Functional Imaging in Different Epileptic Syndromes

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Summary

Epilepsy is diagnosed when persisting cerebral dysfunction causes recurring epileptic seizures. Distinction between different epileptic syndromes requires a comprehensive clinical workup, including functional neuroimaging techniques. The most established techniques are single photon emission computer tomography (SPECT), mainly used to detect local blood flow changes during ictal activity, and positron emission tomography (PET) that detects general or local disturbances in metabolism. More recently, simultaneous recording of EEG and functional MRI (fMRI) has become possible, allowing the detection of blood flow changes due to interictal discharges with very high spatial resolution. An alternative approach to these haemodynamic and metabolic functional imaging procedures represents electric source imaging (ESI) based on the recording of multichannel electroencephalogram (EEG). Source reconstruction algorithms co-registered with the MRI of the patient allows precise localization of the abnormal neuronal activity and to follow the propagation of this activity in the brain in real time. EEG recording with a large number of electrodes is now feasible in clinical practice. The role of the functional neuroimaging techniques (ESI, PET and SPECT, fMRI) for evaluation of the different epileptic syndromes is reviewed in this paper.

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Key words: Epilepsy syndromes, EEG, functional imaging

Funktionelle Bildgebung bei verschiedenen epileptischen Syndromen

Die Diagnose "Epilepsie" wird gegeben, wenn eine persistierende zerebrale Störung zu wiederholten Anfällen führt. Die Unterscheidung zwischen den verschiedenen Epilepsiesyndromen erfordert umfassende klinische Untersuchungen, einschliesslich der funktionellen Bildgebung des Nervensystems. Die am längsten etablierten Techniken sind das SPECT (Single Photon Emission Computer Tomography), häufig zur Messung von lokalen Blutflussänderungen während iktaler Aktivität herangezogen, sowie das PET (Positron Emission Tomography), welches Veränderungen des fokalen oder generalisierten zerebralen Metabolismus misst. Seit kurzem ist auch die gleichzeitige Messung von EEG und funktionellem MRI (fMRI) möglich, was eine exzellente Lokalisation von diskreten Blutflussänderungen durch interiktale Entladungen ermöglicht. Ergänzend zu diesen hämodynamischen und metabolischen funktionellen Bildgebungsverfahren ist die so genannte elektrische Quellenanalyse (Electric Source Imaging [ESI]), welche auf der Ableitung von Multikanal-Elektroenzephalogrammen (EEG) basiert. Algorithmen zur Quellenanalyse erlauben die präzise Lokalisation der initialen abnormen neuronalen Aktivität in dem Patienten-MRI sowie die Propagation dieser Aktivität in Echtzeit. EEG-Ableitungen mit einer sehr hohen Elektrodenzahl sind nun im klinischen Alltag machbar. Die Rolle der funktionellen Bildgebungsverfahren (ESI, PET and SPECT, fMRI) für die Evaluation der verschiedenen Epilepsiesyndrome wird in dem vorliegenden Manuskript diskutiert.

Schlüsselwörter: Epilepsiesyndrome, EEG, funktionelle Bildgebung

Imagerie fonctionnelle de différents syndromes épileptiques

Le diagnostic de l'épilepsie est posé lorsqu'un dysfonctionnement cérébral persistant provoque des crises d'épilepsie. La distinction entre les différents syndromes épileptiques nécessite un bilan clinique complet incluant notamment les techniques d'imagerie cérébrale fonctionnelle. Les techniques les plus utilisées sont la Tomographie à Emission Mono Photonique (TEMP-SPECT), qui permet principalement de visualiser les variations locales de débit sanguin dues à une activité ictale, et la Tomographie à Emission de Positrons (TEP-PET), qui permet de déceler les perturbations locales du métabolisme cérébral. Plus récemment, les progrès techniques ont permis l'enregistrement simultané de l'EEG et de l'IRM fonctionnelle (IRMf-fMRI). Cette technique permet de localiser avec une grande précision spatiale les variations de débits sanguins associés à la présence d'anomalies épileptiques à l'EEG. La reconstruction des sources électriques (ESI) est une approche complémentaire aux mesures de variation du débit sanguins et du métabolisme. Cette technique est basée sur les enregistrements EEG multicanaux. La reconstruction

de source électrique dans l'IRM des patients permet de localiser de manière précise l'activité neuronale anormale. De plus, la résolution temporelle de l'EEG permet de suivre, en temps réel, la propagation des activités épileptiques. L'enregistrement EEG de haute résolution (128 ou 256 canaux) est maintenant possible dans un environnement clinique. Cet article examine le rôle de ces différentes techniques d'imagerie fonctionnelle (ESI, PET, SPECT et fMRI) dans l'évaluation et le diagnostic des différents syndromes épileptiques.

