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FATIGUE IN MG

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What is fatigue?

➤ Fatigue is both:

fatigability: poor muscle activation and weakness with repetitive movement (peripheral)

fatigue: feeling of low energy and tiredness that interferes with routine daily activities (central or generalized)

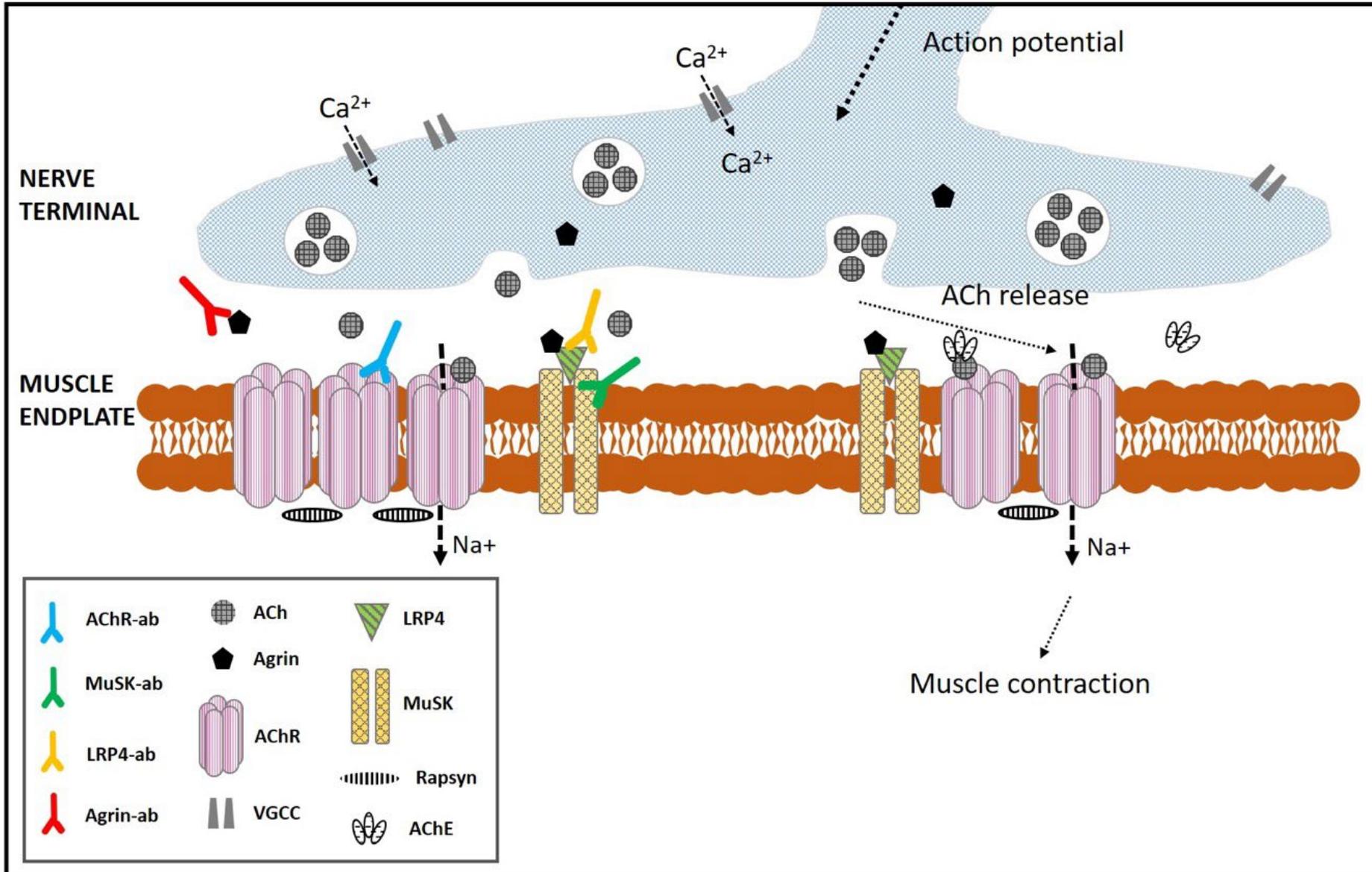


Challenges of measuring fatigue in MG

- Fatigue is both *performance fatigability* and *fatigue perception*
- **Fatigue may be best assessed using multiple measures**
- Clinical MG scores: quantitative MG score (QMG) and MG composite scale (MGC)
- Neurophysiological examination: repetitive nerve stimulation (RNS)
- Fatigue severity scale (FSS); developed primarily for multiple sclerosis
- Functional evaluations: 6 min or 2 min walk tests
- Subjective evaluation forms



MG Fatigability



How do we measure fatigability?

