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Clinical and Psychological Disturbances of Myasthenia Gravis: How Anxiety, Sleep Quality, and Thymectomy Interact

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Abstract: Background: Myasthenia gravis (MG) is an autoimmune neuromuscular disease characterized by fatigue and muscle weakness. Previous research has noted a high incidence of psychological problems, particularly anxiety and depression, as well as alterations in sleep quality among patients with MG. The aim of this study was to assess depression, anxiety, sleep problems, and fatigue in individuals with MG and to analyze the relationships among these variables, as well as to determine the influence of corticosteroid use and thymectomy. Methods: The sample consisted of 72 participants, 42 belonging to the clinical group with MG and 30 healthy participants to the control group. The instruments used were Hospital Anxiety and Depression Scale (HADS), Pittsburgh Sleep Quality Index (PSQI), and Fatigue Severity Scale (FSS). Results: The results showed that MG patients exhibited higher levels of fatigue, anxiety, depression, and poorer sleep quality compared to the control group ($p < 0.05$). Significant differences in sleep quality and anxiety levels were observed between thymectomized and non-thymectomized patients. Additionally, a positive correlation was found between anxiety symptoms and sleep quality. Conclusions: The study demonstrated the presence of anxious and depressive symptoms in patients with MG, as well as poorer sleep quality and increased fatigue, suggesting that MG affects not only neuromuscular function but also the psychological well-being of patients.

Keywords: myasthenia gravis; psychological impact; sleep impairment; fatigue; emotional wellbeing

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1. Introduction

Neuromuscular diseases are conditions that affect the muscles and the nerves controlling them, leading to issues in both the nervous system and the musculature of the affected person. These conditions are characterized by progressive loss of strength, fatigue, and in some cases, muscular dystrophy [1,2].

Among these diseases, myasthenia gravis (MG) is the most common neuromuscular junction disease, accounting for approximately 80% of cases [3]. It is a chronic autoimmune disease in which antibodies target the acetylcholine receptors or other postsynaptic membrane molecules at the neuromuscular junction [4,5], leading to generalized or localized muscle weakness and fatigue.

This weakness primarily affects the extraocular muscles, causing typical symptoms such as diplopia (double vision) and intermittent ptosis (drooping of the upper eyelid). The bulbar musculature can also be involved, resulting in reduced facial expression, dysarthria (speech difficulties), and dysphagia (swallowing weakness) [5,6], as can the proximal muscles of the limbs and trunk, including the neck. In severe cases, respiratory muscles may be affected, leading, in some cases, to myasthenic crises [6].

Existing treatments for this pathology focus on acetylcholinesterase inhibitors (such as pyridostigmine) and immunotherapy, which includes corticosteroids and immunosuppressive or immunomodulatory drugs. Long-term drug treatment is necessary for nearly all patients with myasthenia gravis [4,5]. Another treatment option is surgery to remove the thymus gland, called thymectomy, due to the high percentage of thymic abnormalities in these patients, such as thymoma or thymic hyperplasia [7]. Despite the remarkable clinical improvement observed in many cases following this technique [8], it is not recommended in all patients and drugs do not always achieve symptomatic stability. Consequently, the disease can have a significant impact on patients' lives, negatively affecting physical, mental, and social aspects. This often leads to a progressive deterioration in quality of life, with reductions in functionality in a number of domains [9].

Furthermore, in addition to the physical symptoms, MG patients often face mental health challenges such as higher levels of depression, anxiety, loneliness, and isolation compared to the general population [10], further exacerbating the decline in their overall well-being. Studies report a high prevalence of depression in MG patients, ranging from 3% to 75% [11,12]. Other research has indicated a higher prevalence of depression (17%) compared to global estimates in the adult population of 5.4% and 4.4% [13]. Anxiety is also notably common, with some studies reporting that between 30–50% of MG patients exhibit clinically significant anxiety symptoms [11,14].

Beyond the psychological effects, MG patients often experience additional symptoms, such as sleep disturbances [15]. Previous studies have identified a higher prevalence of daytime sleepiness [16] and limb movements during sleep among people with MG [17]. However, it is important to mention that sleep issues could be related to corticosteroid use rather than the disease itself [18].

