

Epilepsy trigger factors in Saudi Arabia

A missing part of the puzzle

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ABSTRACT

الأهداف: التعرف على مسببات الصرع السائدة في المملكة العربية السعودية للمساعدة في منع النوبات وتقليل عددها.

المنهجية: أجريت هذه الدراسة المقطع العرضي في عام 2020 لدى سكان مقيمين في المملكة العربية السعودية. استخدمنا استبياناً عبر الإنترنت لتقييم عوامل الزناد الأكثر شيوعاً.

النتائج: شارك في الدراسة 546 مريضاً بالصرع، منهم 289 (53%) من النساء. ثمانية وأربعون في المئة لم يكن لديهم نوبة في الأشهر الثلاثة السابقة. خمسة وعشرون في المئة لديهم فرد من العائلة مصاب بالصرع. كان العامل الأكثر إثارة هو الحرمان من النوم (285 (52%)، يليه الإجهاد (225 (41%)، وفقدان الدواء 210 (38.5%)، والقلق 209 (38.3%)، والتعب 184 (33.7%).

الخلاصة: الحرمان من النوم هو العامل الأكثر إثارة للإصابة بالنوبات في المملكة العربية السعودية، يليه الإجهاد، يليه عدم تناول الدواء.

Objectives: To identify epilepsy triggers prevalent in Saudi Arabia with a view to seizure prevention or achieving a reduction in their frequency.

Methods: This is part of a cross-sectional study carried out in 2020 in a Saudi population in the Kingdom of Saudi Arabia (KSA). We used an online questionnaire to evaluate the most common seizure trigger factors.

Results: A total of 546 Saudi patients with epilepsy participated in the study, of which 289 (53%) were women. Of them, 263 (48.1%) had no seizure in the previous 3 months. One hundred and thirty-six (25%) had a family member with epilepsy. The most-reported trigger factor was sleep deprivation reported by 285 (52%), followed by stress 225 (41%), missed medication 210 (38.5%), anxiety 209 (38.3%), and fatigue 184 (33.7%).

Conclusions: Sleep deprivation is the most reported trigger factor for seizures in the KSA, followed by stress, followed by missed medication.

Keywords: epilepsy, trigger factor, Saudi Arabia, seizure

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Contortion is a neurologic confusion identified by an enduring tendency to seizures.¹ A seizure is a sudden, transient brain dysfunction due to repeated, hypersynchronous discharge of central neurons.² Epilepsy is a primary nervous system disease in which brain function fails to work, causing unusual behavior at times, loss of memorably, and sometimes sensations.³ In the Kingdom of Saudi Arabia (KSA), epilepsy occurs in 6.54 of 1000 individuals.⁴ The International League Against Epilepsy classifies seizures according to 2 systems: basic and expanded.⁵ Unusual behavior is classified according to the focal onset and restricted to one side of the brain hemisphere, or great start, with apparent clinical start in both hemispheres.⁶ The expanded unusual behavior Classification is for medical practitioners with extensive knowledge of epilepsy diagnosis and treatment. The skeleton is similar to that of the basic grouping, although particular subtopics are enlarging. Thus, brain-onset failure can carefully be classified depending on whether the first known distinct is, most significant activity, a neuromuscular activity that influences both sides of the patient's brain.

The goal of seizure management is freedom from seizures with no adverse effects of medication, and improvement in the quality of life of the patient.⁷ In a study by Sanya et al,⁸ 89% of the contender register more than one trigger for brain failure causing unusual behavior, and as many as 10 triggers were endorsed.

Examples were stress, trauma, inadequate sleep, and culturally validated concepts such as demonic attacks and spells. However, common causal factors registered by patients were: missed medication (40.9%), reaction stress (31.3%), lack of fear (19.7%), fatigue (15.3%), skipped meals (9.1%), fever (6.4%), and smoking (6.1%). The practical relationship was among commonly reported unusual behaviors (namely, skipped drugs subscription, sleep hardship, fatigue, and psychological stress).

