Clinical and Psychometric Study of Cognitive Functions in Epilepsy of Primary Origin

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This study was conducted on 40 patients suffering from idiopathic epilepsy, 20 control subjects and 25 non - epileptic siblings of the studied epileptic patients. The subjects were chosen from both sexes, their ages ranging from 15-35 years. Half of the patients were already receiving anti-epileptic treatment and the other half were untreated. The patients were submitted to clinical evaluation and EEG studying. Psychometric testing was carried out to all subjects. The untreated patients were tested twice, before and after one month of antiepileptic drug administration by either carbamazepine (CBZ) or sodium valproate (VPA), as monotherapy. Blood samples were taken from patients at VPA in both treated and untreated patients after drug administration. The battery of psychometric tests used in the study included Wechsler Memory Scale (WMS), test of similarities, visual retention test (Benton test A and C), complex key test and maze test. The study showed impairment in cognitive functions in both treated and untreated epileptic patients. CBZ administration for one month in a dose of 15 mg/kg/day led to impairment of attention, concentration and spatial scanning. VPA administration for one month in a dose of 30 mg/kg/day led to impairment of memory, attention, concentration and spatial scanning. Patients with earlier age of onset of epilepsy showed more deterioration of memory than those with later age onset. Patients with higher frequency of fits have more deterioration of memory and abstract thinking than those with lower frequency. Patients with mixed seizures had more deterioration of memory than those with generalized or partial seizures.

(Egypt.J. Psychiat., 1997, 20: 57-73).

Introduction

It has recently become clear that the majority of patients with epilepsy can have their seizures managed successfully. However, there remains a proportion of patients who fail to achieve adequate seizure control with modern anticonvulsant treatments using serum level monitoring and all of the advances or recent technology. Furthermore, there is a significant number of patients, either with or without continuing seizures, who suffer from the neurological and psychosocial consequences of having epilepsy. Important amongst these are cognitive complications.

Although it is hundred years ago that Gowers first paid attention to the problem of memory disturbance in epilepsy, it is only within the last twenty years that the matter has been dealt with a scientific way (Pedersen and Dam, 1986).

In recent years, much work has been carried out on the influence of seizure type and epilepsy treatment variables on cognitive function and the fact that patients with epilepsy may suffer from cognitive disruption has became accepted. Also, the possible adverse effects of antiepileptic drugs (AEDs) on memory, ability to think and other cognitive functions have received much attention (Evans and Gualtieri, 1985, Reynolds and Trimble, 1985; Trimble, 1987; Vin-

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ing, 1987 and Dodrill, 1988).

Possible influential factors are postulated including patient age, duration, frequency, aetiology and type of seizures, hereditary factors, psychosocial issues and antiepileptic drug (AED) therapy. Whereas many of these factors are beyond the physician's control, AED therapy is one element that can be addressed in treatment decisions by recognizing the potential cognitive effects of particular AEDs.

The aim of the present work is to detect changes in cognitive functions occurring in patients with idiopathic epilepsy. Also the study aims at the evaluation of effects of antiepileptic drugs, particularly carbamazepine and sodium valproate on cognitive functions of epileptic patients, and whether the assumed changes occurring in cognitive functions are due to epilepsy, antiepileptic drugs, or both. Lastly, the study aims at finding the relationship between seizure variables, (e.g., age at onset, duration of epilepsy, frequency of fits, seizure pattern and EEG findings), and changes in cognitive functions.

Subjects and Method

The subjects of the present work is formed of 40 patients suffering from idiopathic epilepsy (epileptic seizures with no identifiable cause), whatever its pattern attending the Outpatient Clinic of Sohag University Hospital. The study also included 25 nonepileptic siblings of the studied epileptic patients and 20 control subjects who were nonepileptic and had no epileptic siblings.

Patients and subjects included in the present study (both males or females) had their age ranged between 15 and 35 years. This age range excluded patients below 15 years who are presumably unable to deal with some of the chosen psychometric tests. Moreover, the effect of aging has been abolished by the exclusion of patients aged more than 35 years. The patients were classified into two groups. The first group (treated group) included 20 patients who were already receiving antiepileptic drugs (AEDs). Half of them (10 patients) have been receiving carbamazepine (CBZ) and the other half (10 patients) have been receiving sodium valproate (VPA), either as monotherapy or in combination with other AEDs. The second group of patients (untreated group) included 20 patients who had never received AEDs before the start of the present study.

The patients were submitted to the following:

1- Clinical evaluation:

This included history taking, especially that concerning the fits, such as age at onset, pattern of seizures, average frequency of fits, history of status epilepticus, etc. In addition, a detailed history about AEDs therapy in the treated group was inquired about.

Complete general and neurological examinations were carried out with the exclusion of patients having a history and / or signs suggestive of secondary (symptomatic) epilepsy.

2- Electroencephalography (EEG).

