Huntington's Disease

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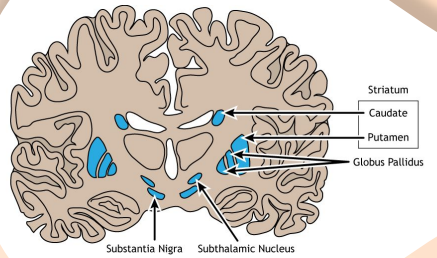
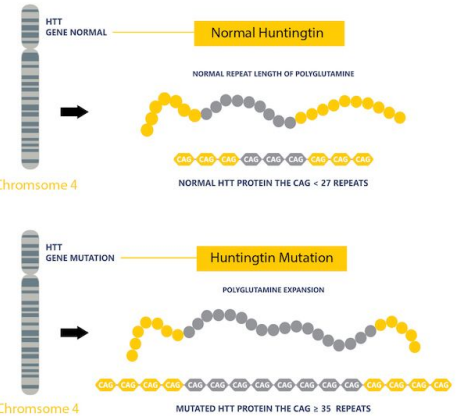
Physiological Process

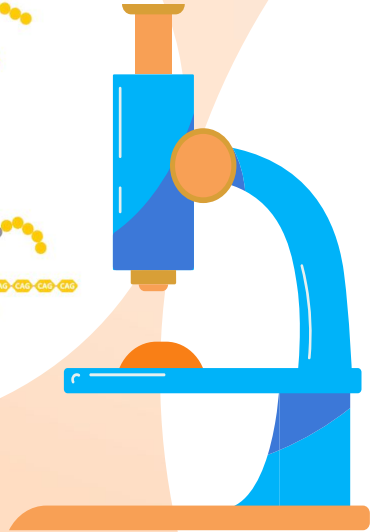
Huntington's disease is a neurodegenerative disorder (Kills neuronal cells) that affects the human brain. From early stages to late in the disease's progression, the most prominently affected area is the Striatal part (Caudate nucleus and Putamen) of the Basal Ganglia. Though many other portions throughout the brain can get affected as the disease continues to progress in severity.



The Basal Ganglia, or Basal Nuclei, is a group of 5 structures within the upper midbrain. It's most associated with the execution of intentional movements of the body, with some connection to cognitive processes like memory, processing of knowledge, and the understanding of different idea's. The caudate nucleus being specifically linked to the planning of movement, ability to learn, remember, focus, and have or express emotion. The putamen has similar properties to the caudate nucleus, but can also be associated with speech articulation and the facilitation of precise movements.

Mutations





- Huntington's disease is caused by a mutation in the HTT gene which creates the huntingtin protein
- The HTT gene is found on chromosome 4
- The CAG codon repeats 36 or more times which is greater than normal
  - Between 10-35 repeats is considered normal
- This repeat causes the huntingtin protein to become too long which disrupts the functions of the neurons
- It is a germline mutation because it is inherited
  - If a parent has Huntington's disease, their child has a 50% chance of inheriting it
- This mutation may be considered a chromosomal or an expansion mutation
  - An expansion mutation is an increase in the number of repeats or copies of a codon

Symptoms

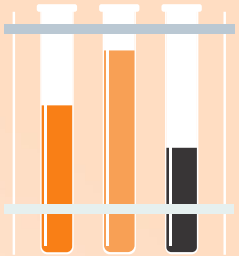
Movement

- Abnormal movement in the eyes (slow movement)
- Body jerks (chorea)
- Muscle contractions
- Abnormalities in walking, balance, and posture
- Swallowing and speech becomes difficult

Psychological

- Difficulty to take in new information
- Challenging to focus and prioritize on certain ideas
- Tendency to get stuck on a recurring thought
- Random outbursts and lack of control
- Slowness in processing ideas and information

Treatment for Huntington's Disease



There are currently no treatments to cure Huntington's Disease, but there are medications to relieve the symptoms.

Medication for movement symptoms:

- Antipsychotic drugs: Haloperidol and fluphenazine can help reduce sudden jerky movements because it is a side effect from taking the medication, but a side effect is that is can cause more muscle contractions.
- Tetrabenazine and Austedo can help control and lessen the unintentional movements that come from Huntington's Disease. Some side effects can be drowsiness and restlessness.

Medication for psychological symptoms:

- Antidepressants: Celexa, Lexapro, Prozac, and Zoloft can help with the obsessive behaviors and thoughts. Side effects may include nausea, diarrhea, drowsiness, and low blood pressure.
- Antipsychotic drugs: Seroquel and Zyprexa can help lessen outbursts and other mood symptoms that come from Huntington's Disease. However, these drugs can worsen chorea.

State of Research on Treatment Plans

Current testing on investigational drugs is leading towards new treatments while also gaining an improved understanding of the disease process. Many classes of drugs have been tested based on those that can control symptoms, slow down the rate of progression, having the effects of excitotoxins blocked, improving neuronal health by providing support factors, or contributing to the development and progression of Huntington's disease by suppressing metabolic defects.

There are also currently groups of scientists who are using gene-editing (CRISPR/CAS9) or specific molecules to use to interfere with HTT production in cells or animals to reduce or elevation the production of HTT.

Current Research Study ↓

HDClarity: A Multi-Site Cerebrospinal Fluid Collection Initiative to Facilitate Therapeutic Development for Huntington's Disease

This study is based on the collection of cerebrospinal fluid (CSF). CSF is the fluid that surrounds the brain and spinal cord. This fluid is used to study biomarkers; looking for the specific biomarkers that influence HD's pathophysiology and progression along with what are the difference better biomarkers in HD participants and non-HD participants. Also, biomarkers may help design and guide future research studies and clinical trials as well as help us better understand who will most likely benefit from a particular treatment.

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