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COGNITIVE ASSESSMENT IN A SAMPLE OF EGYPTIAN PATIENTS WITH GENERALIZED ONSET EPILEPSY

By

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ABSTRACT

Background: Cognitive brain functions constitute the ability to work with information in a meaningful way, apply gained information, perform preferential changes, and someone ability to change opinions about that information. Individuals with epilepsy have a higher prevalence of impaired cognitive performance compared to healthy individuals who are matched for age and education. Numerous factors can have a deleterious impact on cognition in patients, including age at onset of epilepsy, seizure frequency, duration of seizures, structural cerebral damage as a consequence of repetitive or prolonged seizures and medications used for treating seizures.

Objective: Assessing the cognitive functions in patients with generalized onset epilepsy.

Patients and Methods: Our study was conducted, in the neurology department of Sohag general hospital upon 75 individuals divided into 3 equal groups presented with epilepsy selected from the inpatient and outpatient clinics. Patients were divided into three groups: I. Group A: patients diagnosed with generalized onset epilepsy with medication (anti-epileptic drugs). II. Group B: patients diagnosed with generalized onset epilepsy without medication (anti-epileptic drugs). III. Group C: healthy subjects will be included in the study as the control group.

All of the participants were be subjected to the following:

*Full history (demographic data and personal history, detailed history of general health condition and chronic or current diseases) and general and neurological examination

*Special tests including: PEBL Wisconsin (Berg) Card Sort test, PEBL The Conners' continuous performance test, Montreal cognitive assessment (MoCa)

*Brain imaging: MRI brain (to exclude organic cause).

*EEG.

Results: The mean Correct Responses Wisconison card sorting test of study groups was around 76.7±5.65 in group 1, around 78±2.88 in group 2 and 81.8±2.38 in group 3; with significant difference between group 1 and group 3 and significant difference between group 2 and group 3. The mean Target Acc Rate continuous performance test was around 0.956±0.03 in group 1, around 0.970±0.015 in group 2 and 0.974±0.015 in group 3; with significant difference between group 1 and group 2 and significant difference between group 1 and group 3. The mean MoCa of study groups was around 24.1 in epileptic with medication group, 23.96 in epileptic without medication group and 25 in control group with no significant difference between all groups. With high significant difference between Group 1 versus Group 3, and Group 2 versus Group 3. The normal MoCa was around 3 in epileptic with medication group, 2 in epileptic without medication group and 22 in control group with high significant difference between all groups.

Conclusion: All patients with epilepsy reported significant impairment in all cognitive measures such as working memory, inhibitory control, goal maintenance, and mental flexibility. We observed attentional deficits in processes such as alertness and attention span and those requiring sustained and divided attention compared with controls. Attentional and executive impairment was correlated with higher frequency of seizures.

Keywords: Cognitive brain functions, cognition assessment and generalized onset epilepsy.

INTRODUCTION

In 2014, the International League against Epilepsy revised a new definition. Epilepsy is a brain disease defined by either at least two unprovoked seizures occurring more than 24 hours apart or only one unprovoked seizure and with probability of further seizures similar to the general recurrence risk (at least 60%) following two unprovoked seizures, occurring over the next ten years (*Fisher et al.*, 2017).

Almost 50 million people live with epilepsy worldwide. The estimated proportion of the general population with active epilepsy (i.e. continuing seizures or with need for treatment) at a given time is between 4 and 10 per 1000 people. However, several studies in low and middle income nations suggest that the proportion is higher, between 7 and 14 per 1000 people (*Megiddo et al.*, 2016).

Cognitive functions of the brain constitute the ability to work with information in a meaningful way, apply gained information, perform preferential changes, and someone's ability to change opinions about that information. Within psychology, the cognitive brain function idea has been associated with very abstract ideas such as learning, mind, and intelligence. Of course, these ideas are extremely broad, but so are the cognitive brain functions. They are formulated out of memories, and how they relate to

current intake of information (Morita et al., 2016).