3- Blood sampling for measurement of serum levels of AEDs (CBZ and VPA).

4- Psychometric testing:

Both patients, siblings and control subjects were submitted to psychometric testing. The treated patients were tested once with simultaneous blood sampling. Untreated patients were tested twice. The first testing was carried out before any antiepileptic drugs had been taken, then half of them (10 patients) were given conventional CBZ tablets in a dose of 15 mg/kg/day and the other half (10 patients) were given VPA tablets in a dose

of 30 mg / kg/day. After one month, the twenty patients were psychometrically tested again with simultaneous blood sampling for measurement of serum level of CBZ and VPA.

The battery of psychometric tests used in the present study consisted of 5 tests:

1- Wechsler Memory Scale (WMS) (Wechsler, 1945). This scale consists of seven subtests. At the end of the scale, memory quotient (MQ) can be calculated

2- Test of similarities (Anastasi, 1976).

3- Benton visual retention test (forms A & C).

4- Complex key test (El- Behary, in press).

5- Maze test (Badary and Abd El-Rahim, 1985).

Results

The results obtained by studying 40 patients compared with the 20 control subjects and 25 non - epileptic sibs of the studied epileptic patients are demonstrated in the following tables.

Table (1) shows that nonepileptic sibs and control subjects are superior to epileptic patients in all psychometric tests and that superiority is statistically significant in all tests.

Table (2) shows that control subjects are significantly superior to both treated and untreated patients in all psychometric tests.

Table (3) shows that psychometric performance of nonepileptic sibs is significantly better than that of treated and untreated patients in all psychometric tests.

Table (4) shows that the superiority of untreated patients over treated patients is statistically significant in three psychometric tests only.

Table (5) shows that after administration of CBZ for one month, there was a deterioration in results of some psychometric tests and improvement in others. However the changes were statistically significant in two tests only; namely, complex key test and maze test, showing deterioration after treatment.

Table (6) shows that the relation between changes in psychometric performance that occurred after treatment (whether improvement or deterioration) and serum level of CBZ at the time of testing, differed from one test to another. However, this correlation was statistically significant in two tests only. These are the complex key test and the maze test in which the correlation coefficient was positive, which indicates that as the serum level of CBZ increases the deteriorating effects within results of these tests increase and vice versa.

Table (7) shows that after administration of VPA for one month, the deterioration has occurred in all tests, except in one subtest of Wechsler memory scale (personal and current information), which showed a statistically insignificant improvement. The deterioration was statistically significant in most of the other tests.

Table (8) demonstrates the positive correlation between the deterioration which has occurred after VPA administration and serum level of the drug. This positive correlation was statistically significant only in memory quotient, two subtests of Wechsler memory scale (orientation and digit span) and in Benton (A) test. This means that, as serum VPA increases, the deteriorating effects within these tests increase and vice versa. In other tests, the positive correlation was statistically insignificant. Table (9) shows the statistically significant superi-

ority of patients receiving monotherapy over those receiving polytherapy of AEDs in MQ. In other tests, the results were statistically insignificant.

Table (10) shows that the correlation between age at onset of epilepsy in untreated patients and psychometric performance is positive in most of the tests. However, this positive correlation was statistically significant only in one subtest of WMS (personal and current information) and in MQ.

Table (11) shows the negative correlation between duration of epilepsy in untreated patients and psychometric performance in all tests except one subtest of WMS. This negative correlation was statistically significant in two subtests of WMS only, i.e., increased duration of epilepsy was associated with impaired psychometric performance.

Table (12) demonstrates the correlation between average interval between fits and psychometric performance in all patients, whether treated or untreated. In treated patients, the correlation is positive in all tests and is statistically significant in all tests except 3 subtests of WMS. In untreated patients, the correlation is positive in all tests except Benton (C), in which the correlation is significantly negative. The positive correlation in other tests is statistically significant except in complex key tests, maze test and 4 subtests of WMS. Studying all patients (whether treated or untreated) as one group showed that the correlation is positive in all tests, except the Benton (C) in which the correlation was insignificantly negative. The positive correlation in other tests is statistically significant except in maze test and one subtest of WMS.

The comparison between generalized, partial and mixed seizures is shown in Table (13). The results indicate that the lowest score is associated with mixed seizures in all tests and that patients with partial seizures are superior to those with generalized seizures in all tests except in visual reproduction where patients with generalized epilepsy are superior. The results are statistically significant in some subtests of WMS ad in MQ, while are not significant in other tests.

Table (14) shows the statistically insignificant difference between different EEG patterns, as regards psychometric performance in all tests.

Discussion

Results of the present study showed that epileptic patients have statistically significant lower levels of performance in psychometric tests compared with control subjects and nonepileptic sibs (Table 1-3). These lower levels of performance were in all studied psychometric tests which represent memory, abstract thinking, visual perception, visual memory, visuoconstructive abilities, attention, concentration and spatial scanning. These results come in agreement with most of the previous studies starting from those of Maudsley (1974); William Gowers (1881) till Hermann et al. (1987).

