

## Memory Disturbances among Adult Sudanese Patients with Epileptic in Neurologic and Psychiatric Outpatient Clinics in Khartoum State

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### Abstract

**Objectives:** This study aims to identify the factor(s) associated with memory disturbances among adult Sudanese epileptic patients.

**Methodology:** A cross-sectional study was done in different neurologic and psychiatric outpatient clinics in Khartoum State. Out of 63 patients with epileptic, 47 patients completed the interview successfully. Patients in the post-ictal phase and with memory disturbances from different etiologies were excluded. Patients were interviewed by a psychiatry registrar and trained doctors using the memory component of the mental state examination to objectively assess memory disturbances. The subjective component of memory was assessed by a validated questionnaire (The Questionnaire of Memory Efficacy). Anxiety and depression were assessed by the validated Hospital Anxiety and Depression Scale (HADS).

**Results:** Short and long term memory disturbances were objectively detected in 68.1% and 31.9% of patients respectively. There was no significant association in the mean long term memory score among patients with idiopathic generalized epilepsy and temporal lobe epilepsy ( $P = 0.72$ ). However, there was a significant difference in the mean short term memory score among patients with temporal lobe epilepsy compared to idiopathic generalized epilepsy ( $p = 0.02$ ). There was no significant association between the mean memory score and the duration of epilepsy, use of Sodium Valproate, Carbamazepine and polytherapy ( $P = 0.34, 0.07, 0.43, 0.93$ ) respectively. There was a correlation between memory disturbances and both anxiety and depression ( $R = 0.72, R^2 = 0.51, P = 0.00$ ) and ( $R = 0.35, R^2 = 0.12, P = 0.025$ ).

**Conclusion:** Epilepsy causes significant memory disturbances that may be attributable to the disease itself, or associated anxiety and depression.

**Keywords:** Memory Disturbances; Epilepsy; Anxiety and Depression

### Introduction

The term “epilepsy” refers to a group of neurological disorders whose central feature is recurrent unprovoked seizures. Nevertheless, the effects of epilepsy may extend to impaired social functioning, learning difficulties, and memory deficits.

Cognitive dysfunction is often more debilitating than the seizures themselves. The nature of these deficits varies depending upon which areas of the brain are impacted by the disorder [1].

Memory complaints are the most commonly reported cognitive problems in patients with epilepsy. The prevalence of memory problems in patients with refractory epilepsy has been estimated as high as 20 - 50%, and more than half of the patients who are referred for neuropsychological assessment reported memory difficulties in daily life [1]. In another study, 54% of over 700 people with epilepsy regarded memory problems as moderate to severe [2].

Many interacting factors may affect memory function in patients with epilepsy including the underlying neuropathology, seizure activity, localization, frequency, interictal epileptiform discharges, anticonvulsant medications, surgery, age, genetic background and comorbid psychiatric diagnoses such as depression and anxiety [2].

An analysis revealed that impairments in memory encoding and memory retrieval are a common feature in all epileptic disorders. In idiopathic generalized epilepsy (IGE) and frontal lobe epilepsy (FLE), a more prefrontal profile characterizes the memory impairments which resemble those seen in non-epileptic disorders. Retention, in contrast, seems to be almost exclusively affected in mesial temporal epilepsy (MTLE) as it depends on the functional integrity of the hippocampal formation and anterior diencephalic structures [3].

There is good evidence that antiepileptic drugs (AEDs) can hurt cognition, although the field is fraught with methodological difficulties. The most commonly observed effects are slowed mental processing and reduced attention, and these are most marked with high doses and polytherapy. However, a specific impact on memory has been reported in several studies. Some newer drugs may have a better cognitive profile, although topiramate may be a significant exception [2]. A study was done by Vinten., *et al.* 2005 showed that Carbamazepine may further affect mesial temporal lobe memory function [4].

