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Masking of Epileptiform Activity by Propofol during Seizure Surgery

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Propofol has been used extensively at our institution to provide sedation during a variety of neurosurgical procedures performed in "awake" patients. These have included stereotaxic brain biopsy, placement of dorsal column stimulators, and craniotomies for resection of tumors or epileptic foci. Although propofol has proven very satisfactory in these situations, we recently encountered a circumstance in which propofol appeared to interfere with the intended procedure. Our experience with this case suggests that, in the very light stages of propofol sedation, particularly in the emergence phase after a prolonged period of propofol sedation, very marked β activity may occur in the electroencephalogram (EEG) and may hinder recognition of underlying abnormal EEG patterns.

CASE REPORT

The patient was a 27-yr-old, 110 kg woman with a prolonged history of complex partial seizures presumed to be related to birth trauma. Despite attempts to achieve control with several pharmacologic regimens, she continued to have three to five seizures per day. She underwent evaluation by the Epilepsy Program at the University of California, San Diego. All antiseizure medications were discontinued. Subdural and foramen ovale electrodes were placed bilaterally, and scalp and intracranial video-EEG telemetric electrocorticogram recording was performed. The recordings revealed a seizure focus in the left inferior-lateral temporal lobe. Figure 1 presents a sample of the abnormal interictal spike and slow-wave activity that was evident in that region. A Wada test[1] was performed and demonstrated that language function was controlled by the left hemisphere and that there was bilateral representation for memory. The patient was scheduled to undergo craniotomy while awake for partial temporal lobe resection with intraoperative EEG recording and speech and memory testing.

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The patient was brought to the operating room unpremedicated. Monitoring included an automated blood pressure cuff, an electrocardiogram, pulse oximetry, and capnography. The capnography was accomplished by sampling from a 18-G Teflon intravenous catheter placed within one limb of the nasal prongs through which oxygen was administered. Immediately prior to infiltration of the scalp with local anesthetic, propofol 1 $mg \cdot kg^{-1}$ was administered intravenously, and a propofol infusion was instituted at a rate 75 $\mu g \cdot kg^{-1} \cdot min^{-1}$. This regimen was not sufficient to achieve unresponsiveness. A supplementary bolus of 0.5 $mg \cdot kg^{-1}$ was administered, and the infusion rate was increased in increments to 125 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Immediately after scalp infiltration, the head holder was applied. Propofol administration was then discontinued. Within 3 min the patient was responsive to commands. The patient remained awake during the period of skin preparation and application of the drapes. Propofol sedation was reinstituted (bolus 1.25 mg/kg; infusion 125 $\mu g \cdot kg^{-1} \cdot min^{-1}$) immediately prior to skin incision and was discontinued immediately upon completion of the bone flap. During subsequent attempts to reflect the dura, the patient experienced considerable discomfort in association with dural traction. The discomfort was only incompletely relieved by infiltration of additional local anesthetic. Accordingly, the propofol sedation regimen was reinstituted and was continued until completion of dural reflection. Up to this point, the patient had received 2,100 mg propofol. Within 5 min the patient was again conversant.

The neuropsychologist began the explanation of the speech and object-recognition testing that was to be performed during the resection, and simultaneously the surgeon began the application of an array of electrodes over the prerolandic and lateral temporal cortex. The initial electrocorticogram recordings revealed high-amplitude, high-frequency (β) activity in all leads (fig. 2A), and the abnormalities that had been consistently evident in previous interictal recordings could not be identified. The patient was at this time conversing with the neuropsychologist. That interaction was discontinued. Recording was attempted with the patient's eyes open and eyes closed. The substantial β activity persisted in all circumstances. This pattern of activity continued for approximately 10 min, at which time there was some reduction in its amplitude, and the abnormalities that had been observed in the preoperative period could then be detected in the inferior lateral temporal leads superimposed on the β activity (fig. 2b). The resection proceeded with intermittent evaluation of speech function. No further propofol was administered. Approximately 2 h later repeat cortical electrocorticogram recordings were performed. Neither β activity nor the abnormal pattern was observed, and the procedure was concluded.