In our study, although lower level of performance was manifest in both patients who were already receiving AEDs for long periods and those who had never received AEDs before. The treated patients showed more impairment of performance than untreated patients. This impairment was statistically significant in tests representing visual memory, attention, concentration and spatial scanning (Table 4).

This denotes an additional impairing effect accompanying the chronic administration of AEDs regardless of their types and doses. Nevertheless, AEDs admiration is not the only parameter that differentiates between these two groups of patients (treated and untreated), but

Table 1
Comparison between Epileptic Patients, non-Epileptic Sibs and Control Subjects as Regards PsychometricPerformance (Mean ± SD)

Psychometric Tests	Control (n= 20)	Sibs (n= 25)	Patients (n= 40)	P value
1- Wechsler memory scale (WMS)				
- Personal & current inf.	4.85±0.37	4.88±0.33	4.50±0.60	<0.01
- Orientation	4.95±0.22	4.96±0.20	4.50±0.75	<0.01
- Mental control	2.55±0.10	2.72±1.14	1.20±1.00	<0.001
- Logical memory	11 .60±1.15	11.34±1.18	6.36±2.88	<0.001
- Digit span	10.95±0.39	11.0±0.71	8.10±1.97	<0.001
- Visual reproduction	11.25 ± 1.94	13.08±1.00	7.45±3.50	<0.001
- Associate learning	15.63±2.16	16.26±1.93	9.86±3.77	<0.001
- Memory quotient (MQ)	97.85±8.23	100.00±6.44	72.72±13.30	<0.001
2- Similarities	13.75±2.42	14.16±2.67	7.80±3.70	<0.001
3- Visual retention test (Benton)				
- Administration (A)	7.40±0.99	7.88±1.05	4.25±2.40	<0.001
- Administration (C)	8.55±1.10	9.08±0.91	5.80±2.84	<0.001
4- Complex key test	24.35±1.50	23.60±2.22	12.97±2.84	<0.001
5- Maze test	16.25±2.88	19.08±4.00	7.50±5.30	<0.001

Table 2
Comparison between Control Subjects, Untreated and Treated Patients as Regards Psychometric Performance (Mean ± SD)

Psychometric Tests	Control (n= 20)	Untreated (n= 20)	Treated (n= 20)	P value
1- Wechsler memory scale (WMS)				
- Personal & current inf.	4.85±0.37	4.65±0.59	4.40±0.60	<0.05
- Orientation	4.95±0.22	4.60±0.60	4.45±0.89	<0.05
- Mental control	2.55±0.10	1.40±1.14	1.05±1.10	<0.001
- Logical memory	11 .60±1.15	7.10±2.84	5.65±2.80	<0.001
- Digit span	10.95±0.39	8.35±1.75	7.80±2.17	<0.001
- Visual reproduction	11.25 ± 1.94	8.50±3.24	6.40±3.51	<0.001
- Associate learning	15.63±2.16	10.47±3.89	9.25±3.64	<0.001
- Memory quotient (MQ)	97.85±8.23	7.60±13.35	69.85±12.92	<0.001
2- Similarities	13.75±2.42	8.20±3.61	7.45±3.78	<0.001
3- Visual retention test (Benton)				
- Administration (A)	7.40±0.99	5.00±2.10	3.50±2.44	<0.001
- Administration (C)	8.55±1.10	6.15±2.87	5.45±2.84	<0.001
4- Complex key test	24.35±1.50	15.05±4.22	10.90±5.8	<0.001
5- Maze test	16.25±2.88	9.65±4.92	5.40±4.82	<0.001

Table 3
Comparison between Untreated and Treated Patients with their Own non-Epileptic Sibs as Regards Psychometric Performance (Mean ± SD)

Psychometric Tests	Sibs (n= 20)	Untreated (n= 13)	Treated (n= 12)	P value
1- Wechsler memory scale (WMS)				
- Personal & current inf.	4.88±0.33	4.70±0.63	4.58±0.51	<0.05
- Orientation	4.96±0.20	4.77±0.44	4.75±0.62	<0.05
- Mental control	2.72±1.14	1.23±1.01	1.42±1.10	<0.001
- Logical memory	11.34±1.18	7.46±2.90	6.33±2.64	<0.001
- Digit span	11.0±0.71	18.85±1.57	8.33±12	<0.001
- Visual reproduction	13.08±1.00	9.61±2.69	750±3.23	<0.001
- Associate learning	16.26±1.93	11.65±3.13	10.29±3.32	<0.001
- Memory quotient (MQ)	100.00±6.44	77.23±10.1	73.92±11.28	<0.001
2- Similarities	14.16±2.67	8.54±3.28	8.08±3.60	<0.001
3- Visual retention test (Benton)				
- Administration (A)	7.88±1.05	5.31±1.70	3.58±2.27	<0.001
- Administration (C)	9.08±0.91	6.77±2.80	5.75±2.56	<0.001
4- Complex key test	23.60±2.22	15.85±4.28	12.50±5.55	<0.001
5- Maze test	19.08±4.00	11.23±4.90	6.58±5.35	<0.001

