



## Electroencephalography Findings in Infants Diagnosed with Brief Resolved Unexplained Event

Ahmad Hammoud<sup>1</sup>, Rolla Shbarou<sup>2</sup>, Mona Hnaini<sup>3</sup> and Chadi Al-Alam<sup>4\*</sup>

<sup>1</sup>Pediatrics and Pediatrics Neurology, Makassed General Hospital, Beirut, Lebanon

<sup>2</sup>Pediatric Neurology Faculty, American University of Beirut Medical Center, Beirut, Lebanon

<sup>3</sup>Pediatrics and Pediatrics Neurology, Lebanon

<sup>4</sup>Pediatrics and Pediatrics Neurology, Haykel Hospital, El Koura, Lebanon

\*Corresponding Author: Chadi AL-Alam, Pediatrics, Pediatrics Neurology, Haykel Hospital, El Koura, Lebanon.

**Received:** November 06, 2020

**Published:** November 21, 2020

© All rights are reserved by **Chadi Al-Alam., et al.**

### Abstract

An apparent life-threatening event (ALTE) was defined in 1986 by the National Institutes of Health as an episode that frightens the observer, characterized by a combination of apnea, color changes, and a marked drop in muscle tone, accompanied by either choking or gagging [1]. In 2016 the American Academy of Pediatrics adopted the term Brief Resolved Unexplained Event (BRUE), in order to emphasize the transient nature and lack of clear cause for the incident, while eliminating the fear that the term ALTE instilled. We have observed that some electroencephalograms (EEG) in infants admitted to our hospital following ALTE or BRUE were in many cases considered dysmature.

This is a retrospective chart review of infants diagnosed with ALTE or BRUE, over a 10-year period, looking at those who received an EEG. We found that 21% of EEG recordings were dysmature.

**Keywords:** Electroencephalogram; EEG; Dysmature EEG; BRUE; ALTE; Dysmaturity

### Introduction

An apparent life-threatening event (ALTE) is a terrifying event for parents and caregivers. It was defined in 1986 by the National Institutes of Health as an episode that frightens the observer, characterized by a combination of apnea (either central or occasionally obstructive), color changes (usually cyanotic or pallid but occasionally erythematous or plethoric), and a marked drop in muscle tone, accompanied with either choking or gagging [1].

Multiple etiologies have been linked to this diagnosis, ranging from gastroesophageal reflux and lower respiratory tract infections to cardiac arrhythmias, infections, or even metabolic disorders and seizures [2,3].

In 2016 the American Academy of Pediatrics adopted the term Brief Resolved Unexplained Event (BRUE), in order to emphasize the transient nature and lack of clear cause for the incident, while

eliminating the fear that the term ALTE instilled. BRUE was subdivided into low-risk and high-risk groups. In the low-risk group, only observation is advised, whereas, in the high-risk group, a thorough evaluation is warranted [4].

Clinical evaluation testing includes electroencephalography, especially if no apparent gastroesophageal reflux is present [5,6]. The recent Clinical Practice Guideline in Pediatrics discourages the performance of EEG in the low-risk group [7]. Nevertheless, it continues to be ordered by some pediatricians. We have observed that some EEG recordings in these infants, do not show ictal or inter-ictal epileptiform discharges, and were in many cases dysmature. EEG in neonates matures with age, and if the recording is not commensurate with the infant's age, it is deemed dysmature. This concept was not recognized until 1975 when Lombroso., *et al.* mentioned that a diseased infant might show EEG findings consistent with younger gestational age [8].

Dysmaturity on EEG has been later reported in children with neurologic diseases [9]. It has even been found in systemic diseases (such as bronchopulmonary dysplasia) [10]. This finding on EEG has been linked to a poorer neurologic outcome in infants with prematurity [11].

In this study, we studied retrospectively infants presenting with the diagnosis of ALTE or BRUE, who received an EEG. The aim was to look at the percentage of dysmature EEGs in this cohort, and whether this finding carries any clinical significance.

