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Lupus and Multiple Sclerosis: Understanding the Pathophysiology of Under- Funded Autoimmune Diseases and Potential Treatments

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Abstract

The immune system is a body system made up of cells, organs, and proteins that work together to defend the body against foreign invaders. However, there are times when the immune system attacks and kills its healthy tissue and cells, a condition known as autoimmunity. An autoimmune disease occurs when the immune system doesn't know the difference between the body's cells and foreign pathogens, so it attacks its cells. This paper will examine two autoimmune diseases: Lupus and Multiple Sclerosis (MS). Lupus is a chronic autoimmune disease that is often separated into five types. Lupus is mostly characterized by the inflammation it causes throughout the body, including a noticeable facial butterfly rash. Over 5 million people are affected by Lupus and there is no cure for Lupus, but trials have had varying results depending on the severity of the disease, with some treatments including NSAIDs inhibitors. MS is a chronic autoimmune disease characterized by fatigue, impaired vision, and tremors. MS is caused when the immune system destroys the protective sheath of nerve fibers, disrupting the flow of information in the nervous system, and causing nerve damage. There are about 2.3 million people diagnosed with MS. As of 2022, Lupus received over $139 million in funds while MS received over $20 million. Although MS and Lupus are both autoimmune diseases that affect a significant population, they do not receive nearly as much funding when compared to diseases like Cancer or Parkinson's. This paper is dedicated to increasing awareness of the widespread effects of autoimmune diseases and the need for more funding. We have compiled background information and statistics using credible search engines and peer-reviewed studies for collective understanding.

Keywords: Autoimmunity, Lupus, Multiple Sclerosis, Funding, Immune System, Treatments, Clinical Trials

1. Introduction

Lupus is one of the hardest diseases to diagnose because of its complexity and how its symptoms overlap with other disorders one common symptom is shown in Figure 1. Therefore, multiple tests must be taken before it is confirmed that a patient has lupus. Put simply, a combination of blood and urine tests, as well as a physical diagnosis, will help identify whether someone has lupus. However, symptoms vary from person to person, making it hard to know whether someone has lupus.

MS is another disease that is hard to diagnose due to its complexity and varying symptoms. Some of the symptoms include tremors, pain, mood swings, slurred speech, vertigo, and involuntary movement caused by damage to the protective layer of a neuron called Myelin Sheath, as shown in Figure 2. Once the neurologist suspects the patient has MS, they will use a checklist known as the "McDonald criteria" to

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diagnose the patient. Some of the tests include MRIs, Blood tests, Spinal taps, and Evoked potentials. An MRI is used to detect inflammatory lesions in the brain which appear as irregular, white matter on the scan, similar to Figure 3.

Figure 1. Lupus Facial Rash also known as the "Butterfly Rash"

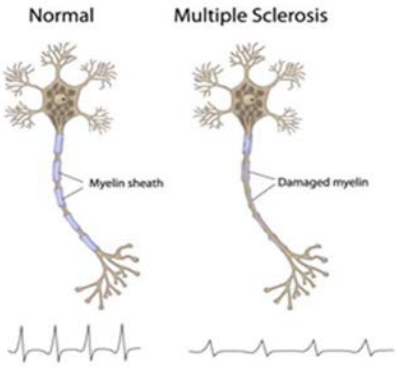

Figure 2. Difference between a normal neuron and a neuron that is affected by Multiple Sclerosis

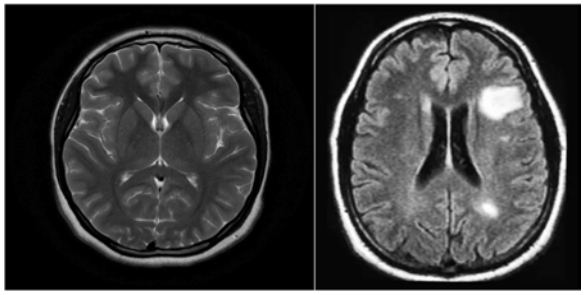

Figure 3. Difference between a normal MRI (left) and a MRI of a Multiple Sclerosis patient (right).

However, the test isn't very reliable because it's not specific, so a patient can receive a false positive and be mistakenly diagnosed with MS. Spinal Taps analyze your spinal fluid to check for elevated spinal fluid protein and white blood cell count. The elevation in immunoglobulin G (IgG) levels indicates MS as it is a sign of an autoimmune response. The least useful test is the Evoked potentials test as it simply checks for response times to stimuli to indicate if your nerves are damaged, and factors, such as age, can easily affect them.

