The classification and differential diagnosis of absence seizures with short-term video-EEG monitoring during childhood

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Absence seizures are idiopathic epilepsies characterized by impairment of consciousness and generalized 2.5-4 Hz spike and slow wave discharges. This prospective study was performed to classify and define properties of subgroups of absence epilepsies. We included 31 patients, of whom seven were in the differential diagnosis group. On admission, absence epilepsy provisional diagnosis was considered in 16 patients clinically and in the other 15 patients based on routine EEG findings. Ictal EEGs were recorded by video-EEG monitoring in 23 of the patients (totally 202 ictal recordings). Patients were diagnosed as childhood absence epilepsy (n=8), juvenile absence epilepsy (n=10), juvenile myoclonic epilepsy (n=3), eyelid myoclonia with absences (n=2), and perioral myoclonia with absences (n=1). Neuroimaging, video-EEG monitoring and especially ictal recordings are important for classification of epilepsies in addition to history, physical examination and routine EEG findings. Video-EEG monitoring is required to classify, to make differential diagnosis and to determine the treatment plan and prognosis.

Key words: absence, childhood absence epilepsy, juvenile absence epilepsy, symptomatic absence epilepsy, video-EEG monitoring.

There is no other field in medicine in which the symptom “seizure” or diagnosis “epilepsy” represents numerous disorders with different clinical features, etiology, prognosis, and response to treatment. Defining epileptic syndromes and disorders increases the diagnostic accuracy and improves the quality of epileptic care. For this purpose, the International League Against Epilepsy (ILAE) published proposals for the classification of seizures and syndromes, which was revised recently. Absence seizures cause a transient impairment of consciousness and staring unresponsive for few seconds usually accompanied by 3 Hz spike and slow wave activity on EEG. In 2001, ILAE classified the idiopathic generalized epileptic syndromes with typical absences into four groups as: childhood absence epilepsy (CAE), juvenile absence epilepsy (JAE), juvenile myoclonic epilepsy (JME), and myoclonic absence epilepsy (MAE). There are also syndromes with typical absences that are not officially recognized by the ILAE: eyelid myoclonia with absences (EMA) and perioral myoclonia with absences (PMA).

In this study, we performed video-EEG recordings of 31 patients (total 202 ictal recordings) with a provisional diagnosis of absence epilepsy that was considered based on either clinical history or routine EEG findings. We classified the absence seizures by syndromic approach. We also considered the differential diagnosis of absence seizures and categorized them as symptomatic absence epilepsy.

Material and Methods
Children with clinical presentations and/or routine EEG evaluations -generalized spike and wave- compatible with absence seizures were included prospectively in this study in Hacettepe University, Pediatric Neurology Department. Absence epilepsy was suspected in patients with a history of impairment of consciousness and blank stare, sometimes with automatisms and without postictal confusion.
The routine EEGs were performed on 21-channel EEGs according to the international 10–20 system on a Nihon Kohden EEG (Irvine, CA, USA). Patients’ demographic factors, seizure-related characteristics (age of seizure onset, frequency and type of seizures as witnessed by parents, triggering factors, history of febrile seizures, etc.), family history of convulsive disorders, neurological examinations, and cranial magnetic resonance imaging (MRI) findings were noted.

**Video-EEG Recordings**

All patients underwent video-EEG monitoring with 16 channels referential unipolar, longitudinal and transverse montages by Grass-Telefactor computer system according to the international 10-20 system. The children had intermittent photic stimulation using 1–16 Hz flash frequencies and period of hyperventilation (HPV) for 5 minutes (min), during which the levels of awareness and consciousness were interpreted by close observation, with either verbal or visual stimuli. Some patients were also recorded during sleep. The duration of video-EEG recordings was 1-3 hours. The video-EEG recordings were reviewed by a pediatric neurologist concerning duration, frequency and morphology of discharges (clinical or subclinical), and the absence seizures were classified as follows.

