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NEUROIMAGING BIOMARKERS FOR ASSESSING THE PROGRESSION OF MYASTHENIA GRAVIS

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Abstract: This thesis explores the use of neuroimaging biomarkers as essential tools for assessing the progression of Myasthenia Gravis (MG). MG is a chronic autoimmune disease that affects neuromuscular transmission, resulting in muscle weakness and fatigue. Assessing the progression of MG is fundamental for clinical management and for personalizing treatment. The thesis investigates how advanced neuroimaging techniques, such as magnetic resonance imaging (MRI), positron emission tomography (PET) and MR spectroscopy (MRS), can provide objective and quantitative insights into the brain changes associated with MG. It also discusses the challenges and future prospects in the clinical use of these biomarkers.
Keywords: Myasthenia Gravis; Biomarkers; Neuroimaging

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune neuromuscular disease characterized by weakness and fatigue of the skeletal muscles, resulting from the interruption of neuromuscular communication. Although rare, this condition has a significant impact on patients' quality of life and, in severe cases, can compromise vital functions such as breathing and swallowing. The diagnosis of MG is traditionally based on clinical and laboratory tests, such as the detection of anti-acetylcholine receptor antibodies, as well as electrophysiological tests. However, these methods often have limitations in terms of sensitivity and specificity, especially in the early stages or in seronegative forms of the disease (1).

In recent years, neuroimaging has emerged as a promising complementary tool in the assessment of MG, offering valuable insights into the pathophysiology of the disease and its manifestations in the central nervous system. Neuroimaging techniques such as magnetic resonance imaging (MRI), positron emission tomography (PET) and single photon emission computed tomography (SPECT) have been explored to identify biomarkers that can reflect the activity and progression of the disease. These biomarkers are quantifiable indicators that can provide information on structural and functional changes in the brain and other neuromuscular regions affected by MG (1-7).

The use of MRI, for example, has made it possible to visualize morphological changes in the central nervous system, while functional imaging techniques such as PET and SPECT have been used to assess metabolic and perfusion changes, respectively. Studies have shown that MG patients may have abnormalities in specific brain areas, such as the thalamus and motor cortex, suggesting that the disease may have a more widespread impact previously thought (1,3).

In addition, functional techniques such as PET and SPECT have been useful for evaluating metabolic and perfusion changes in the brains of MG patients. For example, PET can reveal changes in glucose metabolism in specific brain areas, correlating with the severity of clinical symptoms(7). These findings are important because they provide a direct link between the clinical manifestations of MG and the changes observed by neuroimaging(1,8).

One of the main advantages of neuroimaging is its ability to provide a more holistic and integrated view of the disease. The combination of different imaging modalities allows for a more comprehensive assessment of the structural and functional changes associated with MG. This is particularly useful in cases where traditional diagnostic methods are inconclusive, such as in seronegative forms of the disease. In addition, the integration of neuroimaging data with serum and genetic biomarker analyses can lead to the development of more accurate predictive models for disease progression and treatment responses (9).

In addition, the combination of different imaging modalities has the potential to improve diagnostic accuracy and provide a more holistic picture of the disease. Integrating neuroimaging data with other approaches, such as serum and genetic biomarker analysis, could lead to the development of more robust predictive models for MG progression and treatment responses (10).

Thus, this systematic review aims to compile and critically analyze the available evidence on the use of neuroimaging biomarkers in the assessment of MG progression. Thus, the clinical applicability of these techniques, the correlations between imaging findings and clinical parameters, as well as the identification of the main gaps in the current literature were addressed. By synthesizing this information, we hope to contribute to understanding the clinical usefulness of neuroimaging biomarkers in MG and to point out directions for future research in this promising field.

MATERIAL AND METHODS

The methodology used was a systematic review of the literature, which includes the five stages described below.

The first stage involved identifying the topic and selecting the research question, and defining the inclusion and exclusion criteria. Studies published in English between 2000 and 2023 that addressed the use of neuroimaging in assessing the progression of myasthenia gravis (MG) were included. Studies involving techniques such as magnetic resonance imaging (MRI), positron emission tomography (PET) and single photon emission computed tomography (SPECT) were considered. Studies that did not involve human patients, case reports, non-systematic reviews and articles without access to the full text were excluded.