2. Data Collection Methods

For this research paper, articles from the past 10 years were found using the National Center for Biotechnology Information (NCBI) search engine and EBSCO information center. Words such as autoimmunity, immune system, lupus, multiple sclerosis, diagnosis, tests, etc., were used to find accurate information on the two autoimmune diseases. These keywords were used in the Google search engine to find credible sources, such as the Mayo Clinic. This paper focuses on two rare autoimmune diseases, Lupus, and MS. Lastly, the figures in this paper are taken from articles in which information on the diseases was given or used by NCBI.

3. Results

There has been a significant number of studies and trials done regarding treatments and more efficient management of Lupus. Some clinical trials, studies, and possible treatments have been described. A research study was conducted on the pipeline to automate the classification of glomeruli features in renal biopsy. The researchers concluded that they "propose a complete pipeline for the classification of WSIs into various LN stages based on glomeruli features" (Gupta, et al., 2021). A Pilot Study of CC-220 to Treat SLE (Systemic Lupus Erythematosus) was also done, and results indicated that the drug had improvements to be made but was more successful than the placebo (Celgene, 2020). From an engineering perspective, author Xubin Hao and authors from the Department of Rheumatology and Immunology at the Hospital of Nanjing University Medical School reviewed the engineering technologies and proposed their challenges in SLE treatment. In their review article titled "Developing engineering technologies for the treatment of

systemic lupus erythematosus", they explain that "Compared with traditional therapeutic methods, nanocarriers have multiple advantages in agents delivery for the treatment of SLE, such as enhanced drug solubility, sustained release, and passive accumulation at inflammatory sites…active targeting of tissues or cells in need of delivery can also be achieved… mainly used for the selective delivery of glucocorticoids and immunosuppressants". They further discuss other technologies such as CAR-T cell therapy and noted how "the largest sample in the study of CAR-T treatment of lupus is only 5 patients, and further research is needed on larger samples and whether it can treat early or mild SLE". Lastly, they review the efficiency of nanoparticles which are "encapsulated in RBC membrane and tumor CM has been effectively tested in MRL/lpr mice, but other CM could also be introduced to treat lupus" (Hao et al., 2023). This research study concluded that engineering technologies such as the ones shown in Figure 4 have a high probability of treating and curing SLE in comparison to the relatively static development of drugs.

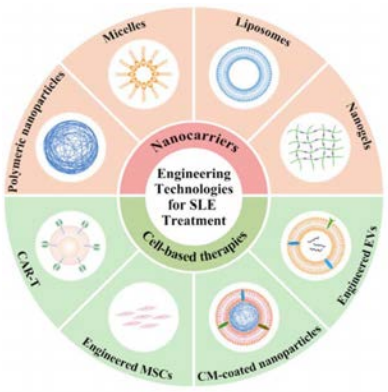

Figure 4: Schematic illustration of recent engineering technologies for Systemic lupus erythematosus (SLE)

There have been many clinical trials and studies that have been conducted for MS as well, and some have promising results. One of them includes a study of Rebif® (interferon beta-1a) in Subjects With Relapsing Multiple Sclerosis. The study with interferon beta-1a was successful and interferon beta-1a can be used to treat MS (Merck KGaA, Darmstadt, Germany, 2018). Another study compared "Oral Ponesimod Versus Teriflunomide In Relapsing MS" indicated that "Ponesimod" or "PONVORY™" was more successful than Teriflunomide at reducing symptoms in those with relapsing MS (Actelion, 2022). However, Ponesimod was noted to have mild to severe side effects including hypertension and upper respiratory infections. Researcher Masoud H. Manjili from the Department of Microbiology & Immunology at the Virginia Commonwealth University School of Medicine conducted research on a new approach to MS therapy and treatment. In his paper "The adaptation model of immunity: A new insight into aetiology and treatment of multiple sclerosis", Manjili notes that current treatment for MS consists of immune suppressive interventions because of the self–nonself (SNS) model and the danger model. These models state that "inflammatory immune responses towards the central nervous system (CNS), triggered by breakage of tolerance to self-antigens (SNS model)1 or by damage-associated danger signals triggered by events such as menstrual cycle result in MS" (Manjili, 2023). However, he proposed the adaptation model of immunity which offers a different approach for MS treatment. This theory "suggests that inflammatory immune responses are required for neuronal homeostasis in the CNS as well as restoration of remyelination process in patients with MS… This immunological function is coordinated through the adaptation receptors (AdRs) expressed on the CNS, and their nominal adaptation ligands (AdLs) or co-receptors expressed on immune cells, that is signal IV. I…However, alterations in the expression of the neuronal AdRs could shift neuroprotective T cells into neurodegenerative T cells. This theoretical model can incite new direction for research and drug development for patients with MS" (Manjili, 2023). As the medical field advances over time, new discoveries and experiment trials will yield more promising treatments, and hopefully, a tentative cure.