Table 4
Comparison between Untreated and Treated Patients as Regards Psychometric Performance (Mean ± SD)

Psychometric Tests	Untreated (n= 20)	Treated (n= 20)	P value
1- Wechsler memory scale (WMS)			
- Personal & current inf.	4.65±0.59	4.40±0.60	NS
- Orientation	4.60±0.60	4.45±0.89	NS
- Mental control	1.40±1.14	1.05±1.10	NS
- Logical memory	7.10±2.84	5.65±2.80	NS
- Digit span	8.35±1.75	7.80±2.17	NS
- Visual reproduction	8.50±3.24	6.40±3.51	NS
- Associate learning	10.47±3.89	9.25±3.64	NS
- Memory quotient (MQ)	7.60±13.35	69.85±12.92	NS
2- Similarities	8.20±3.61	7.45±3.78	NS
3- Visual retention test (Benton)			
- Administration (A)	5.00±2.10	3.50±2.44	<0.05
- Administration (C)	6.15±2.87	5.45±2.84	NS
4- Complex key test	15.05±4.22	10.90±5.8	<0.05
5- Maze test	9.65±4.92	5.40±4.82	<0.01

Table (5)
Comparison between Psychometric Performance Prior to and one Month after Administration of Carbamazepine to Untreated Patients (Mean ± SD)

Psychometric Tests	Before treatment (n=10)	After treatment (n=10)	P Value
1- Whechsler memory scale (WMS)			
- Personal & current inf.	4.40 ±0.52	4.70 ±0.48	NS
- Orientation	4.80± 0.42	4.60± 0.70	NS
- Mental Control	1.60 ±1.26	1.30 ±1.34	NS
- Logical memory	7.60 ± 3.41	7.95 ± 3.19	NS
- Digit span	7.70 ± 3.47	8.60 ± 2.91	NS
- Visual reproduction	10.05 ± 4.64	9.85 ± 4.62	NS
- Associate learning	73.4 ±14.61	74.2 ±15.50	NS
- Memory quotient (MQ)	8.40 ± 4.30	8.50 ± 3.98	NS
2- Similarities	87.40 ± .30	8.50 ± 3.98	NS
3- Visual retention test (Benton)			
- Administration (A)	5.10 ± 2.73	5.50 ± 2.80	NS
- Administration (C)	5.60 ± 3.44	5.90 ± 3.07	NS
4- Complex key test	15.40 ± 5.48	1.40 ± 5.27	<0.01
5- Maze test	12.20 ± 5.33	11.20 ± 5.16	<0.05

Table 6
Correlation Coefficient (r) between Serum Levels (n=10) of Carbamazepine and Changes in Psychometric Performance after Drug Administration

Psychometric Tests	Correlation Coefficient (r)	P value
1- Wechsler memory scale (WMS)		
- Personal & current inf.	-0.1385	NS
- Orientation	0.1385	NS
- Mental control	0.0536	NS
- Logical memory	-0.3566	NS
- Digit span	-0.2616	NS
- Visual reproduction	-0.147	NS
- Associate learning	0.4177	NS
- Memory quotient (MQ)	-0.2907	NS
2- Similarities	-0.0593	NS
3- Visual retention test (Benton)	0.1143	
- Administration (A)		NS
- Administration (C)	0.0321	NS
4- Complex key test	0.5956	<0.01
5- Maze test	0.8138	<0.05

Table 7
Comparison between Psychometric Performance Prior to and one Month after Administration of Sodium Valproate to Untreated Patients (Mean ± SD)

Psychometric Tests	Before treatment (n= 10)	After treatment (n= 10)	P value
1- Wechsler memory scale (WMS)			
- Personal & current inf.	4.70±0.67	4.80±0.42	NS
- Orientation	4.40±0.70	4.20±0.63	NS
- Mental control	1.20±1.03	0.30±0.48	<0. 05
- Logical memory	6.55±2.19	5.75±1.80	<0.01
- Digit span	8.80±1.62	8.00±1.63	<0.05
- Visual reproduction	9.30±2.90	7.10±2.88	NS
- Associate learning	10.90±3.17	9.10±2.04	<0.05
- Memory quotient (MQ)	77.80±12.34	70.9±12.29	<0.01
2- Similarities	8.00±2.98	7.50±2.59	NS
3- Visual retention test (Benton)			
- Administration (A)	4.90±1.37	3.70±1.42	<0.01
- Administration (C)	6.70±2.21	6.30±2.06	NS
4- Complex key test	14.7±2.71	13.7±2.21	<0.01
5- Maze test	7.10±	6..30±2.58	<0.01

