assessment of cognitive impairment

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Abstract

Objective: assessment of the usefulness of quantitative electroencephalographic analysis as an indicator of cognitive impairment, we examined the correlation between Mini-Mental State Examination (MMSE) scores & Montreal Cognitive Assessment(MoCA) & intelligence quotation (IQ) on one hand and quantitative electroencephalographic (QEEG) power values in elderly patients and healthy controls on the other hand and conducting Stepwise multiple regression analysis to calculate the predicted MMSE score from the QEEG power values.

Methods: We evaluated brain function using QEEG in 29 elderly patients with memory complaints and 29 healthy volunteer and compared their results with their MMSE &MoCA& IQ scores.

Results: in our study we reached to a significant negative correlation between MMSE &MoCA& IQ scores. and QEEG relative theta Θ and delta δ power values and significant positive correlation was found between MMSE &MoCA& IQ scores. and QEEG relative alpha α and beta β power values. And the regression model created using relative QEEG and gender for predicting MMSE scores had an adjusted R^2 of 0.69.

Conclusions: These results suggest that QEEG analysis can be a helpful tool of cognitive testing in patients with abnormalities in memory.

Key words : quantitative electroencephalography, cognitive impairment , Mini-Mental State Examination, Montreal Cognitive Assessment, intelligence quotation , regression analysis.

Introduction

Many attempts done to precisely define cognitive impairment and we can say that cognitive impairment refers to decreased capacity to know the world that is why it has become a global problem that gets more and more attention all over the world.**(Francisco J et al.2013)**.

Dementia as one of the most common causes of cognitive decline is a degenerative disorder leading to decline in memory with impairment of at least one other cognitive function, such as skilled movements (different types of apraxia), language (aphasia) or executive function (e.g., planning, attention and abstract reasoning). It was found that the commonest type of dementia among the elderly people is Alzheimer's disease (AD), which represents 50– 60 % of different dementia cases. **(Jorm and Jolley 1998).**

The possibility of occurrence of AD doubles nearly every 5 years after age of 65. After age of 85 the risk reaches nearly 50 % **(Kim et al. 2012).**

Despite the fact that the diagnosis of the vast majority of cognitive disorders is mainly through clinical examination, and different psychometric tests, the electroencephalography has a role in assessment and following up some of these disorders **(Kotchoubey B et al.2005).**

Patients with cognitive impairment show different changes in their

electroencephalography record (EEG) and the most obvious changes are the slowing of different frequencies and decreased bands of fast waves as alpha and beta bands and increased bands of slow waves as delta and theta bands.

Several researchers have studied the changes detected by QEEG in patients with impaired cognition and by the time it has got more trust as a reliable method for evaluation of different functions of the brain**(Pollock VE et al .1991).**

Although different studies found positive correlation between the increase of relative power of slow frequencies bands theta and delta and the dementia stage , others reported that along the course dementia the relative power of fast frequencies band alpha and beta decreases **(Coben LA, et al 1985).**

Some studies found significant relations between power values of different bands and the scores of different psychometric tests performed by patients with cognitive impairment **(Soininen H et al.1990).**

Different findings of the clinical use of QEEG are waiting for validation by independent investigators and confirmatory clinical follow-up studies , that is why we did our study to validate the usefulness of QEEG as a tool for assessment of cognitive impairment.

Methods:

Subjects

Participants in our study were 58 elderly patients divided into two groups 29 patient in case group with cognitive impairment (mean age, 59.34 ±7.3 SD) and control group of 29 healthy volunteers (mean age, 57.67 ±6.1 SD) who attended the Sohag University Hospital's Neuropsychiatric outpatient clinic or who were admitted to the Hospital between May 2015 and May 2016 due to memory complaints. 31 of participants were males and 27 were females. the neurologist who Clinically diagnosed patients were not involved in the EEG analyses and they relied upon clinical findings and psychometric tests (MMSE &MoCA& IQ) and brain Magnetic resonance imaging (MRI) . We excluded from the study patients with serious physical illness as renal failure , liver cell failure or primary brain tumor , secondary tumor (metastasis) and major cerebrovascular lesion (>1cm). We obtained a written informed consent from the participants after receiving a complete description of the study.

