and controls, after

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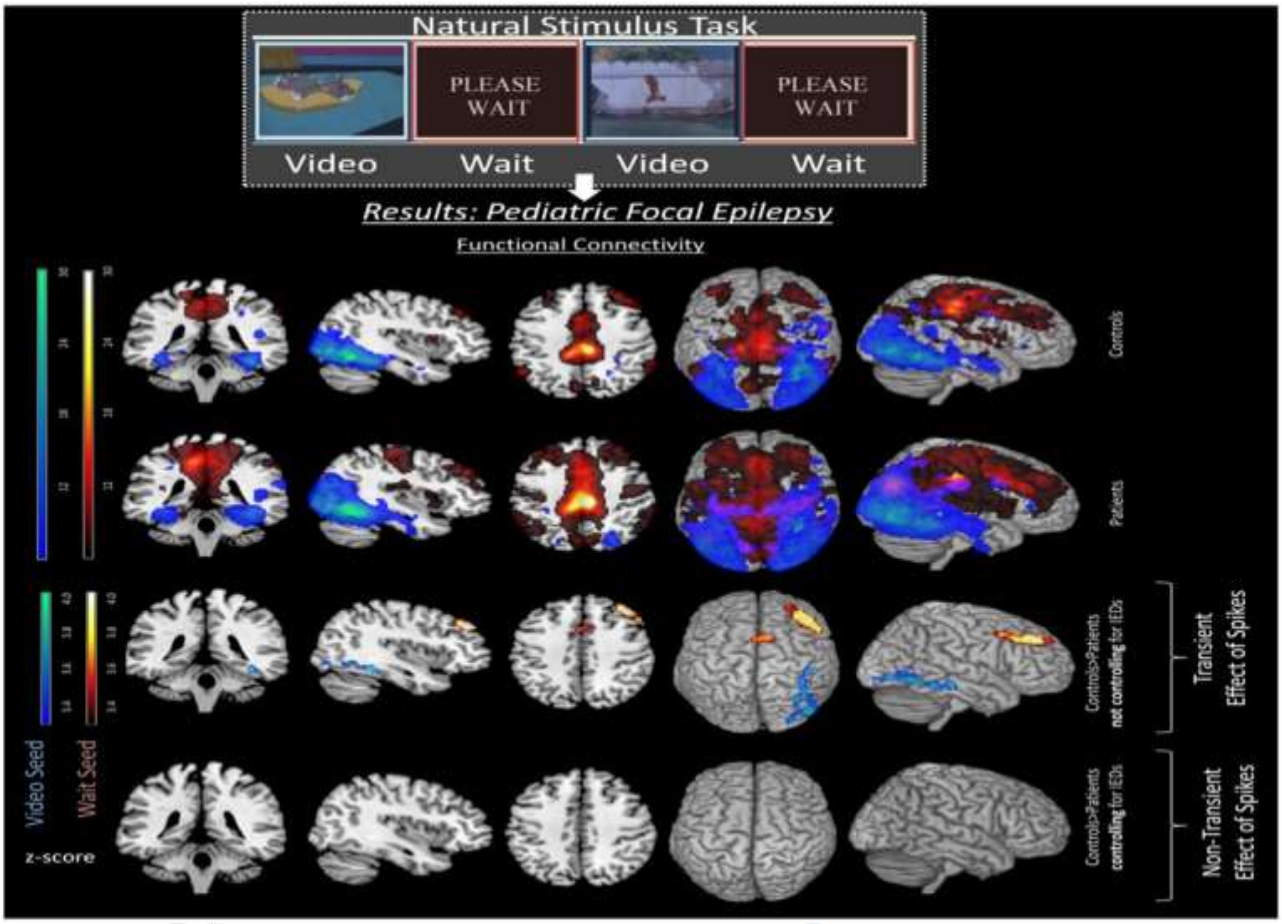
accounting for IED effects . These results were also consistent with a MEG study in children with focal epilepsy patients by Ibrahim et al., but are inconsistent with those studies mentioned above , possibly due to differences between adult and pediatric populations and their respective variability in plasticity and disease duration . Instead, for BECTS patients, several studies reported decreases in functional connectivity regardless of the presence of IEDs . These patients showed decreased FC in the inferior frontal gyrus, anterior cingulate cortex, and the striatum, which have previously been related to cognitive control . This is particularly interesting as patients with BECTS often display behavioral difficulties and language delays.



