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THE ROLE OF FUNCTIONAL MRI IN PRE-SURGICAL PLANNING FOR PATIENTS WITH EPILEPSY: REVIEW

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Abstract

No prior comprehensive analysis has been undertaken to examine all the available information on mapping eloquent cortex (namely motor, language, and memory areas) using modern functional neuroimaging techniques like as functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG) for children who are candidates for epilepsy surgery. The majority of research in this field has mostly focused on adult populations, and the effectiveness of these strategies in pediatric populations is not as well-established. A comprehensive study was conducted utilizing an advanced systematic search and retrieval method to analyze all published publications that investigate the use of functional neuroimaging in pediatric patients who are candidates for epilepsy surgery. Studies that have been obtained suggest that both fMRI and MEG are capable of providing evidence for the lateralization and localization of motor and linguistic functions. An important discovery from the analysis is the lack of research (n = 34) that specifically examine the demographic of children undergoing epilepsy surgery. The ideal activation produced by different language and memory paradigms in children is still uncertain, as well as how to accurately quantify it using rigorous statistical methods. Consensus must be reached for statistical analyses and the consistency and effectiveness of linguistic, motor, and memory paradigms. Extensive research are necessary to provide patient series data that doctors may use to objectively assess outcomes. In order for functional imaging methods to be a reliable option for mapping the eloquent cortex in children before surgery, it is necessary to create paradigms and studies that show agreement with independent measurements.

Keywords: Paediatric, Epilepsy surgery, fMRI, MEG, Memory, Language, Motor

1. Introduction

Paediatric epilepsies are prevalent neurological illnesses in childhood, impacting around 0.5-1% of children and young individuals below the age of 16 years [1]. Childhood epilepsies are linked to a significant level of psychological and mental illness, with psychopathology rates three to six times higher than in the general childhood population [2]. Epilepsies have been shown to substantially impair behavior, emotion, cognition, and learning [2], [3], [4], [5]. Some forms of epilepsy do not show improvement when treated with anti-epileptic medicines. However, alternative therapies such as the ketogenic diet, vagal nerve stimulators, and surgical procedures including resective and functional surgery have been developed as options [6], [7], [8].

Epidemiological studies suggest that the potential beneficiaries of resective surgery for epilepsy in children are estimated to be 27 out of every million. Approximately 405 children in the UK have this treatment each year, although only around 25% of these surgeries are actually performed. Adult-onset epilepsy may result in impairment of previously acquired cognitive abilities. Nevertheless, in the case of a kid, the acquisition of language, memory, and motor functioning occurs gradually, and seizures disrupt both the ongoing development and the previously learned skills [10]. The International League Against Epilepsy (ILAE) suggests that resective surgery should be taken into account for cases of medically refractory epilepsies, in which a patient has not shown improvement after trying two or three anti-epileptic medicines, or when seizure activity is severely impairing [9]. The main objective of resective surgery is to obtain relief from seizures, however this outcome is not always attained. The probability of achieving independence from seizures is influenced by the cause of the epilepsy and the scope of the operation performed [9]. For example, surgery for developmental abnormalities such hemimegalencephaly has been linked to a lower probability of achieving total seizure independence compared to other anomalies [11]. After controlling seizures, the focus shifts to the impact on cognition and behavior. Studies have shown that achieving seizure independence or reducing seizures is linked to decreased psychopathology and aggressive behaviors.

Traditionally, the determination of eligibility for surgery has been made by the use of semiology, structural neuroimaging, vEEG, and neuropsychological examination [9], [14]. These studies continue to be crucial. The objective of epilepsy surgery is to eliminate or substantially decrease epileptic episodes that are resistant to therapy. Nevertheless, the degree of removal is restricted because to the possibility of cognitive, perceptual, and motor impairments [15]. Precisely identifying the specific regions of the brain responsible for language, memory, and motor function is crucial for treating difficult-to-control epilepsies. Although there are known drawbacks, the intracarotid amobarbital test, often known as the Wada test, is still used to assess the risk of language and memory damage after surgery [15], [16].

