Seizure: European Journal of Epilepsy 79 (2020) 86–89

Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

Absence seizure provocation during routine EEG: Does position of the child during hyperventilation affect the diagnostic yield?

Tal Rozenblat[a,*], Dror Kraus[b], Muhammad Mahajnah[c], Hadassah Goldberg-Stern[b], Nathan Watemberg[a]

[a] Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[b] Department of Neurology, Schneider Children's Medical Center of Israel, Petah Tiqva, Israel
[c] Institute, Hillel Yaffe Medical Center, The Ruth and Bruce Rappaport Faculty of medicine, Technion University, Israel

ARTICLE INFO

Keywords:
Epilepsy
Absence seizures
Childhood Absence Epilepsy
Hyperventilation
EEG
Position

ABSTRACT

Purpose: When performed correctly, hyperventilation (HV) for three minutes provokes absence seizures in virtually all children, a finding suggestive of a diagnosis of childhood absence epilepsy (CAE). Interestingly, some children experience absence seizures while performing HV in the office yet do not experience absences during HV on subsequent routine EEG. In most instances, HV during routine EEG is performed in the supine position, while in the office HV is done with the child sitting-up. Therefore, we hypothesized that the position in which HV is performed may influence its yield in provoking absence seizures.
Methods: We conducted a randomized multi-center controlled trial among children (4-10 years old) with suspected CAE. During a routine EEG, children were asked to perform HV twice, in the supine and sitting positions.
Results: Twenty children (four males) diagnosed with CAE were included in the analysis. Seventeen of the 20 patients experienced absence seizures while sitting and 13 experienced seizures during supine HV ($p = 0.031$). All patients that had absence seizures during supine HV also had seizures during sitting HV. Among patients with absences in both positions, seizure duration was significantly shorter during sitting HV (mean 8.69 seconds) than during supine HV (mean 12 seconds) ($p = 0.042$).

An opposite tendency was seen in the younger age group (4-7 years), with shorter seizures in the supine HV group (5.6 seconds supine, 7.57 seconds sitting, $p = 0.019$).
Conclusions: HV in the sitting position may increase the yield of provoking absence seizures during routine EEGs, thereby improving its sensitivity in the diagnosis of CAE.

1. Introduction

Absence seizures are generalized epileptic seizures with a characteristic ictal electroencephalographic (EEG) pattern of generalized, 3 Hertz (Hz) spike-and wave discharges.[1,2] The mean duration of an absence seizure is 4-20 seconds (range 3-40 seconds), and it begins and ends abruptly, manifesting as cessation of activity, unresponsiveness, and staring with/without eye flutter, lip-smacking or head dropping.

Absence seizures are mostly seen in childhood absence epilepsy (CAE) and Juvenile Absence Epilepsy (JAE). CAE onset is between four and ten years of age and resolves spontaneously in 60-80% of patients by the age of 12.[3,4] Seizures may occur many times a day and may go unrecognized by caregivers for weeks or even months.[3,4] Diagnostic criteria include: age between four and ten years at onset, normal neurological state and development, brief and frequent occurrence with abrupt and severe impairment of consciousness, and the classic EEG pattern of 3 Hz generalized spike and wave.[3,5]

EEG is diagnostic of absence seizures.[5,6] Resting hyperventilation (HV), when performed correctly, provokes absence seizures in virtually all children. Hence, HV is used as a maneuver to enhance the possibilities of capturing absences during routine EEG.[5,7,8] The American Clinical Neurophysiology Society Guidelines recommends performing HV for at least three minutes, with continued recording for a minimum of one minute after cessation of over breathing.[9] Recently, we demonstrated that the vast majority of children experience an absence seizure within less than 90 seconds from onset of hyperventilation.[10]

Abbreviations: AED, antiepileptic drugs; CAE, Childhood Absence Epilepsy; HV, hyperventilation; JAE, Juvenile Absence Epilepsy

* Corresponding author at: Rabin Medical Center-Beilinson Hospital, Petach Tikva 4941492, Israel.
E-mail addresses: tal.hakim@gmail.com (T. Rozenblat), Kraus.dror@gmail.com (D. Kraus), MohamedM@hy.health.gov.il (M. Mahajnah), Hagoldberg@clalit.org.il (H. Goldberg-Stern), watembergn@walla.co.il (N. Watemberg).

https://doi.org/10.1016/j.seizure.2020.03.013
Received 7 November 2019
1059-1311/ © 2020 British Epilepsy Association. Published by Elsevier Ltd. All rights reserved.

