Myasthenia Gravis Misunderstood: Identifying the Historical Misinterpretations, Miscommunication, and Misconceptions

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ABSTRACT

Myasthenia Gravis (MG) is a serious disease and can present clinically with very severe symptoms in many patients; however, the *fluctuating* severity of MG results in the disease being commonly misdiagnosed as other conditions, including conversion disorder. The earliest recorded literature on MG provides evidence of the variability of signs and symptoms, including many patients who appeared to have mild symptoms initially but died suddenly and unexpectedly from MG. Often, these patients were initially believed to be suffering from hysteria.

This review analyzes some of the most prominent MG literature still cited today. It found that many communication errors have led to today's misunderstandings and have continued to cause difficulties in diagnosis and difficulty in understanding the MG patients' lived experiences. These errors include the intended meaning for 'gravis' being misinterpreted as 'severe' instead of the intended meaning of 'a painful weight in the limbs', the false belief that 'gravis' is Latin for 'grave' and how the miscommunication of the early 1900's MG autopsy studies added to this confusion, where MG continued to be referred to as a 'grave' condition. The continued omission of the sensory symptoms associated with MG from the literature has also been miscommunicated for decades, however such symptoms are now becoming recognized as a result of increasing patient led research.

Myasthenia Gravis should continue to be regarded as a serious disease, due to the devastating effect on quality of life for many people, and the unpredictability of the myasthenic crisis potentially occurring in *all* people living with MG, including those who are undiagnosed. The dismissing of mild symptoms results in many MG patients remaining undiagnosed. The possibility that individuals in this group go on to become victims of Sudden Adult Unexplained Death (SUD) is yet to be investigated, and there is a need for research in this area.

Miscommunication also includes omitting 'old knowledge,' not listening to the patient's lived experience, and failing to integrate relevant interdisciplinary knowledge. Good examples of these are The Mary Walker Effect, and combining patient lived experience with ocular anatomy and physiology knowledge to develop new MG-specific ocular motility clinical tests. A new test is presented for evaluating MG eye signs utilizing knowledge of the 'Safety Factor,' and is referred to as The SLOWLY Test (Significant Level Of Weakness, Loci in Y Axis).

Awareness of the historical misinterpretations, miscommunications, and misconceptions is crucial to preventing delay in diagnosis in MG patients, developing new clinical tests, rehabilitation interventions, and helping doctors and others understand the lived experience of MG patients.

Keywords: myasthenia gravis, conversion disorder, neuromuscular junction, misdiagnosis, The Mary Walker Effect

Introduction

Acquired Autoimmune Myasthenia Gravis (MG) is a potentially fatal, chronic neuromuscular disease affecting the post-synaptic neuromuscular junction (NMJ). The most well-known symptoms of MG include *fluctuating* fatigue and *variable* weakness of the voluntary muscles affecting limbs, trunk, neck, face, eyes, breathing, and swallowing.[1] The eye muscles are the most susceptible muscle group to an autoimmune-mediated attack on the NMJ, and, therefore, accurate ophthalmic examination is vital to aid in an early diagnosis.[2] MG eye signs (MGES) can help to diagnose MG; however, when eye signs are subtle or latent, diagnosis can be difficult. A study of ocular myasthenia gravis (OMG) patients in 1997 found 64% of uncertain cases of OMG converted to generalized MG within 2 to 4 years, whereas only 12% of those treated with immunosuppression converted to generalized MG within 2 to 4 years,[3] hence early diagnosis through eye signs is crucial.

Even though today there is the knowledge that MG is variable, there remains a common misconception where many physicians only diagnose MG at the point where weakness is obvious or 'severe enough.' This misconception can be traced back to miscommunication and misinterpretation of early MG literature. A review of historical etymology literature and German to English translation of medical terms of the late 1800's shows that the intended meaning for 'gravis' was misinterpreted as 'severe' instead of the intended meaning of 'painful heavy limbs.'[4] Case studies from the earliest diagnosed MG patients, 124 years ago, show that even some patients with mild MG signs died suddenly, yet others with more severe symptoms lived for years. Those earlier reports also documented the variable nature of MG known today. This information should provide insight into the dangers for undiagnosed MG patients today and highlight the importance of diagnosing MG earlier in patients who show milder or more subtle signs.

