


Reflex Seizures Triggered by Exposure to Characters With Numerical Value: A Case With Right Temporal Cortical Dysplasia

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Abstract

Reflex seizures can be triggered by a variety of stimuli. We present a case with drug-resistant complex partial seizures originating in right temporal lobe triggered extensively by visual, auditory, and mental exposure to multidigit numbers. The patient was investigated in video-EEG monitoring unit and seizures were triggered by numerical stimuli. Scalp EEG findings suggested a right temporal focus but ictal semiological findings suspicious for an extratemporal area necessitated the invasive EEG study. A right anterior temporal seizure focus was established with invasive monitoring and cortical stimulation studies. Magnetic resonance imaging showed a cortical dysplasia in right anterior temporal lobe and ictal single-photon emission computed tomography confirmed the epileptogenic focus, leading to a right temporal lobectomy and amygdalohippocampectomy and a pathological diagnosis of focal cortical dysplasia type Ia. The patient is seizure-free at the end of the second postoperative year despite repeated exposures to numbers. To our knowledge, this is the first report of seizures triggered by numbers. It is also of particular importance as the reflex seizures are associated with a cortical lesion and it may suggest involvement of right anterior temporal lobe in numerical processing.

Keywords

reflex seizures, temporal lobe, numbers, cortical dysplasia, video-EEG monitoring

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Introduction

Reflex seizures can be triggered by a wide variety of stimuli.^{1–6} They can rarely be associated with cortical lesions,⁷ providing clues to understand also neurobiology of specific cognitive processes. Although calculation-induced seizures are well known,^{2,6,8} there is no previous report on seizures triggered with exposure to characters with numerical value. Here we present a case with complex partial seizures associated with cortical dysplasia and induced exclusively by numbers.

Case Study

A 36-year-old right-handed female patient was experiencing seizures since she was 12 years old. The seizures occurred after seeing numbers with multiple digits, such as telephone numbers or price tags, but they could also be induced by hearing, thinking about, or writing down such numbers. Besides those provoked seizures, she could also experience spontaneous ones as well. Seizures were refractory to levetiracetam and carbamazepine. The neurologic examination was normal.

The patient was admitted to our video-electroencephalography (video-EEG) monitoring unit for seizure recording. Interictal EEG

revealed sharp waves and spikes on the right frontotemporal areas. Typical seizures were triggered by keeping the patient look at a table with multiple-digit numbers or at a telephone keypad. The recorded seizures were alike; onset was a few minutes after the patient started looking at the numbers. Only one seizure was triggered as the patient unexpectedly heard a telephone number on TV; this time the seizure started approximately 2 seconds following stimulus. Initial ictal sign was numbness in chest, left arm, and shoulder. It was followed by a facial expression of

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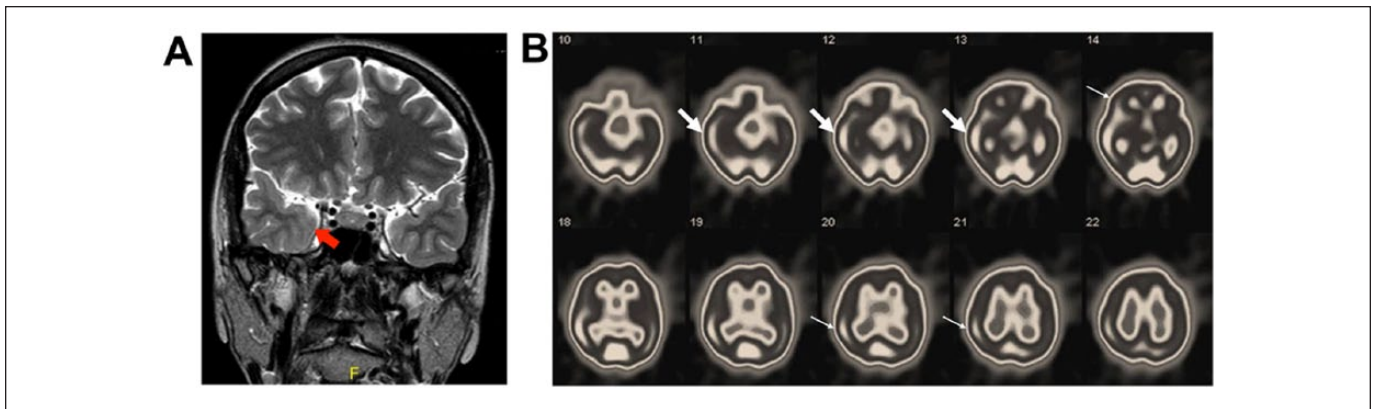