Individuals with epilepsy have a higher impaired cognitive prevalence of compared healthy performance to individuals who are matched for age and education. However, most individuals with epilepsy have IQs that are in normal range. Numerous factors can have a deleterious impact on cognition patients, including age at onset of epilepsy, seizure frequency, seizures duration, structural cerebral damage as a consequence of repetitive or prolonged seizures and medications used for treating seizures (Realmuto et al., 2015).

The present work aimed to assess cognitive functions in patients with generalized onset epilepsy.

PATIENTS AND METHODS

Ethical considerations:

- The study protocol was approved by the ethics committee of the faculty of medicine Al-Azhar University.
- An informed written consent was taken from all of the participants in the study.

Patients:

Our study was conducted, in the Neurology Department of Sohag General hospital upon 75 individuals divided into 3 equal groups presented with epilepsy selected from the inpatient and outpatient clinics. Patients were divided into three groups:

- **I. Group A:** patients diagnosed with generalized onset epilepsy with medication (anti-epileptic drugs).
- **II. Group B:** patients diagnosed with generalized onset epilepsy not receiving medication (anti-epileptic drugs).
- **III. Group C:** healthy subjects will be included in the study as the control group.

Inclusion criteria:

- Patients were diagnosed according to Classification and Terminology of the International League against Epilepsy (Fisher et al., 2017).
- Control group: healthy individuals who will be selected from volunteers, with no evidence with psychiatric or medical disorder controls matched with respect to age, sex, educational level, socioeconomic status (Sadr et al., 2018).

Exclusion criteria:

- Brain diseases that may affect cognitive function (such as fever, infection, head injury, cerebrovascular disease, brain tumors), current Substance abuse use of other medication rather than antiepileptic medication, symptoms or signs of illnesses other than epilepsy.
- Psychiatric illness.
- Systemic illness (renal diseases, liver disease).
- Alcoholic abuse.

All of the participants were subjected to the following:

 Full history (demographic data and personal history, detailed history of

- general health condition and chronic or current diseases) and general and neurological examination
- Special tests including:
 - PEBL Wisconsin (Berg) Card Sort Test (Mueller and Piper, 2014).
 - PEBL the Conners' Continuous Performance Test (*Mueller and Piper*, 2014).
 - Montreal cognitive assessment (MoCa) (Julayanont et al., 2014).
- Brain imaging: MRI brain (to exclude organic cause).
- EEG.

Statistical analysis:

- Statistical package for social sciences (IBM-SPSS), version 24 IBM-Chicago, USA (May 2016) was used for statistical data analysis.
- Data expressed as mean, standard deviation (SD), number and percentage. Mean and standard deviation were used as descriptive value for quantitative data, while number and percentage were used to describe qualitative data.
- Student t test was used to compare the means between two groups, and oneway analysis of variance (ANOVA) test was used to compare means of more than two groups with LSD post-HOC test for individual inter-group p values.
- Mann Whitney test and Kruskal-Wallis tests were used instead of t test and ANOVA - respectively - in cases of non-normally distributed data.

- Pearson Chi square was used to compare

percentages of qualitative data.

RESULTS

The majority of cases were males, and there was non-significant difference between groups regarding gender of the patients (p value = 0.832). In the 1st group there were 16 males and 9 females, in the 2nd group there were 18 males and 7 females while in the 3rd group there were 17 males and 8 females.

The mean age of the study groups is around 26 years in epileptic with medication group, 23 years in epileptic without medication group and 25 years in control group with no significant difference between all groups.

The majority of cases have a low education degree with percentage of 62.5% with 28% high education. Most of cases were single with percentage of 68%, and non-significant difference among the three groups (p value = 0.576).

The majority of cases have no family history and -ve consanguinity with 72% with and non-significant difference among the three groups (p value = 0.214).

All of cases had neither history of status epilepticus, febrile convulsions, nor history of substance, with normal MRI brain.

33.3 % of the sample take AED whom were the 1st group epileptic with medication, while 66.7% did not take any

AED medication, equally divided between the two other groups epileptic without medication and control group, with significant difference between groups (p value = <0.001).

20 % of the sample have monotherapy while 13.3% have polytherapy. 66.7% have no medication whom were divided equally between the two groups, i.e. epileptic without medication and control group.

