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Propofol withdrawal seizures: non-epileptic nature of seizures in a patient with recently controlled status epilepticus

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ABSTRACT – Seizures or seizure-like phenomena which are mostly convulsive have been observed during the induction, maintenance and withdrawal phases of propofol administration. The nature and mechanism of this phenomenon are not well understood and several case reports on these phenomena have presented only indirect evidence. We report on a patient who was administered propofol in order to control status epilepticus with success. However, every attempt at propofol withdrawal was followed by convulsive seizure-like activity. Continuous EEG monitoring showed muscle artefacts without any ictal discharges. Based on this finding, the propofol treatment was withdrawn and the seizure-like activity eventually attenuated and resolved. We propose that seizure-like phenomena associated with propofol withdrawal may not be ictal in nature and should not lead to unnecessary resumption of propofol infusion without documentation of an epileptic origin by EEG.

Key words: seizure-like phenomena, propofol, propofol withdrawal, status epilepticus, EEG

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Propofol is a short-acting anaesthetic frequently used in the intensive care unit for sedation and anaesthesia, as well as for termination of status epilepticus. Although propofol has antiepileptic properties and has an established role in the control of refractory status epilepticus (Brown and Levin, 1998), its use may also be associated with seizure-like phenomena (SLP) (Walder *et al*., 2002). The nature of

these phenomena has been debated, with some authors favouring an epileptic and others a non-epileptic nature (Hickey *et al*., 2005; Zeiler and Kaplan, 2008; Sutherland and Burt, 1994). To the best of our knowledge, no study has provided concomitant video-EEG during SLP to confirm seizure activity on EEG. We present a patient who had SLP which was observed at the time of propofol withdrawal, however, video-EEG failed to show ictal discharges, consistent with the non-epileptic nature of this phenomenon in this instance.

Case report

A 41-year-old woman with a history of long-standing partial epilepsy was admitted with generalised convulsive status epilepticus. She had a left temporal resection ten years previously, after which she was seizure-free for 18 months. She had status epilepticus upon medication withdrawal, followed by recurrent complex partial seizures despite treatment with levetiracetam and carbamazepine. On the day of admission, she presented with generalised tonic clonic status epilepticus lasting 45 minutes and was unresponsive to lorazepam and fosphenytoin. She was intubated and placed in a propofol-induced coma with continuous EEG showing a burst suppression pattern. The bursts included mixed frequency (theta, delta and alpha) low to medium-voltage irregular activity, without ictal or interictal epileptiform discharges. The next day, propofol was withdrawn and EEG activity became continuous with more irregular asynchronous than synchronous activity and generalised delta as well as theta activity. Again, no ictal or interictal epileptiform discharges were seen. About ten minutes after propofol discontinuation the patient started experiencing convulsive activity involving her upper extremities and torso. The motor activity was best described as persistent high frequency coarse rhythmic shaking. This activity was interpreted as recurrent status epilepticus and prompted the treating physicians to restart propofol treatment, without analysing the concomitant EEG. The epilepsy service was consulted and noted only muscle artefact on the EEG in association with the motor activity *(figure 1)*. A second trial of propofol withdrawal was performed with an epileptologist at the bedside. Similar convulsive motor activity occurred again, about five minutes after stopping propofol treatment, but the concomitant EEG showed muscle artefact without any ictal activity. Propofol treatment was not restarted and the patient was sedated with fentanyl. The abnormal movements attenuated and stopped after approximately 30 minutes. She slowly returned to her baseline in the next three days and was discharged on levetiracetam and carbamazepine.

Discussion

Propofol is a non-barbiturate anaesthetic agent with a proposed mechanism which involves activation of GABA-A receptors, inhibition of NMDA receptors and modulation of calcium influx through slow calcium ion channels (Kotani *et al*., 2008). It has been postulated that propofol acts at different binding sites to those of benzodiazepines and barbiturates and can work synergistically with these drugs in controlling seizures (Brown and Levin, 1998). Despite its antiepileptic properties, propofol has been associated with a variety of motor phenomena including clonus, myoclonus, opisthotonus, generalised tonic clonic activity, and focal motor activity (Walder *et al*., 2002; Cochran *et al*., 1996). It is because of their resemblance to epileptic seizures that these motor phenomena are referred to as SLP. A review article (Walder *et al*., 2002) suggested that this phenomenon is associated with a change in cerebral concentration of propofol as SLP occur mostly during escalation or withdrawal of the drug and only infrequently during the maintenance phase.

The nature of SLP has been a subject of debate. Several investigators have argued for a non-epileptic nature of SLP since propofol consistently reduces seizure duration during electroconvulsive therapy, controls refractory status epilepticus, and protects against seizures in animal models of epilepsy (Borgeat, 1997) (Rossetti *et al*., 2004). In one study using propofol as sedation prior to MRI in children with epilepsy or learning difficulties, no SLP were recorded and propofol caused transient suppression of spike-and-wave discharges in patients with epilepsy, confirming its antiepileptic properties (Meyer *et al*., 2006). On the other hand, some authors proposed that propofol produces excitation in subcortical structures at low doses (Dolin *et al*., 1992). One recent case report argued in favour of an epileptic nature based on elevation of serum prolactin level following SLP (Zeiler and Kaplan, 2008), however, no EEG monitoring was performed during the SLP.

