

Case Study 2: Neurological Degenerative Disease FDA Regulatory and Clinical Background

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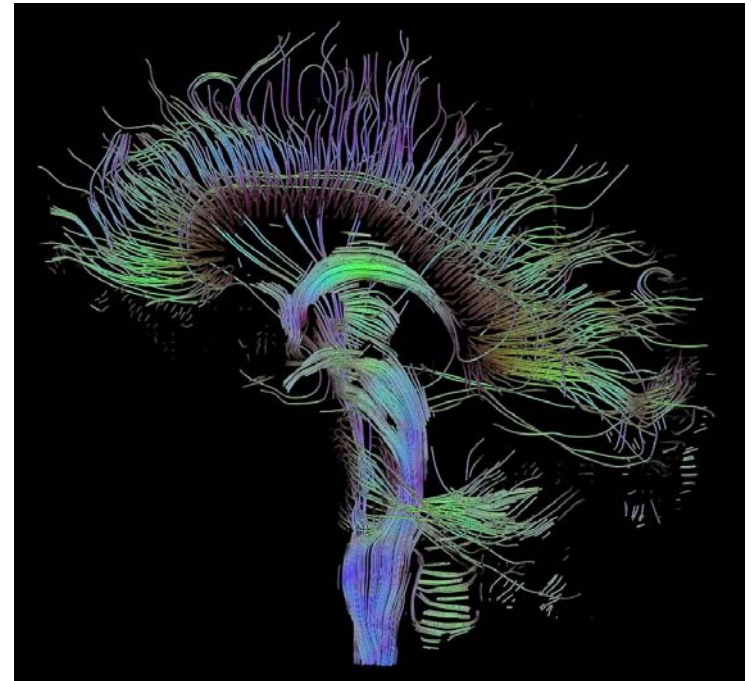
Neurological Degenerative Diseases

Neurodegenerative Diseases

- Parkinson's disease
- Huntington's disease
- Alzheimer's disease
- Dementia
- Amyotrophic lateral sclerosis (ALS)

Common Non-Motor Symptoms

- Memory loss
- Forgetfulness
- Agitation
- Mood changes

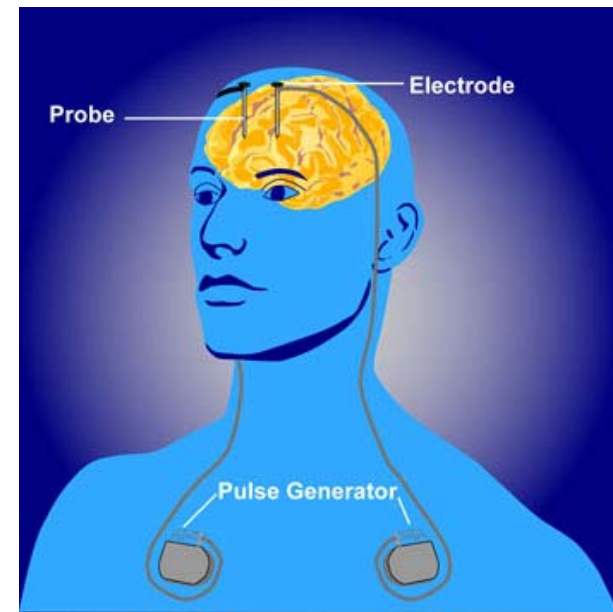


Neurological Degenerative Disease Example: Parkinson's Disease: Symptoms

- **Primary motor symptoms** include resting tremor, bradykinesia, rigidity, and postural instability.
- Non-motor symptoms may include **cognitive impairment, mood disorders, and sleep disturbances.**
- Symptoms vary among patients. The progression of Parkinson's disease may **differ markedly from patient to patient.**
- There is **no cure** for Parkinson's disease. The goals for treatment are to improve quality of life and manage the symptoms of the disease.

Neurological Degenerative Disease Example: Parkinson's Disease: Treatment Options

- Several treatment options for Parkinson's disease are available and involve a wide range of administration routes, including tablets, capsules, patches, subcutaneous injections, intramuscular injections and intrajejunal infusions.
- Deep brain stimulation, a medical device implanted in the brain, is also a therapeutic option for patients with advanced Parkinson's disease.



Neurological Degenerative Disease Example: Parkinson's Disease: PFDD

- Parkinson's disease is a progressive, devastating disease. Participants emphasized the **difficulty of living with the unexpected onset and progression of symptoms**.
- Parkinson's disease **impacts all aspects of patients' lives**. Participants described severe limitations in performing at work, caring for self and family, and maintaining relationships.
- Participants shared the **emotional toll of living with social isolation** and adjusting to significant lifestyle changes to manage their Parkinson's disease.
- Participants emphasized that the **side effects of treatments were often as debilitating as the underlying disease symptoms**.

Neurological Degenerative Disease Example: Huntington's Disease: Symptoms and Treatment

- Huntington's disease (HD) is a hereditary, progressive, and fatal brain disorder that causes a range of **physical, mental, and emotional disabilities**, including uncontrolled movements, loss of cognitive abilities, and behavioral manifestations.
- There is **no cure** for HD, and current treatments attempt to reduce the symptoms of HD.
- As symptoms progress, individuals become increasingly or totally dependent on others for care.

Neurological Degenerative Disease Example: Huntington's Disease: PFDD

- HD is a devastating and debilitating disease that has a tremendous impact on patients and their families. **Participants emphasized that psychiatric and behavioral issues were the most significant symptoms of HD.** Many participants commented on the destructive impact of HD on multiple generations of their families.
- Participants said that current treatments do not adequately manage their most disabling symptoms.
- **HD impacts all aspects of patients' lives.** Participants described severe limitations on physical activity, loss of independence and increased reliance on others for care, the devastating impact on relationships, and a constant fear of passing the disease onto their children. Participants shared that the cognitive impairments of HD often left them or their loved ones socially isolated, which worsened their depression and anxiety.



Examples: Preference-Sensitive Questions

- At what stage of the disease (mild to severe symptoms) do patients prefer to undergo a treatment that involves more risk?
- How important are the side effects associated with a treatment?
The number of medications a patient takes?
- What are patient preferences about a tradeoff between device invasiveness and device effectiveness? Device duration?
- How do patients weigh the trade-off between urgency for new treatments and uncertainty about a new treatment's benefit-risk profile?



Regulatory Preference Study Considerations

- How can the sponsor demonstrate that study design has minimized potential cognitive biases?
- How can the sponsor demonstrate that study participants fully understand the harm, risk, benefit, uncertainty and other medical information being communicated to them?
- How could the sponsor think about potential subgroups for the patient preference survey?