Table 8
Correlation Coefficient (r) between Serum Levels (n=10) of Sodium Valproate and Changes in Psychometric Performance after Drug Administration

Psychometric Tests	Correlation Coefficient (r)	P value
1- Wechsler memory scale (WMS)		
- Personal & current inf.	0.1460	NS
- Orientation	0.7476	<0.01
- Mental control	0.1334	NS
- Logical memory	0.3662	NS
- Digit span	0.5791	<0.01
- Visual reproduction	0.0703	NS
- Associate learning	0.2822	NS
- Memory quotient (MQ)	0.5571	<0.05
2- Similarities	0.3680	NS
3- Visual retention test (Benton)		
- Administration (A)	0.6931	<0.05
- Administration (C)	0.1768	NS
4- Complex key test	0.3961	NS
5- Maze test	0.3373	NS

Table 9
Comparison between Psychometric Performance of Already Treated Group (Polytherapy Vs. Monotherapy) (Mean ± SD)

Psychometric Tests	Polytherapy (n= 9)	Monotherapy (n=11)	P value
1- Wechsler memory scale (WMS)			
- Personal & current inf.	4.22±0.07	4.54+0.52	NS
- Orientation	4.33±1.00	4.54+0.82	NS
- Mental control	1.11±1.05	1.00+1.18	NS
- Logical memory	4.50±2.98	6.59+2.36	NS
- Digit span	7.11±2.03	8.36+2.20	NS
- Visual reproduction	5.00±3.16	7.54+3.50	NS
- Associate learning	7.89±3.54	10.36+3.48	NS
- Memory quotient (MQ)	62.78±10.57	75.64+12.08	<0.05
2- Similarities	6.22±3.56	8.45+3.80	NS
3- Visual retention test (Benton)			
- Administration (A)	2.78±1.86	4.09+277	NS
- Administration (C)	5.33±3.00	5.54+2.84	NS
4- Complex key test	8.67±3.74	12.73+6.68	NS
5- Maze test	6.22±4.60	4.73+5.10	NS

Table 10
Correlation Coefficient (r) between Age at Onset of Epilepsy and Psychometric Performance in Untreated Patients (n= 20)

Psychometric Tests	Correlation Coefficient (r)	P value
1- Wechsler memory scale (WMS)		
- Personal & current inf.	0.3868	<0.05
- Orientation	-0.1898	NS
- Mental control	0.0000	NS
- Logical memory	0.0228	NS
- Digit span	0.3142	NS
- Visual reproduction	0.2256	NS
- Associate learning	0.3647	NS
- Memory quotient (MQ)	0.4081	<0.05
2- Similarities	0.1889	NS
3- Visual retention test (Benton)		
- Administration (A)	0.3549	NS
- Administration (C)	-0.1469	NS
4- Complex key test	0.1805	NS
5- Maze test	-0.1120	NS

Table 11
Correlation Coefficient (r) between Duration of Epilepsy and Psychometric Performance in Untreated Patients (n=20)

Psychometric Tests	Correlation Coefficient (r)	P value
1- Wechsler memory scale (WMS)	-0.2521	
- Personal & current inf.	-0.0746	<0.05
- Orientation	0.2380	NS
- Mental control	-0.1115	NS
- Logical memory	-0.5049	NS
- Digit span	-0.2250	<0.05
- Visual reproduction	-0.4780	NS
- Associate learning	-0.3419	<0.05
- Memory quotient (MQ)	-0.1556	NS
2- Similarities		NS
3- Visual retention test (Benton)		
- Administration (A)	-0.2431	NS
- Administration (C)	-0.2542	NS
4- Complex key test	-0.2490	NS
5- Maze test	-0.1907	NS

Table 12
Correlation Coefficient (r) between Psychometric Performance and Average Intervral between Fits in Epileptic Patients

Psychometric Tests	All patients (n= 40)	Untreated (n= 20)	Treated (n= 20)
1- Wechsler memory scale (WMS)			
- Personal & current inf.	0.1912	0.1717	0.3433
- Orientation	0.281*	0.2412	0.4568*
- Mental control	0.4703**	0.6147**	0.3233
- Logical memory	0.3243*	0.3960*	0.3534
- Digit span	0.3406*	0.2011*	0.6917***
- Visual reproduction	0.4206**	0.4032*	0.6932****
- Associate learning	0.2777*	0.2343	0.4720*
- Memory quotient (MQ)	0.4521**	0.4105	0.7097**
2- Similarities	0.5900***	0.5970**	0.7232***
3- Visual retention test (Benton)		0.5216**	0.7671***
- Administration (A)	0.5037***	-0.3992*	0.6770**
- Administration (C)	-0.0436		
4- Complex key test	0.2970*	0.2797	0.5960**
5- Maze test	0.2275	0.2308	0.4714*

