Comprehensive analysis of motor endplate pathology in AChR-Ab-positive myasthenia gravis

Dr. rer. nat. Corinna Preuße | EAN, June 2025

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Conflicts of Interest

Speaker's fee: argenx
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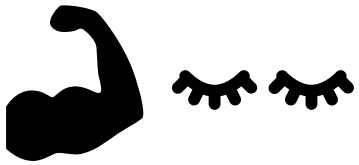
Memberships: Myositis-Netz e.V., DGM, WMS

Very short introduction

Myasthenia gravis

symptoms 

Autoantibodies

AChR, LRP4, MuSK

Study background

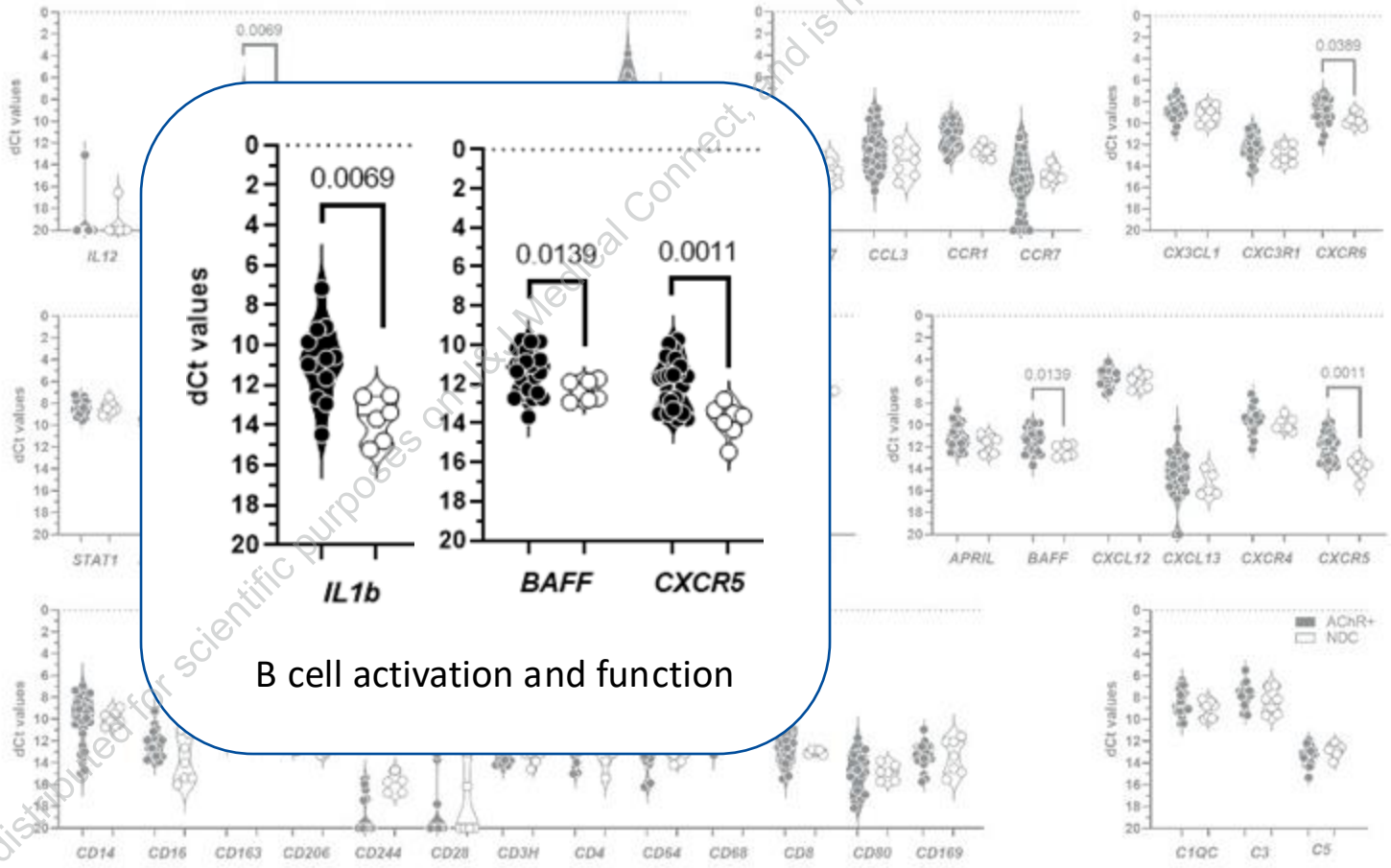
1970s:
"complement deposition at the NMJ leads to motor endplate destruction"