The increase in MG survival rate today is due to improved treatments for diagnosed MG patients; however, myasthenic crisis still occurs in 20% of MG patients and

may be triggered by events such as infection, severe MG exacerbation, certain medications, and anesthesia.[5] In recent years, Takotsubo Cardiomyopathy (TC) has also been reported in MG associated with myasthenic crisis (MC) along with MC in previously undiagnosed MG.[6] Undiagnosed MG patients should be of concern, as their mortality rate is a higher risk due to lack of treatment for their MG, and the risk of inadvertently being exposed to conditions or drugs that can exacerbate MG and place them at risk of MC, TC or choking. As with any disease, awareness leads to knowledge for patients, allowing them to mitigate risk factors that may worsen the disease. This concern about the undiagnosed MG patients in our communities has not previously been reported, and research in this area is essential.

Discussion of Historical Misinterpretations, Miscommunication, and Misconceptions.

This article highlights six issues that have led to today's misunderstandings about MG, which have continued to cause difficulties in diagnosis and poor understanding of MG patients' lived experiences. They include: 1) Misinterpretation of the intended meaning for 'gravis' as being 'severe' instead of the intended meaning of 'a painful weight in the limbs,'[4] through incorrect translation of the intended meaning of the word 'gravis'; 2) misinterpretation of meaning of 'gravis,' through miscommunication of MG severity that led to the incorrect use of the word 'grave' to describe MG; 3) misinterpreting a prominent MG case series paper by Campbell & Bramwell led to the incorrect belief that sensory symptoms are not associated with MG and continued miscommunication about sensory symptoms in MG; 4) miscommunication by omission of 'old knowledge'; 5) not listening to patient lived experience to further understand MG; and 6) failing to communicate and integrate relevant interdisciplinary knowledge to increase knowledge of MG.

1. Incorrect translation of the intended meaning of the word 'gravis'

The term Myasthenia Gravis Pseudo-paralytica was first introduced by the German physician Friedrich Jolly in 1895. In November, 1899, 124 years ago, the Berlin Society of Psychiatry and Neurology accepted the name Myasthenia Gravis and is still used today.[7] Another physician at the time, Leopold Laquer, had also suggested 'Allgemeine schwere myasthenia,' which translated to 'general heavy myasthenia.'[8]

'Schwere' refers to painful weight in the limbs. 'Gravis' means heavy

A review of the meaning and translation of the word 'schwere' was performed, including Latin, German, and English etymology textbooks between 1821 and 2003, first looking at the usage of the words 'schwere' and 'schwer' in the late 1800s within the German language. An 1890 *German-English Dictionary of Medical Terms*[9] lists 'schwer' as an adjective meaning heavy, difficult, serious, severe, dangerous and 'schwere' as meaning heaviness weight when describing the difficulty of movement.

The word 'schwere' was used when discussing the medical condition Myxoedema by William Ord in 1877 to describe an illness in which there was '...Schwere in den Gliedern,' translating to 'Heaviness in the limbs.'[10] An 1891 text, 'Encyclopaedic German-English and English-German Dictionary,' lists the German word 'schwere' as meaning heavy, weighty, and more specifically when discussing pathology, 'schwere' meaning 'a painful weight in the limbs.'[4] This is the first evidence that the Latin word 'gravis' appears to have been chosen by the German physician Friedrich Jolly in 1895 to represent the symptoms of painful heavy muscles. However, changes in the meaning of translation in later years caused an incorrect understanding of the meaning. It is important to note that in medical textbooks, 'schwere' continues to be used for 'heavy,' for example, 'schwere beine' when describing heavy legs from a 2017 German medical textbook.[11]

In a German medical text from 1898, 'Die Im Zusammenhang Mit Anderen Krankheiten,' translated to English as 'In connection with other diseases,"[10] the words *schwere* and *schwer* are seemingly interchangeable, meaning heavy, severe, or hard. This interchangeability of *schwere* and *schwer* is present even today.

Understanding the intended meaning of 'a painful weight in the limbs'[4] is essential for understanding the patient's lived experience and for ensuring that the patient's symptoms aren't dismissed if they don't appear 'severe enough' and they display the symptom of painful heavy muscles.

