E40 – The Use of Imaging in Evaluating Progression of Huntington's Disease

2026 Spring Symposium

Abstract

Huntington's Disease (HD) is a fatal hereditary neurodegenerative disorder caused by a gene mutation. Those who are diagnosed with Huntington's typically receive a prognosis of about 10-25 more years, but disease progression may vary. Symptoms can include twitching of the extremities, mood swings, psychosis, and depression. A blood test and genetic testing is used to confirm the diagnosis of Huntington's Disease. Magnetic Resonance Imaging (MRI) and Nuclear Medicine Positron Emission Tomography (PET) scans are the two most common scans to evaluate structural loss due to HD. Management of symptoms is vital for quality of life, as there is currently no treatment or cure. With the advancement of technology and research, hopefully a cure can be found soon.

Keywords: Huntington's Disease (HD), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET)

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Introduction

Hereditary neurodegenerative diseases are among the most misunderstood diseases today. Specifically focusing on Huntington's Disease – this disease process had been clinically described by Dr. George Huntington in 1872. But the genetic mutation that causes this disease was not discovered until over 100 years later in 1993 by the Huntington's Disease Collaborative Research Group (John Hopkins Medicine). There is still no treatment or cure for this disease. With Huntington's affecting both men and women, and approximately 4.1 - 5.2 per 100,000 people in the United States, developing a treatment or a cure would be a major medical breakthrough (Fisher & Semaka, 2024). While genetic testing is used to diagnose the disease, imaging is a powerful tool in evaluating the progression and structural development of the disease. This paper will discuss what Huntington's Disease is, the symptoms of Huntington's Disease, how it can be diagnosed, what imaging modalities are used to evaluate the progression of the disease, and the management of Huntington's Disease post-diagnosis.

Discussion

What is Huntington's Disease?

The Huntington's Disease Society of America (2019) defines Huntington's Disease as "a hereditary neurodegenerative disorder that is characterized by progressively worsening motor, cognitive, behavioral, and psychiatric symptoms". Huntington's Disease is caused by a gene mutation on the Huntingtin (HTT) gene. This signals an abnormal protein to build up in brain cells and overtime cause damage. This damage directly affects the cells that control movement, coordination, mood, and thinking. As well as damaging the cells that communicate between each

other in the brain. There are two main types of Huntington's disease classified based on the age at which symptoms appear. Typical onset is between the ages of 30 and 55. Early-onset (Juvenile) Huntington's is classified by the presence of symptoms before the age of 20. If the first symptoms do not appear until after the age of 20, the disease is considered adult-onset Huntington's (Cleveland Clinic, 2025). According to the Huntington's Disease Society of America (2019), "Juvenile Huntington's Disease (JHD) usually has a more rapid progression rate than adult-onset Huntington's Disease; the earlier the onset, the faster the disease progresses. Death often occurs within 10 years of JHD onset, as opposed to 10-25 years in adult-onset Huntington's".

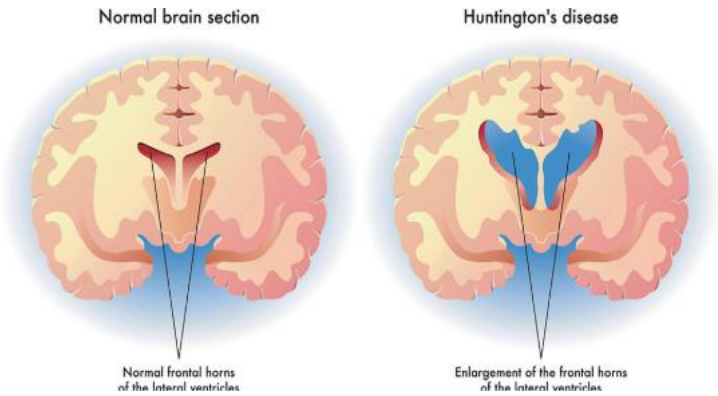
Symptoms of Huntington's Disease

One of the first signs that someone may have Huntington's Disease is an involuntary twitching or jerking movement of the hands, fingers, or face; this is known as chorea. Eventually, this involuntary movement may spread to the upper and lower extremities, as well as the rest of the body. Which can ultimately make it difficult to walk, eat, or speak. Other physical symptoms may include; unexplained weight loss, difficulty with balance and coordination, and dysphagia. While physical symptoms can be very debilitating, this disease also presents mental and emotional symptoms as well. These symptoms can include; mood swings, difficulty with impulse control and concentration, as well as depression and anxiety (Cleveland Clinic, 2025).

How is Huntington's Disease Diagnosed?

