BIOSCIENTIST
The Salford Biomedicine Society Magazine

Stem Cell Regenerative Technologies in Multiple Sclerosis

Faatima Jeylani

Abstract

Multiple sclerosis (MS), an unpredictable attack caused by the immune system to the central nervous system, leaving some with the inability to see, speak or even walk. This condition affects approximately 1.8 million people worldwide and is particularly common amongst females, who are often diagnosed in early adulthood. Between 2013-2020, the number of people diagnosed with multiple sclerosis had increased by 30%. With this rapid increase of the disease, prevalence, detection, the need for effective treatments or a way of slowing down disease progression became crucial. Thus far, clinical studies for neuroprotective therapies in other central nervous system diseases has had limited success. However, for multiple sclerosis, the use of stem cells provides great promise in decreasing disease progression. A stem cell transplant involved multiple sclerosis patients receiving a healthy stem cell donation. Some of the stem cell treatments include autologous haematopoietic stem cell transplantation (aHSCT) and mesenchymal cell therapy. There is evidence that haematopoietic stem cell transplantation is effective for those who have relapsing multiple sclerosis. Due to this, only those meeting specific medical criteria are offered treatment.

Multiple Sclerosis (MS) is a chronic autoimmune disease impacting the central nervous system (CNS) distinguished through primary demyelination and a variable extent of axonal loss[7]. MS is caused by the existence of several merging demyelinated lesions in the grey and white matter of the CNS which is also present in the cortex and brain stem as shown in the MRI (Magnetic Resonance Imaging) of Figure 1[7]. The progression of MS is exceedingly variable and unexpected as most patients experience transient neurological abnormalities at first followed by gradual neurological deterioration[5]. MS is diagnosed based on tests carried out by a neurologist through the observation of a person's symptoms (checking movement, balance, or vision) or from pictures obtained by a magnetic resonance imaging (MRI) of the brain. An MRI monitors the quantity of water in the body[12]. Due to various areas of the brain containing varying amounts of water, the MRI can differentiate them and create images of the central nervous system[12]. The protective myelin covering is fatty and repels water. This implies that we can assess the amount of myelin present since it appears differently on a scan than nerves and other brain cells[12].

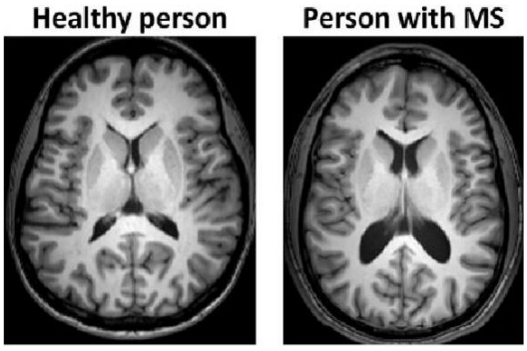

Figure 1: MRI scans comparing brain of a person with and without MS[3].

DOI: https://doi.org/10.57898/biosci.186

Additionally, MS has no established origin although it appears to be caused by a combination of genetic predisposition and non-genetic triggers such as viruses or environmental factors which results in recurring immunological attacks on the CNS[5]. Although MS is not inherited, people with relatives containing the disease are more susceptible of having this disease. The genes linked to the predisposition are *HLA-DRB1* locus in the class II region. Furthermore, earlier studies regarding the heredity of MS had revealed a recurring relative risk for siblings[1]. The possibility of MS is significantly increased when both parents have MS, but the probability of half siblings is lower than that of full siblings being affected by MS[11]. Therefore, the chance of MS recurrence increases in proportion to the amount of genetic sharing with the afflicted family member but not in a liner manner[11]. A review of over 500 research revealed that there was a recurrence rate of 18.2% for monozygotic twins and 2.7% for siblings[11].

Stem cell technologies have been investigated in reducing the progression of aggressive multiple sclerosis. The main ones being autologous haematopoietic stem cell transplantation (aHSCT) and mesenchymal cell therapy (MCT). aHSCT, often referred to as a bone marrow transplant, involves the removal of a person's immune system cell then regrowing it using haematopoietic stem cell which develop into different types of blood cells such as red or white blood cells[13]. Thus, aHSCT infusions enhance bone marrow healing and immunological regeneration, aiming to avoid the progression of neurological impairments[9]. This potentially strengthens neurological function as well as containing numerous benefits, it aids bone marrow function by 'rebooting' the body's immune system via renewal and re-diversification of the T and B-cell repertoire, as well as heightened regulatory T-cell activity[14]. In a prospective investigation of MS patients who underwent aHSCT, over half lived without neurological deterioration for 5 years following the transplant[9]. Additionally, it generates functional cells that replace dysfunctional nerve cells in diseases other than MS such as immune deficiency syndromes[6]. From the beginning to numerous weeks after the procedure, the patient requires monitoring and additional treatments. In recent times, improvements to AHSCT process have resulted in a reduction in treatment-related mortality (TRM) from 7.3% to less than 0.5%[8]. Fifty percent of patients treated with aHSCT recovered from their condition after ten years[8].