Upon reviewing the literature, we found no data on trigger factors (TFs) for epilepsy in the KSA. This study is carried out to identify epilepsy triggers prevalent in Saudi Arabia, intending to prevent and mitigate seizures.

Methods. The research was based on a cross-sectional of 2020 in a Saudi population in KSA. The university of Abdulrahman Bin Faisal accepted the Research procedure that was to be carried out ethically with regards to the ethical standards as was declared by Helsinki in 2020 review.

Between March 2020 and April 2020, we recruited male and female patients with epilepsy aged 18-50 years at an epilepsy clinic in the KSA.

To determine the most common TFs for seizures, we employed an online questionnaire incorporating the Delphi technique. We included only patients diagnosed with epilepsy (**Figure 1**). Preparing the survey, we tested the validity of each question in a pilot study with 10 participants, with an evaluation of the results by a panel of 4 experts. Issues with a reliability coefficient >0.6 were retained.

Statistical analysis. We used the Statistical Analysis for Social Sciences version 26 (Armonk, NY: IBM Corp). Descriptive analyses of sociodemographic characteristics are presented in a table using numbers and percentages. Data is analyzed descriptively using frequency and rates. The research uses the Pearson Chi-square and Fisher's exact tests' carry out the statistical examinations. The tool uses the formula, "A p -value <0.05". Based on "Qualtrics", sample-size calculator, 384 patients is the minimal number of epileptic patients should be recruited in the general population of KSA (which was 6.54/1000 in 2009),⁹ and confidence intervals of 95% with a 5% margin of error.

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The data of each participant were coded and the data file secured by a password. For reasons of confidentiality, the study data are available only to the authors of this research.

Results. A total of 546 Saudi patients with epilepsy participated in this study. Fifty-three percent were female. The most frequent age group was 22-30 years 234 (43%) of participants, followed by 18-21 years 125 (23%) of participants, and 31-40 years 125 (23%) of participants. Higher age groups were infrequent. Patients from all KSA provinces participated in this study; the highest percentage was from the Western area 145 (26.6%) and the lowest was from the Northern region 45 (8.2%). Approximately half of the participants had a university degree, while 158 (29%) had a high school education, and other educational levels were infrequent (**Table 1**).

History taking showed that 263 (48.1%) of participants had been seizure-free over the previous 3 months, 422 (77.2%) were compliant with their treatment plan, and 136 (24.9%) had a family member with epilepsy (**Table 2**).

The prevalence of participant comorbidities, risk factors, and possible etiologic disorders is presented in **Table 3**. The prevalence of smoking was 84 (15.4%); alcohol use 14 (2.6%); and drug abuse 15 (2.7%). The most common comorbidity was asthma at 65 (12%), followed by diabetes at 38 (7%). The most common putative etiologic factors were head trauma at 71 (13%) followed by prenatal hypoxia at 24 (4.4%).

Figure 2 illustrates the TFs reported by the participants. The most-reported factor was sleep deprivation at 212 (52%), followed by stress at 169 (41%), missed medication at 160 (38.5%), anxiety at 150 (38.3%), and fatigue at 138 (33.7%). The least reported factors were decreased coffee consumption, pregnancy, and eating a specific kind of food, each reported by less than 1% of participants.

In **Table 4**, the reported TFs are compared between patients with identified brain factors and those without seizures were idiopathic; applying the accurate Fisher's trial and that of Chi-squared. A higher percentage of participants with specific reasoning factors than those with idiopathic epilepsy reported the following TFs: fever, alcohol use, prolonged reading, studying for an examination, and an extended computer session lower percentage of participants with an etiologic factor than without reported hunger as a TF.

