NMC Case Report Journal 2017; 4: 127–130
DOI: 10.2176/nmccrj.cr.2017-0031

Case Report

The Involvement of Sensory-motor Networks in Reflex Seizure

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Reflex seizures are epileptic events triggered by specific external stimuli, or less commonly, internal mental stimuli. Understanding the characteristics of reflex seizures is important to elucidate the mechanisms underlying network abnormalities in epileptic conditions. This report details a patient with medically intractable reflex seizures provoked by sensory stimuli to the patient's right foot. Single-photon emission computed tomography (SPECT) during the seizure induced by sensory stimulation showed hyperperfusion in broad sensory-motor networks (dorsal column-medial lemniscus pathway, left thalamus, bilateral postcentral gyri and posterior parietal cortices, left supplementary motor area (SMA), and left paracentral lobule) and left caudateputamen. The irritative zones and ictal onset zone were localized to the left medial frontoparietal (SMA, anterior and middle cingulate gyrus, and paracentral lobule) and lateral posterior parietal cortices, as evidenced by amelioration of reflex seizures following intracranial electroencephalography and surgical resection of these areas. The neuroradiological and electrophysiological findings in our case study illustrate that the mechanism of reflex seizures may be associated with hyperexcitability of the broad sensory-motor networks, including the basal ganglia. Disconnection of these networks is necessary to treat reflex seizures.

Keywords: reflex seizure; sensory stimulation; supplementary motor area; somatosensory network

Introduction

Reflex seizures are epileptic events triggered by specific motor, sensory, or cognitive stimulation, and can be associated with generalized and focal epilepsy.[1)] Surgery is a treatment option; however, difficulties are associated with defining seizure-onset zones.[2)] The mechanisms underlying this type of seizure are still unknown. Thus, expanding our understanding of these mechanisms is critical for creating treatment strategies for patients with reflex seizures, as well as elucidating network abnormalities associated with epilepsy. Here, we report a case of reflex seizure provoked by sensory stimuli to the patient's right foot, in which presurgical evaluations revealed the prominent involvement of the sensory-motor networks and basal ganglia in the generation of reflex seizures.

Case Report

An 18-year-old right-handed girl presented with reflex and spontaneous seizures refractory to medical treatment since the age of 12 years old. She had been suffering with two types of seizures, including hypermotor seizures and right foot sensory aura followed by bilateral asymmetric tonic posturing and generalized tonic-clonic seizures. Both seizures could spontaneously occur; however, the latter type of seizure was also evoked by loud sounds, and more commonly somatosensory stimuli to her right foot. Her reflex seizures were exaggerated by sudden unexpected stimulation. She avoided any activities inducing seizures, including gaiting, wearing stockings, and foot care, and her quality of life (QOL) was greatly impaired (Fig. 1a). Magnetic resonance imaging (MRI) of the brain revealed no structural abnormalities, and fluorodeoxyglucosepositron emission tomography (FDG-PET) showed no focal hypometabolism (Figs. 1b and 1c). Interictal scalp epileptiform discharges were localized to the left posterior quadrant and ictal activities were nonlocalizible using long-term video electroencephalography (EEG) monitoring. Following magnetoencephalography (MEG) analysis, equivalent current dipoles (ECDs) of interictal spikes were revealed in the left paracentral lobule and left precuneus (Fig. 1d). Following these non-invasive evaluations, the patient underwent the first invasive evaluation with chronic subdural electrodes at the age of 16. The subdural electrodes were placed over the medial and lateral surfaces of the left frontal-parietal lobe. The most frequent interictal spikes were observed in left paracentral lobule, and other interictal spikes were detected in the middle cingulate gyrus and superior parietal lobule (Fig. 1e). The ictal onset zone was localized to the left middle cingulate gyrus, and seizures spread to left paracentral lobule, pre-and postcentral gyri, and superior parietal lobule (Fig. 1f). Subsequently, the left middle cingulate gyrus, parts of the precuneus, and superior parietal lobule were resected, sparing the left paracentral lobule to prevent right foot motor deficit (Fig. 1g). Thereafter, the patient's seizures ceased temporarily; however, three months after surgery the seizures reoccurred. Vagal nerve stimulation

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Received: February 26, 2017; Accepted: April 24, 2017
Online September 11, 2017