### Aim of the Study

The goal of this study is to identify the factor associated with memory disturbances among adult Sudanese epileptic patients and to determine the association between memory disturbances and type of seizure:

- To determine the association between memory disturbances and duration of epilepsy
- To determine the association between the memory disturbances and type of and number of antiepileptic drugs
- To determine the association between memory disturbances and anxiety and depression

### Materials and Methods

**Study design:** Cross-sectional facility-based study.

#### Study area

The study was conducted in neurological referral clinics of the following hospitals in Khartoum state:

- Soba University Hospital: The first teaching hospital in Sudan, which is affiliated with the University of Khartoum. It is a tertiary hospital providing therapeutic and diagnostic services to patients from all over the country
- Daoud Charity Clinic: A neurological referral clinic, receiving patients on Friday nights from different parts of the State.

#### Study population

##### Inclusion criteria

Sudanese epileptic patients of both genders aged 18-70 years who have been seizure-free for the past 24h (or reported that they had returned to baseline functioning at the time of the interview, after experiencing a seizure within 24h).

### Exclusion criteria

Age below 18 or more than 70, patients known to have memory problems before epilepsy; blindness, hearing, speech impairment, or other physical disability precluding participation; the current intake of medications known to affect the central nervous system (other than AEDs), including anxiolytics, sedative, hypnotics, anti-depressants, anti-psychotics, narcotics, and tranquilizers); patients who had undergone any type of surgery for epilepsy.

### Sample size

Out of 63, 47 patients completed the interview successfully and this was less than the number calculated by the equation because the clinics were very crowded and were not specialized for Epilepsy only. We have to assess the diagnosis first. Many patients refused to give consent and 16 questionnaires were excluded because patients did not complete the interview.

$N = z^2 pq/t$  (multiplied by non-respondents)

Whereas:

$Z = Z$  value (e.g. 1.96 for 95% confidence level)

$p$  = prevalence of the disease in Sub-Saharan Africa based on a study by the WHO = 2.2/1000 to 58/1000 (as mentioned in "Epilepsy in the WHO African region, the global campaign against epilepsy "out of the shadows prevalence; page 5-6)

$q = 1 - \text{prevalence}$

$t$  = is a constant, it equals 0.05

$N = 80$ , chosen by systematic random sampling over 5 randomly chosen outpatient visits.

### Memory assessment

Patients were interviewed by a psychiatrist and trained doctors using the following:

- Structured questionnaire with the following variables: Age, gender, duration of epilepsy, type of epilepsy, frequency of seizures per month, type and number of antiepileptic drugs.
- The memory component of the mental state examination to objectively assess memory disturbances.
- The subjective component of memory was assessed by a validated questionnaire, The Questionnaire of Memory Efficacy, developed by Giovagnoli and colleagues and is made up of 28 questions [5]. It was developed to assess memory disturbances in different aspects of every day's life. It is made up of the following components: concentration and orientation (items 1 - 2), pre-illness knowledge (items 3 - 6), learning (items 7 - 12), episodic memory (items 13 - 17), prospective memory (items 18 - 19), reactions to memory difficulties and the use of memory aids (items 20 - 26) and awareness of memory problems (items 27 - 28).

The frequency of occurrence of each memory problem will be assessed on a five-point scale: never (5 points), seldom (4 points), sometimes (3 points), often (2 points) or always (1 point). The possible score ranged from 28 to 140 points, higher scores reflecting a subjective impression of better memory.

- Anxiety and depression were assessed by the validated Hospital Anxiety and Depression Scale (HADS). HADS is commonly used by doctors to determine the levels of anxiety and depression that a patient is experiencing. The HADS is a fourteen item scale that generates ordinal data. Seven of the items relate to anxiety and seven relate to depression.

### Analysis plan

SPSS version 20 was used for data entry and analysis, with chi-square significant value less than or equal 0.05

**Ethical concern**

Detailed explanation of the nature of the study and its objective was done by the interviewer before obtaining written consent to all participants. The study was approved by the scientific committee of Professor Daoud’s research group.