Our patient had SLP with concurrent EEG which failed to show any ictal discharge. This led us to discontinue propofol treatment and the motor activity ceased within about 30 minutes. The patient was extubated easily the following day and returned to baseline at the time of discharge. Non-epileptic SLP should be considered as an alternative diagnosis to epileptic convulsive seizure activity after propofol withdrawal. The occurrence of SLP during propofol withdrawal should not automatically result in resumption of propofol. Instead, an EEG should be obtained promptly to resolve the nature of the motor activity. □

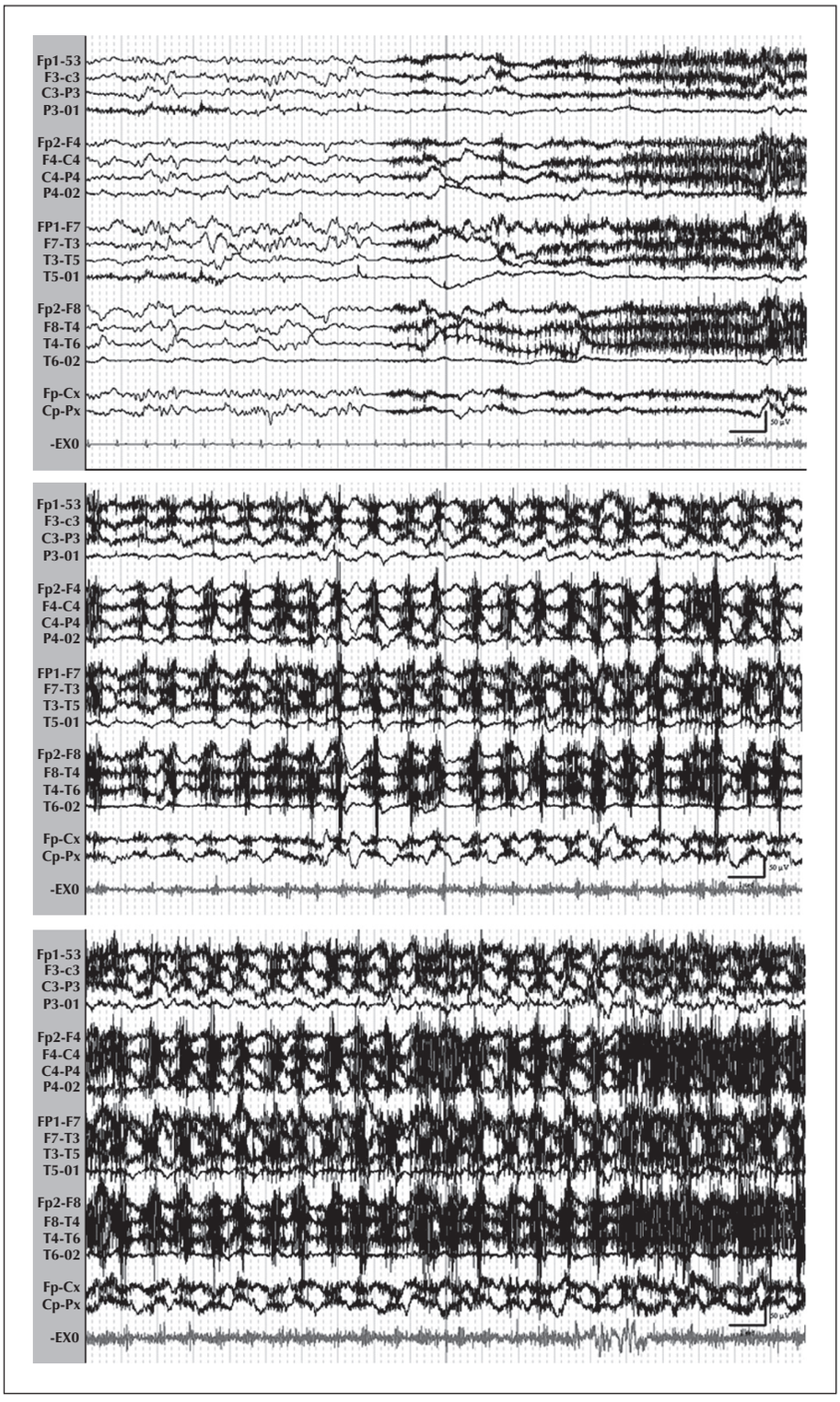

Figure 1. EEG at onset of seizure-like activity. The three panels are consecutive 20-second windows. The EEG shows muscle artefact without any ictal discharge.

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