Figure 1. (A) Coronal T2-weighted magnetic resonance imaging (MRI) series showing a probably dysplastic cortex (arrow) in right anterior temporal lobe. (B) Ictal brain perfusion single-photon emission computed tomography (SPECT) images demonstrates significant right temporal hyperperfusion (thick arrows) slightly extending to the right parietal and frontal regions (thin arrows).

pain or crying, tonic posture in left arm, oral and right-sided automatisms (supplementary video, available at <http://eeg.sagepub.com/content/by/supplemental-data>). Each seizure typically lasted for 45 seconds followed by postictal paresis in left arm for 3 minutes. The ictal EEG findings revealed a short-lasting initial rhythmic sharp theta activity in right temporal lobe followed by rhythmic delta waves. Magnetic resonance imaging (MRI) demonstrated mild T2A hyperintensity and corticomedullary blurring in right anterior temporal lobe, suggesting a cortical dysplasia (Figure 1A). There was no pathological sign in parietal cortices. Ictal brain perfusion single-photon emission computed tomography (SPECT) was obtained and it showed significant right temporal hyperperfusion slightly extending through the right parietal and frontal regions (Figure 1B). Furthermore, her neuropsychological examination revealed moderate right parietal and hippocampal dysfunctions.

Although all neuroimaging and scalp EEG findings supported the presence of a right temporal epileptogenic area, an extratemporal focus was considered because of the initial ictal semiology findings like paresthesias. We performed invasive EEG recording including the right temporal and parietal area (Figure 2A). Very frequent interictal spikes were recorded in right mesial temporal electrodes and also in right inferior parietal areas. Interictal epileptiform activity increased with visual numerical stimulation. Initial ictal EEG changes revealed right temporal lobe onset (Figure 2B; supplementary video). Cortical mapping study was performed with 50-Hz, 300-ms electrical stimulation of subdural electrodes. When posterior mesial temporal electrodes were stimulated with 2.5 mA current, frequent epileptiform discharges appeared in posterior and anterior temporal electrodes simultaneously with numbness symptom in left shoulder. Ten seconds later, a typical complex partial seizure was recorded with similar ictal EEG changes as reported above. Stimulation of extratemporal areas did not end up with clinical seizure or epileptiform activity.

After confirming the seizure focus as a right mesial temporal lobe and considering the right hippocampal dysfunction on her neuropsychological tests, the patient underwent right anterior

temporal lobectomy and amygdalohippocampectomy within the same year of initial evaluation. Pathological examination of temporal lobe revealed microcolumnar neuronal alignment and subpial gliosis in upper cortical layers. There was glial fibrillary acidic protein (GFAP)-positive gliosis and ectopic neurons in white matter and deep cortical layers. These findings were found to be consistent with focal cortical dysplasia, type Ia, according to ILAE 2011 classification. The patient had no postoperative seizures during 2 years follow-up, even after exposure to numerical stimuli. Postoperative EEG showed no epileptiform discharges when the patient is still on carbamazepine and levetiracetam treatment. She also had no cognitive problems on her postoperative neuropsychological tests.

Discussion

The aforementioned case experienced, till date, the first reported type of reflex seizures triggered by visual, auditory, or mental exposure to numbers. Besides the unique nature of the triggering stimuli, association of seizures with a biopsy-proven cortical dysplasia in right temporal lobe, successful preoperative demonstration of the ictal focus and cure of seizures following surgery are also of particular interest.