2. Misinterpretation of the meaning of 'gravis' and miscommunication of MG severity

'Gravis' is not 'Grave'

The word 'grave' originates from the Latin word 'gravis,' meaning heavy or weighty,[12] *and* the French meaning 'serious.'[13] Today, the incorrect statement is that Gravis originates from Grave, such as the common phrase that 'Gravis is Latin meaning grave.' This has led to the common belief that MG is a disease that presents with severe symptoms and causes patients who display less severe symptoms during medical consultation very often to be dismissed. A 1961 Lecture titled *The History of Myasthenia Gravis* by Sir Geoffrey Keynes from the University of Durham, UK refers to 'gravis' as severe but discusses how the name is inappropriate, as "there are many times when the symptoms of MG patients are not severe," questioning whether the name MG should be changed.[14] By this time, people believed that Jolly had named MG using the Latin word 'gravis' due to the severity of the disease; however, as discussed by choosing the Latin word 'gravis,' it is evident that Jolly was referring to painful heavy muscles.[4]

Historical Misinterpretation and Miscommunication of MG Severity

For over a century, many authors have noted that the diagnosis of MG was frequently dismissed in the early stages, as the disease is characterized by daily fluctuations and partial or complete remissions, sometimes for long periods.[1, 15-19]

MG presentation, even in the late 1800s, varied between mild to severe, with the potential of escalating suddenly to death as a result of choking or respiratory failure. In 1893, Samuel Goldflam published an article in German describing three patients with fluctuating weakness of the extra ocular muscles (EOMs), limbs, and breathing difficulties.[20] The article's title translates to "about a seemingly curable bulbar paralytic symptom complex with the participation of extremities."[20] In 1900, Campbell and Bramwell noted that "a characteristic feature of the disease is its tendency to fluctuate in severity from day to day, or from week to week, or even to disappear for months or years, to reappear."[15]

The textbook *The Principles and Practice of Medicine: designed for the Use of Practitioners and Students of Medicine (1901)*, by prominent physician William Osler (1849–1919), provides further evidence that MG was considered a variable disease with many patients initially presenting with mild signs and symptoms. Osler is "generally regarded as one of the greatest and most admired physicians in the history of medicine, [and his text] became the most popular and widely read treatise on medicine in the world."[21] In it, Osler discussed MG's variability, stating there are "...remarkable variations in intensity..." and "...the patient may live for many years; recovery may take place." Of the 180 collected cases, 72 (40%) proved fatal.[22] Many subsequent authors described this variability in severity.[1, 8, 15, 17-19] The mortality rate that can be ascertained in Osler 1901 of 40% is less than the estimate of 75% that has been reported by other authors.[23] Noting this discrepancy from different studies reporting on the same period raises concerns. Further research to find a more accurate mortality rate of the early 1900s would help to understand the true risk of undiagnosed MG patients today since they are untreated and could inadvertently be subjected to substances and situations that are known to cause the risk of death in MG. Is the 40% mortality rate close to the mortality rate for the undiagnosed today? Research to find the answer could include analyzing SUD cases by looking at old photos of the person during their life and looking for MGES, e.g., ptosis and lid retraction, which is variable between photos, or even consistent ptosis or lid retraction that is unexplained by the victim's medical history could indicate undiagnosed MG during their life. The other figure of 75% is likely to be high due to skewing from including the autopsy studies of the time. Further research in this area is important as it will improve knowledge of the importance of early diagnosis and treatment in MG.

Autopsy Studies Led to the Misconception That Nearly All MG Patients Died of MG.

As the cause of MG was unknown at the time, some reports in the early 1900s investigating the cause of MG focused on the autopsies of positive cases; these reports were presented as a case series of MG patients who died suddenly from respiratory failure or choking. One such autopsy report series was documented by Dr. Charles Myers in 1902,[24] where he presented a review of 22 cases provided by several prominent physicians. This report was presented as his thesis for his MD Degree. It included many patients, including one of his own, who were initially misdiagnosed with hysteria and died suddenly and unexpectedly from respiratory failure. Charles Myers is remembered as a respected physician; in later years, he became the president of the British Psychological Society and later president of the Psychology Section of the British Association for the Advancement of Science and editor of the Journal of Psychology. In his thesis, he noted

