

Case Report

Location-specific reflex epilepsy: a novel reflex epilepsy phenotype

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ABSTRACT

Reflex epilepsies are rare syndromes where seizures are triggered by particular stimuli or activities that may be motor, sensory or cognitive in nature. Triggers are diverse, may be extrinsic or intrinsic in nature and heterogeneous phenotypes have been described over the years. We give an account of a case of location-specific reflex epilepsy which we suggest is a novel reflex epilepsy phenotype relating to higher cortical function (HCF), and review the literature in relation to features of HCF reflex epilepsies described to date.

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1. Introduction

Epileptic seizures are considered to be reflex in nature if they are consistently evoked by the presence of a particular stimulus or by a specific activity of the person, which may be motor, sensory or cognitive in nature. Reflex epilepsies are specific syndromes where all of an individual's seizures are precipitated by certain, often sensory stimuli [1,2], whereas reactive seizures [3] can be triggered by transient systemic disturbances such as alcohol excess, sleep deprivation or intercurrent illness. On this basis, the question of whether reflex and spontaneous seizures form a continuum has been raised [4], with an underlying predisposition (genetic or structural causing functional network instability) interacting with various facilitating factors that may lower the seizure threshold. Reflex seizures can occur in the context of a range of epilepsy syndromes including generalized and focal syndromes as well as in association with focal structural pathology/brain lesions [5], and triggers may be extrinsic (for example, lights flashing, music playing), or intrinsic (such as complex thought processes, emotion), and may also be classified as simple (such as intermittent lights) or more complex (higher cortical function) in nature [6]. Various epilepsies relating

to higher cortical function with cognitive stimuli have been described, examples include seizures occurring with praxis [7] (contemplating complicated spatial tasks in a sequential fashion, making a decision and responding by using part of the body) including construction, written calculation and board games; as well as reading, talking, writing, listening to or playing music. These more complex triggers typically have longer latencies prior to an event [8], and may activate broader functional circuitry than more simple ones [9].

Here, we give an account of a case with what we have termed "location-specific reflex epilepsy", which we believe is of particular interest as it highlights the manner in which higher cortical processes relating to being present in a particular location could serve as a trigger in reflex epilepsy.

1.1. "Location-specific reflex epilepsy"

We describe a 53-year-old right-handed woman who had her first seizure at 34 years of age. Her initial event happened as she was in a car driving home with her partner - she had just driven through a crossroads junction close to her home seconds before onset of the event. Semiology was consistent with behavioral arrest with staring, progressing to bimanual automatisms, lip smacking and automatic speech (focal impaired awareness seizure) lasting for 2 minutes, with no memory for the event afterward. There were no focal to bilateral tonic-clonic seizures. Thereafter, frequent recurrent similar stereotyped events would happen predictably 50 m after travelling through this crossroads with

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over 90% of visits/journeys resulting in a similar event. Seizures could occur regardless of the time of day, weather, mode of transport (including walking) or speed and direction of travel, with no evident difference in circumstances during the journeys that did not result in a seizure. There was no obvious visual stimulus identified. A new T-junction was built close to her home some years afterwards, and following this, she also had rare events at this intersection resulting in her avoiding it as well. There was no stressful event in her history relating to such an intersection in the past. These events were resistant to anti-seizure medications, and occurred frequently while on combination therapy with levetiracetam and lamotrigine. There was a family history of epilepsy in her maternal grandmother. Brain MRI showed no epileptogenic lesion. Inter-ictal EEG showed bilateral independent epileptiform discharges over the temporal regions, with a right-sided emphasis. A clinical seizure was captured in the video-telemetry unit shortly after watching a video of a journey through the crossroads, and while discussing it afterwards with her partner. Just after he began to describe the crossroads, she had a seizure. A rhythmic ictal discharge evolved from the right mid-temporal region, maximal at T4 (see Fig. 1). Following a full pre-surgical evaluation, she underwent a right temporal lobectomy resulting in seizure freedom. She is now able to travel through the crossroads seizure-free, and is not taking anti-seizure medication.

2. Discussion

We describe a reflex epilepsy, which to the best of our knowledge is novel due to events triggered by a specific location familiar to the patient. How these locations could trigger an epileptogenic response is interesting. We know from previous studies that visuospatial attention is

lateralized predominantly to the right hemisphere in right-handed individuals, albeit with variability across subjects [10,11]. The crossroads and T-junction might represent items of 3-dimensional space, with resultant non-dominant parietal activation in this case. Furthermore, we hypothesize that the temporal EEG findings seen may represent spread of changes from parietal areas, as ictal and interictal EEG can often be non-localising in epilepsies of parietal origin [12]. The fact that seizure freedom has successfully been achieved surgically in this non-lesional case following temporal lobectomy suggests that there has been surgical disruption of the epileptogenic network.