Mots clés : Syndromes épileptiques, EEG, imagerie fonctionnelle

Introduction

Epilepsy is one of the most common serious brain disorders, which can occur at all ages and has different possible presentations and causes. The two major categories of epilepsies and epilepsy syndromes are referred to as localization related (also: focal or partial epilepsy) or generalized [1]. Seizures that originate from focal brain regions are termed localization related epilepsy whereas generalized epilepsy is characterized by seizures with diffuse bilateral cerebral involvement, either directly at onset (primary generalized) or as endpoint in the evolution of a focal seizure (secondary generalized). In both cases, "generalized" implies the recruitment of bilateral cortical and subcortical structures. While the role of the neuroimaging methods in localization related epilepsies is obvious (to define the epileptic focus with high spatial precision), their application in generalized epilepsies is less frequent. However, recent functional imaging studies in generalized epilepsies indicate the possibility that some of them in fact might have a focal origin, and that location in deep brain structures or very fast propagations might lead to an erroneous classification of these epilepsies.

Magnetic resonance imaging (MRI) is the primary imaging modality that guides clinicians in the determination of the syndrome, treatment and prognosis of epilepsy because of it's capability to detect cerebral structural abnormalities [2]. Identifying a structural lesion alone is not always a reliable indicator of identifying the site of seizure onset, and many focal epilepsies do not have visible structural lesions. Therefore, the functional imaging methods like single photon emission computer tomography (SPECT) and positron emission tomography (PET) have become important tools in the clinical evaluation of epilepsy. These methods allow to localize and measure blood flow changes between ictal and interictal states (SPECT), or to determine the sites of metabolic deficit (PET). In the last decade, functional magnetic resonance imaging (fMRI) has been investigated as a tool for focus localization; as a result of the possibility to record the patient's scalp EEG in the scanner.

Despite these sophisticated modern neuroimaging techniques, the EEG, in conjunction with the seizure semiology assessed with synchronized video recordings, remains the most important tool for the diagnosis of epilepsy and the classification of seizure types and epileptic disorders. EEG alone has the temporal resolution that allows the precise characterization of neuronal activity at the moment of initiation and during different stages of propagation of the epileptic activity. Since the principal characteristic of epileptic activity is the fast (within milliseconds) propagation to different areas in the brain, this feature of EEG is crucial. In recent years, mathematical algorithms became available allowing the localization of the neuronal activity in the brain based on multichannel scalp EEG. These electric source

imaging (ESI) techniques have also been applied successfully in patients with pharmacoresistant epilepsy. The possibility to quickly record the EEG from a large number of electrodes (up to 256 channels) makes ESI a valuable clinical tool in the evaluation of epilepsy [3-5]. In this review, we illustrate the use of these different functional imaging techniques (ESI, PET and SPECT, fMRI) in the diagnosis and evaluation of different epileptic syndromes.

A. Localisation related epilepsies

1. EEG Source imaging

Electric source imaging (ESI) is increasingly being recognized as a valuable noninvasive technique to localize the epileptic focus in partial epilepsies. The method has mostly been applied to the analysis of interictal epileptic activity [6] but some studies have also looked into its ability to localize the onset of seizures [7]. In combination with high resolution EEG systems (128-256 channels), source imaging in epilepsy is now possible with excellent localizing precision [8].

