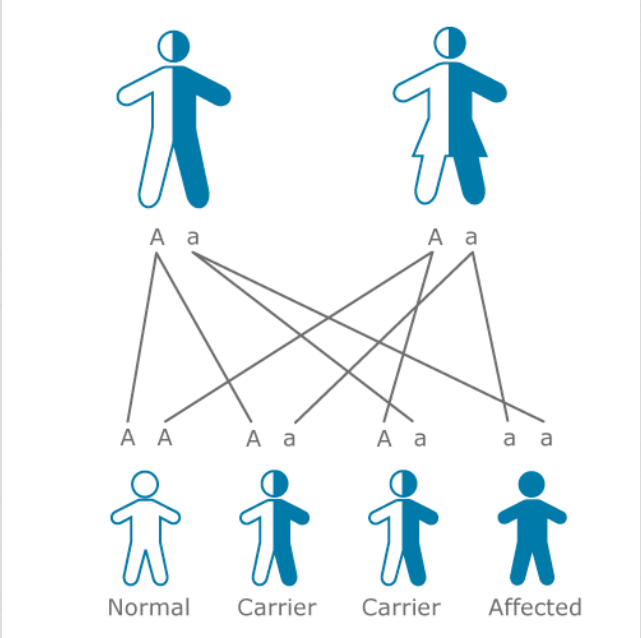
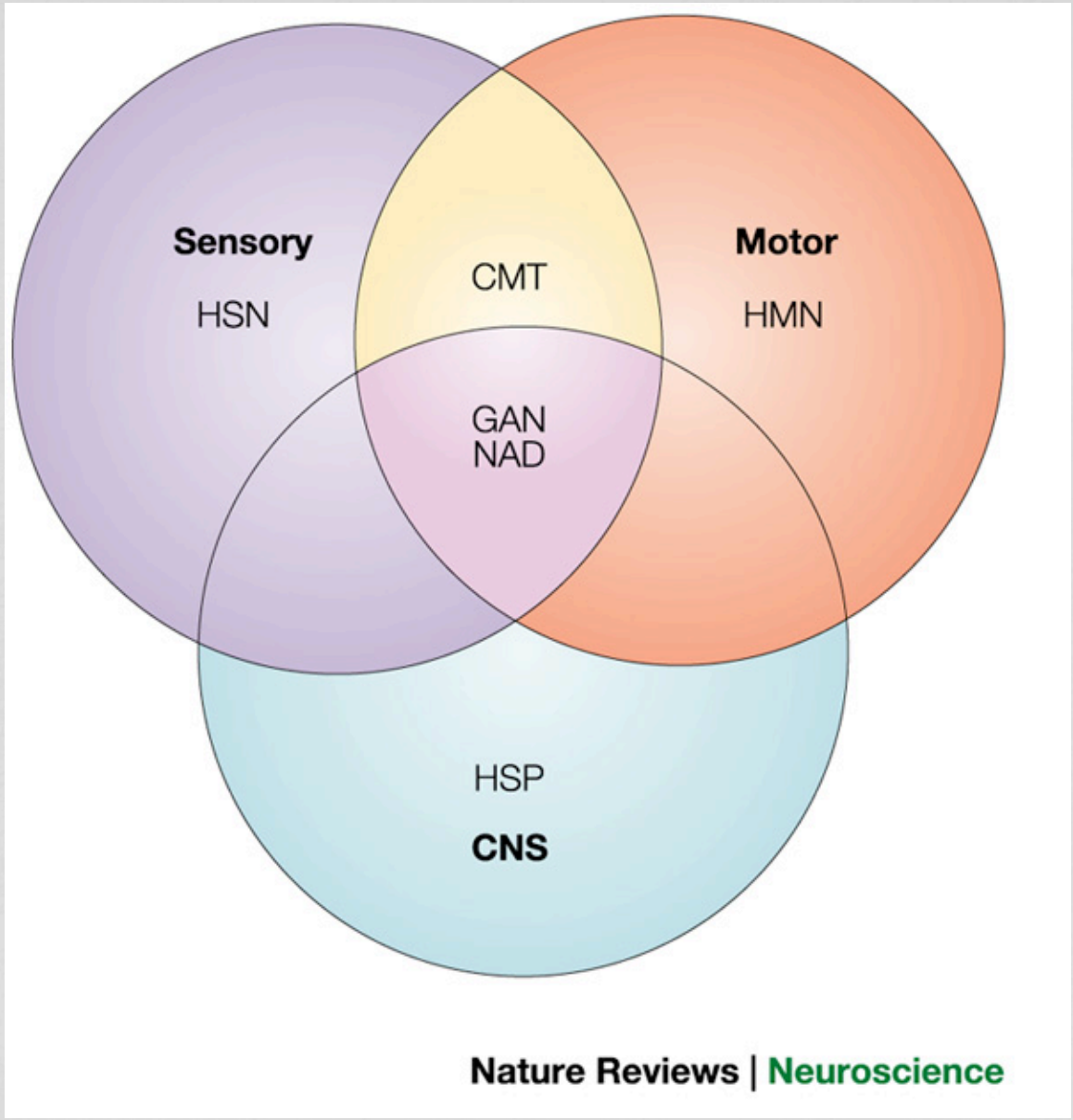
Giant Axonal Neuropathy