Research has shown correlations between poor sleep quality and the intensity of depressive and anxious symptoms in patients with MG [19,20]. Moreover, studies have concluded that poor sleep quality and emotional distress can exacerbate fatigue in individuals with MG, creating a cycle that further diminishes patients' quality of life [21]. This interplay between sleep quality, emotional well-being, and fatigue highlights the importance of comprehensive treatment approaches that address both physical and mental health aspects in managing MG.

To sum up, considering that severe and prolonged mental stress and emotional arousal can affect immune function [22], the aim of this study was to assess depression, anxiety, sleep problems, and fatigue in people with MG and determine whether the use of corticosteroids and thymectomy have an influence on these conditions. Finally, the study aimed to examine the relationship between these variables.

2. Materials and Methods

2.1. Design

A cross-sectional research study was carried out using convenience sampling. Data were collected from two different groups: a clinical group of patients with a diagnosis of MG and a healthy control group at a single point in time. Participants were recruited based on their accessibility and willingness to participate.

2.2. Sample

The study involved a sample of 72 people, 42 with MG, recruited from multiple sources, including association from Spain, Asociación Miastenia de España (AMES), and, from Argentina, Asociacion Miastenia Gravis Rosario (AMiGRo) and Asociación Santafesina de Miastenia (ASaMi) as well as Cruces University Hospital, Bilbao, Spain. The rest of the sample were healthy volunteers without this pathology. They were matched to the clinical group for age, years of education, and sex. This matching allowed more accurate comparisons between the groups.

The clinical group, composed of patients, had a mean age of 47.60 years (SD = 9.68), while the control group consisted of participants with a mean age of 48.47 years (SD = 9.40).

Both groups included people from Spain and Latin America. The chi-square test was employed to ascertain whether there were any significant differences between the two groups in the qualitative variables. The results indicated that there were no statistically significant differences in between the groups χ^2 (1) = 0.411, p = 0.521 and age χ^2 (5) = 7.231, p = 0.204.

For the clinical group, the inclusion criteria were to have an age between 18 and 75 years, to present the diagnosis of MG by a neurologist, and to be of Spanish nationality or from a Spanish-speaking country. For the control group, the inclusion criteria were an age between 18 and 75 years and being of Spanish nationality or from a Spanish-speaking country.

2.3. Instruments

After the collection of socio-demographic data through an ad hoc questionnaire, the following variables were included in the assessment protocol: anxiety-depression symptoms, sleep quality, and fatigue.

The Hospital Anxiety and Depression Scale (HADS) [23,24] was used to assess anxiety and depression levels. This scale consists of 14 items divided into two subscales, with seven items addressing anxiety and the other seven focusing on depression. The standard cut-off score for the HADS is 8 for both anxiety and depression. The internal reliability results were satisfactory (α = 0.90).

The Pittsburgh Sleep Quality Index (PSQI) [25,26] provides seven scores that assess different aspects of sleep quality: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. The Spanish version demonstrated good internal consistency in the general population, with a Cronbach's α coefficient of 0.81.

The Fatigue Severity Scale (FSS) [27,28] was used to measure fatigue levels. The scale consists of nine Likert-type items, each offering seven response options ranging in intensity from 1 to 7. In terms of reliability, the data indicated a Cronbach's alpha of 0.870.

2.4. Procedure

Considering the characteristics of the target population, convenience sampling was carried out. Participants were recruited through the AMES, AMiGRo, and ASaMi associations, as well as from the Cruces University Hospital, Bilbao, Spain, and included individuals from various Spanish-speaking countries. Participants in the clinical group were diagnosed by a neurologist.

The study was carried out online through the Google Forms platform, which required the questionnaires to be specifically adapted for this modality to ensure clarity and ease of use for participants. In the control group, tests were administered in the same way as for the clinical group. The total duration of the study was one year (April 2021–April 2022).

2.5. Ethical Considerations

It is stated that this study complied with the criteria of the Psychologist's Code of Ethics, ensured compliance with the international standards proposed in the Declaration of Helsinki, and was approved by the Research Ethics Committee of the University of Deusto (ETK-54/21-22).