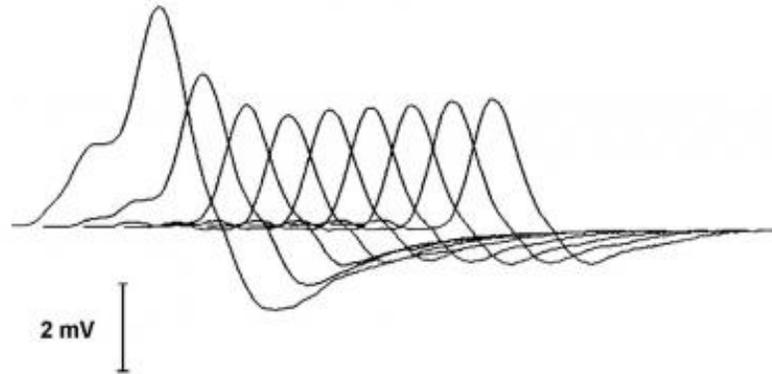
Clin muscle exam



MGC
QMG



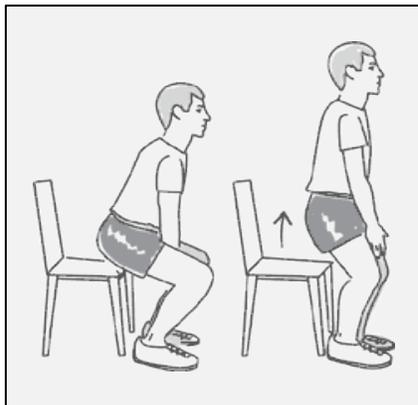
Neurophysiology



Questionnaires

MG-ADL

Physical performance tests



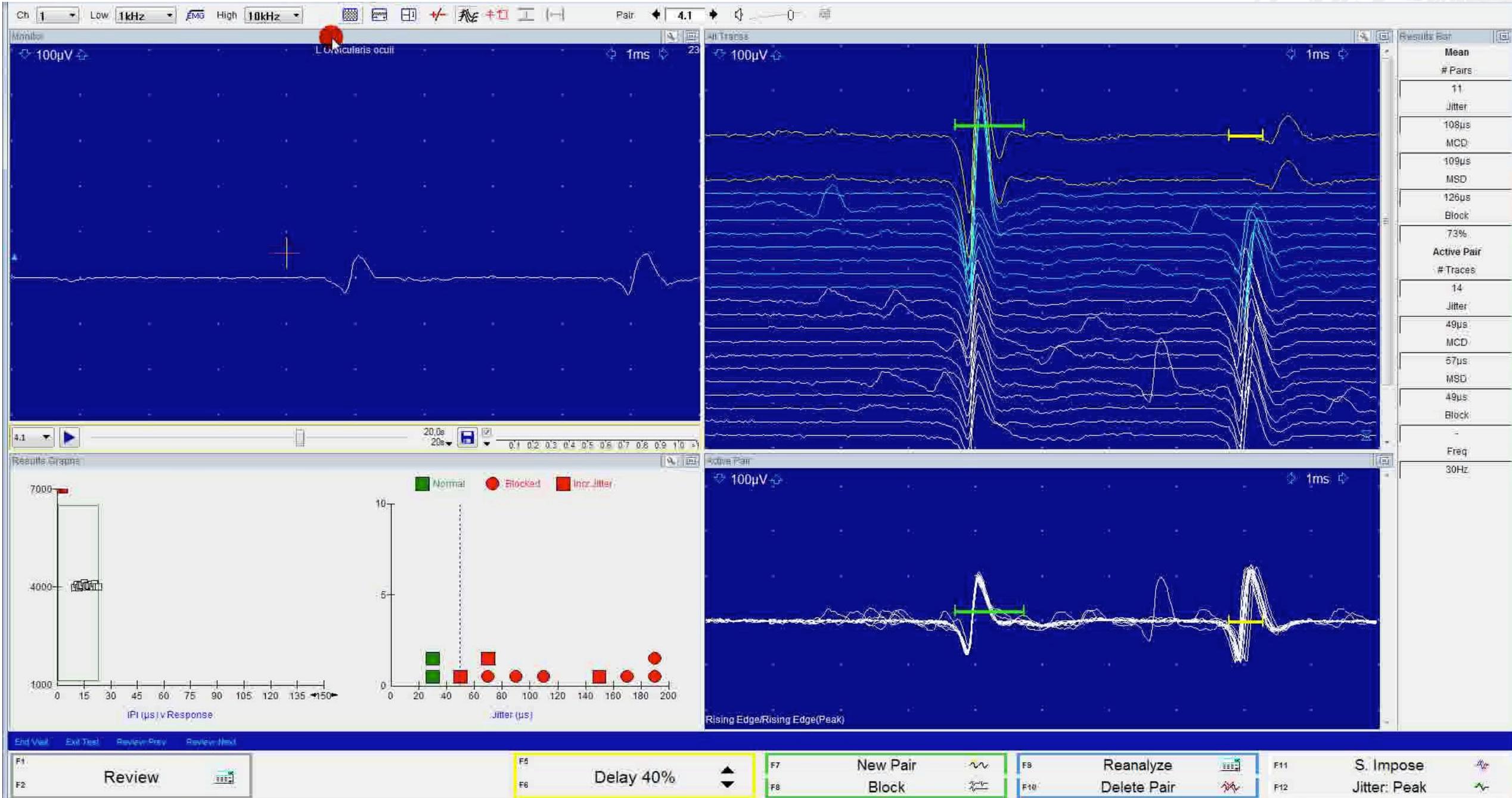
“Timed Up and Go”

6/12 min walking test

30- sec chair test



SINGLE FIBER EMG= neuromuscular transmission failure



How do we measure "fatigue"?



Questionnaires

Fatigue Severity Scale (FSS)

Chalder Fatigue Scale

MGQoL, Neuro-QoL etc

Epworth sleepiness scale, Pittsburgh Sleep Quality Index

More.....



Fatigue Severity Scale

Choose a number from 1 to 7 that indicates your degree of agreement with the following statements where **1 indicates strongly disagree** and **7 indicates strongly agree**. Please answer the questions with reference to how you have been feeling **on average over the last week**.

	Strongly disagree						Strongly agree
1. My motivation is lower when I am fatigued	1	2	3	4	5	6	7
2. Exercise brings on my fatigue	1	2	3	4	5	6	7
3. I am easily fatigued	1	2	3	4	5	6	7
4. Fatigue interferes with my physical functioning	1	2	3	4	5	6	7
5. Fatigue causes frequent problems for me	1	2	3	4	5	6	7
6. My fatigue prevents sustained physical functioning	1	2	3	4	5	6	7
7. Fatigue interferes with carrying out certain duties and responsibilities	1	2	3	4	5	6	7
8. Fatigue is among my three most disabling symptoms	1	2	3	4	5	6	7
9. Fatigue interferes with my work, family or social life	1	2	3	4	5	6	7



Chalder Fatigue Scale

ITEM	Question
Item 1	Do you have problems with tiredness?
Item 2	Do you need to rest more?
Item 3	Do you feel sleepy or drowsy?
Item 4	Do you have problems starting things?
Item 5	Do you start things without difficulty but get weak as you go on?
Item 6	Are you lacking in energy?
Item 7	Do you have less strength in your muscles?
Item 8	Do you feel weak?
Item 9	Do you have difficulty concentrating?
Item 10	Do you think as clearly as usual?



