

## Factors triggering epileptic seizures in patients over 50 years

Serkan Demir<sup>1\*</sup>, Rifat Erdem Togrol<sup>1</sup>, Ali Riza Sonkaya<sup>2</sup>, Mustafa Tansel Kendirli<sup>1</sup>, Semih Alay<sup>3</sup>, Tugba Yanar Celik<sup>4</sup>, Sakir Delil<sup>1</sup>, Mehmet Fatih Ozdag<sup>1</sup>

### Abstract

**Objective:** In this study the factors that trigger the seizures in epileptic patients over the age of 50 were investigated and the frequencies of seizures were analysed regarding to different age, gender, type of seizure and etiological groups.

**Material and Methods:** For this purpose, 387 patients were included in the studies who were admitted to neurology outpatient clinic with the diagnosis of epilepsy. The patients are divided into groups based on those characteristics: male / female, generalized seizure / partial seizure, age between 50 and 65 / age over 65, they were evaluated in terms of seizure triggers.

**Results:** The most common precipitating factor in all groups were found as stress (37%), sleeplessness (27%) and forgetting to take the medication (20%). 31% of the patients were on Carbamazepine, 21% were on Levetiracetam and 19% were on Valproic Acid. The most common etiological causes were identified as idiopathic (39%), post stroke (24%) and dementia (15%). Regarding the triggering factor, some statistically significant differences were found between the following groups and control groups; the group with patients between the age 50 and 65: stress, fatigue, waking and sleeping; the group with female patients: sleeplessness; the group with the generalized seizures: alcohol and sleep.

**Conclusion:** In conclusion 68% of our patients complained about at least one seizure precipitant and the most common precipitants were stress, sleeplessness and missing dose of medication. In this study, age between 50 and 65 group is more affected by triggers.

**Keywords:** Epilepsy, Seizure precipitants, Stress, Sleeplessness, Missing

### Introduction

Epileptic seizure is the unavoidable overactivity of a part or the whole of the central nervous system (CNS) as a result of sudden, paroxysmal, high-voltage electrical discharges (1). If the loss of consciousness, abnormal sensory or motor activity and behavioural dysfunction that is seen during a seizure is of a repetitive nature, the term 'epilepsy' is used (2). Epilepsy is a common health problem in the whole world.

Neurological problems are seen fairly commonly in patients of the geriatric age group. Epilepsy is the most common neurological disease after cerebrovascular disease and dementia in the elderly. Since it is projected that by the year of 2050, 20% of the world's population will be the aging, it is necessary to focus more seriously on diseases of elderly (6,7).

The studies done in patients from other age groups should also be done in older patients; elderly epileptics are equally entitled to research on diagnosis and treatment of epileptic seizures (8). Many studies have been done on the factors triggering seizures and therapy in children and young adults and many endogenous (stress, fatigue, fever, menstrual cycle, sleep, etc.) and exogenous (alcohol, caffeine, eat, sleep, flickering light, temperature, humidity etc.) triggers have been defined. Yet, there aren't enough studies on these issues in the elderly (9). Information on this subject for epileptic people over 50 years is mostly based on data from personal experiences or claims. In this article, we are presenting the results of the survey study which we think is addressing these missing issues, and want to share the results to attract attention to the issue.

**Received: 31-10-2015, Accepted 22-12-2015, Available Online 15-01-2016**

1 Gulhane Military Medical Academy Haydarpasa Training Hospital Department of Neurology

2 Erzurum Mareşal Çakmak Military Hospital, Department of Neurology Erzurum, Turkey

3 Gulhane Military Medical Academy Ankara, Department of Neurology Ankara, Turkey

4 Malkara State Hospital department of Neurology, Malkara, Turkey

\*Corresponding Author: Serkan Demir E-mail: [drsrkndemir@gmail.com](mailto:drsrkndemir@gmail.com)