* p <0.05 ** p <0.01 *** p <0.001

Table 13
Comparison between Different Seizure Patterns as Regards Psychometric Performance (Mean ± SD)

Psychometric Tests	Generalized (n= 30)	Partial (n= 3)	Mixed (n= 7)	P value
1- Wechsler memory scale (WMS)				
- Personal & current inf.	4.60±0.56	5.00±0.00	4.00+5.77	<0.05
- Orientation	4.56±0.73	5.00±0.00	4.14+0.90	NS
- Mental control	1.23±1.16	2.00±0.00	0.86+1.07	NS
- Logical memory	6.40±2.75	9.33±2.02	4.93+3.02	NS
- Digit span	8.43±1.83	9.00±0.00	6.14+1.86	NS
- Visual reproduction	8.13±3.14	7.67±1.53	4.43+4.28	<0.05
- Associate learning	10.45±3.26	12.83±4.25	6.07+3.46	<0.05
- Memory quotient (MQ)	74.93±12.28	80.33±6.03	60.0+12.87	<0.01
2- Similarities	8.30±3.77	9.67±1.15	5.00+2.45	NS
3- Visual retention test (Benton)				
- Administration (A)	4.50±2.40	5.67±1.53	2.57+1.81	NS
- Administration (C)	5.83±2.78	8.00±1.73	4.71+3.20	NS
4- Complex key test	13.33±5.28	16.33±6.03	10.00+5.32	NS
5- Maze test	7.07±4.87	13.33±8.02	7.00+5.10	NS

Table 14
Comparison between Different EEG of Epileptic Patients Patterns as Regards PsychometricPerformance (Mean ±SD)

Psychometric Tests	Focal EEG (n= 21)	Centercephalic (n= 13)	Normal EEG (n= 6)	P value
1- Wechsler memory scale (WMS)				
- Personal & current inf.	4.62±0.59	4.23±0.60	4.83±0.41	NS
- Orientation	4.67±0.66	4.23±0.83	4.67±0.82	NS
- Mental control	1.14±1.01	1.38±1.26	1.17±1.33	NS
- Logical memory	6.83±2.89	5.27±2.63	7.08±3.28	NS
- Digit span	8.24±1.84	7.54±2.07	8.67±2.25	NS
- Visual reproduction	7.29±3.35	7.46±3.71	8.00±4.15	NS
- Associate learning	10.59±3.96	9.11±2.84	8.92±4.89	NS
- Memory quotient (MQ)	74.71±12.98	68.85±12.55	74.17±16.36	NS
2- Similarities	8.62±3.44	6.61±4.13	7.67+3.14	NS
3- Visual retention test (Benton)				
- Administration (A)	4.81±2.48	3.54±2.29	3.83+1.94	NS
- Administration (C)	6.38±2.65	4.69±2.72	6.17+3.49	NS
4- Complex key test	13.86±5.62	12.69±4.53	10.50+6.53	NS
5- Maze test	8.48±5.71	5.77±4.06	8.00+5.83	NS

there are other factors, the most important of which is the duration of the disease, which is much longer in the treated group. Long duration of epilepsy may have an adverse effect on cognitive functions and the lower scores in the treated group may be attributed to this effect. On the other hand, the treated group had the advantage of having a lower frequency of fits than the untreated group, which may be the reason why the results in some tests showed insignificant difference between the two groups. Therefore, the conclusion that the obtained results are due to chronic use of AEDs only is questionable.

Regardless of the mentioned other variables (duration of epilepsy and frequency of fits), the obtained results have come into agreement with previous studies, such as that of Brodie et al. (1987), who stated that the performance of the untreated group was statistically superior to that of the treated group for the same tasks.

The results showed that CBZ produce variable effects (Table 5). A statistically in-significant improvement occurred in tests measuring memory, abstract thinking, visual perception, visual memory, and visuo-constructive abilities, while a significant deterioration occurred in the tests measuring attention, concentration and spatial scanning.

When these results are compared with those of previous studies, agreements with some studies and disagreements with others are found. For example, defects were found in attention and vigilance by Rodin et al. (1974), whereas Marchesi et al. (1980) found unchanged performance as regards these functions after CBZ administration. These same inconsistencies were found with other functions. For example, memory defects were found by Thompson et al. (1980) and Andrews et al. (1986), but were not detected in the comparable studies of Marchesi et al (1980) and Butlin et al. (1984). Other investigators reported improvement following CBZ administration, e.g., Rodin et al. (1974) reported improvement in attention and arousal; Dodrill and Tropin (1977) in vigilance; and Thompson and Timple (1980) in memory.