Discussion. Several potential causes for epilepsy exist such as family history, brain pathology including

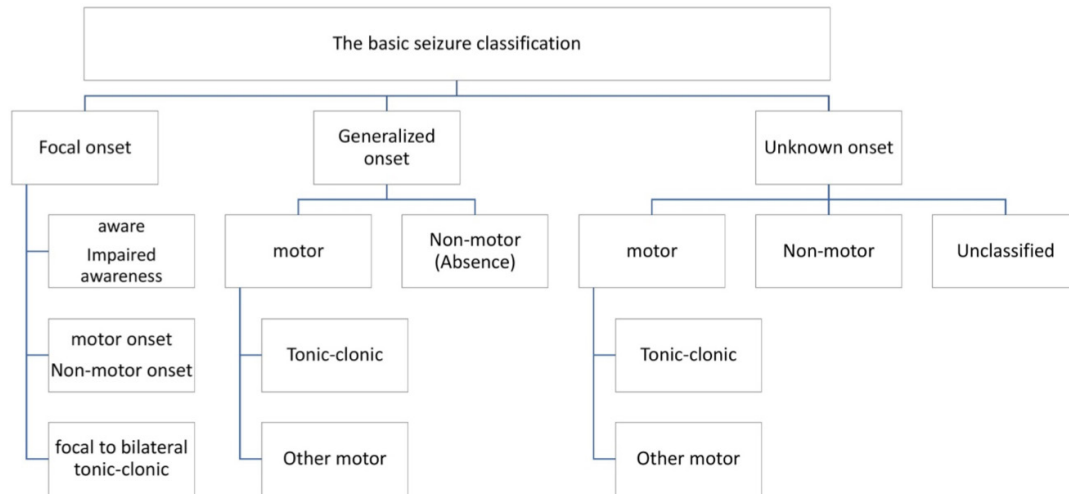


Figure 1 - The basic seizure classification.

Table 1 - Characteristics of participants.

Characteristics	n	(%)
<i>Gender</i>		
Female	289	(52.9)
Male	257	(47.1)
<i>Age</i>		
18-21	125	(22.9)
22-30	234	(42.9)s
31-40	125	(22.9)
41-50	44	(8.1)
>50	18	(3.3)
<i>Region</i>		
Central province	121	(22.2)
Eastern province	115	(21.1)
Northern province	45	(8.2)
Southern province	120	(22.0)
Western province	145	(26.6)
<i>Education</i>		
None	22	(4.0)
Primary	20	(3.7)
Intermediate	19	(3.5)
High School	158	(28.9)
Bachelors	307	(56.2)
Master of Arts	15	(2.7)
Doctor of Philosophy (PhD)	5	(0.9)

Table 2 - Epilepsy history.

History	Women (%)	Men (%)	Total (%)
<i>Duration of illness (years)</i>			
Since childhood	100 (18.3)	76 (13.9)	176 (32.2)
For the past 15-20	47 (8.6)	57 (10.4)	104 (19.0)
For the past 10	41 (7.5)	41 (7.5)	82 (15.0)
For the past 5	101 (18.4)	83 (15.2)	184 (33.7)
<i>Number of attacks per month (last 3 months)</i>			
None	139 (25.4)	124 (22.7)	263 (48.2)
1-3	11 (2.0)	105 (19.2)	116 (21.1)
>3	39 (7.1)	28 (5.1)	67 (12.3)
<i>Committed to treatment plan</i>			
No	69 (12.6)	55 (10.0)	124 (22.6)
Yes	220 (40.2)	202 (36.9)	422 (77.3)
<i>Family history of epilepsy</i>			
No	211 (38.6)	199 (36.4)	410 (75.0)
Yes	78 (14.2)	58 (10.6)	136 (24.9)
<i>Affected family member</i>			
First degree relative	41 (30.1)	31 (22.7)	72 (52.9)
Second degree	24 (17.6)	24 (17.6)	48 (35.2)
Third degree	15 (11.0)	7 (5.1)	22 (16.1)

Table 3 - Comorbidities, risk factors, and possible etiologic disorders.

