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Intractable Epilepsy Controlled by Neurofeedback and Adjunctive Treatments: A Case Report

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Abstract

This case report documents the treatment of a female patient with intractable temporal lobe epilepsy with secondary generalization. At the age of 13, the patient was hospitalized with ~120 seizures in a day, some of which were life-threatening. After hospital discharge, despite a regimen of multiple antiseizure medications, the patient still experienced ~90 seizures per day. After the interventions described in this work, over 500 neurofeedback sessions guided by EEG or qEEG data and adjunctive treatments including mental skills coaching, the patient became seizure- and medication-free, progressing from poor academic performance and inability to carry out normal daily life to attending university as a student athlete playing an NCAA Division I sport. This case emphasizes that, with professional guidance and supervision, it is possible for people with epilepsy or their caregivers to provide the extensive, long-term neurofeedback and adjunctive training necessary for reduction and control of intractable seizures.

Keywords: epilepsy; qEEG; EEG; neurofeedback; mental training; case report

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Introduction

Epilepsy is a common disorder affecting approximately 85 million people worldwide (Singh & Trevick, 2016), including an estimated 470,000 children in the United States. Epilepsy requires self-management to optimize seizure control and minimize impact (Centers for Disease Control and Prevention, 2020). Current allopathic treatments for epilepsy include antiseizure medications, but at least one-third of people with epilepsy (PWE) still have persistent, uncontrolled seizures, currently defined as “intractable epilepsy” (Asadi-Pooya et al., 2016). Children on antiseizure medications demonstrate worse educational and health outcomes, more hospitalizations, and increased morbidity and mortality when compared with age-matched peers (Fleming et al., 2019).

PWE are often referred for possible epilepsy surgery, though reported success rates vary by center. At one center, more than 75% of patients who underwent appropriate epilepsy surgery experienced a meaningful improvement in quality of life (QOL; Benevides et al., 2021), and another center has reported that 47% of those who underwent epilepsy surgery were seizure free at 5-year follow-up (Mohan et al., 2018). Risks and complications of epilepsy surgery may include visual field defects, motor impairments, intracranial complications, and neurocognitive dysfunction (Kohlhase et al., 2021). Given that epilepsy is a disease of neural networks, it is to be expected that focal resective epilepsy surgical interventions are often unable to render freedom from seizures (Engel, 2013; Engel et al., 2013).

Adjunctive or complementary treatments for epilepsy approaches often address the broader health aspects affecting seizures in PWE. These interventions include nutritional therapies, lifestyle changes, cognitive training, and behavioral treatments that are likely underutilized in the treatment of epilepsy (Haut et al., 2019; Yardi et al., 2020). In a 2021 physician survey, approximately 70% of 1,000 physicians from 25 countries endorsed the use of complementary or alternative modalities (Mesraoua et al., 2021). It is likely that patients and caregivers will continue to seek out these alternative strategies in situations where antiseizure medications fail to control seizures or produce unacceptable side effects (Nagai et al., 2019).

Biofeedback (BFB) and Neurofeedback (NFB) as an Alternative Treatment

Electroencephalogram (EEG) BFB, also called NFB, was first reported by M. B. Sterman, who identified and operantly trained the sensorimotor rhythm (SMR) in cats (Sterman et al., 1969; Wyrwicka & Sterman, 1968). This led to successfully applying SMR NFB training to PWE (Sterman et al., 1974). Examples of case studies (Selaa & Shaked–Toledanob, 2014) and small group nonrandomized studies (Frey, 2016; Kohlhase et al., 2021) have reported favorable results. A meta-analysis reported SMR training significantly decreased seizure rate in more than 70% of the cases reviewed (Tan et al., 2009). A 2019 review concluded that NFB is possibly efficacious in the treatment of pediatric epilepsy, though lacking sufficient research (Nigro, 2019). A recent double-blind, sham-controlled study of children and adolescents with epilepsy noted significant improvements in cognitive functioning and quality of life measures following NFB training (Morales-Quezada et al., 2019).

Case Presentation

Ethical Approval

IRB approval is not required for case reports. The patient, now an adult, read and approved this document prior to publication and provided informed consent for use of her medical history.

Early Evidence of Epilepsy

Table 1 lists a brief chronology of the patient's symptoms, attempted interventions, as well as any symptom changes that correlated in time with interventions. The information presented was retrieved from the patient's medical records and contemporaneous notes maintained by her mother.

