Myasthenia Gravis

http://www2.mrc-lmb.cam.ac.uk/group-leaders/emeritus/nigel-unwin/
Myasthenia Gravis

http://neuromuscular.wustl.edu/musdist/dag2.htm
Myasthenia Gravis

NMJ

NORMAL

compound action potential

time of somatic efferent neuron stimulus

compound action potential

time of somatic efferent neuron stimulus

MYASTHENIA GRAVIS

no decrement in amplitude in response to repeated stimulation

decline in amplitude with repeated stimulation because fewer muscle fibers in motor unit are firing action potentials
Other Myasthenic Syndromes

**Congenital Myasthenic Syndromes:**
Arise from mutations in genes that code for critical components of NMJ
- Change function, trafficking or modification of proteins required for proper function

**Lambert-Eaton Myasthenic Syndrome:**
Often associated with certain forms of cancer (~60% with SCLC)
Autoantibodies produced against many components of the NMJ

**Neonatal Myasthenia Gravis:**
Maternal antibodies targeting the γ-subunit of the fetal nAChR
Typically abates as ε replaces γ-subunits in mature nAChRs,
but can produce muscular development delays
Group Activities

1. Treatments for MG and Myasthenic Syndromes
2. Case Study
Treatment for Myasthenia Gravis

• Acetylcholinesterase Inhibitors
  Physostigmine, Donepezil, Rivastigmine

• K⁺ Channel Blockers
  4-aminopyridine; 3,4-diaminopyridine

• Immunosuppressants
  Cyclosporin, Prednisone

• Plasmapharesis

• Thymectomy

Choose 2 or more treatment options and describe:

1. How it works to reduce symptoms
2. If it would work for MG as well as congenital syndromes
Case Study

From Milone et al, Neurology, 66; 2006

Patient 1 (A):
Age 7, has required artificial ventilation since birth
Severe weakness in all skeletal muscles, no tendon reflexes
Anti-nAChR antibody test is negative

Patient 2 (B,D):
Age 44, muscle weakness progressed since age 2,
wheelchair-bound since age 10
Anti-nAChR antibody test is negative

In both cases, parents and siblings are unaffected

With what you know about Myasthenic Syndromes and synaptic neurotransmission at the NMJ, suggest 2 or more potential proteins that could be involved in the pathology of these patients and explain why.