58.7% of sample have abnormal EEG half of them have AED medication and the other group have no AED medication, with high significance between study group (p value <0.001).

The mean age at onset of epilepsy of the study groups was around 21 years in epileptic with medication group and around 23 years in epileptic without medication group.

The mean frequency of seizures of the epileptic with medication group was around 1 per year, and 8 in epileptic without medication group, with a highly significant difference (p value <0.001).

The mean of last fits of the epileptic with medication group was 3 months and 0.5 month in 2nd group, with significant difference (p value <0.001 - **Table 1**).

	GROUPS	MEAN ± S.D	P VALUE
Age at onset of	epileptic with medication	20.96 ± 4.75	0.232
epilepsy	epileptic without medication	22.72 ± 5.51	
Frequency of seizures	epileptic with medication	1.12 ± 0.44	< 0.001
(per year)*	epileptic without medication	8.24 ± 4.08	
Last fits (in months)*	epileptic with medication	3.13 ± 4.66	< 0.001
	epileptic without medication	0.54 ± 0.35	

^{*} Non parametric tests were done due to non-normally distributed data.

Regarding the Wisconison Card Sorting test of the study groups (Table 2), the mean correct responses test of the study groups was around 76.7±5.65 in group 1, around 78±2.88 in group 2 and 81.8±2.38 in group 3 with significant difference between group 1 and group 3 (p value <0.001), and significant difference between group 2 and group 3 (p value =0.001).

The mean total errors test of the study groups was 39.2 ± 3.9 in group 1, 39.4 ± 3.4 in group 2 and 35.8 ± 2.34 in group 3, with significant difference between group 1 and group 3 (p value <0.001) and significant difference between group 2 and group 3 (p value <0.001).

The mean perseverative responses test of the study groups was 28±5.23 in group 1, 30.8±3.24 in group 2 and 28.6±3.62 in

group 3, with significant difference between group 1 and group 2 (p value <0.019).

The mean non-perseverative errors test of the study groups was 11.2 ± 6.62 in group 1, 8.6 ± 2.59 in group 2 and 7.2 ± 2.88 in group 3, with significant difference between group 1 with group 3 (p value = 0.009), and significant difference between group 2 and group 3 (p value = 0.042).

The mean trials to complete test of the study groups was 16.1 ± 7 in group 1, 15.5 ± 4.85 in group 2 and 15.3 ± 5.42 in group 3, with no significant difference between groups (p value = 0.964).

The mean failure to maintain set test of the study groups was 1.2 ± 0.99 in group 1, 0.68 ± 0.8 in group 2 and 1.1 ± 0.81 in group 3, with no significant difference between groups (p value = 0.096 - **Table 2**).

Table (2): Wisconison card sorting test between study groups.

	GROUPS	MEAN ± S.D	P VALUE
Correct responses	Group 1	76.7 ± 5.65	1 vs 2: 0.246
	Group 2	78 ± 2.88	1 vs 3: <0.001
	Group 3	81.8 ± 2.38	2 vs 3: 0.001
	Total	78.8 ± 4.43	All :<0.001
	Group 1	39.2 ± 3.94	1 vs 2: 0.873
Total arrors	Group 2	39.4 ± 3.41	1 vs 3: <0.001
Total errors	Group 3	35.8 ± 2.34	2 vs 3: <0.001
	Total	38.1 ± 3.65	All :<0.001
	Group 1	28 ± 5.23	1 vs 2: 0.019
Perseverative	Group 2	30.8 ± 3.24	1 vs 3: 0.610
responses	Group 3	28.6 ± 3.62	2 vs 3: 0.063
	Total	29.1 ± 4.24	All : 0.047
	Group 1	11.2 ± 6.62	1 vs 2: 0.168
Non-perseverative	Group 2	8.6 ± 2.59	1 vs 3: 0.009
errors*	Group 3	7.2 ± 2.88	2 vs 3: 0.042
	Total	8.98 ± 4.68	All : 0.014
Trials to complete*	Group 1	16.1 ± 7	1 vs 2: 0.836
	Group 2	15.5 ± 4.85	1 vs 3: 0.829
	Group 3	15.3 ± 5.42	2 vs 3: 0.867
	Total	15.7 ± 5.76	All : 0.964
Failure to maintain set*	Group 1	1.2 ± 0.99	1 vs 2: 0.068
	Group 2	0.68 ± 0.8	1 vs 3: 0.842
	Group 3	1.1 ± 0.81	2 vs 3: 0.055
	Total	0.97 ± 0.89	All : 0.096

Group 1: epileptic with medication, Group 2: epileptic without medication, Group 3: control.

