

INTRODUCTION

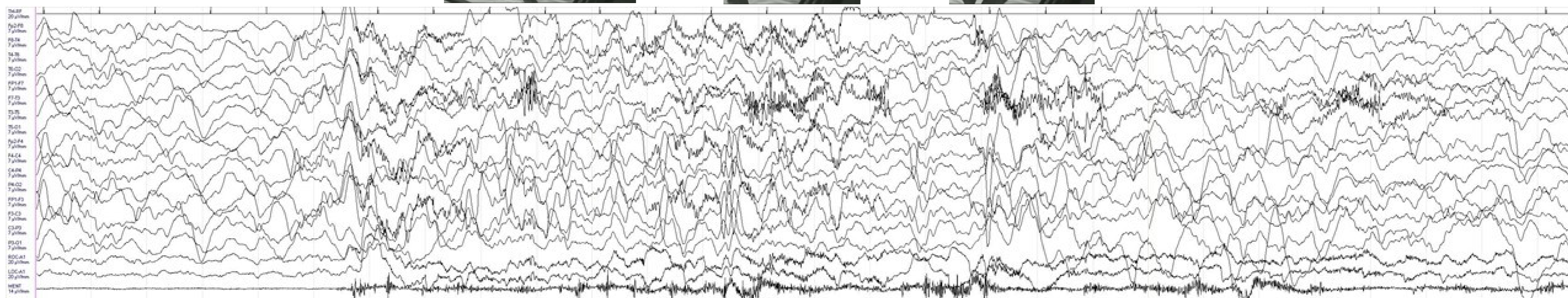
Nocturnal frontal lobe epilepsy (NFLE) counts a complex clinical spectrum of distinct paroxysmal sleep-related attacks of variable duration and intensity, including paroxysmal arousals, nocturnal paroxysmal dystonias and epileptic nocturnal wanderings. Scalp EEG and brain MRI are unable to reveal abnormalities in a considerable amount of patients. In those cases the epileptic nature of NFLE is supported by the stereotypical clinical presentation of the episodes and the often dramatic response to antiepileptic drugs (AEDs).

METHODS

We report two patients affected by drug-refractory NFLE successfully treated with lacosamide (LCM).

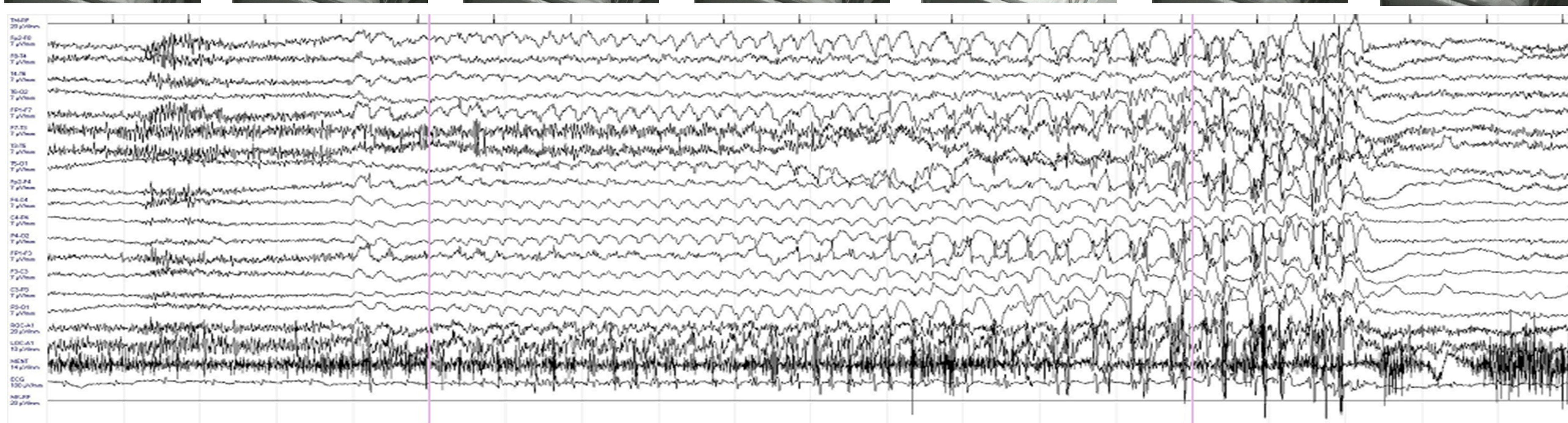
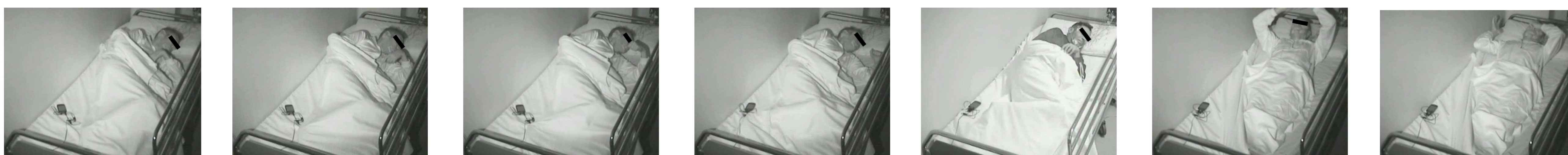
PATIENT 1