**Results**

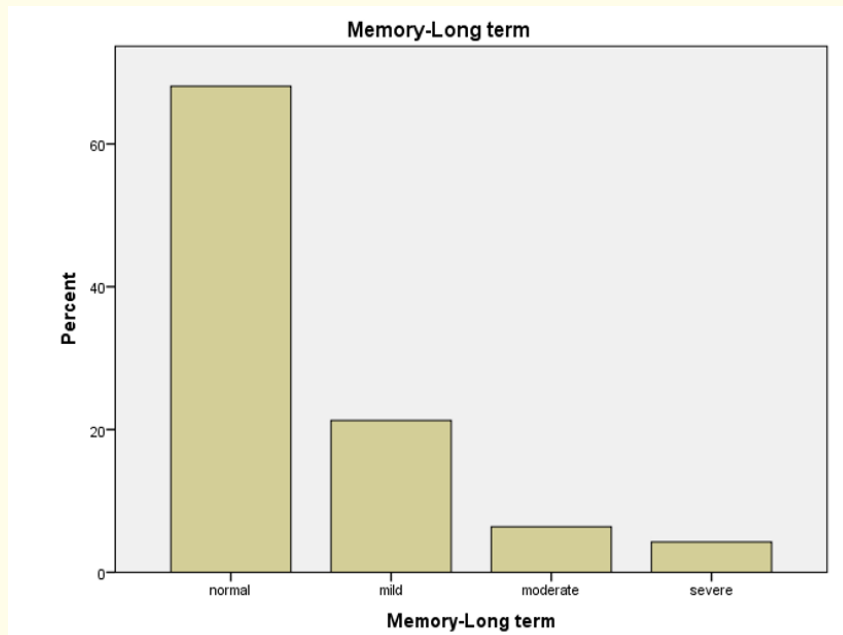
Of the 47 interviewed patients, 60% were males. 57% of the population was under 30 years. 88.6% had idiopathic generalized epilepsy.

Short and long term memory disturbances were objectively detected in 68.1% and 31.9% of patients respectively. In figure 1 and 2, normally refers to a full score memory component of the mini-mental state examination. Mild, moderate and severe refer to scores of 3, 2 and 1 or less respectively.

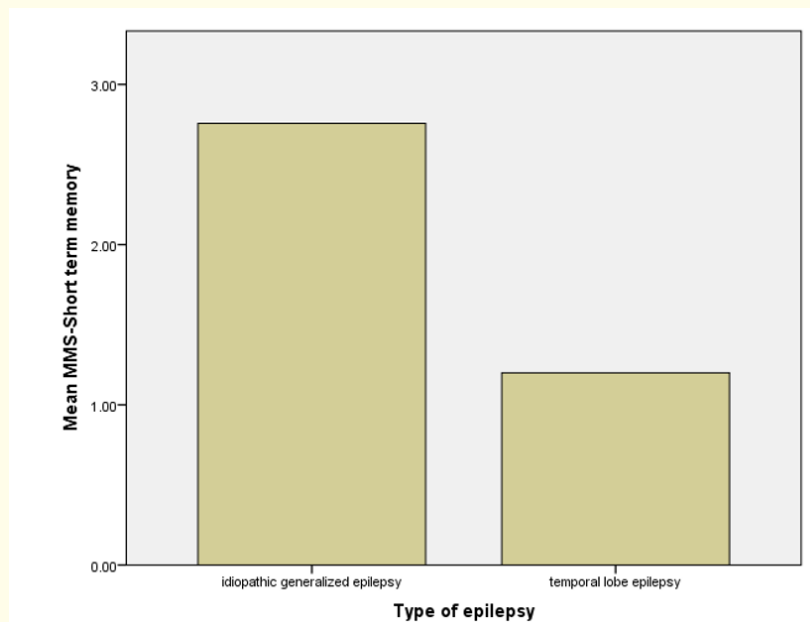
The Mann-Whitney test was used to determine the association between the mean memory score in both long and short term memory and the type of epilepsy. There was no significant association between the mean long term memory score among patients with idiopathic generalized epilepsy and temporal lobe epilepsy ( $P = 0.72$ ). However, there was a significant difference in the mean short term memory score among patients with temporal lobe epilepsy compared to idiopathic generalized epilepsy ( $p = 0.02$ ).



