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Different Neurological Pathologies Found in Humans Can Be Modelled into Mice Brains

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Abstract: Amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) are neurological diseases that affect a considerable population around the world. In this research two articles that implement trials on mice regarding these diseases were analyzed and compared to determine which advancement is most significant to human process. The articles were: Boosting a gut bacterium helps mice fight an ALS-like disease, and a protein helps disease-causing immune cells invade patients' brains. Gene expression in healthy mice and human brains can provide data to explore the capability of modeling neurological diseases in these rodents. Therefore, if different neurological pathologies found in mice can be modeled into the human brain, both research papers equally contribute to the scientific knowledge. The approach used was a direct compare and contrast method of both papers. In addition, a meta-analysis implementing different criteria to identify trends in different data. After the investigation was carried, it was found that 31% of genes were similar between human and mice brains. This provides a pronounced framework for human diseases to be modeled onto mice; this could open the possibility to discover new treatments and further understand the diseases' etiologies. Although there is still margin for error. Considering there is a lot still unknown about ALS when compared to MS, it was concluded that both research papers contribute to the scientific community, but not equally. The ALS article provides a new framework for finally understanding and treating this disease. Some factors that influenced the findings were the difficult access to information and the timeframe implemented.

Keywords: Disease Modeling, Clinical Trials, Mice, Neurodegenerative Diseases, ALS, Immune Disease, MS

1. Introduction

Autoimmune and neurodegenerative diseases affect millions of people worldwide. With people aging in the USA, there is an increase of the people affiliated with these types of diseases. [1] Amyotrophic lateral sclerosis, better known as ALS, is a neurodegenerative disorder "that affects nerve cells in the brain and spinal cord, causing loss of muscle control." [2] On the other hand, multiple sclerosis (MS) "is an unpredictable disease of the central nervous system that disrupts the flow of information within the brain, and between the brain and body." [3] ALS affects 1.5 to 3 per 100,000 people. MS affects 35.9 per 100,000 people. The scope of this case study investigation was to assess which of two articles regarding MS and ALS treatments contribute the most to the scientific knowledge. Both of these employ transgenic mice, which have been used for more than 20 years. [4] The articles that were analyzed were: Boosting a gut bacterium helps mice fight an ALS like disease, and a protein helps disease-causing immune cells invade patients' brains. [5, 6] "Genetic animal models of inherited neurological diseases provide an opportunity to test potential treatments and explore their promise for translation." [7] Therefore, if different neurological pathologies found in mice can be modeled into the human brain, both research papers equally contribute to the scientific knowledge.

2. Methodology

This investigation was approached by using a direct compare and contrast method. First, the articles were read and similarities between both papers were found and analyzed to come with a question that could prove which paper contributed most to the medical knowledge. Followed by in-depth research that elaborated on the articles being compared. Information regarding human disease projecting

into mice was consulted while using academic sources from trusted authors. As well as articles that have been previously peer-reviewed e.g., National Center for Biotechnology Information, National Multiple Sclerosis Society, Mayo Clinic, etc. To gather these articles different keywords were used to substantiate the information implemented, these were: neurological, pathologies, disease, immune disease, mice, brain, human brain, clinical trials brain mapping/modeling, ALS, and multiple sclerosis. In addition, different criteria were used to assess the advancement's importance. Such as: the population that each disease affects, preliminary results, how long has the disease been studied for, how aggressive the disease is, and other researchers' opinions on this particular topic. A meta-analysis was implemented to provide a quantitative assessment of how well human disease projecting into mice works. Moreover, a graph was made to analyze the given statistics. This methodology was implemented because it helped identify overall trends from researched data to conclude.

3. Findings

Research A *("Boosting a gut bacterium helps fight an ALS-like disease"*) talks about how rodents that develop a similar disease to ALS performed better when B3 producing bacteria were found in their intestines. A rise in Akkermansia muciniphila bacteria slowed the progression of the disease. On the other hand, some elevated bacteria were associated with more severe symptoms. [5] This is just a summary of the research; the full paper is: Potential roles of gut microbiome and metabolites in modulating ALS in mice. [8]

Research B (*"A protein helps disease-causing immune cells invade MS patients' brains")* talks about B cells that help immune diseases reach leaky barriers of the brain. They found that B cells in mice that lack activated leukocyte cell adhesion molecules (ALCAM) struggled getting into the brain. This could open the opportunity for new MS treatments. [6] This is just a summary of the research; the full paper is: Role of B Cells in Multiple Sclerosis and Related Disorders. [9]

Gene expressions in healthy rodents and human brains are studied and compared, providing the framework for mice to simulate neurodegenerative illnesses of the human brain, according to research published in 2007. They performed an identical analysis on certain brain regions from mice and compare them separately to human neurological functions. They discovered that particular brain regions have distinctive expression profiles, but regionally enriched genes were very similar in both species. [10]

Another research conducted in 2017 by the Department of Bioinformatics in SCAI, Germany, compared and contrasted neuroinflammatory mechanisms in mice and humans to test disease modeling in rodents. [11] They gathered 42 pathways from the human brain and 29 from mice models. Pathways are "a series of connected neurons that send signals from one part of the brain to another." [12]

When these pathways were analyzed at a molecular level, 27% of cytokine (number of substances a cell from the immune system secrets, which affect other cells) interactions were comparable in both species; 15% of interactions in mice traveled in opposite direction; 58% of interactions can only be found in humans. On the other hand, when compared at a cellular level, more similarities can be found. 62% of cellular interactions were similar between mice and humans; 28% of interactions can only be found in humans; only 10% of interactions traveled in opposite direction. [11] To see this data, refer to Figure 1.

