THE PRION PROTEIN AND ITS EFFECTS ON THE HUMAN BRAIN IN RELATION TO NEURODEGENERATION

Maria Habean, Hans Bogenrief, and Cheyenne Stambaugh
Advised by Dr. Anton Komar

INTRODUCTION

- A prion is an infectious protein responsible for numerous infectious neurodegenerative diseases.
- The word "Prion" was used to distinguish the proteinaceous infectious particles from viruses and viroids.
- The prion was discovered as an accidental byproduct of unsuccessful attempts to unravel the nature of the scrapie agent – for over two decades (Prusiner, 2004).
- The prion was first thought to be a virus, but as further research was made, this idea was revised (Prusiner, 2004).
- The cause of most of the neurodegenerative diseases that are connected to prions are from the protein PrP^{C} misfolding and becoming the infectious agent known as PrP^{Sc} (Prusiner, 2004).
- Currently, researchers have settled on the protein only hypothesis (Prusiner, 2004).

OBJECTIVE

- Obtain a better understanding of the prions and to see how prions can affect humans.

METHODS

- Databases for academic journals such as Google Scholar and Ebsco Host were used to gather resources.
- Keywords such as “prion proteins,” “nerves,” & “nervous system” were used to locate sources.
- The book "Prion Biology and Diseases" was also used for reference.

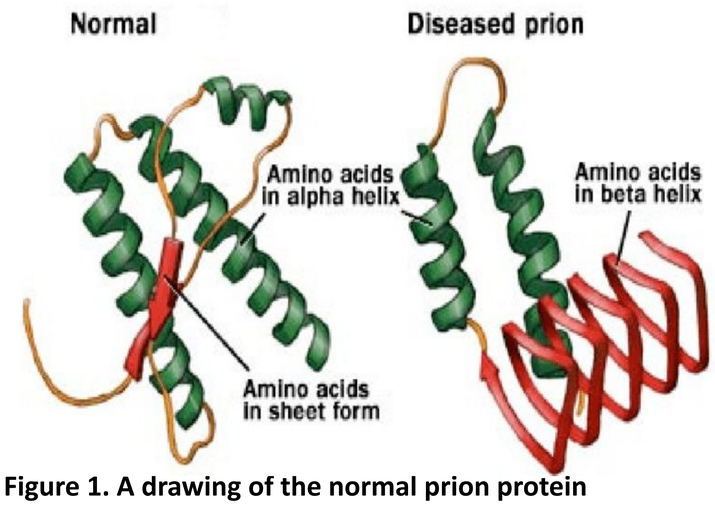

Figure 1. A drawing of the normal prion protein compared to the disease-causing protein. https://www.researchgate.net/figure/Normal-and-abnormal-form-of-prion-protein-Normal-prion-protein-has-amino-acids-in-alpha_fig1_326330981

FINDINGS

Various Diseases Associated with Prions

- Scrapie, originally only a disease observed in sheep, was one of the first diseases determined to be caused by prion proteins.
- Various other diseases caused by prions include:
  - Creutzfeldt-Jacob Disease - human-inherited variant of the same condition known as “mad cow disease” (BSE). Contracted by contaminated medical equipment or ingesting contaminated meat. It is often fatal.
  - VPSPr - affects the digestive system
  - GSS - an extremely rare condition that affects the brain
  - Kuru - observed in New Guinea in rare cases; contracted by consuming contaminated human brain tissue
  - Fatal Insomnia - leads to trouble sleeping; it is a hereditary disease but there is a sporadic form that can't be inherited
  - Chronic Wasting Disease – Rapidly spreading disease affecting Deer, Elk, Moose, and other species (CDC, 2019).

Identification & Treatment

- The most common symptoms that people come in with are confusion, fatigue, hallucinations, and rapid developing dementia. Many of these symptoms are similar to other diseases. MRIs, Spinal taps, blood tests, and neuro exams are used to diagnose prion diseases (John Hopkins, 2019).
- Currently, the timeline for treatment for these diseases is small; found between the initial synapse degeneration and terminal cell loss (Prusiner, 2004).
- In that interval, an effective therapeutic treatment could prevent further degeneration. Once cleared of the infectious proteins, a test of the dendrite trees is done to see if they will regrow (Prusiner, 2004).