Various other epilepsies have been described relating to higher cortical function. Praxis-induced seizures tend to relate to the thought of, followed by the execution of complicated motor tasks or movements that usually involve sequential spatial processing - such as playing board games including chess, cards or drawing. These cognitive tasks that involve the use of the hands have been found to be more epileptogenic than others including mental calculation [13] but it has been shown in some studies that the mere planning of precipitating actions can trigger an epileptogenic response [8,14]. Studies in praxis-induced epilepsy with fMRI have shown increasing coactivation of the primary motor cortex and supplementary motor area with increasing cognitive demand, with impaired deactivation of the default mode network [15]. Rarely thinking-induced seizures (often relating to solution of complex mathematical tasks) without a significant motor component have been described [16–18], although typically these are absence seizures with generalized EEG changes, as opposed to the focal findings seen with our patient. Research in such cases has also shown that calculation is more language dependant (recruiting networks involving the

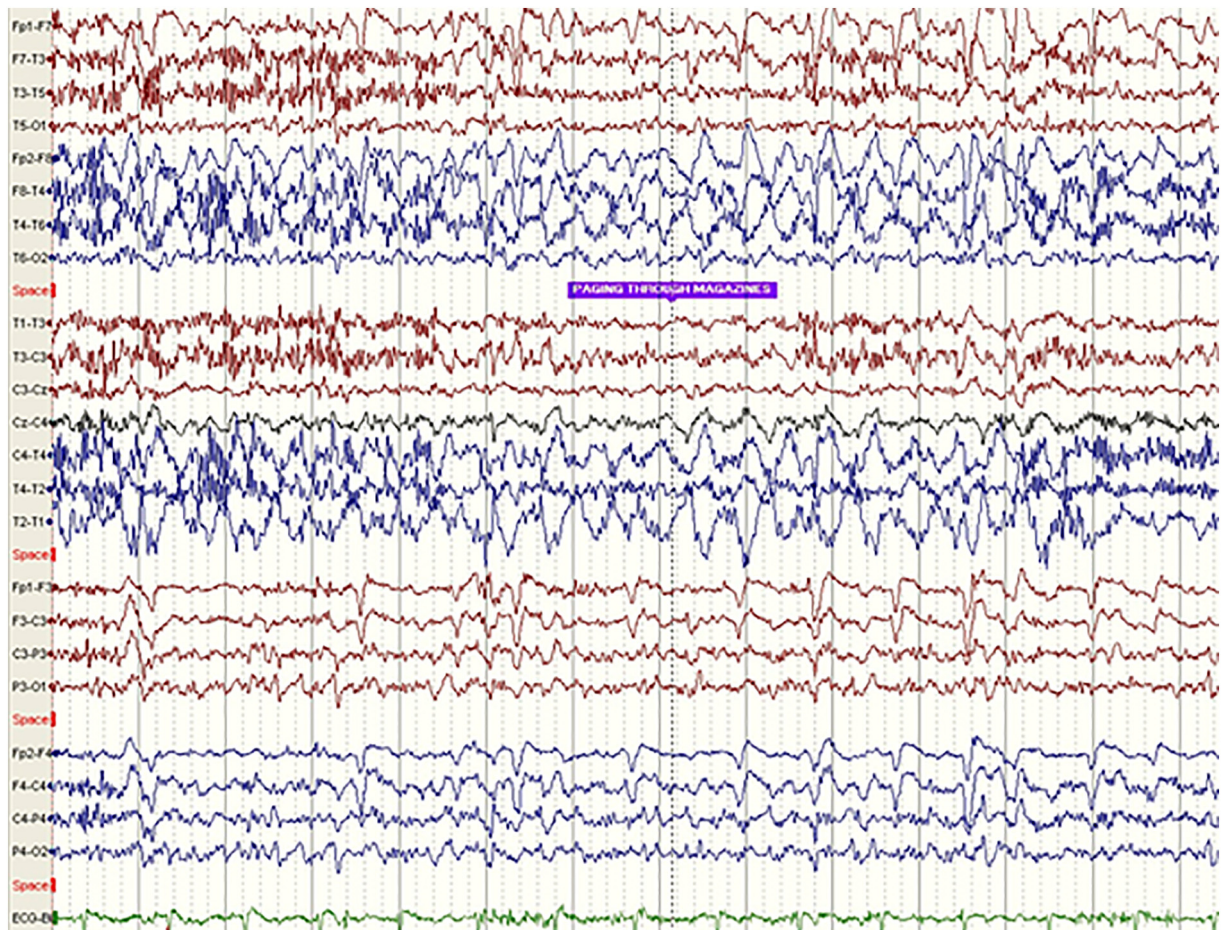


Fig. 1. Shortly after watching a video of a journey through crossroads, a rhythmic ictal discharge evolved from the right mid-temporal region, maximal at T4.

dominant hemisphere) than more complex arithmetic which preferentially involves non-verbal visuospatial networks of both parietal lobes [19].

Other language-related tasks can induce seizures, including reading, writing and talking. Reading requires the recruitment of a complex cognitive network for visual analysis, memory, grapheme-to-phoneme conversion, and articulation [20], and it has been shown that multiple dominant hemispheric cortical areas are involved [21]. Epileptogenic discharges are provoked more readily with difficulty pronouncing text, and with mis-readings [8], indicating also that stress is a facilitator for these seizures. In general, with reflex epilepsies, it is thought that simple triggers activate circumscribed areas of cortex, whereas more complex inputs may activate broader functional circuitry [9], and one might consider reflex epilepsies as a case of synthesis, whereby hyperexcitable areas may overlap with areas which are physiologically activated by particular stimuli.

3. Conclusion

We have presented an interesting and novel phenotype of location-specific reflex epilepsy, which we postulate is a form of seizures induced by HCF. Overall, reflex epilepsies lend themselves as an ideal model to further investigate the dynamics and pathophysiology of system network epilepsies. Further study of aberrant network dysfunction in these individuals may offer insights into precision therapies including (but not limited to) non-pharmacological options.

Ethical statement

The authors have obtained signed informed consent from the patient for publication of their case details. This information has been anonymised in the paper to the extent that this is possible.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Professor Norman Delanty serves on the editorial board of *Epilepsy and Behaviour Reports*.

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