Comorbidities and risk factors	n	(%)
Smoker	84	(15.4)
Alcoholic	14	(2.6)
Drug abuser	15	(2.7)
Asthma	65	(11.9)
Thyroid disease	30	(5.5)
Hypertension	37	(6.8)
Diabetes mellitus	38	(7.0)
Cardiac disease	14	(2.6)
Stroke	7	(1.3)
Metabolic disease	3	(0.5)
Malignant disease	9	(1.6)
Human immunodeficiency virus infection or acquired immune deficiency syndrome	2	(0.4)
Autism	10	(1.8)
Neurofibromatosis	3	(0.5)
Possible etiologic disorders		
Meningitis	16	(2.9)
Brain tumor	15	(2.7)
Head trauma	71	(13.0)
Viral encephalitis	2	(0.4)
Prenatal hypoxia	24	(4.4)
Stroke	7	(1.3)
Human immunodeficiency virus infection or acquired immune deficiency syndrome	2	(0.4)

vascular and space occupying lesions and trauma. And multiple TFs described by previous studies, it is difficult sometimes for the patients to determine the exact TF for the seizure. Combination of more than one TF can exist. This study achieved our aim of identifying the common TFs for epilepsy in the KSA, which was carried out as a self-administered survey which could be a limitation compared to the usual seizure diaries and long-term monitoring. Earlier studies have focused on seizure TFs but not in the KSA. The present research fills this gap in the literature. We tried to limit the misunderstandings of some of the questions and carried a risk of subjectivity in the answers given by doing a pilot study in 10 participants. The reliability coefficient was found to be >0.6 , which confirmed that the questionnaire was suitable for use in this study.

In the present study, TF associated with oversleeping has been reported on many occasions. In a study of 71 patients, Haut et al found that seizure conditions are associated with much anxiety, oversleeping and depression.¹⁰ A survey by Sanya et al,⁸ 27 participants (30%) mentioned inadequate sleep as the TF for their first seizure. In the present study, 258 patients (52.2%) reported a history of seizure after sleep deprivation. This has an importance for more sleep hygiene for better seizure control.

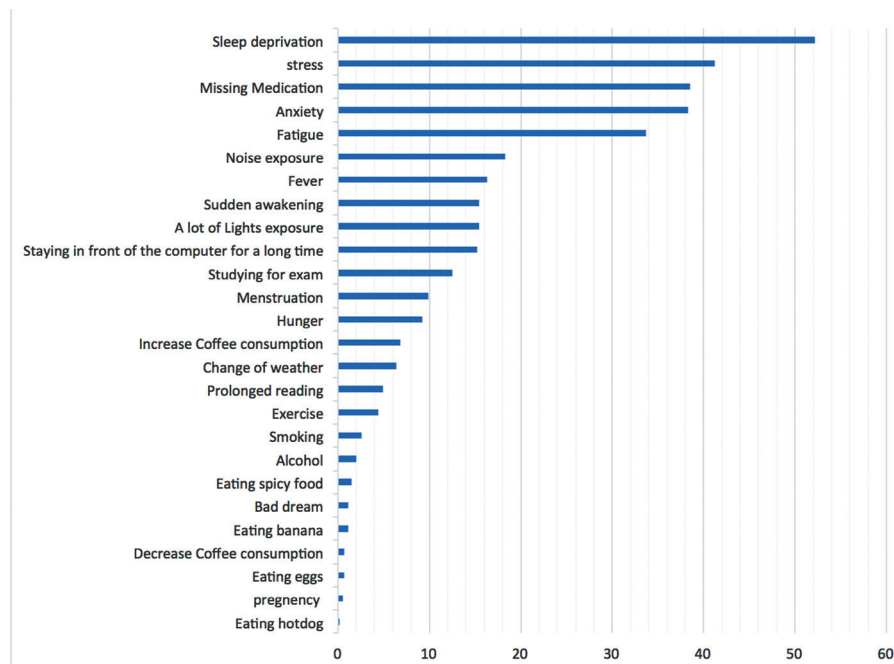
**Figure 2** - Triggering factors as percentage reported by participants.

Table 4 - Epilepsy triggers versus etiological status.