Diagnosis of reflex seizures was evident in this patient as all seizures occurred shortly after being exposed to a multidigit number. Seizures under monitoring took a little longer than normal to start, probably because of the patient's expectancy for triggering stimuli, as reflex seizures are mainly triggered by unexpected sensory stimuli.¹ Seizure semiology strictly suggested right temporal lobe involvement, apart from the initial aura of numbness in left arm, which would point to a parietal lobe focus. MRI and ictal SPECT studies suggested a lesion in right anterior temporal lobe. Invasive EEG study clearly demonstrated a right posterior mesial temporal ictal onset. Reflex activation of seizure focus would then be followed by prominent epileptiform activity on dysplastic cortex and then seizure activity would rapidly spread to frontoparietal areas. Sensory symptoms at the beginning of seizures therefore would be related to

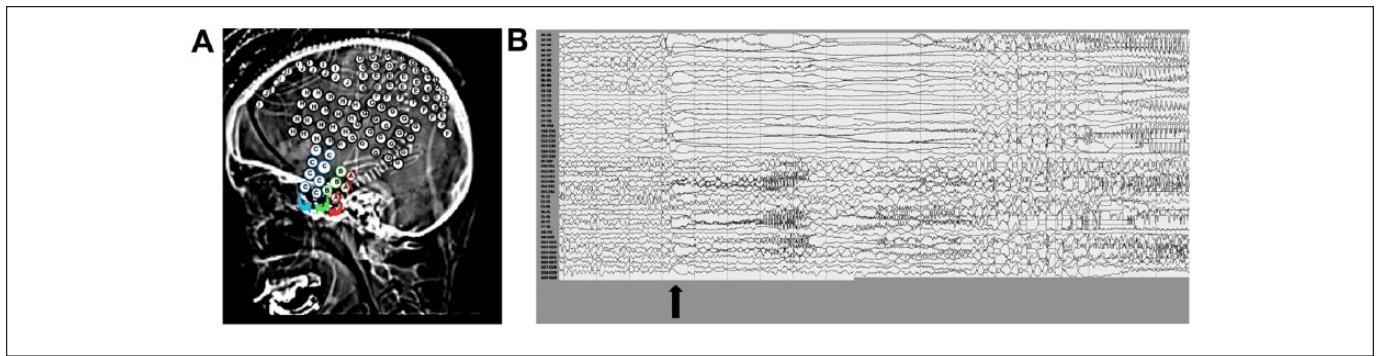


Figure 2. (A) The subdural strips and grids covered the right parietal, temporal (lateral, mesial, and basal), and frontal lobes. A, B, and C were on the temporal lobe. D to G were on the parietal lobe. H was on the temporo-parietal and part of frontal region. I and J were on part of frontal region. (B) Ictal EEG onset was beginning with attenuation and fast activity on right mesial temporal electrodes A, B, and C (black arrow). High-pass filter, 70 Hz; low-pass filter, 0.1 Hz.

propagation of epileptic activity to parietal lobe. Besides prominent hyperperfusion in the right temporal lobe, slightly increased perfusion in the frontal and parietal regions on ictal brain SPECT supports this rapid propagation of epileptic activity. Right temporal lobectomy with amygdalohippocampectomy totally cured seizures and pathological examination finally confirmed the diagnosis of cortical dysplasia.

Reflex seizures can be triggered by a variety of stimuli, which can eventually be highly surprising. Triggers such as flashing lights or visual patterns, somatosensory stimulation, reading, eating, listening to music, thinking, playing chess, exposure to hot water have been reported in the literature.¹⁻⁶ Triggering stimuli in our case was highly exceptional. It could not be regarded as a visual pattern-sensitive epilepsy because exposure to single-digit numbers individually was not causing seizures; the patient needed to see a multidigit number, like a telephone number. Moreover, the patient was not dependent on visual stimuli for seizures; hearing a number on TV or just trying to tell someone a phone number would always end up with seizures. Although a calculation attempt would inevitably result in a seizure, the patient did not need to make a mental arithmetic operation to have a seizure, excluding calculation-triggered seizures for our case. These observations suggested involvement of a higher cortical center as an association area for numerical value representations. Stimulation of critical amount of cortical tissue in this area either visually, auditory, or mentally was initiating seizure activity. Numbers with higher digits were probably stimulating a higher mass of hyperexcitable cortex, resulting in a greater probability of seizure, a common feature of reflex seizures.^{9,10}