4. Funding

Compared to other neurological diseases such as ALS or Parkinson's, MS has the least publication rate in medical journals. A review of publications from 1985 to 1999 showed that MS also had the least

productivity in scientific papers. MS has relatively high funding, as evidenced by The National Institutes of Health (NIH) shown in Figure 6 where MS receives over 20 million dollars annually for research. This is more than typically expected, but the money isn't as equally distributed amongst all aspects of research. The funding is mostly given to the most promising and innovative research proposals. However, another aspect of research in MS that is underfunded is the recruitment of high-achieving and credible researchers who can deliver the most accurate information on this chronic neurodegenerative disease. Lupus gets about 139 million dollars per year in funding as of 2022. While Lupus only gets 139 million dollars in funding, Cancer gets about 6.25 billion dollars of funding from the National Cancer Institute (NCI). $139 million in funding to dig deeper into Lupus is a good amount compared to the $90 million given in 2014. Although Cancer is a more common disease and therefore received much more funding, it's evident that Lupus is getting more attention as the medical field is expanding.

Figure 5: The graph demonstrates the amount of money (in millions) the NIH is funding for Lupus across the United States from 2008-2022.

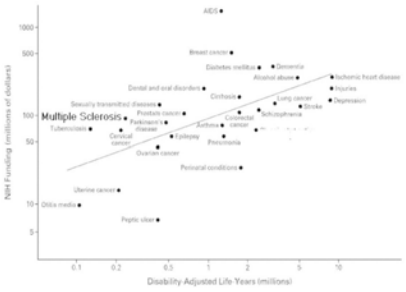

Figure 6: The graph demonstrates the relationship between the amount of NIH funding (1996) and the Disability Adjusted Life Years of patients across 27 different diseases/conditions.

5. Conclusion

Both Lupus and Multiple Sclerosis are difficult to diagnose because there is no single test to assuredly diagnose them. Many of the symptoms of these autoimmune disorders overlap with other conditions and therefore require rounds of testing for a positive diagnosis. Compared to MS, Lupus gets much higher funding.

According to the Lupus Foundation of America, 1.5 million Americans, and around 5 million people worldwide have a form of lupus. It is diagnosed mainly between the ages of 15 - 44 with around 16,000 cases of lupus appearing annually. About 10% - 15% of people with lupus die prematurely due to the disease. Worldwide, about 2.3 million people are diagnosed with MS, while in the US specifically, over 1 million people are affected by it. About 200 cases of MS are diagnosed weekly. As of 2022, lupus receives $139 million in funding annually as shown in Figure 5, while MS receives only $20 million for its research. While Lupus has been getting more attention from the medical field, as evidenced by its increase in funding (in 2014, lupus received $90 million annually), MS has been relatively the same. MS has the least publication rates and productivity rates in scientific journals, especially compared to other neurodegenerative diseases such as ALS or Parkinson's, while its funding is primarily used to look into new, innovative treatments for the disease instead of being used to bring in more credible researchers who can deliver more accurate and useful information on the disease. MS receives less attention than lupus primarily because it is far rarer than lupus. Thus, lupus has a higher public awareness that gives it an edge over MS in receiving funding for it treatments. The social stigma surrounding these two diseases also distinctly separates them. Many see MS as affecting only older people, aged well into their 60s and 70s, while lupus is more prevalent in younger populations. Of course, this isn't true, yet the misconception remains, and so Lupus is regarded as a more pressing issue compared to MS. To solve the disparities between MS and Lupus funding there must be increased public awareness about the two diseases. Eliminating such misconceptions as MS affecting older populations and lupus affecting

younger people, as well as highlighting the need for support for MS patients, among other things, would give the public a more well-rounded understanding of why both diseases need to be addressed seriously and equally.

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