2.6. Statistical Analysis

This study used SPSS (Statistical Package for Social Sciences) version 28.0, a software product developed by IBM Corporation, based in Armonk, New York, USA, to perform the analyses. The normal distribution of the sample was tested using the Kolmogorov–Smirnov test. The direct scores were converted into z-scores to carry out the analyses.

In order to analyze the differences between groups with respect to sociodemographic and clinical data, the Chi-square statistic and the Mann–Whitney U test were used for

categorical and quantitative variables, respectively. To analyze the differences in regard to psychological assessment, the Mann–Whitney U test was used for intergroup differences.

Finally, to analyze the relationships between variables, Spearman's Rho correlation analysis and simple linear regression test were employed to assess the influence between related variables. Values with a *p*-value of less than 0.05 were accepted as significant (95% confidence interval).

3. Results

3.1. Variations in Sociodemographic and Clinical Characteristics

A description of the main socio-demographic and clinical indicators of the sample can found in Table 1.

Table 1. Sociodemographic and clinical characteristics of the total sample.

Variable	Clinical Group (*n* = 42)	Control Group (*n* = 30)	*U* χ^2	*p*-Value
	M (*SD*)/*n* (%)	*M* (*SD*)/*n* (%)		
Gender			0.411	0.521
Women	36 (85.7%)	24 (80.0%)		
Men	6 (14.3%)	6 (20.0%)		
Age (years)	47.60 (9.68)	48.47 (9.40)	662.500	0.710
Country			7.231	0.204
Spain	16 (38.1%)	17 (56.7%)		
Argentina	8 (19.0%)	8 (26.7%)		
Mexico	9 (21.4%)	1 (3.3%)		
Uruguay	7 (16.7%)	3 (10.0%)		
Other	2 (4.8%)	1 (3.3%)		
Years with the disease	10.27 (8.05)	-		
Age of symptom onset	32.62 (13.48)	-		
MG crisis suffered	2.53 (2.86)	-		
Hospitalizations for MG	2.59 (3.13)	-		
Corticosteroids				
Yes	16 (38.1%)	-		
Thymectomy				
Yes	18 (42.9%)	-		

Note. *n* = number of participants; *M* = mean; *SD* = standard deviation; *U* = Mann–Whitney U; χ^2 = chi-squared; MG = myasthenia gravis.

3.2. Differences in Recognition Between Clinical and Control Group

Differences between the clinical and control groups across all assessed variables are presented in Table 2 and were demonstrated to be significant for anxiety ($p = 0.017$), depression ($p = 0.001$), fatigue ($p < 0.001$), and sleep quality ($p < 0.001$). Patients with MG consistently reported higher scores in each of these domains compared to the control group, indicating greater levels of psychological distress and neurophysiological impairment in the clinical population. These differences had a high effect size for fatigue and sleep quality, and a medium one for anxiety and depression.

Considering the different indicators provided by the PSQI test, the analysis showed significant differences between the clinical group and the control group in several dimensions. Latency ($p < 0.001$) and dysfunction ($p < 0.001$) presented the largest differences with large effect sizes ($r = 0.475$ and $r = 0.513$, respectively). There were also significant differences in quality ($p = 0.004$), efficiency ($p = 0.041$), and disturbances ($p = 0.005$), with medium effect sizes. No differences were found in duration or medication between two groups.

Table 2. Comparison of psychological and petrophysical performance between groups.

Variable	Clinical Group (n = 42) Mdn (Range)	Control Group (n = 30) Mdn (Range)	U	Z	p	r
HAD-A	9.00 (14)	7.50 (12)	421.500	−2.393	0.017 *	0.282
HAD-D	6.00 (12)	3.00 (14)	343.500	−3.290	0.001 *	0.388
PSQI	10.00 (17)	5.00 (16)	250.000	−4.353	<0.001 **	0.513
Quality	1.00 (2)	1.00 (2)	388.500	−2.892	0.004 *	0.341
Latency	2.00 (3)	1.00 (2)	289.500	−4.034	<0.001 **	0.475
Duration	1.00 (3)	1.00 (3)	618.500	−0.142	0.887	0.017
Efficiency	0.00 (3)	0.00 (2)	484.500	−2.043	0.041 *	0.226
Disturbances	2.00 (3)	1.00 (3)	400.500	−2.806	0.005 *	0.331
Medications	1.00 (3)	1.00 (2)	470.000	−1.917	0.055	0.241
Dysfunction	2.00 (3)	1.00 (3)	232.500	−4.353	<0.001 **	0.513
FSS	44.00 (54)	20.50 (59)	291.500	−3.869	<0.001 **	0.456