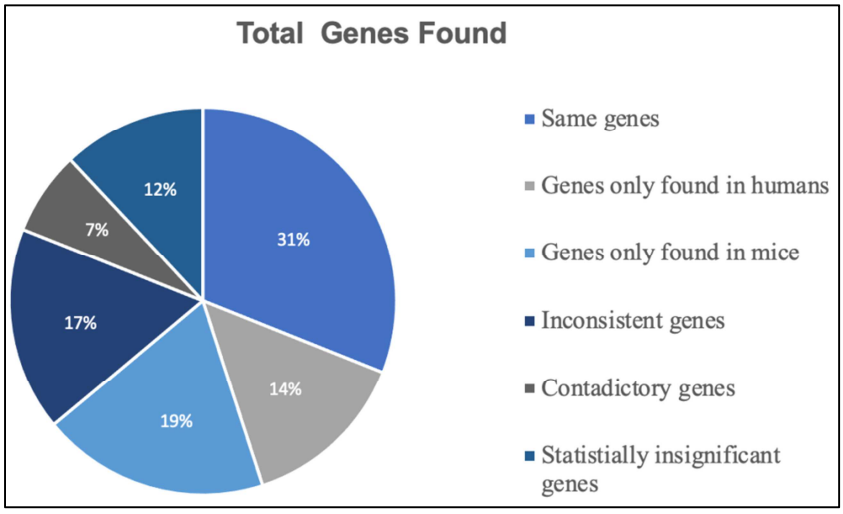

Figure 1. *Genes found in both mice and humans.*

Meta-Analysis Results

When the two articles are compared using different criteria, refer to Table 1, it can be perceived how both papers due contribute to the scientific knowledge because both are supported by other research on mice disease modeling. Although, more articles talk about disease modeling in neurodegenerative pathologies, results can still be very accurate when modeling MS into mice. However, when

diseases are well transcribed into mice brains, results are not always as expected. Drugs functioning well in the treatment for pathologies found in rodents are commonly not successful in clinical trials. These can fail due to other factors like poor design, dose quantity, etc. [11]

To sum up everything that has been stated so far: mince and humans share different genes in their brain pathways. This accounts for 31% of the genetic factors studied. The other 69% percent of genes are not correlated between the two species, although only 7% of genes were contradictory.

Table 1. *Criteria for Evaluation.*

Criteria	Research A	Research B
Population	Around 1,000,000 people have a diagnosis of MS in the US	There are just 16,000 people with ALS in the US
How prelaminar are the results?	Results are very important to understand MS, although a lot is already known about this disease.	A conclusion cannot be done with the early results, we still don't know much about ALS.
How long has the disease been studied for	1930	1939
How aggressive is the disease	Late-stage MS is rarely debilitating or fatal	ALS is completely debilitating leading to paralysis and death
What investigations say	Mimicking neurological diseases in human brains can be effective, although some variations on physiology can alter results when tested on the human brain.	

4. Discussion

Genes found in both species suggest that human and mice brains can definitely be associated when compared at a molecular and cellular level. Even though, many differences can be found, when the number of genes existing in both brains is taken into consideration, it can be seen that they are significantly correlated. When we put together the molecular and cellular interactions seen in Figure 1, we can notice how an outstanding 31% of genes are the same in both humans and mice. Although there is still a remaining 69% of genes that cannot be compared to one another; this 31% opens the ability to project certain pathologies into the mice brain to seek treatment and understand diseases' etiology. Alzheimer's disease, prion encephalopathies, motor neuron illness like amyotrophic lateral sclerosis and fragile X syndrome are among these diseases. [13]

Previous publications have shown how illness modeling in mice can be erroneous owing to the significant distinctions between mice and humans. However, due to uncorrelated genes, there will always be a margin for error. The collected data proved to be statistically significant. demonstrating that illnesses may be modeled with a large margin of error and yet provide satisfactory outcomes

When taking into consideration the criteria used, it can be perceived that both diseases share the similarity of being studied since the 1930s, but not much is known about ALS. [14], [15] It should be noted that MS affects 35.9 per 100,000 people, while ALS affects 1.5 to 3 per 100,000 people. The advancement presented in the ALS article provides information that could open the possibilities to finally treating and understanding the etiology of this disease. On the other hand, the MS article provides what could be just a new treatment for a disease that is somehow understood and that someone can live with. Therefore, both research papers contribute to the scientific knowledge, but not equally, the ALS article provides a bigger advancement for the scientific community.

Some factors should be taken into consideration when assessing the effectiveness of this research. A limited breadth of information due to inadequate access to publications was one factor that impacted the outcomes. As well as the timeframe which was not very extensive.

5. Conclusion

Human disease modeling into mice is a subject that still has plenty of questions unanswered. Mice and humans share plenty of genes in different brain pathways, 31% to be precise. This opens the possibility of transcribing amyotrophic lateral sclerosis and multiple sclerosis into mice, which are both neurodegenerative disorders. This can be effective at discovering the treatment and etiology for different pathologies. Although there is still plenty left before clinical trials start on humans, these are great discoveries. Therefore, both research papers contribute to the scientific community, but not equally. The ALS article provides a new framework for finally understanding and treating this disease.

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