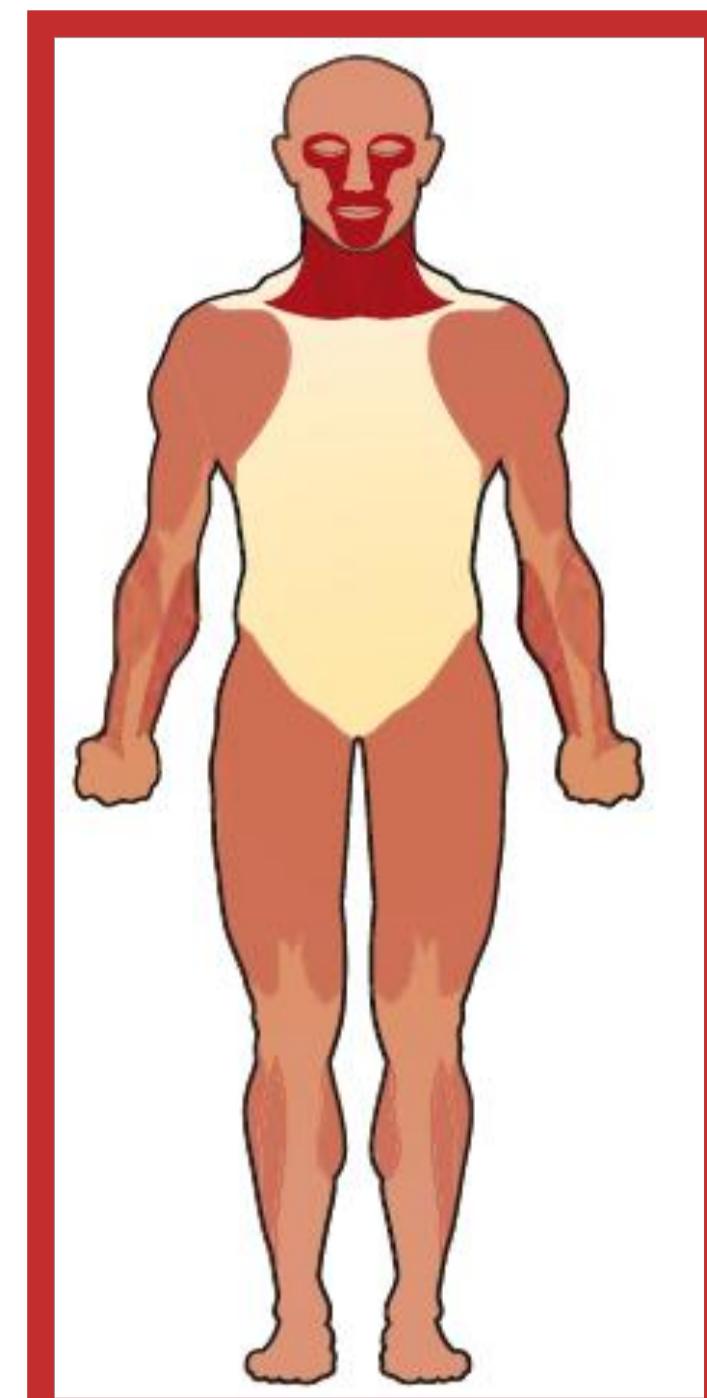
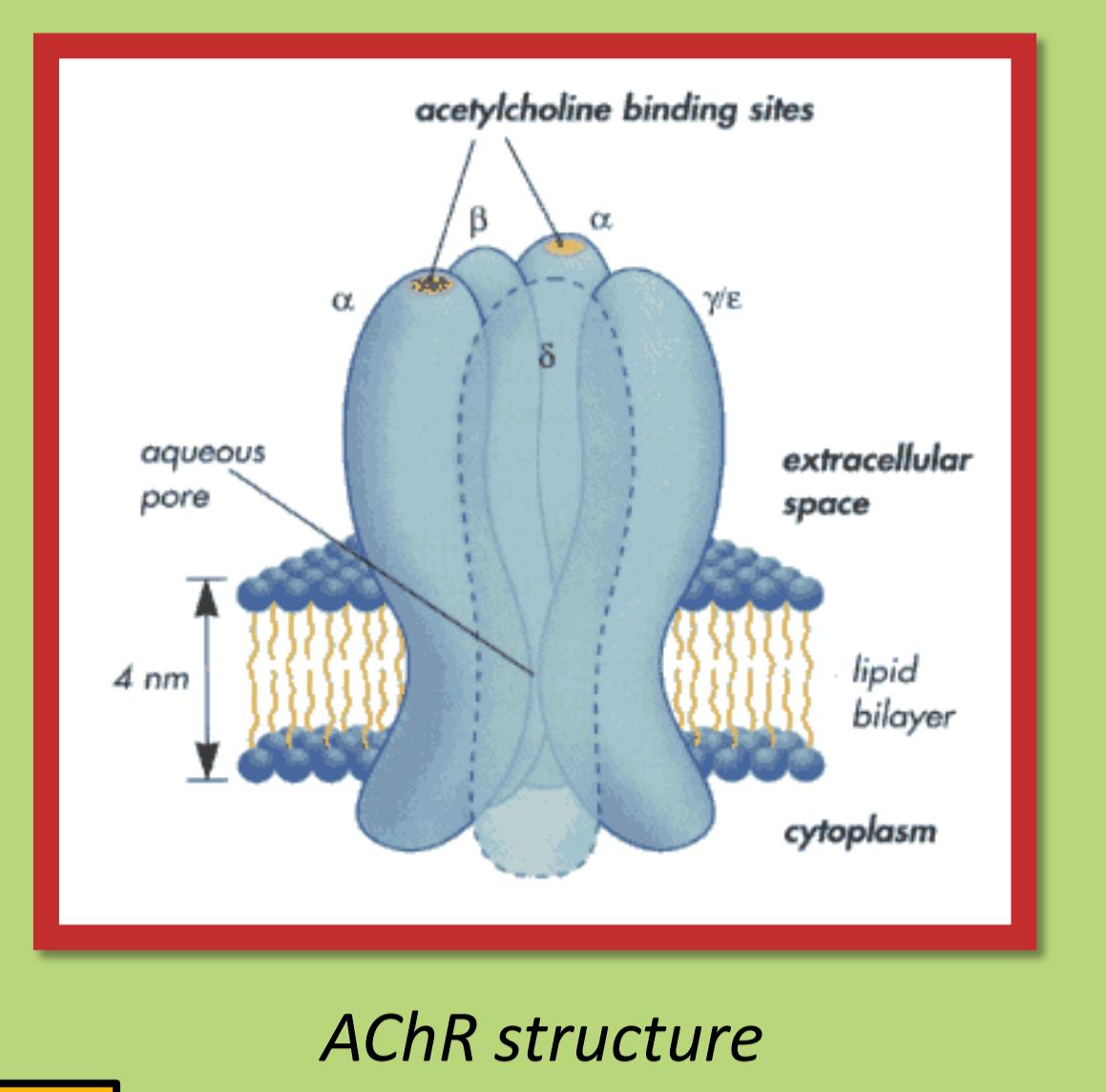