In a recent study we showed that ESI applied to standard clinical EEG recordings provides good localizing precision, particularly in extratemporal lobe epilepsy [9]. Preoperative EEGs recorded from 19 to 29 scalp electrodes in 30 pediatric patients were reviewed, and interictal epileptiform activity was analyzed by using a linear source-imaging procedure in combination with statistical parametric mapping. The ESI localization was considered as correct when the majority of the active voxels were within the resected area that rendered the patients seizure-free or almost seizure free. In 90% of the patients, the ESI result was correct. This number compared favorably with the results from the other functional imaging techniques in the same patients (PET correct in 82%; ictal SPECT correct in 70%). In the cases with extratemporal epilepsy, ESI was correct in all cases (100%), however, in those with temporal lobe epilepsy, only 10 of 13 (77%) cases were correct. In two of the three patients with incorrect ESI, a 128-channel recording was performed, leading to correct localization in both cases. Thus, while ESI analysis based on routine long-term recordings with a limited electrode number provided already good localization in patients with extratemporal lobe epilepsy, patients with basal temporal foci benefit from larger electrode set-ups, since these foci are outside the standard electrode array.

Further, we evaluated the question of how many electrodes are needed to correctly identify the epileptic focus. 14 patients with partial epilepsy were recorded with 123-channel EEG [8]. Epileptic discharges were determined on the basis of the 123-channel recordings and the electrode configuration was later downsampled to 63 and 31 electrodes. The correct underlying sources were then estimated for the three different electrode configurations, by determining the distance from the inverse solution maximum of each single spike to the epileptogenic lesion. In 9/14 patients, ESI was significantly more precise with 63 than with 31 electrodes, and increasing the number of electrodes to 123 increased this number of patients from 9 to 11. Thus, multichannel EEG recordings are an effective clinical tool, allowing significant higher source location accuracy.

In a subsequent study, we evaluated prospectively the clinical yield and localization precision of 128-channel scalp EEG source imaging of interictal epileptic activity in a consecutive series of patients with intractable epilepsy of various causes, including children and adults [4]. Presurgical workup identified a focal epileptogenic area in 32 patients and ESI correctly localized this area in 30 of these patients (93.7%). The sub-lobar precision of the ESI was evaluated in the subgroup of 24 patients who were operated by calculating the distance of the source maximum to the resected area. The analysis revealed zero distance in 19 cases (79%). These results indicate that the yield of ESI is comparable to other imaging procedures which are currently used in the presurgical workup of patients with intractable partial epilepsy.

Interictal epileptiform discharges (IEDs) represent a very specific marker of epilepsy, the delineation of the irritative zone being of particular interest for presurgical evaluations of epileptic patients. Although the irritative zone in most cases is concordant with the seizure onset zone [10], this is not necessarily always the case [11]. Therefore, comparison of interictal and ictal epileptic activity is needed. Studies on ictal EEGs are rare [12], and to date, no data with multichannel EEG are available. Scalp long-term monitoring with 128 or 256 electrodes EEG is now possible, however, the methods that reliably identify the time point of seizure onset are required, either based on temporal [13] or frequency analysis of the EEG [14]. It is thought that appropriate algorithms which reliably localize ictal and interictal EEG activity will diminish the need for invasive recordings.

2. PET and SPECT in partial epilepsies

Visualization of increased focal cerebral blood flow (CBF) during seizures and its comparison with interictal blood flow form the basis of SPECT imaging. Imaging of cerebral metabolism, most often measured with a radioactive glucose tracer, is carried out with PET and has also an important role in presurgical epilepsy evaluation, particularly in MRI-negative partial epilepsy [15] and focal cortical dysplasias. Peri-ictal SPECT imaging of CBF has good accuracy in determining the region of ictal onset, but may also show areas of pre-

dominant propagation in refractory partial epilepsies [16, 17]. When the radiopharmaceutical agent is injected during the electrographic seizure or within 30 seconds after the seizure, over 90% of patients with unilateral temporal lobe epilepsy (TLE) have regional hyperperfusion in the affected temporal lobe [18]. Extratemporal seizures are often brief and difficult to localize. Studies have shown that ictal SPECT also has a high diagnostic yield in extratemporal epilepsies [19] albeit somewhat lower than in temporal lobe epilepsies. Sensitivity and spatial accuracy of ictal SPECT findings can be enhanced by using subtraction analysis methods between ictal and interictal SPECT images, coregistered with the patient's MRI [20].

SPECT-studies also help in better understanding the neuroanatomical correlates of certain aspects of the seizure semiology. Partial seizures that cause greater impairment of consciousness (without causing a full generalized tonic-clonic seizure) are more likely to show hyperperfusion of the thalami and midbrain, in addition to cortical hyperperfusion, than are simple partial seizures [21, 22]. Greater impairment of consciousness and the presence of motor phenomena during seizures are associated with greater CBF increases in the contralateral hemisphere [23]. Focal seizures can also be seen when originating in deep structures as shown in a SPECT-study of a patient with hypothalamic hamartoma [24].

