bring on seizures by thinking about certain, often emotional, scenes or events; or inhibit seizures by changing their train of thought or interrupting forced thinking. Such activating or interrupting mechanisms may be more common than previously suspected.

References

1. Fenwick P. Evocation and inhibition of seizures: behavioral treatment. Adv Neurol 1991;55:163–183.
2. Dahl J, Melin L, Brorson L, Schollin J. Effects of a broad-spectrum behavior modification treatment programme on children with refractory epileptic seizures. Epilepsia 1985; 26:303–309.
3. Wolf P. Behavioral therapy. In: Engel J Jr, Pedley TA, eds. Epilepsy: a comprehensive textbook. Philadelphia, PA: Lippincott-Raven; 1997:1359–1364.
4. Palmini A, Gambardella A, Andermann F, et al. The human dysplastic cortex is intrinsically epileptogenic. In: Guerrini R, Andermann F, Canapicchi R, et al., eds. Dysplasias of cerebral cortex and epilepsy. Philadelphia, PA: Lippincott-Raven; 1996: 43–52.
5. Avoli M, Bernasconi A, Mattia D, Olivier A, Hwa GG. Epileptiform discharges in the human dysplastic neocortex: in vitro physiology and pharmacology. Ann Neurol 1999;46:816–826.
6. Belichenko P, Dahlström A. Mild cortical dysplasia: a three-dimensional study of dendritic morphology. In: Guerrini R, Andermann F, Canapicchi R, et al., eds. Dysplasias of cerebral cortex and epilepsy. Philadelphia, PA: Lippincott-Raven; 1996: 65–70.
7. Preul MC, Leblanc R, Cendes F, et al. Function and organization in dysgenic cortex: case report. J Neurosurg 1997;87:113–121.
8. Spreafico R, Battaglia G, Arcelli P, et al. Cortical dysplasia: an immunocytochemical study of three patients. Neurology 1998;50:27–36.
9. Li LM, Cendes F, Andermann F, et al. Surgical outcome in patients with epilepsy and dual pathology. Brain 1999;122: 799–805.
10. Gloor P. Experiential phenomena of temporal lobe epilepsy. Brain 1990;113:1673–1694.

EEG discharges on awakening: A marker of idiopathic generalized epilepsy

Article abstract—In a series of 24-hour ambulatory EEG recordings from 1,000 consecutive adult outpatients (44.5% with generalized and 55.5% with partial epilepsy, one recording per patient), the authors found only 46 (4.6%) activations of epileptiform discharges on awakening. All recordings came from patients with idiopathic generalized epilepsy, predominantly with juvenile myoclonic epilepsy and generalized tonic-clonic seizures on awakening. Multiple spike discharges that develop with an unusually delayed onset after arousal (more than 10 minutes) might help to discriminate juvenile myoclonic epilepsy.

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The paroxysmal EEG discharges typical of generalized epilepsy often show circadian fluctuations. Clinical and EEG manifestations of juvenile myoclonic epilepsy (JME)—a type of idiopathic generalized epilepsy (IGE)—bear a strict relationship to the sleep–wake cycle, particularly during the transition phases.[1] Most patients with JME show myoclonic jerks on awakening, occasionally terminating in a convulsive seizure. Owing to its widely varying clinical presentations, JME sometimes remains undiagnosed even by experienced neurologists,[2-3] but its generally benign and drug-dependent course emphasizes the importance of a correct diagnosis. Therefore, a pressing diagnostic need is to identify a pattern of brain activity as a specific EEG marker of JME.

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Methods. We retrospectively reviewed 1,000 consecutive ambulatory EEG (A-EEG) recorded from 1,000 adult outpatients with epilepsy (aged 19 to 72 years, mean 30 years), one cassette per patient. A-EEG were recorded with an eight-channel cassette recorder (Oxford Medilog 9000, Oxford Instruments, Abingdon, Oxfordshire, UK) before, during, or after antiepileptic treatment. Recording lasted 22 to 25 hours and included one nocturnal sleep–wake cycle. Patients slept and woke naturally at home. Patients or their relatives marked the occurrence of clinical seizures on the recording by a push-button option.

One author (M.M.) classified patients as having generalized or partial epilepsy according to the International League Against Epilepsy criteria[4] (table 1). Patients with generalized epilepsy were further classified as having idiopathic (IGE), secondary, or cryptogenic generalized epilepsy. Patients with IGE were finally classified as having JME, epilepsy with generalized tonic-clonic seizures on awakening (A-GTCS), epilepsy with generalized tonic-clonic seizures at random (R-GTCS), or childhood absence epilepsy (CAE) (table 2). Patients with partial epilepsy were classified as having idiopathic, secondary, or cryptogenic partial epilepsy (see table 1). Patients with epilepsy of uncertain classification or with diagnoses other than epilepsy were excluded from the study.

