

Diagnosis and treatment of absence seizures

J. Kiffin Penry, M.D.¹

Absence seizures are characterized by a brief, blank stare. Such seizures occur suddenly, without an aura, and likewise end suddenly, without mental confusion. They may be associated with mild clonic movements, an increase or decrease in postural tone, or automatisms. The ictal electroencephalogram (EEG) reveals generalized spike-and-wave discharges, usually at 3 Hz, though the interictal EEG is usually normal. Seizures usually begin between five and 15 years of age and usually subside with adulthood. Half the patients have a history of one or more generalized tonic-clonic seizures, which may precede or follow the onset of absence seizures. One third have a family history of seizures. Ethosuximide is the preferred treatment in individuals who have absence seizures alone, while valproic acid is preferred for those with a history of generalized tonic-clonic seizures. Once the dose is adjusted to provide an effective trough drug level, nearly all seizures can be completely (or at least satisfactorily) controlled.

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¹ Professor of Neurology, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina. Submitted for publication and accepted Oct 1983.

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Absence seizures have been studied in great detail and their characteristic components established.^{1,2} Clinical and electroencephalographic (EEG) correlations have been defined, along with ictal and interictal impairment of performance^{3,4}; quantitative studies of antiepileptic drugs have provided a choice of effective treatments^{5,6}; and seizure occurrence beginning in childhood has been clarified as part of the natural history and prognosis for a syndrome of the epilepsies.⁷ These findings are summarized briefly below.

Diagnosis

Absence seizures are characterized by a brief, blank stare which occurs suddenly, without an aura, and ends just as suddenly, without mental confusion. It may be associated with mild clonic components, usually involving the facial muscles; there may be a slight nod of the head or semipurposeful movements of the mouth or hands, forming automatisms. Rarely, there is an increase in tone, with the head moving backward. The pupils are usually dilated, and other autonomic phenomena can occur as well. While there may be no response to verbal stimulation, a loud or repetitive stimulus could evoke an impaired response or terminate the attack; frequently, the patient will resume preattack activities as though nothing had happened. Two thirds of patients have their first attack between five and 15 years of age; one fourth start before the age of five and the remaining few, after 15. In 50% of cases, seizures will remit or become clinically insignificant in the decade following adolescence. Occurrence does not vary with race or sex. Though early control probably improves prognosis, I know of no statistically controlled studies to prove what seems clinically apparent. Approximately 50% of patients with recurring absence seizures have a history of one or more generalized tonic-clonic seizures as well, though the prognosis is much better for an individual having only absence seizures.⁷ One third of patients have a family history of seizures, while at least one fourth report experiencing photosensitivity or reveal it when tested.

Electroencephalography: Though the first clinical description of absence seizures appears to have been given by Poupart in 1705,⁸ it was not until 1935 that Gibbs et al⁹ described the accompanying 3/sec generalized spike-wave discharge. The interictal EEG is normal in about 90% of patients and slowed, asymmetric, or characterized by multifocal sharp waves or spikes in 10%. Asymmetrical onset of generalized spike-wave bursts and polyspikes has been reported. Slow spike-wave bursts (2 cps) have also been described, but usually correlate with drowsiness, mental retardation, or atonic attacks in patients classified as having atypical absence seizures. It has been shown that sleep may alter many abnormal EEG findings.¹⁰ Hyperventilation administered during EEG will precipitate spike-wave bursts in nearly all patients prior to medication and photic stimulation in about one fourth of

cases; drowsiness also activates spike-wave bursts, but they may be brief and less synchronous.

Closed-circuit TV/EEG: When the clinical and EEG manifestations of absence seizures are recorded simultaneously on videotape, they may be analyzed in great detail¹ and both responsiveness and performance tested.^{3,4} These latter factors, as well as memory, are impaired but not obliterated. During a generalized spike-wave burst, an individual may recall hearing voices, but not recall what was said. More errors are made on pursuit rotor performance during spike-wave bursts than between them; however, fewer errors are made during spike-wave bursts in patients than during visual occlusion of similar duration in normal controls.¹¹ Finally, performance is impaired more during completely generalized (full-voltage) spike-wave bursts than during poorly generalized bursts.³ Though TV/EEG is rarely required, it may be valuable in differentiating absence seizures from complex partial seizures with impairment of consciousness (alone or with automatisms). Long-term telemetered EEG with or without TV is valuable in assessing drug response.

Precipitating absence seizures: It has already been noted that drowsiness, hyperventilation, and photic stimulation may precipitate absence seizures, and the physician should always explore the possibility of these factors as well as anxiety, boredom, and inactivity. Happy, active children will have about one-third fewer attacks during the day than those who are inactive and bored.¹² Anxiety is often more difficult to determine and measure. Recurring absence seizures may persist in the presence of adequate drug levels until the factors provoking anxiety are removed. There are methods of studying the frequency of EEG events in relation to activity.¹³ Finally, total sleep deprivation (TSD) may activate absence seizures after many months or years of complete control by medication and could even be the underlying cause of absence status.