## Material and Methods

In this study, 387 patients over 50 years of age, who were evaluated between February 2013-June 2013 in GATA Haydarpaşa Training Hospital Neurology Department Outpatient Polyclinic, GATA Ankara Neurology Department Clinic, Cerrahpaşa Faculty of Medicine Neurology Department Epilepsy Polyclinic and Haydarpaşa Numune Training and Research Hospital Neurology Department Epilepsy Outpatient Polyclinic, who have been diagnosed as having epilepsy by a neurologist, who were over 50 years of age, and who have been followed up for more than 6 months were included. These patients were evaluated for the “factors that trigger seizures in epileptic patients over the age of 50”. Metabolic disorders, post-infectious causes, fever and other causes that may present with symptomatic seizures that last less than six months were excluded from the study. To investigate this issue, a random sample of 387 epilepsy patient volunteers selected from those being followed up in the outpatient departments were asked to complete the screening questionnaire. While developing the instrument, a pre-test consisting of open-ended questions was administered to 30 patients in order to determine the factors that determine the factors that trigger the seizures. The information obtained from these patients was used to identify the triggering factors and these factors were added to the survey. An open-ended item was also included; thus nothing was left out and all the factors could be evaluated.

### Statistical method:

Statistical analysis of the study was carried out by using the SPSS 18:00 program. Qualitative variables were summarized with frequency and percent values, numerical variables were summarized by mean  $\pm$  standard deviation values. Basic topics investigated in this study are the age group with the triggering factors, age of onset of seizures, sex, disease, type of seizure types. The relationship between all variables was investigated. To investigate this relation, chi-square test, which is the statistical test to investigate the difference between qualitative variables, was used. To investigate the relation between the treatment groups and the variables evaluated, Spearman's rho coefficient was used. Since the types of treatment and the types of disease variables were more than two level, linear association test statistic, which is a specialized version of Chi-squared test was used.

Our study was given "ethical approval" by the GATA Haydarpaşa Training Hospital Non-Invasive Clinical Research Ethics Committee with project number 2013-14 in the 13th session on February 28, 2013.

## Results

387 patients were included in the study and 52 % were men. 59% were between 50-65 years, 54% were

patients whose seizures started after the age of 50 and 52% had partial seizures. (Table 1). The 31% of the patients in the study were using carbamazepine as therapeutic, and 21% levetiresetam 19% valproic acid and %9 fenitoin for epilepsy treatment (Table 2).

**Table 1:** Sex, age group, age of seizure onset and type of seizures descriptive statistics

Groups		n	%
Sex	Male	201	52%
	Female	186	48%
Age group	> 65 years	160	41%
	50-65 years old	227	59%
Age of seizures	<age 50 years	209	54%
	>50 years	178	46%
Type of seizure	Generalized	184	48%
	Partial	203	52%

**Table 2.** Treatment type variables descriptive statistics

Drugs type	n	%
Carbamazepine	119	31
Levetirecetam	83	21
Valproic Acid	75	19
Fenitoin	35	9

Idiopathic causes were found in 39% of patients, cerebrovascular diseases in 24%, and dementia was present in 15% (Table 3).

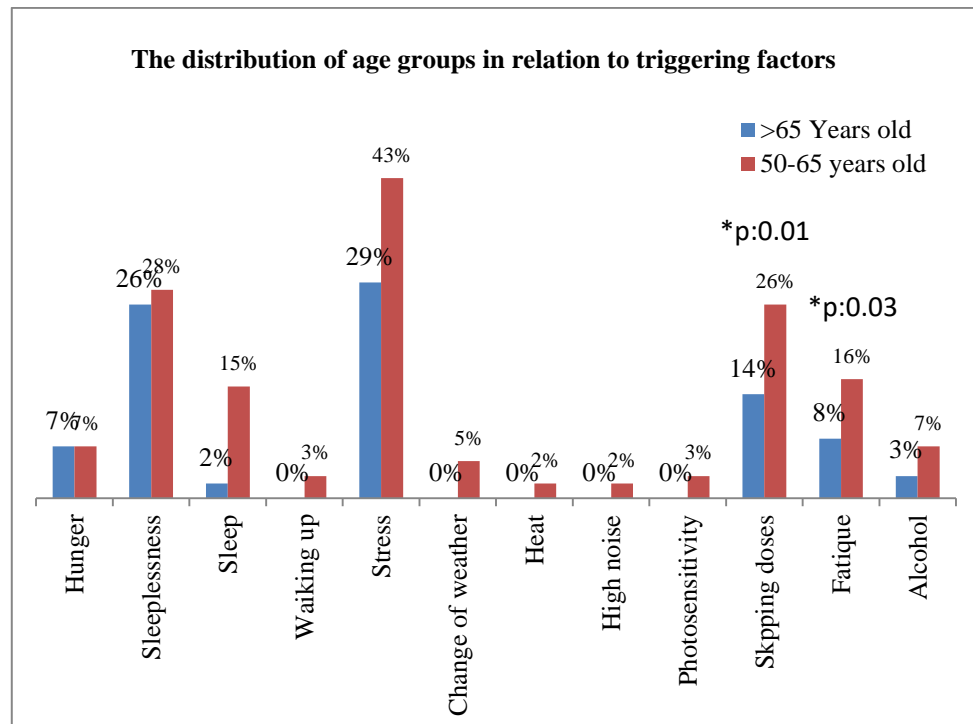
**Table 3.** Etiology variables summary statistics