Table 1

Chronology of Symptoms, Signs, and Interventions

Age (Years)	Symptom Summary	Intervention	Any Apparent Symptom Changes After Intervention
8–10	Forgetful, anxious, epigastric pain, ADHD diagnosis. EEG: single paroxysm consistent with seizure.	NFB: begins training series for ADHD symptoms.	Slight improvement in emotions, but attention problems persisted.
11–12	Difficulty with peers, emotional, can't recall instructions; blank staring. EEG: epileptiform discharges	NFB: same; Other: social skills training.	Better outward management of emotions. Sport: won regional titles.
13 (Jan–Apr)	Sharp school decline, eye flutters, TLE diagnosis, absence seizures every 5–10 min, fatigue. Sport: impaired but some wins; EEG: seizure activity; MRI: No struct defect.	NFB: same; Sleep: naps for fatigue.	
13 (Late Apr)	Admitted to ER; episode of status epilepticus; first tonic-clonic seizures, peak of 250 seizures/day.	Med: (in ER) DZP, MDZ; (later in hospital) LEV, LAC; NFB: now treating epilepsy.	Sedated by meds. Seizures reduced to ~90 per day. EEG: seizures reduced during NFB recording sessions.
13 (May–Jun)	Hospital discharge, multiple tonic-clonic seizures/day, poor memory/coherence, weak, seizures more severe during menses.	Med: LEV, LAC, CBZ; NFB: same; Sleep: extended daily naps.	Seizures reduced to ~80 per day with continued aura, epigastric pain, sleep seizures, heart and lung stoppage.

Table 1

Chronology of Symptoms, Signs, and Interventions

Age (Years)	Symptom Summary	Intervention	Any Apparent Symptom Changes After Intervention
14 (Jul)	~80–90 seizures/day, with LOC 70% of time, drop seizures with unbearable epigastric pain.	Sport: mental skills train; Diet: low glycemic, supplements, probiotics, CBD, homeopathy, acupuncture; Med: reduced; NFB: 5–8 1-min sessions/day; BFB: diaphragmatic breathing/HRV; Sleep: same.	Able to do more activities; fitness level improved, able to use visualization of sports skills. Doctors pleased with seizure reduction progress.
14 (Aug–Oct)	Drop seizures while playing sports during shifts in emotion, sharp, unbearable epigastric pain; most intense when striking the ball; ~60 episodes/day.	Sport: mental skills train, daily practice between seizures but none during menses; Diet: low glycemic, supplements, probiotics; homeopathy; Med: none; NFB/BFB: increased; Sleep: same.	Won sports tournament in spite of multiple seizures during matches. Still weak.
14 (Nov–Feb)	Epigastric pain, fatigue despite long sleep, fewer seizures overall, but intense 2- to 5-min lung-stopping tonic-clonics during week of menses (~15/day). Anxious and tearful.	Sport: same; Diet: low glycemic, probiotics, zinc, selenium, magnesium, B-complex; NFB: target seizure foci, increased session time; BFB: increased; Sleep: same.	Seizures reduce to 30–40/day with fewer lung stoppages; reduced fatigue/epigastric pain; fewer tonic-clonics; Sport: played well, 2–3 tonic-clonics during games; EEG: elevated beta but no waking seizures; Sleep EEG: no night seizures.
14–15 (Apr–Jul)	Improved sleep and strength, able to play many sports matches except during menses. Seizures: fewer with LOC; able to remain coherent, hand stiffening common.	Diet: low glycemic, supplements; NFB: same; BFB: learned to use HRV and diaphragm breathing to reduce length of seizures and avoid onset of lower intensity seizures; Sleep: same.	Epigastric pain ceases, reduced LOC during seizures with more ability to communicate/function. Sport: attained international ranking; EEG: reduced beta amp from 16 SD to 8 SD; BFB: felt empowered to prevent or blunt seizures.
15 (Aug)	Shorter, milder seizures, ~8/day, LOC uncommon (< 2%). Hand stiffening only.	Diet, NFB, BFB, Sleep: same.	Felt increased control. EEG: beta amp dec further; Sport: professional tournaments, played during menses.
15 (Oct–Dec)	~5 episodes/day; last drop seizure noted; dizzy but no LOC; EEG: slowing but no discharges, beta amp improved.	Diet: low glycemic; NFB, BFB: same; Sleep: naps discontinued.	Reduced to ~3 episodes/day; Reduced anxiety, went on walks alone, straight A's, built peer relationships, less anxiety; Sport: games now possible during menses.
16–17	Occasional dizziness, no LOC, no drop seizures; hands can stiffen for 10–15 s if fatigued. Improved focus under stressful conditions.	Diet: dairy-free and reduced gluten; NFB, BFB: focused on motor quieting for performance, rather than seizures, 1–2/week.	Academic improvement, able to travel on flights; Sport: increased stamina for multiple matches, awarded full NCAA Division I university scholarship.
17 (Mar–Jun)	Two brief, mild episodes of epileptic activity, both associated with lack of sleep. No LOC.	Diet: gluten- and dairy-free; NFB: intense 30 sessions over 6 weeks; BFB: same.	EEG: beta amplitudes normalized. Sport: semifinalist in two professional tournaments.
18	Seizure-free, difficulty with sleep.	NFB: 1/week; BFB: 2–3/week.	Attended university away from home as an athlete.