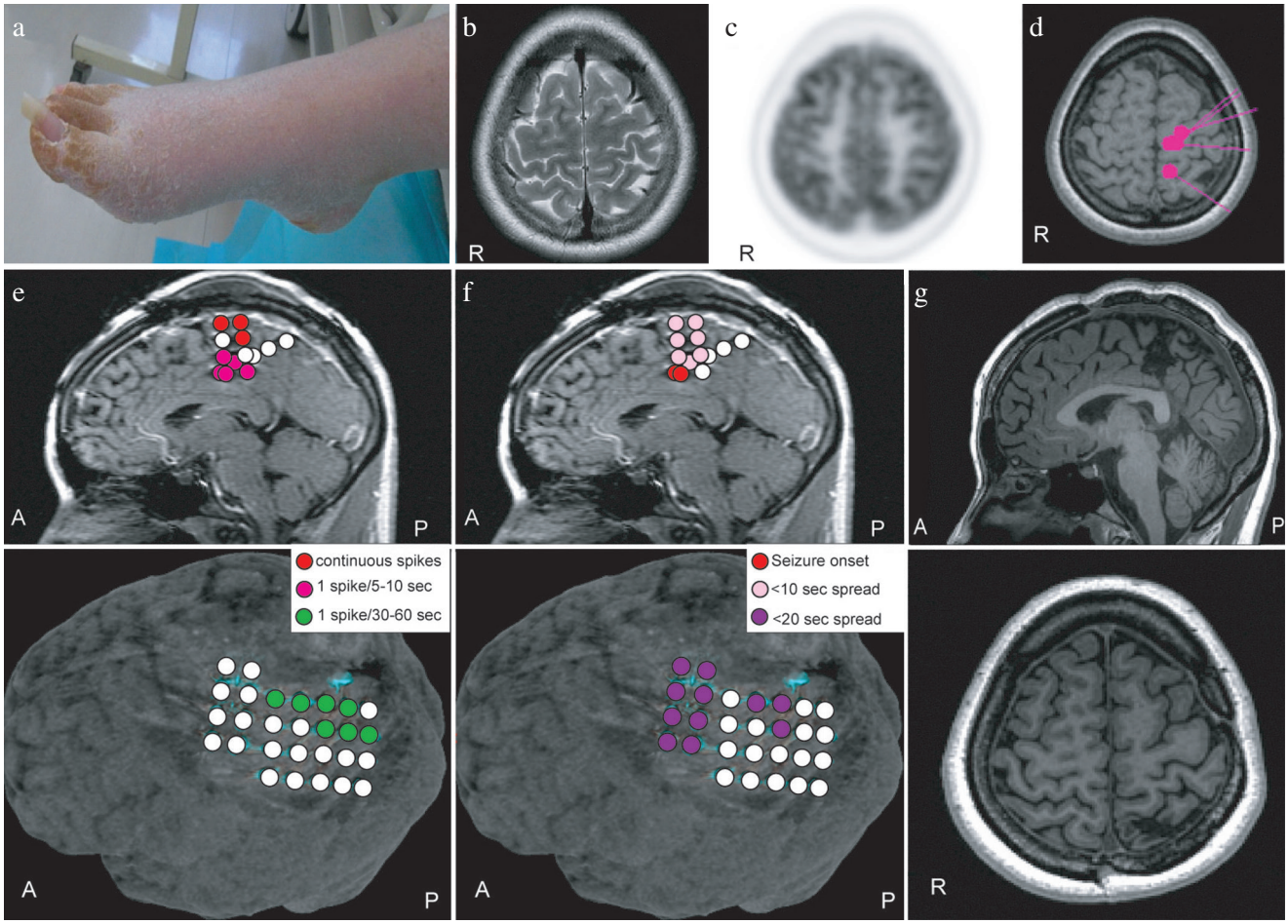

Fig. 1 (a) A picture of the patient's right foot with long nails. The patient avoided any activities inducing seizures, including gaiting, wearing stockings, and foot care. (b) Magnetic resonance imaging (MRI) of the brain revealed no structural abnormalities. (c) Fluorodeoxyglucose-positron emission tomography (FDG-PET) showed no focal hypometabolism. (d) In the analysis of magnetoencephalography (MEG), equivalent current dipoles of spikes were revealed in the left paracentral lobule and left precuneus. (e) Distribution of the interictal spikes in the first invasive evaluation. Continuous spikes were observed at the red circle. One spike was seen every 5–10 s at the area of the magenta circle and one spike every 30–60 s in the area of the green circle. (f) Seizure onset and spread areas in the first invasive evaluation. Seizures started in the area of the red circle, then spread to the pink circles within 10 s, and to the purple within 20 s. (g) Postoperative MRI after the first resection revealed that the left middle cingulate gyrus, parts of precuneus, and the superior parietal lobule were resected.