Disease	n	%
Idiopathic	151	39%
Cerebrovascular disease	92	24%
Dementia	57	15%
Brain tumour	49	13%
Post-traumatic	38	10%

At this point 68% of the participants (n = 122) reported at least one triggering factor for seizures. At Table 4 all factor that are thought to trigger seizures and their frequencies are listed. 37% of the patients have reported seizures triggered by stress. Insomnia was a triggering factor in 27%, while missing doses was mentioned as a triggering factor in 20%.

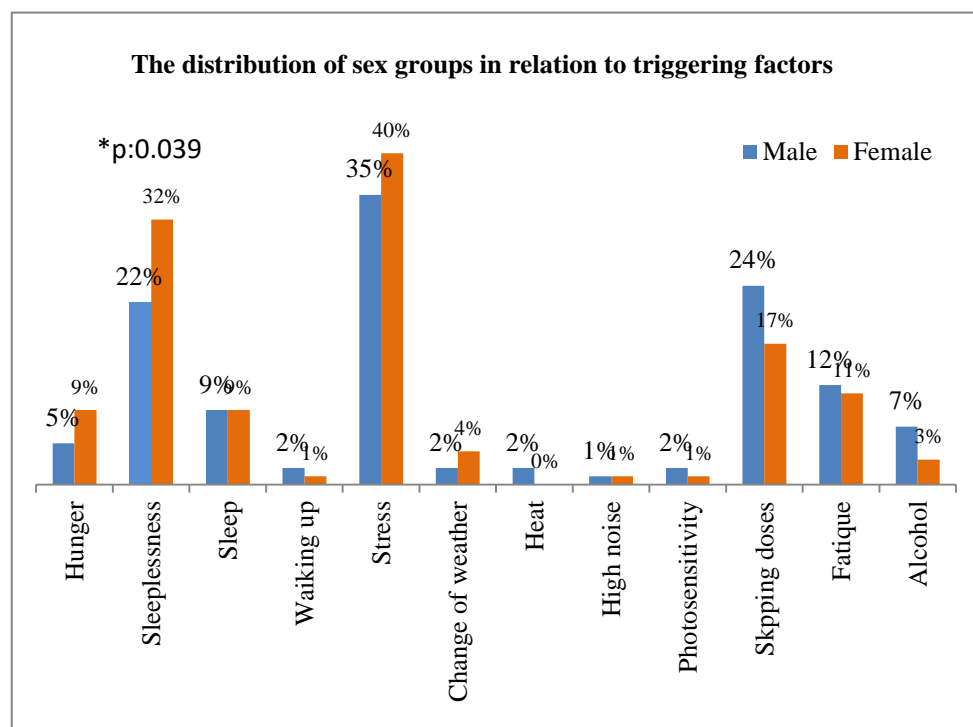
**Table 4** Seizure Triggers

Triggering factor	n	%
Hunger	27	7%
Insomnia	104	27%
Sleep	36	9%
Waking	6	2%
Stress	145	37%
Weather Changes	12	3%
Heat	4	1%
(high sound)	4	1%
Photosensitivity	6	2%
Missing doses	79	20%
Fatigue	45	12%
Alcohol	21	5%