BFB: biofeedback; CBD: cannabidiol; CBZ: clobazam; DZP: diazepam; HRV: heart rate variability training; LAC: lacosamide; LEV: levetiracetam; LOC: loss of consciousness; MDZ: midazolam; MSC: mental skills coaching; NFB: neurofeedback; TLE: temporal lobe epilepsy.

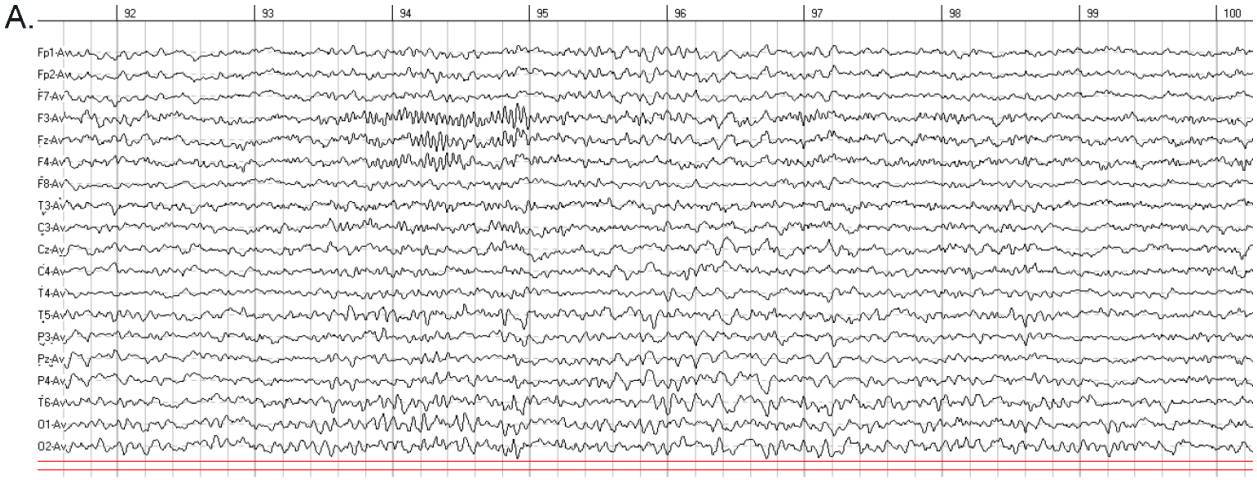
At 8 years of age (2010), the patient's teachers reported attention issues such as forgetting instructions and assignments, and over the following year she developed anxious behaviors and difficulty relating to her peers.

At 10.5 years old, an EEG recorded the first report of possible epileptiform activity, although there were no apparent outward or behavioral manifestations of epilepsy. On a follow-up EEG at age 11 (2013), the neurologist highlighted that the EEG was "consistent with epileptic seizure activity" (Figure 1). In this recording, 20–24 Hz beta spindles are present frontally and fast 12–13 Hz alpha frequencies are present posteriorly, both indicating CNS overarousal. Subtle spikes and slower activity are also noted left temporally (T5). All EEGs for this case review were collected in the eyes-open (EO) and eyes-closed (EC) conditions according to the American Clinical Neurophysiology Society guidelines using the International 10–20 electrode placement system, and all were reviewed and interpreted by neurologists before an NFB specia list decided on training locations and frequencies. The EEGs were processed using a 4-s epoch Hanning window, with a 50% overlapping "sliding window" to process deartifacted epochs.