Clinical observations reveal that some children, especially younger children, experience absence seizures while performing bedside HV (during office visits), yet HV performed during a subsequent routine EEG fails to provoke clinical or electrographic seizures. In most instances, HV during a routine EEG is performed in the supine position, while office HV is usually performed while sitting up. Therefore, we hypothesized that the position in which HV is performed may influence its yield in provoking absence seizures and that, in some cases, routine EEG recording may not elicit the seizures. The aim of this study was to investigate whether, in children with absence seizures, HV performed in a sitting position increases the likelihood of provoking an absence seizure compared to HV in a supine position.

2. Methods

This randomized multi-center controlled trial was performed under the authorization of the institutional review boards in all participating medical centers. Children's parents or guardian have received information regarding the study protocol and approved their children's participation by signing a consent form.

The study included children with suspected absence seizures referred for a routine EEG. Data was collected between 2016 and 2017 in three academic medical centers in Israel.

Inclusion criteria were: children four to ten years of age, not receiving antiepileptic drugs (AEDs), who were deemed capable of performing HV. Children were allocated into two groups: Group A performed HV first in the supine position and then while sitting, group B performed the procedure in the reverse order.

During routine EEG recordings, patients performed three minutes of HV in both supine and sitting (without reclining on the chair) positions, with a resting period of five minutes between both maneuvers while EEG recording continued. Only records in which the child succeeded in performing the full study protocol were included.

The following parameters were examined in each position: occurrence of absence seizures, duration of seizures (in seconds) and latency (in seconds) from onset of HV until onset of seizure. All studies were done using the 10-20 system for electrode placement. All records were reviewed by one of the authors (D.K., M.M., N.W.).

2.1. Statistical analysis

Data was gathered using a Microsoft Excel spreadsheet. Data analysis was performed using SPSS version 25. Descriptive statistics are presented using prevalence and percentage values for categorical variables, while continuous variables are presented with mean ± standard deviation.

Continuous variables were compared by the Wilcoxon non-parametric test, nominal parameters were compared by chi-square test. Age groups were compared by Mann-Whitney non-parametric test. All analyses were performed using a significance threshold of 0.05.

3. Results

Between 2016 and 2017, 78 children with suspected absence seizures were referred to perform diagnostic EEG. Among them, 20 children were eventually diagnosed with CAE and comprised the study cohort. Most participants were girls (80%); mean age at diagnosis was 7.3 ± 1.6 years (range; 4.3-9.9 years). Group A consisted of 9 children (45%) while group B included 11 patients (55%). Patient demographics are summarized in Table 1.

As depicted in Table 2, absence seizures were recorded in 17 of 20 patients (85%). All 17 children experienced a seizure while sitting, compared with 13 children (65%) who experienced a seizure in the supine position (p = 0.031).

The mean duration of absences was 8.69 ± 4.85 seconds (range 3-20 seconds) in the sitting position and 12 ± 9.77 seconds (range 2-34 seconds) in the supine position (p = 0.042) (Table 3).

The latency to first seizure was 86.6 ± 50.1 seconds (range 28-196 seconds) in a sitting position and 98.2 ± 83 seconds (range 20-325 seconds) in a supine position (p = 0.591) (Table 4).

Table 5 presents a subgroup analysis of the patients divided by the first HV position. The order in which HV was performed did not significantly affect the occurrence of an absence seizure. Moreover, absence seizures did not differ between groups A and B in the sitting position (p = 0.109) or in the supine position (p = 0.333). We did not detect a difference in the mean duration of absence seizures between groups A and B in the sitting position (p = 0.308) or in the supine position (p = 0.592). Similarly, the latency to occurrence of the first seizure did not differ between groups in either sitting (p = 0.87) or supine position (p = 0.29).

Analysis of absence seizure occurrence according to age revealed that absence seizure duration in the supine position was shorter in children aged 4-7 than in children aged 8-10 (5.6 ± 3.4 vs 16 ± 10.5 seconds respectively, p = 0.019). Conversely, age did not significantly affect absence duration in the sitting position. Moreover, latency to first seizure did not differ between sitting and supine positions (Table 6).

Table 1
Demographic distribution of the patient population.

