Drug Effects on EEG

Warren T. Blume

Abstract: Although excess beta activity and a mild theta increase may be the most common EEG alterations associated with medication, more remarkable changes may also appear. Although changes such as diffuse delta, triphasic waves, bisynchronous spikes or polyspikes, burst suppression or electrocerebral inactivity may indicate a dismal prognosis under many circumstances; these patterns may fully resolve to a normal EEG if drug administration is the unique or principal cause.

Key Words: Drug effects, EEG, Prognosis.

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As a substantial proportion of patients undergoing electroencephalography (EEG) take one or more medications of various kinds, the electroencephalographer must bear their effects in mind when reading the EEG and phrasing its clinical interpretation. Moreover, an asymmetry of drug effects may reflect a focal or hemispheric lesion whose EEG effects may not have been otherwise recognized.

PRINCIPLES OF DRUG EFFECTS

Factors

Quantity of medication in the patient influences the EEG. This quantity varies according to dose, volume of distribution, and rate of metabolism.

Systemic effects of medication, e.g., hyponatremia from Carbamazepine, may diffusely perturb the EEG. Any preexisting systemic disorder may augment this effect. Additionally, anecdotal experience suggests that prominence of drug-related EEG alterations vary among patients beyond the aforementioned factors. Anomalous target or multidrug transporter mechanisms may apply (Loscher et al., 2006).

Principal Modifications

Table 1 lists features discussed in the following sections. Typically, these should appear symmetrically and possibly diffusely. Less effect in one hemisphere or region may indicate a lesion there (Blume et al., 2002a). A greater effect, usually as beta activity, may relate to a skull defect, i.e., a breach rhythm (Blume et al., 2002b).

Professor Emeritus of Neurology, University of Western Ontario, London, Ontario, Canada

Address correspondence and reprint requests to Warren T. Blume, MDCM, FRCPC, Professor Emeritus of Neurology, University of Western Ontario, London, Ontario, Canada N6A 5A5; e-mail: Warren.Blume@lhsc.on.ca

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SPECIFIC MODIFICATIONS

Beta

An augmentation of voltage, field distribution, and persistence of normally appearing 15 to 25 Hz Beta activity most commonly indicates the presence of a medication effect on the EEG (Figs. 1–3). Barbiturates and benzodiazepines most prominently produce this effect (G. Bauer and R. Bauer, 2005; Van Cott and Brenner, 2003). Greater than usual theta activity may accompany such beta excess (Blume et al., 2002). Central nervous system stimulants such as cocaine, amphetamines, and methylphenidate as well as tricyclic antidepressants may evoke greater beta activity at low voltage (G. Bauer and R. Bauer, 2005; Van Cott and Brenner, 2003). Withdrawal from alcohol and barbiturates may produce a similar low voltage EEG with beta activity.

Beta activity is more abundantly expressed by medication in children than in adults and with acute rather than chronic administration.

Epileptiform Activity

High doses of several types of medications may elicit spikes or poly spikes that usually appear bisynchronously in bursts, either spontaneously (Fig. 4) or as a photoparoxysmal response. Drugs known to possess this capability include Clozapine, (Fig. 5) Lithium, Phenothiazines, selective serotonin reuptake inhibitors, and tricyclic antidepressants.

Acute withdrawal of alcohol or barbiturates may also elicit bursts of spikes and polyspikes, particularly as a photoparoxysmal response (G. Bauer and R. Bauer, 2005; Van Cott and Brenner, 2003).

Reduction of antiepileptic drugs (AEDs) may augment focal spikes or spike waves. This increase may reflect seizure occurrence (Van Cott and Brenner, 2003; Kaibara and Blume, 1988). Young and DaSilva (2000) noted reversible EEG findings of spikes and periods of attenuation in neonates on morphine.