**Childhood Absence Epilepsy**

The diagnosis of CAE was made according to the 2005 ILAE Task Force for Classification and Terminology. The inclusion criteria are: 1) Age at onset between 4 and 10 years (peak at 5 to 7 years); 2) Normal neurologic state and development; 3) Brief and frequent (tens per day) absence seizures with abrupt and severe loss of consciousness; 4) EEG ictal discharges of generalized, 3 Hz, high-amplitude spike and double (maximum 3 spikes are allowed) spike and slow wave complexes with a duration from 4 seconds (sec) to 20 sec.

**Juvenile Absence Epilepsy**

The age at onset is usually between 10 and 17 years. Juvenile absences are much more sporadic and the extent of loss of consciousness might be less severe compared to CAE. The EEG is characterized by symmetrical, generalized spike-wave discharges with a frequency of 3.5 Hz to 4.5 Hz precipitated by HPV.

**Juvenile Myoclonic Epilepsy**

The age of onset is in the second decade. JME is characterized by sudden, brief, bilaterally symmetrical and synchronous muscle contractions, frequently of the upper extremities, soon after awakening. Absence seizures occur in 15-30% of patients with JME. The ictal EEG reveals 10- to 16-Hz medium-high amplitude spikes followed by irregular slow waves.

**Statistical Analysis**

All data analyses were conducted using SPSS for Windows, version 11.5 (SPSS Inc, Chicago, IL, USA). Kolmogorov-Smirnov test was performed to test the normal distribution of data. Differences between the groups were compared by Student’s t or chi-square as appropriate. A value of p ≤ 0.05 was considered statistically significant.

**Results**

Between September 2002 and March 2004, 31 (45.2% male) patients were included in the study. The provisional diagnosis of absence epilepsy was considered in 16 children with clinical history and in the remaining 15 with routine EEG findings. In the whole study population, the mean age of onset of epilepsy was 8.8 ± 4.1 years.

**Childhood Absence Epilepsy (n=8)**

We diagnosed 8 patients (25% male) with CAE. Age at onset of absences ranged from 4.2 to 9 years, with a mean age of 6.3 ± 1.5 years. Three children had febrile seizures (Table I). The cranial MRIs of the patients were normal except in 2 patients with nonspecific cysts. The background video EEG rhythms were within normal limits. There was no asymmetry between hemispheres. In the interictal period, there were generalized 2.5-4 Hz spike and wave discharges [11 (3.8-16.3) discharges/patient] lasting 1-26 sec [1.8 (1.1-5.8) sec]. The mean frequency of interictal discharges per 100 min was 12.7/patient in CAE.
We recorded 31 absence seizures in 8 patients [4 (2-5.8) seizures/patient], of which 18 seizures occurred during HPV. The absence seizures lasted 10.78 ± 5.27 sec accompanied by loss of consciousness, blank stare, unresponsiveness to verbal stimuli, pause in HPV, and eye-blinking (n=3 patients). Automatisms including lip-licking and chewing (n=4), rubbing abdomen (n=1) and stretching (n=1) were observed. The EEG revealed high amplitude 2.5-4 Hz spike and slow wave complexes [3 Hz frequency most common (87.5%)] (Fig. 1). Patient 13 had two absence seizures lasting 60 and 130 sec with 3 Hz spike and slow waves with fragmentation.

Video-EEG findings were recorded in 5 patients also during sleep. There were 2.5-4 Hz spike-wave and sharp slow wave discharges (0.5-16 sec).

**Juvenile Absence Epilepsy (n=10)**

Ten patients (50% male) were classified as JAE. Febrile seizures were observed in 5 patients, 2 of whom used phenobarbital as prophylaxis (Table I). Patient 21 had coincidental hippocampal atrophy on the left side detected by cranial MRI.

The interictal video-EEG recordings revealed generalized 2-4 Hz spike-wave and sharp wave discharges [5 (3.3-10.8) discharges/patients] with duration of 2.5 (1-4.5) sec. The mean frequency of interictal discharges per 100 min was 5.8/patient in JAE.