^{*} Non parametric tests were done due to non-normally distributed data.

The mean target acc rate was 0.956 ± 0.03 in group 1, 0.970 ± 0.015 in group 2 and 0.974 ± 0.015 in group 3, with significant difference between group 1 with group 2 (p value = 0.031), with significant difference between group 1 and group 3 (p value = 0.007).

The mean foil acc rate of the study groups was 0.446 ± 0.14 in group 1, 0.406 ± 0.11 in group 2 and 0.449 ± 0.14 in group 3, with no significant difference between all groups.

The mean commission errors of the study groups was 20.36±6.15 in group 1, 21.20±4.87 in group 2 and 20±6.16 in group 3, with no significant difference between all groups.

The ommission errors of the study groups was 13.88 ± 10.1 in group 1, 9.68 ± 4.62 in group 2 and 8.56 ± 4.80 in group 3, with significant difference between group 1 and group 3 (p value = 0.025).

The mean correct RT mean of the study groups was 449.4± 55.7 in group 1, 401.7±44.8 in group 2 and 391.3±58.6 in

group 3, with significant difference between group 1 and group 2 (p value = 0.002), significant difference between group 1 and group 3 (p value <0.001).

The mean correct RT SD of the study groups was 194.6 ± 66.3 in group 1, 165.6 ± 52.4 in group 2 and 136.2 ± 55.9 in group 3, with significant difference among all groups (p value = 0.005), significant difference between group 1 and group 3 (p value = 0.002); and significant difference between group 2 and 3 (p value = 0.035).

The mean error RT mean continuous performance test of the study groups was 562.5 ± 143.3 in group 1, 511.7 ± 107.4 in group 2 and 434.5 ± 90.8 in group 3, with significant difference between group 1 and group 3 (p value <0.001), with significant difference between group 2, and group 3 (p value = 0.021).

The mean error RT SD continuous performance test of the study groups was 441.1±278.8 in group 1, 421.1±203.2 in group 2, and 314.2±257.7 in group 3, with no significant difference between all groups (**Table 3**).

Table (3): Continuous performance test between study groups.

	GROUPS	MEAN ± S.D	P VALUE
Target acc rate	Group 1	0.956 ± 0.03	1 vs 2: 0.031
	Group 2	0.970 ± 0.015	1 vs 3: 0.007
	Group 3	0.974 ± 0.015	2 vs 3: 0.575
	Total	0.967 ± 0.022	All : 0.018
Foil acc rate*	Group 1	0.446 ± 0.14	1 vs 2: 0.233
	Group 2	0.406 ± 0.11	1 vs 3: 0.877
	Group 3	0.449 ± 0.14	2 vs 3: 0.273
	Total	0.434 ± 0.13	All : 0.414
Commission errors*	Group 1	20.36 ± 6.15	1 vs 2: 0.711
	Group 2	21.20 ± 4.87	1 vs 3: 0.734
	Group 3	20.00 ± 6.16	2 vs 3: 0.431
	Total	20.52 ± 5.70	All : 0.747
Ommission errors*	Group 1	13.88 ± 10.1	1 vs 2: 0.147
	Group 2	9.68 ± 4.62	1 vs 3: 0.025
	Group 3	8.56 ± 4.80	2 vs 3: 0.255
	Total	10.71 ± 7.25	All : 0.061
Correct RT mean	Group 1	449.4 ± 55.7	1 vs 2: 0.002
	Group 2	401.7 ± 44.8	1 vs 3: <0.001
	Group 3	391.3 ± 58.6	2 vs 3: 0.491
	Total	414.1 ± 58.5	All : 0.001
Correct RT SD*	Group 1	194.6 ± 66.3	1 vs 2: 0.133
	Group 2	165.6 ± 52.4	1 vs 3: 0.002
	Group 3	136.2 ± 55.9	2 vs 3: 0.035
	Total	165.4 ± 62.5	All : 0.005
Error RT mean	Group 1	562.5 ± 143.3	1 vs 2: 0.126
	Group 2	511.7 ± 107.4	1 vs 3: <0.001
	Group 3	434.5 ± 90.8	2 vs 3: 0.021
	Total	502.9 ± 126.0	All : 0.001
Error RT SD*	Group 1	441.1 ± 278.8	1 vs 2: 0.720
	Group 2	421.1 ± 203.2	1 vs 3: 0.059
	Group 3	314.2 ± 257.7	2 vs 3: 0.073
	Total	392.2 ± 251.6	All : 0.100