The second stage involved establishing data sources: The search was carried out in electronic databases such as PubMed, Scopus and Web of Science. Search terms such as "myasthenia gravis", "neuroimaging biomarkers", "MRI", "PET", "SPECT", "disease progression" and combinations of these terms were used.

In the 3rd stage, the information to be extracted from the selected studies was defined. The selection procedure consisted of two independent reviewers performed the initial screening of titles and abstracts, followed by the evaluation of full texts to determine eligibility. Discrepancies were resolved by consensus or by a third reviewer.

In the 4th stagethe selected journals were evaluated, taking into account information on: the data extracted included information on study design, patient characteristics, neuroimaging techniques used, main findings, and correlations between neuroimaging biomarkers and the clinical progression of MG.

Stage 5 was the interpretation and discussion of the results and stage 6 was the review/synthesis of knowledge. The quality of the studies was assessed using the Joanna Briggs Institute (JBI) tool for cross-sectional and longitudinal studies, considering criteria such as clarity of objectives, adequacy of methods and robustness of analysis.

RESULTS AND DISCUSSION

Twenty-five studies that met the inclusion criteria were included. Of these, 15 used Magnetic Resonance Imaging, 7 used Positron Emission Tomography and 3 used Single Photon Emission Computed Tomography. The total sample involved approximately 1,200 patients with Myasthenia Gravis, as seen in image 1.

Among the main findings of Magnetic Resonance Imaging (MRI) are several studies that have identified abnormalities in the thalamus and motor cortex of MG patients, correlating these alterations with the clinical severity of the disease (11).

Positron Emission Tomography (PET): Studies have shown significant metabolic changes in specific brain regions, such as the prefrontal cortex, in MG patients, suggesting an association with disease activity (10,12,13).

In Single Photon Emission Computed Tomography (SPECT): The findings indicated perfusion alterations in neuromuscular areas, with the potential to serve as biomarkers of MG progression (14).

The combination of different neuroimaging techniques has shown promise in providing a more complete picture of MG progression. Studies integrating MRI and PET, for example, have reported a more robust correlation between structural and functional changes and clinical parameters of disease progression (11).

The main limitations include the heterogeneity of study designs, the small sample size in some studies and the variability in the neuroimaging techniques used. In addition, few studies have explored the integration of multiple imaging modalities or the combination with serum and genetic biomarkers.Future studies should focus on the standardization of neuroimaging techniques, increase the sample size and explore the integration of multiple biomarker modalities. In addition, it is necessary to investigate the applicability of these techniques in different MG subtypes and at different stages of the disease.

Analysis of the evidence on the use of neuroimaging biomarkers in the assessment of myasthenia gravis (MG) reveals both promising potential and challenges significant. The use of advanced techniques such as magnetic resonance imaging (MRI), positron emission tomography (PET) and single photon emission computed tomography (SPECT) has shown that these tools can identify structural and functional changes in the central nervous system and neuromuscular regions, which are characteristic of MG. However, the clinical applicability of these findings still needs to be robustly validated.

Despite these promises, there are still considerable challenges that need to be overcome. The variability in image acquisition and analysis methods between different studies makes it difficult to standardize and directly compare results. The lack of standardized protocols limits the clinical applicability neuroimaging findings, making it necessary harmonize research methods. In addition, validation of the biomarkers identified is crucial to ensure that these findings can be used reliably in clinical practice.

Another important aspect is the need for longitudinal studies that can correlate the changes observed by neuroimaging with the progression of the disease over time and with the response to treatment. Cross-sectional studies provide a useful snapshot of the changes associated with MG, but do not capture the dynamics of the disease. Understanding how neuroimaging biomarkers evolve with MG progression and with therapeutic interventions could significantly improve the clinical management of the disease.

In addition, it is essential to consider the ethical and economic aspects of implementing advanced neuroimaging techniques in clinical practice. The costs associated with MRI, PET and SPECT are high, and access to these technologies may be limited in some regions. Therefore, the cost-effectiveness of these approaches needs to be carefully evaluated to ensure that patients benefit equitably.