We defined epileptic discharges on awakening (EDA) as the appearance of EEG discharges on awakening, or a 30%

Table 1 *Occurrence of epileptiform discharges on awakening (EDA) in adult patients with epilepsy*

	Patients, n (%)	EDA positive, n (%)
Generalized epilepsy		
Idiopathic	348 (78.2)	46 (13.2)
Symptomatic	54 (12.2)	0 (0)
Cryptogenic	43 (9.6)	0 (0)
Subtotal	445 (100)	46 (10.3)
Partial epilepsy		
Idiopathic	89 (16.1)	0 (0)
Symptomatic	245 (44.1)	0 (0)
Cryptogenic	221 (39.8)	0 (0)
Subtotal	555 (100)	0 (0)
Total	1,000 —	46 (4.6)

increase in the amount (number and duration) of discharges compared with the preawakening hours. Awakening was defined as the 60 minutes following the onset of EEG signs of arousal.

We analyzed EDA occurrence in the various syndromes, and the EEG pattern and duration (in seconds) of discharges during the event. We also measured EDA latency from awakening (minutes). Frequency variables were subjected to χ^2 test; values for duration and latencies to one-way analysis of variance (significance for $p < 0.05$).

Two of the authors (L.F., F.F.) reviewed all A-EEG and were blinded to the patients' classification, with a high interobserver reliability and 100% concordance in selecting EDA-positive recordings.

Results. Of the 1,000 recordings reviewed, 46 (4.6%) showed EDA. All A-EEG came from patients with IGE (22 men and 24 women; aged 20 to 56 years, mean 24 years) (IGE versus symptomatic generalized epilepsy, χ^2 8.1, $p = 0.004$; IGE versus cryptogenic generalized epilepsy, χ^2 6.4, $p = 0.01$) (see table 1).

EDA had a similar occurrence in JME and A-GTCS (22/105, 20.9%; and 13/48, 27%; χ^2 0.7, $p = 0.4$). It occurred more frequently in both of these syndromes than in R-GCTS (7/75, 9.3%; JME versus R-GCTS: χ^2 4.4, $p = 0.036$; A-GTCS versus R-GTCS χ^2 6.8, $p = 0.009$) and CAE (4/120, 3.3%; JME versus CAE: χ^2 17, $p = 0.000$; A-GTCS versus CAE χ^2 21, $p = 0.0000$). EDA occurrence in R-GCTS and CAE was similar (χ^2 3.1, $p = 0.76$) (see table 1).

Recordings from patients with EDA rarely indicated clinical seizures (6/46 EDA-positive recordings, 13.1%). Four of these six recordings were from patients with JME manifesting myoclonic jerks on awakening. One recording came from a patient with A-GCTS manifesting a convulsive seizure, and another from a patient with CAE showing multiple clinical absences during the waking hours (see table 2).

The EEG pattern of EDA varied in the same patient and even in the same cluster of discharges. Although the pathologic activity occasionally predominated in one hemisphere, all recordings mainly showed synchrony and symmetry. EDA events consisted of generalized discharges of polyspikes or spike-and-wave complexes. Recordings belonging to patients with JME and A-GTCS showed remarkably similar discharges, frequently including multiple spikes, isolated or irregularly intermingled with typical spike-and-wave complexes or with single or multiple arrhythmic slow waves. In EEG tracings recorded from patients with R-GTCS and CAE, the epileptiform discharges had a more regular, rhythmic pattern, consisting mainly of spike-and-wave complexes (see table 2; figure).

Discharges lasted longer in CAE than in the other groups ($F = 8.4$, $p < 0.01$)—on average more than 7 seconds. Discharges from patients with JME and A-GTCS were brief and irregular, rarely lasting up to 7 seconds. Discharges longer than four seconds were often intermingled with physiologic background EEG activity. Tracings from patients with R-GTCS epilepsy showed brief but regular discharges. The overall duration of EDA events was similar between groups ($F = 0.6$, $p = 0.6$).

The latency between EEG arousal and EDA onset clustered interestingly in early and late subgroups. In 39 out of 46 A-EEG from patients with all IGE sub-syndromes (84.7%), the latency varied from 1 to 10 minutes. In the remaining seven A-EEG, all belonging to patients with JME (15.3%), the abnormalities appeared between 20 and 50 minutes after awakening. Overall, EDA latency was longer in JME than in the other IGE subsyndromes ($F = 5.23$, $p = 0.003$).