In patients with mesial temporal lobe (mTLE) epilepsy, the area of hypometabolism as determined by the PET often exceeds the temporal lobe; the significance of this is poorly understood. Nelissen et al. found that

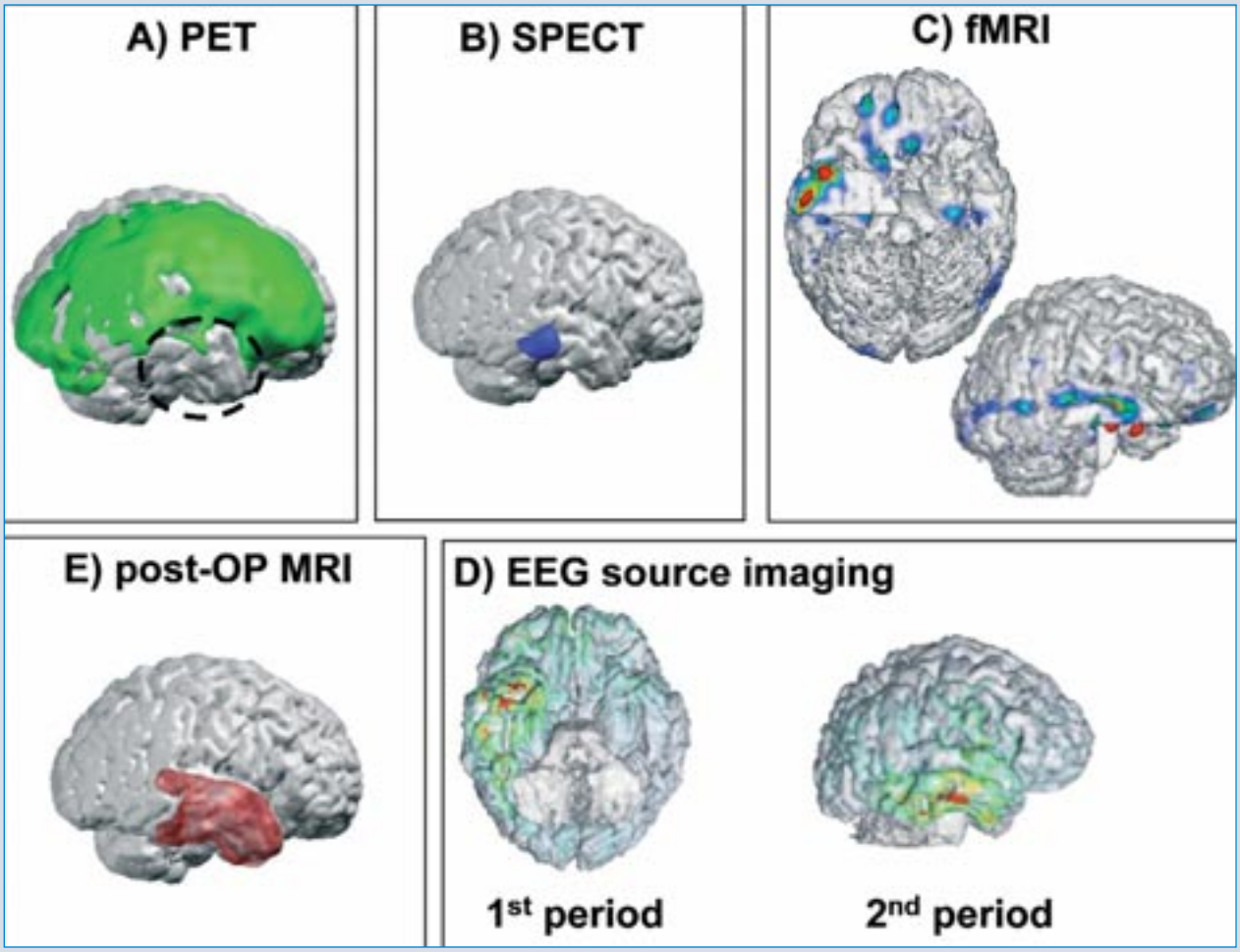

Figure 1: Multimodal functional neuroimaging in a 43 year-old right-handed lady suffering from pharmaco-resistant partial epilepsy since 12 years. The structural MRI did not show any abnormality. The long-term Video-EEG monitoring indicated a seizure focus in the right mid- to posterior temporal lobe. FDG-PET (A) showed hypometabolism (not green) in the right mid- to posterior temporal lobe. The ictal SPECT (B) revealed increased blood flow in the right middle temporal lobe (blue area). EEG-triggered functional MRI (C) showed several areas of increased BOLD response in the right middle and posterior temporal lobe, also in the anterior pole of the right temporal lobe. The electric source imaging based on the scalp EEG (D) showed a temporal propagation of the interictal activity from the anterior pole of the right temporal lobe (1st period) to mid-and posterior areas of the temporal lobe (2nd period). Similar seizure propagation was later found in the intracranial EEG. The surgery included the resection of the right anterior and middle temporal lobe, sparing the posterior part (E).

interictal hypometabolism in mTLE-patients was also important in the ipsilateral frontal lobe, and probably reflects a seizure-related dynamic process [25]. The authors proposed that the surround inhibition in the frontal lobe is a defense mechanism against seizure propagation, and may be responsible for other neuropsychological deficits frequently observed in mTLE.

In extratemporal localization-related epilepsies, interictal FDG PET often demonstrates a region of pathological hypometabolism, both in adults and children [26]. Many individuals with lesional or non-lesional neocortical localization-related epilepsies have a more widespread hypometabolic zone, which has graded transitions from areas of severe hypometabolism to areas of normal metabolism, similar to patterns of hypometabolism in limbic TLE. However, the zone of most severe hypometabolism, excluding the site of a foreign-tissue lesion, usually contains the electrophysiologically defined ictal onset zone. In any case, the correct interpretation of SPECT or PET images require EEG monitoring before, during and probably also after image acquisition, in order to understand the exact cerebral condition at the moment of tracer injection.

3. EEG triggered functional MRI