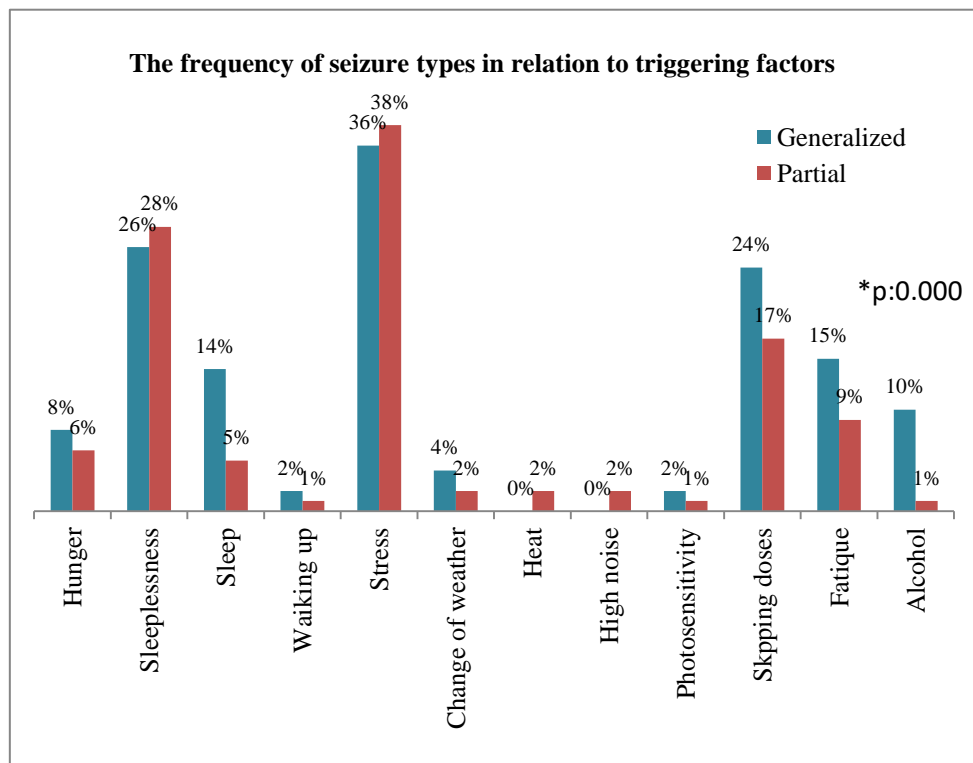
**Figure 1:** The distribution of triggering variables in relation to age

Comparing sex groups, females were found to have significantly more seizures in case of insomnia ( $p = 0.039$ ) (Figure 2).



**Figure 2:** The distribution of triggering variables in relation to sex groups

In patients with generalized seizure types, sleep ( $p = 0.006$ ) and alcohol ( $p = 0.000$ ) were found to trigger seizures at a significantly higher frequency. (Figure 3).



**Figure 3:** The frequency of seizure types in relation to triggering factors

When the two age groups were compared, patients in the 50-65 years age group had significantly more seizures during sleep ( $p = 0.000$ ), while waking up ( $p = 0.038$ ), with stress ( $p = 0.006$ ), weather changes ( $p = 0.003$ ), photosensitivity ( $p = 0.038$ ), missing doses ( $p = 0.013$ ) and fatigue ( $p = 0.033$ ). Additionally, patients in the 50-65 years age group had significantly more seizures. In general, triggering factors had a significantly higher probability to trigger seizures in the 50-65 age group. (Figure 1).

### Discussion

Epileptic seizure is the unavoidable overactivity of the whole or a part of the central nervous system (CNS) as a result of sudden, paroxysmal, high-voltage electrical discharges (1). Its incidence increases again after the age of 50 years and after 65 years the incidence of epilepsy reaches the highest incidence of all age groups. The incidence of epilepsy is at its lowest values in the 40s (30-40 / 100,000), its incidence rapidly increases in the 50s. In ages around 80s, the average value is at the 140- 160/100,000 level (6-8).

Although definitions vary according to the resources, the term “elderly” is mainly used for individuals over 65 years.