Twenty-one absence seizures in 10 patients [2 (1-2.8) seizures/patient] were observed (7.64 ± 3.39 sec) during video-EEG monitoring, and 9 of them were due to HPV. The clinical features included loss of consciousness, blank stare, pause in HPV, unresponsiveness to verbal stimuli, and eye-blinking. Only 1 patient had lip-licking as automatism. The EEG findings were high amplitude, 3-4 Hz spike (usually 2, occasionally 3 spikes) and slow waves in all JAE; additionally, in 2 patients, sharp slow wave activity was noted. The discharges were 3.5-4 Hz at the onset followed by 3 Hz frequency of waves (Fig. 2).

EEG recordings were made in 4 patients with JAE during sleep, revealing 2.5-3 Hz spike-wave and sharp slow wave activities lasting 0.5-6 sec.

**Juvenile Myoclonic Epilepsy (n=3)**

The onset of symptoms was 10 to 15.4 years of age and the diagnosis of JME was made at the age of 13 to 15.6 years of age. The presenting symptoms were myoclonic jerks usually upon awakening and loss of consciousness. There was family history of convulsive disorders in 2 of the patients and no child had a history of febrile seizures. The neuroimagings were normal.

<table>
<thead>
<tr>
<th>Table I. Demographic Characteristics of Patients with CAE and JAE</th>
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<td><strong>Gender, male (%)</strong></td>
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<tr>
<td>Age at onset of seizure (years)</td>
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<td>Age at diagnosis (years)</td>
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<tr>
<td>History of febrile seizures (%)</td>
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<tr>
<td>Family history for convulsive disorders</td>
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*Independent samples T test
CAE: Childhood absence epilepsy. JAE: Juvenile absence epilepsy.
In the interictal period, video-EEG showed generalized 2-4 Hz spike-slow wave and sharp slow wave discharges lasting 1-6 sec (5-46 discharges/patient). The photic stimulation did not induce seizure or epileptic discharges. We could record video-EEG during sleep in 2 patients. Patient 19 exhibited 21 myoclonic jerks (0.5-1 sec) after awakening accompanied by multiple spike-wave activities between which bilateral synchronous high amplitude 2 Hz spike-wave and sharp wave discharges occurred (Fig. 3). There were 2.5-3 Hz spike-wave and sharp wave activities (1-5 sec) on sleep interictal EEG of Patient 20.

**Eyelid Myoclonia with Absences (n=2)**

Two patients (9.8 and 9.5 years old) were diagnosed as EMA. The patients admitted to our clinic because of eyelid blinking, numbness of hands and generalized tonic-clonic convulsions. Family history for convulsive disorders existed for both of the patients, and cranial MRI findings were normal.

Patient 4 exhibited interictal bilateral, high amplitude 3-4 Hz spike-slow wave, sharp slow wave and multiple spike-waves on video-EEG when the eyes were closed. After 4-5 sec of eye closure, the discharges decreased and isolated sharp waves were seen on posteriors of both hemispheres. Seven ictal periods (1-3 sec) were recorded as generalized 3-4 Hz spike-slow wave, sharp slow wave and multiple spike-wave activities accompanied by eyelid myoclonia. The seizures were not provoked by HPV and photic stimulations.

![Figure 2. Ictal EEG findings of Patient 17 with JAE with loss of consciousness and pause in hyperventilation and lip-licking.](image1)

![Figure 3. Ictal EEG recording of Patient 18 with JME with myoclonic jerks.](image2)

We recorded 49 seizures as eyelid myoclonia (6 during HPV, 11 during photic stimulation) of Patient 23. The ictal EEG demonstrated 3-4 Hz multiple spike-waves and sharp waves (1-13 sec). At the onset of photic stimulation, the frequency of discharges was 4-5 Hz followed by 2-3 Hz multiple spike-waves and sharp waves.