Triggering factors	Etiology		Total	P-value
	Idiopathic (no specific etiology)	Having an etiologic factor		
Stress	169 (41.8)	56 (39.4)	225 (41.2)	0.618
Anxiety	150 (37.1)	59 (41.5)	209 (38.3)	0.351
Flashing light	57 (14.1)	27 (19.0)	84 (15.4)	0.163
Noise	74 (18.3)	26 (18.3)	100 (18.3)	0.999
Sleep deprivation	212 (52.5)	73 (51.4)	285 (52.2)	0.827
Fatigue	138 (34.2)	46 (32.4)	184 (33.7)	0.702
Fever	55 (13.6)	34 (23.9)	89 (16.3)	0.004*
Exercise	16 (4.0)	8 (5.6)	24 (4.4)	0.403
Missed medication	160 (39.6)	50 (35.2)	210 (38.5)	0.355
Hunger	44 (10.9)	6 (4.2)	50 (9.2)	0.018*
Sudden awakening	65 (16.1)	19 (13.4)	84 (15.4)	0.442
Smoking	7 (1.7)	7 (4.9)	14 (2.6)	0.058
Bad dream	3 (0.7)	3 (2.1)	6 (1.1)	0.185
Change of weather	26 (6.4)	9 (6.3)	35 (6.4)	0.967
Alcohol	5 (1.2)	6 (4.2)	11 (2.0)	0.040*
Pregnancy	2 (0.5)	1 (0.7)	3 (0.5)	1.000
Menstruation	45 (11.1)	9 (6.3)	54 (9.9)	0.099
Decreased coffee consumption	3 (0.7)	1 (0.7)	4 (0.7)	1.000
Increased coffee consumption	26 (6.4)	11 (7.7)	37 (6.8)	0.593
Prolonged reading	15 (3.7)	12 (8.5)	27 (4.9)	0.025*
Studying for exam	40 (9.9)	28 (19.7)	68 (12.5)	0.002*
Prolonged computer session	54 (13.4)	29 (20.4)	83 (15.2)	0.044*
Eating spicy food	6 (1.5)	2 (1.4)	8 (1.5)	1.000
Eating banana	4 (1.0)	2 (1.4)	6 (1.1)	0.653
Eating hotdog	0 (0.0)	1 (0.7)	1 (0.2)	0.260
Eating eggs	1 (0.2)	3 (2.1)	4 (0.7)	0.056

*significant

Depression came the second-highest TF followed by stress and AED noncompliance, a combination of 2 or more TFs were founded. A similar result was seen in this study which was comparable with a study of 266 patients carried out by Privitera et al¹¹ reported that depression that is caused by seizures can be related to chronic or acute sadness and may be associated with an increase of anxiety tests. Exercise is one stress reduction mechanism that most patients with depressed condition often employ for them to come out of such situations. However, in a study of 100 patients, Neufeld et al¹² found that acute external emotions are the contributors to the

epilepsy control. However, Thapar et al¹³ concluded that anxiety predicts changes in seizure recurrence. In the present study, 225 patients (41.2%) described a history of seizure after stress. The level of psychological stress should be measured in future articles. Stress itself can lead to sleep deprivation and fatigue and make it difficult to determine which factor was the attributed to the seizure episode. In a study of 1677 patients, Nakken et al¹⁴ found that those with generalized epilepsy more commonly reported flashing lights as a TF than those with localized forms of epilepsy. However, in a study of 400 patients by Frucht et al,¹⁵ only 4% noted seizures induced by flashing lights. In our study, 84 patients

(15.4%) had a history of seizure upon exposure to flashing lights.

Balamurugan et al¹⁶ and Jallon et al¹⁷ reported that emotional stressors might initiate epileptic seizures, especially when combined with fatigue and chronic sleep deficit. In our study, 184 patients (33.7%) described a history of seizure after exhaustion. Cross¹⁸ states that following febrile seizures, other seizure types may develop promptly as a direct result. In different scenarios, an epilepsy syndrome develops with a delay after the occurrence of febrile seizures. In the present study, 89 patients (16.3%) described a history of seizure after fever. Loud sound can be one of the TFs of reflex epilepsy. Ozer et al¹⁹ found that this type of seizure is mostly seen in elderly patients known to have epilepsy. In our study, 100 patients (18.3%) described a history of seizure after noise exposure.