A 16-year old boy showed from age 6 nocturnal seizures characterized by stereotyped motor behaviors, associated with dystonic posturing of the upper limbs or simple motor acts such as head scratching, limb flexion, pelvic movements and gestural automatisms (swiping nose by right hand). Ictal video-polysomnography documented bilateral frontal monomorphic slow waves arising from non-REM sleep. Brain MRI was unremarkable and mutations in nAChR were not detected. Although he was treated with oxcarbazepine 900 mg/day and clonazepam 1 mg/night, nocturnal seizures endured. Therefore LCM 200 mg/day was added with abrupt reduction of seizures. After collecting parental informed consent, oxcarbazepine and clonazepam were stopped and the patient remained on LCM monotherapy, then he was seizure-free at 12-month follow-up.



PATIENT 2

A 43-year old man presented from age 17 stereotyped nocturnal seizures characterized by left head deviation, left arm elevation and right arm flexion, sometimes accompanied by jerks involving lower extremities and secondary generalization. Ictal video-polysomnography showed the abrupt transition from non-REM sleep to slow activity localized in bilateral frontal regions followed by spikes and slow waves discharges. No family history of epilepsy and/or parasomnia was reported. Brain MRI was unremarkable and mutations in nicotinic acetylcholine receptor (nAChR) were not detected. Seizures were refractory to carbamazepine as monotherapy (up to 800 mg/day) or associated with valproic acid (1500 mg/day), zonisamide (400 mg/day), phenobarbital (100 mg/day), topiramate (up to 300 mg/day) and clobazam (up to 30 mg/day). Therefore, LCM 200 mg/day was added to carbamazepine and topiramate and nocturnal seizures were dramatically abolished. After signing informed consent, the patient slowly withdrew carbamazepine and topiramate remaining on LCM monotherapy with a seizure-free period at 12-month follow-up.



CONCLUSIONS

NFLE is widely considered a benign clinical entity because seizures occur during sleep and are commonly controlled by carbamazepine; however, other effective treatments are topiramate, oxcarbazepine and acetazolamide.

Our report showed that LCM may be efficacious in NFLE, either in add-on or as conversion monotherapy. The remarkable effect of LCM in our patients may arise from the multiple mechanism of action of the drug. In fact, LCM acts not only on the slow inactivation of voltage-gated sodium channels, but also inhibits carbonic anhydrases. Then, LCM shares the main molecular target with carbamazepine and the latter with topiramate and acetazolamide.

Although larger samples are needed to confirm our observation, this report proposes LCM as a new therapeutic possibility in NFLE patients.