Measurements:

All patients underwent a complete physical and neurologic examination, standard laboratory tests as renal function ,liver function, complete blood count , cerebral MRI, and EEG followed by cognitive assessments by using (MMSE &MoCA& IQ).

Electroencephalography:

All spontaneous EEGs were recorded in a resting awake condition with eyes closed. The technician continuously monitored the subjects' vigilance to make sure that they did not become drowsy. computer-based system (Nihon Kohden) from 16 electrode locations according to the 10/20 system) : Fp1, Fp2, F7, F3, F4, F8, T3, C3, C4, T4, T5, P3, P4, T6, O1, and O2. The EEG was band pass- filtered at 1–30 Hz before digitizing, using a sampling rate of 128 Hz. For each subject, a single 21-second sample was extracted beginning 1 minute after the start of the recording to get a minimum of ten 2-second epochs of the EEG record. If the points were not free of eye blinks, drowsiness, muscle movements, or any other kinds of artifacts, the closest 21 seconds of data were extracted . Frequency analysis was

performed in the range of 0–24 Hz, using a Fast Fourier Transform algorithm with an epoch of 2.0 seconds and resolution of 0.5 Hz.

The EEG variables chosen were the relative power values in four conventional frequency bands: δ (1.0-3.9) ,Θ (4.0–8.0 Hz), α (8.5–14 Hz) and β(14.5–24.0 Hz), and the mean frequency of the averaged spectrum (4.0–24.0 Hz).

The analysis was performed using the Win EEG software package by (MITSAR Brain Diagnostic Solutions). The EEG variables chosen were the relative & absolute power values in four conventional frequency bands: δ(1.0-3.9) ,Θ(4.0– 8.0 Hz),α(8.5–14Hz) and β(14.5–24.0).

Relative power values were calculated as the ratio of the power in 1 frequency band to the total power across all bands and was expressed as a percentage).

Statistical Analysis:

Data was analyzed using statistical software package SPSS for Windows (Version 16.0; SPSS Inc, Chicago, IL). Quantitative data was represented as mean, standard deviation. Data was analyzed using student t-test to compare means of two groups. Qualitative data was presented as number and percentage and compared using Chi square test. Multiple regression analysis was conducted to calculate the predicted MMSE score. Graphs were produced by using STATA program. P values were considered significant if it was less than 0.05, all tests were two-tailed.

RESULTS

The baseline characteristics of the participants in our study are shown in **table (1).**There is no significant difference between males and females in MMSE &MoCA& IQ as shown in **table (2)**and the age is negatively correlated with MMSE & IQ &MoCAin all participants as shown in **table(3).**

Table (1) Characteristics of studied population

Criteria	Cases N=29	Controls N=29	P value
Age (Mean ± SD)	59.34±7.30	57.76±6.10	0.07
Gender Females Males	 14 (48.28%) 15 (51.72%)	 16 (55.17%) 13 (44.83%)	0.04
MMSE (Mean ± SD)	20.86±1.95	27.72±1.29	<0.0001
IQ (Mean ± SD)	73.62±9.42	95.79±5.72	<0.0001
MoCA (Mean ± SD)	21.28±2.55	27.14±0.94	<0.0001

Table (2) The mean MMSE &MoCA& IQ

Criteria	Male	Female	P value
MMSE (Mean ± SD)	24.3 ±4.31	24.29±3.12	0.952
MoCA (Mean ± SD)	24.35±4.05	24.06±2.79	0.202
IQ (Mean ± SD)	84.73±16.04	84.56±10.26	0.861

Table(3) Correlation of age with cognitive functions in all subjects

character	MMSE		MoCA		IQ	
	Pearson's r	P value	Pearson's r	P value	Pearson's r	P value
age	-0.255	<0.0001	-0.213	<0.0001	-0.259	<0.0001

The mean electroencephalographic power values in cases and controls:

There is significant increase in theta (Θ) power in cases in relation to controls in all leads except T3&T4 as shown in **table(4)**

There is significant increase in alpha (α) power in controls in relation to cases in all leads as shown in **table(5).**

There is significant increase in beta (β) power in controls in relation to cases in some leads as shown in **table(6)**

There is significant increase in delta (δ) power in cases in relation to controls in most leads as shown in **table(7)**