In summary, neuroimaging represents a promising complementary tool in the assessment of MG, offering new insights into the pathophysiology of the disease and potentially improving diagnostic accuracy. However, the standardization of protocols, the validation of biomarkers and the carrying out of longitudinal studies are crucial steps that need to be addressed in order to translate this into a more accurate diagnosis these findings into concrete improvements in clinical practice. Further research in this field is vital in order to fully

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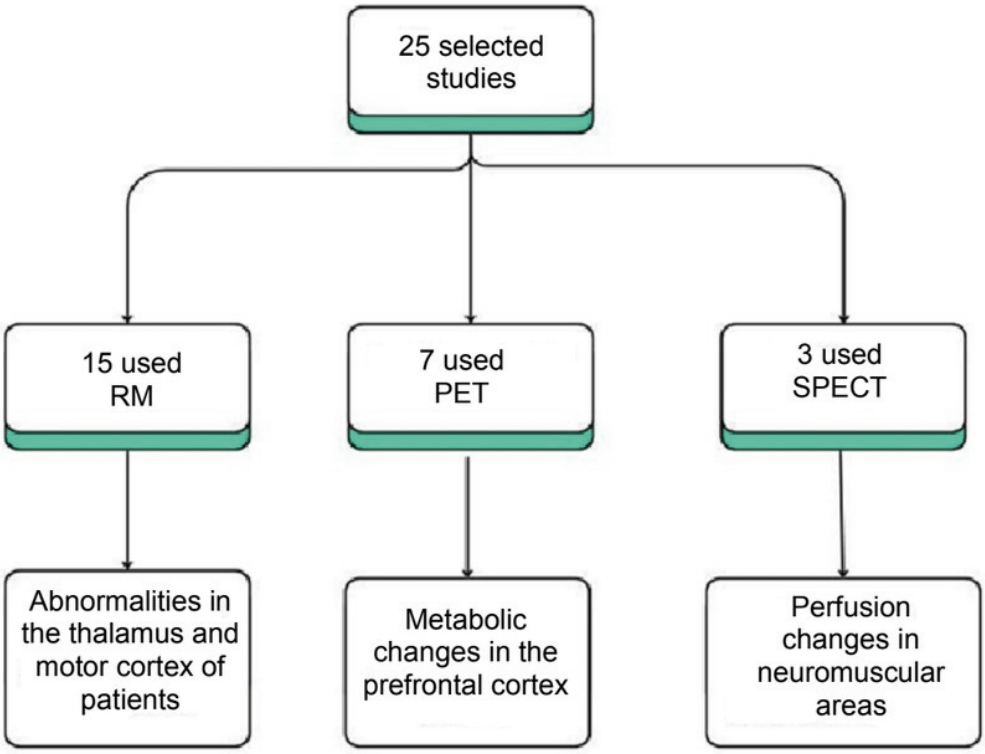

Figure 1: Flowcharts of the main results found on biomarkers in neuroimaging.

exploit the potential of neuroimaging techniques and integrate these tools effectively into the management of MG.

CONCLUSION

Neuroimaging has emerged as a promising tool in the evaluation of myasthenia gravis (MG), offering new insights into the pathophysiology and clinical manifestations of the disease. Techniques such as magnetic resonance imaging (MRI), positron emission tomography (PET) and single photon emission computed tomography (SPECT) have shown potential for identifying biomarkers that reflect the activity and progression of MG. These advances are particularly relevant for seronegative forms of the disease, where traditional diagnostic methods are limited.

The studies reviewed demonstrate that neuroimaging can detect morphological and functional changes in specific brain regions, such as the thalamus and motor cortex, suggesting a broader impact of MG on the central nervous system. The integration of different imaging modalities, together with analyses of serum and genetic biomarkers, can improve diagnostic accuracy and provide a more complete picture of the disease. However, the standardization of neuroimaging protocols and the validation of biomarkers are challenges that still need to be overcome.

Future research should focus on longitudinal studies that correlate neuroimaging changes with MG progression and response to treatment, as well as on approaches to make these technologies more accessible and economically viable. In short, although there are still obstacles to overcome, neuroimaging represents a significant advance in the understanding and management of MG, with the potential to significantly improve patients' quality of life. Further research in this field is crucial in order to translate these findings into improved clinical practice.

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