Huntington's Disease is considered an autosomal dominant inherited condition. Meaning that even if only one parent is a carrier of the gene, there is a possibility of inheriting the disease. But this mutation can also occur in people with no family history of having the

gene. Huntington's Disease is diagnosed by looking at symptomology and family history. If symptoms correlated with Huntington's are present alongside a family history, then genetic testing will be done to confirm the presence of the gene mutation. Once it is confirmed that the gene is present, an MRI of the brain is typically ordered to evaluate any structural changes within the brain tissue (Cleveland Clinic, 2025). "On imaging Huntington's Disease is classically characterized by atrophy of the caudate nucleus with enlargement of the frontal horns of the lateral ventricles" (Gaillard, 2008). Figure 1 below shows the structural differences between a normal brain and a brain with Huntington's Disease.



Huntington's Disease. https://www.healthdirect.gov.au/huntingtons-disease

Imaging Modalities that Aid in Evaluating the Progression of Huntington's Disease

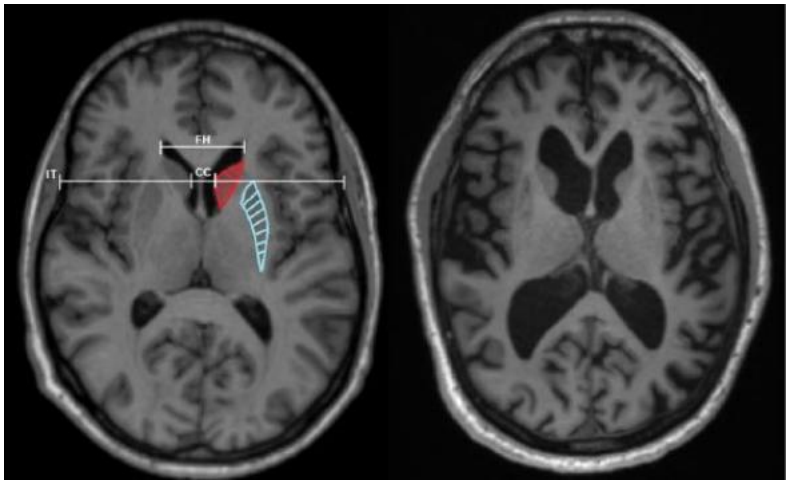
Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) is a "non-invasive imaging technology that produces three-dimensional detailed anatomical images" (National Institute of Biomedical Imaging and Bioengineering, n.d.). MRI uses strong magnetic fields to interact with protons in the body and produce very detailed anatomic images. MRI and Computed Tomography (CT) are similar in that they both produce cross-sectional images of the body. But they differ in that MRI produces much more detailed images of soft tissue structures like the brain, spinal cord, ligaments, and tendons. MRI is also preferred over CT when it comes to conditions that require

frequent imaging as it does not use ionizing radiation, therefore reducing the risk of biological damage from imaging.

While a blood test is used to confirm the diagnosis of Huntington's, Magnetic Resonance Imaging is a tool used as a biomarker to evaluate and track the progression of structural changes within the brain as the disease progresses. An MRI of the brain will typically be ordered after diagnosis to develop a baseline image of the brain, and as needed later to evaluate the brain structure depending on the development of symptoms. While those involved in research studies or clinical trials will typically receive an MRI annually.

According to the National Library of Medicine (2014), "the most consistent change in the HD brain is a significant volumetric loss of the striatum. A reduction of 50%-54% in putamen volume, and 28%-29% in mean caudate volume has been reported in patients with mild to moderate HD". It is also mentioned that volumetric putamen atrophy is correlated with motor impairments, while mental and cognitive assessments are inversely correlated with the amount of caudate volume loss in the brain. The image below demonstrates a comparison of a control brain and a brain of someone with Huntington's Disease. The putamen of the brain is shown in blue, and the caudate is shown in red. The following measurements are evaluated "CC: inter-caudate distance; FH: frontal horn distance of lateral ventricles; IT: inner table of skull" (Goh et al, 2018).

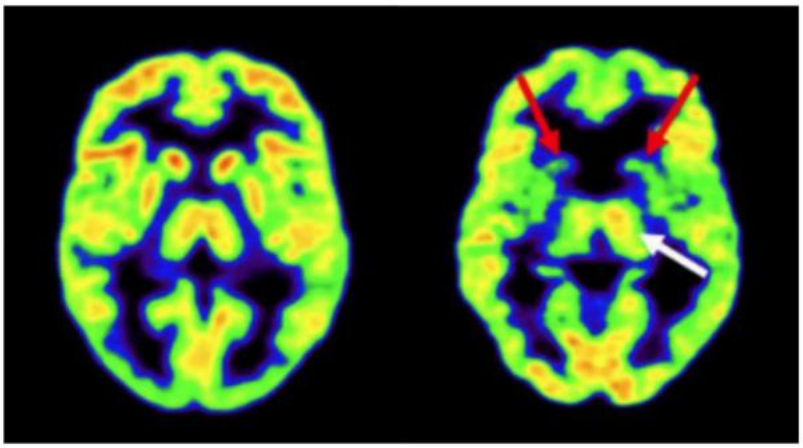


Neuropsychiatric Manifestations of Huntington's Disease: https://www.researchgate.net/publication/326442062_Neuropsychiatric_manifestations_of_Huntington's_disease