Behavioral Signs and Clinical Diagnosis of Epilepsy

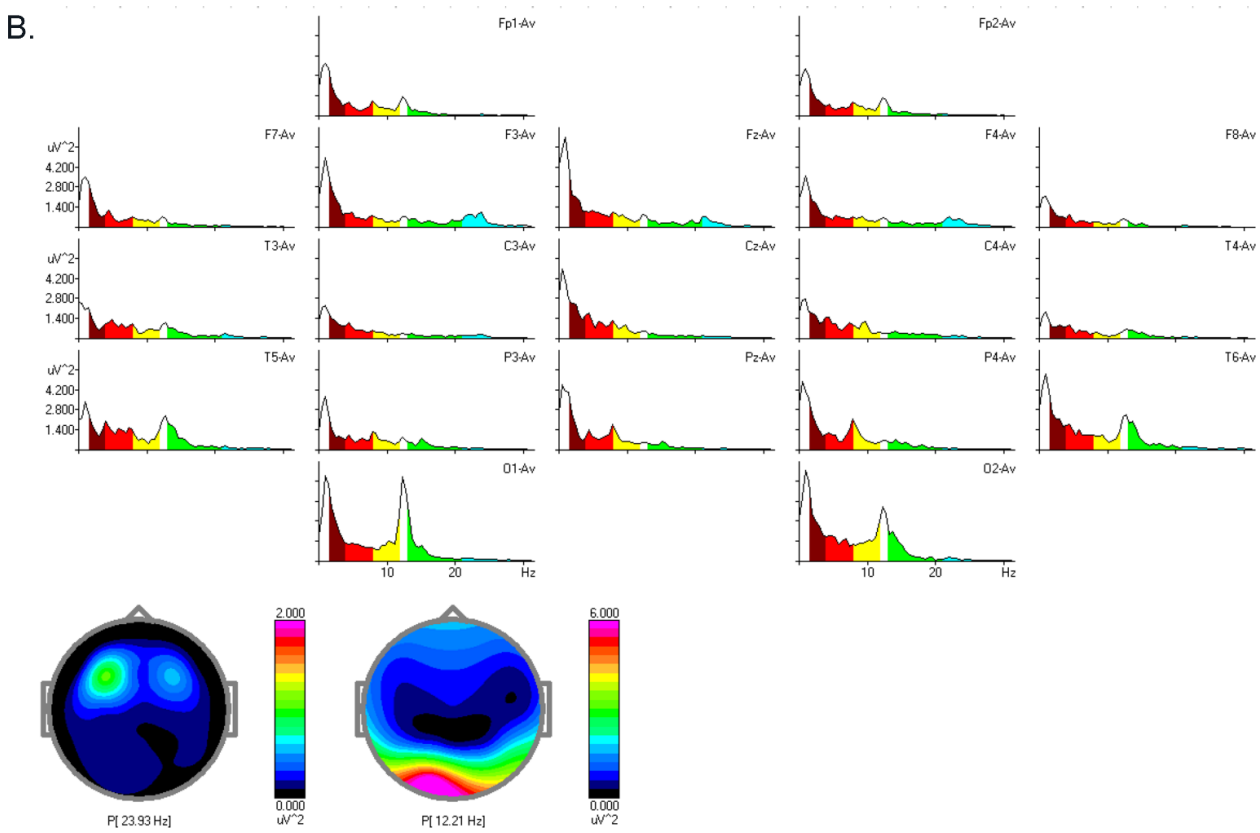
At age 13 (2015), the first outward signs of seizures were recognized, with rapid eye-blinking, difficulty with breathing, and choking sounds. Neurologists diagnosed temporal lobe epilepsy (TLE) and recommended medications should be considered, although no antiseizure medication was prescribed at that time. The patient's seizures became progressively worse, with more frequent and intense episodes over the next 2 months. In one day, she experienced over 120 seizures, including full body and lung stoppages, and was admitted to the emergency room, followed by an episode of status epilepticus. While hospitalized over the next week, she experienced a peak of ~250 visible seizures per day, including tonic rigidity followed by clonic convulsive activity, choking, cessation of breathing, loss of consciousness and eye. Auras of intense abdominal pain were reported during each seizure.

Figure 1. *Early EEG and qEEG Recordings*.



Note. These recordings were collected in 2013 when the patient was 11 years old, 2 years before she was diagnosed with TLE. (A) EEG and qEEG from EC baseline were collected during the evaluation for NFB for ADHD. Note the 20–24 Hz beta spindles seen frontally, with very fast 12–13 Hz alpha frequencies posteriorly. Subtle spikes and slower activity are also noted left temporally (T5).

Figure 1. *Early EEG and qEEG Recordings*.



Note. (B) In the power spectrum graphical display and topographic mapping, these faster alpha and beta spindles can be seen, indicating CNS overarousal. The temporal epileptiform transients are not seen in the qEEG's averaged spectral displays.