> So far, I have been speaking of the disease as if it were invariably fatal. But although I intend to confine my remarks mainly to those cases in which necropsy has been performed with negative (or practically negative) results I ought to insist at once that, as our knowledge of the disease has increased, numerous cases have been published in which the patient appears to have quite recovered.[24]

It appears that some authors of the day had a misconception regarding the severity and prognosis of MG that originated from the misinterpretation of these types of MG autopsy reports. In 1903, the first textbook that appeared to have based MG prognosis on autopsy papers stated the "prognosis is grave."[25] The text was *Savill's System of Clinical Medicine Dealing with the Diagnosis, Prognosis, and Treatment of Disease for Students and Practitioners.* This misconception was repeated in subsequent texts,[25, 26] with the statement "the outcome is usually fatal" in the 1923 edition.[27]

Historical Similarities to MG Today

In 1911, Oppenheim discusses that "suffering reveals its insidious, treacherous nature, because not only can relapses occur at any time, but in many cases, death occurs just then, as a patient at a stage, of complete or relative well-being left out of treatment and was no longer thought to be serious or even lethal."[8] These statements are still relevant today, as around 20% of MG patients suffer a MC involving sudden severe respiratory symptoms requiring intervention and may result in death.[5] Even today, many undiagnosed MG patients are also at risk of death, as they are not undergoing appropriate treatment for their MG and may unwittingly be subjected to substances or situations that trigger MC, TC or choking.

A clinical review of 87 cases observed between 1915 and the early part of 1932, described an MG mortality rate

of 39%.[28] Out of the 34 documented deaths, MG had been present for a variable time ranging between six months to 22 years, with an average of four and a half years. Symptoms were noted to be variable, with most cases taking two to four years to diagnose after the initial symptoms, ranging between one month and 25 years. At times, patients complained of weakness for years without any objective symptoms, and many of these patients were believed to be "neurotics."[28] As no treatment was available at the time, this study is a good indication of mortality rates in untreated disease. Today, many undiagnosed MG patients are misdiagnosed as having a conversion disorder and are at risk of dying from sudden MC, TC or choking.

A prominent textbook written by Robert Bing in 1921, who was considered one of Europe's most "illustrious neurologists" of his time,[29] titled "A Textbook of nervous disease for Students and Practicing Physicians; in thirty lectures," describes MG as a disease that:

> Has a great tendency to intermissions, in when the patients for weeks, months and years can be entirely free from trouble; termination in recovery is, on the other hand, rare, and the prognosis is on this account unfavourable since the harmless initial stage of the disease can stretch over an exceedingly long period characterized by long intermissions and short exacerbations, (In one case mentioned [of Cushman's], twenty-two years). Once the myasthenia has reached its full development, however, the situation is exceedingly dangerous. The pseudo-paralysis is constantly more permanent; the muscles recover almost not at all.[17]

He also discussed the importance of rest: "during the exacerbations of the disease, rest in bed; during the intermissions, long periods of entire rest are introduced into the regime of the day."[17] This text provides evidence that milder early signs of MG were documented even in the early 1900s before effective treatments were discovered. Most importantly, it acknowledges that even in the early stages of remission, the MG patient is still in danger of recurrence of potentially dangerous symptoms.

The Dangers of Misconception of MG Severity Today

There is a common misconception today that a patient is required to present with severe muscle weakness to be diagnosed with MG. The reality, as already discussed, is that a patient may have mild or moderate symptoms that can escalate to sudden MG, TC or choking. Too often, a wait-and-see-if-symptoms-worsen approach is undertaken, leaving many patients suffering for years with poor quality of life. Literature often states that MG is not as 'grave' as it had been in the early days; it appears that the clinical course of the mild cases reported from the earlier case reports have been forgotten. It is true that the mortality rate gradually fell associated with the improvements in the medical treatment of MG; however, such statements have resulted in the misconception that MG always presents with severe muscle weakness, and mild symptoms were no longer considered serious. The historical miscommunication of MG is a result of authors continuing to reprint incorrect statements about MG. This misconception persists today in many popular medical textbooks, MG research, and MG information websites.