(VNS) was performed, but did not result in any reduction in seizure frequency. Interictal and ictal scalp epileptiform discharges were localized to the left fronto-central region. Single-photon emission computed tomography (SPECT) during seizures provoked by sudden right foot sensory stimulation showed hyperperfusion in broad sensory-motor networks (dorsal columnmedial lemniscus pathways, left thalamus, bilateral postcentral gyri and posterior parietal cortices, left supplementary motor area (SMA), left paracentral lobule) and the left caudate-putamen (Fig. 2a). A second MEG analysis of interictal spikes revealed ECD clusters in the left SMA and paracentral lobules (Fig. 2b). These findings suggest that the seizure onset zone remained at the anterior edge of the resection. At the age of 18, the patient underwent a second invasive evaluation. Subdural electrodes covered the lateral surface of the left fronto-parietal lobe (premotor, sensorimotor and posterior parietal areas) and the medial surface of left frontal lobe (SMA, anterior and middle cingulate gyrus). Interictal epileptiform discharges and ictal onset zones were localized to the medial frontal lobes (SMA, middle cingulate gyrus and a part of paracentral lobule) (Figs. 2c and 2d). Functional mapping revealed that these areas controlled motor function of right upper limb, which were likely to be symptoms of SMA. Based on this invasive evaluation, a second resection of these areas was performed (Fig. 2e). Histopathology demonstrated cortical dysplasia (ILAE type Ic)[3] (Fig. 2f). Postoperatively, the patient presented with transient mild right hemiparesis, but recovered within one month. At a follow-up consultation one year later, remission of reflex seizures and hypermotor seizures were observed and there was remarkable improvement of daily life activities. Postoperatively, the patient became able to gait, wear stockings, and receive in foot care. The patient's spontaneous seizures still remained, but had lessened in frequency and severity, characterized by short negative motor seizure; i.e. stopping of the movement instantly, once every 2 or 3 days.