Meanwhile, after the age of 50 years, the incidence of epilepsy increases along with the increasing incidence of many systemic diseases. In our study, we described pre-senile age group as the patients between 50-65 years of age (5-8).

It is not easy to diagnose epilepsy in elderly patients. Usually a generally reliable story cannot be obtained from these patients, and these patients may have different seizures that are not observed by their relatives or that may be confused with or misinterpreted as other conditions. Epilepsy may present very different from young people in the elderly (9).

The etiology of epilepsy in our study was; idiopathic in 39%, cerebrovascular disease in 24%, dementia in 15%. Compared to the literature, our higher rate of idiopathic epilepsies may be due to undiagnosed other etiologies (e.g. meningioma, dementia, or head trauma overlooked in medical history etc.) and also be due to cryptogenic epilepsy patients been considered in this group. There are studies suggesting Alzheimer's disease as a cause of late-onset epilepsy with no identified etiology (10).

The diagnosis of epilepsy in older patients with different presentations may also be difficult because of the patient's current disease and seizures. These patients may respond to low-dose antiepileptic agent. Side effects in a wide range may occur, including sedation, tremor and cognitive disorders, depending on the patient and the AEDs used. The combination therapy should be avoided if possible, due to combination therapies may increase side effects (11). Since elderly patients often use other drugs (antihypertensive, antidiabetic, antidementia, etc.), agents with lower drug interactions, drugs that do not bind to proteins and do enzyme induction should be preferred. Cognitive and psychological effects should be positive. In this age group, the seizures can be controlled with proper treatment at correct doses in 70% of the patients (11,12).

The most common agents used were carbamazepine (31%), levetiracetam (21%) and valproic acid (19%). The relatively high frequency of partial seizures may have been a reason for the neurologists' choice of carbamazepine. The possibility to follow blood drug levels of carbamazepine and valproate, and the long experience related to these agents may be other reasons for their selection of these agents. However, unlike the literature, the second most preferred drug is levetiracetam. The reason for the selection of this drug may be the low drug interactions, its side effect profile being lower than other AEDs, and easy dose titration, with going up to high doses in a relatively short time (13).

68% of the participants in our study reported at least one seizure triggering factor. Results of different studies has revealed a seizure triggering factor (at least one) at a ratio between 53-86.6%. (14-18).

Stress is an automatic response when a condition or force that exceeds the person's ability to deal with is detected. Fear, anxiety and concern are moods that are the reflections of stress in everyday life (19-21). Epilepsy is one of the common areas of study for different disciplines such as neurology, psychiatry, neurosurgery and pediatrics. Specifically, many studies have been done on the neuropsychological aspects of epilepsy in the last century (22-27). Meanwhile, individuals are exposed to stress factor more at old age than young individuals due to affective problems due to physical challenges, loss of self-confidence, feeling helpless, loneliness, hopelessness, inability to fulfill one's responsibilities, and social challenges such as those due to retirement, loss of productivity and economic difficulties. Jalava et al. have demonstrated in their 35- year follow study that patients with epilepsy have a 4-fold increased risk of developing psychiatric disease and are sensitive to stress than normal individuals (28). On the other hand, the relationship between stress and seizures is usually accepted by clinical experience and Nancy et al. have demonstrated in the work they have done that stress is

a factor that triggers seizures (29). In their study on the quality of life of epilepsy patients, Baker et al. have shown that stressful experiences tend to increase seizure frequency. Again it was concluded in this study that the mental and physical fatigue caused by stress results in an increase in seizure frequency (30). Other studies demonstrating that seizures may be triggered by stress are also present (15,17,31-35). Although quite a number of hypotheses have been put forward on how stress triggers seizures, the exact mechanism has not yet been clearly explained (36).

There is an interaction between sleep and epilepsy. The effect of sleep on epilepsy and the effects of epilepsy on sleep, has been intriguing scientists for many years, and despite a number of studies conducted on the subject, it is still not yet fully clear (37,38). In particular, the occurrence of SUDEP usually happening during sleep has increased the interest on the relation of sleep and epilepsy. Especially childhood epileptic syndromes are known to have close relationship with sleep.