But, rapid effects of novel therapies make complete NMJ destruction unlikely

re-examine the NMJ in AChR+ MG

Few changes on transcriptomic level – specifically B cell related genes

46 genes
- activation pathways
- immune cell marker
- Complement-related markers
- antibody-related markers



Proteomic profiling revealed TARSH

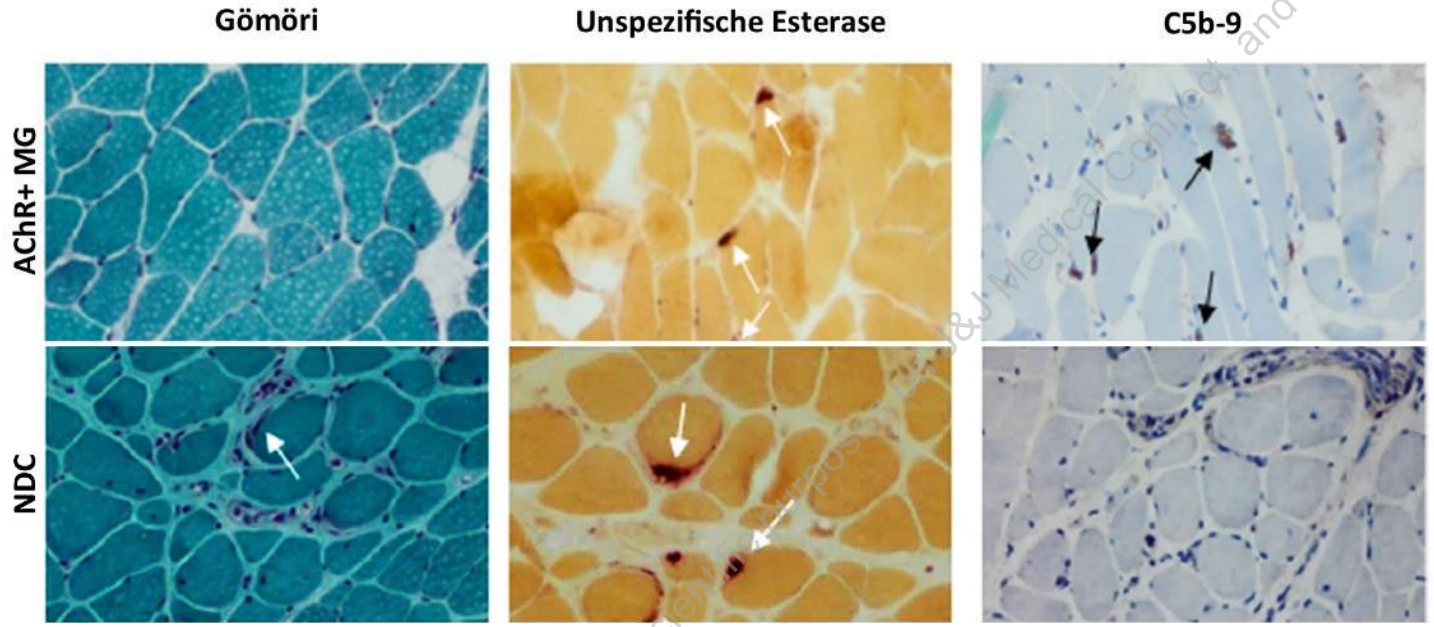
Alpha-1-acid glycoprotein
acute phase protein with inflammatory and immunomodulating properties