DISCUSSION

There have been previous investigations of the effects of propofol on the EEG in humans. Borgeat *et al.* recorded the EEG after administration of bolus doses of propofol 3–5 $mg \cdot kg^{-1}$ to children.[2] They observed a very brief period (2 s) of EEG activation including β activity during the onset of the propofol effect and then a more sustained period of β activity after the period of maximum clinical

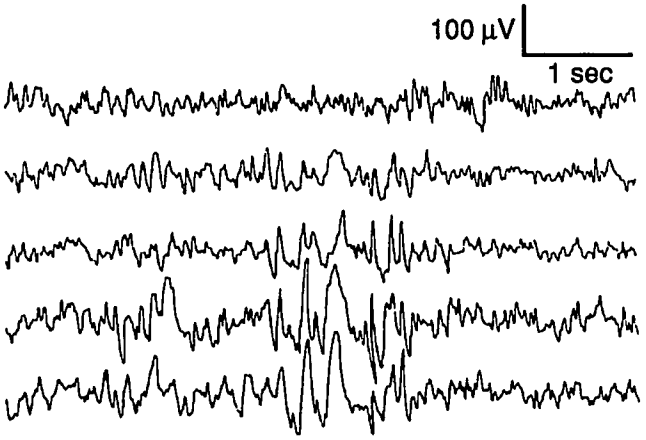

FIG. 1. Electrocorticogram recorded from the lateral and inferior–lateral surface of the left temporal lobe. The interictal spike and slow wave pattern that was recurrent in this patient is evident in the three most inferior leads.

effect during which slow-wave activity predominated. An investigation by Schwilden *et al.* revealed that propofol anesthesia was associated with very substantial reduction of high-frequency EEG activity with a concomitant reduction in both spectral edge and median frequency.[3] However, that investigation also revealed, although the report does not emphasize it, that in the emergence phase after discontinuation of propofol infusion, both spectral edge and median frequency increased to levels above those of the preanesthetic control state. It was a preponderance of activity in the β frequency range that accounted for these increases.

These two reports[2,3] suggest that our observation of β activity in association with probable low residual serum concentration of propofol was not unique. However, in the majority of situations that arise in the operating room, it is EEG effects that occur at or near surgical planes of anesthesia that are of most interest to the anesthesiologist. Customarily, the EEG patterns observed in association with states in which the patient is awake and conversant have little relevance. However, craniotomy in awake patients with cortical mapping may represent an exception to this generalization. Our experience suggests that at times when the degree of residual sedation is clinically minimal, the residual electrophysiologic effect may still be substantial. A similar dissociation between the magnitude of sedative and electrophysiologic effects was recently reported by Kalkman *et al.*[4] in connection with an investigation of motor evoked responses in humans. In that investigation, prolonged suppression of the motor evoked response was observed following propofol administration in subjects in whom the effects on level of consciousness appeared to have resolved.[4]

From the EEG record of the present case, it is not certain whether the patient's typical, abnormal EEG pattern (fig. 1) was suppressed by propofol or merely obscured by it. Although there have been several case reports of postpropofol "seizures" or opisthotonus that have prompted suspicions that propofol may be proconvulsant,[5–7] systematic investigations in both animals and humans strongly suggest that propofol has anticonvulsant effects.[8,9] However, the implications of these two possibilities for the anesthetic management of the type of procedure described in this report are the same. Whatever the mechanism, our experience suggests that propofol's electrophysiologic effects may persist for a short period beyond clinical recovery from propofol-induced sedation and may mask underlying epileptiform activity.