Types of seizures

Absence seizures: An absence seizure is a finite event composed of a limited number of clinical and EEG features resulting from an abnormal and excessive discharge of nerve cells in the brain. Absence epilepsy is characterized by the recurrence of absence seizures and is associated with other characteristics such as childhood onset and a family history of seizures, any of which may determine the prognosis.⁷

Atypical absence seizures: These seizures are similar to absence attacks, but do not conform to the above description. Clinically, they may not begin or end abruptly, and atonic attacks with complete collapse rather than head nodding often occur. Mental retardation is frequently present. Therapy is ineffective in most cases. On the EEG, background activity is usually slow, with fluctuating asymmetry and multifocal epileptiform display. Generalized spike-wave bursts are usually slow (2 Hz) and irregular. Interictal performance may be impaired when only generalized slowing is present. These individuals frequently have a history of cluster recurrence of generalized tonic-clonic seizures. Even with improvement, their EEGs do not return to normal.

Absence status: Absence status is defined as one staring spell after another without complete recovery between spells. The EEG reveals slowing between generalized spike-wave bursts, with some bursts often represented by spikeless high-voltage 3-cps slow waves. The individual may wander about in a fugue state, performing poorly. Speech is usually simple, and thoughts go unexpressed; questions must be repeated. Case reports of absence status most often involve adults because the abnormal behavior attracts attention.¹⁴ Precipitating factors are usually present. About 10% of children with absence seizures will exhibit at least one episode of absence status, and again precipitating factors are present in most cases. Febrile pneumonia or other causes have been noted, as have sleep deprivation and emotional factors. Porter and Penry have recently reviewed this subject.¹⁵

Treatment

No form of epilepsy is easier to treat than absence seizures. Fewer than 5% of cases are truly refractory with optimal application of current knowledge about the disorder and use of marketed antiepileptic drugs. Problems rarely arise unless handicaps or extenuating circumstances are also present. Unfortunately, many patients' seizures remain uncontrolled, most often due to incomplete diagnosis. Such individuals have brief, unrecognized absence attacks which progress to generalized tonic-clonic seizures. Drugs given for generalized tonic-clonic seizures fail to control these attacks and may even aggravate the absence attacks, which may then be confused with side effects of the drugs; additional drugs are then prescribed, further aggravating the effects of the various drugs.

Optimal care will not be achieved until a complete history is taken: this must include a description of all seizure types, age at onset, frequency, duration, magnitude, and evolution, which will facilitate choice of the appropriate drug. The dose must then be adjusted to an effective level for that individual, i.e., one which will result in complete control of seizures without side effects.

Ethosuximide (Zarontin): Ethosuximide is the drug of choice for treatment of absence seizures unaccompanied by other types of seizures. It is rapidly absorbed from the stomach, reaching a peak in one to four hours. It is not bound by protein and reaches the same concentration in the cerebrospinal fluid as in the serum. The biological half-life before adolescence is 30 hours, 60 hours in adults. It may be given three or four times a day in divided dosages; the average daily dose is 20–40 mg/kg, which results in a serum concentration of 40–100 µg/ml. If seizures remain uncontrolled, the dosage should be increased to give a trough level of >60 µg/ml. Side effects (anorexia, nausea, vomiting, headaches, lethargy, and/or dizziness) may be transient and can be relieved by lowering the dosage. Of those patients with absence seizures alone, 60% will achieve complete control, 35% will achieve virtually complete control, and approximately 5% will be refractory. There are few troublesome side effects.^{5,16}

Valproic acid (Depakene, Depakote): Valproic acid is the drug of choice when the patient also has a history of generalized tonic-clonic seizures and is effective for both types. This compound has been available in the U.S. since February 28, 1978; however, the acid form (Depakene) resulted in significant gastrointestinal side effects, which have been largely relieved by the enteric-coated preparation, sodium hydrogen divalproex (Depakote), which has been available since March 18, 1983, and is absorbed rapidly from the small intestine. The initial daily dose is 10–15 mg/kg and the average maintenance dose, 30 mg/kg; dosage should be increased until seizures are controlled without side effects; the guide to dosing is a trough level of 60 µg/ml in the presence of a normal SGOT. Since hepatic failure has been reported with valproic acid on rare occasions, liver function should be monitored. Minor side effects may include weight gain, transient hair loss, and tremor at high serum concentrations. There may be a bimodal onset of action, comprising an initial decrease in the frequency of absence seizures with complete control coming

only after the full dose has been in effect for two to three weeks.⁶

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