TABLE 1. Principal Changes

Background slower
Phenytoin and others
Excess beta
GABA agonists: barbiturates, benzodiazepines
Epileptiform activity
Triphasic waves
Theta and Delta
Coma patterns

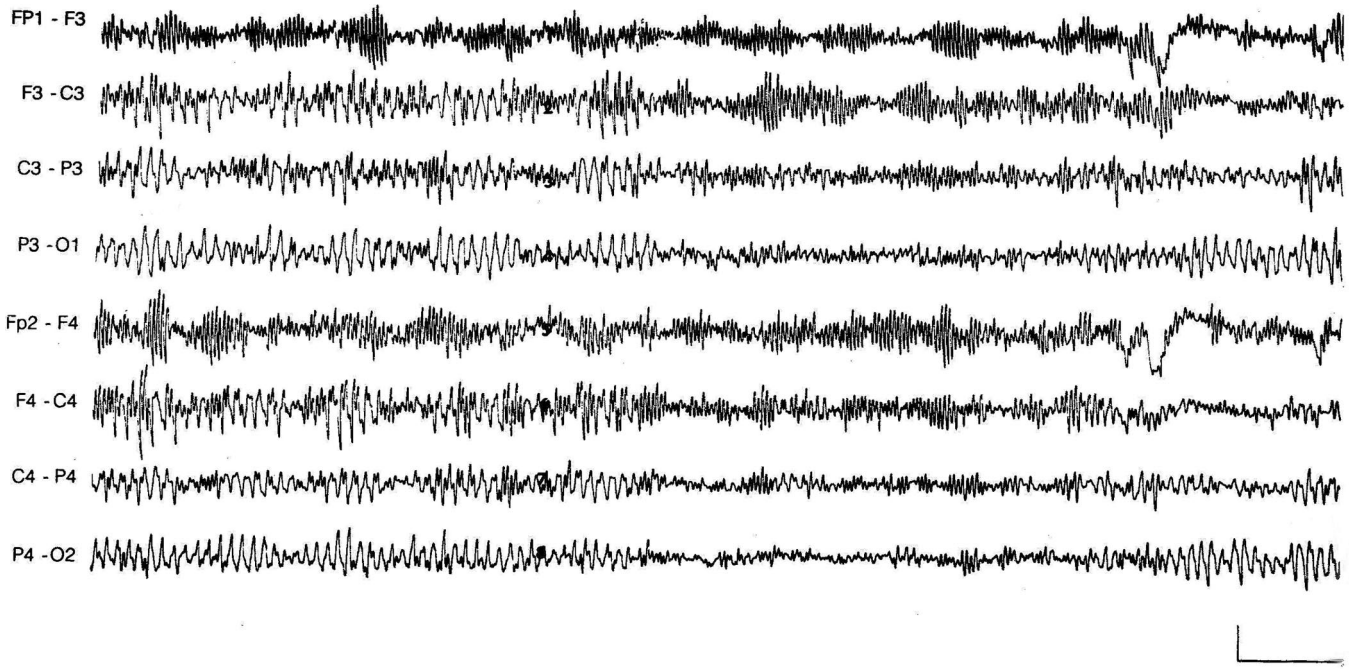

FIGURE 1. Beating of beta. Prominent diffuse predominantly anterior beta is the most common obvious medication effect. As does alpha, the amplitude of beta activity may wax and wane in a regular fashion, producing a "beating" appearance. Note that its combination with 10 Hz alpha (or mu) produces a particularly apiculate appearance in the first 5 seconds. Calibration signal 1 second, 50 μV.