Wada is a rigorous and intrusive test that has some hazards. Its purpose is to determine the lateralization of function rather than its localization. Notable advancements have resulted in the substitution of sophisticated non-invasive methods, including as fMRI and MEG, for mapping motor, linguistic, and memory functions. The references are [17] and [18]. fMRI is used to detect changes in magnetic resonance signals that are linked to changes in blood oxygenation level-dependency (BOLD) when the brain is engaged in a specific activity, such as responding to a cognitive task. This technique forms the foundation for mapping brain function [17]. One related advancement is resting state functional magnetic resonance imaging (rs-fMRI), which focuses on the natural fluctuations in blood oxygen level dependent (BOLD) signals when a person is not engaged in any specific activity. rs-fMRI is considered a dependable technique for studying the connectivity of different brain networks in youngsters [19]. MEG is used for the identification of functional areas by analyzing the magnetic fields generated by neural activity outside the brain. MEG may also provide localized information on the zones where seizures begin [20], [21]. However, this work does not seek to discuss this particular usage.

No prior comprehensive analysis has been performed to examine all the available published data on advanced functional neuroimaging for children who are candidates for epilepsy surgery. None of the evaluations undertaken for this group have used sophisticated search approaches, such as fMRI [17], MEG [20], [22], or function [23] specific. Furthermore, the vast majority of research investigating the use and effectiveness of fMRI and MEG in mapping the eloquent cortex for epilepsy surgery candidates has been concentrated on adult populations [10]. This research aims to identify and evaluate all previously published publications that use functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG) techniques to map motor, language, and memory performance in children who are potential candidates for epilepsy surgery. Furthermore, the study delineates and evaluates the pertinent clinical, methodological, and statistical aspects. This paper provides an overview of the present state of these approaches and offers suggestions to enhance their consistency and productivity.

Studies have shown evidence that both fMRI and MEG may give information on the lateralization and localization of motor and linguistic processes. The provided data indicated a positive predictive value (PPV) of 74% (95% CI 61–87) for the accurate identification of linguistic lateralization using fMRI with validation. The collected research provide proof that these non-invasive approaches are advantageous. Nevertheless, there is a lack of universally established instructions for healthcare professionals identifying the specific group of individuals who are most likely to have positive outcomes from a certain treatment method. The evidence suggests that these modalities should not be used as screening examinations, but rather utilized to address particular inquiries. Typically, localized lesions are examined to determine their connection to the particular eloquent cortex, whereas for mesial temporal epilepsy, language testing is conducted. There was only one study that specifically aimed to assess memory [23].

2. Memory mapping

Memory mapping refers to the process of assigning sections of a computer's memory to specific addresses for efficient and organized data storage and retrieval. There is just one research that was found and it is connected to memory mapping [23]. The dearth of research examining memory is not exclusive to the pediatric group. There is a scarcity of research publications in the adult population that use fMRI [24-27] or MEG [28] to map memory in individuals with epilepsy. Several findings obtained in this research focus on comparing linguistic mapping results with Wada outcomes and emphasize the possibility of non-invasive functional imaging to replace this invasive treatment. Nevertheless, Wada has both a language and memory component, with the memory component being particularly important, especially when it comes to removing a portion of the temporal lobe in the hemisphere responsible for language dominance [29-33].

3. Memory activation task

The specific memory activation task and the baseline imaging state have an impact on both the degree and the specific area of activation in the hippocampus. Richardson et al. [34] investigated the result of verbal memory and found that more activation on the left side was associated with a bigger decrease. Nevertheless, the outcomes from important research using preoperative hippocampal activation techniques have shown inconclusive results [34-38]. The presence of these discrepancies, together with the challenges in accurately measuring signals due to signal drop out or macroscopic field inhomogeneity [39], has resulted in the use of language lateralisationas a means to forecast post-operative memory. The rationale for this approach is based on the advantages of having a broader area of focus, which leads to fewer challenges in measuring. Additionally, there are separate networks for verbal and non-verbal episodic memory, each with distinct patterns of hemispheric lateralization. It has been found that the lateralization of language is significantly correlated with the lateralization of verbal memory. Binder and colleagues [39] demonstrate that the likelihood of experiencing a decline in verbal memory is more strongly associated with the lateralization of memory networks that are specific to material, and are correlated with the lateralization of language as assessed through tasks involving contrasting semantic and tone decisions, rather than stimuli that result in asymmetry in episodic memory. Although the results presented in this study may be considered preliminary owing to the limited sample size and inclusion of adult participants, it offers valuable insights for developing suitable procedures for pediatric patients.

