Epilepsy Research (2014) **108**, 600—603

journal homepage: www.elsevier.com/locate/epilepsyres

SHORT COMMUNICATION

Refractory status epilepticus treated with trigeminal nerve stimulation

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Received 26 August 2013; received in revised form 9 November 2013; accepted 5 December 2013
Available online 30 December 2013

KEYWORDS
Critical care;
Status epilepticus;
Refractory status epilepticus;
Trigeminal nerve stimulation;
TNS

Summary Refractory status epilepticus (RSE) is a neurologic emergency associated with significant morbidity and mortality. Alternative therapies are needed for patients who do not respond to more traditional therapies for RSE. We report on a patient with RSE treated with external trigeminal nerve stimulation (eTNS). On admission, the patient was experiencing consecutive focal dyscognitive seizures with secondary generalization without recovery in between. His seizures remained refractory to multiple therapies, including IV lorazepam, valproic acid, levetiracetam, phenobarbital, and midazolam. Although a burst suppression pattern was achieved with a continuous pentobarbital infusion, seizures returned following attempts to taper it. Given his beneficial response to eTNS during a previous clinical trial, eTNS was initiated. Four days after starting eTNS, the pentobarbital infusion was finally weaned, and his EEG revealed no further seizures. The patient's mental status improved and he was ultimately discharged with only moderately severe disability. Our case demonstrates that eTNS may have antiseizure effects in RSE. Given our patient's quick response, such benefit may have arisen from EEG-desynchronization. If confirmed in larger studies, eTNS could one day be considered along with other adjuvant treatments for RSE.

Introduction

Refractory status epilepticus (RSE) accounts for 30—40% of all cases of status epilepticus (Holtkamp et al., 2005; Mayer et al., 2002). RSE is associated with poor outcome in up to 75% of cases (Hocker et al., 2013). This includes irreversible cognitive/neurologic damage, prolonged hospital stay, and need for inpatient rehabilitation (Novy et al., 2010). Death may ultimately occur in 38% of cases (Sutter et al., 2013). Such outcomes suggest the urgent need for alternative therapies for patients who fail first, second, and third line therapies, or in whom seizures return when such therapies are weaned.

External trigeminal nerve stimulation (eTNS) is an emerging therapy for drug resistant epilepsy (DRE). Its efficacy in DRE has been demonstrated in previous studies, including a Phase II double-blind randomized active-control trial (DeGiorgio et al., 2013). However, the use of eTNS in the

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http://dx.doi.org/10.1016/j.eplepsyres.2013.12.010