Important to separate: Peripheral versus central fatigue

- Central fatigue, rather than peripheral fatigability, is reported in 40-80% of MG patients
- Central fatigue correlates strongly with depressive symptoms and the severity of MG
- 10% of MG patients whose symptoms resolve after treatment still have central fatigue
- Although symptomatic fatigue responds to physical and psychological training, several studies have reported improved fatigue scores in response to intensifying immune therapies





Fatigue in myasthenia gravis: risk factors and impact on quality of life

Sarah Hoffmann^{1,2} | Johanna Ramm¹ | Ulrike Grittner^{3,4} | Siegfried Kohler^{1,2} |
Jana Siedler¹ | Andreas Meisel^{1,2}

- The study aimed to assess the **prevalence of fatigue** and its **relation to ADL and QoL** as well as to identify factors associated with MG fatigue in 200 MG patients.
- Prevalence of fatigue was assessed using the Chalder Fatigue Scale (CFQ). Impact of fatigue on ADL and QoL was assessed by the MG activities of daily living profile (MG-ADL) and the MG-specific quality-of-life instrument (MG-QoL), respectively.
- Association of fatigue with sociodemographics, clinical characteristics of MG, and comorbidities including mood and anxiety disorders as well as sleep disorders.



Fatigue in MG associated with ADL and QoL

- The observed rate of fatigue was 56%, of those 70% fulfilled the criteria of chronic fatigue with a duration of ≥ 6 months
- Fatigue was strongly associated to ADL and QoL
- Other factors for relevant fatigue were: female sex, GMG, positive AchR or MuSK antibody status, medication with cholinesterase inhibitors or opioids, thymectomy, presence of other immunopathies, higher QMG score
- Factors associated with relevant fatigue were disease severity and depressive state
- Positive muscle-specific tyrosine kinase (MuSK) antibody status showed a strong association with fatigue



Diversity in mental fatigue and social profile of patients with myasthenia gravis in two different Northern European countries

Liis Sabre^{1,2*}  | Elisabet Westerberg^{1*} | Maarika Liik² | Anna R. Punga¹

- All patients with a confirmed MG diagnosis were asked to answer two questionnaires including demographic and disease-specific data, lifestyle issues, and mental fatigue (Fatigue Severity Scale [FSS])
- Clinical fatigue was assessed objectively through the Quantitative Myasthenia Gravis Score (QMG)
- 92 Estonian MG patients and 70 Swedish MG patients



TABLE 4 Clinical characteristics on myasthenia gravis patients in Estonia and Sweden

	Estonia	Sweden	p-Value
Subgroups, N (%)			
Juvenile MG	0	2 (5.3)	.49
Early-onset MG	15 (42.9)	16 (44.4)	>.99
Late-onset MG	20 (57.1)	20 (55.6)	.88
Phenotypes, N (%)			
Generalized	29 (80.6)	31 (79.5)	>.99
Bulbar	3 (8.3)	2 (5.1)	.67
Pure ocular	4 (11.1)	6 (15.4)	.74
Antibody serology, N (%)			
AChR ab	23 (71.9)	34 (85)	.06
MuSK ab	0	0	
SNMG	9 (28.1)	6 (15)	.42
Missing antibodies	4 (11.1)	0	<.05*
Thymectomy, N (%)			
Thymoma MG, N (%)	2 (5.5)	4 (10.0)	.77

MG, myasthenia gravis; AChR ab, acetylcholine receptor antibodies; MuSK ab, muscle-specific kinase antibodies; SNMG, seronegative myasthenia gravis. Results are presented as number (%). *Significant difference ($p < .05$).