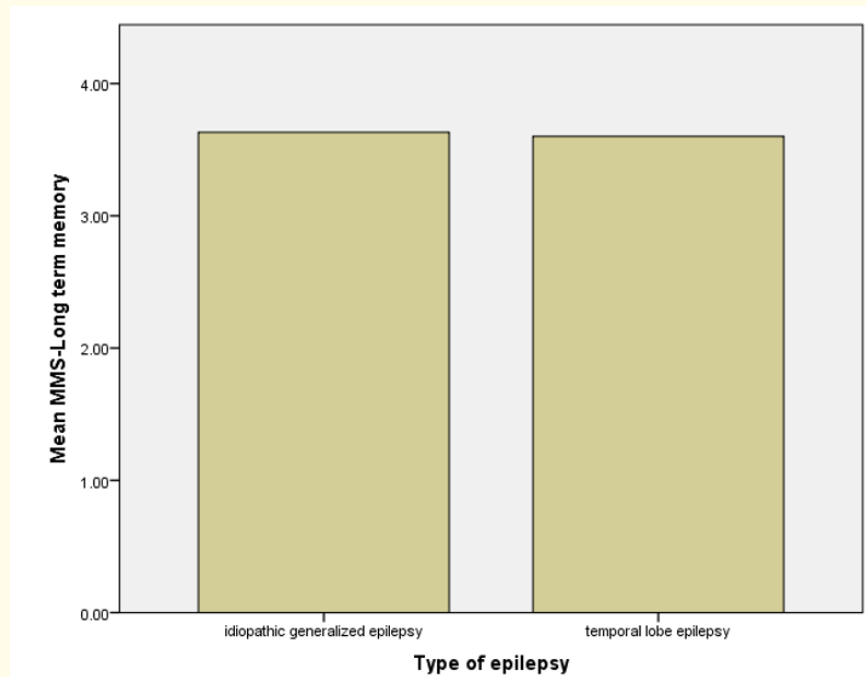
**Figure 1:** The percentage of patients with short term memory disturbances and this was further sub-classified as mild, moderate and severe.



**Figure 2:** The percentage of patients with long term memory disturbances and this was further sub-classified as mild, moderate and severe.



**Figure 3:** The relation between short term memory score and the type of epilepsy: idiopathic generalized epilepsy and temporal lobe epilepsy.



**Figure 4:** The relation between long term memory score and the type of epilepsy: idiopathic generalized epilepsy and temporal lobe epilepsy.

There Kruskal-Wallis test showed no significant association between the mean memory score and the duration of epilepsy ( $P = 0.34$ ). Also, the Mann-Whitney showed no significant association between the mean memory score and the use of Sodium Valproate, Carbamazepine, and polytherapy ( $P = 0.07, 0.43, 0.93$ ) respectively.

Regression analysis revealed a positive correlation between memory disturbances and both anxiety and depression ( $R = 0.72, R^2 = 0.51, P = 0.00$ ) and ( $R = 0.35, R^2 = 0.12, P = 0.025$ ) respectively.

## Discussion

In this study, long and short term memory function was assessed among adult Sudanese Patients with epilepsy attending different neurological and psychiatric clinics in Khartoum state using the memory component of the mental state examination. This is considered to be a simple and clinically relevant assessment as opposed to more sophisticated tests, which are not available in the country. The memory function was related to many epilepsy-related variables including the duration, type of epilepsy, number of antiepileptic drugs and other common comorbidities among epileptics such as depression and anxiety.

The study showed that most epileptics suffered short term memory loss in comparison with long term memory loss, 68.1%, and 31.9% respectively. A study by Helmsteadter, *et al.* [4] showed that short term memory is particularly affected by lateral temporal lobe lesions, while long term memory is affected by mesial temporal lobe lesions. Unfortunately, imaging was not included in our study because it was not readily available for all patients.