In 31/46 (67.4%) EDA-positive recordings, EEG abnormalities recurred throughout sleep and wakefulness. Of the remaining 15 tracings, nine showed occasional discharges only during sleep (two JME, five A-GCTS, and two R-GTCS) and three had rare abnormalities only during wakefulness (one CAE, one JME, and one A-GTCS). Three

Table 2 *Occurrence and EEG patterns of epileptiform discharges on awakening (EDA) in patients with idiopathic generalized epilepsy*

Epilepsy group	Patients, n (%)	EDA positive		Single discharge duration, s, mean ± SD (range)	Latency from EEG awakening, min, mean ± SD (range)	EDA event duration, min, mean ± SD (range)
		n (%)	Seizures, n			
JME	105 (30.2)	22 (20.9)	4	3.1 ± 1.3 (1–6)	13.8 ± 13.2 (1–50)	29.8 ± 28.1 (1–118)
A-GTCS	48 (13.8)	13 (27)	1	3.5 ± 1.8 (1–7)	3.5 ± 2.2 (1–10)	33.5 ± 22.3 (5–63)
R-GTCS	75 (21.5)	7 (9.3)	0	2.3 ± 1.1 (1–4.5)	1.6 ± 1.5 (1–5)	44.4 ± 38.4 (12–120)
CAE	120 (34.5)	4 (3.3)	1	8 ± 4.9 (3–14)	2.7 ± 1.7 (1–3)	24.0 ± 25.6 (2–60)
Total IGE	348 (100)	46 (13.2)	6			

EDA = epileptiform discharges on awakening; JME = juvenile myoclonic epilepsy; A-GTCS = epilepsy with generalized tonic-clonic seizures on awakening; R-GTCS = epilepsy with generalized tonic-clonic seizures at random; CAE = childhood absence epilepsy.