- The patients' objective MG fatigue (QMG) did not differ and the patients' self-perceived health positively correlated with the QMG score
- A strong positive correlation was found between self-related health and FSS
- ***The mean FSS was considerably higher in Estonia compared to Sweden***
- The most commonly mentioned factor affecting health status was psychological stress and infection in both groups
- **72% of Estonian patients did not perform physical exercise training at all compared to 26% in Sweden**



Myasthenia Symptom Burden, Fatigue, and Sleep: Are They Related?

Sarah Yang, MD, Mitchell G. Miglis, MD,† Safwan Jaradeh, MD,† and Srikanth Muppidi, MD†*

Fatigue and Sleep in MG?

- 196 MG patients, online questionnaires
- MG QOL-15, Epworth sleepiness scale, Pittsburgh Sleep Quality Index, fatigue severity score (FSS) and MG-ADL were completed at a follow up call (50%)
- Mean MG-ADL was 6.8, indicating a moderate MG disease burden.
- 24% reported high Epworth sleepiness scale scores, 77% reported high Pittsburgh Sleep Quality Index scores, and 82% reported high FSS scores.



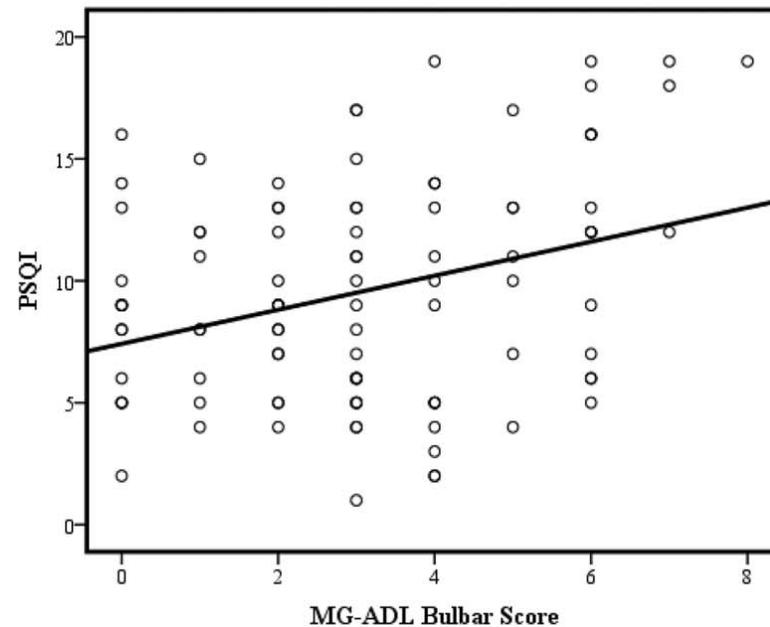
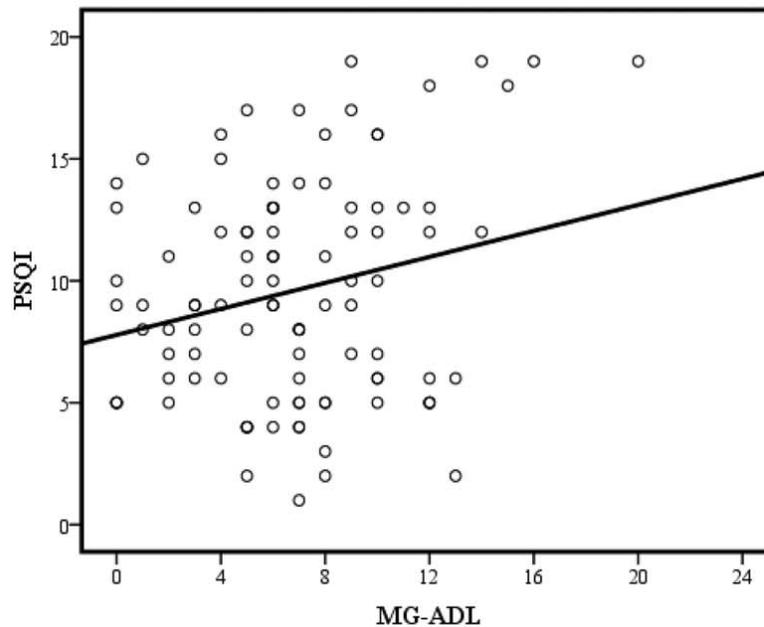
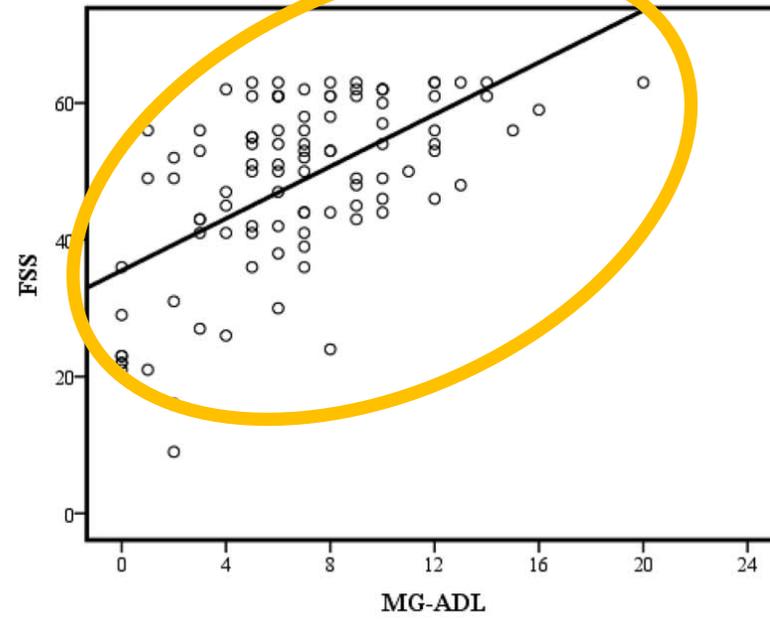
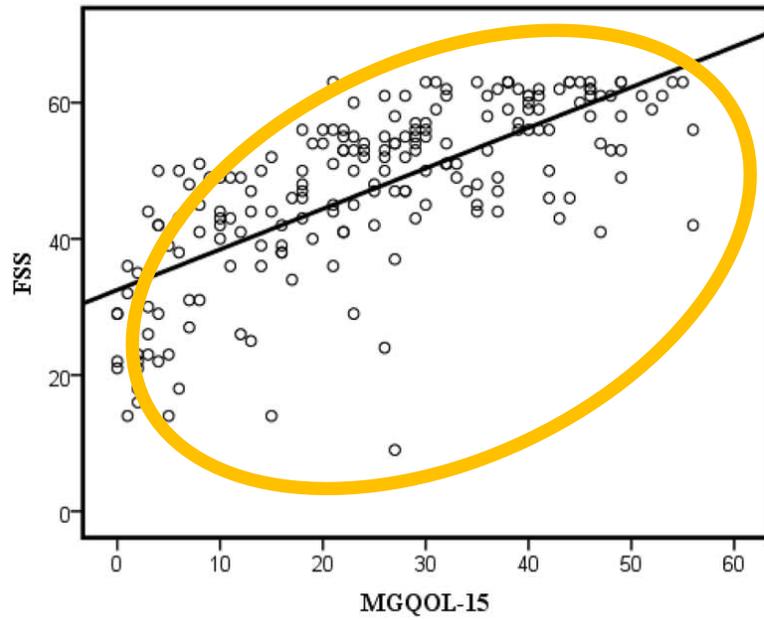


FIGURE 1. Composite scatter plot of MG QOL-15, MG-ADL, FSS, and PSQI measures. Composite scatter plot of MG-Quality of life 15, MG activities of daily living, bulbar subset of MG activities of daily living, FSS, and Pittsburgh Sleep Quality Index.



TAKE HOME MESSAGE

- **MG fatigue** includes both **muscle fatigability** and **general fatigue**,
important to separate
- Generalized fatigue is a common symptom, even in patients with well controlled MG
- There is a moderate positive correlation between various MG-specific outcome measures and fatigue severity.



Thank you!!
Questions?