In the first EEG-fMRI recordings, Warach et al. studied interictal activity in two patients, one of them with generalized epilepsy that showed, surprisingly, a focal response [27]. Most of the subsequent studies looked at spikes in patients with different focal epilepsy syndromes [28, 29, 30, 31]. In many cases, blood oxygenation level dependent (BOLD) activations concordant with the lesion were found, i.e. EEG–fMRI is able to provide localizing information on the generators of the discharges [32]. In some cases, the concordance of the "real" focus was confirmed with intracerebral recordings [33]. However, more work remains to be done to obtain a better understanding of the meaning of BOLD signals. The main problem is that not one but several brain areas show increased BOLD responses, probably due to propagation of the epileptic activity. In these cases the fMRI alone cannot unambiguously define the primary epileptic focus. It is also not yet clear to which extent the BOLD response is related to abnormal neuronal activity and is of functional significance for the patient. For example, extensive BOLD changes related to brief focal electrographic seizures have been described in a patient with right temporo-parietal gray matter nodular heterotopia [34]. The brief focal seizures resulted in high amplitude and widespread signal enhancement. Such brief events could have important behavioural and cognitive consequences despite absent overt manifestations.

B. Generalized epilepsies and syndromes

In the current concept of generalized seizures, idiopathic (primary) generalized seizures, with bilateral diffuse onset, and secondary generalized seizures are distinguished. While it is generally acknowledged that in idiopathic generalized epilepsy (IGE) there are no overt structural abnormalities, recent MRI studies suggest that there may be subtle alterations [35]. In quantitative magnetic resonance imaging studies, increased gray matter versus decreased white matter structures have been found, pointing to aberrant connections between cortical and subcortical structures, which involves both hemispheres [36, 37] .

1. EEG source imaging

Absence seizures were recorded with dense-array 256-channel scalp EEG in five subjects with primary generalized epilepsy [38]. Source analysis was applied to the spike components of each spike-wave burst in each seizure. The onset of seizures was typically associated with activation of discrete, often unilateral areas of the dorsolateral frontal or orbital frontal lobe. Although each patient showed unique features, the absence seizures of all patients showed rapid, stereotyped evolution to engage both mesial frontal and orbital frontal cortex sources during the repetitive cycles of spike-wave activity. This study indicates that absence seizures may not be "generalized" in the sense of simultaneous diffuse activation but involve highly localized activations from mesial frontal and frontopolar sources in both hemispheres.