Patient demographics		
Variable	n	%
Gender		
Female	16	80
Male	4	20
Age		
4-7	10	50
8-10	10	50
Group		
A	9	45
B	11	55

Table 2
Absence seizures incidence

		Occurrence during supine position		Total n (%)
		yes n (%)	no n (%)	
Occurrence during sitting position	yes n (%)	13 (65)	4 (20)	17 (85)
	no n (%)	0 (0)	3 (15)	3 (15)
Total n (%)		13 (65)	7 (35)	20 (100)

Table 3
Absence seizures duration

Position	n	Duration of absence seizure (sec) Mean ± SD	Range (sec)	p
Sitting	13	8.69 ± 4.85	3-20	0.042
Supine	13	12 ± 9.77	2-34	

Table 4
Latency to first seizure

Position	n	Latency to first seizure (sec) Mean ± SD	Range (sec)	p
Sitting	13	86.62 ± 50.08	28-196	0.591
Supine	13	98.23 ± 83.03	20-325	

Table 5
Sub group analysis of groups A and B

Started with	Position	Incidence n (%)	p	Duration of absence seizure (sec) Mean ± SD	Range (sec)	p	Latency to first seizure (sec) Mean ± SD	Range (sec)	p
Group A- Supine	sitting	8 (88.9)	0.109	9.33 ± 2.16	7-18	0.308	78 ± 39.4	33-145	0.87
Group B- Sitting		9 (81.8)		8.14 ± 6.5	3-20		94 ± 59.9	28-196	
Group A- Supine	supine	6 (66.7)	0.333	13.67 ± 8.8	6-30	0.592	70.8 ± 58.29	20-182	0.29
Group B- Sitting		7 (63.3)		10.57 ± 11	2-34		121.7 ± 97.8	46-325	

4. Discussion

HV is an integral component of routine EEG studies in children. HV is usually performed in order to provoke absence seizures in children with CAE and other types of generalized epilepsies, in which absences may occur. EEG recording, including activation procedures, namely hyperventilation and photic stimulation, are generally performed with the patient in the supine position.[3,5] Our study aimed to investigate whether patient position affects the diagnostic yield of HV during a routine EEG, specifically whether performing HV during sitting position increases absence seizure occurrence. Our findings suggest that the occurrence of absence seizures in the sitting position is significantly higher than that seen in the supine position.

The use of activation procedures – namely hyperventilation and photic stimulation during routine pediatric EEG recording has received relatively little attention in recent literature. The necessity of performing HV for a full 3 minutes was questioned by Watemberg et al., who found that most children with CAE experienced an absence seizure less than 90 seconds after HV onset.[10] Craciun et al studied the effect of HV prolongation on interictal EEG abnormalities and seizures among children (20%) and adults (80%). They found that patients benefitted from prolonging HV from 3 to 5 minutes: 16% experienced seizures, and in 30% interictal epileptiform discharges were triggered by the extra 2 minutes of HV.[11]

In our study, HV while sitting triggered absence seizures in 17 patients (85%). Four of these children did not experience a seizure during supine HV, rendering sitting HV essential for diagnosis ($p = 0.031$) in these four children. We also found that absence duration during sitting HV was significantly shorter compared with supine HV ($p = 0.042$).

The 2016 American Clinical Neurophysiology Society Guidelines suggest that other stimulation procedures such as photic stimulation should be performed at least 3 minutes after cessation of HV in order to enable HV-related EEG changes to resolve.[9] Based on this recommendation we allowed a 5 minutes resting period of continuous EEG recording between the two positions of HV.

In fact, the order in which HV positions was performed did not influence absence seizures' incidence, duration or the latency to first seizure. Hypothesizing that thoracic compliance may affect the efficacy of HV in younger children, we analyzed the study cohort by age groups.

Indeed, EEG absence seizures duration in the supine position was shorter among younger children (4-7 years old) compared with older children (8-10 years old) ($p = 0.019$), sometimes as short as 3.3 seconds in the younger group compared with 6 seconds in older children. These findings could explain the clinical observation that children who experience an absence seizure during HV while sitting may not experience an event during a routine EEG recording in the supine position.

Several mechanisms have been proposed to explain how HV induces absence seizures. The hypoxia theory suggests that EEG changes during HV result from cerebral ischemic hypoxia associated with vasoconstriction due to low pCO_2 level.[12] The hypocapnia theory claims that forced reduction of pCO_2 level and blood alkalization raise absence seizures' occurrence with variability in the critical pCO2 level.[13,14] Of note, physical exercise-induced HV, a physiologic mechanism to expel CO2 and raise blood pH, does not increase the occurrence of absence seizures in people with absence epilepsies.[13]

The mechanism through which HV induces absence seizures among CAE patients is yet to be determined. Differences in chest wall compliance and efficacy of hyperventilation could explain, at least in part, the observed higher yield in provoking absence seizures in young children.[15,16] We assume that HV in the supine position may be less effective due to decreased chest wall compliance, while in a sitting position without backrest, younger children may perform HV more efficiently.