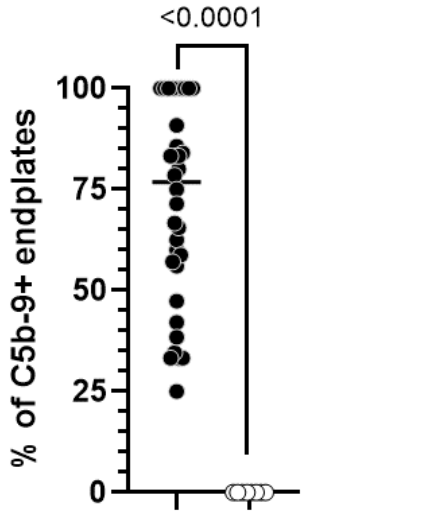
Acyl-CoA-binding protein
facilitate the transport of acyl-CoA within cells

Target of Nesh-SH3 variant 3
enable actin filament binding activity;
Predicted to be involved in several processes, including extracellular matrix organization;
upregulated in congenital Myasthenia

Dynamin 2
mediate vesicle scission at plasma membrane during endocytosis

Histologically only mild changes, but: complement deposition at the neuromuscular endplate

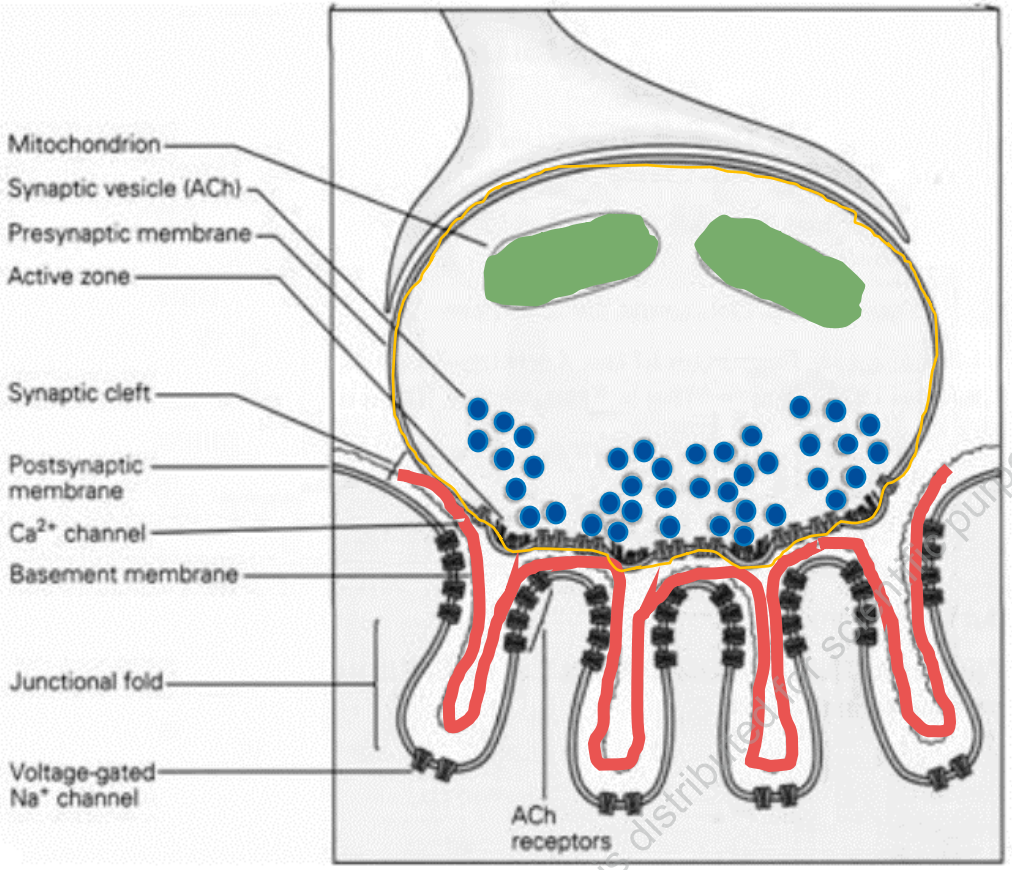


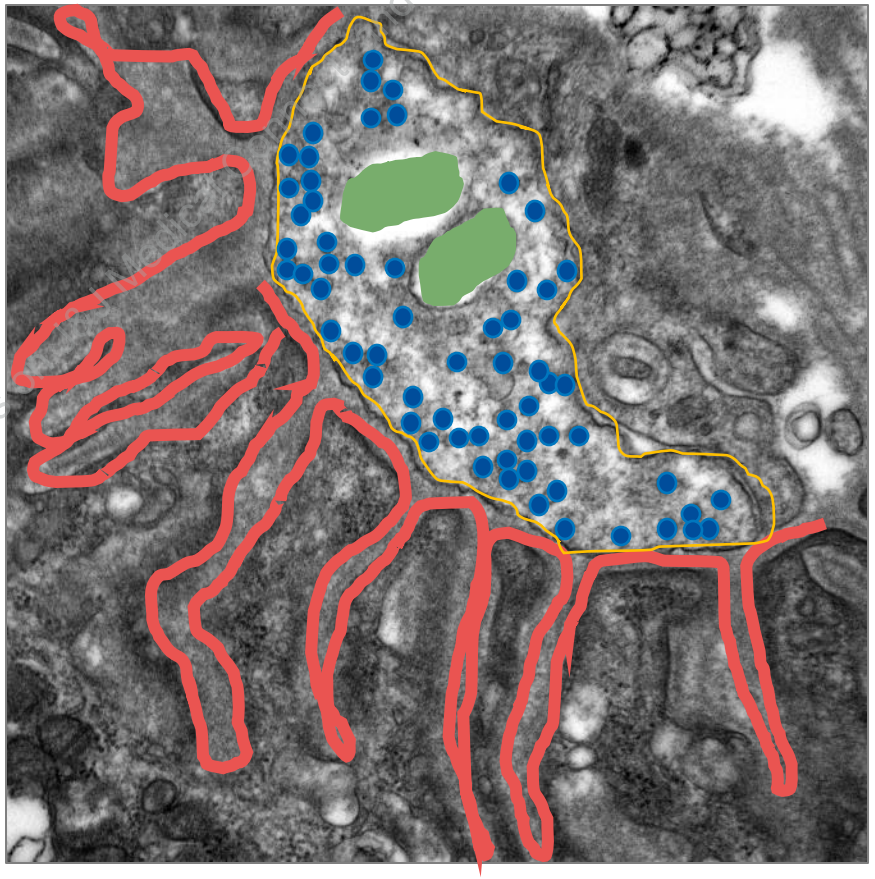


● AChR+ MG, n=27
○ NDC, n=8