Medications and Adjustments

When hospitalized, the patient began antiseizure medications, up to 400 mg of lacosamide (LAC) and 2500 mg of levetiracetam (LEV) daily. These treatments reduced observed seizures from 250/day to about 90/day. One month after her initial hospitalization, clobazam (CBZ) was added and titrated up to 5 mg daily. During this time, she had very forceful, seizure-related automatisms of uncontrolled hand/fist pounding documented with EEG monitoring.

There was significant sedated demeanor, so medications were reduced under medical supervision. LEV was completely tapered over the following 7 weeks, and with its reduction the peri-ictal automatisms completely ceased. Even with LEV discontinued, she continued to have clouding of her sensorium for the next 5 weeks, so LAC was phased out slowly over the following 8 weeks. CBZ was then also tapered over a 10-week period. Although she was still exhibiting clinical seizures, frequency of events decreased, and she exhibited much-improved cognitive functioning and awareness.

Neurofeedback and Adjunctive Treatments

Encouraged by reported cases of success with NFB for control of seizures (Tan et al., 2009), the patient's parents proposed to the hospital's neurologists that medications should be withdrawn due to the side effects and NFB begun for seizures and epilepsy. The hospital neurologists involved in her care were not supportive of NFB. Her parents nonetheless decided to pursue medication taper and EEG/qEEG-guided NFB, along with adjunctive lifestyle changes and mental skills coaching (MSC). Behavioral side effects of the medications were carefully monitored and successfully eliminated during medication taper.

The patient's mother, who had obtained training and supervision in providing NFB for ADHD, sought out a

treatment team of neurologists, epileptologists, and other clinicians experienced with NFB in PWE. She arranged for EEGs to be acquired and EEG monitoring, and the patient began MSC. An NFB-experienced neurologist recommended six NFB sessions to decrease slow 1–5 Hz activity primarily over F3/F4, followed by more sessions of F7/F8 and then over Fz, as well as decreasing fast beta activities of 21–30 Hz at all sites except T3/T4. This did not resolve any behavioral symptoms, and the patient was referred to a pediatric epileptologist /neurologist who was trained and board-certified in pediatric epilepsy as well as EEG, qEEG, and NFB.

The pediatric neurologist emphasized enhancing SMR (Cz, C4, Fz) and suppressing delta and theta at those sites. Despite over 80 NFB sessions, there was little improvement noted. An NFB trainer recommended fine tuning the sites to between T3/C3 and T4/Cz and more sessions of C3/C4. By early December 2015 (age 14), with little change evident after the NFB approaches noted above, a comprehensive consultation was obtained from a qEEG and NFB expert with decades of EEG experience and training in applied clinical psychophysiology, who recommended use of combined EEG and qEEG to provide a complete assessment to guide training. EEGs continued to show right temporal discharges and more frequent left posterior temporal discharges (Figure 2).

