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Analysis of Dynamics and Propagation of Parietal Cingulate Seizures with Secondary Mesial Temporal Involvement

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Summary

Cingulate onset seizures, particularly those originating from parietal cingulate regions are inadequately described and confounded by patterns of propagation. We analyzed scalp and depth electrode recordings in a patient whose seizures originated from a lesion in the right posterior cingulate region and produced secondary seizure activity in ipsilateral mesial temporal structures. Analyses included the matching pursuit (MP) method of time-frequency decomposition and the Gabor atom density (GAD) measure of signal complexity. Although scalp recordings suggested a right temporal onset, seizures recorded with depth electrodes clearly began in the parietal cingulate region before producing a secondary discharge in ipsilateral mesial structures. GAD revealed a significant increase of complexity during ictal cingulate activity and a consistent pattern of subsequent complexity changes in the hippocampus 30 seconds later. MP and GAD measures were valuable supplements to confirm the stereotyped pattern of both time-frequency changes and complexity. This provides additional evidence for pathways between the parietal cingulate region and mesial temporal structures and raises questions as to whether parietal cingulate seizures can produce clinical symptoms independent of regional or remote propagation.

Keywords

Posterior cingulate seizures; Depth electrodes; Seizure dynamics; Gabor atom density (GAD); Matching Pursuit

Introduction

Seizures with similar semiology may originate from disparate brain regions because of propagation from relatively silent cortical regions to more remote areas that produce clinical manifestations. Posterior cingulate seizures, an uncommon subset of parietal lobe seizures, are poorly understood because their patterns of propagation often confound both the classification of clinical semiology and attempts at seizure localization. While more is thought to be known about the semiology and patterns of spread of anterior cingulate gyrus seizures [1-5] than those

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originating in the posterior cingulate region, these more anterior seizures also propagate to produce remote symptomatology. In the rare reports [6,7] where seizures originating in the area of the parietal cingulate gyrus are described, a diagnosis of temporal lobe epilepsy was initially made based on clinical and EEG findings, indicating a propagation pathway from the parietal cingulate area to temporal structures. Conversely, one of the propagation pathways for seizures originating in the hippocampus is to the retrosplenial cingulate gyrus [8]. Accurate determination of seizures originating from the cingulate requires targeted recording arrays since these regions are not routinely sampled even with intracranial recordings.

We present analyses of intracranial recordings of seizures originating from the right posterior cingulate region and propagating to the right mesial temporal structures, producing clinical manifestations in a patient with a known parietal cingulate lesion. Detailed analyses of ictal onset and propagation patterns are done using the Gabor atom density (GAD), a measure of signal complexity derived from the matching pursuit (MP) method for time-frequency decomposition [9]. Multichannel GAD analysis facilitates identification of seizure onset and propagation patterns [10,11].

Methods

Patient History

A 22 year old right-handed male student presented with over a year history of complex partial seizures with rare secondary generalization. Seizures produced staring, unresponsiveness, late oral automatisms, and post-ictal confusion. Less consistently he would have abnormal posturing of his left hand during the seizures. His seizures occurred several times per month despite high therapeutic levels or doses of five antiepileptic drugs.

Imaging

MRI revealed a 1 cm × 0.9 cm × 0.7 cm cortical-based mass in the posterior aspect of the right cingulate gyrus with hypointensity on T1 weighted images and bright signal on T2 weighted images (Fig. 1) and no significant mass effect. The hippocampi were normal in appearance. Serial MRI showed no change in the lesion. MRS of the lesion showed a mild reduction in N-acetyl acetate (NAA) compared to the contralateral hemisphere, with normal levels of creatinine and choline. Positron emission tomography (FDG-PET) revealed moderately decreased activity in the right lateral temporal lobe, in addition to a hypometabolic defect corresponding to the posterior cingulate gyrus mass. Functional MRI (fMRI) revealed the motor regions for toe and hand movements to be anterior to the mass.

Video-EEG Studies

The patient underwent continuous video-EEG monitoring with scalp electrodes for seven days. Ten stereotypical seizures were recorded. The ictal EEG (Fig 2A) was typically characterized by an initial buildup of rhythmic 2-5 Hz activity in the right temporal region that evolved to 8-9 Hz activity. The interictal EEG showed right anterior to mid-temporal spikes and spike-wave complexes, mainly during sleep. No epileptiform activity was seen on the left.

Because of the known cingulate lesion, there was concern that the apparent right temporal seizure onset might reflect secondary spread, so during a subsequent admission, ictal recordings were done following placement of depth electrode arrays targeting the right amygdala, the right hippocampus, and the posterior cingulate lesion. Post-operative MRI confirmed excellent placement of the depth arrays with the deepest contact of the cingulate probe close to or within the cingulate lesion (Fig 1C, 1D).