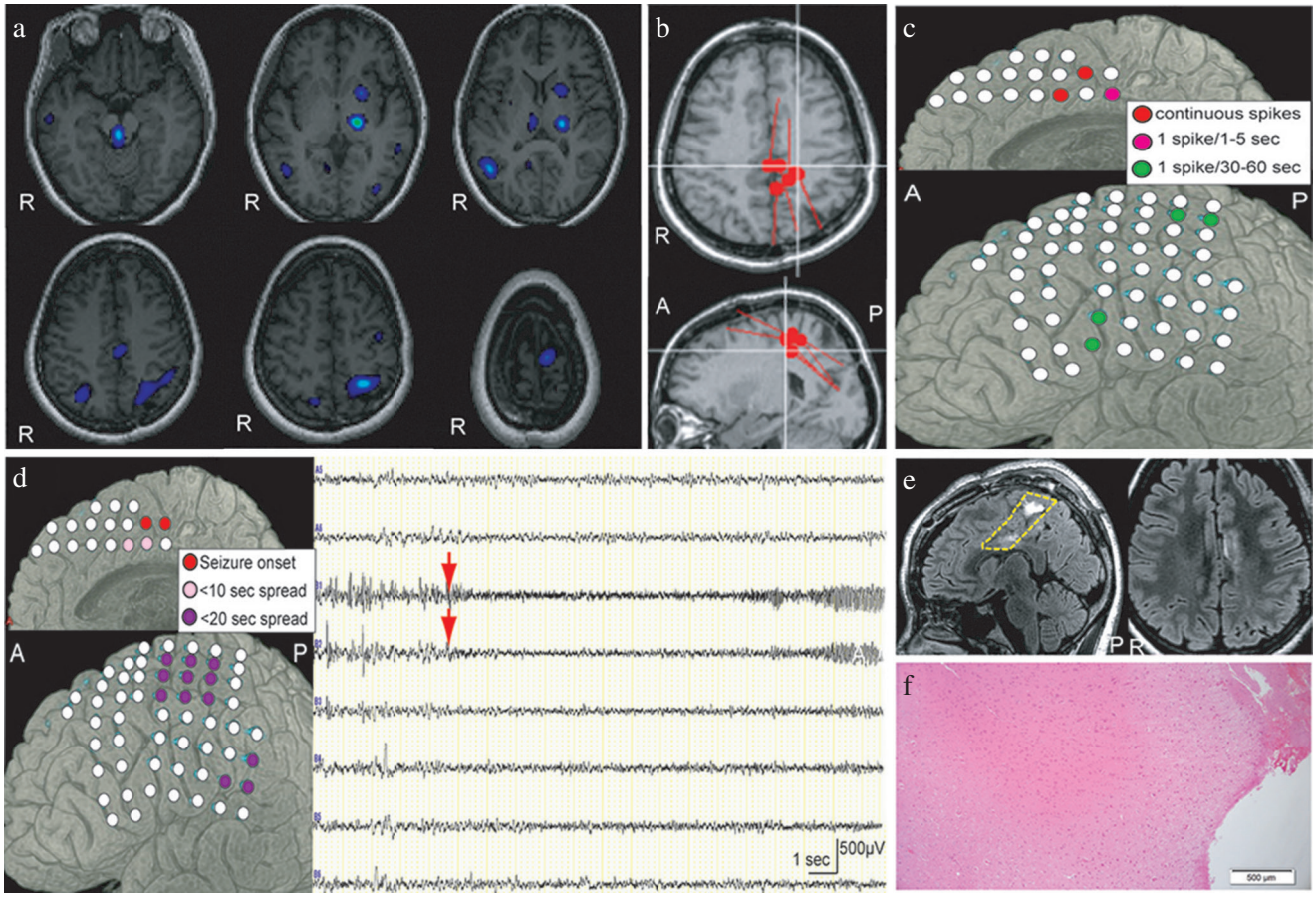

Fig. 2 (a) Single-photon emission computed tomography (SPECT) during seizures induced by right foot sensory stimulation showed hyperperfusion in broad sensory-motor networks, including the dorsal column- medial lemniscus pathway, left thalamus, bilateral postcentral gyri and posterior parietal cortices, left supplementary motor area (SMA), left caudate-putamen, and left paracentral lobule. (b) A second MEG analysis of interictal spikes revealed ECD clusters in the left SMA and paracentral lobules. (c) Distribution of the interictal spikes in the second invasive evaluation. Continuous spikes were observed in the area of the red circle. One spike was seen every 1–5 s in the area of the magenta circle, and one spike every 30–60 s in the green circle. (d) Areas of seizure onset and spread, and the electrocorticographic ictal findings in the second invasive evaluation. The low voltage fast activity started at the red arrow. (e) Postoperative MRI after the second resection revealed that the left SMA, middle cingulate gyrus, and a part of the paracentral lobule were resected (yellow-dashed line). (f) Histopathology findings in FCD ILAE type Ic. A hematoxylin–eosin (HE) stain reveals tangential dyslamination without a dysmorphic neuron.

Discussion

Here, we present a patient with reflex seizures provoked by unexpected loud sounds and somatosensory stimulation to her right foot, which had the characteristics of startle-induced seizures. The patient underwent two invasive evaluations, which revealed irritability of the left medial fronto-parietal areas and left posterior parietal cortices, and ictal involvement of these regions. Furthermore, ictal SPECT analysis during provoked seizures showed hyperperfusion in broad sensory-motor networks and the left caudate-putamen. After resection of the medial frontal and parietal areas, her reflex seizures ceased. Although the first resection could affect the brain network, our electrophysiological and neuroradiological findings suggest the involvement of broad sensory-motor networks, including the basal ganglia in reflex seizure, and provide new insight into mechanisms of reflex seizures. Previous studies suggested that startle-induced seizures could originate in the motor and premotor cortices,[4] SMA,[5,6] the precuneus,[7] and the interaction of all these regions; i.e. parieto-frontal network, including the motor/premotor cortex, the precuneus, and the SMA.[8] The invasive evaluations in our case study revealed the involvement of parieto-frontal networks, consistent with previous reports. In addition, ictal SPECT showed hyperperfusion in broad sensory-motor networks and the left caudate-putamen. This study is the first to demonstrate the hyperexcitability of this sensory-motor network, including the basalganglia, in reflex seizures. Based on functional neuroimaging studies, cortical and subcortical structures, including the precentral and temporal lobe, the thalamus, and the striatum, modulate startle responses.[8,9] Fernandez et al. suggest the functional and anatomic connections between structures associated with voluntary movement (the basal ganglia, the premotor area, and the SMA) and the central nervous system involved in startle responses.[8] As a mechanism of startle seizure, it has been hypothesized that an exaggerated startle response, due to abnormal activity in the brain stem, leads to an increase of proprioceptive feedback to the hyperexcitable motor cortex, evoking a seizure.[10] We speculate that the present findings might reflect hyperexcitability of

this startle-sensory-motor circuit. The hyperperfusion of the left caudate-putamen and sensory tracts (dorsal column-medial lemniscus pathway, left thalamus, bilateral postcentral gyri and posterior parietal cortices) in ictal SPECT may reflect startle responses and an increased response of proprioceptive input, respectively. Hyperperfusion of the medial fronto-parietal motor related areas (left SMA and left paracentral lobule) in ictal SPECT, and the irritability and ictal involvement of these areas during invasive evaluation indicate hyperexcitability of these areas. Both increased proprioceptive feedback via the startle responses and hyperexcitability of motor related areas are thought to be inducing factors of reflex seizures. Resection of the medial frontal lobes might result in disconnection of this circuit and stopped the patient's reflex seizures.

Conclusion

Our study shows that the epileptic networks involved in reflex seizures include the broad sensory-motor networks and the basal ganglia. More cases need to be studied in order to elucidate the mechanisms underlying reflex seizures, as well as the integrative brain functions of sensory-motor networks.

Conflicts of Interest Disclosure

The authors have no personal, financial, or institutional interests in any of the drugs or materials.

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