The correlation between serum level of CBZ and its effect on cognitive functions has been studied (Table 6). Statistically significant correlation coefficients were obtained in two tests only, those measuring attention, concentration and spatial scanning. In these two tests, in which CBZ presumably led to deterioration, the correlation between serum level of the drug and this deterioration was positive. This means that whenever the serum level of CBZ rises, its associated deteriorating effect upon these function increases. The obtained results have come into agreement with some studies, e.g. Andrews et al. (1986), who obtained a negative correlation between serum level of CBZ and performance in a tracking task.

Sodium valproate (VPA) produced impressive effects (Table 7). Its administration was associated with statistically significant deterioration in tests measuring memory, visual memory, attention and concentration and spatial scanning. In other tests (measuring abstract thinking, visual perception and visuo - constructive abilities), these were insignificantly deteriorated.

In view of the previous studies on VPA, nearly the same controversy, as that mentioned with CBZ, has been found, but studies reporting improvement following VPA administration were much less. Sommerbeck et al. (1977) found reduced psychomotor speed and inhibited visuospatial analytic and synthetic functions following VPA administration, whereas Sonnen et al.

(1977) found that VPA has no psychiatric effect. Barnes and Bower (1975) noted that cognitive beneficial effects have been attributed to VPA administration.

A positive correlation was obtained between deterioration that occurred following VPA administration and its serum level in all tests, but the correlation was statistically significant in tests representing memory and visual memory only (Table 8). This means that as the serum level of VPA rises, an associated deterioration increases. It is noteworthy that all serum level of the drugs within the therapeutic range.

Comparing patients on polytherapy with those on monotherapy within the treated group showed that patients on monotherapy did better in all tested functions, but the results were statistically significant with memory quotient (MQ) only (Table 9).

All previous studies concerned with this subject indicated that reduction in polytherapy is often accompanied by neuropsychological improvement. For example, Reynolds, and Shorovon (1981), reported improvement especially in alertness, concentration, drive, mood and sociability following reduction of number of AEDs taken by epileptic patients.

Seizure variable such as age at onset, duration of epilepsy, frequency of fits, seizure pattern and EEG findings were studied as regard their relation to cognitive functions. A statistically significant positive correlation has been obtained between age at onset of epilepsy in untreated patients and MQ in addition to a subtest of Wechsler memory scale (personal and current information), (Table 10). This means that an early age of onset is associated with a more adverse effect on memory and vice versa.

Almost all previous studies on this subject agree that early age at onset has a poor prognosis on intellectual outcome (Rodin, 1968; Harrison and Taylor, 1976; Bourgeois, 1983; and Farwell et al., 1985) with later age at onset conveying a better prognosis (Kriz, 1978).

In our study, although a negative correlation between duration of epilepsy in untreated and treated patients and performance in all psychometric tests was obtained (except one subtest of WMS measuring mental control), the correlation was statistically significant only in two subtests of WMS, namely digit span and associate learning (Table 11). This means that a longer duration of epilepsy has a more adverse effect on performance in these tests.

To study the effect of frequency of fits on psychometric performance, both treated and untreated patients were included in the study. Statistically significant correlations were obtained between average interval in between fits and performance in all studies psychometric tests in treated patients. The only statistically significant negative correlation was in the test of visual memory and visuo-constructive abilities in untreated patients, while in the other tests, the correlation was positive (Table 12). This negative correlation, which seems to be unexplained, can be attributed to the interaction between different seizure variable.

In the view of previous studies, most authors concluded that increased frequency of fits has a detrimental effect on cognitive function. Chaudhry and Pond (1961) and Hung (1968) found a highly significant relationship between the incidence of mental impairment and seizure frequency. Dodrill and Troupin (1976), in twin studies, found that the twin with more frequent seizures performed worse on tests of cognitive function.

It is noteworthy that the mentioned three variables (age at onset, duration of epilepsy and frequency of fits) are interacting with each other and consequently

their effects on cognitive functions will interact too. For example, a patient may have an early age of onset with a long duration of the disease but with a low frequency of fits. In this case, the assumed adverse effects of early age of onset and long duration may be lessened by the effect of the low frequency of fits. In other cases, late age of onset and short duration were associated with high frequency of fits. So, it was difficult, in this study, to deal with each one of these variables independently and hence, the results may not be so expressive. Nevertheless, the results obtained on studying frequency of fits were so impressive that one can state that frequency of fits is the most important variable of the three mentioned ones that can affect cognitive function.

Depending on history obtained from the patients and their close relatives, the clinical types of epilepsy were determined. Comparing the three groups as regards psychometric performance, the results showed that statistically significant results were obtained only in tests representing memory with the lowest scores in patients having mixed seizures and superiority of patients with complex partial seizures over those with generalized epilepsy (Table 13). In other tests, the results had the same direction but they were not statistically significant.

In previous studies, most investigators found that patients suffering from complex partial seizures show more impairment of memory function than patients suffering from primary generalized seizures, although some studies failed to show any differences (Trimble and Thompson, 1981).