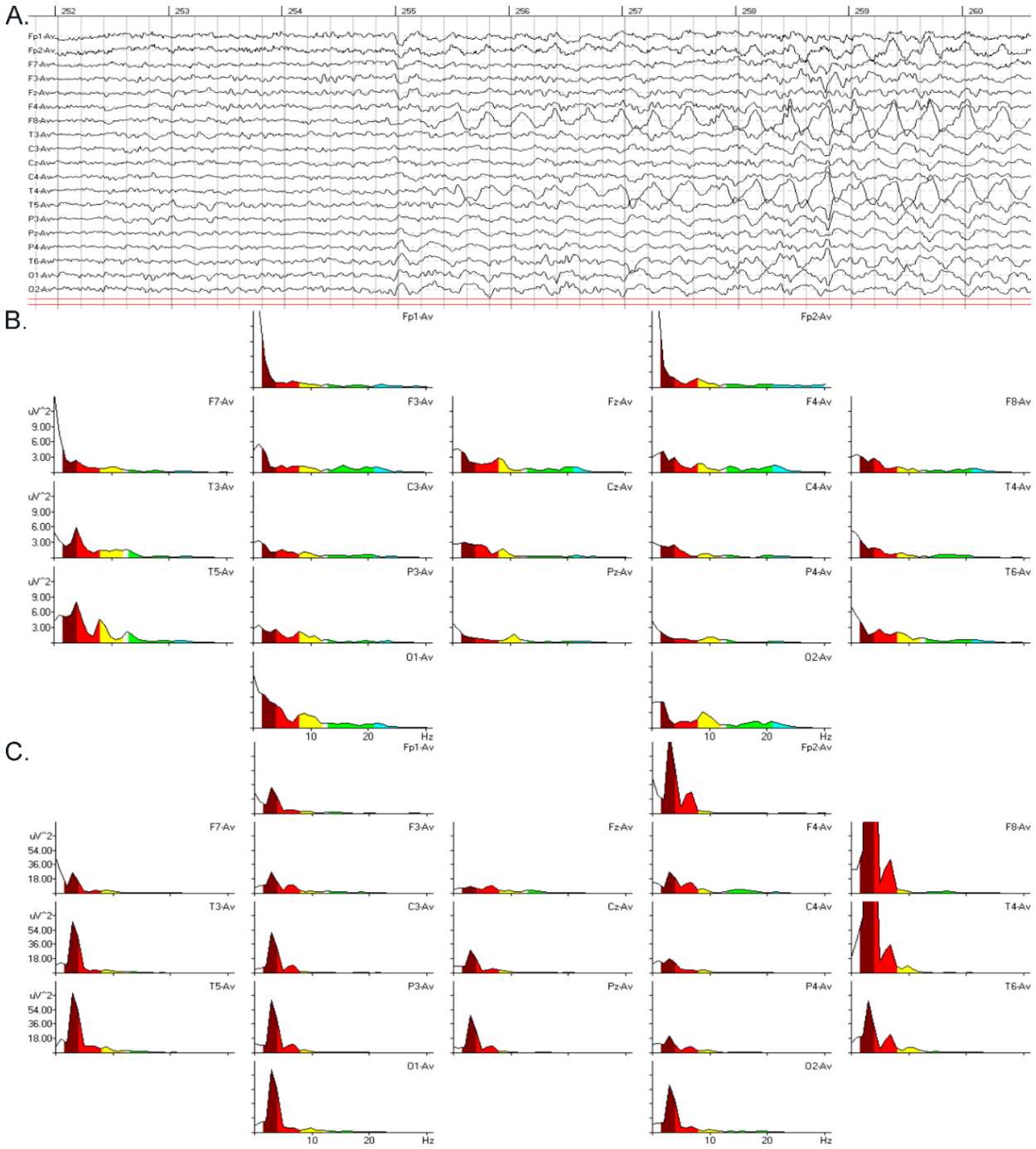
At his direction, the training parameters were altered to enhance SMR at T5-Cz while suppressing both slow (2–7 Hz) and fast (22–30 Hz) activity over 35 sessions. Fifty-one more training sessions followed at T5/T6 and 28 sessions of T5 and O2 training. Following this, neurobehavioral improvements were noted, with fewer akinetic (“drop”) seizures, which generally lasted about 20 seconds, with frequency decreasing to less than 1/day. The patient continued to have drop seizures when participating in sports and would resume play after a seizure. During menstrual periods, seizures were significantly more frequent and severe. Based upon research at the time (Strehl et al., 2005), NFB was changed to 40 sessions of slow cortical potential (SCP) training, but this had little apparent effect. Then, 30 more sessions were conducted using O1 and FCz, followed by 15 sessions of T3-FCz. Following this, “drop” seizures ceased, but clonic/motor seizures (seen as stiffening and clouding, but not total loss, of consciousness) remained. An aura of abdominal pain prior to seizures continued to occur.

Updated EEG/qEEG data suggested NFB training back to SMR at T5-CZ. To address the presumed deep-brain sources of the preictal abdominal pain (Morales-Quezada et al., 2019), training was moved to T3-Cz, with some intermittent training at T5-Fz or T6-Cz. For rationale for these training protocols, the aura of abdominal pain was suggestive of a deep temporal lobe source at or near the Sylvian fissure or insular cortex, where epileptiform discharges may elicit visceral effects, including abdominal pain (Balabhadra et al., 2020; Cerminara et al., 2013). This early aura was one of the most persistent and one of the last symptoms to disappear during treatment. Early treatments were limited by seizure frequency interruptions, and training took place 30, 45, or 60 seconds at a time. Over time, they were extended to six 5-min sessions. The patient had NFB training twice daily for several months (when possible).

Concurrent with NFB, adjunctive treatments were attempted (Table 1). A low glycemic index diet appeared to correlate with improvement in seizures. Other dietary supplements were discontinued due to lack of perceived benefit, including cannabidiol, Omega 3 fish oil, and probiotics (L. rhamnosus and B. longum). Toxicology testing for heavy metals indicated that the patient had elevated copper and low zinc levels. Additional testing including organic acids and infectious/fungi testing, mitochondrial function assessment, levels of oxalates, and other key elemental substances, but these tests did not yield diagnostic clarity. After a monitored chelation and vitamin supplement combination, vitamin and essential metal absorption improved, but had only small impact, if any, on seizure reduction (although there may have been a positive impact on her sleep quality). Homeopathic interventions for one year had no evident impact on seizures.