Mean = 71,47%
Median = 76,79%

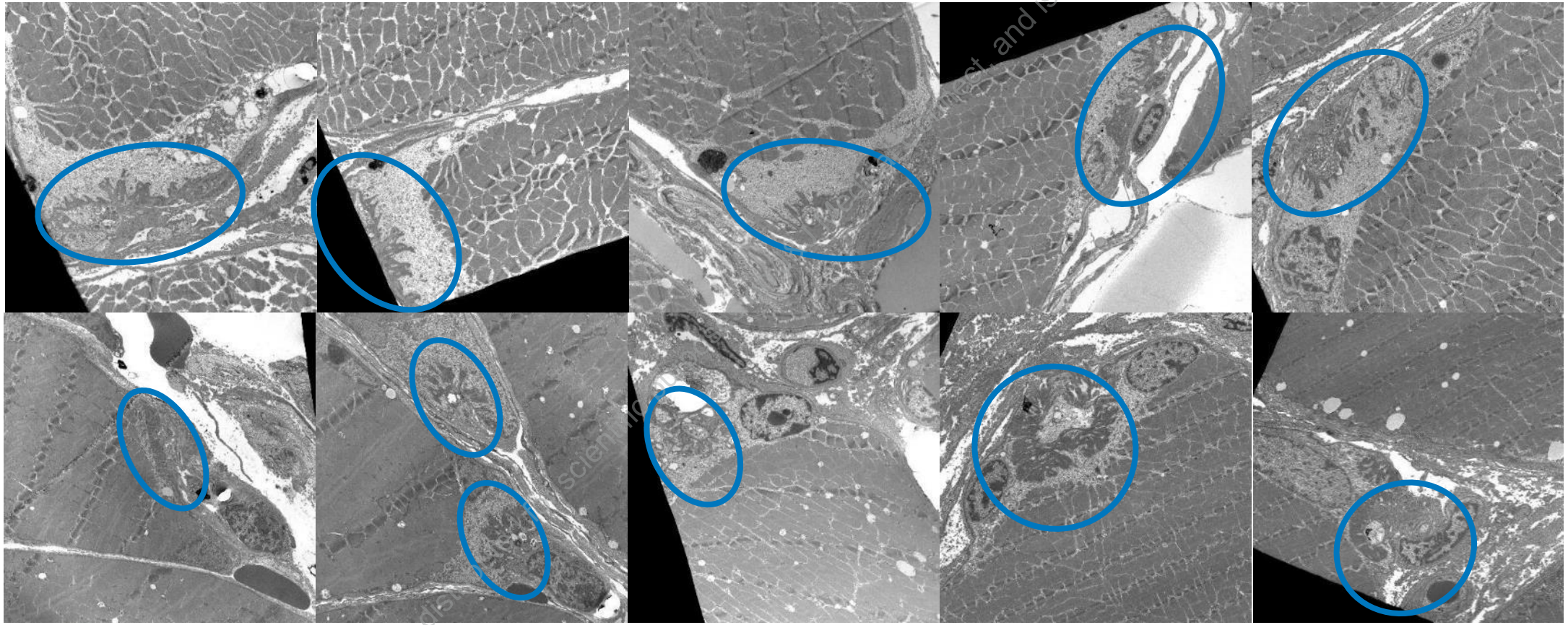
What do the neuromuscular junctions look like?





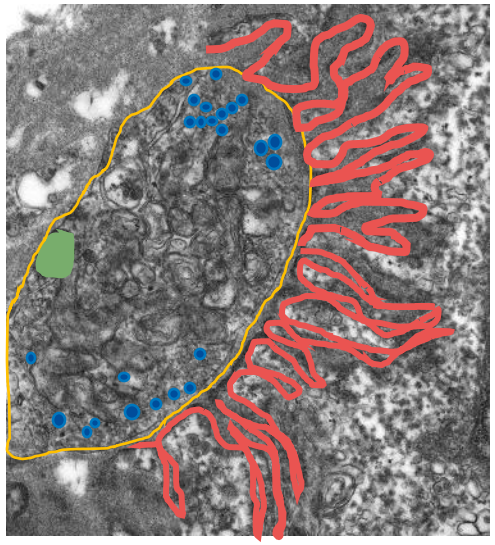
- Bouton terminal
- Postsynaptic membrane
- Mitochondria
- Vesicles

What is the frequency/degree of destruction at NMJ in AChR-ab+ MG?