### Patients and Methods

This was a retrospective chart review, over a period of 10 years (from January 2007 to December 2017), of children aged 0 to 12 months, who were admitted to the American University of Beirut Medical Center with a diagnosis of ALTE or BRUE and who underwent EEG recording.

Patients with the final diagnosis of ALTE or BRUE upon discharge from the hospital, were searched for, on the computerized medical records.

Exclusion criteria included: 1) corrected age for ex-premature babies less than 37 weeks; 2) infants with known structural brain anomaly; 3) infants known to have seizures; 4) infants diagnosed with sepsis and/or bacteremia at the time of BRUE or ALTE, and 5) infants with no EEG done during this admission.

A total number of 39 infants were found, and out of those, 13 did not receive an EEG.

The data of the remaining 26 were collected and studied, 1 patient was eliminated from the group because the corrected age at the time of EEG was less than 37 weeks, and 1 was excluded due to the diagnosis of sepsis.

EEGs of the remaining 24 infants were reviewed by an epileptologist who was different than the one who interpreted them at first, and the diagnosis of: normal, abnormal (Epileptiform findings, or Slowing), or dysmature was confirmed.

A dysmature of the pattern was reported when the recorded findings appear to belong to a post-conceptual age younger than that of the infant's age [12].

Other variables were also assessed in these infants, and those were: gender, brain MRI, other radiologic findings, the description

of symptoms, the duration of symptoms, and whether the ALTE or BRUE on presentation was the first or a repeat event.

### Results

The average age of the remaining 24 patients was 60 days, with a range between one day and 270 days.

The EEG records of the 24 infants were obtained and verified by a second epileptologist and were the following: 16 normal, 3 abnormal, and 5 dysmature (Figure 1). Out of the 3 infants with abnormal EEG, one was 6 months old at presentation and was the oldest infant presenting with ALTE or BRUE. His EEG showed atypical Absence. He was later diagnosed with Glucose Transporter 1 (GLUT1) deficiency. The other 2 had frank epileptiform discharges.

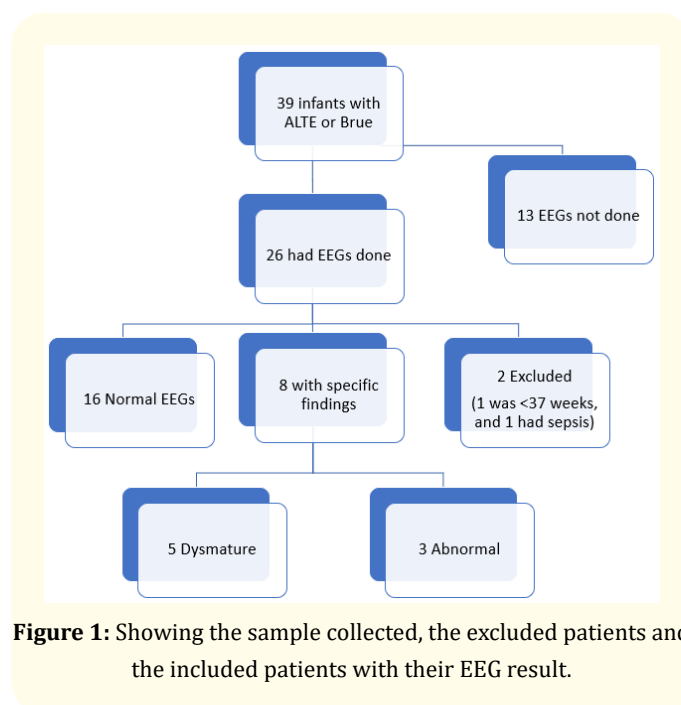
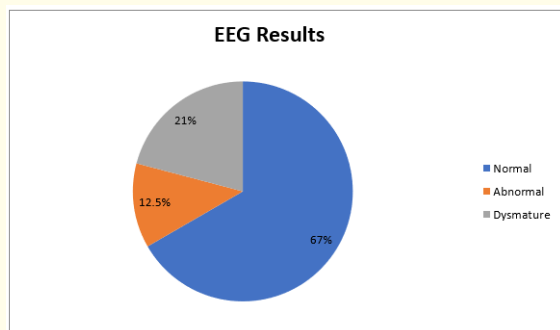


Figure 1: Showing the sample collected, the excluded patients and the included patients with their EEG result.