**Perioral Myoclonia with Absences (n=1)**

A 7-year-old male (Patient 24) was diagnosed as PMA with presenting symptoms as mild loss of consciousness and perioral rhythmical mimics for a few seconds. The age at onset of the condition was 6.1 years, and he did not experience any generalized tonic-clonic seizures. The family history was positive for convulsive disorders, and cranial MRI findings were normal.

The interictal video-EEG was normal. The video-EEG considered 5 seizures clinically as PMA (rhythmical contractions of perioral muscles) with loss of consciousness, unresponsiveness to verbal stimuli and flexion of legs towards abdomen as automatism continuing 7-17 sec. Ictal EEG demonstrated generalized, high amplitude discharges of 4 Hz at the onset followed by 3 Hz spike and slow waves. There were fragmentations in epileptic activities of 2 seizures (14 and 17 sec) during HPV. Photosensitivity was absent.

During sleep, there were 3 generalized 2-2.5 Hz spike-wave and multiple spike-wave (2-7 sec) activities prominent on the frontal area accompanied by movements of legs. Multiple
spike-wave activities (1-4 sec) were also seen
without clinical features.

**Differential Diagnosis Group (Cryptogenic/ Symptomatic Absence)**

i. Absence epilepsy provisional diagnosis based on clinical features

Four patients (7 to 13.3 years of age) were included in this group since they admitted to our department because of a short period of loss of consciousness and blank stare. Two patients had a family history of convulsive disorders. The onsets of symptoms were 6 to 12.8 years of age (Table II, Figs. 4A, B).

ii. Absence epilepsy provisional diagnosis based on routine EEG features

Three patients were considered in this group. The age of onset of symptoms was 2 to 7.8 years of age; they had pathological physical examination, EEG findings and cranial MRI (Table II).

**Discussion**

Even though the syndromic classification of absence epilepsies has been known for the last 30 years, there are still controversies about the definitions, inclusion criteria and disease-related characteristics. In this study, we further clarified the differences between absence epilepsy syndromes and also focused on symptomatic absence epilepsies, which had the potential to cause diagnostic dilemma.

Childhood absence epilepsy (CAE) and JAE were first classified by the ILAE in 1989. The syndrome-related characterization of absence seizures with video-EEG analysis was described by Panayiotopoulos et al., who advanced more strict inclusion and exclusion criteria that were accepted as a proposal by the ILAE in 2005. Panayiotopoulos et al. reported the mean duration of absence seizures in CAE as 12.4 ± 2.1 sec, similar to our findings. However, the duration of absence seizures in JAE in Panayiotopoulos’ study was much longer than in our group (16.3 ± 7.1 vs 7.64 ± 3.39 sec, respectively). This finding by Panayiotopoulos was based on three patients with JAE to be considered as established. In a population-based study, Hedström and Olsson demonstrated the frequency of 3 Hz spike and slow wave activity longer than 10 sec was higher in the group representing CAE than the group representing JAE. They also indicated short episodes (<10 sec) of 2-4 Hz spike and slow wave without clinical correlates were associated with increased risk for future generalized tonic clonic seizures, observed in 80% of JAE. In a recent study by Sadleir et al., although no significant difference was seen between seizure duration in JAE and CAE, there was a trend for absence seizures to be shorter in JAE. Absence seizure duration was affected by the stimulus - shorter when asleep and during intermittent photic stimulation and longer during HPV.

