Assessment of Cognition in Myasthenia Gravis

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Abstract

Purpose: We performed the study to find if there is cognitive impairment in patient with MG and if there is any relationship between its. Methods: We performed clinical evaluation, P300 for 20 cases presenting with MG and 20 normal control subjects. Results: There was statistically significant discrepancy between MG patients and controls demonstrated by clinical cognitive examination and P300 latency (p = 0.007). Conclusion: In contrast with the control group, MG patients had associated with cognitive impairment

KeyWords: Myasthenia Gravis; Cognition; P300.

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Introduction:

Myasthenia gravis (MG) is an immune-mediated neuromuscular junction (NMJ) disorder characterized by muscle fatigue and weakness peaking at the end of the day. MG is mainly caused by antibodies (Abs) against muscle nicotinic acetylcholine receptors (nAChRs) at the postsynaptic membrane resulting in depletion of acetylcholine (ACh) at the NMJ. (1) While the prevailing clinical finding of MG is muscle fatigue and weakness, rarely patients may develop additional nervous system manifestations and syndromes as memory difficulties. (2, 3, 4)

Decreased sleep efficiency leads to cognitive impairment, and psychiatric disorders. Cognitive dysfunctions are common consequence of reduced oxygen saturation during sleep (due to sleep dysfunction) or as a sequence of central abnormities (due to brain ACh deficiency). (5)

Subjects and Methods

This study is a cross-sectional case control study with twenty patients (15 females and 5 males) with a mean age 30.65 ± 13.99 presenting with myasthenia gravis (MG) diagnosed (clinically and electrophysiological).

The age and sex of twenty matched healthy controls (15 females and 5 males), with a mean age 28.90 y ± 8.86.

All included patients and controls subjected to the following P300 parameters.

Excluded from the study patients with any associated medical or metabolic disorder considered to impair cognition, such as hepatic or renal dysfunction, thyroid or parathyroid disease

All included patients subjected to the following:

1) Neurological examination:

Mini mental state examination (MMSE):

MMSE was used to check the time and position orientation of the subject (visuospatial orientation), instant recall, short-term memory, serial reverse spelling subtractions, constructing capacities (copying a design), language usage.

The total score is 30, the score 24 is used to detect cognitive functions impairment. **(6)**

2) P300:

The P300 was carried out for both patients and control groups. Nihon KhodenNeuropack machine, Japan was used to record the responses. The P300 response was identified as the most positive waveform to the target tones occurring after 250 msec and before 600 msec. The responses were shown on a monitor and could be printed out. The P300 latency and amplitude were collected for each subject in order to measure any considerable abnormality.

For most adult subjects aged between 20 and 70 years, the P300 latency ranged between 250-600 msec. **(7)**

Methodology of Statistics

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between groups were done using unpaired t test in normally distributed quantitative variables while non-parametric Mann-Whitney test was used for non-normally distributed quantitative variables. (8) For comparing categorical data, Chi square (2) test was performed. Exact test was used instead when the expected frequency is less than 5. (9) P-values less than 0.05 were considered as statistically significant.

Results

A- **Descriptive results:**

1- Age:

The mean age of patients was 30.65 ± 13.99 y and control was 28.90±8.86 y.

Table (1): Comparison between patients and control as regard age

	Patients					Control					P value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Age	30.65	13.99	32.00	10.00	50.00	28.90	8.86	32.00	15.00	40.00whi	0.602

2- Sex:

Table (2): Comparison between patients and control as regard sex

		Patients		Control		P value
		Count	%	Count	%	
Sex	Female	15	75.0%	15	75.0%	1
	Male	5	25.0%	5	25.0%	

B- **Clinical Results:**

1- **Duration of the illness**:

The mean duration of illness 3.28 ± 2.24 y.

Table (3): Duration of illness

	Patients				
	Mean	SD	Median	Minimum	Maximum
Duration	3.25	2.24	2.50	1.00	7.00

Mini mental state examination (MMSE):

Patients were subjected to MMSE. All patients score ranged from 28-30.

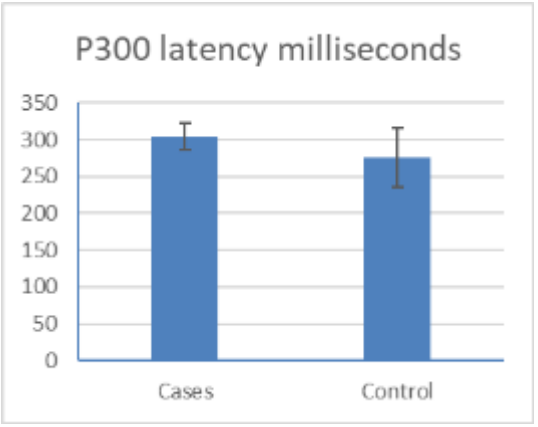
C- **P300 results**:

The means and standard deviations of P300 latency and amplitude for patients with MG and control group are illustrated in Table 4.

Table (4): Comparison between patients and control as regard P300 latency and amplitude

	Patients					Control					P value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
P300 latency milliseconds	303.90	18.02	305.55	275.30	330.30	275.35	39.76	261.70	233.60	342.90	0.007
P300 amplitude µv	7.79	3.29	7.05	3.60	14.10	6.53	6.15	6.80	0.00	17.90	0.426

Figure (1): Comparison between patients and control as regard P300 latency



There was significant relationship between (Age, clinical data &Mini mental state examination) and P300 data in MG patients.

Discussion

The current study was undertaken to analysis the presence of cognitive dysfunction in patient with MG and to find any relation between both in MG patients. In this study as regards cognitive function assessment clinically by using mini mental state examination (MMSE) & electrophysiology by using P300, there was statistically significant discrepancy between MG patients and controls.

Also, Paul et al. in their study analyzed the methods and results of previous researches that studied cognition in MG and reported that mild impairments were observed in learning measures. Authors suggested that these results need to be repeated with enough monitoring of possible confounds before any conclusions on cognition e.g. limited sample size, no exclusion for patients with diminution of vision, insufficient mood assessment, and poor control for the use of prednisone. (10)

While, Paul et al. reported that significant cognitive

dysfunctions in myasthenia gravis patients were not evident and reported that cognitive performances of the MG group were not related to disease duration. (11)

Tüzün reported that most of the MG disease inducing anti-AChR antibodies bind to the α1subunit of AChR. α 9 was found in different locations of CNS (cortex, hippocampus, midbrain, and brainstem). Preliminary studies showed anti- α 9 antibody in serum samples of some of the mice with experimental autoimmune myasthenia gravis (EAMG). So, he concluded that myasthenic serum anti-AChR antibodies can cross-react with the CNS target antigen AChR a9-subunit leading to CNS symptoms. (12)

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