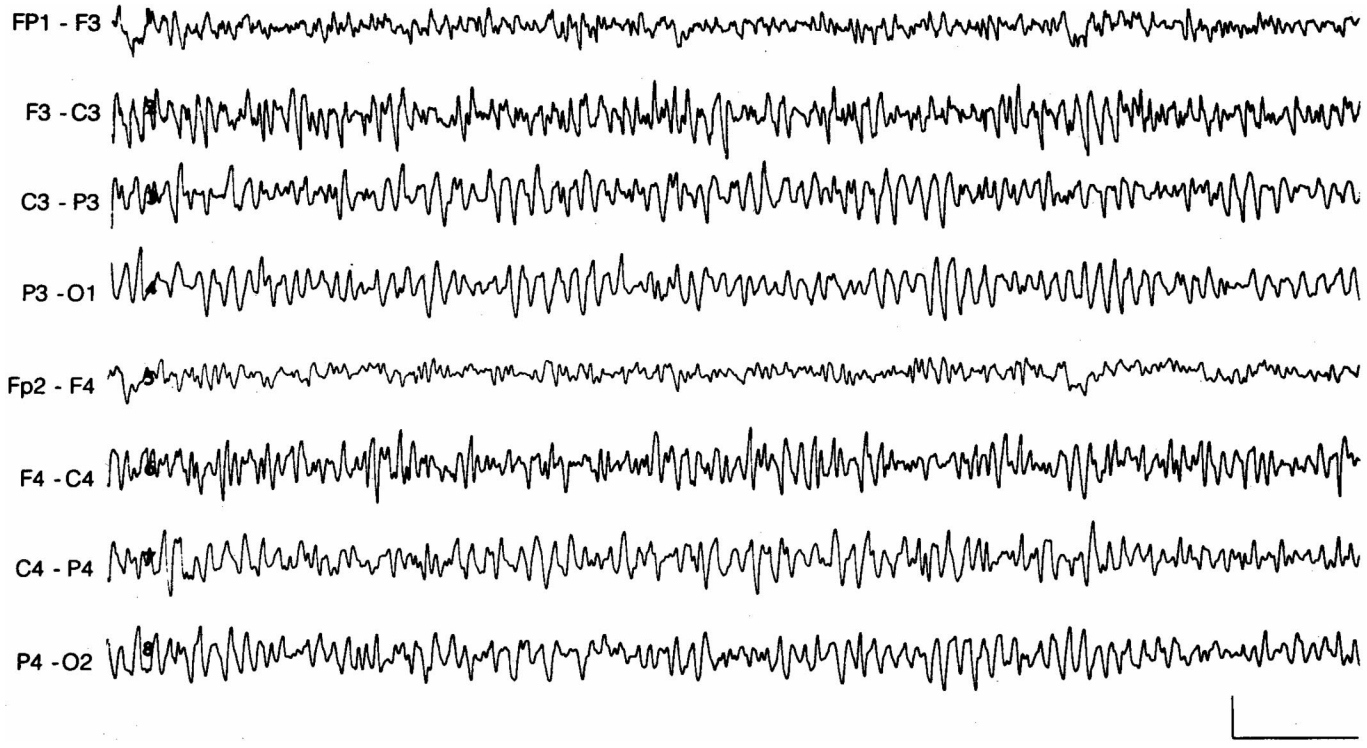

FIGURE 2. Medication effect. 73 years. Benzodiazepines or barbiturates could be responsible for all the modifications in this sample. The most prominent is frontally dominant, symmetric, approximately 20 Hz beta activity. The background rhythm posteriorly has slowed to 7 to 8 Hz. A slight excess of diffuse theta activity also appears. Both the slow background and this quantity of diffuse theta may normally appear with medication. The rich mixture of waveforms produce sharply contoured waves which are not spikes. Calibration signal 1 second, 50 μV.