Analysis of Ictal Dynamics

Intracranial EEGs (ICEEGs) were recorded on a Stellate system at a sampling rate of 1000Hz. All signals were pre-filtered by a 300Hz low pass filter. Time frequency analyses were performed using the MP method which allows the signals to be described as a sum of Gaussian-modulated sinusoidal functions [9]. The complexity of the EEG signal is computed based on the number of those functions needed to represent the EEG and is expressed as the Gabor atom density (GAD) [10,11]. Results from these analyses are represented by a reconstructed image showing the time and frequency repartition of the energy of the signal. The GAD represents the complexity of the EEG signal over time. GAD increases have been previously shown to correlate with seizure onset and duration [10,11]. GAD measurements were made to supplement seizure detection and propagation patterns.

Results

During monitoring with depth electrodes, the patient had three stereotypical complex partial seizures which started with cessation of activity, staring, and confusion, and were associated with amnesia for the events. Electrographically, the seizures began with a right cingulate burst followed by low voltage, 40 Hz activity (Fig 2B). After 20-30 seconds, the mesial temporal depth contacts developed prominent secondary organized rhythmic activity of 6-8 Hz frequency. Frequent interictal epileptiform discharges were seen in the right amygdala and hippocampus, without preceding or concomitant epileptiform activity in the parietal cingulate region.

Analysis of Seizure Dynamics

The time-frequency MP analysis of one seizure with hippocampal and cingulate recordings (the seizure in Fig 2B) is illustrated in Figure 3A and 3C respectively. In addition, the GAD plot of complexity is shown. GAD plots for all three seizures are shown in Fig 3B and 3D. Both the MP plots and the GAD plots clearly show the cingulate onset prior to hippocampal involvement. The MP plots reveal both the initial sharp activity in the cingulate followed by gamma frequency activity (predominantly 25-40 Hz). The increase in signal complexity as measured by GAD occurs first in the posterior cingulate region followed about 30 seconds later by GAD increases in the hippocampal electrodes. The MP and GAD plots, particularly for the early seizure epochs, are similar for all three seizures. The hippocampal activity is of different time-course and predominant frequency suggesting that this is secondary activity, triggered by, but not originating from the cingulate region. The predominant organized rhythmic activity is 7-8 Hz, typical for mesial temporal generators of seizure activity. All seizures terminated around 60 seconds after the propagation to the hippocampus. The cessation of epileptic activity is marked by the return of GAD to baseline level or below when there is postictal EEG depression.

Surgical Pathology and Outcome

Histopathology of the resected lesion revealed mucopolysaccharide-rich tissue of low cellularity with some atypical nuclei, but no proliferative index. No cells were positive on immunohistochemistry for MIB-1. Stains were not specific for either glial or neuronal cells. The myxoid matrix and minimally atypical nuclei are consistent with a dysembryoplastic neuroepithelial tumor (DNET); however, DNET could not be confirmed as there was no clear glialneuronal component. There was no histological evidence of glioma, pleomorphic xanthoastrocytoma or ganglioglioma and the imaging features were consistent with DNET (e.g. Low T1 and high T2 signal). In addition, there has been no recurrence of the mass two years after resection and the patient remains seizure free on reduced antiepileptic monotherapy.

Discussion

In contrast to the more common reports about anterior cingulate seizure manifestations, little is known about posterior cingulate seizures. Wada and Tsuchimochi kindled the posterior cingulate cortex in the Senegalese baboon *Papio papio* producing nonconvulsive seizures characterized by staring [12]. The ictal discharge in these animals was lateralizing to the kindled hemisphere. In the few reports from humans, parietal lobe seizures [13], including those arising from the parietal cingulate gyrus [7], may become manifest clinically only after they spread to other brain regions. Ictal propagation patterns from parietal foci may result in false localization [13]. Whether discharges from the posterior cingulate can produce clinical manifestations without propagation is not resolved. Although clinical symptoms (somatosensory, somatomotor, visceral, emotional, affective behavioral) have been reported in some patients with stimulation of the parietal cingulate gyrus without an afterdischarge, it cannot be established that other brain regions were not involved [8].

The initial ictal discharge in one patient with epileptic nocturnal wanderings was localized to the right temporal lobe with secondary propagation to the cingulate gyrus, including the parietal cingulate cortex [14]. A patient with somnambulism had SPECT activation in the vermis and the posterior cingulate gyrus [15], and another patient with a medial parietal vascular lesion presented with temporal lobe seizures [8]. Williamson et al. [16] concluded that interictal and even ictal EEG findings in parietal lobe epilepsy were unhelpful.