Nuclear Medicine

Nuclear Medicine is another imaging modality used to evaluate anatomical structures throughout the progression of Huntington's Disease. "Nuclear medicine imaging is a test that uses small amounts of radioactive substances (called tracers) to diagnose or monitor diseases or illnesses. After you receive the tracer, a special camera senses the radiation it gives off as it moves through your body. Then, a computer produces detailed images of your organs and tissues" (Cleveland Clinic, 2025). The specific type of imaging used in Nuclear Medicine for Huntington's Disease is called Positron Emission Tomography (PET) scans. During a PET scan, a radiotracer designed to be absorbed by specific diseased cells is injected into the patient's body. The scanner then detects the areas of the body that the radiotracer is absorbed by and creates an image demonstrating the anatomy of interest as "hot spots" (Cleveland Clinic, 2022).

If a PET scan for Huntington's is indicated by symptoms, family history, or past diagnosis; a radiotracer called F18 Fludeoxyglucose (FDG) is used (Ashraf, 2023). This radiotracer monitors glucose accumulations in areas of the body with high metabolic rates. The brain is just one organ that typically has a high glycolytic rate where this tracer tends to heavily accumulate in. Decreased glucose metabolism in the bilateral striatum (putamen and caudate nucleus) is a "well-known and characteristic finding of HD. FDG PET is capable of showing striatal dysfunction in HD even when structural imaging is normal or mild" (Banks, 2023).



PET Imaging in Huntington's Disease Clinical Trials: https://imaging-cro.biospective.com/resources/huntingtons-pet-biomarkers-clinical-trials

The image above demonstrates a comparison of a FDG PET scan done on a healthy control brain on the left, and "premanifest HD gene expansion carrier" (Brown & Bedell, 2025) on the right. The brain on the right is a person who has inherited the gene that causes Huntington's Disease but is not yet presenting symptoms. The red arrows on the brain to the right are pointing at the size and color of the striatum of the brain. Not only are the structures smaller, but they are showing green in comparison to the same area in red on the healthy brain. The red shows the regions where FDG heavily accumulated, whereas FDG is not

accumulating as heavy in the green regions. This demonstrates decreased FDG uptake in the striatum of the brain on the right, indicating that glucose metabolism is not occurring here. This is commonly seen in Huntington's Disease (Brown & Bedell, 2025).

Management of Huntington's Disease

While there is currently no cure or treatment to slow down the progression of Huntington's Disease, there are measures that can be taken to manage the symptoms that come with the disease. These are particularly important to maintain quality of life. Certain medications can be prescribed to lessen the symptoms of chorea that come with HD. Other medications may be prescribed to manage mental health symptoms such as antipsychotics, antidepressants, or mood stabilizers. A speech language pathologist can help to address difficulties swallowing or eating and provide guidance with communication devices if the person with HD requires them. Physical therapists can provide and give instruction on safe exercises to help maintain mobility as long as possible. Occupational therapists can assist those with and caregivers of those with HD on using assistive devices to improve functioning for activities of daily living (Mayo Clinic, 2024).

Conclusion

As stated previously, Huntington's Disease is a fatal hereditary neurodegenerative disorder that affects both cognitive, behavioral, and motor function. Symptoms of the disease include twitching or jerking of the extremities, known as chorea, difficulty or loss of balance and coordination, mood swings, depression, psychosis, dysphagia, etc. This disease is caused by a gene mutation and is passed down from family members but can also occur spontaneously. Genetic testing is used to confirm diagnosis, but imaging is used to evaluate the stages of structural loss at diagnosis and throughout the progression of the disease. Imaging

exams that can be used to evaluate this structural loss include MRI of the brain and PET scans in nuclear medicine. These modalities can visualize the size and function of the caudate nucleus and putamen, and loss of structure and function in these areas is directly correlated with Huntington's disease. Imaging plays a crucial role in clinical trials, improving research, and understanding this disease. Hopefully, with the development of technology and the years of research being put in, a treatment can be found to help those affected by this terrible disease.

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