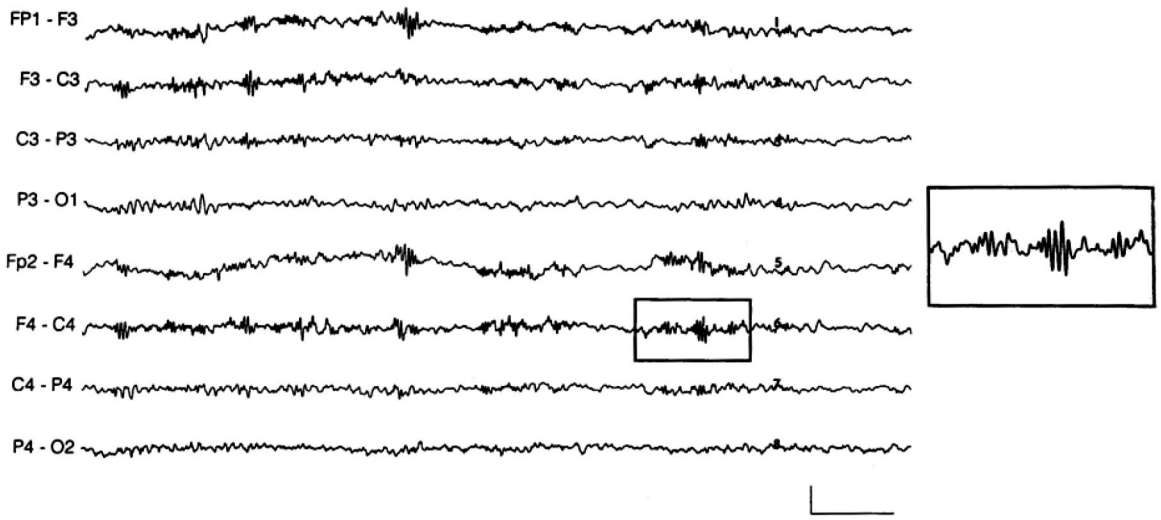

FIGURE 3. Drowsiness and bursting beta. 41 years. Beta activity can appear in alarming bursts during drowsiness. Some components of each burst are apiculate; yet, these are not polyspikes in which all components are usually apiculate and are followed by slow wave. The morphology of beta bursts is depicted in the *square*. Although such beta may be a normal drowsy phenomenon, medication may have enhanced its prominence. Calibration signal 1 second, 70μV.

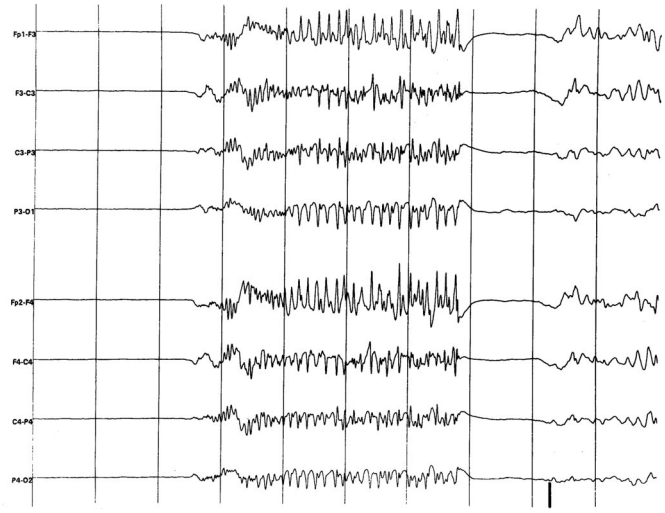

FIGURE 4. Generalized burst-suppression with epileptiform discharges. Thirty-two-year-old woman with a massive carbamazepine overdose. Bursts contain runs of rhythmic waves followed by sequential, bilaterally synchronous spikes without intervening slow waves. Between the bursts, the recording is completely suppressed. With falling carbmazepine serum concentrations, the patient regained continuous EEG rhythms and epileptiform activity disappeared. Calibration signal: dark vertical line 100μV, distance between other ventrical lines: 1 second.

Triphasic Waves

Intoxication with several types of drugs has been associated with triphasic waves. Perhaps the most notable is Valproic Acid-associated hyperammonemic encephalopathy (Kifune et al., 2000) (Fig. 6). Other drugs producing this association have been Baclofen, Lithium, Levodopa, Pentobarbital, and the serotonin syndrome (Chatrian and Turella, 2003; Dike 1997; Hormes et al., 1988; Kubicki and Stolzel, 1970; Lancman et al., 1997; Neufeld, 1992). These triphasic waves always arise from a diffusely abnormal background activity containing a mixture of delta and theta (Blume et al., 2002c). No aspect of triphasic waves distinguishes a specific toxin, nor a toxic from a metabolic encephalopathy (Chatrian and Turella, 2003). Importantly, although triphasic waves represent a moderately severe toxic encephalopathy, the EEG may evolve to normal as the toxic or metabolic encephalopathy recedes (Bickford and Butt, 1955).