Ictal discharge fragmentation/disorganization on EEG is an exclusion criterion for CAE. However, Patient 13, a five-year-old boy (onset of symptoms 4.2) had fragmentation of 3 Hz spike and slow waves in two absence seizures lasting 60 and 130 sec. Even though absence seizures in CAE are brief (4-20 sec), they might be exceptionally longer. In idiopathic generalized epileptic syndromes with typical absences, disorganization was most frequent in
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age of onset</th>
<th>Age adm</th>
<th>Cranial MRI</th>
<th>Routine and/or Video-EEG</th>
<th>Symptoms/etiology</th>
</tr>
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<tbody>
<tr>
<td>Patient 25</td>
<td>6</td>
<td>11.2</td>
<td>Enlarged right temporal lobe</td>
<td>Ictal spike-slow wave and sharp slow waves with loss of consciousness, lip-licking. Interictal 5 Hz sharp waves and spike-waves on right centroparietal and centrottemporal areas.</td>
<td>Mental retardation</td>
</tr>
<tr>
<td>Patient 26</td>
<td>12.8</td>
<td>13.3</td>
<td>Cortical dysplasia and/or hamartoma in left mesial temporal cortex</td>
<td>Multiple sharp waves on F7, T3, T5 electrodes of left hemisphere. Bilateral, high amplitude 3 Hz spike and slow wave.</td>
<td>Cortical dysplasia and/or hamartoma</td>
</tr>
<tr>
<td>Patient 27</td>
<td>10.9</td>
<td>11.1</td>
<td>Parieto-occipital gyral asymmetry</td>
<td>2.5 Hz spike-wave and multiple spike-wave activities prominent on left hemisphere.</td>
<td>Gyral asymmetry</td>
</tr>
<tr>
<td>Patient 28</td>
<td>6.5</td>
<td>7</td>
<td>-</td>
<td>Isolated sharp wave and spike-wave activities on left temporal area. Ictal 3-4 Hz biphasic spike-wave and sharp slow wave with loss of consciousness.</td>
<td>Cryptogenic absence epilepsy, chronic renal failure</td>
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*Absence epilepsy provisional diagnosis by clinical features including loss of consciousness and blank stare*

*Absence epilepsy provisional diagnosis by routine EEG features (3 Hz spike and slow wave)*

<table>
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<tbody>
<tr>
<td>Patient 29</td>
<td>5.5</td>
<td>7.9</td>
<td>Widened left temporal horn and left mesial temporal sclerosis</td>
<td>Generalized 2.5-3 Hz spike-slow waves followed by sharp slow waves during sleep, isolated 4-5 Hz sharp waves on central area on left hemisphere.</td>
<td>Mesial temporal sclerosis</td>
</tr>
<tr>
<td>Patient 30</td>
<td>2</td>
<td>12.8</td>
<td>Tumor in optic chiasm, cystic lesions in caudate nucleus and centrum semiovale</td>
<td>Generalized 3-3.5 Hz spike-slow wave and sharp slow waves, also during HPV with transient loss of consciousness.</td>
<td>Neurofibromatosis</td>
</tr>
<tr>
<td>Patient 31</td>
<td>4</td>
<td>5.8</td>
<td>Periventricular leukomalacia and thinning of corpus callosum</td>
<td>Generalized 3 Hz spike-slow wave and occasionally spike-slow waves, also during HPV with loss of consciousness, eye deviation and chewing.</td>
<td>Periventricular leukomalacia, anoxic birth</td>
</tr>
</tbody>
</table>

Adm: Admission. HPV: Hyperventilation.
JME, followed by JAE and CAE. Older age was associated with more organized discharges\textsuperscript{13}. Patient 13 fulfilled the diagnostic criteria of CAE except fragmentation, which might be due to the younger age and prolonged nature of the seizure.

Automatisms might be important to document. The patients who had automatisms in their clinical seizures had increased risk of relapse of epileptic discharges on follow-up EEGs\textsuperscript{14}. Automatisms were seen in five patients with CAE and one with JAE, with lip-licking being the most common. This incidence of automatisms was lower than in the previous studies, which stated an incidence of 80-100%\textsuperscript{7,15}, because the duration of absence seizures in JAE was shorter.