3. Sensory symptoms miscommunicated as being absent in MG

Interestingly, sensory changes, including ocular pain, headache, paresthesia, and the sensation of heaviness, have been reported throughout literature since the 1800s, including the Campbell & Bramwell report from 1900.[15] However, this well-known report still cited in recent literature had a crucial contradictory remark. The paper stated on the second page of the review that "there are no sensory changes"[15] associated with MG; however, reading the 63 case studies listed in the report, there *are* many sensory symptoms reported, including heaviness, headaches, tenderness, and aching limbs mentioned in detail. This is a significant historical error of interpretation that has been constantly restated in literature even today, resulting in difficulty in diagnosing MG and poor understanding by doctors of the patient's lived experience.

Sensory Symptoms in MG have been Documented Since the Earliest Cases

Even though today MG is commonly believed to be purely a motor disease, there is a long history of recorded sensory symptoms, such as heaviness, ocular pain, muscle pain, headache, and numbness associated with MG. In 1901, Oppenheim described patients reporting sensations such as "heaviness in arms and legs; heavy and unwholesome legs and arms; dizziness, pain in shoulders and neck; paresthesias in legs; paresthesia in the left cheek and severe dizziness and headache."[16] Buzzard, in 1906, recorded the following symptoms in a patient: "He noticed a feeling of heaviness in the right leg, which became easily tired,[30] In 1927, Hart noted in another patient that "she complained at this time of a sensation of heaviness and general exhaustibility, increased by a moderate amount of exertion."[31]

Sensory symptoms have also been documented across other prominent MG literature. A 1908 peer-reviewed textbook titled 'Diseases of the Nervous System' by Dr. Herbert Thomson. Dr. Thomson was a respected physician and vice-president of the Section of Neurology and Psychological Medicine at the Annual Meeting of the British Medical Association, held at Aberdeen in 1914. In his text, he discussed MG, stating, "while the main symptoms are motor, there are occasionally some sensory changes to be noted."[32, 33] He also noted that "transient ocular symptoms are sometimes associated with migraine."[32, 33] Bain, in 1904, reported patients complaining of "premonition, consisting of headache, pain in the neck and back, photophobia, and giddiness have occasionally been noted."[34]

This association of sensory symptoms as a premonition of MG was discussed 40 years later by Dr. Abner McGehee Harvey, who was appointed Chairman of John Hopkins Hospital at age 34. "That sensory disturbances may precede or accompany the first manifestations of weakness is not generally realized. Headache, pain in the eye, numbness and tingling in various regions, and other sensory manifestations were described often enough to deserve some consideration."[35]

Subsequent miscommunication caused by ignoring this knowledge of sensory symptoms has led to the misconception that persists that MG is purely a motor disease. More recent research is acknowledging that "sensory anomalies have been overlooked for decades in myasthenia gravis,"[36] with pain and headaches now recognized by some authors as common symptoms in patients with MG.[37] This knowledge is yet to be communicated to general consulting physicians and in the general MG information that is readily available, contributing to delayed diagnosis and misdiagnosis of the sensory symptoms as being another condition or being "all in the patient's head." This failure to disseminate this important knowledge needs to be urgently remedied.

4. Miscommunication Includes Omitting Information from 'Old Knowledge'

An excellent example of the importance of remembering 'old knowledge' is the clinical sign known as 'The Mary Walker effect,' identified in 1938. Mary Walker, a Scottish physician, observed that exhaustion of one group of voluntary muscles through repetitive use in a patient with MG induced weakness in other groups of muscles that had not been engaged.[38]

The Relevance of The Mary Walker Effect Today

a. Developing new clinical tests

A recently published Case Presentation that introduced the SLOW Test (Simultaneous Lip and Ocular Weakness), by this author showed how knowledge of the Mary Walker Effect could be utilized to develop clinical tests that demonstrate muscle fatigability in MG.[38] The Mary Walker Effect highlights the fact that all eye muscle testing methods that increase fatigability should be performed carefully so as not to overfatigue the MG patient. Further research is recommended as MG is variable among patients and within the same person throughout the day, so testing should be tailored to the individual's level of fatigability at the time of testing.