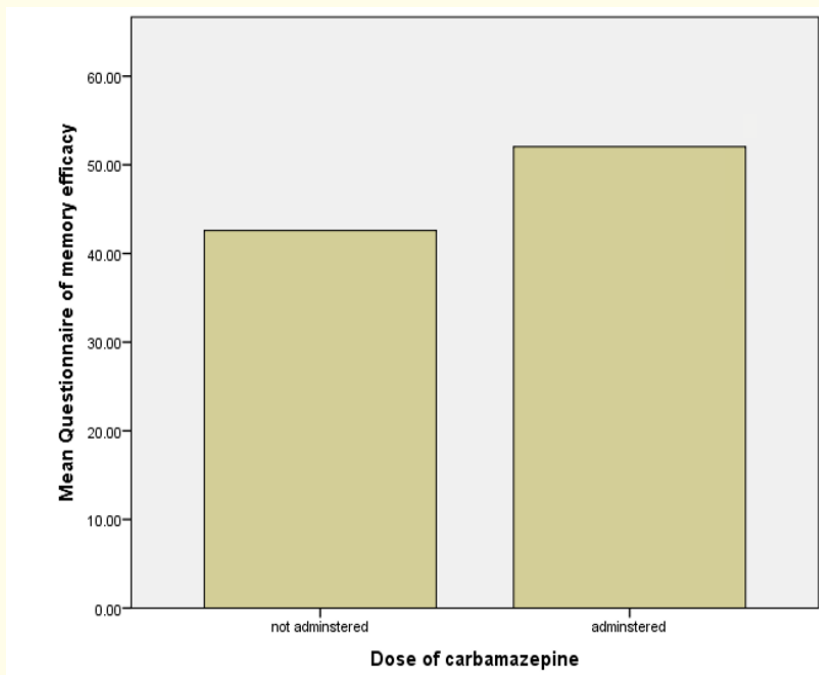


Figure 5: Mean memory score to whether carbamazepine was administered or not.

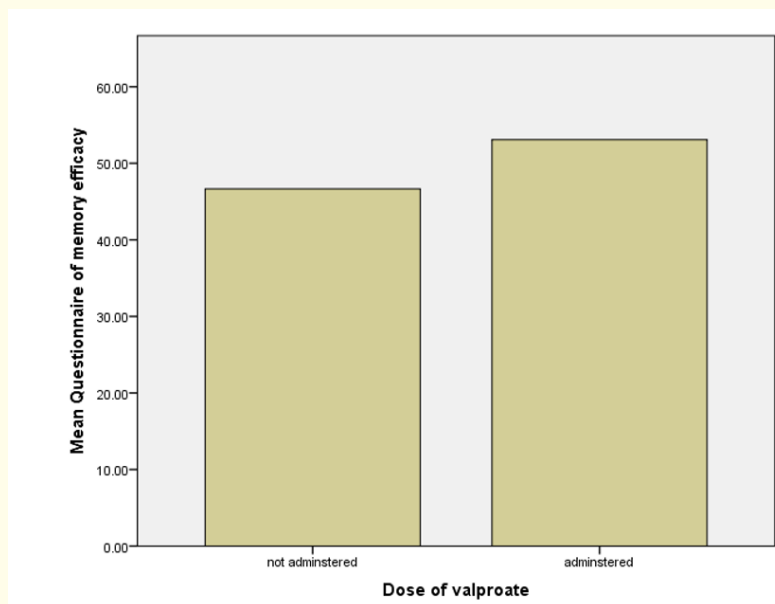
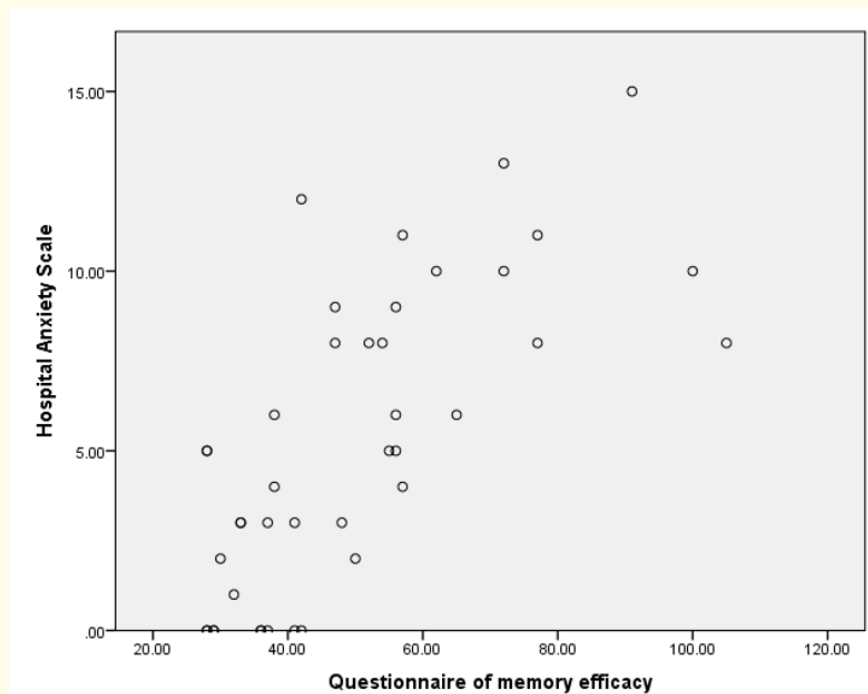