Because menstruation was associated with increased seizures, transdermal progesterone was attempted, which may have correlated with decreased seizure frequency but not intensity. Electrodermal response BFB training was attempted but not perceived as effective for seizure reduction. Other BFB modalities, including heart rate variability (HRV), abdominal breathing, and muscle relaxation had a positive impact on managing anxiety, reducing triggers for seizures, and reducing or shortening seizures.

Figure 2. *EEG/qEEG During Symptomatic TLE, Age 14*.



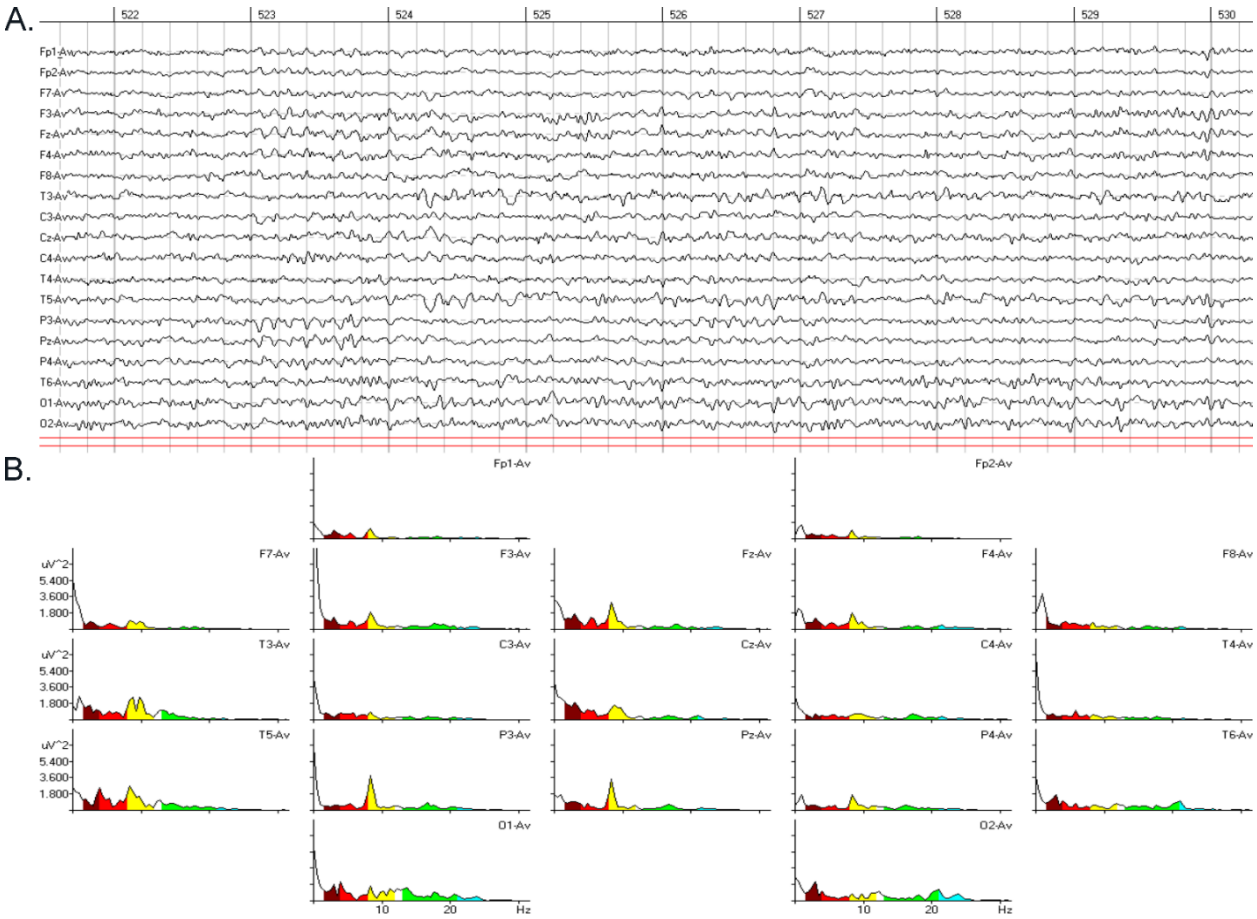
Note. (A) EEG waveforms include a paroxysmal right frontal-temporal discharge. The baseline period showed altered left temporal EEG spectral power, which seemed to trigger the more prominent right hemispheric event. (B) Represents the EEG spectra for the baseline period. (C) Represents the EEG spectra during the right frontal-temporal paroxysmal discharge.