An alternative test to the SLOW Test[38] could be used and could be called 'The Mary Walker Ball Test', based on Mary Walker's experiment demonstrating the Mary Walker Effect.[38] The patient could squeeze a ball to fatigue the hand and forearm muscles while simultaneously testing for MGES, stopping at the first sign of an MGES. This test was successfully trialed by the author, as an MG patient, eliciting MGES within 5 to 10 seconds, e.g., ptosis in upgaze. Research should be trialed on MG patients to assess the effects of fatiguing other muscles simultaneously, and to analyze the efficiency of the test on all MG subgroups.

b. Rehabilitation Strategies

Understanding The Mary Walker Effect is essential for MG patients in their daily life, to help prevent exacerbations escalating when MG medications, combined with a vigilant balance of rest and appropriate activity levels fail to control symptoms adequately, e.g., an MG patient who has an exacerbation of eye muscle restrictions when looking down needs to understand that continuing to fatigue her eye muscle when looking down while cutting vegetables or attempting to eat from a dinner plate at table height, could potentially result in swallowing difficulties and cause choking. The author, who lives with MG, has found that at times of severe exacerbation of downgaze eye restrictions, a useful rehabilitation strategy is raising the dinner plate by around 20 cm to reduce the use of the eye muscles in the direction that they are the most symptomatic. This patient also benefits from routinely performing reading activities at eye level rather than looking down, as it helps to prevent exacerbations of her eye muscle restrictions, and as per The Mary Walker Effect, helps prevent exacerbation of her other MG symptoms. Also, a comfortable chair supporting other muscles like the arm and neck muscles helps prevent exacerbation of her MG symptoms.

c. Understanding Patient-Lived Experience

In the above example, the patient noted that during periods of poor MG control, preparing dinner has caused MG exacerbation of her bulbar muscles, putting her at risk of choking. This knowledge helps her to seek assistance from others with certain chores or find strategies to do things differently. This is an area of knowledge that should be further developed through patient-led research.

5. Miscommunication also includes not listening to the patient's lived experience.

The value of patient experiential expertise in research has increased in recent years, and future studies involving patients at all levels of research is vital to advancing knowledge in MG. Listening to patients describe their condition has excellent potential to increase understanding of MG. The author is an orthoptist living with generalized MG, and the test below was developed by combining lived experience, professional orthoptic knowledge and experience, with interdisciplinary knowledge.

6. Miscommunication also includes failing to communicate and integrate relevant interdisciplinary knowledge.

A good example of this is how anatomy and physiology knowledge may help to develop new disease-specific ocular motility clinical tests to diagnose latent MGES.

Background of The Neuromuscular Junction 'Safety Factor,' EOM Physiology and Anatomy

Neurotransmission in a normal NMJ is a result of the presence of adequate acetylcholine receptors (AChRs) and Na+ channels (NaChs), including a necessary reserve of supply. The safety factor is a measure of excess or reserve of the NaCh and AChR in the NMJ. It has been shown that in MG, the eye muscle fibers that have a lower safety factor are affected earlier in the fatigue process as there is a loss of Na+ channels and AchRs from the endplate, which reduces the safety factor for neuromuscular transmission.[39]

The eyes are the most susceptible muscle group to an autoimmune-mediated attack on the NMJ.[2] Five of the six identified types of fibers in the orbital and global layers of the EOM have a lower safety factor, increasing the likelihood of the extra-ocular muscles (EOM) suffering from fatigable weakness in MG.[40] Recent studies in human EOMs show that they are much more complex than previously thought.[41] Currently, they have been divided into six types: orbital singly innervated, orbital multiply innervated, global red singly innervated, global intermediate singly innervated, global pale singly innervated, and global multiply innervated fibers.[42] It is now known that all extraocular muscle fibers except pale globe fibers have a lower safety factor, which explains why saccades remain fast in MG patients who exhibit restriction of ocular motility.[43] Electromyographic studies of the extraocular muscles indicate that global fibers are less active than orbital layers during eccentric gaze-holding.[44]

Developing the SLOWLY Test

During ocular motility testing, variable EOM fiber types are engaged depending on factors like the starting point, speed, and direction of the eye movement. Advances in knowledge of the anatomy of the oculomotor system, including fibromuscular pulleys, have provided insight into how specific movements influence which EOM fibers are engaged. The clinical implications are still not fully understood; however, for this report, the knowledge that a weak lateral rectus muscle affects the positions of pulleys, which, in turn, influences the pulling directions of muscles with predominantly vertical actions, was considered as part of the design of the new test describe.[43] This test was named the SLOWLY Test, and excludes saccadic movements, instead including only slow, small vertical pursuit in the mid-lateral field of vision.