Focal, in particular frontal, seizures with rapid contralateral propagation may mimic primary generalized epilepsy. ESI should have the capacity to differentiate both conditions, which implies different treatment and prognosis. Rapid contralateral propagation, also termed secondary bisynchrony, has been investigated in patients with tuberous sclerosis (and multiple lesions ["tubers"] in both hemispheres). Seri et al. studied the topographic relationships between cortical and subcortical lesions shown on magnetic resonance images (MRI) and sources of epileptiform activity in a series of nine children with intractable epilepsy and tuberous sclerosis complex [39]. Although video-EEG monitoring was suggestive of a unilateral frontal seizure onset, interictal EEG was, in seven of nine cases, in the form of apparently bisynchronous discharges. In all cases, the use of a short time lag estimation procedure based on a nonlinear correlation function between surface recorded EEG signals allowed the detection of a lateralized onset of EEG paroxysmal activity. Furthermore, ESI co-registered with the patient's MRI provided good topographic concordance between well-defined frontal cortical lesions shown on MRI and site of onset of "generalized" discharges. These findings are of major

relevance for the patient's care, since focal onset in one tuber offers the possibility of surgical epilepsy treatment whereas the presence of diffuse, truly bilateral discharges does not.

2. PET and SPECT in generalized epilepsies

SPECT is not very often used in generalized epilepsy. Nehlig et al. reported cerebral blood flow changes during the ictal and postictal phases of typical childhood absence seizures in four children aged 10-13 years at the time of scan [40]. One scan was performed during the ictal phase and showed diffuse blood flow decreases, while the three other scans performed during the postictal phase, showed generalized blood flow increase. These data indicate that functional alterations may not be limited to the thalamo-cortical circuit, a network considered crucial for the development of absence seizures.

Interictal FDG PET studies have been reported as "normal" in primary generalized epilepsies [41] although 18FDG-PET with SPM analysis showed multifocal hypometabolic areas in a study in children with cryptogenic generalized tonic-clonic seizures (GTCS) from infancy [42]. Using PET, regional cerebral blood flow (rCBF) was measured in eight patients with idiopathic generalized epilepsy in whom typical absence seizures were induced by voluntary hyperventilation [43]. There was a mean global 14.9% increase in blood flow in association with typical absence seizures and a focal increase in thalamic blood flow of 3.9 to 7.8%. There were no significant focal changes in rCBF in the 30 seconds before the onset of spike-wave activity on the EEG. This study provides evidence for the key role of the thalamus in the pathogenesis of absence seizures.

Studies of interictal 11C-flumazenil binding in idiopathic generalized epilepsy have not given uniform results. In one investigation a slight reduction was reported in the neocortex of patients with idiopathic generalized epilepsy in comparison with patients with partial seizures along with increased benzodiazepine receptor density in the cerebellar nuclei and decreased density in the thalamus [44]. Widespread increases in central benzodiazepine receptors (cBZRs) also have been reported in cerebral neocortex, thalamus, and cerebellar cortex [44].

Infantile spasms are age-specific epileptic phenomena with many underlying etiologies and present as generalized seizures, in terms of seizure presentation and in the EEG. However, they may originate from a single lesion. Studies suggest that infantile spasm-associated malformations of cortical development are more likely to be detected in the PET than in the MRI. Unilateral cortical metabolic dysfunctions (hypo- or hypermetabolism) have been reported in West's syndrome [45]; however, many infants have both unilateral cortical metabolic dysfunction and bilateral lenticular and brainstem metabolic dysfunction [46]. Bitemporal hypometabolism is less common, occurring in approximately 15% of infants with spasms [47]. It is thought that infantile spasms begin with a focal cortical abnormality, which induces brainstem activities that are projected symmetrically to the basal ganglia and spinal cord, therefore, unilateral cortical resection can result in the cessation of these spasms. Pathological examination of the resected tissue in patients with West syndrome who underwent surgery typically reveals cortical dysplasia [48]. Functional cerebral imaging PET and SPECT have shown hypometabolism and hypoperfusion in the area of vascular malformation in children with epilepsy due to Sturge-Weber syndrome [49, 50]. In these patients with refractory epilepsy, PET has been useful both in guiding the extent of focal cortical resection and in assessing candidacy for early hemispherectomy.