Her overall treatment plan also included mental skills coaching. The skills included progressive relaxation, imagery, HRV, breathing, attentional focusing, and cognitive restructuring to enhance awareness of the feelings of stress or any sensations prior to onset of a seizure, followed by immediate practice of self-regulation skills to quickly alter the mind and body responses. Her ability to produce these changes was documented with BFB training instruments (HRV and EEG). This provided a link between her behavior and body responses and enhanced her self-control and self-confidence. Consistent coaching improved compliance and seeing changes in her daily life resulted in additional confidence and motivation.

Full Abatement of Epilepsy Symptoms

By age 16 (2017/2018), following two years of daily NFB SMR training sessions, the patient did not experience any witnessed akinetic/“drop” seizures, aura/epigastric pain or motor tremulousness, or tonic “stiffening” seizures. She reached two professional semifinals in her sport, illustrating her ability to perform at elite levels without seizures, despite suboptimal sleep, intense sports-cardiovascular challenges, and the mental stressors of university recruitment interviews. An EEG recording at this time, taken after a 12-hour international flight, demonstrated residual elevated spectral power and slowing over the left temporal regions (Figure 3). However, no spikes or abnormal paroxysmal discharges were noted.

Figure 3. *EEG/qEEG After Epilepsy Symptoms Abated, Age 16.*



Note. (A) EEG waveform and (B) Power spectrum graphical display and topographic mapping. Note subtle residual low voltage slowing left temporally. EEG also demonstrated lack of epileptiform discharges and no abnormal paroxysms, with diminution of frontal beta spindling noted in earlier recordings.

At age 17 (2019), the patient experienced the final two epileptic episodes through the writing of this report. In the first, she experienced a 5- to 8-second period of dizziness that occurred after period of illness and physical exhaustion. In the second, she experienced an 8- to 10-second period of hand stiffening on a 17-hour international flight with a 5-hour layover and no sleep. In both cases, she did not lose consciousness.

Current Status

As of the time of writing, the patient remains seizure- and medication-free and carries a full academic load and daily sports workouts at university. Her NFB training is ongoing, and she reports improved attention/focus in her sport and feels at optimal health when she maintains two NFB training sessions per week. While she has shown some continued epileptiform activity in her EEG up to 20 seconds, she has had no outward signs, with the exception of occasional light headedness. She is aware that, in order to remain seizure- and medication-free, intermittent follow up NFB sessions may be required long-term, perhaps for the rest of her life.

Discussion

This successful approach to controlling severe epilepsy was a multi-disciplinary effort, working with a highly motivated patient and parents or caregivers. Although a case report of only one patient, the authors feel the foundation of her successful achievement of controlling, and ultimately eliminating, epilepsy was NFB training over a long period. The monitoring and tracking of NFB training sessions and their outcomes, with ongoing monitoring of the underlying EEG and qEEG changes, allowed the neurologist and EEG specialists to give personalized recommendations and guidance for fine-tuning of training interventions to maximize the beneficial outcomes. When there was little improvement following NFB sessions targeting the prominent right temporal lobe IEDs, NFB training was altered to target the less-prominent left temporal lobe IEDs, and this was followed by behavioral improvements and, eventually, complete seizure cessation.

Concurrent with NFB, adjunctive modalities and coaching helped to improve motivation and health and facilitated the transfer of self-control from training sessions to real-life situations. Importantly, the patient was able to achieve a sense of competence, motivation, and self-confidence from participating in her own treatment. Her physicians and other healthcare providers were knowledgeable and experienced in EEG, qEEG, epilepsy, and NFB training. All these factors were needed to develop, execute, and sustain a relevant treatment plan that was administered at home. This, supplemented with parental or caregiver support and ongoing coaching, allowed for the patient's success in school, sports, and independence in daily life.

While many PWE cannot attend specialized clinics, this case study documents that, with appropriate EEG equipment, training, and guidance and internet access, it is possible to receive extensive help for epilepsy remediation in a cost-effective manner. Technology allows such training to be largely home-based, professionally supervised, and implemented by a trained caregiver, with online professional supervision as required. The development of more sophisticated mobile apps and equipment should aid in the monitoring and training of an individual's brain/body physiologic states during daily life (Dozières-Puyravel et al., 2020).

Conclusions

This case report documents the use of NFB, along with adjunctive interventions, for a young female who progressed from severe, medically intractable temporal lobe epilepsy to a current performance as a university student and athlete in a NCAA Division I sport. Those of us involved in her clinical care and management believe that her story can bring hope and inspiration to others experiencing intractable epilepsy and that it will encourage research in alternative therapies.

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Author Declaration

There are no financial interests or conflicts to report.

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