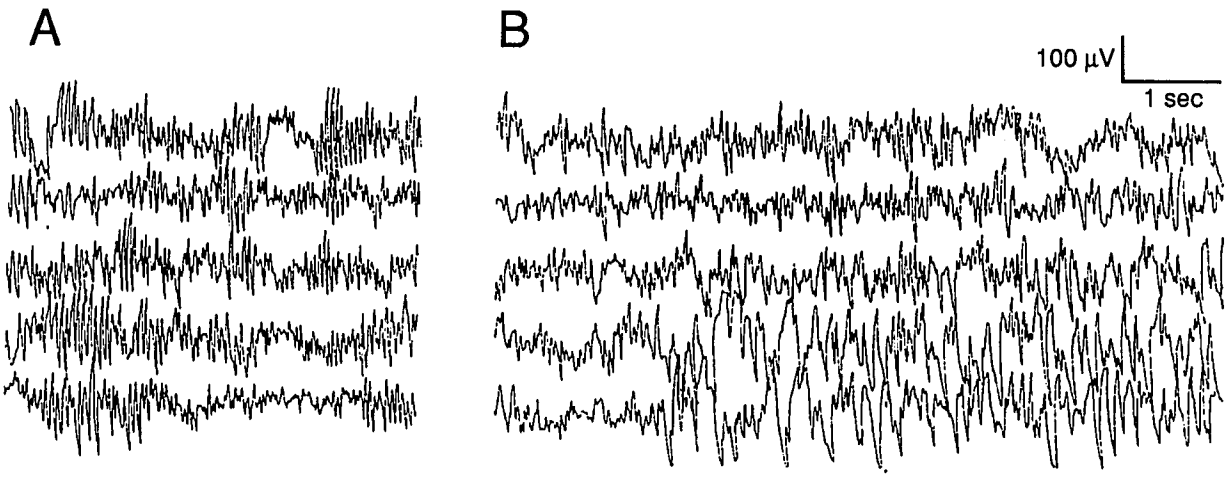

FIG. 2. *A:* The initial electrocorticogram from the inferior and lateral temporal lobe revealing a predominance of activity in the β frequency range. *B:* Recordings from the same leads made 10 min later. The β activity persists but is somewhat attenuated, and the abnormal activity seen in the preoperative recordings (fig. 1) is now evident in several leads.

We have subsequently observed the same β activation phenomenon in the EEG recorded in other patients receiving propofol by infusion during "awake" craniotomy for tumor resection. In general, the phenomenon appears to be short-lived, lasting at most a few minutes. It was rather more prolonged in the patient described in the current report. In fact, we are uncertain of the precise duration because the recording was discontinued following identification of the abnormal focus within the waning β activity. The current patient may in fact represent a relatively extreme case of the phenomenon because of the very large total dose of propofol that was administered. Our experience has not precluded our use of propofol for awake craniotomy with surface mapping but has rather encouraged us to limit the dose and duration of exposure such that there is a substantial propofol-free interval prior to undertaking surface mapping.

We have not yet had the opportunity to evaluate the effects of concurrent administration of other anesthetic or sedative agents on the occurrence of this β activation phenomenon. In some institutions, opioids and benzodiazepines are frequently administered as sedatives for procedures of this nature. These agents, however, have been systematically avoided in our practice. The benzodiazepines have been omitted to avoid the possibility that their anticonvulsant effect will render abnormal areas of cortex more difficult to identify electrophysiologically. The opioids have been restricted because of the perceived hazards of using a respiratory depressant when propofol is being titrated to the point of unconsciousness in a patient in pin fixation with an unsecured airway. It is entirely possible that the addition of these adjunctive agents might alter the β activation phenomenon substantially. However, β activation has also been observed in association with subanesthetic levels of several other intravenous anesthetic agents. It has been reported after administration of thiopental, pentobarbital, amobarbital diazepam, and midazolam,[10–12] although with the two benzodiazepines conspicuous increases in amplitude do not occur. It has not been observed with opioids and etomidate.[13,14] Because β activation does occur with some other agents, it is possible that the EEG effects of propofol that we have observed represent a nonspecific effect of arousal at the time of emergence from anesthesia. The various reports cited above do not make the patients' precise level of function at the time of EEG activation apparent, and as a result interagent comparisons are difficult. It must suffice to say that in the present patient, the β activation was apparent at a time when the patient was oriented and conversant and not in a state of apparent emergence delirium.

In summary, the present case suggests that administration of propofol may result in very substantial β activity in the EEG. This activity appears to be most likely to occur at times when the patient would be considered clinically to be "awake." The activity may be sufficient to obscure other underlying EEG patterns.

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