Quadfasel and Pruyser (1955) found that patients with generalized seizures have normal memory function, but patients with psychomotor seizures showed a verbal memory impairment.

In contrast with the above studies, Loiseau et al. (1983) found that memory function in patients with complex partial epilepsy did not differ from controls, but patients with primary generalized epilepsy showed memory impairment. However, in our study, an important point to be mentioned is that patients having complex partial seizures are three only. This little number reduces markedly the value of statistical significance obtained in this study.

From all factors that have been assumed to affect cognitive function in epileptic patients, AED therapy is the only factor that can be put under the physician's control. Therefore, the physician, when dealing with an epileptic patients, must pay considerable attention to AEDs from cognitive effect point of view.

In the view of the results of this study, we can state two important recommendations regarding the number and dose of AEDs used in the treatment of epileptic patients:

- monotherapy must be tried sufficiently before starting polytherapy
- the doses of antiepileptic drugs must be as small as possible.

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Une Etude Clinique- Psychometrique de Fonctions Cognitives chez Les Malades d'Epilepsie d'Origine Première

On a evalué 40 malades d'epilépsie idiopathique, et un groupe de contrôle (20 individus normals et 25 de leurs frères et soeurs non - épileptiques). L'âgè était 12-35 ans. 20 malades n'ont jamais pris de medicaments (groupe 1) et l'autre 20 (groupe 2) prenaient des medicaments antièpileptiques. L'èvaluation était clinique et éléctroéncéphaalographique. Les malades de groupe 1 ont été evalués avant et après un mois de commenber la therapie (Carcamazepine CBZ, ou Valproate VPA, comme monotherapie). L'évaluation psychometrique a compris l'échelle de la mèmoire de Wechsler, un examen de similartités, L'examen Benton (A,C) et L'examen de labyrinthe. On a trouvé que les fonctions cognitives sont dètèriorèes chez les deux groupes de malades. Un mois de therapie avec CBZ a conduit à la détérioration de l'attention, la concentration et du balayage dans l'espace. VPA a conduit à la détèrioration de la mèmoire, l'attention, la concentration et du balayage dans l'espace. Un debut tôt était associé à plus de détérioration de la memoire. La fréquénce de crises était associée à une détérioration de la mémoire et de la pensée abstraite.

دراسة إكلينيكية - سيكومترية للوظائف المعرفية لدى مرضى الصرع الأولى

أجرى هذا البحث على أربعين مريضا من مرضى الصرع الأولى ومجموعة ضابطة تتكون من عشرين شخصا سليما بالإضافة إلى خمسة وعشرين من أشقاء للمرضى لا يعانون من مرض الصرع، تتراوح أعمارهم بين ١٥و ٣٥ سنة من الجنسين.

وقد قسم المرضى إلى مجموعتين، شملت المجموعة الأولى نصف المرضى الذين يتناولون عقاقير مضادة للصرع، أما المجموعة الثانية فشملت نصف المرضى الآخر الذين لم يتعاطوا أى عقاقير مضادة للصرع من قبل. وقد تم إجراء الفحص الطبى وعمل رسم المخ وتطبيق مجموعة من إختبارات القياس النفسى على جميع المرضى والأشخاص الآخرين. وتضم إختبارات القياس النفسى الآتى: (١) إختبار وكسلر لقياس الذاكره، (٢) إختبار المتشابهات، (٣) إختبار بنتون، (٤) إختبار المفاتيح، (٥) إختبار سرعة تتبع المتاهة. كما تم إعطاء عقارى الكاربامازيين (١٥ مجم / كجم / يوم) وفالبروات الصوديم (٣٠ مجم / كجم / يوم) لمدة شهر للمجموعة التى لم يسبق لها تناول أى عقاقير مضادة للصرع مع إعادة تطبيق إختبارات القياس النفسى بعد إنقضاء هذا الشهر، وتم سحب عينة دم من جميع المرضى أثناء إجراء الإختبار لتحديد نسبة العقارين المذكورين بالدم.

وقد تبين أن مستوى أداء المرضى فى جميع الوظائف المعرفية المذكورة (سواء الذين يتناولون علاجا لمرض الصرع أو الذين لا يتناولون العلاج) أقل من أقرانهم فى المجموعة الضابطة، وكذلك أشقاء المرضى، كما أن تناول عقار الكاربامازبيين لمدة شهر قد صاحب تدهور فى الإنتباه والتركيز والتمعن المكانى، وأنه كلما كان سن المريض عند بدء النوبات الصرعية أقل كلما إزداد التأثير السلبى على ذاكرة المريض، وأنه كلما ازداد معدل حدوث نوبات الصرع كلما زاد التأثير السلبى على الذاكرة والتفكير التجريدى، وأن المرضى الذين يعانون من أكثر من نوع من الصرع يحدث لديهم تدهور فى الذاكرة أكثر من المرضى الذين يعانون من نوع واحد فقط.