Theta And Delta

Diffuse delta and excess theta may reflect clinical neurotoxicity if associated with the institution of one or more traditional AEDs.

Phenytoin and several other "older" AEDs may slow background rhythms to the high theta range, probably reflecting relatively high serum levels (Van Cott and Brenner, 2003; Duncan, 1987). Some AEDs, such as Carbamazepine and Valproate, may mildly augment theta activity diffusely at therapeutic serum levels (personal observation). Carbamazepine (10, 11) epoxide excess may produce this effect, accounting for diffuse theta and possibly delta with normal Carbamazepine levels (G. Bauer and R. Bauer, 2005; Van Cott and Brenner, 2003) (Fig. 7). Little information is available concerning the new AEDs.

Among neuropsychiatric drugs, Clozapine, tricyclic antidepressants, and lithium are among drugs known to be associated with delta and diffusely augmented theta if in excess (G. Bauer and R. Bauer, 2005; Van Cott and Brenner, 2003).

Coma Patterns

All coma patterns have been associated with drug intoxication (G. Bauer and R. Bauer, 2005; Chatrian and Turella, 2003; Fisch, 1999; Ikeda et al., 2003; Young, 2002). In increasing order of severity these are: spindle coma, alpha/theta pattern, burst-suppression, electro-cerebral inactivity (ECI). These pat-