Note: n = number of participants; Mdn = median; U = Mann–Whitney U test; Z = z-scores; * $p \leq 0.05$; ** $p \leq 0.001$; r = r coefficient (effect size); HAD-A = Hospital Anxiety and Depression Scale—Anxiety; HAD-D = Hospital Anxiety and Depression Scale—Depression; FSS = Fatigue Severity Scale; PSQI = Pittsburgh Sleep Quality Index.

For the effects of corticosteroid use, the analyses showed that there were no significant differences in any of the variables studied. However, when thymectomy was analyzed, differences were observed for anxiety (U = 110.5, p = 0.007), with higher anxiety levels in the non-thymectomy group (Mdn = 25.90) compared to the thymectomy group (Mdn = 15.64), and for sleep quality, there was a significant difference between groups (U = 129.5, p = 0.027), with better sleep quality in the thymectomy group (Mdn = 16.69) compared to the non-thymectomy group (Mdn = 25.10). For depression (U = 177.5, p = 0.325) and fatigue (U = 160.5, p = 0.158), there was no significant difference between groups.

Finally, to determine the relationship between the variables sleep quality, fatigue, depression, and anxiety in the clinical group, Spearman's bivariate correlation analyses were carried out (see Table 3). The results showed a positive relationship between anxiety and sleep quality. To determine the relationships among these variables, a linear regression was performed. The model explained 22.9% of the variability in sleep quality, with a moderate correlation (R = 0.479). A higher anxiety score was associated with a decrease in sleep quality, as indicated by a coefficient of 0.563. The analysis showed that the model was statistically significant (F = 11.892, p = 0.001), confirming that as anxiety levels increase, sleep quality tends to worsen.

Table 3. Correlations between the variables sleep quality, fatigue, anxiety, and depression in MG.

	PSQI	FSS	HADS-A	HADS-D
PSQI	1.00			
FSS	0.269	1.00		
HAD-A	0.413 **	0.148	1.00	
HAD-D	0.302	−0.001	0.468 **	1.00

Note: HAD-A = Hospital Anxiety and Depression Scale—Anxiety; HAD-D = Hospital Anxiety and Depression Scale—Depression; FSS = Fatigue Severity Scale; PSQI = Pittsburgh Sleep Quality Index (PSQI). ** $p \leq 0.001$.

4. Discussion

The diagnosis of a rare disease can be a stressful time, with increased levels of anxiety, depression, and fatigue, increasing the likelihood of the disease worsening and impacting the process of adjusting to living with the diagnosis [29,30]. Therefore, the aim of this study was to examine anxiety, depression, fatigue levels, and sleep quality in patients with MG compared to a control group without this pathology. Additionally, we aimed to assess the impact of specific treatments within the MG group, specifically evaluating the effects

of corticosteroid use and thymectomy on these psychological and neurophysiological variables. Finally, the study sought to explore the relationships among anxiety, depression, fatigue, and sleep quality in the MG population.

As anticipated, the results showed that the MG group had significantly higher scores in sleep disturbances, fatigue, anxiety, and depression compared to the control group. These findings are consistent with previous studies that have reached similar conclusions [14,15]. However, contrary to expectations, no significant differences were found regarding corticosteroid use within the MG group. This means that in the present study, the presence of fatigue, emotional disturbances, and sleepiness is not due to the use of this drug.

In these patients, in addition to pharmacological treatment, thymus removal is also used in some cases. This technique has shown improvements in both symptomatology and quality of life [8,9]. In this study, it is observed that patients who have undergone thymectomy have lower levels of anxiety and better sleep quality than those who have not undergone this intervention. With regard to fatigue and depression, although the results were not statistically significant, a reduction in the prevalence of these symptoms was also observed in thymectomized patients. However, it is noteworthy that this technique is not applicable to all patients, for example, it is not recommended for older patients [31]. Therefore, the results may be influenced by the age and gender of patients who have not undergone thymectomy compared to those who have. It would be advisable to control this variable longitudinally in each patient in order to obtain more accurate results.