In a retrospective study of 10 patients who underwent surgery for presumed parietal lobe epilepsy, five patients had complex partial manifestations, of whom three had no auras [6]. Interestingly, the EEG of a patient who had a cavernous angioma in the medial parietal region posterior to the splenium of the corpus callosum showed ipsilateral midtemporal spikes interictally, and bitemporal ictal activity. Thirteen months after resection of the cavernoma, surgical outcome was class I. The authors confirmed previous observations that scalp recordings could be an unreliable indicator of parietal epileptic foci, and disagreements between scalp recordings and neuroimaging should invite further assessments. Similarly, in our patient interictal epileptiform discharges appeared to occur independently in the mesial temporal region, without concomitant activity in the medial parietal region, and seizures were controlled after resection of the cingulate lesion. Cascino et al. found that the initial ictal symptoms in parietal lobe epilepsy often reflected areas of seizure propagation [6]. In addition, misleading EEG findings in parietal lobe epilepsy can, at least in part, account for some of the surgical failures in non-lesional epilepsy patients [13].

Interestingly, although the MRI in our patient with thin cuts through the temporal lobe revealed no evidence of hippocampal atrophy or sclerosis, the interictal PET imaging showed mesial temporal hypometabolism. This is possibly a secondary phenomenon; a post-operative PET has not been performed.

The above reports as well as the patient reported here support the presence of connectivity between the posterior cingulate gyrus and the hippocampal formation. One of the preferential pathways of seizure propagation from the parietal lobe is to the temporal lobe [13,16]. The posterior cingulate cortex is known to project to the hippocampus via the entorhinal cortex [17] and to receive connections from the hippocampus, possibly via the thalamus [18]. In a report of 36 patients with TLE who were monitored with stereo-EEG, ictal propagation to the cingulate gyrus was frequent [19].

There is growing interest in more detailed analysis of ictal onset patterns, particularly high frequency activity. While routine intracranial EEG here reveals the cingulate onset of the seizures, the time-frequency maps highlights and quantifies the high frequency content. Both the time-frequency and GAD analyses also document the remarkable similarity in dynamics

between all recorded seizures. The report presented here provides detailed analyses of symptomatic seizures clearly originating from the posterior cingulate region that produced no clinical manifestations until there was subsequent temporal lobe involvement. This supports the importance of connectivity (direct or indirect) between the posterior cingulate gyrus and temporal lobe and secondary epileptogenesis. Although independent interictal discharges were seen from the mesial temporal regions, no seizures originate independent of cingulate onset. Any conclusions regarding clinical manifestations of cingulate seizures must include sampling from temporal and adjacent parietal regions to determine whether these symptoms reflect seizure propagation. Additional sampling of the cingulate region with targeted recording arrays should perhaps be considered more often in patients with temporal lobe ictal manifestations and no clear temporal lobe focus or lesion. Time-frequency and GAD analyses can be valuable supplements to visual analysis of the seizure onset and propagation.

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Figure 1.

Axial T2 weighted image (A) and sagittal T1 weighted (B) images show the lesion (arrows), centered in the posterior cingulate gyrus. There was only mild patchy enhancement (not shown) and no significant edema or mass effect. Panel C shows a coronal T2 image with a depth contact proximal to the lesion, and panel D shows a sagittal T1 image with the location of another depth electrode. Not all depth contacts are visible because the trajectory of the depth arrays was not in the plane of the MR sections.

A - Scalp EEG

B - Intracranial EEG

Figure 2.

Panel A illustrates one of ten seizures recorded with scalp arrays suggesting a right temporal lobe seizure onset. The ten seizures were similar clinically and electrographically. Scalp recordings were done prior to depth recordings.

Panel B illustrates one of the three seizure recorded with intracranial depth electrode arrays; the two ICEEGs are continuous. A prominent spike is seen from the cingulate region followed by low voltage fast activity better illustrated in the exploded view. Later prominent activity is recorded from the right hippocampal and amygdalar electrodes. No clinical signs or symptoms were seen or reported until the temporal lobe involvement with the seizures. All three seizures recorded with intracranial arrays were similar clinically and electrographically.

Figure 3.

Panels A and C are time-frequency decompositions using the matching pursuit method for the same time periods after seizure onset (time 0) as for the seizure shown in Fig. 2B recorded with intracranial depth arrays; all seizures had similar patterns. The energy of the signal is color-coded (blue is low energy, red is high energy). The GAD is plotted as a black line representing the composite complexity of the signal for the same time period. The cingulate recording (from contact 2-3, see Figure 2B) shows the clear onset in the cingulate region and the gamma frequency bands as well as the increase in complexity represented by increased GAD. No GAD increase or ictal activity is identified in the mesial temporal recordings (hippocampal 2-3 shown) until approximately 30 seconds after seizure onset. At this time prominent activity is present in the hippocampus (7-8 Hz with associated harmonics). Only the first 45 seconds of the seizures are shown on the time-frequency maps. On the right two panels (B and D) the GAD plots for all three seizures are shown for the entire seizure duration showing the similar patterns for all three seizures supporting the cingulate origin of all three seizures with similar latencies of spread to hippocampal regions. The black GAD plot in panels B and D is the same as in panels A and C.