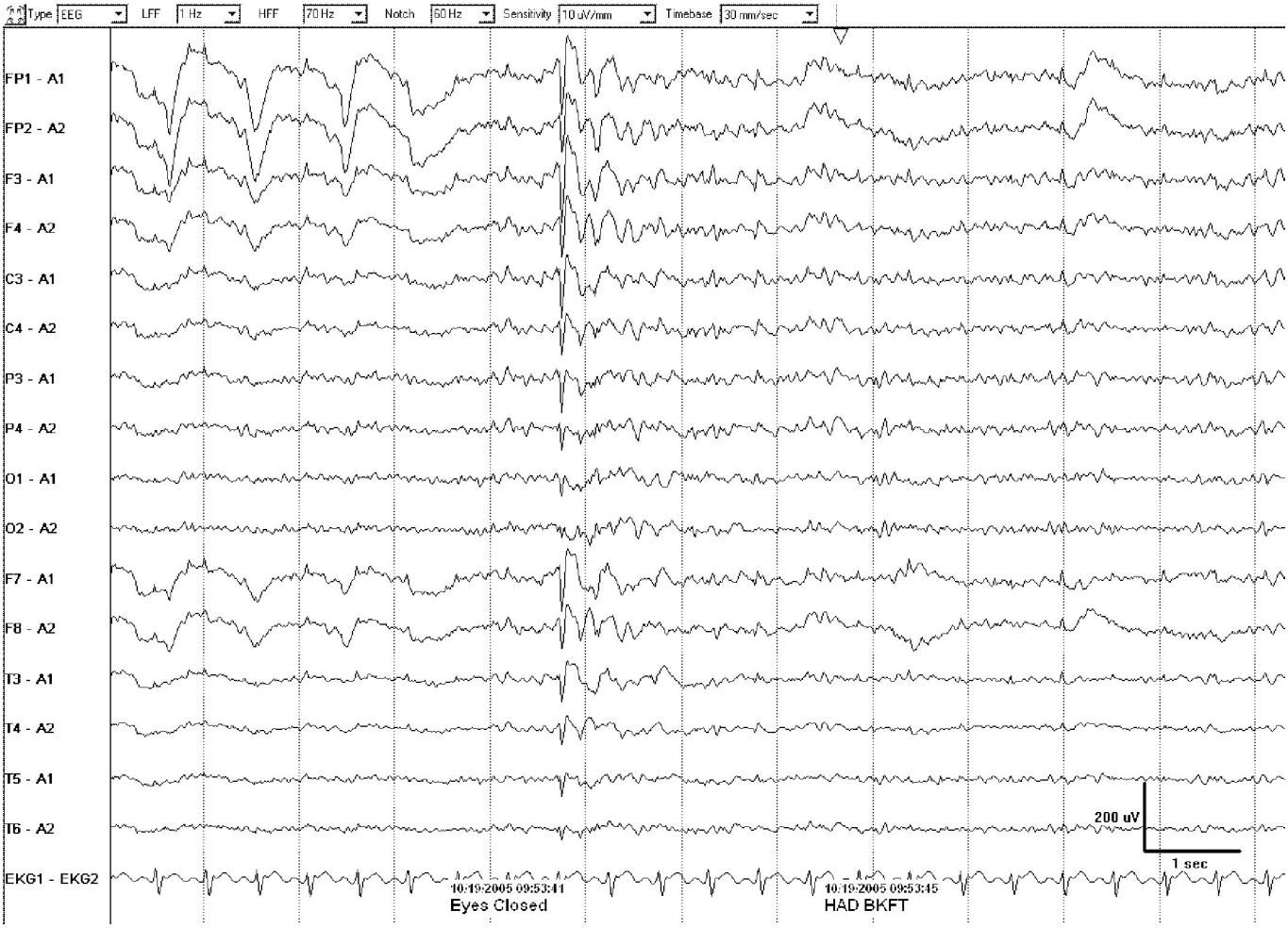

FIGURE 5. Clozapine. Bisynchronous spikes and excess theta may be produced by clozapine, as this segment shows.