A Novel Test - The SLOWLY Test – 'Significant Level of Weakness in the Lateral Y axis mid gaze'

Ocular motility testing in an MG patient has not previously been described in terms of extraocular muscle physiology, including the 'Safety Factor' of each extraocular muscle (EOM) while combined with patient experiential knowledge. This new method involves identifying fixation areas with a 'significant level of weakness in the lateral Y-axis mid-gaze zone.' This area is given the acronym 'SLOWLY' to emphasize the importance of a slow testing speed for MG assessment. The SLOWLY Test induces objective fatigable muscle weakness by utilizing the action of the EOM fibers with the lowest neuromuscular junction (NMJ) 'Safety Factor.' The design for the SLOWLY Test includes testing extra slow, small vertical pursuit eye movements, performed in a manner similar to plotting a blind spot on a confrontation visual field test, alternating with static gaze holding while excluding saccadic movement.

The SLOWLY Test Method

This method is not simply gaze holding but involves small, slow movements not currently tested in standard OM examinations in a zone that is not tested routinely. It consists of asking the patient to follow a target in slow vertical pursuit movements in mid-lateral gaze, with intermittent gaze holding. The procedure involves slowly following a target in this unique pattern to disclose the MGES without initiating saccadic movements. During the SLOWLY Test, as with any OM testing, it is quite easy for patients to become distracted and perform a saccadic movement to regain eye contact with the examiner or at some other target. The examiner must explain to the patient that they should refrain from using fast eye movement and maintain fixation on the target.

It was noted that the patient in this report displayed fatigable weakness associated with a positive SLOWLY Test occurring immediately once a SLOWLY was identified, and remained while the patient maintained their gaze holding in the SLOWLY. However, the MGES disappeared with a change in fixation, a saccadic movement, or a decrease in 'effort' to maintain fixation by the patient. This patient's most significant MGES with a SLOWLY were in right lateral mid-gaze mid-elevation, where she displayed a complete ptosis of the right eyelid and a total left ptosis was identified in left lateral mid-gaze mid-elevation. These MGES were sustained on maintaining fixation in the specific loci. Other MGES, including OM restriction and lid hopping, were also noted in left lateral gaze in other identified loci. These MGES were also more obvious than other traditional methods of testing for MGES previously performed.

The SLOWLY Test is potentially particularly valuable for disclosing latent signs in MG patients, who, due to the variable nature of their disease, may have less obvious signs of objective fatigability at the time of consultation. These patients are often missed with current testing regimes. Further research on groups of the subtypes of MG patients should be undertaken to see if there is a difference in response to the tests between subgroups of MG.

Slow speed for testing for MGES (The SLOW and SLOWLY Test)

Another test designed to elicit latent MGES, the 'SLOW Test,' which is based on the Mary Walker Effect, and examines simultaneous lip and ocular weakness, has also

been previously described by this author.[38] The SLOWLY Test continues with the 'slow' theme, highlighting the importance of a slow-moving target when testing for MGES during ocular motility examination. The SLOWLY Test stands for Significant Level Of Weakness, Loci in the Y axis.

The SLOWLY Test helps explain the fleeting and variable nature of MG eye signs that may occur in some MG patients during ophthalmic clinical assessment. The importance of slowing down the pace of OM testing in MG is explained through a deeper understanding of neuromuscular junction, muscle fiber anatomy, and physiology. This concept also highlights the need for further interdisciplinary studies in OM to develop more effective diagnostic tests for MG, due to the complexity of damage to the NMJ affecting the 'safety factor' in MG and its effect on ocular motility.

Myasthenia Gravis Misunderstood – Conclusion

The historical communication errors regarding MG outlined in this review have contributed to today's misunderstandings of the disease and have continued to cause difficulties in diagnosis and difficulty in understanding MG patients' lived experiences. Myasthenia gravis should continue to be regarded as a serious disease due to the devastating effect on quality of life for many people, and the unpredictability of MC, TC, or choking potentially occurring in *all* people living with MG, including those who are undiagnosed.