The prevalence of dysmature EEG in infants with ALTE or BRUE was 21%, with a confidence interval of 95% that was considered statistically significant (Figure 2). In the total sample, there were 8 (33.3%) males and 16 (66.7%) females. Among infants with a dysmature EEG (5), there were 2 females (40%) and 3 males (60%). A P-value of fisher exact test exploring the association between dysmaturity and gender was 0.289 (> 0.05), therefore it was not statistically significant. In other words, dysmaturity was not significantly associated with gender. The average age of the infants with dysmature EEG was 34 days, which was lower than the average age of the

entire group. The youngest infant was 5 days of age and the oldest was 67 days of age. Only one of these infants was a premature newborn, born at 32 weeks of gestation, with a post-conceptional age at the time of the event of 7 days. The remaining 4 patients were term infants.



**Figure 2:** Pie chart showing the percentage of infants with EEG results showing Normal, Abnormal, or Dysmature EEG. 21% was considered statistically significant with a 95% CI.

Among those who had a brain MRI (9), 3 had an abnormal result, and out of those, 2 had a normal EEG and one had an abnormal EEG. None of the patients with dysmature EEG had any abnormality on MRI.

As for other radiologic findings, out of the 5 infants with a dysmature pattern, 1 had gastro-esophageal reflux on barium swallow, and one had a suspected pneumonia on chest X-ray.

When analyzing the duration of the presenting symptoms of ALTE or BRUE in these infants, no statistical significance was found between infants with Normal and Abnormal EEG versus those with dysmature EEG.

Out of 24 charts, only 19 charts documented whether the BRUE was a first or a repeat event. It was found that 4 out of 5 infants (80%) with a dysmature EEG, presented with their first ALTE or BRUE compared to 5 out of 14 infants (20%) with a normal or abnormal EEG, with a p-value for the association of dysmature EEG with the First ALTE of 0.047 being statistically significant (Table 1).

		First Event	Repeated Event	Total
Normal and Abnormal EEG	Count	5	14	19
	Percentage	26.3%	73.7%	100%
Dysmature EEG	Count	4	1	5
	Percentage	80%	20%	100%
Total	Count	9	15	24
	Percentage	37.5%	62.5%	100%

**Table 1:** Compares infants with normal and abnormal EEGs to infants with dysmature EEG when it comes to, weather the ALTE or BRUE episode they presented with was the first or a repeated episode. The p-value for patients with Dysmature EEG presenting with the first episode was 0.047 (<0.05) which was statistically significant.

**Discussion**

No clear explanation exists for our findings. A theory one can postulate might be: the stressful condition the infant's experience, i.e. the BRUE causes the dysmature appearance of EEG (like the infants suffering from bronchopulmonary dysplasia for example). The reverse theory may also be plausible: the dysmaturity on EEG, heralding an immaturity in the brain, including the brainstem, causes a centrally mediated severe apneic event that may be similar to apnea of prematurity. It would be helpful to perform polysomnograms on these infants to find out the prevalence of central apnea that may not be clinically apparent.

In our study, we have noticed that the female to male ratio was around 2:1, yet in the infants having a dysmature EEG, the number was more or less equal (2 females and 3 males).

When studying brain MRI imaging in these infants, none of the infants with a dysmature the pattern had abnormal imaging. This supports the hypothesis that a dysmature EEG pattern is not due to a structural brain abnormality, but rather due to an immaturity of physiologic mechanisms.

In addition, out of the 5 infants with dysmature EEG, one had gastroesophageal reflux on barium swallow and one had suspected pneumonia, therefore, 3 infants had no other radiologic findings or clinical diagnoses, albeit it is known that a normal barium swallow does not rule out the presence of gastroesophageal reflux in these patients [13]. One question comes to mind: does silent GE reflux lead to respiratory symptoms, and result in cyanosis and transient hypoxemia, thus affecting the brain's physiologic function and causing the dysmature pattern on EEG?