Cortical dysplasias can be epileptogenic, causing formation of a high amount of abnormal connections among cortical and subcortical areas.¹¹ Stimulation of dysplastic or nearby cortex via various afferent stimuli would therefore result in seizures. There is highly limited experience reported in the literature for reflex seizures associated with dysplasias and malformations. Reflex seizures triggered by hot water exposure,^{7,12} eating,¹³ and thinking about a particular object¹⁴ have been associated

with dysplastic lesions. Typical for cortical dysplasia-related seizures, our patient was refractory to antiepileptic drug therapy and excisional surgery was required for seizure relief.

Reflex seizures, especially when lesion associated, provide an opportunity to increase our understanding of certain neurobiological processes. Dendritic rarefaction, decreased interneurons in the brain leading to inhibitory dysfunction has been implicated as a mechanism for reflex seizures¹⁵; and erroneous connectivity within dysplastic cortices may cause local imbalance of excitatory and inhibitory neuronal activity following sensory activation. In our case, electrophysiological seizure focus and anatomical lesion was in right temporal lobe. This would suggest association of the nondominant temporal lobe with higher numerical processing. Previously, a “triple-code” model was suggested for number processing actions in the brain.¹⁶ In this model, the numbers are predicted to be processed in 3 formats: a visual Arabic code, an analogue magnitude code, and a verbal code. The visual code involves the perception of the presented string of digits for representation of a numerical value and manipulation of numbers. Bilateral activity in inferior ventral occipitotemporal areas are suggested to take part in this code. Magnitude code establishes the knowledge for quantity on the represented number with activity in bilateral inferior parietal cortices. Auditory verbal code manipulates verbal representations of numbers, stores arithmetic facts, and takes part in calculation with involvement of dominant perisylvian areas. In our patient, the role of right temporal lobe in triggered seizures, especially the temporal focus that was demonstrated with cortical mapping studies would fit in the visual code representation area in the triple-code model. Ictal activity arising from occipital lobes may cause numerical visual hallucinations¹⁷ and this seizure activity may spread to temporal lobes¹⁷ via rich connections in between.¹⁸ Speculatively, internal processing of numerical data within the occipital cortex may be a rate-limiting step in our patient, causing a lag before triggering the connections to the dysplastic temporal lobe. There was no lesion or electrographic seizure activity in cortical areas involved in the magnitude and verbal codes, and suitably,

seizure triggering in our case did not require mental activity of magnitude comparison or calculations.

It is difficult to explain how the patient's seizures could be triggered by auditory or mental stimuli besides visual ones, as it is not known how the nonvisual stimuli would affect pathways related to the visual number form. It would be useful to consider that in epileptic patients, cortical lesions may shift the representative areas of cognitive functions and neurophysiological data for number processing obtained from healthy controls might not account for these patients in all cases. Accordingly, number processing skills were found to be affected in mesial temporal lobe epilepsy patients involving both right and left temporal lobes.¹⁹

Conclusively, this unique case of "numerical" reflex seizures indicates that structural lesions in right anterior temporal lobe should be investigated in similar patients and these cortical areas may play role in number processing.

Author Contributions

S.E.E, F.I.T, O.K and S.S were involved in the clinical care and investigative workup of the patient. K.K.O performed and evaluated the MRI, E.L.E did the SPECT study and F.S. made the pathological diagnosis. S.E.E. drafted the manuscript, F.I.T and S.S. critically revised the manuscript.

Declaration of Conflicting Interests

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Supplementary Material

Full-color figures are available online at <http://eeg.sagepub.com>

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