In our study, the second most triggering factor was found to be insomnia with 27%. In patients between 50-65 years of age and in women insomnia was found to trigger seizures significantly. At the same time, stress is also a cause of insomnia in women and in the elderly. Stress and insomnia are closely related to each other as triggering factors. Insomnia also may create stress (39). In studies comparing the two sexes, insomnia problem was more prevalent in women than men, similar to our study. Women may not spend enough time to sleep like men, due to their tempo of business life and their responsibility associated with family business and housework. According to the data from the US National Sleep Foundation, women aged 30-60 years allocate only 6 hours 41 minutes to sleep. To be a woman and to have insomnia are associated with each other (40).

Although skipping doses of medication is not counted among endogenous or exogenous triggers, it is one of most common causes of status epilepticus. Antiepileptic drugs are effective with a particular concentration in the blood and instant withdrawal or decrease in concentration is thought to trigger seizures. Usually studies that investigate seizure triggers do not evaluate skipping doses; we wanted to address this issue with the result of our study. In this study, skipping doses was found to be the third most common triggering factor with 20%.

In conclusion, there is at least one trigger for seizures in 68% of our patients. The most common seizure triggers were found to be stress with 37%, insomnia with 27% and skipping doses with 20%. Etiological causes were, idiopathic 15%, Cerebrovascular disease 24%, dementia 39%, brain tumor 13% and posttraumatic 10% respectively. Most commonly used three agents were identified as; carbamazepine 31%,



valproic acid 19% and levetiracetam 21%. When our study groups were evaluated, the effect of seizure triggering factors are statistically significant in the group whose seizures started before the age of 50 and the group with seizures starting 50-65 years of age.

**Conflict of Interest:** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. The first case was presented as poster presentation at the American Academy of Neurology 67th Annual Meeting , 18-25 April 2015, Washington DC, USA.

