Huntington’s Disease and the Basal Ganglia
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Background
- Huntington’s Disease is a genetic disease that breaks down the nerves in the brain.
- Symptoms of the disease can appear in ages 30 to 50 and it will affect a person’s ability to think, eat, move, and speak. Symptoms may describe as having ALS, Parkinson’s and Alzheimer’s disease at the same time.
- HD can be broken down into three stages. The first is chorea and mood swings. The second is involuntary movements that can affect swallowing and speech. The final stage is when voluntary movement is completely lost, in which assistance is necessary and can result in death.
- The basal ganglia is a part of the brain that controls movement and works closely with the frontal lobe.

Methods
- Allan Brain Atlas (http://www.brain-map.org/) was used to collect gene expression data from the basal ganglia area in the brain. The data came from four donors. Donor one: H0351.2001; Donor two: H0351.2002; Donor three: H0351.1009; Donor four: H0351.1012. Venny (http://bioinformatics.cse.edu/tools/venny/index.html) was used to sort through the genes found in the four donors to find all the genes that the donors had in common.
- PythonAnywhere (https://www.pythonanywhere.com/) was used to create a chart showing the different fold changes in the genes taken from the four donors.
- DAVID (https://david.ncifcrf.gov/tools.jsp) is a functional annotation tool used to cluster different genes based on their function.
- STRING (http://string-db.org/) is a database that was used to identify what proteins a specific gene interacts with.
- Gene Wrangler (https://genewrangler.org/index.php?action=search) was used to further investigate the relevance of genes found using the other databases to Huntington’s Disease.

Results
The heat maps above are collected from the basal ganglia region from four donors. The data collected needed the requirement of a fold change greater than 3. The red parts of the maps demonstrate high gene expression and the green express low gene expression. The black section represents equal expression.

Common Genes
The Venny database was used to gather the selected genes from the four donors and compare them to see which genes were found common in all of the donors. 43.1% of genes were common throughout the four donors.

Data Analysis
Python created a histogram showing the different fold changes in each of the four donors. The y-values display gene frequency, while the x-value displays the fold change of the genes.

The histogram is heavily right-skewed for a smaller fold change. The frequency of genes with a fold change of about 5 is approximately 140.

The histogram is right skewed. However, it is not as drastic as Donor One. Between fold change 6 and 10, the genes increase in frequency.

The variation in fold change is sizeable, displaying a heavily right-skewed graph. Genes with a larger fold change decrease at a value of approximately 25; however, after this point, the rest is minimal.

The fold-change variation is right-skewed but not as extreme, similar to Donor Two. However, around the 30 on the x-axis, the value decreases and returns to a stable fold change around 10 on the y-axis.

Common Gene Analysis
The STRING database is used to show how a specific gene interacts with other proteins. Taking the three new genes (DRD1, and DRD2) and placing them into STRING, there was a similar gene that was shown to interact in all three genes is SRP14. The three main genes were used as “fish hooks” to search for more genes related to the behavioral aspect of Huntington’s disease. Gene Wrangler helped to learn more about the genes found in STRING and what their relationship to Huntington’s Disease means.

Network Analysis
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Statistical Analysis
The maximum fold change of all four donors varies, with Donor Two being the lowest (27.877) and Donor Three being the highest (46.238). However, the minimum fold change is very similar in all of the donors. The average ranges between 5 and 9, however, they are still around the same value. Standard deviation also has the same variance as the mean, it fluctuates between 4 and 8.

Conclusion
- The Basal Ganglia contained many genes that deal with the locomotor and behavioral functions of Huntington’s disease.
- Genes such as HTR2C, DRD1, and DRD2 play a function in connecting many genes together that result in the behavior is HD.
- Other diseases, such as ALS, Alzheimer’s, and Parkinson’s share similar functional traits to Huntington’s because the same genes sets that produce similar actions when the disease is present.