Table (4)The mean electroencephalographic power values (theta Θ)

Frequency	Site	Cases Power value (mean ± SD)	Controls Power value (mean ± SD)	P value
Θ Case (3.91-7.32) Controls (4.64-7.32) All (3.91-7.32)	FP1	22.07±1.81	12.45±5.74	<0.0001
	FP2	22.55±3.70	14.00±1.60	<0.0001
	F3	21.90±3.63	8.93±8.39	<0.0001
	F4	20.17±3.13	12.72±9.34	0.0001
	C3	22.66±5.88	7.41±5.67	<0.0001
	C4	16.34±3.17	9.28±5.98	<0.0001
	P3	16.93±4.86	8.55±6.31	<0.0001
	P4	17.27±1.46	7.58±8.38	<0.0001
	O1	16.72±2.58	10.79±9.21	<0.0001
	O2	14.31±3.14	7.76±5.58	<0.0001
	F7	16.41±3.79	13.34±8.25	0.04
	F8	16.90±2.04	12.58±7.65	0.005
	T3	16.93±3.59	11.72±8.40	0.13
	T4	13.76±0.99	11.24±8.21	0.11
	T5	17.09±1.07	10.34±1.13	<0.0001
	T6	18.55±1.38	9.93±5.71	<0.0001
	average	16.55±2.88	10.54±5.43	0.001

Table (5) The mean electroencephalographic power values (alpha α)

Frequency	Site	Cases Power value (mean ± SD)	Controls Power value (mean ± SD)	P value
α Case (8.06-11.23) Controls (7.57-13.43) All (7.57-13.43)	FP1	40.31±6.15	61.10±14.23	<0.0001
	FP2	42.90±6.03	51.48±10.24	0.0003
	F3	45.07±9.08	73.38±21.12	<0.0001
	F4	45.93±7.57	57.38±21.17	0.008
	C3	48.72±7.17	72.93±19.91	<0.0001
	C4	52.24±9.74	70.14±20.86	<0.0001
	P3	48.00±10.24	71.66±19.88	<0.0001
	P4	55.55±4.85	68.72±28.32	0.02
	O1	51.62±7.76	66±19.52	0.0005
	O2	53.93±6.79	72.03±21.20	0.0001
	F7	50.48±8.44	61.90±18.25	0.003
	F8	54.07±4.75	59.03±21.21	0.02
	T3	51.38±10.81	61.21±21.61	0.03
	T4	52.44±5.23	68±18.51	0.0001
	T5	49.21±8.68	68.24±17.49	<0.0001
	T6	53.45±4.11	67.55±21.19	0.0009
	Average	49.71±7.12	65.67±20.61	<0.0001

Table (6)The mean electroencephalographic power values (beta β)

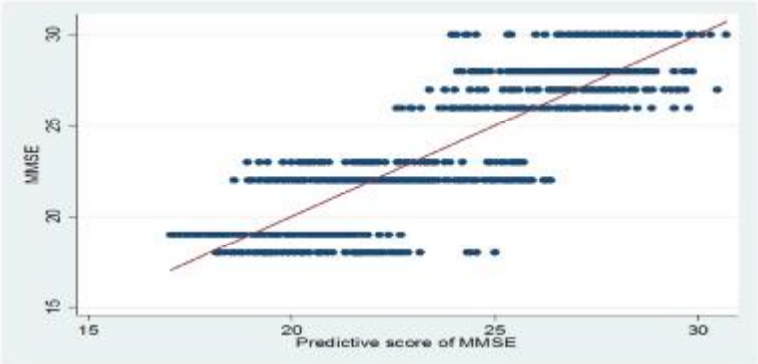
Frequency	Site	Cases Power value (mean ± SD)	Controls Power value (mean ± SD)	P value
β Cases (13.92-18.07) Controls (13.92-19.78) All (13.92-19.78)	FP1	20.59±5.24	20.76±13.98	0.95
	FP2	18.68±4.19	27.79±9.63	0.1
	F3	19.41±5.93	14.62±13.13	0.08
	F4	18.44±3.24	25.48±18.78	0.07
	C3	14.79±1.21	16.00±14.71	0.66
	C4	17.66±4.87	15.20±14.36	0.39
	P3	17.55±6.51	16.55±14.38	0.05
	P4	17.28±2.53	20.66±4.73	0.048
	O1	17.24±1.99	17.90±15.50	0.02
	O2	20.93±4.50	17.13±14.97	0.02
	F7	18.79±5.51	20.34±15.27	0.61
	F8	18.34±3.06	23.97±20.47	0.15
	T3	19.21±5.63	22.38±18.96	0.39
	T4	22.17±3.06	16.93±13.06	0.04
	T5	16.55±2.16	17.58±15.17	0.72
	T6	16.76±3.75	17.38±14.28	0.82
	average	18.41±4.51	19.44±16.12	0.196