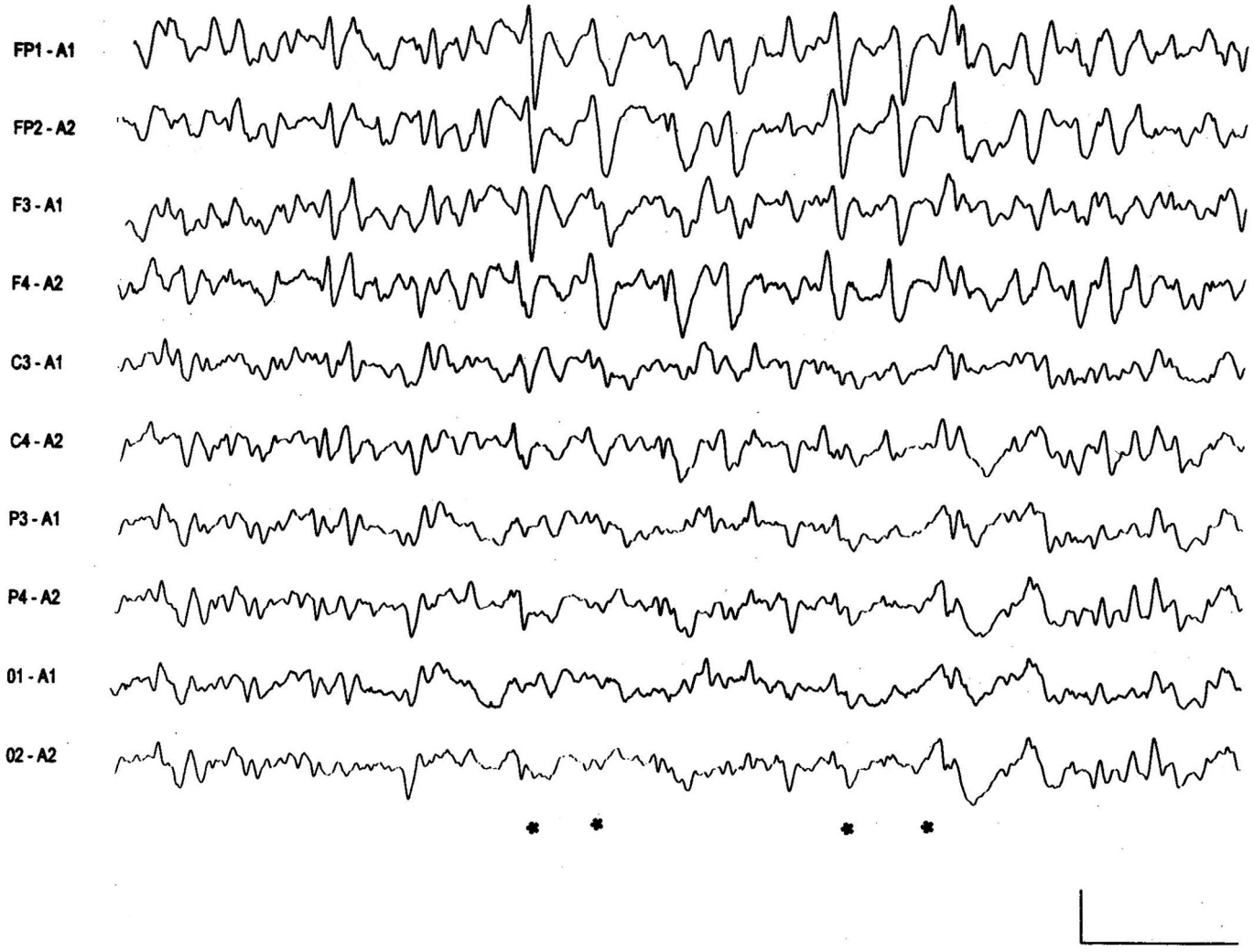

FIGURE 6. Triphasic waves and diffuse delta. This referential montage depicts the frontally predominant triphasic waves (*asterisks*) together with diffuse delta activity. Triphasic waves and delta may represent a toxic or a metabolic encephalopathy. The low-voltage apiculate waves at A2 may represent ECG. Calibration signal 1 second, 100μV.

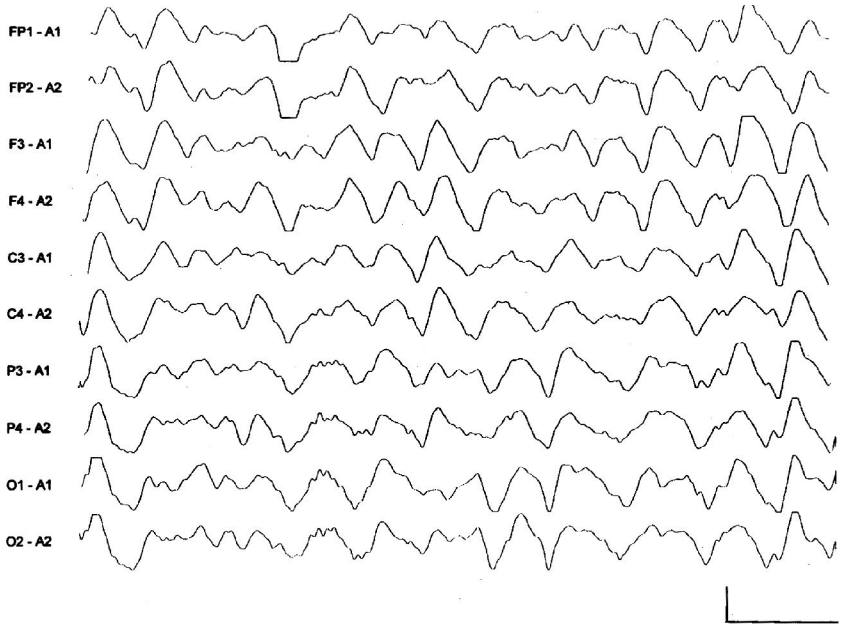

FIGURE 7. Generalized, high voltage, persistent delta. 19 years. The patient had taken a deliberate overdose of valproic acid. The recording is dominated by diffuse, high-voltage rhythmic delta activity with a minimum of faster frequencies superimposed. The relative lack of mixtures of frequencies with little variability and no reactivity to stimulation indicates a severe encephalopathy. She recovered completely. Calibration signal 1 second, 70μV.

terns persist throughout a recording. Spindle coma and alpha/theta coma may minimally react to afferent stimuli in some patients, but no reactivity occurs with burst suppression or ECI.

Importantly, if these patterns are entirely due to drug overdose, gradual return to a normal awake EEG will occur.

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