Figure 6: Mean memory score to whether sodium valproate was administered or not.



**Figure 7:** Scatter graph which shows the relation between memory score and anxiety score as measured by the HADS scale.

The study revealed no association between long term memory and the type of epilepsy, whether idiopathic generalized or temporal lobe epilepsy ( $P = 0.72$ ). This was supported by a study done by Upton., *et al.* [2] and La., *et al.* [2]. On the other hand, it revealed a significant association between short term memory in temporal lobe epilepsy compared to idiopathic generalized epilepsy ( $P = 0.02$ ). This was consistent with a study done by M Centeno., *et al.* and CR Butler., *et al.* [1,2]. This can be explained by the direct involvement of memory-related structures including the hippocampus by seizure activity. Consolidation, retention and delayed recall are greatly affected in patients with temporal lobe epilepsy.

The study did not show any association between the mean memory score and the duration of epilepsy ( $P = 0.34$ ). A study by AR Giovaloni., *et al.* found no correlation between the duration of epilepsy and memory disturbances [5]. However, Thompson and Corcoran found greater subjective memory difficulties in patients with later seizure onset. Previous studies using laboratory tests reported that early-onset, long disease duration and high seizure frequency are associated with greater memory impairment but Thompson claimed that the effect of clinical factors was not always consistent [5].

There was no significant association between the mean memory score and the use of carbamazepine and sodium valproate alone or in combination ( $P = 0.07, 0.43, 0.93$ ) respectively. A study was done by Vinten., *et al.* showed that Carbamazepine may further affect mesial temporal lobe memory function [4]. Two studies found a positive correlation between remote semantic memory loss and the number of anticonvulsants taken Lah., *et al.* interpretation of this result is confounded by the close relation between medication dose and the severity of epilepsy [2].

The study revealed a correlation between the mean memory score and both anxiety and depression ( $R = 0.72, R^2 = 0.51, P = 0.00$ ) and ( $R = 0.35, R^2 = 0.12, P = 0.025$ ) respectively. This was consistent with a study done by Hennrik Jokeit., *et al.* and Anne Elixhauser., *et al.*



[3,4]. Both depression and anxiety are more common in epileptic patients compared to controls. Both of these disorders affect different cognitive domains such as attention and concentration which in turn affect memory function.

### **Recommendations**

- Patients with Epilepsy should be asked whether they are facing any memory disturbances affecting their daily activities.
- Memory function should be frequently assessed in Patients with Epilepsy using simple clinical methods.
- Depression and anxiety should be routinely assessed as they are common in Patients with Epilepsy and can hurt their memory.

### **Conclusion**

Epilepsy causes significant memory disturbances that may be attributable to the disease itself, or associated anxiety and depression.

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