By Joshua Khani

What is Giant Axonal Neuropathy (GAN)?

- Dysfunction or disorganization in nerve cells
  - Swellings of axons caused by bundles of neurofilaments
- Autosomal recessive disorder
  - 25% chance of inheriting
- Incidence is unknown
- Progressive neurodegeneration
  - Generally appears in infancy




Sensory
HSN
CMT
Motor
HMN
GAN
NAD
HSP
CNS
Nature Reviews | Neuroscience

Signs and Symptoms

Initial (1st Decade)	Advanced (2nd Decade)	Late (3rd Decade)
• trouble walking	• inability to walk	• bedridden
• unusual posture	• loss of sensation and strength in limbs	• seizures
• curly, lackluster hair	• loss of muscle control and coordination (ataxia and dysarthria)	• dementia
• impaired reflexes	• hearing and visual problems	• mental retardation

Example of GAN

Clinical Testing

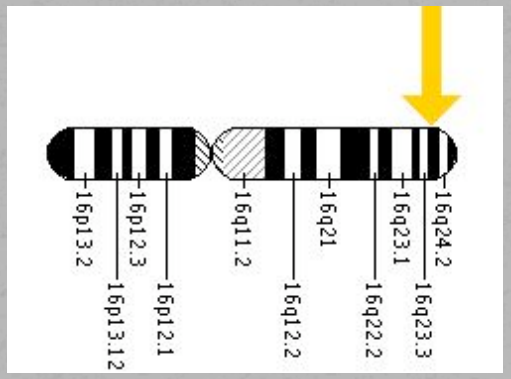
- Biopsy of peripheral nerve cells and other areas of the nervous system
  - Shows swollen axons
- Microscope examination of hair
  - Abnormal variations in diameters of the follicles and twisting of the hair along the long axis
- Electron Microscope of skin
  - Shows accumulation of spiraling filaments
- Other signs
  - Abnormal responses to stimulation in the visual and auditory cortex
  - MRI show white matter abnormalities
  - Moderate to complete reduction of nerve conduction velocity

Genetics of GAN

- Only one gene associated with Giant Axonal Neuropathy
- No other phenotypes correlated with a mutation of the GAN gene
- GAN encodes for the protein gigaxonin
- Gigaxonin plays a role in the architecture of the neurofilaments
  - Gigaxonin controls degradation of a microtuble-associated-proteins (MAPs)
  - The accumulation of MAP-1 B-LC, MAP8, and TBCB in a cell leads to neuron death
- The test for the GAN is done by sequence analysis
  - Located on chromosome 16 at locus 16q24.1

More Genetics

- Mutations: Missense, nonsense, frameshift
- GAN is ~65,000 base pairs long



Treatments

After assessment of abilities and progression of disorder, treatments are symptomatic and include a team of professionals.

- Neurologists, ophthalmologist, orthopedic surgeons, physiotherapists, psychologists, and speech and occupational therapists

- Even with this team, the disease cannot be stopped and life cannot be prolonged significantly

Questions?

Resources

- http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=gan#gan.Resources
- http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=gan#gan.Clinical_Description
- http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=605379
- http://ghr.nlm.nih.gov/condition=giantaxonalneuropathy
- http://www.ninds.nih.gov/disorders/gan/GiantAxonalNeuropathy.htm
- http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=256850
- http://www.webmd.com/brain/neuropathy-giant-axonal
- http://www.nature.com/nrn/journal/v4/n9/fig_tab/nrn1196_F5.html
- http://video.aol.com/category/giant-axonal-neuropathy
- http://ghr.nlm.nih.gov/gene=gan
- http://journals.cambridge.org/download.php?file=%2FDMC%2FDMC46_10%2FS0012162204001215a.pdf&code=6b07cc7f754eadb7d298f403f4d38dc7
- http://neuromuscular.wustl.edu/time/child.html#gan