Group 1: epileptic with medication, Group 2: epileptic without medication, Group 3: control.

The mean MoCa of the study groups was 24.1 in epileptic with medication group, 23.96 in epileptic without medication group and 25 in control group

with no significant difference between all groups, with high significant difference between group 1 versus group 3 and group 2 versus group 3 (**Table 4**).

Table (4): Montreal cognitive assessment (MoCa) between study groups.

GROUPS	$MEAN \pm S.D$	P VALUE
Epileptic with medication	24.08 ± 1.152	1 vs 2: 0.682
Epileptic without medication	23.96 ± 1.020	1 vs 3: <0.001
Control group	26.92 ± 0.909	2 vs 3 : <0.001
Total	24.99 ± 1.712	

ANOVA = 65.93, P value < 0.001

^{*} Non parametric tests were done due to non-normally distributed data.

Montreal cognitive assessment (MoCa) of the study groups showed that the normal MoCa was 3 individuals in epileptic with medication group, 2 individuals in epileptic without

medication group and 22 individuals in control group, with high significant difference between all groups (p value = <0.001 - **Table 5**).

Table (5): Montreal cognitive assessment	(MoCa) of the study groups.
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Groups Parameters	Epileptic With Medication	Epileptic Without Medication	Control Group	Total
Normal	3	2	24	29
	12%	8%	96%	39%
Abnormal	22	23	1	46
	88%	92%	4%	61%
Total	25	25	25	75
	100%	100%	100%	100%

DISCUSSION

Our study aimed to assess cognitive functions in patients with generalized onset epilepsy.

Individuals with epilepsy have a higher prevalence of impaired cognitive performance compared to healthy individuals who are matched for age and education, this result is consistent with the result of *Realmuto et al.* (2015).

The majority of cases were males, and there was non-significant difference between groups regarding gender of the patients. The mean age of the study groups was around 26 years in "epileptic with medication" group, 23 years in "epileptic without medication" group and 25 years in control group with no significant difference between all groups. The majority of cases had a low education degree with percentage of 62.5% with 28% high education; these results are consistent with the result of *Sunmonu et al.* (2009).

The family history of similar condition in the study groups, we observed that the majority of cases have no family history and -ve consanguinity with 72% with and non-significant difference among the three groups, these results are consistent with the result of *Desoky and Gabra* (2019).

Like *Luton et al.* (2010), this study reported that the higher frequency of seizures was associated with more ED in patients with generalized epilepsy, which may be attributed to the structurally damaging effect and cognitive dysfunction of the long-lasting frequent uncontrolled seizure disorders.

The mean frequency of seizures of the "epileptic with medication" group was around 1 per year and 8 in "epileptic without medication" group; with a highly significant difference.

By using Wisconsin card sorting test (WCST) in study groups statistically there was significant difference between study groups as regard to WCST. Patient with generalized epilepsy had worse performance on this executive test: This indicates that the patients had deficits mental flexibility, goal maintenance and

concept building and this is agreed with different studies. These results are consistent with the result of *Zhang et al.* (2017).

By using continuous performance test (CPT) in study groups there was statistically significant difference between study groups in all parameters of CPT (target accuracy rate, foil accuracy rate, commission errors, omission errors, correct response time mean, and error response time mean), which was in line with *Parente et al.* (2013).