In both CAE and JAE, we observed generalized 2.5-4 Hz spike-wave and sharp wave discharges in the interictal period in all patients, and these activities were more frequent in CAE than JAE (p<0.05); however, the durations were similar. Fragments of generalized spike and waves were demonstrated in 31% to 94% of children with absence seizures during the interictal period\textsuperscript{13,15}. On sleep EEG, we also demonstrated brief 2.5-4 Hz spike-wave and sharp waves. Nobili et al.\textsuperscript{16} stated that in CAE, generalized spike-wave discharges increased in the second phase of non-rapid eye movement (REM) sleep and decreased in REM sleep. Sleep EEG might have prognostic value. In adults who were originally diagnosed as CAE or JAE, fast discharges of rhythmic spikes (10-15 Hz) during sleep was a marker of drug resistance in absence epilepsy\textsuperscript{17}. In children with CAE, the presence of polyspikes and polyspikes and waves during sleep was associated with persistence of absence seizures or further development of generalized tonic clonic seizures\textsuperscript{18}. One might consider sleep EEG in patients with a provisional diagnosis of absence seizures in case of inefficient HPV, lack of video-EEG monitoring and normal interictal EEG.

Video-EEG recordings are important in the precise diagnosis of EMA. In EMA, myoclonic jerks of the eyelids precipitated by eye closure are prominent\textsuperscript{19,20}, whereas in CAE or JAE, random eye movements and eye-blinking are seen. One of our patients with EMA did not exhibit photosensitivity even though typical seizures were recorded upon eye closure by video-EEG. There are some other patients in the literature diagnosed as EMA in whom photosensitivity was not noticed\textsuperscript{21,22}. Video-EEG recordings are also required for the differential diagnosis of JME from other myoclonic disorders of childhood.

Symptomatic absence seizures are a heterogeneous group of disorders that have not been documented well. Olsson and Hedström\textsuperscript{23} defined the epidemiological features of absence epilepsies: besides generalized 3 Hz spike-wave activities, there were asymmetric, disorganized or multiple spike-waves in a group of patients (10% of absence epilepsies) with cerebral palsy, Down syndrome, and non-progressive encephalopathy, etc. We diagnosed four patients provisionally with clinical features (blank stare and loss of consciousness) and three patients with routine EEG findings (3 Hz spike and slow wave) as absence epilepsy. In the differential diagnosis, in the clinical features group, the evaluation of both cranial MRI findings and video-EEG recordings pointed out the involvement of the temporal lobe. Complex partial temporal lobe seizures present with an alteration of consciousness accompanied by a staring spell or eye deviation, and associated automatisms such as lip smacking or chewing. The disturbances of consciousness both in temporal lobe epilepsies and absence epilepsies might suggest they share common underlying circuit mechanisms including thalamocortical circuits\textsuperscript{24}. In young children, the initial manifestations of temporal lobe epilepsies might be generalized in character\textsuperscript{25}. In the differential diagnosis, in the routine EEG group, the patients admitted with a wide spectrum of clinical findings including difficulty in learning and generalized tonic clonic seizures. The video-EEG recordings of two of these children (Patients 30 and 31) revealed generalized 3 Hz spike-slow wave discharges, also during HPV, with loss of consciousness compatible with absence seizure. There were no focal discharges. We also classified this group as symptomatic absence seizure. The cranial MRI findings might be coincidental in this group.

It can be difficult to make an accurate diagnosis and classification of epilepsy. A detailed history and routine EEG recordings can provide evidence to confirm the diagnosis, but these
might not be sufficient in some cases. In this study, short-term video-EEG monitoring enabled us to record interictal and sleep EEG and also ictal EEG, which was important to define seizure type. Video-EEG monitoring was also required for the differential diagnosis of symptomatic absence epilepsy.

There are some limitations of the study. We had small numbers of children in each category, which did not allow us to do further statistical analysis. This was not a population-based study. Participants of this study were followed in a tertiary hospital; thus, results might not reflect all the children with absence seizures in the whole population.

In conclusion, video-EEG monitoring considering one hour of sleep and awake status is the gold standard in syndrome classification of absence epilepsies. The findings of our study confirmed the importance of sleep and interictal video-EEG in the diagnosis of patients with absence epileptic syndromes besides HPV. Long-term follow-up of patients is required to decrease morbidity and provide the best prognosis for patients.

REFERENCES