## References

- Shovon S.D. Epidemiology, classification, natural history and genetics of epilepsy. *Lancet* 1990;336: 93- 96
- Banerjee PN, Filippi D, Hauser WA. The descriptive epidemiology of epilepsy. *Epilepsy Research* 2009; 85:31-45
- Hauser WA. Seizure disorders: the chances with age. *Epilepsia* 1992;33(suppl4):6-7
- Spector S, Cull C, Goldstein LH. Seizure precipitants and perceived self-control of seizures in adults with poorly-controlled epilepsy. *Epilepsy Research* 2000; 38; 207- 216
- Courte DL, Breteler MM, Meinardi H, Hauser A, Hoffman A. Prevalence of epilepsy in the elderly: the Rotterdam study. *Epilepsia* 1996;37:141-147
- Stephen L, Brodie M. Epilepsy in elderly people. *The Lancet* 2000;355:1441-1446
- DeToledo JC. Changing presentation of seizure with aging: Clinical and etiological factors. *Gerontology* 1999;45:329-335
- Cloyd J, Hauser W, Towne A, Ramsay R, Mattson R, Glim F, Walczak T. Epidemiological and medical aspects of epilepsy in the elderly. *Epilepsy Research* 2006;68:39-48
- Tascilar NF, Bozdemir H, Aslan K, Sarica Y, Seydaolu G. Yaşlı epilepsi hastalarında elektroensefalografinin yeri. *Epilepsi* 2006;12(1):32-41
- Mendez MF, Catanzaro P, Doss RC. Seizures in Alzheimer's disease: Clinicopathologic study. *J Geriatr Psychiatry Neurol* 1994;7:230-233
- Wilmore LJ. Management of epilepsy in the elderly. *Epilepsia* 1996;37(6):23-33
- Stephen L, Brodie M. Epilepsy in elderly people. *The Lancet* 2000;355:1441-1446
- Berkovic SF. Treatment with anti- epileptic drugs. *Aust Fam Physician*. 2005; 34: 1017-1020.
- Dorothee GA. Provoked and reflex seizures: Surprising and common? *Epilepsia* 2012; 53(4):105-112
- Pinikahana J, Dono J. Age and gender differences in initial symptoms and precipitant factors of epileptic seizures: An Australian study. *Epilepsy and Behaviour* 2009; 16: 231-239
- Lunardi MDS, Sukys-Claudino L, Guarnieri R, Walz R, Lin K. Seizure precipitants and inhibiting factors in mesial temporal lobe epilepsy. *Journal of the neurological sciences* 2011;308:21-24
- Spector S, Cull C, Goldstein L. Seizure precipitants and perceived self-control of seizures in adults with poorly-controlled epilepsy. *Epilepsy Research* 2000;38:207-216
- Fang PC, Chen YC, Lee IC. Seizure precipitants in children with intractable epilepsy. *Brain & Development* 2008; 30 527-532
- Oto R, Apak İ, Arslan S, Yavavlı A, Altındağ A, Karaca EE. Epilepsinin psikososyal etkileri. *Klinik Psikiyatri Dergisi* 2004; 7:210-214
- Baker GA, Jacoby A, Buck D. Quality of life people with epilepsy. *Epilepsia* 1997; 38: 353-362
- Nancy RT, Gay D. Stress as a risk factor for seizure among adults with epilepsy. *Epilepsia* 2008; 43: 456-468
- Chadwick D. Epilepsy. *J Neurol Neurosurg Psychiatry*. 1994;57(3):264-77
- Swinkels WA, Kuyk J, van Dyck R, Spinhoven P. Psychiatric comorbidity in epilepsy. *Epilepsy Behav*. 2005;7:37-50.
- Sachdev P. Schizophrenia-like psychosis and epilepsy: the status of the association. *Am J Psychiatry*. 1998;155:325-336.
- Kristensen O, Sindrup EH. Psychomotor epilepsy and psychosis. I. Physical aspects. *Acta Neurol Scand*. 1978;57:361-369
- Slater E, Beard AW, Gliethero E. The schizophrenialike psychoses of epilepsy. *Br J Psychiatry*. 1963;109:95-150
- Suurmeijer TP, Reuvekamp MF, Aldenkamp BP. Social functioning, psychological functioning, and quality of life in epilepsy. *Epilepsia* 2001;42(9):1160-1168
- Jalava M, Sillanpaa M. Concurrent illness in adult with childhood-onset epilepsy: a population-based 35 year follow up study. *Epilepsia* 1996;1155-1163
- Nancy RT, Gay D. Stress as a risk factor for seizure among adults with epilepsy. *Epilepsia* 2008; 43: 456-468 Silber MH. Sleep Disorders. *Neurol Clin* 2001;1,173-186
- Baker GA, Jacoby A, Buck D. Quality of life people with epilepsy. *Epilepsia* 1997; 38: 353-362
- Nakken KO, Solaas MH, Kjeldsen MJ. Which seizures precipitating factors do patients with epilepsy most frequently report? *Epilepsy Behav* 2005;6:185-189
- Frucht MM, Quigg M, Schwazer C. Distribution of seizure precipitants among epilepsy syndromes. *Epilepsia* 2000;41:1534-1539
- Sperling MR, Schilling CA, Glosser D, Tracy JI. Self-perception of seizure precipitants and their relation with anxiety level, depression, and health locus of control in epilepsy. *Seizure* 2008;17:302-307

34. Hart YM, Shorvon SD. The Nature Of Epilepsy In Teh General Population: I: characteristics of of patients receiving medication for epilpsy. *Epilepsy Res* 1995; 21:43-49
35. Cull CA, Fowler M, Brown SW. Perceived self control of seizures in young people with epilpsy. *Seizure* 1996;5:131-138
36. Friedman RA, Cacheaux LP, Ivens S, Kaufer D. Elucidating the complex interactions between stres and epileptogenic pathways. *Cardiovasc Psychiatry Neurol.* 2011; 10; 1-8
37. Salgado PC, Souza EA. Quality of life in epilepsy and perception of seizure control. *Arg Neuropsiquiatr* 2001; 59: 537-40.
38. Birbeck GL, Ron D, Hays RD et al. Seizure reduction and quality of life improvements in people with epilepsy. *Epilepsia* 2002; 43:535-8.
39. Silber MH. Sleep Disorders. *Neurol Clin* 2001;1,173-186
40. [www.sleepfoundation.org](http://www.sleepfoundation.org) Women and Sleep