It is necessary to have paradigm advances for children in order to get the best possible activation and precise prediction of episodic memory degradation before surgery. It is important to acknowledge that the conflicting results regarding hippocampus activation in fMRI language lateralization have led to its use in assessing the danger to memory before surgery. However, it is worth noting that no research has yet tried to develop the best memory activation methods for pediatric patients. This paper does not propose that Wada testing has been discontinued prematurely. However, in order for functional imaging techniques to be a reliable substitute for evaluating paediatric epilepsy patients before surgery, it is crucial to establish protocols that can show agreement with independent measures. Wada is a diagnostic test that might result in failure, indicating a high probability of serious impairment to post-operative memory. The literature that was obtained does not provide any specific criteria for determining failure.

4. Mapping of languages

MEG and fMRI may accurately and non-invasively identify language function in children, and these results align with estimates obtained from Wada and electrical stimulation techniques. These remain constant throughout different scanning sessions and across researchers. There are other options or methods that are also accessible. For instance, ECoG is used to identify the specific regions of the brain responsible for language function in children who are being evaluated as prospective candidates for epilepsy surgery. These data are then utilized to confirm the findings. Nevertheless, the quantity of validation research conducted on youngsters is very limited, necessitating a higher level of meticulousness in regards to stimuli and analysis. A significant number of MEG investigations use comparable paradigms, comprising of spoken nouns and a roster of target nouns that need to be recognized. There has been little research conducted on improving language procedures particularly for children. One of the primary obstacles in MEG research with young persons is to minimize their mobility. In order to do this, it is necessary for scanning processes to be concise while yet guaranteeing sufficient signal-to-noise ratio.

During fMRI, it is customary to provide a letter to the patient using an intercom system, after which they are instructed to mentally produce words that start with that letter. This strategy has been shown to be quite effective. Nevertheless, it might be advantageous to recognize a broader spectrum of linguistic paradigms that are efficacious. For instance, a young patient may have a lower score in phonemic abilities but a higher score in semantic naming abilities. In such cases, it may be more appropriate to use a different language paradigm. These issues are crucial, especially since one of the retrieved publications emphasized the many connections between the language network and the specific kind of cortical lesion [35]. Each person should have distinct particular implementations. For instance, some articles use a 30-second 'on-off' design. Alternatively, if the patient can produce words at a typical speed, a 15-second 'on-off' pattern might be more suitable. This would allow for twice as many repeats within the same time frame, significantly increasing the effectiveness of future statistical tests.

5. Mapping of somatosensory and motor functions

A possible reason for the limited research on mapping the motor cortex in MEG and fMRI studies including children and adults is the use of straightforward procedures and analysis. Both motor and somatosensory paradigms are equally successful in localizing the central sulcus in individuals, making them viable alternatives to other methods for patient groups who are unable to endure other operations. The motor paradigms showed a high degree of consistency across many experiments. Some individuals used auditory cues via an intercom system, while others relied on visual cues. For youngsters who have no difficulty reading, words may serve as cues for movement. Colored images, such as a cartoon hand on a green backdrop and a cross on a red background, may be efficiently used in younger persons. The measured responses are often robust, allowing for the monitoring of the patient's performance throughout the task. To assess bilateral motor function efficiently, the most expedient approach is to alternate the movement of the left and right hands. However, in the case of very young patients, it may be more advantageous to determine the function of each hand separately in order to prevent the patient from disrupting the order of activation. Similar to the motor paradigms previously addressed in MEG, these paradigms generally function well and have a brief duration, despite minor variances. Several studies document the process of scanning infants, which, while more time-consuming and requiring more preparation compared to scanning adults, is undeniably feasible.

6. Summary

Paediatric epilepsies are the predominant and significant neurological illnesses that occur throughout childhood. Surgeries are a very successful kind of therapy, yet in the UK, they account for just around 25% of all medical operations [9]. fMRI is the primary instrument used, and all the studies that were obtained show changes in cerebral blood flow and oscillatory biomagnetic signals that are connected to the stimuli. These strategies were also shown to be effective in infants and toddlers. While there were variations in the precise protocols used, there were accounts of several methods that youngsters could endure and that resulted in meaningful changes in their signals. A significant drawback is the scarcity of functional imaging studies, specifically pertaining to memory, that specifically target the pediatric population. Approximately 76% of the research obtained Level 3 evidence level [25].

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