When comparing infants with dysmature EEG to infants with normal or abnormal EEG, we found that the ALTE or BRUE episode was more likely to be the first episode in the infants with dysmature EEG, whereas infants with normal or abnormal EEG were more likely to have a repeat episode. This finding was significant with a p-value of 0.047; this finding can be explained by the fact that the dysmature group was the younger group of patients, and therefore more likely to have an "immature brain".

### Limitations

This was a retrospective study, with a small number of patients. In addition, the computerized system could only check for the admitting diagnosis of ALTE or BRUE, if this diagnosis was also mentioned in the discharge diagnosis. Therefore, this could have led to the loss of a significant number of patients over a 10-year period.

### Conclusion

We have observed in this study the significant presence of dysmature EEGs in infants with ALTE and BRUE, and more in infants presenting with the first attack. Whether a dysmature EEG is a direct cause of ALTE or BRUE remains to be seen.

A larger prospective study should be performed to further investigate this hypothesis, with an adequate follow-up that would include a careful neurologic evaluation and determination of developmental milestones.

### Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

### Funding

The authors received no financial support for the research, authorship, and publication of this article.

### Bibliography

1. "National Institutes of Health Consensus Development Conference on Infantile Apnea and Home Monitoring, Sept 29 to Oct 1, 1986". *Pediatrics* 79.2 (1987): 292-299.
2. Genizi J., et al. "Apparent life-threatening events: neurological correlates and the mandatory work-up". *Journal of Child Neurology* 23.11 (2008): 1305-1307.
3. Okada K., et al. "Discharge diagnoses in infants with apparent life-threatening event". *Pediatric International* 45.5 (2003): 560-563.
4. Arane K., et al. "Brief resolved unexplained event: New diagnosis in infants". *Canadian Family Physician* 63.1 (2017): 39-41.
5. Hewertson J., et al. "Epileptic seizure-induced hypoxemia in infants with apparent life-threatening events". *Pediatrics* 94 (1994): 148-156.
6. Fuger M., et al. "[Relevance of electroencephalography in infants presenting to an emergency department who have had an apparent life-threatening event]". *Archives of Pediatrics* 21.11 (2014): 1206-1212.
7. Tieder JS., et al. "Brief Resolved Unexplained Events (Formerly Apparent Life-Threatening Events) and Evaluation of Lower-Risk Infants: Executive Summary". *Pediatrics* 137.5 (2016).
8. Lombroso CT. "Neurophysiological observations in diseased newborns". *Biological Psychiatry* 10.5 (1975): 527-558.
9. Scher MS. "Neurophysiological assessment of brain function and maturation. II. A measure of brain dysmaturity in healthy preterm neonates". *Pediatric Neurology* 16.4 (1997): 287-295.
10. Hayakawa F., et al. "Dysmature EEG pattern in EEGs of preterm infants with cognitive impairment: maturation arrest caused by prolonged mild CNS depression". *Brain Development* 19.2 (1997): 122-125.
11. Le Bihannic A., et al. "Prognostic value of EEG in very premature newborns". *Archives of Disease in Childhood: Fetal and Neonatal* 97.2 (2012): F106-109.
12. Shany E and I Berger. "Neonatal electroencephalography: review of a practical approach". *Journal of Child Neurology* 26.3 (2011): 341-355.
13. van der Pol R.J., et al. "Diagnostic accuracy of tests in pediatric gastroesophageal reflux disease". *Journal of Pediatrics* 162.5 (2013): 983-7 e1-4.

#### Assets from publication with us

- Prompt Acknowledgement after receiving the article
- Thorough Double blinded peer review
- Rapid Publication
- Issue of Publication Certificate
- High visibility of your Published work

Website: [www.actascientific.com/](http://www.actascientific.com/)

Submit Article: [www.actascientific.com/submission.php](http://www.actascientific.com/submission.php)

Email us: [editor@actascientific.com](mailto:editor@actascientific.com)

Contact us: +91 9182824667