## Introduction

- Myasthenia Gravis (MG) is an autoimmune disease (AID) that causes muscle weakness and fatigue. It especially affects the ocular, facial and bulbar muscles.
- MG is caused by the production of antibodies against proteins of the neuromuscular junction:

IgG

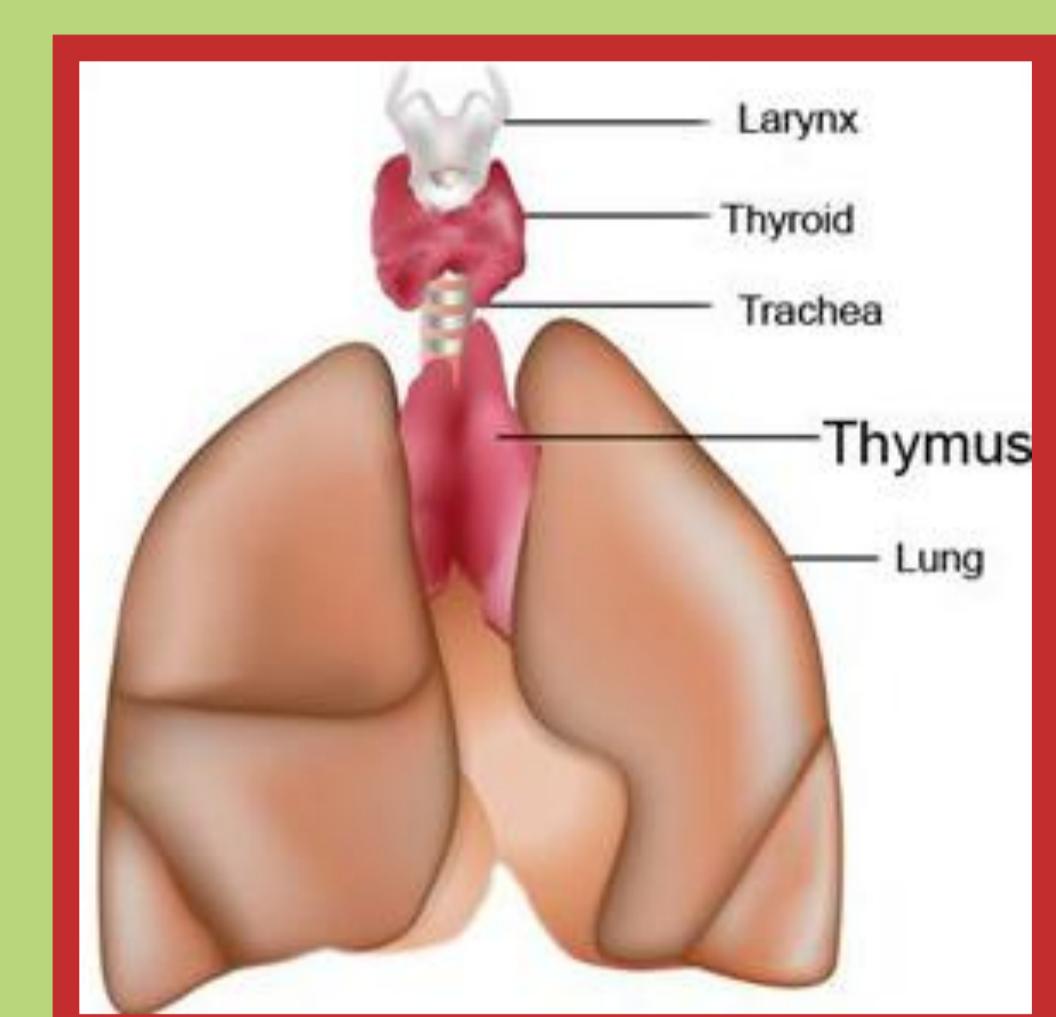
→ Acetylcholine Receptor **AChR**  
 → Muscle Specific Kinase **MuSK**  
 → Low-density lipoprotein receptor-related protein **LRP4**