This study did help to increase the awareness of the patients to the possible TF of their seizure and try to avoid them and more seizure control. Prospective studies may clarify the relationship between these seizure TFs and their mechanisms to predispose seizures.

In conclusions, the present study designed to identify abnormal functioning of brain triggers prevalent in the KSA with a view to seizure prevention or a reduction in their frequency. Sleep deprivation was the most reported TF, followed by stress, then missed medication.

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References

- Nasir BB, Berha AB, Gebrewold MA, Yifru YM, Engidawork E, Woldu MA. Drug therapy problems and treatment satisfaction among ambulatory patients with epilepsy in a specialized hospital in Ethiopia. *PLoS One* 2020; 15: e0227359.
- Duan L, Lian Z, Chen J, Qiao Y, Miao J, Li M. Classification of epilepsy period based on combination feature extraction methods and spiking swarm intelligent optimization algorithm. *Concurr Comp-Pract E* 2020: e5550.
- Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE official report: a practical clinical definition of epilepsy. *Epilepsia* 2014; 55: 475-482.
- Pottoo FH, Alshayban DM, Joseph R, Al-Musa F, Al-Jabran O, Aljaafari D. Impact of adherence to antiepileptic medications on quality of life of epileptic patients in the Eastern Province of Saudi Arabia: A cross-sectional study. *Imam J Appl Sci* 2020; 5: 1.
- Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, 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: 522-530.
- Fisher RS. The new classification of seizures by the International League Against Epilepsy 2017. *Curr Neurol Neurosci Rep* 2017; 17: 48.
- Uijl SG, Uiterwaal CS, Aldenkamp AP, Carpay JA, Doelman JC, Keizer K, et al. Adjustment of treatment increases quality of life in patients with epilepsy: a randomized controlled pragmatic trial. *Eur J Neurol* 2009; 16: 1173-1177.
- Sanya EO, Mustapha K, Ademiloyi A, Bello A, Alaofin O. Self-perceived seizure precipitants among patients with epilepsy in middle-belt Nigeria. *Niger J Clin Pract* 2014; 17: 701-705.
- Benamer HTS, Grosset DG. (2009). A systematic review of the epidemiology of epilepsy in Arab countries. *Epilepsia* 2009; 50: 2301-2304.
- Haut SR, Hall CB, Masur J, Lipton RB. Seizure occurrence: precipitants and prediction. *Neurology* 2007; 69: 1905-1910.
- Privitera M, Walters M, Lee I, Polak E, Fleck A, Schwieterman D, et al. Characteristics of people with self-reported stress-precipitated seizures. *Epilepsy Behav* 2014; 41: 74-77.
- Neufeld MY, Sadeh M, Cohn DF, Korczyn AD. Stress and epilepsy: the Gulf war experience. *Seizure* 1994; 3: 135-139.
- Thapar A, Kerr M, Harold G. Stress, anxiety, depression, and epilepsy: investigating the relationship between psychological factors and seizures. *Epilepsy Behav* 2009; 14: 134-140.
- Nakken KO, Solaas MH, Kjeldsen MJ, Friis ML, Pellock JM, Corey LA. Which seizure-precipitating factors do patients with epilepsy most frequently report? *Epilepsy Behav* 2005; 6: 85-89.
- Frucht MM, Quigg M, Schwaner C, Fountain NB. Distribution of seizure precipitants among epilepsy syndromes. *Epilepsia* 2000; 41: 1534-1539.
- Balamurugan E, Aggarwal M, Lamba A, Dang N, Tripathi M. Perceived trigger factors of seizures in persons with epilepsy. *Seizure* 2013; 22: 743-747.
- Jallon P, Zifkin BG. In: Engel J, Pedley TA, Aicardi J, editors. *Epilepsy: a comprehensive textbook*. Lippincott Williams & Wilkins; 2008.
- Cross JH. Fever and fever related epilepsies. *Epilepsia* 2012; 53: 3-8.
- Ozer F, Mutlu A, Ozkayran T. Reflex epilepsy and non-ketotic hyperglycemia. *Epileptic Disord* 2003; 5: 165-168.