Our study limitations consist of the relatively small size of the cohort. There may have also been slight differences in the technique of hyperventilation among the 3 medical centers.

In conclusion, contrary to the current standard of performing HV in the supine position, HV in the sitting position without reclining on chair (i.e., without backrest) increases the probability of provoking absence seizures during routine EEG recordings. In younger children absence seizure duration in the supine position is shorter compared with that observed in older children. Since currently routine EEG is recorded in the supine position, absence seizures may not be induced in some children, particularly in younger ones. Further prospective studies on larger patient populations are needed to corroborate our findings.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

None.

Acknowledgments

None.

Table 6
Sub group analysis of age groups

Position	Group	n	Duration of absence seizure (sec) Mean ± SD	Range (sec)	p	Latency to first seizure (sec) Mean ± SD	Range (sec)	p
Sitting	4-7	7	7.57 ± 5.03	3-18	0.278	94.71 ± 63.58	28-196	0.807
	8-10	10	9.6 ± 5.13	3-20		79.6 ± 33.47	30-131	
Supine	4-7	5	5.6 ± 3.36	2-11	0.019	111.6 ± 124.7	20-325	0.661
	8-10	8	16 ± 10.47	7-34		89.88 ± 52.2	41-182	

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.seizure.2020.03.013.

References

[1] Fisher RS, Cross JH, French JA, et al. Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. Epilepsia 2017;58:522–30.
[2] Brigo F, Trinka E, Lattanzi S, et al. A brief history of typical absence seizures- Petit mal revisited. Epilepsy Behav 2018;80:346–53.
[3] Panayiotopoulos CP. (Chrysostomos P., International League against Epilepsy. The epilepsies : seizures, syndromes and management : based on the ILAE classifications and practice parameter guidelines. Bladon Medical Pub 2005.
[4] Mikati MA. Seizures in Childhood. Nelsontextb Pediatr. 19th Ed. 2011. p. 2013. Philadelphia: PA.
[5] Ma X, Zhang Y, Yang Z, et al. Childhood absence epilepsy: Elctroclinical features and diagnostic criteria. Brain Dev 2011;33:114–9.
[6] Dlugos D, Shinnar S, Cnaan A, et al. Pretreatment EEG in childhood absence epilepsy: associations with attention and treatment outcome. Neurology 2013;81:150–6.
[7] Sadleir LG, Farrell K, Smith S, et al. Electroclinical features of absence seizures in childhood absence epilepsy. Neurology 2006;67:413–8.
[8] DALY DD. Epilepsy and syncope. Curr Pract Clin Electroencephalogr 1990:269–334.
[9] Sinha SR, Sullivan L, Sabau D, et al. American Clinical Neurophysiology Society Guideline 1: Minimum Technical Requirements for Performing Clinical Electroencephalography. J Clin Neurophysiol 2016;33:303–7.
[10] Watemberg N, Farkash M, Har-Gil M, et al. Hyperventilation During Routine Electroencephalography: Are Three Minutes Really Necessary? Pediatr Neurol 2015;52:410–3.
[11] Craciun L, Varga ET, Mindruta I, et al. Diagnostic yield of five minutes compared to three minutes hyperventilation during electroencephalography. Seizure 2015;30:90–2.
[12] Davis H, Wallace WM. Factors affecting changes produced in electroencephalogram by standardized hyperventilation. Arch Neurol Psychiatry. 1942.
[13] Esquivel E, Chaussain M, Plouin P, et al. Physical exercise and voluntary hyperventilation in childhood absence epilepsy. Electroencephalogr Clin Neurophysiol 1991;79:127–32.
[14] Wirrell EC, Camfield PR, Gordon KE, et al. Will a critical level of hyperventilation-induced hypocapnia always induce an absence seizure? Epilepsia 1996;37:459–62.
[15] Papastamelos C, Panitch HB, England SE, et al. Developmental changes in chest wall compliance in infancy and early childhood. J Appl Physiol 1995;78:179–84.
[16] Keslacy S, Carra J, Ramonatxo M. Role of respiratory system impedance in the difference of ventilatory control between children and adults. Respir Physiol Neurobiol 2008;161:239–45.