Patients with the Lennox-Gastaut syndrome have multiple regions of bilateral cortical hypometabolism interictally on FDG scans, but sometimes have predominantly unilateral hypometabolism, when patients with structural lesions are included [51]. A series of 32 children with "cryptogenic epileptic encephalopathies", which presumably included mainly children with secondary generalized epilepsies, demonstrated generalized metabolic dysfunction in most cases, regional metabolic dysfunction in some cases, and normal metabolism in only two cases [52]. The FDG scans in this series detected thalamic hypometabolism in 90% of cases, which was usually bilateral, but thalamic metabolism was lower on the side of more severe cortical hypometabolism.

Unilateral focal or multifocal sites of hypermetabolism during sleep, with more nearly normal cerebral glucose metabolism during waking, are typical of electrical status of slow wave sleep [53]. The sites of metabolic dysfunction were found mainly in the association cortex. This childhood syndrome of continuous generalized spike-and-wave discharges during slow wave sleep (CSWS), usually with dementia or progressive aphasia, and with clinically evident epileptic seizures, thus provides another example of secondary generalized epilepsy where generalized EEG phenomena are associated with focal or multifocal cortical metabolic dysfunction.

3. EEG-fMRI in generalized epilepsy studies

The first series in generalized epilepsy patients explored photosensitivity, but later on, emphasis was placed on spontaneous generalized discharges, showing involvement of the thalamus and the presence of widespread frontal, parietal and posterior cingulate region deactivation. Archer et al. performed a study that included five patients with generalized epilepsy, four of whom showed both activation and deactivation [54]. Activations involved different cortical areas and

the thalami (in two studies), and deactivations were seen in the posterior cingulate regions. In a group analysis, they confirmed this consistent posterior cingulate deactivation and found scattered activation in the precentral sulci, bilaterally, but no response in the thalami.

Aghakhani et al. studied a group of 15 patients with idiopathic generalized epilepsy (IGE), selected on the basis of frequent bursts of generalized spike or polyspikes and wave activity. In this group, 14 of 15 studies (93%) in which EEG bursts were present showed a response. Responses were found in the thalamus, most often in the form of activation (increased BOLD), and were widespread, bilateral and symmetrical in the cerebral cortex, predominantly in the form of deactivation (decreased BOLD). This study clearly demonstrated an involvement of the thalamus in generalized spike-wave bursts of IGE, providing further evidence for the thalamocortical circuit involvement in the generation of interictal and ictal spike-and-wave activity [55]. In contrast to the predominantly frontal EEG distribution of the spike-and-wave activity, the BOLD response was more diffuse and the posterior regions were almost as involved as the frontal areas. A group analysis later performed in this series of IGE patients [56], showed bilateral activations in the thalamus, mesial frontal region, insulae, midline cerebellum and on the borders of the lateral ventricles. Deactivations were found bilaterally in the anterior frontal and parietal regions and in the posterior cingulate gyri, in a pattern very similar to that seen in the default or resting state of the brain.

Salek-Haddadi et al. described ictal EEG-fMRI results in a patient with juvenile absence epilepsy, who had four absence seizures with generalized spike-wave discharges during the 35-minute scanning period [57]. They also found bilateral thalamic activation and widespread symmetrical cortical deactivation with frontal predominance.

In summary, EEG-fMRI studies in generalized epileptic discharges show a widespread activation involving both anterior and posterior head regions, with important involvement of the thalami. Deactivation seems to follow the spatial distribution seen in the resting mode of the brain, and might represent the effect of the bursts of discharges on normal brain function.

Conclusions

A variety of structural lesions and neurochemical disturbances are associated with epilepsy, often also outside the structures that are supposed to be implicated. The dissociation between localization related and primary generalized epilepsy is of utmost importance for proper diagnosis and treatment. Modern brain imaging techniques help in correctly classifying the underlying syndrome. Studies indicate that many of the epilepsies that are usually considered as generalized might in fact be due to a focal structural or functional abnormality. The combination of the different imaging techniques allow to identify these focal abnormalities with high spatial precision. Precise localization of a focal abnormality may lead to successful surgical intervention in cases that have so far not been considered as surgical candidates.

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