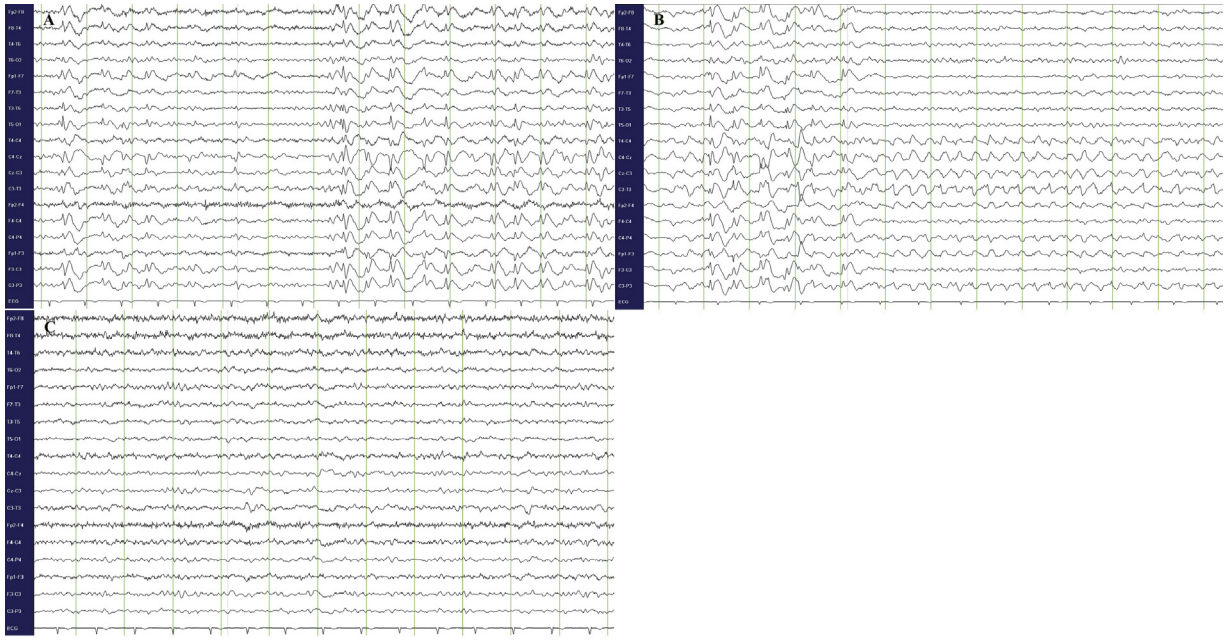

Figure 1 Treatment of refractory status epilepticus with trigeminal nerve stimulation.
(A) On admission, the patient's EEG revealed a continuous trains of spike and wave and periodic epileptiform discharges merging with periods of suppression associated with clinical seizure activity and impairment of awareness.
(B) These occasionally evolved into rhythmic discharges in the centrotemporal head regions. These discharges were often associated with right or left arm jerking, stereotyped vocalizations, and facial grimacing. These discharges persisted despite lorazepam, phenobarbital, levetiracetam, midazolam, and a pentobarbital infusion. Clinical and electrographic seizures returned each time an attempt to wean pentobarbital was attempted.
(C) A trial of eTNS was undertaken to allow weaning of pentobarbital. Following 4 days of eTNS, the pentobarbital infusion was finally weaned. The EEG revealed no further clinical/electrographic seizures.

treatment of status epilepticus has not been previously explored. We report on a case where eTNS was used as an adjunctive treatment in RSE.

Methods

Case-report and review of the literature.

Results

A 32 year-old male with severe drug resistant epilepsy was admitted for status epilepticus. He had suffered from multifocal dyscognitive seizures with secondary generalization since childhood. He had unsuccessfully tried multiple antiepileptic drugs, including phenobarbital, primidone, phenytoin, lamotrigine, levetiracetam, zonisamide, vigabatrin, gabapentin, topiramate, carbamazepine, pregabalin, clonazepam, valproic acid, lacosamide, and rufinamide. His pre-surgical evaluation had included an MRI brain, which revealed hyperintensities in the left opercular, left temporal, and left frontal regions. However, prolonged video electroencephalography (EEG) monitoring revealed seizures arising independently from the left and right frontal regions, precluding resective epilepsy surgery.

The patient had been part of a randomized, double blind parallel trial of eTNS for intractable epilepsy. At baseline, he average 2.86 seizures/day (80 seizures/month). During the clinical trial, he was randomized to control (sham) stimulation therapy and was a non-responder, with less than 50% reduction in seizures. He was crossed over to active eTNS stimulation during long-term follow-up. He subsequently reported 1.07 seizures/day at 3 months (a 63% reduction from baseline) and 1.16 seizures at 6 months of long-term follow-up (a 59% reduction from baseline). During this time, he experienced skin irritation. Although such irritation may have been secondary to his pre-existing eczema, he ultimately elected to exit the long-term protocol to try another antiepileptic drug.

Admission was prompted by an acute worsening of seizures in the setting of a lacosamide and rufinamide taper for side effects (nausea). The seizures were marked by motor arrest, right or left arm jerking, stereotyped vocalizations, facial grimacing, and secondary generalization. The patient's mental status failed to return to baseline in between seizures. His EEG revealed continuous trains of spike and wave and periodic epileptiform discharges merging with periods of suppression (see Fig. 1A). These occasionally evolved into rhythmic discharges in the centrotemporal head regions (see Fig. 1B). Such discharges were associated with clinical seizure activity and continued impairment of consciousness. Such a sequence of EEG changes has been previously described during generalized convulsive status epilepticus (Treiman et al., 1990).