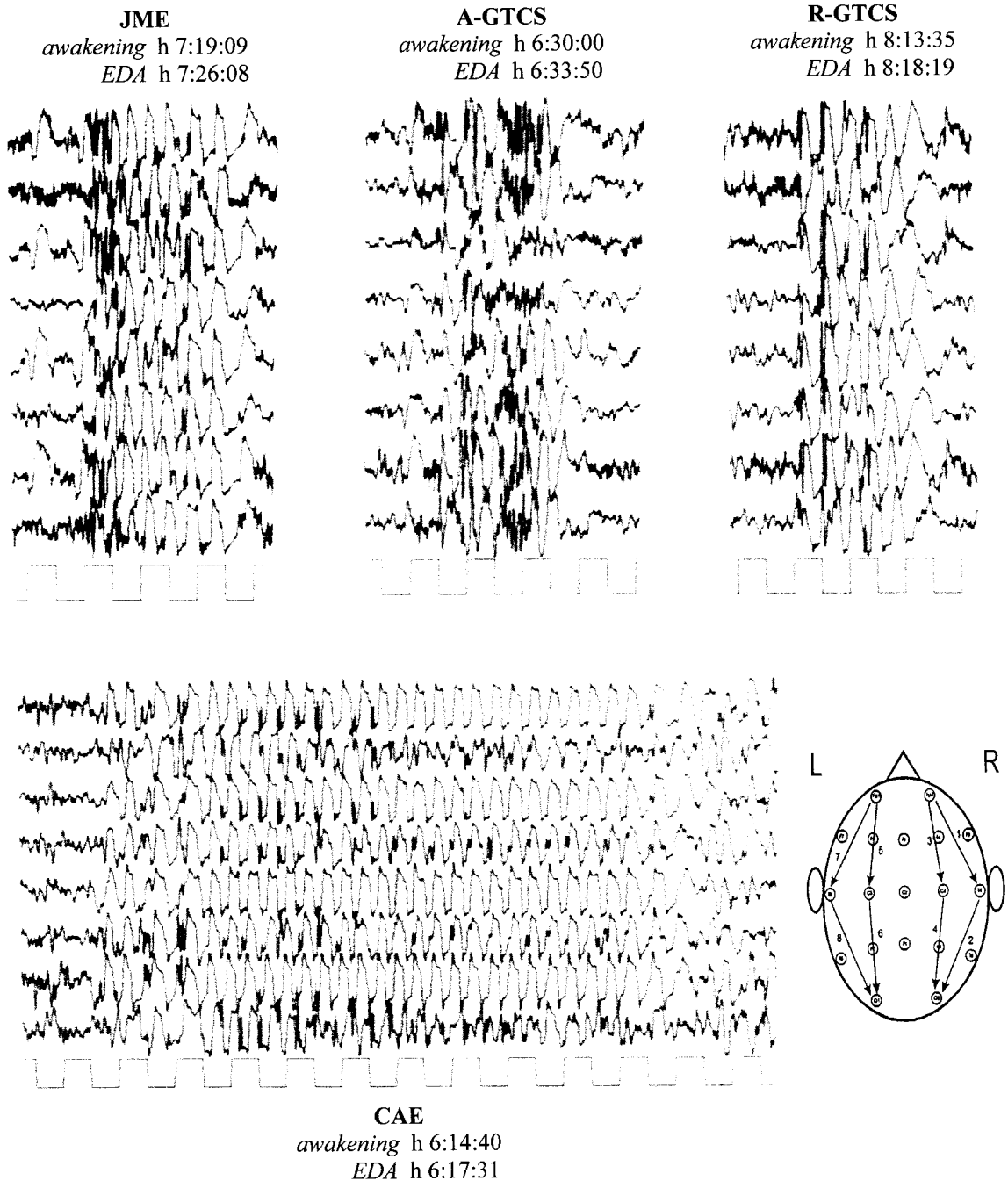

Figure. Sample tracings from patients with idiopathic generalized epilepsy. Ambulatory EEG were recorded at a speed of 15mm/s and an amplitude of 50 μV/7mm. EDA = epileptiform discharges on awakening; JME = juvenile myoclonic epilepsy; A-GTCS = epilepsy with generalized tonic-clonic seizures on awakening; R-GTCS = epilepsy with generalized tonic-clonic seizures at random; CAE = childhood absence epilepsy. Time is reported in hours:minutes:seconds.

recordings contained no abnormalities other than EDA. The circadian distribution of discharges was similar between groups.

Discussion. EDA is a rare A-EEG phenomenon in adult outpatients with epilepsy, and was identified in only 4.6% of the 1,000 recordings in this series. All EDA-positive tracings belonged to patients with IGE and accounted for 13.2% of the 348 patients. The diagnostic workup for patients suspected of having IGE should therefore include A-EEG monitoring when standard EEG recordings and photic stimulation are nondiagnostic. Because few patients in this series reportedly had clinical seizures, these events do not seem to be a target for A-EEG. Although rare, EDA is highly specific of IGE, and when associated with consistent clinical features, it might render further investigation unnecessary.

None of the 97 A-EEG from patients with symptomatic or cryptogenic generalized epilepsy and none from the 555 patients with partial epilepsy showed

EDA. This supports the observation that seizures activated on awakening are rarely focal, but does not exclude possible activation of partial epilepsy in the ensuing hours of the morning.

Our finding that EDA are a specific EEG pattern of IGE confirms previous knowledge, which attributes a crucial role in triggering EEG discharges and seizures in IGE to the transition between sleep and wake. Janz[5] introduced the concept of "awakening epilepsy," and subsequently Niedermeyer[6] coined the term "dyshormia" to indicate faulty or deviant arousal. In patients with IGE, arousing stimuli generate K complexes contaminated with spikes that are maximal over the frontal midline and precipitate paroxysmal EEG discharges.[7]

In IGE subsyndromes, EDA occurred more frequently in patients with JME and A-GTCS than in those with R-GTCS and CAE. Rather than depending on an altered circadian distribution of discharges, which is similar in all groups of patients, the difference probably reflects the fact that seizures in JME and A-GTCS tend to recur on awakening and are facilitated by lack of nocturnal sleep, fatigue, and unexpected awakening. In addition, JME and A-GCTS may be subtle phenotypic variants of the same underlying genetic process.[8-9]

Even if EDA will not distinguish JME from otherIGE subsyndromes, irregular, multiple-spike discharges of late onset may help to discriminate JME. Late-onset discharges (20 to 50 minutes) appear only in JME. Despite their presence in few cases, they render patients vulnerable to seizures during walking or driving to school or work.

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References

1. Panayiotopoulos CP, Obeid T, Tahan AR. Juvenile myoclonic epilepsy: a 5-years prospective study. Epilepsia 1994;35:285–296.
2. Grunewald RA, Chronni E, Panayiotopoulos CP. Delayed diagnosis of juvenile myoclonic epilepsy. J Neurol Neurosurg Psychiatry 1992;55:497–499.
3. Editorial. Diagnosing juvenile myoclonic epilepsy. Lancet 1992; 340:759–760.
4. Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for classification of epilepsies and epileptic syndromes. Epilepsia 1989;30:389–399.
5. Janz D. Aufwach–Epilepsien. Arch Psychiatr Nervenkr 1953; 191:73–98.
6. Niedermeyer E. Generalized seizure discharges and possible precipitating mechanisms. Epilepsia 1966;7:23–29.
7. Niedermeyer E. Primary (idiopathic) generalized epilepsy and underlying mechanisms. Clin Electroencephalogr 1996;27:1–21.
8. Delgado–Escueta AV, Greenberg DA, Treiman L, et al. Mapping the gene for juvenile myoclonic epilepsy. Epilepsia 1989; 30(suppl 4):S8–18.
9. Greenberg DA, Durner M, Resor S, Rosenbaum D, Shinnar S. The genetics of idiopathic generalized epilepsies of adolescent onset: differences between juvenile myoclonic epilepsy and epilepsy with random grand mal and with awakening grand mal. Neurology 1995;45:942–946.