Table(7) The mean electroencephalographic power values (delta δ)

Frequency	Site	Cases Power value (mean ± SD)	Controls Power value (mean ± SD)	P value
delta δ cases (1.46-3.91) Controls (1.46-3.91) All (1.46-3.91)	FP1	9.41±1.40	5.52±2.89	0.001
	FP2	10.66±1.65	6.10±3.35	0.001
	F3	8.83±4.26	2.82±1.89	0.001
	F4	7.66±4.48	3.83±2.10	0.001
	C3	11.83±3.39	4.10±2.71	<0.0001
	C4	12.62±1.68	6.48±3.28	<0.0001
	P3	8.51±8.15	3.45±2.11	<0.0001
	P4	9.89±4.97	2.86±2.82	<0.0001
	O1	10.83±5.02	4.89±2.51	<0.0001
	O2	11.00±3.98	4.48±1.62	<0.0001
	F7	9.31±6.55	4.45±1.90	<0.0001
	F8	8.28±2.07	4.20±1.37	<0.0001
	T3	10.51±2.67	5.07±2.67	<0.0001
	T4	9.83±2.80	3.79±1.66	0.001
	T5	8.17±5.97	3.86±1.98	0.001
	T6	8.03±3.23	5.34±3.03	0.001
	average	7.26±2.85	4.85±2.75	0.001

The regression analysis is created by extracting significant variables for predicting MMSE scores had an adjusted R2 of 0.69 (P <0.001)

Figure (1) Scatter diagram showing correlation between the score of Mini-Mental State Examination (MMSE) and the predictive score of MMSE derived from the electroencephalographic power values (r=0.85, p<0.0001).



Disscusion

Many studies have reported on the EEG changes associated with cognitive impairment. In particular, QEEG has been receiving much attention as a reliable method to evaluate brain function quantitatively (Hooijer et al., 1990).

In our study we compare patients with a complaint of cognitive impairment and controls who are healthy volunteers. We aim at assessment of the utility of QEEG analysis as an objective electrophysiological indicator of cognitive impairment by comparing different power values in cases and controls and finding relations between power values and psychometric tests as MMSE &MoCA& IQ.

In our study the The MMSE &MoCA& IQ scores were significantly negatively correlated with age (r=-0.255 p= <0.0001) & (r= -0.213 p=<0.0001) & (r= -0.259 P= <0.0001) respectively this result is in agreement with (Joji et al., 2005) and (Ji-Sun et al ., 2012).

There was no significant difference in the scores of psychometric tests in relation to sex this result is in agreement with (Joji et al ., 2005) and (Gawel et al ., 2009) and (Christian et al ., 2008).

Although, it was revealed that AD is more prevalent in females (Andersen et al. 1999) but our result could be explained by larger number of males participating in our study and presence of other types of dementia rather than Alzheimer .

In our study we found that there was significant global increase in theta (Θ) and delta (δ) relative powers in patients in comparison with controls (16.55±2.88 vs 10.54±5.43 respectively, p value0.001) & (7.26±2.85 vs 4.85±2.75 respectively , p value 0.001) and this result is in agreement with(Francisco et al .,2013)& (Chiaramonti et al ., 1997) , (Rodriguez et al ., 1998) and (Kowalski et al.,2001) and this could be explained as theta wave is thought to be involved in memory, synaptic plasticity, and long-range synchronization (Vertes 2005) and(Von Stein et al., 2000).