As regard the Montreal cognitive assessment (MoCa) between study groups, found patients had that "epileptic with performance in both medication" and "epileptic without medication" groups while patients in control group had good performance. This result is consistent with the result of Phabphal and Kanjanasatien (2011).

It was found that MoCa is normal in 3 individuals in "epileptic with medication" group, 2 individuals in "epileptic without medication" group and 22 individuals in control group with high significant difference between all groups.

CONCLUSION

Our findings indicated the need for comprehensive neuro psychological batteries in patients with generalized epilepsies, in order to provide a more extensive evaluation of attentional and executive functions and to show that some relevant deficits have been overlooked. Evidence was accumulating that 'benign' generalized epilepsies also have cognitive sequelae which can interfere with learning and social adaptation. The impact of these

epilepsies on cognition and behavior was far from being negligible.

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تقييم الوظائف المعرفية في عينة من المرضى المصريين المصابين بمرض الصرع العام

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خلفية البحث: تشكل وظائف المخ المعرفية القدرة على التعامل مع المعلومات بطريقة مجدية، وتطبيق المعلومات المكتسبة، وإجراء تغييرات تفضيلية، وقدرة شخص ما على تغيير الآراء حول هذه المعلومات. والأفراد المصابون بالصرع لديهم معدل إنتشار أعلى للأداء الإدراكي الضعيف مقارنة بالأفراد الأصحاء في نفس العمر والتعليم. هناك العديد من العوامل تأثير ضار على الإدراك لدى المرضى، بما في ذلك العمر عند ظهور الصرع، وتواتر النوبة، ومدة النوبات، والتلف المخي الهيكلي نتيجة للنوبات المتكررة أو المطولة والأدوية المستخدمة لعلاج النوبات.

الهدف من البحث: هو تقييم الوظائف المعرفية لدى المرضى الذين يعانون من الصرع العام.

المرضى وطرق البحث: أجريت در استنا في قسم الأمراض العصبية في مستشفى سوهاج العام على 75 شخصًا مقسمًا إلى 3 مجموعات متساوية ، يعانون من الصرع وقد تم اختيارهم من عيادات المرضى. تم تقسيم المرضى إلى ثلاث مجموعات: المجموعة الأولى (أ) وهم المرضى الذين تم تشخيصهم يعانون من الصرع العام ويتلقون الدواء (الأدوية المضادة للصرع). والمجموعة الثانية (ب) وهم المرضى الذين تم تشخيص إصابتهم بالصرع العام ولا يتلقون الدواء (الأدوية المضادة للصرع). والمجموعة ضابطة.

تعرض جميع المشاركين لما يلى:

1. التاريخ الكامل (البيانات الديموغرافية والتاريخ الشخصي، والتاريخ التفصيلي للحالة الصحية والأمراض المزمنة أو الحالية) والفحص العام والفحص العصبي.

2. إختبارات خاصة بما في ذلك: اختبار الفرز ببطاقة PEBL ويسكونسن (بيرج)، اختبار الأداء المتواصل لكونبيرز، التقييم المعرفي في مونتريال (MoCa).

3. تصوير المخ: التصوير بالرنين المغناطيسي للمخ (لاستبعاد السبب العضوي).

4. رسم المخ.

نتانج البحث: متوسط الإجابات الصحيحة لاختبار فرز بطاقة ويسكونسون لمجموعات الدراسة كان حوالي 76.7 ± 5.65 في المجموعة أ، وحوالي 78.2 في المجموعة بالمجموعة بال

الخلاصة: جميع المرضى الذين يعانون من الصرع يظهرون ضعفاً كبيراً في جميع التدابير المعرفية مثل الذاكرة العاملة، والمتحكم المثبط، والحفاظ على الهدف، والمرونة العقلية. لاحظنا وجود حالات عجز في الانتباه واليقظة وهولاء يحتاجوا إلى اهتمام مستدام ومنقسم مقارنة بالمجموعة الضابطة. وارتبط ضعف الإنتباه واليقظة بإرتفاع عدد نوبات الصرع.