Transient effects of IEDs in pediatric focal epilepsy patients. Image with permission Shamshiri et al.illustrating the effects of spikes on FC networks of a resting state task. Differences between controls (top row) and patients (second row) can be seen in the third row. These differences are including both transient and long-term effects of spikes as spikes are not controlled for in the analysis. However, once the transient effects of spikes are accounted for, the group differences disappear (fourth row), emphasizing the effect of IEDs on ICNs.

Perspectives

The study of IED-related effects on cognitive networks may be difficult in many patients, given the lack of frequent IEDs to model. Other approaches to model pathologic activity using EEG topographies or other EEG features such as decomposition using Independent Component Analysismay offer alternative markers of epileptic activity to correlate with cognitive network alterations.

Simultaneous intracranial EEG and fMRI would allow to better map fMRI network alterations correlated to intracranial pathological EEG activity. Such recordings focused on the mapping of

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epileptic network and the coupling between neuronal activity and hemodynamic changes, which is related to the fundamental assumptions underlying fMRI studies. These fMRI studies take advantage of the relationship between neuronal activity (mainly post-synaptic potentials) and deoxyhemoglobin concentration to show the focal changes related to the epileptogenic zone, and reveal distant BOLD modulations related to the interictal epileptic network . Simultaneous recordings of intracranial EEG and scalp EEG could also uncover new non-invasive markers of epileptic activity that are currently undetectable on scalp EEG but could nevertheless affect cognitive processing. Such markers could be used to refine EEG-fMRI analysis .

The possibility to inform fMRI analysis using EEG-derived brain activity offers several perspectives to study the spatio-temporal aspects of cognitive networks, at rest or engaged in specific tasks, in a more selective way than using fMRI, EEG or MEG alone. The characteristics of task-related EEG evoked responses (amplitude, latency) can be included in the fMRI analysis to model and map the network involved in such responses, such as attention and error monitoring and therefore also study interactions with epileptic activity. EEG measures of arousal (e.g., drowsiness or sleep) could also be valuable to study alterations of cognitive networks. Changes in arousal have a significant effect on fMRI connectivity patterns than can even be used to monitor drowsiness during scanning . This could be particularly relevant when studying patients with epilepsy vs. controls when drowsiness could show group differences, notably related to drug-induced sedation, sleep deprivation or scanner related anxiety. Antiepileptic drugs affect fMRI brain networks in healthy controls and the effect other drugs, such as donepezil and memantine in the field of dementia, have also been documented. This contribution of medication is hard to disentangle from the effect of disease, notably due to the high variability of drug regimes in patient groups and the difficulty to recruit drug naïve patients. EEG markers of medication, such as beta activity or increased drowsiness could be used to try to model this effect in the analysis.

Conclusion

Overall, the temporal and spatial effects of epileptic activity and medication can all influence changes in ICNs and cognitive functioning. Although there has been an increase in interest regarding EEG-fMRI and the effects of epileptic activity on ICNs, as reflected by the number of results from our search, there is still much to learn about how to use this information to understand the long-term impact of interictal activity and cognition and improve the decision making regarding the therapy of patients with epilepsy. Globally, there are differences between focal/non-focal epilepsies, especially in regards to which ICNs or task-related networks are more sensitive to IEDs and how the epileptogenic network influenced the findings. Nevertheless all groups show a widespread influence of interictal activity but also some IED-independent alterations.

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