Furthermore, increased theta wave activity is thought to reflect drowsy mentality (Fernandez et al., 1999) and (Lee et al., 2006); also increased theta activity has been associated with reduced cerebral blood flow (Rodriguez et al., 1999) and (Mattia et al., 2003) and diminished cholinergic neuronal activity (Kai et al., 2005).These mechanisms have pathogenic relevance in the course of dementia on the other hand increase in delta relative power in demented patients occurred due to progressive cortical disconnection by slow conduction along cortico-subcortical pathways leading to memory and recall problems in those patients (Christian et al ., 2008).

In contrast to our result Some studies as (Ji- Sun et al ., 2012) showed that there was no change in delta (δ) relative power in patients with dementia in comparison with controls and this occurred as delta wave may be affected late in demented patients and this study did not include late stages of the disease (Ji-Sun et al ., 2012).

Also we found that there was significant global decrease in alpha (α) relative power in patients in comparison with controls (49.71±7.12 vs 65.67±20.61 respectively , p value <0.0001)and this result is in agreement with (Francisco et al.,2013) and (Joji et al., 2005) and this could be explained as the major source of alpha activity is thought to lie in the reciprocal relay activity of thalamic and

cortical neurons, and in the activity of intercortically projecting neurons (Steriade et al., 1990)and(Lopes da Silva, 1991).

Cortical disconnectivity and thalamic atrophy are, however, recognized neuropath logical changes of AD that have recently been described also for the MCI stage by magnetic resonance based diffusion tensor imaging and morphometry (Pennanen et al., 2005),(Chen et al ., 2006) .(Rossini et al., 2006) found that there is decrease in alpha relative power particularly in parietal & occipital leads in patients in comparison with controls and correlate it with progression of Mild cognitive impairment to Alzheimer disease but the global decrease in alpha average power in our result could be explained by heterogeneity of study subjects .

In contrast to our result few studies as (Ji-Sun et al ., 2012) showed that there was no change in alpha (α) relative power in patients with dementia in comparison with controls and this occurred as alpha wave may be significantly affected late in demented patients and this study did not include late stages of the disease . (Ji-Sun et al ., 2012) .

We found that there was decrease in regional beta (β) relative power mainly in occipital ,parietal

,temporal leads in patients in comparison with controls although the global decrease in beta (β) relative power did not reach statistical significance (18.41±4.51 vs 19.44±16.12 respectively , p value 0.196) and this result is in agreement with (Francisco et al .,2013),(Ji-Sun et al ., 2012) and (Christian et al ., 2008).

This could be understood through the fact that beta wave is associated with functional capacity in global cognition, memory, visuospatial function, and attention, and beta power decreased mainly at the temporal, occipital and parietal leads. (Ji-Sun et al ., 2012).

In (Joji et al., 2005) there was no significant decrease in average beta power in patient in comparison with controls and this occurred as a result of difference in the classification of frequencies for QEEG analyses and the heterogeneity of study subjects.

In our study The regression analysis created by extracting significant variables for predicting MMSE scores had an adjusted R2 of 0.69 (P<0.001) which was higher than that in (Joji et al., 2005) R2 of 0.471 (P 0.001) . also we found significant correlation between the score of Mini- Mental State Examination (MMSE) and the predictive score of MMSE derived from the electroencephalographic power values (r=0.85, p<0.0001) so QEEG findings could be useful tool for assessment of cognitive impairment .

Our study has some limitations that need to be addressed . First, Findings reported here are based on a sample size of 58 participants,Future studies should focus on a larger pool Secondly, the AD and NC groups had a greater non statistically significant proportion of male subjects. although, it was revealed that AD is more prevalent in females(Kim et al.,1999), a few authors have stated that the prevalence was higher in males (Wang et al., 2000).

Thirdly , the use of few electrodes in EEG recording which gave us limited information about each lobe of the brain so in the next studies we will need larger number of electrodes.

Conclusion:

we find that there is increase in delta and theta power values in patients with cognitive impairment in comparison

with normal people, also we find that there is decrease in alpha and beta power values in patients with cognitive impairment in comparison with normal people, and there is positive correlation between psychometric test results and alpha and beta power values in both groups and there is negative correlation between psychometric test results and theta and delta power values in both groups and we were able to predict more than two thirds of MMSE scores by using power values of EEG different frequencies through regression analysis so we can conclude that QEEG is a reliable,noninvasive ,simple, objective electrophysiological indicator of cognitive impairment.

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