Analyzing the neurophysiological variables in more detail, the PSQI test assesses various aspects of sleep, including the time it takes a person to fall asleep (latency), the perception of sleep quality, or the presence of interruptions during the night. In the results obtained, it was found that participants had an increase in sleep latency, indicating that they took longer to fall asleep. In addition, dysfunction in sleep quality and efficiency is manifested in the perception of poor sleep, which may be associated with problems such as fatigue and impaired general well-being [21,22]. Finally, sleep disturbances reflect a higher frequency of night-time awakenings and difficulties in maintaining sleep, highlighting the need for interventions that address these problems and improve sleep quality in this population.

Continuing the analysis to gain a deeper understanding of the relationships among the variables, we observed that in MG group, correlation analyses showed a relationship between anxiety levels and sleep quality. Furthermore, linear regression analyses show that anxiety explains 22.9% of the variability in sleep quality, and this impact is statistically significant. As anxiety levels increase, sleep quality tends to worsen. The same is confirmed by other studies which also find a positive relationship between sleep quality and anxiety in the general population [32]. Furthermore, other studies focusing on the target population find that sleep disorders and emotional problems may be associated with more severe symptoms in these patients, affecting their quality of life [19,21,33]. This highlights the importance of interventions aimed at improving mental health and sleep quality in these patients.

Limitations and Strengths

Despite the significant findings of this study, several limitations should be acknowledged. First, the sample size is relatively small, which is common in rare disease research and may affect the robustness of statistical analyses and limit the generalizability of the results.

Another limitation is the cross-sectional design. This provides only a momentary description of the sociodemographic and clinical characteristics of the participants, without establishing a causal relationship. A longitudinal study could better examine the long-term effects of treatments such as thymectomy on disease progression and quality of life, and could clarify whether the observed associations persist over time or are transient. In addition, although the study takes into account the treatments received, an extension of the list of drugs included could provide a deeper insight into the effects of treatment.

Finally, the study used convenience sampling, recruiting participants mainly from associations and hospitals in Spain and Latin America. Although efficient, this method may introduce selection bias and limit the generalizability of the results.

Despite these limitations, this study provides useful information about the experience of people affected by MG. Additionally, it includes both a clinical group of patients with MG and a control group. This allows meaningful comparisons between the two groups while controlling for important socio-demographic factors such as age, gender, and education. The inclusion of participants from both Spain and Latin America increases the diversity of the sample. This makes the findings more relevant to a broad, Spanish-speaking population. These strengths contribute to the study's comprehensive approach to understanding the clinical and psychosocial aspects of MG, providing important insights for future research and clinical practice.

5. Conclusions

In conclusion, the present study highlights that patients with MG experience significantly higher levels of anxiety and depression, as well as poorer sleep quality and increased fatigue, when compared to healthy subjects. Notably, these psychological factors do not appear to be influenced by the use of corticosteroids. Conversely, patients who underwent thymectomy exhibited improvements in these areas, indicating a potential therapeutic benefit of this surgical intervention. Additionally, a significant relationship was found between anxiety and sleep quality, suggesting that these factors may be interrelated and could contribute to the overall symptomatology of MG. Therefore, it is crucial to address these psychological dimensions in the management of MG, as they may play a significant role in exacerbating the disease's symptoms and affecting patients' quality of life. By considering both the physical and psychological components of the disease, the specialists can offer more comprehensive care that improves patient outcomes. Moreover, these findings underscore the importance of incorporating psychological assessments and interventions as part of routine care for MG patients. Future research should explore the long-term effects of treatments on mental health and investigate the mechanisms linking anxiety, sleep disturbances, and fatigue to develop more targeted interventions for improving quality of life in this patient population.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Research Ethics Committee of the University of Deusto (ETK-54/21-22 on 26 April 2022).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The datasets presented in this article are not readily available because they belong to the University of Deusto. Requests to access the datasets should be directed to the corresponding author (Maddalen García-Sanchoyerto).

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