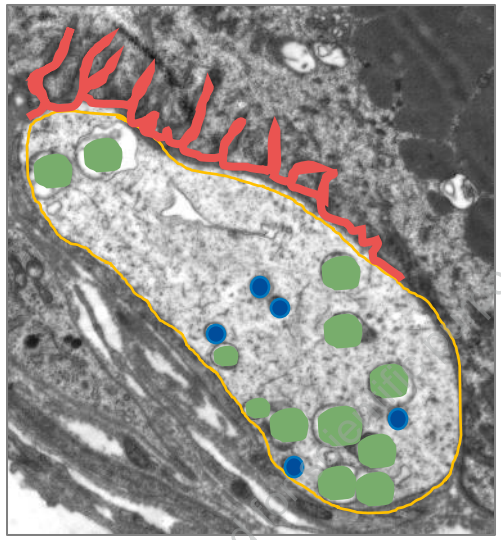


Electron microscopy in n = >30 NMJ shows different degree of …

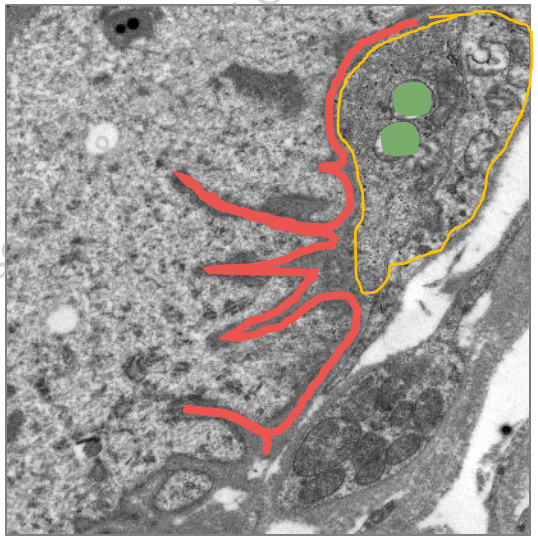
“normal” appearing



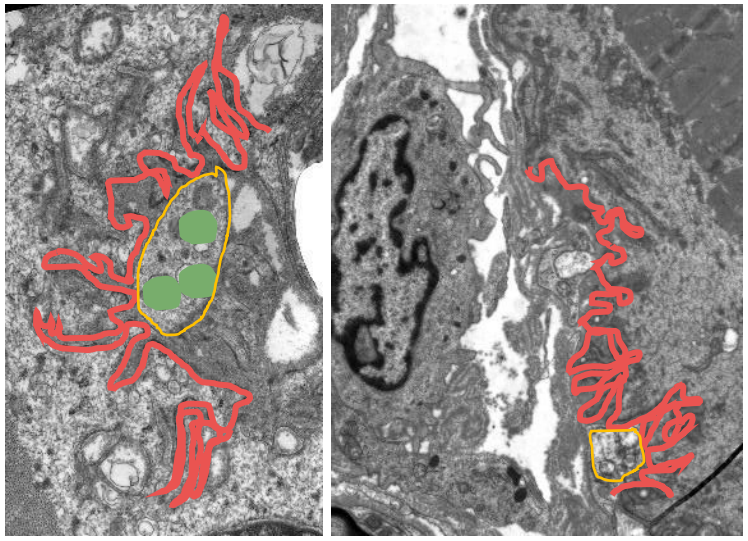
shortening



rarefication



plumping of postsynaptic clefts



CHARITÉ | Bouton terminal | Postsynaptic membrane | Mitochondria | Vesicles

Conclusion

Detailed evaluation and quantification pending, but …

- different NMJ is the same patients are not affected the same!
- It´s a spectrum – from “healthy appearing” to completely plumed

Question long-standing statements,
if they are not proven convincingly

lasting success is only possible as a team

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janssen

DGM Deutsche Gesellschaft für Muskelkranke e. V.

European Reference Networks for rare or low prevalence complex diseases
Network Neurological Diseases (ERN-RND)

EUROPEAN NEUROMUSCULAR CENTRE

AFMTÉLÉTHON INNOVER POUR GUÉRIR

DFG Deutsche Forschungsgemeinschaft German Research Foundation

MYOSITIS NETZ