Acknowledging the symptom of 'painful heavy muscles' should help with diagnosis and understanding the patient's experience. Patient-led research recording MG patients describe how their muscles feel are vital, and should be compared with the descriptions of painful heavy muscles that been recorded since the early 1900's.[16, 30] This is an important area for future research to document and emphasize Jolly's intended meaning of Myasthenia Gravis as 'weak, painful heavy muscles.'

The dismissing of mild symptoms results in many MG patients remaining undiagnosed, or having a delayed diagnosis, resulting in poorer outcomes for quality of life. The possibility that individuals in the undiagnosed group go on to become victims of Sudden Adult Unexplained Death (SUD) is yet to be investigated, and research should be performed in this area. Awareness that clinical symptoms may be mild and fluctuating, not necessarily severe at the time of clinical assessment and that sensory symptoms are often associated, is crucial to prevent further misdiagnosis. Awareness that clinical tests of fatigability can cause exacerbation of the other muscles that are not engaged is essential for the clinician to not overfatigue the patient and to understand the patient's lived experience. Awareness that interdisciplinary knowledge, such as the physiological and anatomical features of the eye muscles is crucial to further develop accurate clinical assessments to disclose latent and fleeting eye signs in MG.

Awareness of the issues addressed in this paper will directly positively impact patients' lives through earlier diagnoses, initiation of earlier treatment and understanding lived experiences by their doctors, loved ones, and the community. This knowledge will lead to further research to find methods for earlier diagnosis, development of rehabilitation interventions, and improved knowledge to update the incorrect information prominent in the MG field.

Summary

Historical miscommunication and misinterpretations have resulted in misconceptions and MG being a misunderstood disease. This article highlights six issues that have led to today's misunderstandings of MG. These have continued to cause difficulties in diagnosis and difficulty in understanding the MG patients' lived experiences; they include:

1. Misinterpretation of the intended meaning for 'gravis' being misinterpreted as 'severe' instead of the intended meaning of 'a painful weight in the limbs.'[4]

2. Misinterpretation that led to the incorrect use of the word 'grave' to describe MG in a popular 1903 medical textbook, and has been repeated in many subsequent medical texts even today.

3. Misinterpreting a prominent MG case series paper by Campbell & Bramwell led to the incorrect belief that sensory symptoms are not associated with MG. Even though MG patients have reported having sensory symptoms for over 124 years, including in the above-mentioned MG case series paper by Campbell & Bramwell.[15]

4. Miscommunication that occurs when important 'old knowledge' like The Mary Walker Effect is forgotten. Remembering that 'wearing out one muscle group causes exhaustion and weakness in the other muscle groups that have not been stimulated' in MG will help in many ways, like developing new clinical tests,[38] developing new rehabilitation strategies, and helping understand the patient's lived experience. Examples of the latter are described in this paper.

5. Miscommunication involving not listening to the patient's lived experience. Patient experiential knowledge can help develop further understanding in many aspects of MG, including understanding Jolly's intended meaning of weak painful heavy muscles, developing new clinical tests, like the Mary Walker Effect Tests (The SLOW Test and the Mary Walker Ball Test) and the new test named the 'SLOWLY Test;' the latter 2 tests are described in this paper.

6. Miscommunication involving failing to communicate and integrate relevant interdisciplinary knowledge. A good example is how anatomy and physiology knowledge may help develop new ocular motility clinical tests specific to MG. The SLOWLY Test described in this paper was developed in this way.

Future Directions

Patient-led research recording MG patients describe how their muscles 'feel' during periods of exacerbation is an important area for future research to clearly document and emphasize Jolly's intended meaning of Myasthenia Gravis as 'weak, painful heavy muscles.'

Further research utilizing the Mary Walker Effect is recommended to develop new tests, and improve understanding of Patient Lived Experience by doctors. The research should involve patients at every stage.

Interdisciplinary knowledge, such as the physiological and anatomical features of the eye muscles is crucial to the further develop accurate clinical assessments to disclose latent and fleeting eye signs in MG. This area could be further developed with patient-led research.

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The author is an orthoptist living with generalized myasthenia gravis, diagnosed in 2016.

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