MCT involves eliminating a person's MCT from their bone marrow or tissue which is multiplied in a laboratory then numerous MCT are re-introduced[13]. MCT has emerged as a possibly safe cellular treatment for MS however the dosage, method, and administration must be examined and further quantified[4]. Stem cells are similar to tumour cells in certain ways because of their capacity to proliferate for an extended length of time, high vitality, and resistance to apoptosis[10]. Their ability to proliferate for pro longed amount of time is dependent on their ability of dividing. Patients who are transplanted with stem cells frequently have long-term chemotherapy or radiation, so their immune system does not perform correctly, which can also relate to the risk of tumorigenesis[10]. Effects of chemotherapy include constant fatigue, being sick and increased risks of infections.

Whereas, the aHSCT technique has been found to provide long term sustained emission but also requires more research to determine the conditioning plan to be implemented[4]. More research is required due to increased risk of infection due to immunodeficiency which are current concerns of aHSCT as well as associations of rare cases of death. As aHSCT can cause residual cancer and requires a donor that is suitable, fitting to the recipient, they are the current focus of research[2]. Whereas for MCT, the current focus for research is finding a way to ease the side effects which include fever, headaches, and urinary tract infection.

DOI: https://doi.org/10.57898/biosci.186

References:

Alfredsson, L., & Olsson, T. (2019). Lifestyle and Environmental Factors in Multiple Sclerosis. *Cold Spring Harb Perspect Med*, *9*(4). https://doi.org/10.1101/cshperspect.a028944

Bazinet, A., & Popradi, G. (2019). A General Practitioner's Guide to Hematopoietic Stem-cell Transplantation. *Current Oncology*, *26*(3), 187-191. https://www.mdpi.com/1718-7729/26/3/5033

Crommelin, D. J., Broich, K., Holloway, C., Meesen, B., Lizrova Preiningerova, J., Prugnaud, J.-L., & Silva-Lima, B. (2016). The regulator's perspective: How should new therapies and follow-on products for MS be clinically evaluated in the future? *Multiple Sclerosis Journal*, *22*(2_suppl), 47-59. https://doi.org/10.1177/1352458516650744

Cuascut, F. X., & Hutton, G. J. (2019). Stem Cell-Based Therapies for Multiple Sclerosis: Current Perspectives. *Biomedicines*, *7*(2).

Goldenberg, M. M. (2012). Multiple sclerosis review. *P t*, *37*(3), 175-184.

Khaddour, K., Hana, C. K., & Mewawalla, P. (2024). Hematopoietic Stem Cell Transplantation. In *StatPearls*. StatPearls Publishing

Lassmann, H. (2018). Multiple Sclerosis Pathology. *Cold Spring Harb Perspect Med*, *8*(3). https://doi.org/10.1101/cshperspect.a028936

Mohammadi, R., Aryan, A., Omrani, M. D., Ghaderian, S. M. H., & Fazeli, Z. (2021). Autologous Hematopoietic Stem Cell Transplantation (AHSCT): An Evolving Treatment Avenue in Multiple Sclerosis. *Biologics*, *15*, 53-59. https://doi.org/10.2147/btt.S267277

Muraro, P. A., Pasquini, M., Atkins, H. L., Bowen, J. D., Farge, D., Fassas, A., Freedman, M. S., Georges, G. E., Gualandi, F., Hamerschlak, N., Havrdova, E., Kimiskidis, V. K., Kozak, T., Mancardi, G. L., Massacesi, L., Moraes, D. A., Nash, R. A., Pavletic, S., Ouyang, J., . . . Group, f. t. M. S. A. H. S. C. T. L.-t. O. S. (2017). Long-term Outcomes After Autologous Hematopoietic Stem Cell Transplantation for Multiple Sclerosis. *JAMA Neurology*, *74*(4), 459-469. https://doi.org/10.1001/jamaneurol.2016.5867

Musial-Wysocka, A., Kot, M., & Majka, M. (2019). The Pros and Cons of Mesenchymal Stem Cell-Based Therapies. *Cell Transplant*, *28*(7), 801-812. https://doi.org/10.1177/0963689719837897

Patsopoulos, N. A. (2018). Genetics of Multiple Sclerosis: An Overview and New Directions. *Cold Spring Harb Perspect Med*, *8*(7). https://doi.org/10.1101/cshperspect.a028951

Roberts, K. (2017). *MRI and MS: 7 things you need to know*. MS Society. Retrieved 22/02/2024 from https://www.mssociety.org.uk/research/latest-research/latest-research-news-and-blogs/mri-and-ms-7-things-you-need-to-know

Rowden, A. (2021). *Stem cell therapy for multiple sclerosis*. Retrieved 22/02/2024 from https://www.medicalnewstoday.com/articles/stem-cell-multiple-sclerosis

Snowden, J. A., Sharrack, B., Akil, M., Kiely, D. G., Lobo, A., Kazmi, M., Muraro, P. A., & Lindsay, J. O. (2018). Autologous haematopoietic stem cell transplantation (aHSCT) for severe resistant autoimmune and inflammatory diseases – a guide for the generalist. *Clinical Medicine*, *18*(4), 329. https://doi.org/10.7861/clinmedicine.18-4-329