Recent Research

- Parkinson’s Disease, another neurodegenerative disease, is believed to have protein misfolding and aggregation similar to that of prion diseases (Brundin & Melki, 2017; Borghammer, 2018).
- Distribution of prion proteins in regions throughout the brain surprisingly aren’t always correlated with sites of neurodegeneration (Alibhai et al., 2016).

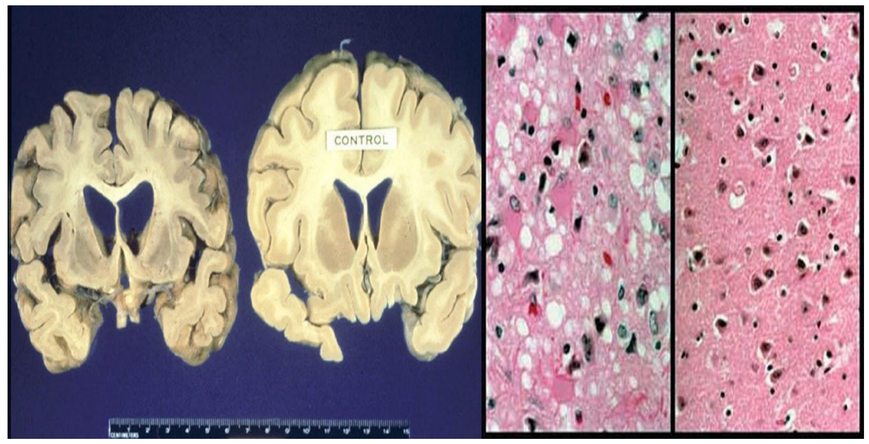

Figure 2. The effect the prion protein has on the brain. On the left for each side shows a brain and tissues affected with infectious prions, while the right shows a healthy brain and tissues. http://biologicalexceptions.blogspot.com/2016/01/an-infectious-genetic-disease-better.html

Recent Research (cont.)

- The course a prion disease takes is instead dependent on response from microglial cells within the brain, where regions with an inflammatory response are sites that are vulnerable to neurodegeneration (Alibhai, et al., 2016).

CONCLUSION & FUTURE WORK

Over the past few decades, human understanding of the prion protein has increased immensely. They not only have pathogenic, medicinal, and agricultural consequences in the human population, but also have an ecological effect on various species. Medical treatment for these diseases is still advancing as many of the diseases are fatal and have no known cure. Further research should be made into utilizing gene therapy to prevent these diseases on a hereditary basis, as well as more efficient treatment methods of those infected with pathogenic prions.

References

Alibhai J, Blanco RA, Barria MA, Piccardo P, Caughey B, et al. (2016). Distribution of Misfolded Prion Protein Seeding Activity Alone Does Not Predict Regions of Neurodegeneration. *PLOS Biology,* 14(11): https://doi.org/10.1371/journal.pbio.1002579

Borghammer, P. (2018). How does Parkinson’s disease begin? Perspectives on neuroanatomical pathways, prions, and histology. *Movement Disorders*, (1), 48. https://proxy.ulib.csuohio.edu:2096/10.1002/mds.27138.

Brundin, P., & Melki, R. (2017). Prying into the prion hypothesis for Parkinson’s disease. *Journal of Neuroscience*, 37(41), 9808–9818.

Chronic Wasting Disease (2019). *CDC.* Retrieved from https://www.cdc.gov/prions/cwd/index.html https://proxy.ulib.csuohio.edu:2096/10.1523/JNEUROSCI.1788-16.2017

Prusiner, S. B. (2004). Prion biology and diseases. New York: Cold Spring Harbor Laboratory Press.

Prion Diseases (2019). *John Hopkins Institution*. https://www.hopkinsmedicine.org/health/conditions-and-diseases/prion- diseases

Acknowledgments

We would like to thank Dr. Anton Komar for being an advisor for this research project.