Muscles affected in MG

## Thymus

- The function of the thymus is to establish tolerance to self antigens.
- In a normal thymus there is more production of autoreactive T cells against AChR than against other antigens.
- Structural and functional changes in the thymus are associated with the AChR-MG.



Localisation of the thymus

THYMOMA

THYMIC FOLLICULAR HYPERPLASIA

AChR-MG

## OBJECTIVE: TO REVIEW THE CURRENT LITERATURE ON THE ROLE OF THE THYMUS IN MG

The **methodology** is based on reading and understanding bibliographical references and the subsequent drafting of the report on summarizing and linking all the information of interest.

## THYMOMA

> 50 years old  
Men=Women

Tumor of cortical epithelial cells of the thymus: types AB, B1 and B2.

Changes in the thymus caused by thymoma:

- Medullary area reduced compared to cortical area (imbalance in the cell density)
- Low expression of AIRE (defect in negative selection)
- High number of immature T cells (CD4 + and CD8 +, DP)
- High proliferation of cortical thymocytes increases genetic mutations
- Reduced number of dendritic cells (defect in negative selection)
- MHCII deficiency (defect in positive selection)
- FoxP3 deficiency (deregulation of Treg)
- Treg deficiency (increases survival of autoreactive T cells in the periphery)
- High levels of expression of type I interferons



Autoreactive T cells are able to move to the periphery and be functional

AChR-MG

## THYMIC FOLLICULAR HYPERPLASIA

<50 years old  
> Women

Many germinal centers (GCs) are formed in the thymus.

Changes in the thymus caused by thymic follicular hyperplasia:

- Thymus overexpression of proinflammatory cytokines and genes induced by IFN-γ
- Abnormal cytokine network that alters the balance between Th1, Th2 and Th17
- Defect in Treg (increases survival of autoreactive T cells in the periphery)
- Reduced number of dendritic cells (defect in negative selection)
- Low expression of AIRE (defect in negative selection)
- High expression of TNF-α (chronic inflammation in thymus)
- Expansion of perivascular spaces, displacement of miod cells
- The complement proteins and autoreactive T cells against AChR attacks miod marrow cells
- High expression of Bcl-2 prevent apoptosis of autoreactive cells

Recruitment of B cells and dendritic cells

Formation of GCs

- Increasing antibody production
- Antibody-producing cells could be exported to the periphery
- Altearing the thymus function

## THYMECTOMY

Only for AChR-MG patients

The removal of the thymus.

## -Thymoma:

Eliminates the production site of autoreactive T cells

## -Thymic follicular hyperplasia:

Eliminates the production site of antibodies anti-AChR



More studies are needed

## -Thymoma:

Autoreactive T cells that were exported to periphery could be still functional

## - Thymic follicular hyperplasia:

Plasma cells and/or memory cells that were exported to periphery still produce antibodies anti-AChR



## Conclusions

- Thymus plays a very important role in the AChR-MG
- Thymoma affects the proper functioning of the thymus and favors the generation and the exportation of autoreactive T cells to periphery.
- The presence of GCs in the thymus increases antibody production, favours the exportation of antibody-producing cells to periphery and alters the thymus function.
- There is evidence that thymectomy is useful in some cases but not fully effective in others.

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